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Supplementary information

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Lymph node-targeted, mKRAS-specific amphiphile vaccine in pancreatic cancer: the randomized phase 2 AMPLIFY-7P trial

In the format provided by the authors and unedited

Supplementary Information
Table of Contents

Supplementary Table 1 . . . . . Page 2

Supplementary Figure 1 . . . . . Page 3

Supplementary Figure 2 . . . . . Page 4

Supplementary Table 2 . . . . . Page 6

Supplementary Figure 3 . . . . . Page 7

Supplementary Table 3 . . . . . Page 8

ELI-002-201 Protocol . . . . . Page 10

Phase 2 Statistical Analysis Plan (SAP) . . . . . Page 147

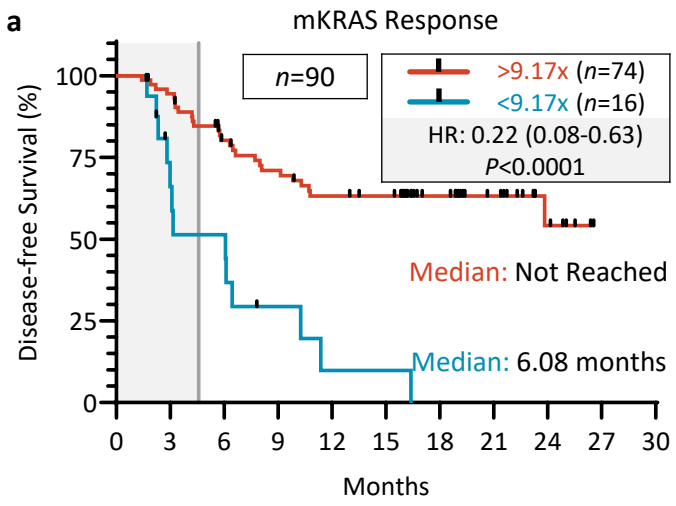
Supplementary Table 1 | Prior Chemotherapy Intent

ITT	Camupepimut *n*=96	Observation *n*=48	Overall *n*=144
Prior Chemotherapy Intent *n* (%)			
Adjuvant only	44 (45.8)	16 (33.3)	60 (41.7)
Neoadjuvant only	25 (26.0)	10 (20.8)	35 (24.3)
Perioperative (neoadjuvant + adjuvant)	27 (28.1)	22 (45.8)	49 (34.0)

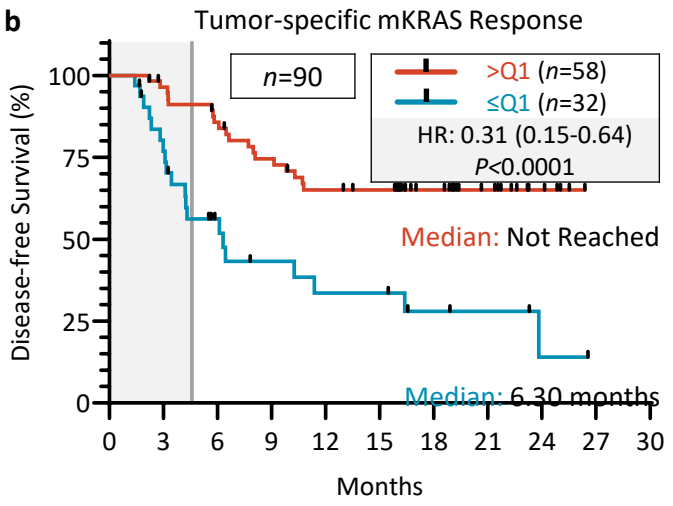
ctDNA Negative	Camupepimut *n*=62	Observation *n*=31	Overall *n*=93
Prior Chemotherapy Intent *n* (%)			
Adjuvant only	35 (56.5)	11 (35.5)	46 (49.5)
Neoadjuvant only	13 (21.0)	7 (22.6)	20 (21.5)
Perioperative (neoadjuvant + adjuvant)	14 (22.6)	13 (41.9)	27 (29.0)

No Prior Radiation	Camupepimut *n*=73	Observation *n*=33	Overall *n*=106
Prior Chemotherapy Intent *n* (%)			
Adjuvant only	42 (57.5)	13 (39.4)	55 (51.9)
Neoadjuvant only	11 (15.1)	6 (18.2)	17 (16.0)
Perioperative (neoadjuvant + adjuvant)	20 (27.4)	14 (42.4)	34 (32.1)

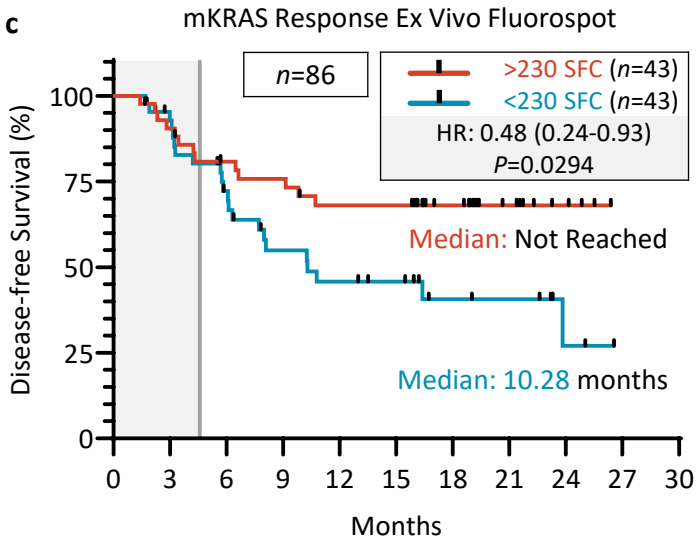
Supplementary Figure 1: At risk tables for indicated Kaplan Meier plots.
a, mKRAS response (from Fig. 5j), **b**, Tumor-specific mKRAS response (from Fig. 5k), **c,**mKRAS response ex vivo Fluorospot (from Extended Fig. 4e), **d,** mKRAS response ex vivo ICS (from Extended Fig. 4f), **e,** Known mKRAS presenting HLA-1 (from Extended Fig. 5b)



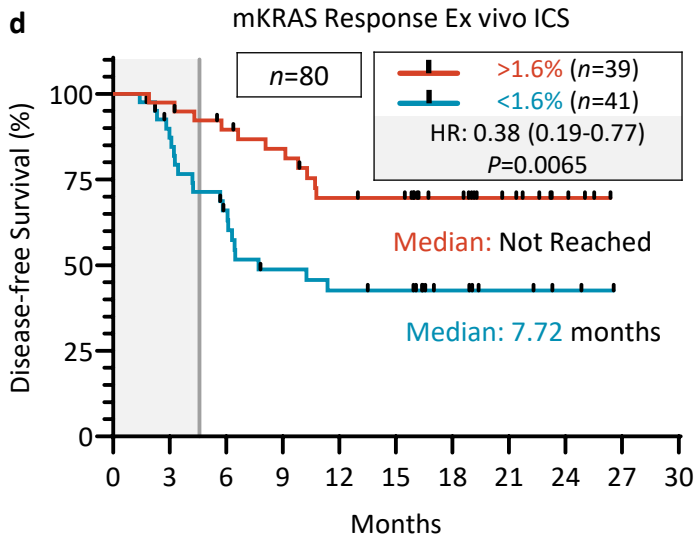
At risk										
>9.17x	74	68	53	46	40	38	24	15	6	0
<9.17x	16	9	7	3	1	1	0			



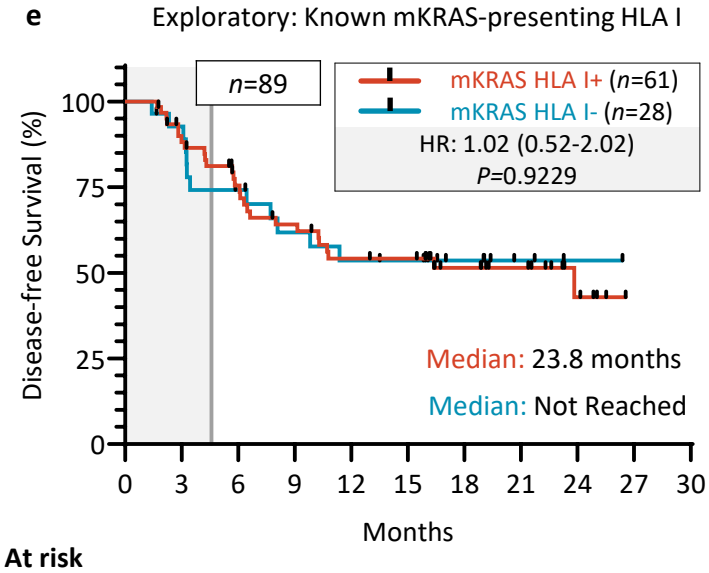
At risk										
>Q1	58	54	47	40	34	32	20	12	5	0
≤Q1	32	23	13	9	7	7	4	3	1	0



At risk										
>230 SFC	43	38	32	30	26	26	17	9	4	0
<230 SFC	43	37	26	18	15	13	7	6	2	0



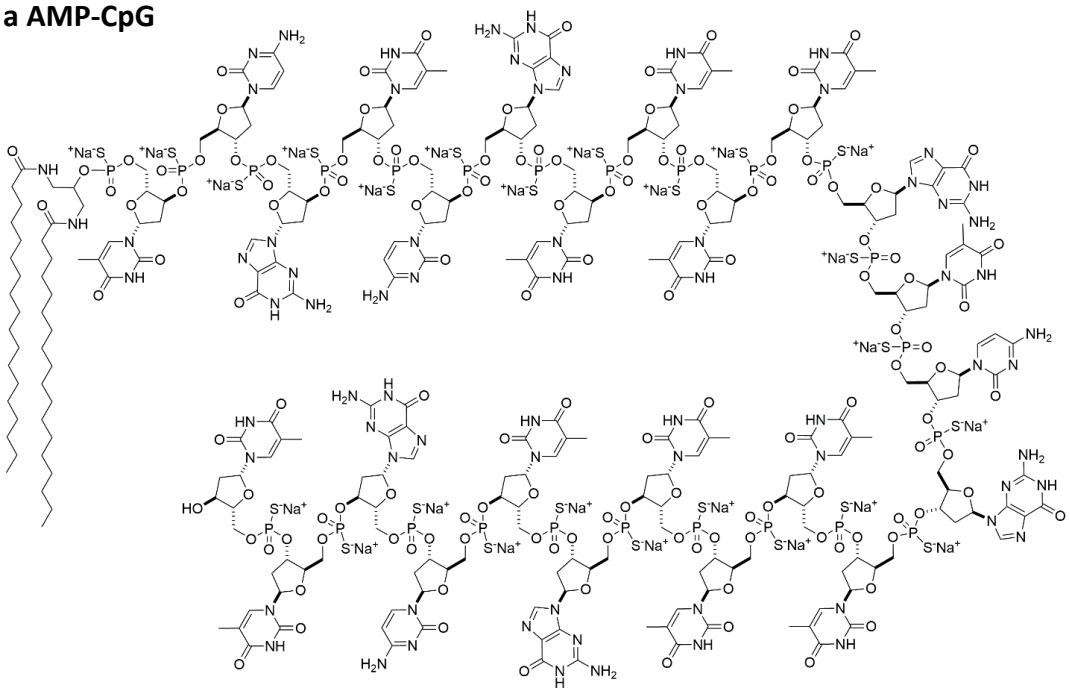
At risk										
>1.6%	39	38	33	30	24	23	15	9	4	0
<1.6%	41	33	23	16	14	13	7	4	2	0



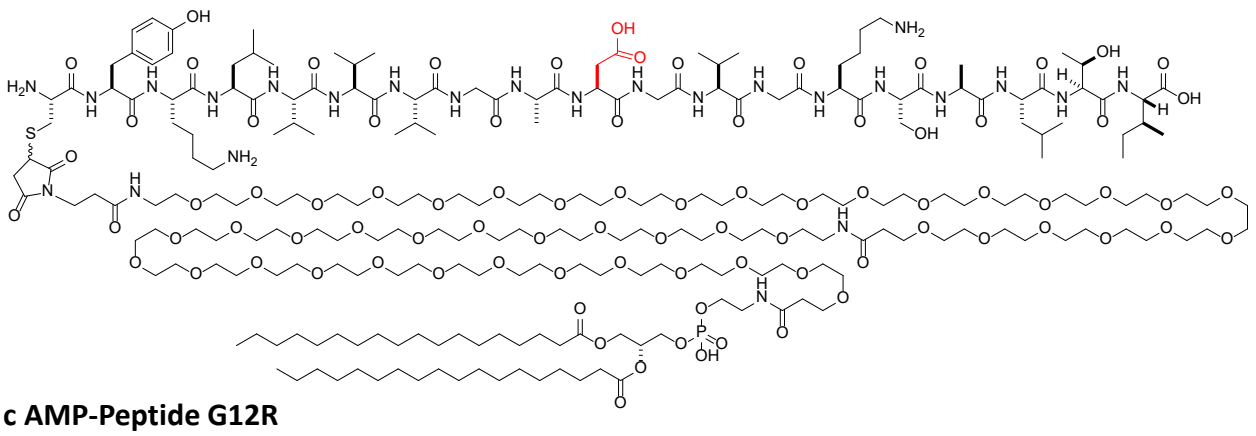
At risk										
mKRAS HLA-I+	61	51	40	33	27	26	16	12	5	0
mKRAS HLA I-	28	25	19	15	13	12	7	3	1	0

Supplementary Figure 2: Chemical structures for camupepimut components.
Chemical structures for **a,** AMP-CpG-7909, **b**, AMP-Peptide G12D, **c,** AMP-Peptide G12R, **d,** AMP-Peptide G12V, **e,** AMP-Peptide G12A, **f,** AMP-Peptide G12S, **g,** AMP-Peptide G12C, **h,** AMP-Peptide G13D. Amino acid side chains are shown in red.

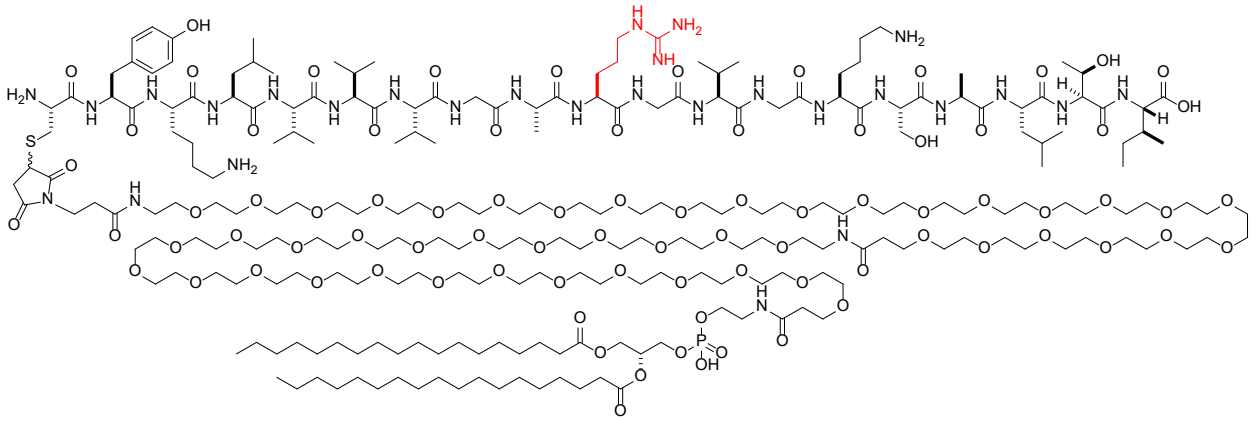
a AMP-CpG



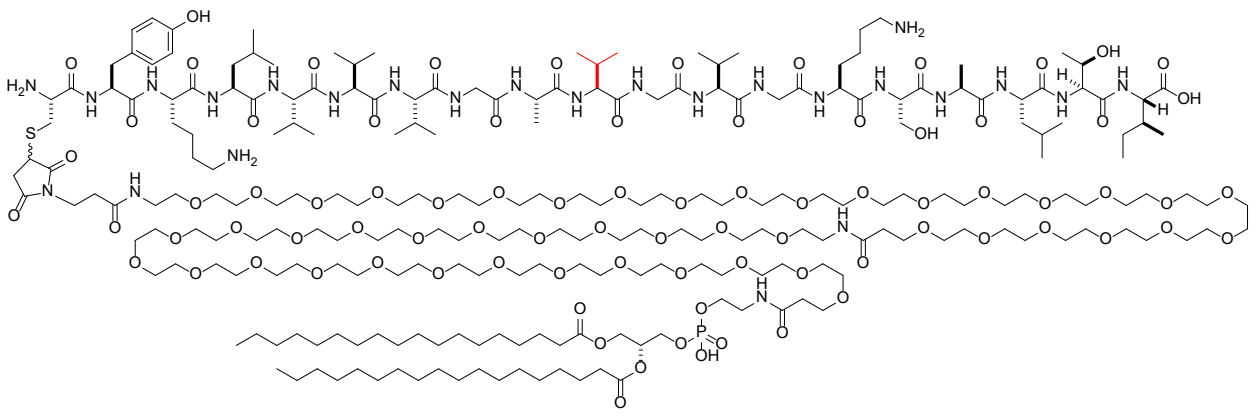
b AMP-Peptide G12D



c AMP-Peptide G12R

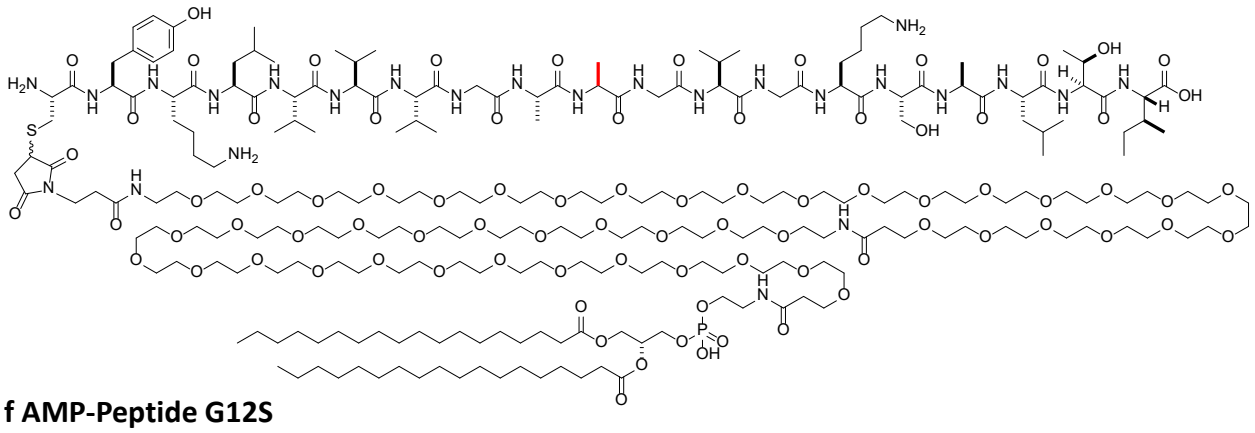


d AMP-Peptide G12V

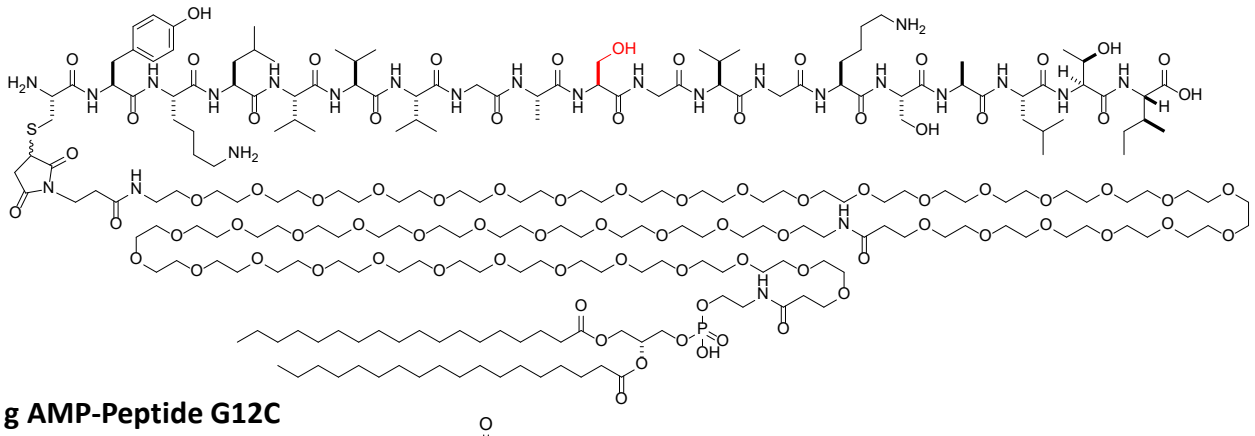


Supplementary Figure 2 continued: Chemical structures for ELI-002 2P components.

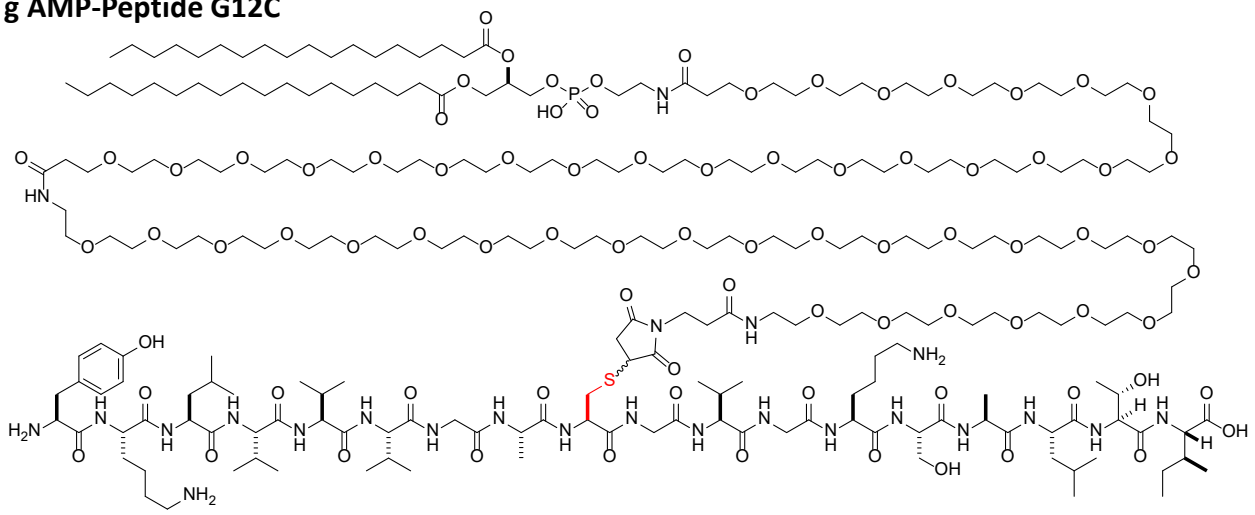
e AMP-Peptide G12A



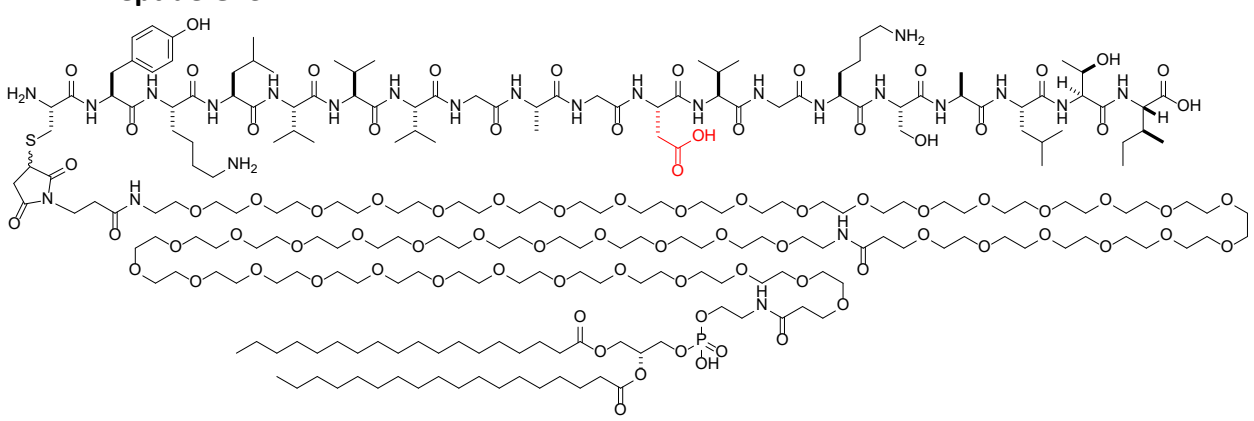
f AMP-Peptide G12S



g AMP-Peptide G12C



h AMP-Peptide G13D



Supplementary Table 2: Stimulation peptides used for immunogenicity analysis.

Peptide Name	Peptide Sequence	Peptide Length
G12D Long	YKLVVVGADGVGKSALTI	18
G12D Short 9-1	YKLVVVGAD	9
G12D Short 9-2	KLVVVGADG	9
G12D Short 9-3	LVVVGADGV	9
G12D Short 9-4	VVVGADGVG	9
G12D Short 9-5	VVGADGVGK	9
G12D Short 9-6	VGADGVGKS	9
G12D Short 9-7	GADGVGKSA	9
G12D Short 9-8	ADGVGKSAL	9
G12D Short 9-9	DGVGKSALT	9
G12D Short 10-1	YKLVVVGADG	10
G12D Short 10-2	KLVVVGADGV	10
G12D Short 10-3	LVVVGADGVG	10
G12D Short 10-4	VVVGADGVGK	10
G12D Short 10-5	VVGADGVGKS	10
G12D Short 10-6	VGADGVGKSA	10
G12D Short 10-7	GADGVGKSAL	10
G12D Short 10-8	ADGVGKSALT	10
G12D Short 10-9	DGVGKSALTI	10

Peptide Name	Peptide Sequence	Peptide Length
G12V Long	YKLVVVGAVGVGKSALTI	18
G12V Short 9-1	YKLVVVGAV	9
G12V Short 9-2	KLVVVGAVG	9
G12V Short 9-3	LVVVGAVGV	9
G12V Short 9-4	VVVGAVGVG	9
G12V Short 9-5	VVGAVGVGK	9
G12V Short 9-6	VGAVGVGKS	9
G12V Short 9-7	GAVGVGKSA	9
G12V Short 9-8	AVGVGKSAL	9
G12V Short 9-9	VGVGKSALT	9
G12V Short 10-1	YKLVVVGAVG	10
G12V Short 10-2	KLVVVGAVGV	10
G12V Short 10-3	LVVVGAVGVG	10
G12V Short 10-4	VVVGAVGVGK	10
G12V Short 10-5	VVGAVGVGKS	10
G12V Short 10-6	VGAVGVGKSA	10
G12V Short 10-7	GAVGVGKSAL	10
G12V Short 10-8	AVGVGKSALT	10
G12V Short 10-9	VGVGKSALTI	10

Peptide Name	Peptide Sequence	Peptide Length
G12R Long	YKLVVVGARGVGKSALTI	18
G12R Short 9-1	YKLVVVGAR	9
G12R Short 9-2	KLVVVGARG	9
G12R Short 9-3	LVVVGARGV	9
G12R Short 9-4	VVVGARGVG	9
G12R Short 9-5	VVGARGVGK	9
G12R Short 9-6	VGARGVGKS	9
G12R Short 9-7	GARGVGKSA	9
G12R Short 9-8	ARGVGKSAL	9
G12R Short 9-9	RGVGKSALT	9
G12R Short 10-1	YKLVVVGARG	10
G12R Short 10-2	KLVVVGARGV	10
G12R Short 10-3	LVVVGARGVG	10
G12R Short 10-4	VVVGARGVGK	10
G12R Short 10-5	VVGARGVGKS	10
G12R Short 10-6	VGARGVGKSA	10
G12R Short 10-7	GARGVGKSAL	10
G12R Short 10-8	ARGVGKSALT	10
G12R Short 10-9	RGVGKSALTI	10

Peptide Name	Peptide Sequence	Peptide Length
G12A Long	YKLVVVGAAGVGKSALTI	18
G12A Short 9-1	YKLVVVGAA	9
G12A Short 9-2	KLVVVGAAG	9
G12A Short 9-3	LVVVGAAGV	9
G12A Short 9-4	VVVGAAGVG	9
G12A Short 9-5	VVGAAGVGK	9
G12A Short 9-6	VGAAGVGKS	9
G12A Short 9-7	GAAGVGKSA	9
G12A Short 9-8	AAGVGKSAL	9
G12A Short 9-9	AGVGKSALT	9
G12A Short 10-1	YKLVVVGAAG	10
G12A Short 10-2	KLVVVGAAGV	10
G12A Short 10-3	LVVVGAAGVG	10
G12A Short 10-4	VVVGAAGVGK	10
G12A Short 10-5	VVGAAGVGKS	10
G12A Short 10-6	VGAAGVGKSA	10
G12A Short 10-7	GAAGVGKSAL	10
G12A Short 10-8	AAGVGKSALT	10
G12A Short 10-9	AGVGKSALTI	10

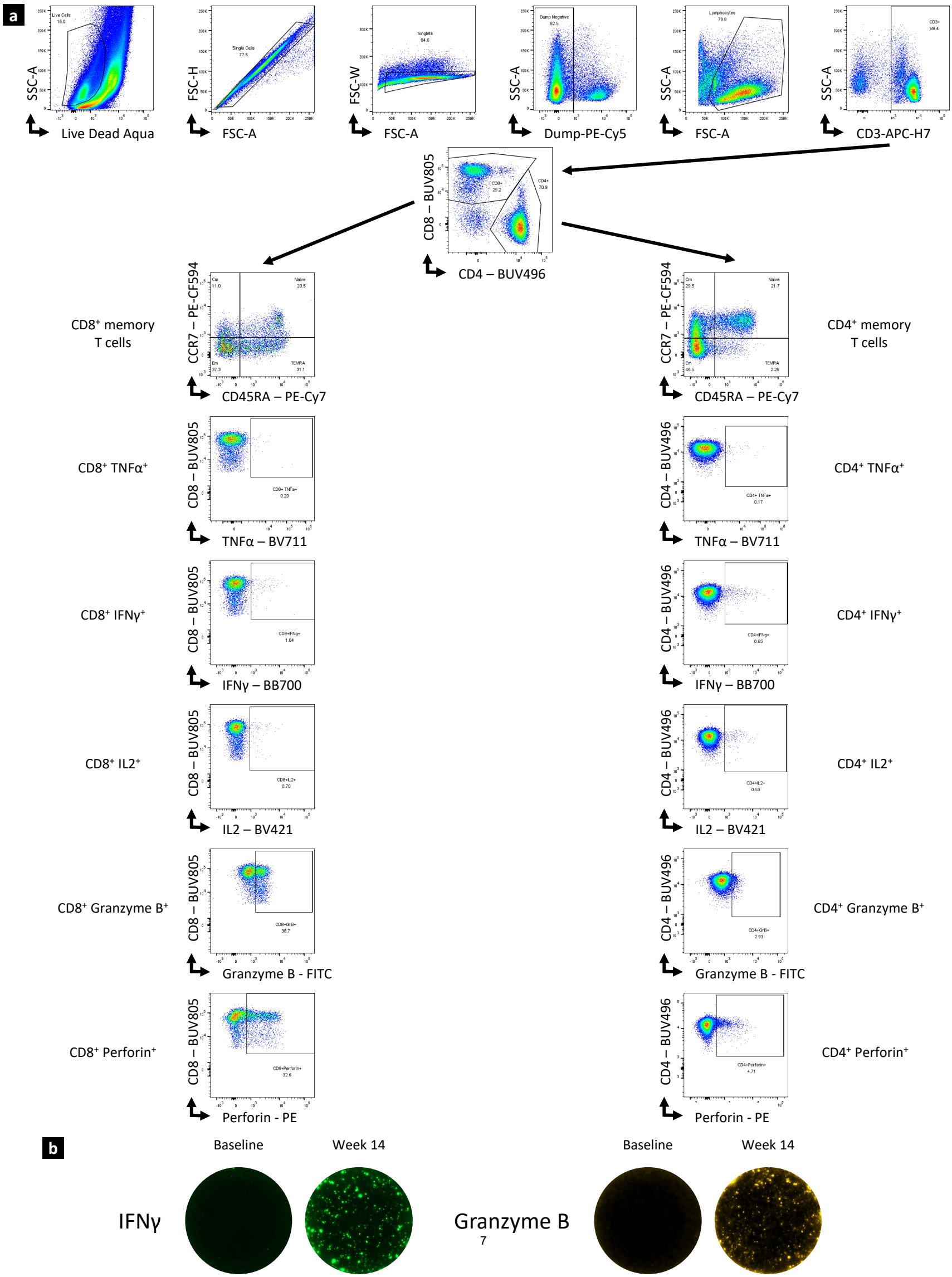
Peptide Name	Peptide Sequence	Peptide Length
G12S Long	YKLVVVGASGVGKSALTI	18
G12S Short 9-1	YKLVVVGAS	9
G12S Short 9-2	KLVVVGASG	9
G12S Short 9-3	LVVVGASGV	9
G12S Short 9-4	VVVGASGVG	9
G12S Short 9-5	VVGASGVGK	9
G12S Short 9-6	VGASGVGKS	9
G12S Short 9-7	GASGVGKSA	9
G12S Short 9-8	ASGVGKSAL	9
G12S Short 9-9	SGVGKSALT	9
G12S Short 10-1	YKLVVVGASG	10
G12S Short 10-2	KLVVVGASGV	10
G12S Short 10-3	LVVVGASGVG	10
G12S Short 10-4	VVVGASGVGK	10
G12S Short 10-5	VVGASGVGKS	10
G12S Short 10-6	VGASGVGKSA	10
G12S Short 10-7	GASGVGKSAL	10
G12S Short 10-8	ASGVGKSALT	10
G12S Short 10-9	SGVGKSALTI	10

Peptide Name	Peptide Sequence	Peptide Length
G12C Long	YKLVVVGACGVGKSALTI	18
G12C Short 9-1	YKLVVVGAC	9
G12C Short 9-2	KLVVVGACG	9
G12C Short 9-3	LVVVGACGV	9
G12C Short 9-4	VVVGACGVG	9
G12C Short 9-5	VVGACGVGK	9
G12C Short 9-6	VGACGVGKS	9
G12C Short 9-7	GACGVGKSA	9
G12C Short 9-8	ACGVGKSAL	9
G12C Short 9-9	CGVGKSALT	9
G12C Short 10-1	YKLVVVGACG	10
G12C Short 10-2	KLVVVGACGV	10
G12C Short 10-3	LVVVGACGVG	10
G12C Short 10-4	VVVGACGVGK	10
G12C Short 10-5	VVGACGVGKS	10
G12C Short 10-6	VGACGVGKSA	10
G12C Short 10-7	GACGVGKSAL	10
G12C Short 10-8	ACGVGKSALT	10
G12C Short 10-9	CGVGKSALTI	10

Peptide Name	Peptide Sequence	Peptide Length
G13D Long	YKLVVVGAGDVGKSALTI	18
G13D Short 9-1	KLVVVGAGD	9
G13D Short 9-2	LVVVGAGDV	9
G13D Short 9-3	VVVGAGDVG	9
G13D Short 9-4	VVGAGDVGK	9
G13D Short 9-5	VGAGDVGKS	9
G13D Short 9-6	GAGDVGKSA	9
G13D Short 9-7	AGDVGKSAL	9
G13D Short 9-8	GDVGKSALT	9
G13D Short 9-9	DVGKSALTI	9
G13D Short 10-1	YKLVVVGAGD	10
G13D Short 10-2	KLVVVGAGDV	10
G13D Short 10-3	LVVVGAGDVG	10
G13D Short 10-4	VVVGAGDVGK	10
G13D Short 10-5	VVGAGDVGKS	10
G13D Short 10-6	VGAGDVGKSA	10
G13D Short 10-7	GAGDVGKSAL	10
G13D Short 10-8	AGDVGKSALT	10
G13D Short 10-9	GDVGKSALTI	10

Peptide Name	Peptide Sequence	Peptide Length
WT Long	YKLVVVGAGGVGKSALTI	18
WT Short 9-1	YKLVVVGAG	9
WT Short 9-2	KLVVVGAGG	9
WT Short 9-3	LVVVGAGGV	9
WT Short 9-4	VVVGAGGVG	9
WT Short 9-5	VVGAGGVGK	9
WT Short 9-6	VGAGGVGKS	9
WT Short 9-7	GAGGVGKSA	9
WT Short 9-8	AGGVGKSAL	9
WT Short 9-9	GGVGKSALT	9
WT Short 9-10	GVGKSALTI	9
WT Short 10-1	YKLVVVGAGG	10
WT Short 10-2	KLVVVGAGGV	10
WT Short 10-3	LVVVGAGGVG	10
WT Short 10-4	VVVGAGGVGK	10
WT Short 10-5	VVGAGGVGKS	10
WT Short 10-6	VGAGGVGKSA	10
WT Short 10-7	GAGGVGKSAL	10
WT Short 10-8	AGGVGKSALT	10
WT Short 10-9	GGVGKSALTI	10

Supplementary Figure 3: ICS and cytotoxic gating strategy and example Fluorospot well images.
a Gating strategy and example scatter plots for ICS assay. **b** Example well images for baseline and Week 14 PBMC IFNγ and Granzyme B Fluorospot assay.



Supplementary Table 3: Stimulation peptides used for immunogenicity analysis.

Patient ID	2-78	2-58	2-104
# neoantigens tested	10	10	10
# neoantigens positive	10	1	1
Neoantigen 1	TP53 (I162N) pgtrvramanykqsqhmt	TP53 (G245S) ymcnsscmgsmnrrpilt	ABCC8 (G1433S) ilqdpvlfsstirfnldp
Neoantigen 2	ADAM23 (R688W) iptsfyhqgwvidcsgah	ANKRD31 (N929I) cstggkkhyifkenltnk	BUD13 (R477H) grkrnlklehleqrrkae
Neoantigen 3	CD81 (K148N) dannakavvntfhetldc	CDH8 (P714A) qfmprqglaavpngvdvd	DCLK1 (R326C) tpgsqlstpcsgkspsps
Neoantigen 4	DNAH5 (K3920N) kheefltlinggasldlk	DGKG (D484G) glnffrdtpgfrvlacgg	GAK (P370L) glalaeydqlyggfldil
Neoantigen 5	GRM7 (A30V) levllcalavaargqemy	GPRASP1 (S78C) savggarpkckkaipvsr	IL4I1 (R193H) vpeklgyalhpqekghsp
Neoantigen 6	MYLIP (R317S) gkkyvfdikstskevydh	LPIN3 (R602W) slrlssdqiwrlnlqega	KANSL1L (Q246E) qarrtqkhlemllakhvv
Neoantigen 7	PDLIM2 (A594T) ekharqrystpatlssra	PROB1 (A353V) lqseekiqevrktrfpre	PRDM5 (R414Q) qceeckalfqtpfslqrh
Neoantigen 8	PLXNB2 (R1624Q) kaiteiyltqllsvkgtl	SMAD4 (R100S) phviyarlwswpdlhkne	SLX4 (V1747M) gevsasqaamqaadtdea
Neoantigen 9	SENP1 (W534C) lvpihlgvhcclavvdfr	TCP11L1 (C401Y) vlttigekvylevsscls	SQSTM1 (E242G) svnflknvggsvaaalsp
Neoantigen 10	STAB1 (R1796W) hrdklaailwghmirnve	WDFY4 (R1871Q) qaptkahpaqrklreftq	ZCCHC5 (P252S) tfsgdsqklseflvqlys
Neoantigen 11			
Neoantigen 12			

Patient ID	2-81	2-114	2-33
# neoantigens tested	10	10	10
# neoantigens positive	10	4	5
Neoantigen 1	ABCF2 (T1571I) tremppsdkiplhcvmev	TP53 (G279E) evrvcacperdrrteee	CDH8 (R782H) fdylsdwgphfkrlgely
Neoantigen 2	COL4A4 (R877W) mkglpglpgwpgahgppg	ABLIM2 (R381Q) slgrytptsqspqhysrp	CLCA1 (N256S) vefcteqnhskeapnkqn
Neoantigen 3	GATAD2B (P268R) mlmsqrviarnpaqlqgq	FANCA (A1157V) pslmvdfilvkcqtkcpl	DOCK2 (K485N) yrsvvyyqvkqprwmetv
Neoantigen 4	KIF2B (R40Q) yvaiqrsdkqihlavvte	FRMPD4 (A532V) fnmankkntvtqetgpen	EPPK1 (R855L) rrrqllrrylqrevtlgq
Neoantigen 5	NCKAP5L (R1304I) stsdmaeegivasggppg	MROH2B (G1326R) atlrqmairrlgntasga	HEATR5B (R818H) ecvkqakgvhqqavqlni
Neoantigen 6	RTP1 (R174H) cygerggqyhihvasrqd	PDZRN3 (R941H) yitkrpvrdhllreralk	IGSF22 (T624M) haitvkvghmahikvpfr
Neoantigen 7	SLITRK5 (N137H) lrglrrlhlhnnklellr	RLIM (T128N) nqswravsrtnpnsgdfr	MUC16 (R5966K) vtslltsgrhktidmldt
Neoantigen 8	SPOP (T37A) kvvkfsymwainnfsfcr	SCRN1 (D349N) tqspcfgddnpakkeprf	CD1E (R225H) scgpspgpghlqlvchvs
Neoantigen 9	TMEM201 (L229P) laflacaflpttalygas	TNRC6A (R1677C) pstsawssicasnynvpl	SYCE1 (A293T) khgmqvpaqtqstqeeea
Neoantigen 10	UBE2U (T60I) Lvfqltihfiseynyapp	UHRF1BP1 (H825L) vhmlvhspalvrvrldhy	XKR4 (R586C) ptapstpsscpprieesv
Neoantigen 11			
Neoantigen 12			

Patient ID	2-16	2-142	2-117
# neoantigens tested	11	11	5
# neoantigens positive	3	3	4
Neoantigen 1	CDH13 (E196D) ivvspilipdnqrqpfpr	ATP2C2 (T381M) ccsvlcsdkmgtltanem	TP53 (Y163C) gtrvramaickqsqhmte
Neoantigen 2	SOX13 (A515V) krlrvgeykvlmrtrrqd	EML1 (L54P) vqmqeddiqplksaladv	HEATR1 (D1269A) lnicqklspaggkipkdi
Neoantigen 3	KIR2DL4 (A23S) gffldqsvwshvggqdkp	ZFHX4 (A2686V) cpfcralfkvksaleshi	PCDHA4 (T136A) ndnppvfpaaqknlsiae
Neoantigen 4	SOBP (R626H) rsevvdltrhagsppgpp	SRRM2 (R730W) rgrsgsssewknksrtsq	RPS2 (L139R) igdynghvgrgvkcskev
Neoantigen 5	ENTPD8 (I174V) gqaegafgwvtvnyglgt	PRMT8 (K60Q) tqpscpgrgqmskllnpe	TSPYL2 (N281H) nhprisilihrrdedifr
Neoantigen 6	RBFOX1 (E60K) appqngipakytaphphp	PIN1 (A140S) qkpfedasfslrtgemsg	
Neoantigen 7	ZNF142 (R287H) aaaaeplplhcfqegcsy	PAX3 (A411V) vphqpqtdyvlspltggl	
Neoantigen 8	PABPN1L (A204T) fatkgsvqatveldqslf	LRFN1 (A495V) graydlcvlvvyddgata	
Neoantigen 9	PCDHAC2 (D252N) isvrvldtnnnspafdqs	RHEB (R161Q) enqtavdvfqriileaek	
Neoantigen 10	OR10H3 (R81H) ilftvaitphmladllft	EPHA4 (R973Q) kilssvqamqtqmqqmhg	
Neoantigen 11	TP53 (D259V) piltiitlevssgnllgr	CDKN2A (D84Y) plprrpghdygqrpsgga	
Neoantigen 12			

Supplementary Table 3 continued

Patient ID	2-126	2-112	2-82
# neoantigens tested	11	12	11
# neoantigens positive	1	0	11
Neoantigen 1	PDZRN4 (A804T) aktteqgcsteskekvle	IRX2 (D71N) fgsplqysanaaaaaagf	ZNF501 (Q33K) csecgkfftkrssltqhq
Neoantigen 2	MYH2 (T1860M) rrvkeltyqmeedrknil	TPRX1 (A54G) plvpaasasgpqrgpsgi	NLRP4 (V282M) aslliaikpmcpkelrdq
Neoantigen 3	ATP10B (G134S) vlfvimikdsmedfkrhr	SMAD4 (H92R) qvagrkgfprviyarlwr	HMGCS2 (R92H) kytvglgqthmgfcsvqe
Neoantigen 4	STXBP5L (R815H) eenrensynhsrsssiss	ZBTB25 (R295H) nensealechrlssfivk	CDKN2A (T93R) daaregfldrlvvlhrag
Neoantigen 5	ADAMTS12 (R442H) skcseeyithfldrgwgf	ACVR1B (S243F) kifssreerfwfreaeiy	SPG7 (G632R) fermcmalgrrasealsf
Neoantigen 6	ZBTB46 (A187T) anssgdsaitschdggss	EPHX2 (E444A) epslsrmvtaeeiqfyvq	ACSBG2 (V147L) tnsaeacqylithakvni
Neoantigen 7	IRS4 (S299T) qyfflevgrttvigpgel	PCDH18 (Y734C) nrekkdtrscncrvaest	KRTAP19-3 (R33C) gygcgcgsfcrlgsgcgy
Neoantigen 8	KIF26A (R1125H) evsvctadshdptpqprf	TLE2 (S436L) gqmqpvpfpldalvgagi	RP1 (R125W) dldkarrrpwpwlssrai
Neoantigen 9	REPS1 (D299N) vnqfktiqpnlngfipgs	SYNE2 (E5174A) leqllesitasenkiqil	FNDC1 (R632H) qspssvlrdhssvhpgak
Neoantigen 10	TP53 (V172F) ykqsqhmtefvrrcphhe	KIF1A (R1662H) atetdkepqhllvpdiqe	PRSS1 (V25I) apfddddkiiggynceen
Neoantigen 11	CDKN2A (H83Y) qqplprrpgyddgqrpsg	TP53 (R175H) sqhmtevvrhcphhercs	TP53 (M237V) dcttihynyvcnsscmgg
Neoantigen 12		CDKN2A (P48R) napnsygrrriqvmmmgs	

Patient ID	2-76	2-107	2-130
# neoantigens tested	6	11	6
# neoantigens positive	2	7	0
Neoantigen 1	TP53 (G279E) duplicate	CHRNA9 (R84H) qiltaylwihqiwhdayl	ABCB5 (A986V) eyskaksgavhlfallek
Neoantigen 2	ATRX (D421G) dlnseframgavnkeknt	CYLD (G512R) gleledecarctdgtfrg	BFSP1 (P578S) srrpcamvtsgaeepsip
Neoantigen 3	AXIN2 (R158T) lkpatktyitdgikkqqi	HS6ST1 (D87E) slrfdmkgdevivflhiq	CHD1 (R815Q) rvlifsqmvqmldilaey
Neoantigen 4	CDKN2A (T93K) daaregfldklvvlhrag	NFRKB (G567V) hkaftfrmhvfesvvgpv	IFIT1B (I353T) vdlaetyaetghhrkaee
Neoantigen 5	GNAS (T397M) piptpgrplmpqpiqmpg	NPIPB5 (P622R) vcgfrfhhqrmiisrhlp	NF1 (S2829C) qvqkqrsagcfkrnsikk
Neoantigen 6	NTRK3 (R343W) hwlhngqplweskiihve	NPIPB5 (H620P) lsvcgfrfhpqpmiisrh	ZNF503 (C432F) taslcrdpyplsyhcash
Neoantigen 7		PIDD (V96I) qslsclrslilkggqrrd	
Neoantigen 8		RYR2 (V1664I) yhtlrlysaicalgnhrv	
Neoantigen 9		SPN (R283W) lllwrrrqkwrtgalvls	
Neoantigen 10		TP53 (V272G) nllgrnsfegrvcacpgr	
Neoantigen 11		CDKN2A (H83Y) qqplprrpgyddgqrpsg	
Neoantigen 12			

Protocol Number: ELI-002-201

Protocol Name: AMPLIFY-7P

First in Human Phase 1/2 Trial of ELI-002 7P Immunotherapy as Treatment for Subjects with Kirsten Rat Sarcoma (KRAS)/Neuroblastoma RAS viral oncogene homolog (NRAS) Mutated Pancreatic Ductal Adenocarcinoma (PDAC) and Other Solid Tumors

SPONSOR

Elicio Therapeutics, Inc.

Sponsor Contact: [redacted]

Phone: [redacted]

Email: [redacted]

Lead Medical Monitor: [redacted]

Phone: [redacted]

Email: [redacted]

Protocol Version: Version 8.0, Dated 06 February 2026

SIGNATURE PAGE

[redacted]
Chief Medical Officer
Elicio Therapeutics, Inc.

Date

[redacted]
Senior Vice President, Clinical Development
Elicio Therapeutics, Inc.

Date

[redacted]
Senior Vice President, Regulatory Affairs
Elicio Therapeutics, Inc.

Date

INVESTIGATOR'S AGREEMENT

I have read and reviewed the ELI-002-201 Protocol, version 8.0, 06 February 2026, and agree to conduct the trial as outlined and with all applicable regulations including the current International Conference on Harmonization guidelines.

I agree to provide copies of the ELI-002-201 Protocol and the Investigator's Brochure for ELI-002 7P, provided by the Sponsor (Elicio Therapeutics), to all members of the study team. I will ensure that all members of the study team are fully trained regarding the study drug and conduct of the study.

I agree to make available to Elicio Therapeutics, their representatives, and regulatory authorities, the study records of each subject in order to verify the data that Elicio Therapeutics has entered into the case report forms. I am aware of my responsibilities as a study investigator as provided by the Sponsor.

_____

Printed Name of Investigator

_____

Signature of Investigator

_____

Date

PROCEDURES IN CASE OF EMERGENCY

Emergency contact information is provided in Table 1.

Table 1: Emergency Contact Information

Role in Trial	Name	Email and Telephone Number
Clinical Operations	[redacted]	[redacted]
Responsible Physician	[redacted]	[redacted]
24-Hour Emergency Contact	[redacted]	[redacted]

1. SYNOPSIS

<table>
<tr><td colspan="3">Name of Sponsor/Company: Elicio Therapeutics, Inc. (hereafter, referred to as Elicio)</td></tr>
<tr><td colspan="3">Name of Investigational Product: ELI-002 7P</td></tr>
<tr><td colspan="3">Name of Active Ingredient: ELI-002 7P is an 8-component product consisting of: 7 lipid-conjugated peptide-based antigens (amphiphilic peptides, referred to as ‘Amph-Peptides 7P’) and a lipid-conjugated immune-stimulatory oligonucleotide (‘Amph-CpG-7909’) dosed after an admixing procedure of the respective Amph-Peptides 7P and Amph-CpG-7909 drug products.</td></tr>
<tr><td>Protocol Number: ELI-002-201</td><td>Phase: 1/2</td><td>Country: United States (of America)</td></tr>
<tr><td colspan="3">Title of Trial: First in Human Phase 1/2 Trial of ELI-002 7P Immunotherapy as Treatment for Subjects with Kirsten Rat Sarcoma (KRAS)/Neuroblastoma RAS viral oncogene homolog (NRAS) Mutated Pancreatic Ductal Adenocarcinoma (PDAC) and Other Solid Tumors</td></tr>
<tr><td colspan="3">Trial centers: Multicenter</td></tr>
<tr><td colspan="3">Investigators: Multicenter</td></tr>
<tr><td colspan="3">Studied period:
Estimated date first subject enrolled: 2Q2023
Estimated date last subject completed: 4Q2027</td></tr>
<tr><td colspan="3">Phase 1 Hypothesis: ELI-002 7P is safe at the same recommended Phase 2 dose (RP2D) of Amph-CpG-7909 as ELI-002 2P, established in protocol ELI-002-001.
Phase 2 Hypothesis: ELI-002 7P is safe and prolongs disease-free survival (DFS) with a hazard ratio (HR) less than 1.</td></tr>
<tr><td colspan="3">Phase 1 Primary Objective:
To assess the safety and tolerability of ELI-002 7P as adjuvant therapy for subjects with KRAS/NRAS mutated solid tumors who have minimal residual disease (MRD) identified using either ctDNA or a serum tumor biomarker
Phase 1 Secondary Objective:
To assess circulating tumor deoxyribonucleic acid (ctDNA) reduction and clearance, defined as reduction or clearance in ctDNA compared to baseline, or if ctDNA was not detectable at baseline, serum tumor biomarker (such as carbohydrate antigen [CA]19-9 and carcinoembryonic antigen [CEA]) reduction and clearance compared to baseline
Phase 1 Exploratory Objectives:
To report the median DFS (per investigator) and the median overall survival (OS)
To assess the change relative to baseline in:
Phase 1A only: Serum cytokines interleukin (IL)-2, interferon gamma (IFNγ), IL-6, IL-10, and tumor necrosis factor alpha (TNFα)
Patient reported outcomes (PROs): European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire [QLQ]-C30 and QLQ-PAN26, or QLQ-CR29
To evaluate the immunogenicity of ELI-002 7P. T cell responses to ELI-002 7P will be assessed using assays such as intracellular cytokine staining (ICS), Fluorospot, and/or dextramer+ T cells for subjects with human leukocyte antigen (HLA) alleles for which dextramer/s is/are available</td></tr>
</table>

  - Biomarker levels (ctDNA, CA19-9, and CEA)
  - To evaluate tumor-infiltrating T cells and the tumor microenvironment after dosing with ELI-002 7P
- To correlate biomarker data to clinical safety and efficacy (DFS, OS)

Phase 2 Primary Objective:

- To compare ELI-002 7P versus standard of care (SOC; observation) in DFS (per investigator)

Phase 2 Secondary Objectives:

- To compare OS between subjects randomized to ELI-002 7P versus SOC (observation)
- To compare ctDNA reduction and clearance, defined as reduction or clearance in ctDNA compared to baseline, or if ctDNA was not detectable at baseline, serum tumor biomarker (such as CA19-9 and CEA) reduction and clearance compared to baseline in subjects randomized to ELI-002 7P versus SOC (observation)
- To assess the safety and tolerability of ELI-002 7P

Phase 2 Exploratory Objectives:

- To assess objective response rate (irORR) in subjects who crossover to ELI-002 7P from observation after relapse according to Immune Response Evaluation Criteria in Solid Tumors (iRECIST)
- To assess the change relative to baseline in:
  - To evaluate the immunogenicity of ELI-002 7P. T cell responses to ELI-002 7P will be assessed using assays such as ICS, Fluorospot, and/or dextramer+ T cells for subjects with HLA alleles for which dextramer/s is/are available
  - Biomarker levels (ctDNA, CA19-9, and CEA)
  - To evaluate tumor-infiltrating T cells and the tumor microenvironment after dosing with ELI-002 7P

Phase 1 Primary Endpoint:

- To evaluate safety as assessed by the incidence of adverse events (AEs) and clinically significant changes in laboratory tests and vital signs

Phase 1 Secondary Endpoint:

- To report the proportion of subjects with ctDNA reduction and clearance, defined as reduction or clearance in ctDNA compared to baseline, or if ctDNA was not detectable at baseline, serum tumor biomarker (such as CA19-9 and CEA) reduction and clearance compared to baseline

Phase 1 Exploratory Endpoints:

- Median DFS (per investigator) and median OS
- Duration of biomarker (ctDNA or serum tumor biomarker) reduction or clearance, defined as the time from the date of the first decreased and/or negative biomarker to the earliest date of any of the following events:
  - Subsequent increased/positive biomarker
  - Subsequent disease relapse
  - Death due to any cause
- Change relative to baseline in:
  - Phase 1A only: Serum cytokines IL-2, IFNγ, IL-6, IL-10, and TNFα

- PROs: EORTC QLQ-C30 and QLQ-PAN26, or QLQ-CR29
- Immunogenicity of ELI-002 7P determined by magnitude of response and fold-change from baseline, using assays such as ICS, Fluorospot, and/or dextramer+ T cells for subjects with HLA alleles for which dextramer/s is/are available
- Biomarker levels (ctDNA, CA19-9, and CEA)
- Immune cell infiltrate and tumor microenvironment if standard-of-care biopsies are obtained to confirm new lesions

Phase 2 Primary Endpoint:

- DFS (per investigator)

Phase 2 Secondary Endpoints:

- 1-year DFS rate
- OS
- Biomarker response rate (BRR) - Proportion of subjects with biomarker response (ctDNA or serum tumor biomarker), defined as reduction or clearance in biomarker compared to baseline
- Safety as assessed by the incidence of AEs and clinically significant changes in laboratory tests and vital signs

Phase 2 Exploratory Endpoints:

- irORR in subjects who crossover to ELI-002 7P from observation after relapse according to iRECIST
- Change relative to baseline in:
  - Immunogenicity of ELI-002 7P determined by the magnitude of response and the fold-change from baseline, using assays such as ICS, Fluorospot, and/or dextramer+ T cells for subjects with HLA alleles for which dextramer/s is/are available
  - Biomarker levels
  - Immune cell infiltrate and tumor microenvironment in the event that standard-of-care biopsies are obtained to confirm new lesions

Trial Design:

ELI-002-201 is an open-label, Phase 1/2 trial of ELI-002 7P immunotherapy as adjuvant treatment for subjects with KRAS/neuroblastoma ras viral oncogene homolog (NRAS) mutated pancreatic ductal adenocarcinoma (PDAC) and other solid tumors who are at high risk for relapse (ie, presence of isolated tumor cells in the subject's body, in which the primary tumor has been removed and is currently without clinical signs of disease).

This protocol builds on the experience obtained with a related product, ELI-002 2P (with Amph-Peptides G12D and G12R), which was studied in protocol ELI-002-001 under IND 26909. ELI-002-001 evaluated escalating doses of the adjuvant Amph-CpG-7909 when admixed with a fixed dose of Amph-Peptides 2P (1.4 mg [700 µg of each peptide]). Therefore, the dose carried forward into this protocol will be the RP2D of Amph-CpG-7909, determined to be 10.0 mg. This Amph-CpG-7909 RP2D will be evaluated in Phase 1A with two dose levels of Amph-Peptides 7P (G12D, G12R, G12V, G12A, G12C, G12S, G13D): 4.9 mg total (700 µg of each peptide) and 1.4 mg total (200 µg of each peptide).

Phase 1A is planned to enroll 12 subjects, 6 subjects at each Amph-Peptide 7P dose (designated Cohort 1) with mutant KRAS (mKRAS)/mutant NRAS (mNRAS) solid tumors (PDAC and CRC). If 2 or more of the 6 subjects in Phase 1A (Cohort 1) at either of the Amph-Peptide 7P dose levels experience a dose-limiting toxicity (DLT) in the first 28 days following ELI-002 7P administration,

then, prior to opening Phase 2 to enrollment, the independent data monitoring committee (IDMC) will review the events and may recommend a change in the ELI-002 7P dose (ie, RP2D−1 of Amph-CpG-7909 or an updated dose level of Amph-Peptides 7P), and if so, an additional 6 subjects will be enrolled in Phase 1A at the changed dose level. An additional 6 subjects at the RP2D−1 may also be added if further characterization of the Phase 2 dose is required. Following IDMC review of the Phase 1A safety data, if the IDMC recommends on a dose level to proceed to Phase 2, Phase 1A enrollment of PDAC subjects may continue at this dose level until Phase 2 is opened to enrollment. Phase 1B (Cohort 2, CRC) may be opened to enrollment by Elicio either concurrent or subsequent to Phase 2. If Cohort 2 is opened this will be documented in a study memo sent to all clinical sites and maybe submitted to IRBs, per IRB guidance.

The Phase 2 portion of the study (Cohorts 3A, 3B and 3C) will proceed contingent on the observation of antitumor activity with ELI-002 during the clinical development program. In Phase 2, approximately 135 subjects with PDAC will be randomized 2:1 to ELI-002 7P or SOC (observation), respectively. Subjects randomized to ELI-002 7P will receive subcutaneous (SC) injections of ELI-002 7P during the Immunization Period and the Booster Period. Subjects randomized to SOC (observation) will be able to cross over to ELI-002 7P treatment following confirmed disease progression.

Randomization in Phase 2 will be stratified according to the following:

- Nodal status: node negative versus node positive (0 versus 1)

Subject replacement: In Phase 1A, if any of the first 12 subjects discontinue for any reason other than toxicity prior to completing 28 days of ELI-002 7P therapy, a replacement subject will be added to the cohort until 12 subjects (6 at each Amph-Peptide 7P dose, depending on whether the 1.4 mg dose is evaluated) complete 28 days of ELI-002 7P therapy. In Phase 2, once a subject is randomized, they will not be replaced for any reason.

DLT definition (Phase 1A, first 12 subjects): A DLT will be defined as any event at least possibly related to ELI-002 7P as follows:

a. Any Grade ≥ 3 non-hematologic toxicity except asymptomatic laboratory abnormalities (see Section 12.2.1.1)
b. Any Grade ≥ 3 toxicity involving major organ systems for greater than 72 hours and occurring within 28 days of SC administration
c. Grade 3 CRS that does not resolve to ≤ Grade 2 within 7 days
d. Any Grade 4 CRS that does not improve to < Grade 2 within 72 hours
e. Any Grade ≥ 3 autoimmune disorder
f. Any Grade ≥ 3 rash that does not resolve to ≤ Grade 1 within 7 days with appropriate treatment

The DLT observation period will be 28 days following the first SC administration of ELI-002 7P.

Grade 3 maculo-papular or acneiform rashes are commonly observed after SC delivery of therapeutic cancer vaccines and are not dose-limiting.

The trial will consist of a Screening Period, an Immunization Period, a No Dosing 2-Month Period, a Booster Period, and a Follow-up Period.

A Booster Period is provided as further lymph node antigen exposure may be required to maintain effective levels of antigen-specific T cells. All subjects will receive booster doses unless they have unresolved toxicity.

All subjects will be observed for safety and tolerability. Radiographic imaging with contrast will be performed at screening, approximately 3 months after the first dose, and at additional timepoints until confirmed radiographic relapse is observed.

The central laboratory will confirm if at least 1 of the 7 mutant KRAS/NRAS alleles targeted by ELI-002 Amph-Peptides 7P (G12D, V, R, S, A, C, G13D) is present, and for Phase 1 only, central laboratory ctDNA must be positive or there must be serum tumor biomarker (such as CA19-9 and

CEA) elevation at ≥21 days post-surgery or after the last administration of adjuvant therapy (whichever comes last in the specific subject's treatment plan). KRAS data are required to determine a subject's eligibility and inclusion into all cohorts in the trial. Results confirming ctDNA positivity and/or serum biomarker elevation are required to determine a subject's eligibility and inclusion into Phase 1 of the trial.

Immunologic biomarkers of response may include HLA typing, ICS, Fluorospot, and dextramer^{+} T cells for subjects with appropriate HLA alleles will be determined when matching dextramer/s is/are available. Tumor biopsy assessments may include gene expression and/or immunofluorescence to examine immune cell infiltration and tumor microenvironment phenotype.

Local laboratories will be utilized for tumor biomarkers CA19-9/CEA (as appropriate per tumor type), and all other safety laboratory tests.

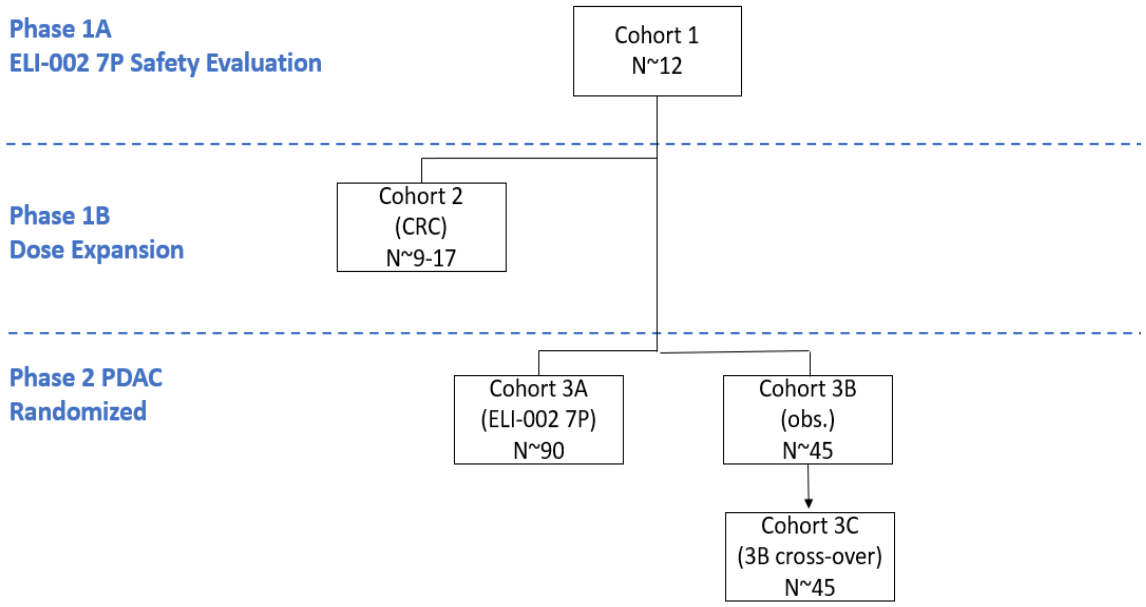
Central laboratories will be utilized for ctDNA analysis, HLA typing, peripheral blood mononuclear cell (PBMC) isolation, tumor microenvironment and T-cell infiltration, and immunogenicity assessment (such as Fluorospot, ICS, and/or T cell dextramer testing) as detailed in the central laboratory manual.

While HLA testing will be performed prior to the first dose at Visit 2, cohorts will be enrolled regardless of the HLA subtype.

Discontinuation of Trial Treatment or Crossover from SOC (Observation) to ELI-002 7P: Subjects with confirmed radiographic relapse (using iRECIST criteria; not judged as pseudoprogression) during treatment with ELI-002 7P may discontinue trial treatment or could continue for clinical benefit per Section 6.1.2. Discussion should take place with Elicio Clinical prior to early treatment discontinuation to ensure potential pseudoprogression is considered. In Phase 2, subjects randomized to SOC (observation) will be eligible to crossover to intervention (ELI-002 7P) after confirmed relapse is documented using iRECIST criteria, and regardless of their election to crossover or not, they will continue to be followed for OS. For subjects who cross over, response to treatment will be characterized using iRECIST criteria.

The design of the Phase 1/2 trial is outlined in the following figures.

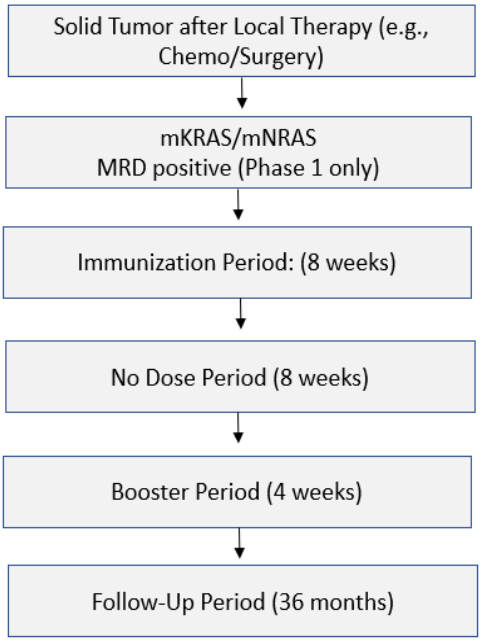
ELI-002-201 Cohort Schematic



CRC=colorectal cancer; PDAC=pancreatic ductal adenocarcinoma

Protocol ELI-002-201

- Phase 1A, Cohort 1: approximately 12 subjects to receive ELI-002 7P (Amph-CpG-7909 at RP2D + Amph-Peptides 7P [6 subjects at 4.9mg and 6 subjects at 1.4mg)
- Phase 1B, Cohort 2: approximately 9-17 subjects to receive ELI-002 7P (sponsor may open cohort at later date, sites to be notified via study memo)
- Phase 2 (Randomized), Cohort 3: approximately 135 subjects randomized 2:1 (ELI-002 7P: Observation). Subjects randomized to observation will have an opportunity to cross-over to ELI-002 7P treatment following confirmed radiographic progression
  - Cohort 3A: 90 subjects randomized to ELI-002 7P
  - Cohort 3B: 45 subjects randomized to observation
  - Cohort 3C: cross-over to ELI-002 7P from Cohort 3B
- Collect safety, clinical and immune response data including: ir-ORR by iRECIST, immunologic responses, ctDNA reduction/clearance



Sample Size Justification: For Phase 1A, the 12 subject safety evaluation is empiric and will achieve the protocol objective of confirming the safety of the RP2D of Amph-CpG-7909 admixed with Amph-Peptides 7P.

For Phase 1B Cohort 2 (CRC), Bayesian Optimal Phase 2 (BOP2) design assumes a null hypothesis of biomarker (ctDNA or serum tumor biomarker) response (reduction/clearance) rate ≤0.05 and the alternate hypothesis of biomarker response rate ≥0.3. The BOP2 is designed with 90% power to reject the null hypothesis that the true biomarker response rate is ≤0.05 with a sample size of 17 subjects. An interim analysis for go/no-go decision for expansion to a sample size of 17 subjects will occur after 9 biomarker evaluable subjects are available and have been on study for at least 28 days. If ≥1 biomarker response is observed, then the Phase 1B cohort will continue to enroll until it reaches 17 subjects with the criteria of ≥3/17 biomarker responses to reject the null hypothesis at alpha=0.05 (1-sided). Enrollment will stop if there are 0 responses observed in the first 9 subjects (ie, no-go).

For Phase 2 (PDAC), approximately 135 subjects will be randomized 2:1 to receive ELI-002 7P or SOC (observation), respectively. Randomization will be stratified by nodal status (N0 vs N1). Assuming the true HR is 0.53 (median DFS [per investigator] of 7 months vs. 13.2 months), a 2-sided alpha of 0.10, (or equivalent 1-sided alpha 0.05), and a power of 80%, approximately 71 DFS events will be required to detect the hypothesized HR. One interim analysis and one final analysis is planned. A safety evaluation is also planned when approximately 20 biomarker evaluable subjects are available who had been on study for at least 28 days. See Section 13.7 for further details on interim analysis.

Number of Subjects (planned):

- Phase 1A: approximately 12 subjects are planned to enroll in Cohort 1.
- Phase 1B Expansion: approximately 9-17 subjects are planned to enroll in Cohort 2.
- Phase 2: Approximately 135 subjects are planned to enroll.

Diagnosis and Main Criteria for Inclusion: Males or females ≥18 years of age with histologically or cytologically confirmed diagnosis of solid tumor with central laboratory analysis confirming the presence of at least 1 of the 7 KRAS/NRAS mutations targeted by ELI-002 Amph-Peptides 7P.

Investigational Product, Dosage and Mode of Administration: ELI-002 7P is an investigational product consisting of 7 lipid-conjugated peptide (G12D, G12R, G12V, G12A, G12C, G12S, G13D) based antigens (amphiphilic peptides, referred to as 'Amph-Peptides 7P') and a lipid-conjugated immune-stimulatory oligonucleotide ('Amph-CpG-7909') dosed after an admixing procedure of the respective Amph-Peptides 7P and Amph-CpG-7909 drug products (referred to as ELI-002 7P in this protocol).

The cohorts planned to be evaluated are as shown below:

Cohort	Tumor Type	Treatment
Phase 1A: ELI-002 7P Safety Evaluation		
1	mKRAS/mNRAS solid tumors	ELI-002 7P
Phase 1B: Dose Expansion Cohort		
2	CRC	ELI-002 7P
Phase 2: Randomized Cohorts		
3A	PDAC	ELI-002 7P
3B	PDAC	Observation
3C	PDAC	ELI-002 7P (crossover)

CRC=colorectal cancer; mKRAS=mutant Kirsten Rat Sarcoma; mNRAS=mutant neuroblastoma ras viral oncogene homolog; PDAC=pancreatic ductal adenocarcinoma

Duration of Treatment: The total duration of participation for each subject is approximately 3.5 years, and includes a Screening Period, an Immunization Period, a No Dosing 2-Month Period, a Booster Period, and a Follow-up Period. Subjects who crossover after observation in the Phase 2 portion of the study will be followed for a minimum of 3 years after the final administration of ELI-002 7P.

Subjects who remain in the trial until the end of the required Booster Period may be eligible to enroll in an Extension Protocol.

Reference Therapy, Dosage and Mode of Administration: None

Criteria for Evaluation:

Safety: Adverse events will be recorded and categorized using CTCAE, Version 5.

Standard clinical chemistry, hematology assays, physical examinations, vital sign measurements, electrocardiograms, and Eastern Cooperative Oncology Group performance status will be assessed/performed at specified times during the trial.

Efficacy: DFS and 1-year DFS rate will be assessed through imaging using iRECIST criteria; subjects will be followed for OS. In addition, biomarker (ctDNA or serum tumor biomarker) response rate will be calculated. Biomarker response is defined as reduction or clearance, as measured by the reduction or absence of the biomarker, and the duration of biomarker reduction and/or clearance will be recorded.

Immunogenicity: Subjects will have leukapheresis and blood samples drawn to evaluate the immunogenicity of ELI-002 7P. T cell responses in PBMCs will be assessed by immune assays such as IFNγ Fluorospot, ICS, and/or dextramers. Tumor biopsy assessments may include gene expression and/or immunofluorescence to examine immune cell infiltration and tumor microenvironment phenotype. Serum cytokine, CEA, and CA19-9 levels will also be examined.

Statistical Methods:

General considerations for both phases:

Descriptive statistics will be computed for demographics, medical history, and safety data.

Continuous variables will be summarized using mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized using frequency counts and percentages. Time to event data will be summarized using the Kaplan-Meier method. Where appropriate, confidence intervals around point estimates will be presented, and estimates of the median and other quantiles, as well as individual time points (for time to event data) will be produced.

The IDMC is anticipated to meet at least 3 times during the trial to review the phase 1A safety, the Phase 2 safety evaluation (approximately 20 biomarker evaluable subjects who had been on study for at least 28 days) and the planned efficacy/futility interim analysis (approximately 67% of total DFS [per investigator] events) for the Phase 2 PDAC subjects.

Efficacy:

For Phase 2, DFS is defined as the time from randomization until recurrence/death due to any cause. The OS (in months) is defined as the time from randomization until death from any cause.

Subjects who are lost to follow-up or do not have a date of death at the time of data cut-off will be censored at the last date that they were known to be alive. The median DFS and OS will be estimated using the Kaplan-Meier method.

Interim Analyses:

Phase 1A: If 2 or more of the 6 subjects in Phase 1A (Cohort 1) at either of the peptide dose levels experience a DLT in the first 28 days following ELI-002 7P administration, then, prior to opening Phase 2 to enrollment, the IDMC in partnership with the Sponsor, will review the data and may recommend a change in the ELI-002 7P dose (ie, RP2D−1 of Amph-CpG-7909 or an updated dose level of Amph-Peptides 7P), and if so, an additional 6 subjects will be enrolled in Phase 1A at the changed dose level. An additional 6 subjects at the RP2D−1 may also be added if further characterization of the Phase 2 dose is required. Following IDMC review of the Phase 1A safety data, if the IDMC recommends on a dose level to proceed to Phase 2, Phase 1A enrollment of PDAC subjects may continue at this dose level until Phase 2 is opened to enrollment. Phase 1B (Cohort 2, CRC) may be opened to enrollment by Elicio either concurrent or subsequent to Phase 2. If Cohort 2 is opened this will be documented in a study memo sent to all clinical sites and maybe submitted to IRBs, per IRB guidance.

Phase 1B: The trial will have futility interim analyses for Cohort 2 CRC, to determine further progression of the cohort. The analyses will be performed by the CRO and reviewed by the IDMC, which will make recommendations to the Sponsor regarding continuation of the trial.

Phase 2: One safety evaluation is planned when approximately 20 biomarker evaluable subjects who had been on study for at least 28 days are available, one efficacy analysis (including a non-binding futility analysis) is also planned when approximately 67% of the required total number of DFS events is observed. The final analysis will be conducted after observing the total number of DFS events. Additional details are provided in Section 13.7.

2. TABLE OF CONTENTS, LIST OF TABLES, AND LIST OF FIGURES

TABLE OF CONTENTS

TITLE PAGE 1
INVESTIGATOR'S AGREEMENT 3
PROCEDURES IN CASE OF EMERGENCY 4
1. SYNOPSIS 5
2. TABLE OF CONTENTS, LIST OF TABLES, AND LIST OF FIGURES 14
3. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS 21
4. INTRODUCTION 25
4.1. Summary of Pancreatic Cancer and Other Solid Tumors 27
4.1.1. Pancreatic Cancer 27
4.1.2. Colorectal Cancer 31
4.1.2.1. Introduction 31
4.1.2.2. Adjuvant Therapy in the Case of Localized CRC Disease 31
4.1.2.3. Rectal Cancer 32
4.1.2.4. Colorectal Liver Metastases 32
4.1.2.5. Frequency of KRAS and NRAS Mutations in CRC 33
4.1.2.6. Importance of ctDNA and CEA Assessment and Follow up in CRC 34
4.1.2.7. Colorectal Cancer and Vaccines 35
4.2. Brief Summary of Nonclinical Pharmacology 35
4.3. Brief Summary of Pharmacokinetics and Toxicokinetics 42
4.4. Brief Summary of Toxicology 42
4.4.1. Repeat-Dose Toxicity Studies 42
4.4.1.1. Study No. 2795-001: Amph-CpG-7909 (with and without Amph-Peptide-G12D): A 4-Week Subcutaneous Injection Tolerability Study in Male C57BL/6 Mice 42
4.4.1.2. Study 2795-002: A GLP 3-Month Study of ELI-002 by Subcutaneous Injection in C57BL/6 Mice with a 5-Week Recovery Period 43
4.5. Safety Pharmacology 43
4.6. ELI-002 7P: An Investigational Treatment for KRAS/NRAS Mutated Solid Tumors 44
4.6.1. Mechanism of Action 44

4.6.2. Amphiphile Lymph Node Delivery Background 44
4.6.3. Known and Potential Risks and Benefits....45
4.6.4. Trial Rationale 47
4.6.5. Rationale for Endpoints 48
4.6.6. Rationale for Dose Selection 49
5. TRIAL OBJECTIVES 50
5.1. Phase 1 Primary Objectives 50
5.2. Phase 1 Secondary Objective....50
5.3. Phase 1 Exploratory Objectives....50
5.4. Phase 2 Primary Objective....50
5.5. Phase 2 Secondary Objectives 51
5.6. Phase 2 Exploratory Objectives....51
6. INVESTIGATIONAL PLAN....52
6.1. Overall Trial Design 52
6.1.1. Criteria for Booster and Additional Booster Vaccines 55
6.1.2. Criteria for Treatment with ELI-002 7P After Disease Progression 56
6.1.3. Screening for Human Leukocyte Antigen Subtypes 56
6.1.4. Schedule of Assessments for ELI-002 7P Treated Subjects....56
6.1.5. Schedule of Assessments for Standard of Care/Observation Subjects 66
6.1.6. Risk Determination for Investigational In Vitro Diagnostics....75
6.1.6.1. Description of the IVDs....76
6.1.6.2. Applying the IVD Results in the Clinical Trial 77
6.2. Endpoints 77
6.2.1. Phase 1 Primary Endpoints 77
6.2.2. Phase 1 Secondary Endpoint 78
6.2.3. Phase 1 Exploratory Endpoints....78
6.2.4. Phase 2 Primary Endpoints 78
6.2.5. Phase 2 Secondary Endpoints....78
6.2.6. Phase 2 Exploratory Endpoints....79
6.3. Number of Subjects 79
6.4. Treatment Assignment....79
6.5. Dose Adjustment Criteria 80

6.6. Safety Criteria for Temporarily or Permanently Stopping the Trial....80
6.7. Management of Study Drug-Related Events....80
6.7.1. Temporarily Suspending Treatment Administration....80
6.7.2. Permanent Stopping Treatment Administration....80
6.7.3. Dose-limiting Toxicity Guidelines....81
6.8. Management of Risks and Toxicities....81
6.8.1. Management of On-target Off-tumor Toxicity....81
6.8.2. Management of Maculo-Papular or Acneiform Rashes, Injection Site Reactions....82
7. SELECTION AND WITHDRAWAL OF SUBJECTS....83
7.1. Subject Inclusion Criteria....83
7.2. Subject Exclusion Criteria....85
7.3. Phase 2 Subject Crossover Eligibility Criteria....86
7.4. Subject Withdrawal Criteria....87
7.4.1. Subject Replacement....88
7.4.2. Subjects Lost to Follow-up....88
8. TREATMENT OF SUBJECTS....89
8.1. Concomitant Medications....89
8.1.1. Prohibited Concomitant Medications....89
8.2. Treatment Compliance....89
8.3. Randomization and Blinding....89
9. TRIAL DRUG MATERIALS AND MANAGEMENT....90
9.1. Trial Drug....90
9.2. Trial Drug Packaging and Labeling....90
9.3. Trial Drug Storage....90
9.4. Trial Drug Preparation....90
9.5. Administration and Dosage....90
9.6. Trial Drug Accountability....91
9.7. Trial Drug Handling and Disposal....91
10. TIMING OF TRIAL PROCEDURES....92
10.1. Screening and Observation Period....92
10.1.1. Rescreening....93
10.2. Immunization Period....93

10.3. No Dosing 2-Month Period 98
10.4. Booster Period 99
10.5. Follow-up Period 102
10.6. Crossover from SOC (Observation) to ELI-002 103
11. CLINICAL ACTIVITY, IMMUNE ASSESSMENTS, AND SUBJECT REPORTED OUTCOMES 105
11.1. Mixed Response/Tumor Flare 105
11.2. Immunogenicity 105
11.3. ctDNA Levels 106
11.4. Future Use of Biospecimens 106
12. ASSESSMENT OF SAFETY 108
12.1. Safety Parameters 108
12.1.1. Demographics and Medical History 108
12.1.2. Vital Signs 108
12.1.3. Physical Examinations 108
12.1.4. Electrocardiogram 108
12.1.5. Eastern Cooperative Oncology Group 108
12.1.6. Laboratory Assessments 108
12.1.6.1. Hematology 109
12.1.6.2. Blood Chemistry 109
12.1.6.3. IL-6 at Screening 109
12.1.6.4. Viral Laboratory at Screening 110
12.1.6.5. Pregnancy Screen 110
12.2. Adverse and Serious Adverse Events 110
12.2.1. Definition of Adverse Events 110
12.2.1.1. Adverse Event 110
12.2.1.2. Serious Adverse Event 111
12.2.1.3. Reactogenicity to the Vaccine 111
12.3. Relationship to Trial Drug 112
12.4. Severity of Adverse Events 112
12.5. Recording Adverse Events 113
12.6. Pregnancy 113
12.7. Reporting Adverse Events 114

12.8. Extension Protocol 114
13. STATISTICS 115
13.1. General Statistical Considerations 115
13.2. Sample Size 115
13.3. Randomization 116
13.4. Analysis Population 116
13.4.1. Full Analysis Set (FAS) / Intention-to-Treat (ITT) 116
13.4.2. Safety Analysis Set 116
13.4.3. Per Protocol Set 116
13.4.4. PD/Biomarker Evaluable Set (BES) 116
13.5. Missing Data 117
13.6. Statistical Analyses 117
13.6.1. Efficacy Analysis 117
13.6.1.1. Disease-free Survival (DFS) 117
13.6.1.2. Overall Survival (OS) 118
13.6.1.3. Biomarker Response Rate (BRR) 118
13.6.1.4. Objective Response Rate (irORR) 118
13.6.1.5. Duration of Biomarker Response (DBR) 118
13.6.1.6. Multiplicity Adjustment 119
13.6.2. Safety Analysis 119
13.7. Interim Analyses 119
14. DATA INTEGRITY AND QUALITY ASSURANCE 121
14.1. Data Management and Case Report Forms 121
14.2. Source Documentation 121
14.3. Study Drug Accountability 121
14.4. Laboratory Assessments 122
14.5. Trial Monitoring 122
14.6. Protocol Deviations 122
14.7. Audits and Inspections 122
14.8. Institutional Review Board and Other Committees 123
14.8.1. Institutional Review Board 123
14.8.2. Independent Data Monitoring Committees 123

15. ETHICS 125
15.1. Ethical Conduct of the Trial 125
15.2. Written Informed Consent 125
16. DATA HANDLING AND RECORDKEEPING 126
16.1. Retention of Records 126
17. PUBLICATION POLICY 127
18. LIST OF REFERENCES 128
19. APPENDICES 137
19.1. ECOG Performance Status Scale 137

LIST OF TABLES

Table 1: Emergency Contact Information 4
Table 2: Abbreviations and Specialist Terms 21
Table 3: Peptide Elements of Amph-Peptides 26
Table 4: KRAS Mutation Spectrum in Pancreatic Cancer 30
Table 5: Colon and Rectal Cancer KRAS and NRAS Mutation Spectrum 33
Table 6: Nonclinical Pharmacology studies of mKRAS Vaccine in Support of ELI-002 (Model = Female C57BL/6 Mice, 5, 10 or 15/group) 37
Table 7: Schedule of Assessments: Screening and Observation 57
Table 8: Schedule of Assessments: Immunization Period 59
Table 9: Schedule of Assessments: No Dosing 2-Month Period 61
Table 10: Schedule of Assessments: Booster Period 62
Table 11: Schedule of Assessments: Follow-up Period (Year 1 to Year 2) 63
Table 12: Schedule of Assessments: Follow-up Period (Year 2 to Year 3) 65
Table 13: Schedule of Assessments: Screening and Observation 67
Table 14: Schedule of Assessments: Immunization Period 69
Table 15: Schedule of Assessments: No Dosing 2-Month Period 70
Table 16: Schedule of Assessments: Booster Period 71
Table 17: Schedule of Assessments: Follow-up Period (Year 1 to Year 2) 72
Table 18: Schedule of Assessments: Follow-up Period (Year 2 to Year 3) 74
Table 19: Phase 1 and Phase 2 Cohorts and Doses 91

Table 20: ECOG Performance Status Scale.....137

LIST OF FIGURES

Figure 1: Structure of Amph-CpG-7909 26
Figure 2: ELI-002 Trial Cohort Schematic 54
Figure 3: Protocol ELI-002-201: Phase 1/2 Trial Design 55
Figure 4: Flow Diagram of Eligibility Determination for Protocol ELI-002-201 76

3. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

The following abbreviations and specialist terms are used in this trial protocol.

Table 2: Abbreviations and Specialist Terms

Abbreviation or Specialist Term	Explanation
ADL	Activities of daily life
AE	Adverse event
AIDS	Acquired immune deficiency syndrome
AJCC	American Joint Committee on Cancer
ALT	Alanine aminotransferase
APC	Antigen-presenting cell
AST	Aspartate aminotransferase
ASTCT	American Society for Transplantation and Cellular Therapy
BES	Biomarker Evaluable Set
BOP2	Bayesian Optimal Phase 2
BRR	Biomarker response rate
CA	Carbohydrate antigen (cancer antigen)
CAP	College of American Pathologist
CAR	Chimeric antigen receptor
CBC	Complete blood count
CEA	Carcinoembryonic antigen
CI	Confidence interval
CLIA	Clinical Laboratory Improvement Amendment
CPD	Confirmed progressive disease
CRC	Colorectal cancer
CSF	Cerebrospinal fluid
CT	Computed tomography
CTCAE	Common Terminology Criteria for Adverse Events, Version 5
ctDNA	Circulating tumor deoxyribonucleic acid
Da	Daltons
DFS	Disease-free survival
DLT	Dose-limiting toxicity
EEG	Electroencephalogram

Abbreviation or Specialist Term	Explanation
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Report Form
FAS	Full Analysis Set
FDA	Food and Drug Administration
5-FU	5-fluorouracil
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GM-CSF	Granulocyte-macrophage colony-stimulating factor
GMP	Good Manufacturing Practices
HbA1c	Hemoglobin A1c
HbsAG	Hepatitis B virus surface antigen
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen
HR	Hazard ratio
ICH	International Conference on Harmonization
ICS	Intracellular cytokine staining
IDMC	Independent Data Monitoring Committee
IFNγ	Interferon gamma
IL	Interleukin
IND	Investigational New Drug
INR	International normalized ratio
IPM	Investigational Product Manual
irAE	Immune related adverse event
IRB	Institutional Review Board
iRECIST	Immune Response Evaluation Criteria in Solid Tumors
ITT	Intent to Treat
IV	Intravenous(ly)
IVD	In vitro diagnostic
IxRS	Interactive voice/web response system
KRAS	Kirsten rat sarcoma

Abbreviation or Specialist Term	Explanation
MHC	Major histocompatibility complex
mKRAS	Mutant Kirsten rat sarcoma
mNRAS	Mutant neuroblastoma ras viral oncogene homolog
MRD	Minimal residual disease
MRI	Magnetic resonance imaging
MSI	Microsatellite instability
MTD	Maximum tolerated dose
MW	Molecular weight
NCCN	National Comprehensive Cancer Network
NED	No evidence of disease
NGS	Next-generation sequencing
NOAEL	No-observed-adverse-effect level
NRAS	Neuroblastoma ras viral oncogene homolog
irORR	Objective response rate
OS	Overall survival
PBMC	Peripheral blood mononuclear cell
PCR	Polymerase chain reaction
PDAC	Pancreatic ductal adenocarcinoma
PE	Physical examination
PK	Pharmacokinetics
PI	Primary Investigator
Poly IC	Polyinosinic:polycytidylic acid
PRO	Patient reported outcome
PT	Prothrombin time
PTT	Partial thromboplastin time
QLQ	Quality of life questionnaire
QoL	Quality of Life
ROA	Route of administration
RP2D	Recommended Phase 2 dose
RP2D−1	One dose level below the recommended Phase 2 dose
SAE	Serious adverse event

Abbreviation or Specialist Term	Explanation
SAP	Statistical Analysis Plan
SARS	Severe acute respiratory syndrome
SC	Subcutaneous
SEER	Surveillance, Epidemiology, and End Results
SOC	Standard of care
SUSAR	Suspected Unexpected Serious Adverse Reaction
TNFα	Tumor necrosis factor alpha
TLR-9	Toll-like-receptor-9
ULN	Upper limit of normal
US	United States (of America)
WT	Wild type
XRT	Radiation therapy

4. INTRODUCTION

ELI-002 7P is a structurally novel amphiphilic therapeutic vaccine being studied as post-surgical adjuvant treatment of minimal residual disease (MRD) in subjects with Kirsten rat sarcoma (KRAS) viral oncogene homolog mutated pancreatic ductal adenocarcinoma (PDAC) and other KRAS mutated solid tumors.

ELI-002 7P uses amphiphile lymph node targeting which was developed at the Massachusetts Institute of Technology and licensed to Elicio Therapeutics. In cancer subjects, visual identification of sentinel lymph nodes during surgery is accomplished by injections of dyes that bind to endogenous albumin, targeting these compounds to draining lymph nodes. Amphiphiles were developed as an approach to improve the potency and safety of vaccination by harnessing the ability of the lipid component to bind to albumin and deliver a payload to lymph node antigen-presenting cells (APCs) [Liu et al., 2014]. Initial studies showed that amphiphiles markedly increase lymph node accumulation and decrease systemic dissemination relative to their parent soluble compounds, leading to 30-fold increases in T-cell priming and enhanced anti-tumor efficacy with reduced systemic toxicity. Subsequently investigation of the mechanism of action of amphiphiles using Batf3 knockout mice determined that the pharmacology requires cross-presenting dendritic cells in lymph nodes, and that combinations of amphiphiles with tumor-antigen-targeting antibodies, cytokines, and checkpoint inhibition using PD1 antibodies were able to destroy large established transplanted and genetically induced tumors in mice curing a majority of cancers in experimental settings previously considered intractable [Moynihan et al., 2016]. Most recently, amphiphile combinations with chimeric antigen receptor (CAR) T cells demonstrated potent enhancement of their activity including modulation of their phenotype to increase the proportion of central memory T cells, to extend the longevity of these cells, and to confer the ability to induce antigen spreading, which together led to cures of the majority of tumors in the models studied [Ma et al., 2019; Singh and June, 2019].

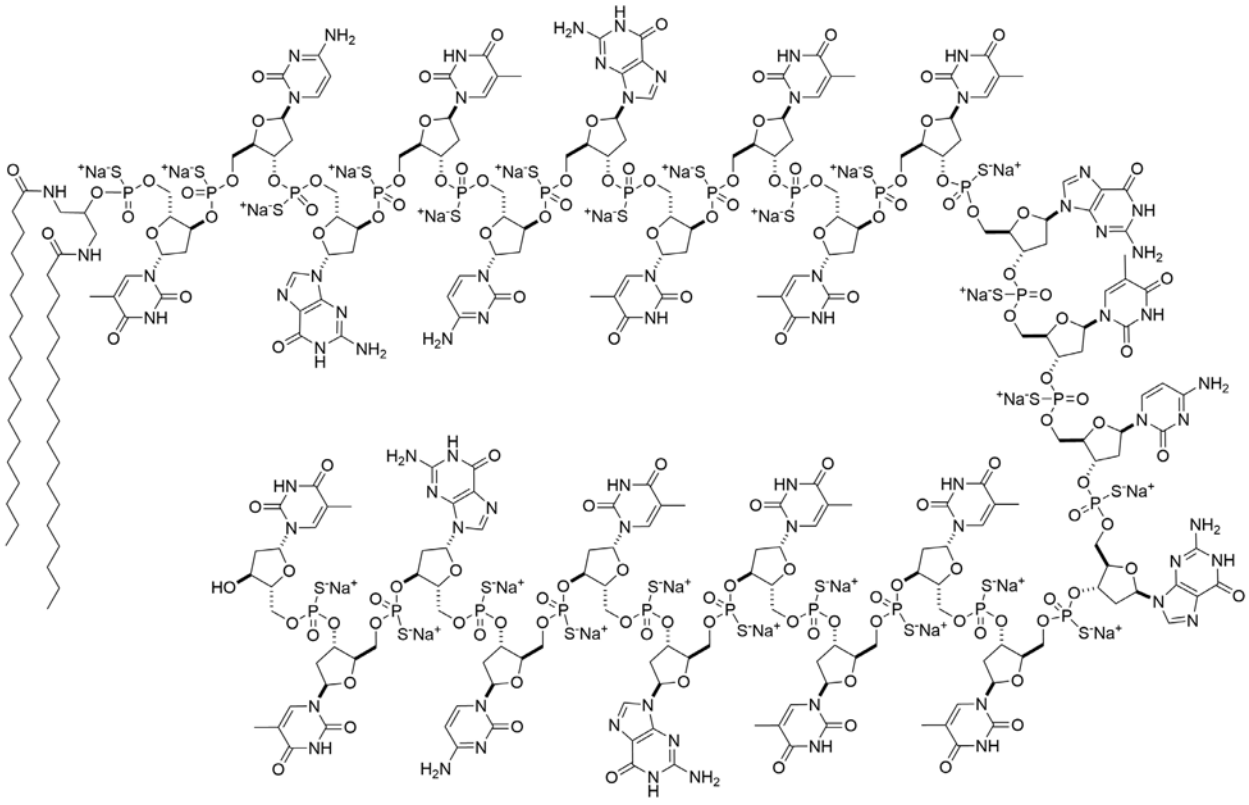
For the first clinical translation of the amphiphile technology, Elicio is developing ELI-002, a mutant KRAS (mKRAS)/mutant neuroblastoma ras viral oncogene homolog (mNRAS) lymph node targeting immuno-oncology product candidate. ELI-002 is comprised of up to 7 lipid-conjugated peptide-based antigens (‘Amph-Peptides’) described in Table 3, and a lipid-conjugated immune-stimulatory oligonucleotide (‘Amph-CpG-7909’) depicted in Figure 1.

Table 3: Peptide Elements of Amph-Peptides

Peptide Name	Peptide Sequence[a]	Peptide MW (Da)[b]	Residues[b]	Amph-Peptide MW (Da)[b]
G12D 4-21	CYKLVVVGADGVGKSALTI	1790	18	5049
G12V 4-21	CYKLVVVGAVGVGKSALTI	1774	18	5033
G12R 4-21	CYKLVVVGARGVGKSALTI	1831	18	5090
G12A 4-21	CYKLVVVGAAGVGKSALTI	1746	18	5005
G12S 4-21	CYKLVVVGASGVGKSALTI	1762	18	5021
G12C 4-21	YKLVVVGACGVGKSALTI	1778	18	4934
G13D 4-21	CYKLVVVGAGDVGKSALTI	1790	18	5049

[a] Variable residues: aspartic acid (DG and GD); valine (V); arginine (R); alanine (A); serine (S); cysteine (C)
[b] Peptide MW and Residues exclude *N*-terminal cysteine (C) required for Amphiphile sulfhydryl-maleimide coupling; Da=Daltons; MW=molecular weight

Figure 1: Structure of Amph-CpG-7909



Structurally, each amphiphile (Amph) component is a fusion comprised of 3 domains:

- An 18-carbon diacyl lipid that mediates association with albumin to facilitate trafficking to the lymph nodes and permits cell membrane insertion;
- A flexible linker that improves pharmaceutical properties in Amph-Peptides; the flexible linker is omitted in Amph-CpG-7909;
- A bioactive peptide or oligonucleotide.

Results of in vivo preclinical pharmacology studies showed that the greatest T cell responses to mKRAS peptides were achieved when the animals were administered Amph-Peptide(s) in combination with Amph-CpG adjuvant. The 7 peptide antigens included in ELI-002 7P have been previously evaluated in humans (without amphiphile modification) and were observed to be safe and well tolerated after subcutaneous (SC) administration in studies sponsored by Targovax ASA [Palmer et al., 2020].

ELI-002 7P targets mKRAS-driven malignancies expressing the most common oncogenic mutant forms of KRAS. Upon SC injection, the components of the vaccine are drained from the peripheral tissues into the lymph nodes. Here mKRAS Amph-Peptides are taken up by antigen-presenting immune cells for processing through the proteasomal pathway. Moynihan et al. reported that the immunogenicity of peptide vaccines could be increased by maximizing delivery to lymph nodes, where T-cell responses generated using the amphiphile approach were increased compared to soluble controls [Moynihan et al., 2018] (see Section 4.6.2).

In this protocol, ELI-002-201, the safety and efficacy of ELI-002 7P (Amph-CpG-7909 admixed with Amph-Peptides 7P) will be evaluated in subjects with KRAS/NRAS mutated solid tumors who have MRD. Specifically, the ELI-002 7P admixture will consist of Amph-CpG-7909 at the recommended Phase 2 dose (RP2D; determined in Study ELI-002-001 to be 10.0 mg). This Amph-CpG-7909 RP2D will be evaluated in Phase 1A with two dose levels of Amph-Peptides 7P (G12D, G12R, G12V, G12A, G12C, G12S, G13D): 4.9 mg total (700 µg of each peptide) and 1.4 mg total (200 µg of each peptide).

The trial will be monitored in accordance with the Sponsor's procedures, which comply with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

4.1. Summary of Pancreatic Cancer and Other Solid Tumors

4.1.1. Pancreatic Cancer

With an estimated number of 60,430 new cases in the United States (US) in 2021, PDAC is among the most common malignancies. Moreover, it is one of the most lethal cancers, as indicated by mortality estimated at 48,220 (~80%) [Siegel et al., 2021]. PDAC is the third leading cause of cancer death [Siegel et al., 2020], with 133,300 estimated deaths for 2018 in the US and Europe [Malvezzi et al., 2018].

Surgery (pancreatectomy) is the only curative option in PDAC. Even with surgery, prognosis remains poor due to the high propensity of the tumor for loco-regional and hepatic recurrence. In the National Cancer Database population, the 5-year survival in subjects undergoing pancreatectomy was only 23.3% [Sener et al., 1999]. Therefore, surgery alone is clearly an

inadequate approach to achieve long-term disease control in subjects with resectable PDAC. Historical use of adjuvant therapy with gemcitabine, or FOLFIRINOX combination chemotherapy improved the disease-free survival (DFS) and overall survival (OS) outcomes for subjects with resectable disease, but the majority of these subjects relapsed and died from recurrent disease [Oettle et al., 2007; Conroy et al., 2018]. Contemporary neoadjuvant therapy with FOLFIRINOX-based neoadjuvant therapy is a standard approach for locally advanced pancreatic cancer since it has been shown to improve the surgical resection rates and clinical outcomes in locally advanced PDAC [Chawla and Ferrone, 2019], and promising phase 2 data with neoadjuvant gemcitabine/nab-paclitaxel [Philip et al., 2020] indicate that an alternative regimen has activity. Fluoropyrimidine-based chemoradiation may be used as well [NCCN PDAC guidelines Version 2.2021]. Despite this, there is a need for improved adjuvant therapies for subjects who have undergone pancreatic resection surgery as survival rates for pancreatic cancer have mostly remained unchanged since the 1970s [Ansari et al., 2016; Macdonald and Mair, 2016].

PDAC is a disease that is almost entirely related to *KRAS* mutations. The *KRAS* gene encodes the KRAS protein, which is a small (21 kDA) guanosine triphosphatase (GTPase) that functions as a simple binary ON–OFF molecular switch, cycling between active GTP-bound and inactive guanosine diphosphate (GDP)-bound states [Vigil et al., 2010]. Cancer-associated *RAS* genes contain missense mutations that encode single amino acid substitutions primarily (98%) at 1 of 3 mutational hot spots: glycine-12 (G12), glycine-13 (G13), or glutamine-61 (Q61) [Waters and Der, 2018]. These mutations render KRAS persistently GTP-bound and constitutively active, resulting in overstimulation of effector signaling pathways to drive cancer growth.

The majority of KRAS mutations occur at codon 12. A conversion of the amino acid glycine (G) to aspartic acid (D) at this site (KRAS G12D) is the most frequent KRAS mutant in human gastrointestinal cancers and has been identified in approximately 33% to 52% of pancreatic cancers [Biankin et al., 2012; Guo et al., 2020; Hendifar et al., 2020] and 34% to 37% of CRCs [Gong et al., 2017; Price et al., 2020; Prior et al., 2012]. KRAS G12D plays a vital role in the control of tumor metabolism [Vigil et al., 2010].

In addition to G12D, there are 5 other clinically relevant but less frequently identified mutants with amino acid substitutions at the same site (G12V, G12R, G12A, G12S, and G12C) and 1 peptide with a mutation at codon 13 (G13D). After G12D, G12V mutation is the next most frequent mutation in PDAC, identified in about 36% of these tumors, followed by G12R (about 12% of mutations) [Biankin et al., 2012]. The remaining codon 12 mutations (G12A, G12C, and G12S) each account for about 3% to 4% of PDAC-associated codon 12 KRAS mutations [Prior et al. 2012]. G13D is the most frequent codon 13 mutation but is only identified in <1% of PDAC tumors.

Administration of a combination of these peptides provides coverage for multiple potential mutations that might be present.

Circulating tumor deoxyribonucleic acid DNA (ctDNA) is a promising biomarker in the management of many cancers, including breast, colorectal [Bettegowda et al., 2014; Reinert et al., 2019; Tie et al., 2016; Tie et al., 2019], non-small cell lung cancer (NSCLC) [Abbosh et al., 2017], bile duct [Jensen et al., 2020], and pancreatic cancers [Diaz and Bardelli, 2014; Lee, Lipton, et al., 2019].

In the metastatic setting, PDAC subjects with positive MRD, as measured by mKRAS ctDNA, exhibit shorter OS [Perets et al., 2018]. Presence of MRD pre-surgery predicted for poor outcomes. Similarly, measurement of mKRAS ctDNA identifies PDAC subjects who have undergone pancreatectomy but are at high risk of recurrence. For example, persistence of ctDNA immediately following the postoperative period was associated with a high rate of recurrence and shorter median recurrence-free survival (5 months) than those without detectable postoperative ctDNA (15 months) [Groot et al., 2019]. Similar data were obtained by analysis of a prospective cohort in Australasia who underwent surgery and adjuvant gemcitabine-based chemotherapy; ctDNA 4-8 weeks post-surgery was assessed [Lee, Lipton, et al., 2019]. In this study, ctDNA detection post-surgery had 100% positive predictive value at a median follow up of 38.4 months; ctDNA predicted relapse free (hazard ratio [HR]: 5.4; 95% confidence interval [CI]: 1.9-15.2; $p<0.0001$). Likewise, high pre-operative ctDNA levels associated with shorter overall survival (HR: 2.8, 95% CI: 1.8-4.6, $p = 0.001$) and were an independent prognostic factor compared to pathologic features of pancreatic cancer in multivariate analysis of an operable pancreatic cancer patient cohort [Singh et al., 2015].

Multiple studies have also shown the prognostic value of postsurgical serum carbohydrate antigen 19-9 (CA19-9), with failure to normalize correlating with early recurrence. Most patients are assessable for CA19-9, with the exception of 5-10% of the population who lack Lewis blood antigen expression and cannot synthesize the sialylated carbohydrate. For example, in a retrospective analysis of 525 patients, postsurgical elevations in CA19-9 predicted subsequent radiographic relapse [Rieser et al., 2018]. In a Japanese cohort of 119 patients who completed adjuvant chemotherapy, median relapse-free survival (RFS) was significantly shorter in patients with CA19-9 above the upper limit of normal (ULN) versus those with lower levels (10.4 vs 29.6 months, $p<0.001$), median overall survival was also shorter (24.7 vs 92.1 months; $p<0.001$), and CA19-9 was an independent prognostic factor (HR: 2.72) associated with short RFS [Imaoka et al., 2016]. Prospective studies have also found that postoperative CA19-9 predicts overall survival: among 385 RTOG9704 patients, those with a CA19-9 ≥90 U/mL had a 3-year survival of 2%, whereas those with CA19-9 <90 U/mL had a 3-year survival of 32% [Berger et al., 2008]. In Protocol ELI-002-201, pancreatic cancer subjects in the Phase 1 cohort will be enrolled based on high risk ctDNA or serum tumor biomarkers, while subjects in the Phase 2 cohorts, with the DFS endpoint, will be enrolled assuming all patients are at elevated relapse risk, given that 90% of resected PDAC patients experience relapse [Chawla and Ferrone, 2019].

Activating KRAS mutations turn on canonical cancer-related pathways but also contribute to extensive metabolic reprogramming of pancreatic cancer cells. KRAS is mutated in >90% of PDACs and is a well-validated driver of not only initiation but also PDAC growth and maintenance [Eser et al., 2014]. Recently FDA approval of small molecules targeting $KRASG^{12C}$ such as sotorasib [Hong et al., 2020] suggest it may be possible to target cysteine containing KRAS alleles, however G12D and G12V are predominate in pancreatic cancer, and non G12C alleles are also common in colorectal and NSCLC, making it clear that additional immunotherapy strategies are urgently needed.

In a small trial from Norway, Palmer et al. utilized a vaccine containing the same mKRAS peptides present with amphiphile modification in ELI-002 7P. Prolonged survival was observed in one quarter (8 of 32) of the pancreatic cancer subjects who underwent resection surgery and were immunized; this trial also provided evidence that humans can mount T-cell responses

against KRAS peptides and established a dosing schedule that was the basis for the design of the ELI-002-001 trial [Palmer et al., 2020]. Building on this observation of the promise of KRAS-directed immunotherapy, Leidner et al. utilized adoptive transfer of KRAS exon 2 G12D mutant-specific TCR-T cells and observed an objective response in one of two patients [Liedner et al., 2022]. Thus, KRAS directed immunotherapies such as ELI-002 represent a promising strategy to target this lethal cancer.

ELI-002 7P is well suited to pancreatic cancer since it covers common mutations in KRAS that are present in the majority of pancreatic adenocarcinoma cases. A large comprehensive trial of 3,594 pancreatic tumor samples submitted for analysis at Foundation Medicine (Cambridge, MA) has recently been published [Singhi et al., 2019]. In this analysis 3,150 of the 3,594 (88%) tumors harbored an mKRAS allele. Similar high prevalence of mKRAS was evident in the international consortium trial of US, Australian, and Canadian pancreatic tumors where 93% of 142 tumors had exon 2 mutations (Table 4); 46% were G12D, 36% were G12V, and 12% were G12R [Biankin et al., 2012]. The proportion and specific mKRAS alleles identified are consistent across studies, as confirmed by the Cancer Genome Atlas Network, where 93% (140 of 150) tumors harbored mKRAS including 44% that were G12D, 29% that were G12V, and 20% that were G12R [Cancer Genome Atlas Network, 2017]. Likewise, the Johns Hopkin's cohort identified KRAS mutations in 96% (49 of 51 pancreatic tumors), with 42% G12D, 27% G12V, 21% G12R, 6% G13D and 2% G12C [Sausen et al., 2015] and a German trial identified KRAS mutations in 79% (141 of 179 pancreatic tumors); 49% were G12D, 34% G12V, 14% G12R and 2% G12C [Haas et al., 2017].

Therefore, the majority of pancreatic cancer subjects are anticipated to have a KRAS mutation appropriate for ELI-002-201 trial participation. KRAS is a validated oncogene that when mutated is required for PDAC growth and maintenance so that target loss is not anticipated. Enhancing the T-cell immune response to PDAC by utilizing the targeted KRAS ELI-002 product candidate has the potential to improve the outcomes of subjects who have undergone pancreatic resection surgery.

Table 4: KRAS Mutation Spectrum in Pancreatic Cancer

	G12D (%)	**G12V** (%)	**G12R** (%)	**G13D** (%)	**G12C** (%)	**G12A** (%)	**G12S** (%)	**Reference:**
Pancreatic	46	36	12	0	0	0	0	Biankin et al., 2012
Pancreatic	42	27	21	6	2	0	2	Sausen et al., 2015
Pancreatic	49	34	14	nr	2	nr	nr	Haas et al., 2017
Pancreatic	44	29	20	nr	nr	nr	nr	Cancer Genome Atlas Network, 2017
Pancreatic	33	23	11	nr	1	nr	nr	Hendifar et al., 2020
Pancreatic	52	28	12	4	4	0	0	Guo et al., 2020

4.1.2. Colorectal Cancer

4.1.2.1. Introduction

Colorectal cancer (CRC) is the fourth most frequently diagnosed cancer and the second leading cause of cancer death in the US. In 2018, 97,220 new cases of colon cancer and approximately 43,030 cases of rectal cancer have been diagnosed. During the same year, an estimated 50,630 people died of colon and rectal cancers combined [Miller et al., 2019; Siegel et al., 2020].

Non metastatic colon cancer is generally treated with curative intent by colectomy and, in many cases, adjuvant chemotherapy. The prognosis for patients with CRC depends on the stage at diagnosis: the 5-year survival rate is up to 90% for stage I, but only <15% for advanced stages. Over half of the cases are diagnosed at a higher stage of disease (III and IV). Treatment usually involves complete primary tumor resection and appropriate chemotherapy.

4.1.2.2. Adjuvant Therapy in the Case of Localized CRC Disease

Adjuvant therapy confers a survival advantage in patients with stage III or high-risk stage II resected colon cancer. High risk stage II colon cancer are defined as stage T4 tumor, poor differentiation, cancer embolus, lymph node harvested number less than 12 and obstruction or perforation, baseline carcinoembryonic antigen (CEA) >5 ng/L, large vessel invasion, perineural invasion, and extramural vascular invasion [Amri et al., 2016].

For patients with high-risk stage II or stage III colon cancer, adjuvant chemotherapy with fluoropyrimidine and oxaliplatin reduces the risk of recurrence and death by approximately 30%. Oxaliplatin is associated with peripheral neurotoxicity. Consideration of disease stage and pathologic features, microsatellite instability (MSI) status, toxicity profiles, and patient age, comorbidities, aid in decision-making regarding the use of adjuvant therapy.

The National Comprehensive Cancer Network (NCCN) guidelines are based on the IDEA study, published in 2018, an academic collaboration of clinicians and statisticians who were involved in 6 randomized, Phase 3 clinical trials enrolling in 12,834 patients with stage III colon cancer in 12 countries. The 3-year rates of DFS were 74.6% in the 3-month adjuvant therapy group as compared with 75.5% in the 6-month therapy group. The 3-year rates of DFS were 64.4% in high-risk patients: T4 (61.8%), or N2 (61.4%) [Grothey et al., 2018].

Tumor (T) and nodal (N) stage were grouped together to make a pragmatic choice between low-risk (T1–T3,N1) and high-risk (T4 and/or N2). A difference of approximately 20% at 3 years was shown between these cancers.

According to the NCCN Guidelines for patients with low-risk stage III disease (T1–3,N1), the preferred regimen is CAPEOX for 3 months or FOLFOX for 3 to 6 months. For patients with high-risk stage III disease (T4,N1–N2 or any T and N2), the preferred regimen is CAPEOX for 3 to 6 months or FOLFOX for 6 months. Other options include capecitabine (6 months) and 5-fluorouracil (5-FU) for 6 months [Grothey et al., 2018].

After adjuvant cytotoxic therapy, no further treatment is recommended. Circulating tumor DNA is positive in 28.6% defining a subgroup of high-risk Stage II (T4N0) and a 39.4% subgroup of high-risk Stage III (T4, N1 or T Any, N2) patients [Kasi et al., 2020]. Overall, Stage III CRC

patients are at elevated relapse risk, with 30% relapses observed within 5-years of diagnosis [Cardoso et al., 2022].

4.1.2.3. Rectal Cancer

Patients with rectal cancer were specifically excluded from the previously mentioned studies assessing adjuvant chemotherapy in colorectal cancer because of potential toxicity and the confounding impact of radiotherapy.

Although conclusive data on the benefits of adjuvant therapy in patients with stage II/III rectal cancer are lacking, the NCCN panel recommends its use. Choice of regimen depends on initial clinical staging and predicted circumferential resection margin status during excision surgery (such as total mesorectal excision). Pathologic evaluation of the resection margin on the excised rectum has been considered important for determining the risk of local recurrence. A margin of ≤1 mm is considered by some to be a negative prognostic factor for local recurrence [Benson et al., 2018].

FOLFOX or CAPEOX are preferred adjuvant regimens, with 5-FU/leucovorin or capecitabine used in some circumstances, such as when strong neoadjuvant responses to 5-FU or capecitabine were previously obtained during therapy. Neoadjuvant or adjuvant 5-FU or capecitabine-based chemoradiation, or total neoadjuvant therapy are all standard options for rectal cancer [NCCN rectal cancer guidelines V2.2021].

4.1.2.4. Colorectal Liver Metastases

Aside from localized CRC, up to 25% of patients with CRC present with simultaneous metastases and the liver is frequently the only metastatic site.

Approximately 35% to 55% of patients will develop hepatic metastases during the course of their disease. In some cases, colorectal liver metastases (RLM) are resectable, ie, an R0 resection can be performed, leaving at least a 20% to 25% of total liver volume as future liver remnant. Surgical resection represents the only chance of long-term survival [Akgul et al., 2014].

Preoperative factors found to be independent predictors of poor survival are a primary tumor at stage T4, ≥4 liver metastases, the largest liver metastasis ≥5 cm in diameter, and a serum CEA level ≥5 ng/mL. According to these factors, resectable patients could be divided in high-risk patients (3 or more factors) and low-risk patients (less than 3 factors) [Adam, et al., 2012].

The optimal sequencing of systemic therapy and resection in RLM remains unclear. Most studies report on perioperative (neoadjuvant plus postoperative) systemic therapy [Krell et al., 2019], with some series reporting on patients with resectable disease who undergo resection first, followed by postoperative adjuvant chemotherapy.

A 2012 meta-analysis identified 3 randomized clinical trials comparing surgery alone to surgery plus systemic therapy. The analysis showed a benefit of chemotherapy in progression-free survival and DFS but not in OS. Another meta-analysis combined data on 1,896 patients and also found that perioperative chemotherapy improved DFS but not OS [Ciliberto et al., 2012].

In high-risk patients, perioperative combination chemotherapy should be administered. Those who had received neoadjuvant chemotherapy had a better median OS (38.9 months versus 28.4 months) than those who had not received it, and 5 years OS rate of 39% versus 33%

(p=0.028). In low-risk patients, no significant difference in median survival (60.0 m versus 60.0 m) was observed.

4.1.2.5. Frequency of KRAS and NRAS Mutations in CRC

KRAS genotyping is done for every CRC patient because of its impact on the treatment and patients are classified as KRAS wild type (WT) or KRAS mutated.

Since 2008, anti-epidermal growth factor receptor (EGFR) therapy is restricted to KRAS WT patients as it has been shown that KRAS mutated tumors do not respond [Boeckx et al., 2015; Modest et al., 2016].

KRAS mutations occur in approximately 40% of the cases, especially in exon 2, codons 12 (70%-80%) and 13 (15%-20%) (Table 5) [Gong et al., 2017; Price et al., 2020; Prior et al., 2012; Zhang et al., 2015]. In exon 2, mutations are common in codons 12: G12D, G12V, G12C and G12A. Much less frequent KRAS mutations are mainly located in exon 3, codons 59–61, and in exon 4, codons 117 and 146 [Afrasanie et al., 2019].

Since the amino acid sequence surrounding positions 12 and 13 are identical in KRAS and NRAS, T cells generated to these mKRAS epitopes cross-react and are effective in targeting mNRAS at the same amino acids [Chatani and Yang, 2020]. NRAS mutations also occur in CRC in approximately 4% of cases, also in exon 2, codons 12 and 13 [Douillard et al., 2013; Summers et al., 2017; Zhang et al., 2015]. Therefore, ELI-002 7P can additionally target NRAS mutations at positions 12 and 13, and subjects whose tumors harbor these will be eligible to enroll.

Table 5: Colon and Rectal Cancer KRAS and NRAS Mutation Spectrum

	G12D (%)	G12V (%)	G12R (%)	G13D (%)	G12C (%)	G12A (%)	G12S (%)	Reference
KRAS								
Colon	34	12	0	7	0	1.4	5.1	Gong et al., 2017
Colon	41	20	0.7	20	6	3.6	8	Zhang et al., 2015
Colon	35	20	0.9	19	10	6	7	Prior et al., 2012
Colon	37	23.6	Nr	13.3	9.6	10.7	4.4	Price et al., 2020
Rectal	33	23	0.7	17	8	7	6	Prior et al., 2012
NRAS								
Colon	45	14	nr	nr	14	4	nr	Douillard et al., 2013
Colon	25	13	nr	nr	62.5	nr	nr	Summers et al., 2017
Colon	52	4	nr	9	13	nr	nr	Zhang et al., 2015

nr=not reported

The full analysis of the RAS gene exons 2, 3, and 4 revealed that these mutations correlate with certain typical clinical, pathological and molecular features. The mutations of exon 2 and codon 12 are associated with the well/moderately differentiated adenocarcinoma subtype and the mucinous subtype [Dobre et al., 2015].

Limited data is available evaluating the possible prognostic role of mKRAS at the initiation of the treatment. One study showed that patients with KRAS mutation who presented with stage IV had a higher mortality rate (34% versus 18.5%) and reduced OS (23.5 months versus 14 months) compared to patients without this mutation. Also, the presence of the KRAS mutation was found to be an independent risk factor for reduced survival [Heinemann et al., 2009].

4.1.2.6. Importance of ctDNA and CEA Assessment and Follow up in CRC

Different authors reported that the detection of ctDNA in CRC patients with stage I, II, or III after treatment was associated with a shorter survival and disease recurrence. Patients with higher levels of mutant ctDNA and higher mutation loads for the detected mutations in *KRAS* or *BRAF* genes evinced shorter OS. Diehl et al. observed that CRC patients with detectable ctDNA after surgery generally relapsed within 1 year and considered ctDNA as a highly specific biomarker of tumor dynamics. This might indicate that ctDNA levels in plasma after surgery represent a reliable marker of residual disease [Diehl et al., 2008]. Subsequent studies have now confirmed the utility of serial ctDNA sampling for relapse prediction. Reinert et al. observed a 2 to 15 (mean 10) months lead time on detection of metastatic recurrence compared to conventional follow-up [Reinert et al., 2016].

These all support the further development of ctDNA as a biomarker for the detection of early disease and MRD following curative resection, relapse assessment, treatment response, and the development of chemoresistance [Vymetalkova et al., 2018]. Fan et al. systematically reviewed comprehensive data from published studies and showed that a ctDNA-positive status after treatment was associated with a worse prognosis [Fan et al., 2017].

In addition, ctDNA assessment using a personalized ctDNA method for 535 colon cancer patients in a real-world sample have confirmed the association with relapse and allow precise definition of the risk subgroups. High risk stage 2 (T4N0 with MRD rate 28.6%), high risk stage 3 (T4N1-2;TanyN2 with MRD rate 39.4%) and surgically resected oligometastatic patients (MRD rate 49%) have high rates of ctDNA detection indicating their unmet need for effective therapy [Kasi et al., 2020]. In a prospective, multicohort study [Tarazona et al., 2020] with 84 patients where MRD+ status after adjuvant chemotherapy was determined using a personalized ctDNA assay, all MRD+ patients relapsed and the association was strongly statistically correlated (HR 27.9, 95% CI 9.2-85.1 months, $p<0.0001$). Another study in a cohort of 230 patients with Stage II colon cancer further confirmed that a plasma-based ctDNA analysis predicts recurrence [Tie et al., 2016]. Patients who were ctDNA-positive postoperatively were at extremely high risk of radiologic recurrence (HR 18), and ctDNA positivity immediately after completion of chemotherapy was associated with poorer relapse-free survival (RFS; HR 11). Postsurgical ctDNA analysis using a plasma-based ctDNA assay in 100 patients with Stage III colon cancer demonstrated that MRD^+ status was associated with inferior RFS [Tie et al., 2019].

Likewise, the association between elevations in serum CEA with relapse following surgery and adjuvant chemotherapy in colorectal cancer was examined in a large patient series. The CEAwatch study, consisting of 3223 patients with Stage I-III R0 resected CRC in the Netherlands, evaluated recurrence outcomes in patients followed with usual care versus patients with intensified follow-up, including CEA monitoring every 8 weeks, with more frequent monitoring if the CEA value was >2.5 ng/mL or if there was a 20% increase compared with the previous value. The results showed that with the intensified follow-up protocol a significantly

higher proportion of radiographic relapse was detected compared with usual care (odds ratio: 1.8; 95% CI: 1.33-2.50; p=0.0004), indicating earlier detection [Verberne et al., 2015; Verberne et al., 2017]. A Memorial Sloan Kettering review of 728 R0 resected patients showed that individual CEA measurements above a threshold of 15 ng/mL had a low (2%) false positive rate, and no elevations above 35 ng/mL were false positive [Litvak et al., 2014].

4.1.2.7. Colorectal Cancer and Vaccines

Approaches under investigation to further improving therapy are vaccinations with peptides alone, peptide-expressing viruses, peptide-loaded APCs or application of peptide-specific T cells.

In the process of cancer development mutations resulting in neoantigens can emerge in every coding region of the DNA. Neoantigens caused by KRAS are one example for point mutations in CRC. Early approaches could prove that peptides derived from mKRAS can stimulate cytotoxic T-lymphocytes in vitro [Gedde-Dahl et al., 1994] as well as in CRC [Shono et al., 2003]. A subsequent study also investigated the cytotoxic activity of mKRAS peptide-induced cytotoxic T lymphocytes [Khleif et al., 1999]. Only 2 of 10 CRC patients showed induction of peptide-specific $CD8^+$ but in addition, these cytotoxic T cells were able to lyse HLA-A2-positive target cells incubated with the 10-mer mutant peptide. Similar results were obtained in a xenograft study, where peptide-specific T cells were able to delay the growth of KRAS-mutant pancreatic tumors [Wang, et al., 2016].

In vaccination trials with peptides derived from mKRAS, there were early indications of potential clinical benefits for patients. Two of 7 CRC patients had an immune response to a mKRAS peptide vaccine, and vaccination correlated to DFS [Toubaji et al., 2008]; the treatment was well tolerated with no serious systemic effects and Grade 1 to 2 reactogenicity. In a case report, 1 CRC patient was treated with activated T cells recognizing G12D KRAS [Tran et al., 2016]. After a single infusion, all 7 lung metastases regressed until 1 metastatic lesion progressed at 9 months. This patient underwent surgical resection for the single relapsed site and has now been in ongoing remission for >4 years [Chatani and Yang, 2020].

To further enhance the immunological response in CRC patients, Rahma et al. combined the peptide vaccination of mKRAS with IL-2 or granulocyte-macrophage colony-stimulating factor (GM-CSF) [Rahma et al., 2014]. The strongest immune response could be detected in the group with GM-CSF as adjuvant; all CRC patients had an increase in interferon gamma (IFNγ) producing, specifically activated T cells. Despite the high immune response rate, none of these advanced metastatic patients showed clinical response and disease progressed in all cases.

4.2. Brief Summary of Nonclinical Pharmacology

A subset of nonclinical studies evaluated ELI-002a, an investigational product consisting of 8 components: 7 lipid-conjugated KRAS peptide-based antigens (Amph-Peptides, Table 3) and a lipid-conjugated immunostimulatory oligonucleotide adjuvant (Amph-CpG-7909, Figure 1). Nonclinical studies with ELI-002a or components of ELI-002a have been performed to support the clinical investigation of the multivalent product.

The objective of the nonclinical pharmacology program for ELI-002 7P was to demonstrate, in a C57BL/6 mouse model, the improved potency of the amphiphile-conjugated subunits (both

antigens and adjuvant) in eliciting cellular immune responses to KRAS peptides. The C57BL/6 model was selected because there is no readily available immunocompetent animal model of cancer related to KRAS mutations and because the primary objective of these studies was to justify the components of the vaccine by demonstrating differential immunogenic responses between amphiphile-conjugated and nonconjugated vaccines. The CpG-1826 adjuvant was used in place of the clinical ELI-002 CpG-7909 adjuvant in most mouse pharmacology studies because it is more potent to agonize mouse Toll-like-receptor 9 (TLR-9). The nonclinical pharmacology program for ELI-002 7P is outlined in Table 6.

Table 6: Nonclinical Pharmacology studies of mKRAS Vaccine in Support of ELI-002 (Model = Female C57BL/6 Mice, 5, 10 or 15/group)

Study Title	Groups and Test Article Test Article Manufacturing Site/Batch #	Doses/Dose Volume	ROA/Treatment Regimen
KRAS Imgen #4	7 groups: sKRAS-WT + CPG sKRAS G12D + Amph-CpG; sKRAS G13D + Amph-CpG; Amph-KRAS G12D + Amph-CpG; Amph-KRAS G13D + Amph-CpG; KRAS G12D + pIC; No Treatment (PBS)	KRAS peptide (Amphiphilic or soluble): 20 µg[1]; CpG-1826 (Amphiphilic or soluble) at 5 nmol and pIC at 50 µg. Dose volume: 100 µL administered divided as a SC injection on either side of the tail head (50 µL per injection site)	ROA: SC Prime: Day 0 Boost: Day 14
KRAS Imgen #7	12 groups: sKRAS-WT + CPG sKRAS G12D + CpG-1826; sKRAS G12A + CpG-1826; sKRAS G12R + CpG-1826; sKRAS G12V + CpG-1826 sKRAS G12R + pIC; sKRAS G12V + pIC; Amph-KRAS G12D + Amph-CpG-1826; Amph-KRAS G12A + Amph-CpG-1826; Amph-KRAS G12R + Amph-CpG-1826; Amph-KRAS G12V + Amph-CpG-1826; No Treatment (PBS)	KRAS peptide (Amphiphilic or soluble): 20 µg[1]; CpG-1826 (Amphiphilic or soluble) at 5 nmol and pIC at 50 µg. Dose volume: 100 µL administered divided as a SC injection on either side of the tail head (50 µL per injection site)	ROA: SC Prime: Day 0 Boost: Day 14

Study Title	**Groups and Test Article** **Test Article Manufacturing Site/Batch #**	**Doses/Dose Volume**	**ROA/Treatment Regimen**
KRAS Imgen #8	6 groups: sKRAS WT + CpG-1826 sKRAS G12D + CpG-1826 sKRAS G12R/V + CpG-1826 Amph-KRAS G12D + Amph-CpG-1826 Amph-KRAS G12R/V + Amph-CpG-1826 No Treatment (PBS)	KRAS peptide (Amphiphilic or soluble): 20 µg[1]; CpG-1826 (Amphiphilic or soluble) at 5 nmol. Dose volume: 100 µL administered divided as a SC injection on either side of the tail head (50 µL per injection site)	ROA: SC Prime: Day 0 Boost: Day 14, Day 23
KRAS Imgen #9	7 groups: sKRAS WT + CpG-1826 (bw) sKRAS WT + CpG-1826 (w) sKRAS G12D + CpG-1826 (bw); sKRAS G12D + CpG-1826 (w); Amph-KRAS G12D + Amph-CpG-1826 (bw); Amph-KRAS G12D + Amph-CpG-1826 (w); No Treatment (PBS)	KRAS peptide (Amphiphilic or soluble): 50 µg[1]; CpG-1826 (Amphiphilic or soluble) at 5 nmol. Dose volume: 100 µL administered divided as a SC injection on either side of the tail head (50 µL per injection site)	ROA: SC Prime: Day 0 (w and bw) Boost: Day 7 (w) Boost: Day 14 (w and bw)
KRAS Imgen #12	7 groups: sKRAS G12D + sol CpG-1826 sKRAS G12D + Amph-CpG-1826 sKRAS G12D + pIC Amph-KRAS G12D + Amph-CpG-1826 sKRAS WT + sCpG-1826 Amph-CpG-1826 (No antigen) No Treatment (PBS)	KRAS peptide (Amphiphilic): 18.75 µg[1] (50 µg based on total construct mass); KRAS peptide (soluble): 50 µg[1]; CpG-1826 (Amphiphilic or soluble) at 5 nmol; pIC 50 µg. Dose volume: 100 µL administered divided as a SC injection on either side of the tail head (50 µL per injection site)	ROA: SC Prime: Day 0 Boost: Day 14, Day 27, Day 41, Day 55, and Day 66

Study Title	**Groups and Test Article** **Test Article Manufacturing Site/Batch #**	**Doses/Dose Volume**	**ROA/Treatment Regimen**
KRAS Imgen #14	7 groups: sKRAS G12D + sol CpG-1826 sKRAS G12D + Amph-CpG-1826 sKRAS G12D + pIC Amph-KRAS G12D + Amph-CpG-1826 sKRAS WT + sol CpG-1826 Amph-CpG-1826 PBS (No treatment control group)	KRAS peptide (Amphiphilic): 7.5 µg[1] (20 µg based on total construct mass); KRAS peptide (soluble): 20 µg[1]; CpG-1826 (Amphiphilic or soluble) at 5 nmol and pIC at 50 µg. Dose volume: 100 µL administered divided as a SC injection on either side of the tail head (50 µL per injection site)	ROA: SC Prime: Day 0 Boost: Day 14, Day 28, Day 42
KRAS Imgen #14.2	5 groups: Vehicle (5% EtOH, 3.3 mM HCl) Adjuvant (Amph-CpG-7909) alone Amph-KRAS mutant pool (7 peptides) + 0.6 nmol Amph-CpG-7909 Amph-KRAS mutant pool (7 peptides) + 3 nmol Amph-CpG-7909 Amph-KRAS mutant pool (7 peptides) + 15 nmol Amph-CpG-7909	KRAS peptide pool: 30 µg/dose of Amph-KRAS G12D; 3 µg/dose of all others: Amph-KRAS G12A, Amph-KRAS G12C, Amph-KRAS G12S, Amph-KRAS G12R, Amph-KRAS G12V, Amph-KRAS G13D for a total of 48µg of Amph-Peptide per dose Amph-CpG-7909 alone at 15 nmol (125 µg/100 µL) Amph-CpG-7909 in combination with Amph-KRAS peptide pool at 0.6, 3 and 15 nmol (5, 25 and 125 µg/100 µL) Dose volume: 100 µL administered divided as a SC injection on either side of the tail head (50 µL per injection site)	ROA: SC Prime: Day 0 Boost: Days 10, 17, 24, and 39
KRAS Imgen #15	9 groups: Untreated Amph-KRAS G12D + 0.1nmol Amph-CpG-1826 Amph-KRAS G12D + 1nmol Amph-CpG-1826 Amph-KRAS G12D + 5nmol Amph-CpG-1826 Amph-KRAS G12D + 5nmol sCpG-1826 sKRAS G12D + 0.1nmol Amph-CpG-1826 sKRAS G12D + 1nmol Amph-CpG-1826 sKRAS G12D + 5nmol Amph-CpG-1826 sKRAS G12D + 5nmol sCpG-1826	KRAS peptides (Amphiphilic): 7.5 µg[1] (20 µg based on total construct mass); KRAS peptides (soluble):20 µg[1]; Amph-CpG-1826 was dosed at 0.1, 1 and 5 nmol and soluble CpG-1826 was dosed at 5 nmol Dose volume: 100 µL administered divided as a SC injection on either side of the tail head (50 µL per injection site)	ROA: SC Prime: Day 0 Boost: Day 14, Day 28, Day 74

Study Title	Groups and Test Article Test Article Manufacturing Site/Batch #	Doses/Dose Volume	ROA/Treatment Regimen
KRAS Imgen #26	PBS (vehicle) Amph-KRAS G12D (fresh preparation) + 5 nmol Amph-CpG-1826 Amph-KRAS G12D (aged preparation) + 5 nmol Amph-CpG-1826	Amphiphilic KRAS peptides (fresh or aged) were dosed at 30 µg based on total construct mass; Amph-CpG-1826 was dosed at 5 nmol Dose volume: 100 µL administered divided as a SC injection on either side of the tail head (50 µL per injection site)	ROA: SC Prime: Day 0 Boost: Day 13, Day 27
BLAST P Report	In silico BLAST search for Amph-Peptide sequences	N/A	N/A

KRAS= Kirsten rat sarcoma; mKRAS = mutant Kirsten rat sarcoma; PBS = phosphate-buffered saline, pIC = polyinosinic:polycytidylic acid; ROA = route of administration; SC = subcutaneous; w = weekly; bw = biweekly; Amph-G#X = Amph-KRAS G#X, eg, Amph-G12D = Amph-KRAS G12D
[1]Based on peptide mass alone.

These nonclinical pharmacology studies demonstrate that despite the historically poor immunologic responses of mice to mKRAS peptides, they consistently mounted potent immune responses to the amphiphile conjugated vaccine that were superior to control soluble vaccines lacking the amphiphile modification.

- The weight of evidence of in vivo data indicates that immunization with amph-mKRAS peptides and amph-CpG1826 or soluble mKRAS and Amph-CpG-1826 stimulated a stronger memory immune response, as indicated by cytokine release, to the corresponding short and long peptides than did immunization with soluble mKRAS and soluble CpG-1826 or soluble mKRAS + pIC. (KRAS Imgen #7; KRAS Imgen #12, KRAS Imgen #8, KRAS Imgen #9).
- The immunologic response was characterized by a strong Th1 response and cytolytic function against KRAS-specific targets, both in vitro and in vivo. Very low amounts of Th2 cytokines like IL4 and IL10 were generated in vitro (KRAS Imgen #12, KRAS Imgen #14).
- The most robust responses were generated when both peptide and adjuvant were amph-conjugated (KRAS Imgen #4).
- Restimulation with short peptides elicited a weaker response than restimulation with long peptides (KRAS Imgen #14, KRAS Imgen #7, KRAS Imgen #8).
- Restimulation with long wide type (WT) peptide did elicit responses in cells from animals vaccinated with mutant peptide but responses were lower than those induced by the corresponding mutant peptide (Imgen #4, Imgen #14). During toxicity evaluation WT Ras tissues were unaffected, suggesting that low level responses to WT peptide may not present a safety concern.
- Increasing the frequency of dosing did not affect the immune response towards long peptide stimulation. However, it did seem to improve responses to short-peptide stimulation (KRAS Imgen #9).
- Amphiphilic CpG-7909 (Amph-CpG-7909) dose-dependently increased the immune response to KRAS antigen. No significant immune response was detected at the lowest concentration of CpG; however, medium and high concentrations generated robust immune responses (KRAS Imgen #14.2).
- The minimum adjuvant (aCpG) dose needed to achieve a robust immune response was 5 nmol (KRAS Imgen #15, KRAS Imgen #14.2).
- The minimum effective dose (MED) identified for immunogenicity of ELI-002 in mice, based on available data, was 48 µg total peptide (30 µg 12D and 3 µg/peptide of the other 6 peptides; 5 nmol or 25 µg aCpG7909) (KRAS Imgen #14.2).
- There was no effect of the vehicle formulation change on immunogenicity (KRAS Imgen #14.2).
- There was no effect of the formation of the Amph-TM-G12D thiomorpholinone isomer on immunogenicity of Amph-G12D (KRAS Imgen #26).

- Despite the lower dosage of Amph-KRAS peptide used when based on peptide mass alone, the T-cell responses in mice treated with the Amph-KRAS peptide vaccines surpassed the responses of mice treated with soluble equivalents (KRAS Imgen #12, KRAS Imgen #14, KRAS Imgen #15).
- BLAST searches using either the wild type or mutant sequence demonstrated identity with sequences in over 300 human proteins, and particularly those that are other products of human RAS genes [BLAST Results Summary], however there has been no evidence of autoimmune phenomena described in other KRAS vaccine trials using the same peptide sequences. There was no non-RAS potential cross-reactivity identified by BLAST-P alignment.

Since antitumor activity of mKRAS specific T cells can lead to durable clinical response [Tran et al., 2016; Chatani and Yang, 2020, Liedner et al., 2022], the ELI-002 in vivo pharmacology observations demonstrating increased antigenicity and potent CD4 and CD8 T cell responses suggest potential for antitumor activity and clinical benefit. T cell therapeutics such as CD19 chimeric antigen receptor (CAR) T cells [Park et al., 2018] show enhanced remission duration and OS when administered to patients who have microscopic nests of tumors cells (MRD) compared to those with bulky disease. Therefore, ELI-002 7P will be evaluated in MRD^+ $mKRAS^+$ solid tumors in order to maximize the ratio of elicited T cells to target tumor cells.

4.3. Brief Summary of Pharmacokinetics and Toxicokinetics

Pharmacokinetics/toxicokinetics (PK/TK) are not assessed for vaccinations since systemic exposure is not observed. Therefore, PK/TK will not be assessed in the nonclinical development program for ELI-002 7P.

4.4. Brief Summary of Toxicology

ELI-002a (an investigational version of ELI-002) was used in nonclinical toxicology testing. ELI-002a consists of all 7 Amph modified KRAS peptides (Amph-Peptides, Table 3) and the lipid-conjugated immunostimulatory oligonucleotide adjuvant (Amph-CpG-7909, Figure 1). Nonclinical studies with ELI-002a or components of ELI-002a have been performed to support the clinical investigation of the multivalent product.

4.4.1. Repeat-Dose Toxicity Studies

4.4.1.1. Study No. 2795-001: Amph-CpG-7909 (with and without Amph-Peptide-G12D): A 4-Week Subcutaneous Injection Tolerability Study in Male C57BL/6 Mice

Subcutaneous administration of the adjuvant (Amph-CpG-7909) with and without peptide (Amph-G12D) to male C57BL/6 mice once weekly for 4 weeks was well tolerated. Moderate to severe erythema noted at 200/80 µg adjuvant/peptide (0.2 mL total dose volume) was deemed to be adverse.

Based on the available data, Amph-CpG-7909 alone was tolerable up to 100 µg (0.2 or 0.4 mL total dose volume) and Amph-CpG-7909 + Amph-Peptide was tolerable at 100/80 µg adjuvant/peptide (0.2 or 0.4 mL total dose volume) as well as 200/80 µg adjuvant/peptide at a

higher dose volume (0.4 mL total dose volume). Based on these data, the high dose of adjuvant was set at 125 µg in a total injection volume of 300 µL.

4.4.1.2. Study 2795-002: A GLP 3-Month Study of ELI-002 by Subcutaneous Injection in C57BL/6 Mice with a 5-Week Recovery Period

Two control groups (a phosphate-buffered saline control and an adjuvant only control) were included. Groups of mice (15-20/sex/group) were dosed on Days 1, 8, 15, 22, 29, 36 and 64 and euthanized on Days 8, 43, 71, and 99. Three dose levels were employed, with the same dose of Amph-Peptide (48 µg of the aggregate of 7 peptides) at each dose level; only the adjuvant dose varied.

The administration of 48 µg Amph-Peptides with either 5 µg or 25 µg Adjuvant was well tolerated with a dose-dependent reduced (relative to the high dose) incidence and severity of local irritation and limited associated effects. However, high dose adjuvant (125 µg Adjuvant alone and 48 µg Amph-Peptides/125 µg Adjuvant) was not well tolerated, with 3 of 90 animals in each group (with and without peptide) animals euthanized in extremis as a result of increased severity of clinical observations around the injection site. There were also positive dermal scores; clinical pathology and organ weight including increased lymph node size, effects indicative of an immune/inflammatory response; and histopathology consisting of injection site ulceration, inflammation and osseous proliferation, as well as the spread of extensive abdominal/peritoneal and regional inflammation. These effects were all considered subsequent to exacerbated local toxicity at the injection site and were considered adverse. Therefore, the no-observed-adverse-effect level (NOAEL) was 48 µg Amph-Peptides/25 µg Adjuvant.

The mouse toxicology data indicate that the adjuvant, rather than the peptide, was primarily responsible for the observed toxicity in these studies. During toxicity evaluation WT RAS tissues were unaffected, suggesting that low level responses to WT peptide may not present a safety concern. The dose multiples from the highest dose of adjuvant that was well tolerated in mice (25 µg) to the proposed adjuvant doses in humans of 0.1, 0.5, and 2.5 mg are 599x, 120x, and 24x, respectively (based on body surface area). As a large molecule expected to undergo intracellular rather than hepatic or renal clearance, a fixed dose of ELI-002 will be administered in this study.

4.5. Safety Pharmacology

Safety pharmacology studies were not conducted since soluble mKRAS peptides identical in amino acid sequence to those in ELI-002 7P have been well tolerated when previously evaluated in clinical studies in cancer subjects [Gjertsen et al., 2001; Wedén et al., 2011; Abou-Alfa et al., 2011; Rahma et al., 2014; Toubaji et al., 2008; Palmer et al., 2020] and Amph-mKRAS peptides are not expected to have any effects on core physiological systems that are different from those of soluble mKRAS peptides.

Similarly, soluble CpG-7909 has been previously evaluated and found to be well tolerated in clinical studies in normal volunteers and cancer subjects [Cooper et al., 2004; Krieg et al., 2004] with an MTD observed in one oncology study of myalgia and constitutional effects [Zent et al., 2012] and Amph-CpG-7909 is not expected to have any effects on core physiologic systems that are different from those of soluble CpG-7909. Interim results from the dose escalation of Amph-

CpG-7909 in the related product ELI-002 2P demonstrated no dose limiting toxicity at the RP2D of 10.0 mg [O'Reilly et al., 2023].

4.6. ELI-002 7P: An Investigational Treatment for KRAS/NRAS Mutated Solid Tumors

4.6.1. Mechanism of Action

Therapeutic vaccines for cancer commonly seek to stimulate the expansion of cytotoxic T cells specific to antigens from malignant cells. Following activation, these antigen-specific cells infiltrate tumor sites, recognize tumor cells expressing antigen through major histocompatibility complex (MHC) presentation, and execute cytotoxic effector functions to kill target cells. ELI-002 7P employs this general paradigm to target mKRAS and mNRAS-driven malignancies expressing mutant forms of KRAS/NRAS. The sequence of amino acids is identical between KRAS and NRAS surrounding positions 12 and 13, and the National Cancer Institute has demonstrated that RAS-specific T cells cross recognize both mKRAS and NRAS tumors [Chatani and Yang, 2020]. Upon SC injection, the components of the vaccine are drained from the peripheral tissues into the lymph nodes. KRAS/NRAS Amph-Peptides are then taken up by antigen-presenting immune cells for processing through the proteasomal pathway. Peptide fragments produced through proteasomal degradation are loaded onto MHC molecules and presented on the cell surface for recognition by T lymphocytes through T-cell receptor interactions. In parallel, Amph-CpG-7909 is taken up by lymph node resident immune cells for endocytic processing. Immune cells expressing TLR-9 are activated by CpG, a process which leads to expression and secretion of pro-inflammatory factors supportive of adaptive immunity including T lymphocyte activation. Within this pro-inflammatory context, T-cells capable of specific recognition of antigen engage with APCs and are clonally expanded, activated, and licensed for killing of antigen-bearing target cells [Yang et al., 2016a; Yang et al., 2016b; Yang et al., 2017].

4.6.2. Amphiphile Lymph Node Delivery Background

Subunit vaccines are an attractive strategy for eliciting therapeutic immunity given the ease, speed, and low cost of manufacturing for small molecules and biopolymers such as peptides and oligonucleotides [Liu et al., 2014]. However, subunit vaccines consisting of linear peptides and molecular adjuvants often elicit only minimal immunological responses in animals and humans. Previous studies have demonstrated that poor lymphatic drainage, and thus inefficient delivery to immune cells, is a significant factor leading to the observed lack of potency for these vaccination strategies.

Empirical studies have established 2 competing mechanisms for solute drainage from peripheral tissues: (1) passage through the endothelial basement membranes into systemic blood circulation and (2) drainage from the tissue into lymphatic vessels and circulation through the lymph system. The predominant pathway taken for any individual molecule following SC injection is determined by molecular size. Specifically, solutes <3 nm in size easily pass through the endothelial basement membranes and are rapidly cleared from the tissues into the blood before elimination in the kidneys and liver. Importantly, molecules of this size are not delivered to draining lymph nodes. Conversely, for solutes >3 nm in size, passage into blood vessels is

inefficient, and molecules >5 nm in size are excluded completely via physiological barriers from clearance into the blood. Rather molecules of this size are drained through convective transport through the tissues into lymphatic vessels and perfuse the lymph nodes prior to re-entry into the blood via the thoracic duct through the subclavian vein. Thus, the minimal potency observed for subunit vaccines can be attributed, in substantial part, to their lack of delivery into the lymph nodes based on their size of <3 nm. Consequently, improved delivery of these subunit vaccine components to lymph nodes holds promise for greatly enhancing overall immunological responses and therapeutic efficacy.

Correlative to the established size-dependent biodistribution paradigm, clinical studies have demonstrated that compounds <3 nm in size which bind avidly to albumin after injection are effectively concentrated in draining lymph nodes rather than being cleared through the systemic circulation. Further, these albumin-binding compounds efficiently accumulate in antigen-presenting immune cells once delivered into the draining lymph nodes. The basis for this paradoxical observation is the innate biodistribution pattern of endogenous albumin. Albumin, a 66.5 kDa protein, is present at high concentrations throughout the body, and is exclusively drained from the peripheral tissues into the lymphatics due to its high molecular weight. Therefore, compounds which otherwise would be cleared into the blood due to their small molecular size take on the biodistribution properties of albumin by binding to the larger molecule.

Vaccine responses have been boosted by the use of altered peptide ligands that enhance T-cell responses against tumor antigens. Moynihan et al. found that vaccines that were modified with albumin-binding domains helped to transport these molecules throughout the lymphatic system and increased T-cell response [Moynihan et al., 2018]. Liu et al. reported this lymph-node targeting as “albumin hitchhiking.” In mice, structurally optimized CpG-DNA/peptide-amph-vaccines increased lymph node accumulation and resulted in a 30-fold increase in T-cell priming and enhanced anti-tumor efficacy with reduced systemic toxicity [Liu et al., 2014].

Building on these observations, the amphiphile approach seeks to improve vaccine potency by targeting conventional vaccine components for specific delivery to the lymph nodes through simple chemical modifications which impart affinity for albumin. Specifically, peptide antigens or molecular adjuvants are chemically conjugated to fatty-acid moieties which take advantage of the natural function of albumin as a fatty-acid transporter. Antigens and adjuvants modified in this way reversibly and persistently associate with albumin at the injection site and are carried by albumin into lymph nodes where they efficiently engage immune cells to promote the expansion of antigen-specific immunity.

4.6.3. Known and Potential Risks and Benefits

Elicio will evaluate safety and tolerability of ELI-002 as adjuvant therapy for subjects with KRAS/NRAS mutated PDAC and other solid tumors who have MRD to determine whether the potential for clinical benefit is sufficient to warrant further testing while minimizing risk. ELI-002 7P is an investigational therapy, therefore, not all aspects pertaining to potential risks and benefit from it are completely known at this time. However, there is an extensive body of preclinical studies as well as human studies conducted by other institutions on soluble versions of the peptide and CpG components used in ELI-002 7P which are reassuring.

In addition, there are considerable data available on the risks and benefits from cancer vaccines as a class of therapy. The technologies for cancer vaccination have been extensively reviewed by Kudrin [Kudrin, 2012]. In brief, therapeutic cancer vaccines can be available off-the-shelf (recombinant antigen cocktails, recombinant microorganisms, whole tumor cell derived (allogeneic), oncolytic viruses, anti-idiotypic antibodies, DNA and gene-therapy based products) which could be manufactured and distributed worldwide and personalized cancer vaccines (autologous cells and antigens, adoptive cell transfer) which are heavily dependent on specialized centers of expertise and manufacturing. With extensive prior efforts and trials, one cancer vaccine: Dendreon's PROVENGE® (sipuleucel-T), a dendritic cell for metastatic castration-resistant prostate cancer, was approved by the Food and Drug Administration (FDA) in 2010 which has established the clinical application of cancer vaccines.

These cancer vaccines were generally well tolerated and most infusion-related side effects lasted 1 or 2 days. These are the potential risks which have been associated with PROVENGE cancer vaccine: acute infusion reaction, chills, fever, and fatigue back pain, joint ache, fatigue, nausea, headache and fever [PROVENGE® USPI].

As reported by Wedén et al., no signs of toxicity were reported and no serious adverse events (SAEs) attributable to the vaccine treatment were observed in any of the subjects following soluble mKRAS peptide vaccination, including long-term survivors who received up to 30 injections each [Wedén et al., 2011].

Likewise, 5 subjects with advanced pancreatic cancer were treated with synthetic RAS peptides used as a cancer vaccine. All subjects were vaccinated at Day 0, and booster vaccinations were performed similarly on Days 7-10 and at 1 month. Further booster vaccinations were performed at 4-6–week intervals or as long as the subject's immunological response and overall performance status permitted over a period of 2 to10 months. The treatment was well tolerated and could be repeated multiple times in the same subject. No sign of toxicity and no adverse events (AEs) were observed [Gjertsen et al., 1996].

ELI-002 7P is expected to elicit common side effects often associated with vaccines such as local skin reaction, fever, fatigue, pain, among others which generally subside within a day or two. Reactogenicity refers to a subset of reactions that occur soon after vaccination and are a physical manifestation of the inflammatory response to vaccination. In clinical trials, information on expected signs and symptoms after vaccination is actively sought (or 'solicited'). These symptoms may include pain, redness, swelling or induration for injected vaccines, and systemic symptoms, such as fever, myalgia, headache, or rash. The broader term "safety" profile refers to all AEs that could potentially be caused/triggered or worsened at any time after vaccination, and includes AEs, such as anaphylactic reactions, diseases diagnosed after vaccination and autoimmune events.

The administration of 48 µg Peptide with either 5 or 25 µg Adjuvant was well tolerated in the rodent Study No. 2795-002 with a dose-dependent reduced incidence and severity of local irritation and limited associated effects. Therefore, the NOAEL was 48 µg Amph-Peptides/25 µg Adjuvant. Local reactions were considered adverse at the high adjuvant Amph-CpG-7909 dose in the GLP toxicity study which confirms the importance of reactogenicity monitoring. Local reactions and some flu-like symptoms are expected in subjects who receive peptide injections, and there is always a possibility of hypersensitivity reactions. Injection site reaction is the only

AE known to be attributed to ELI-002. Reactogenicity monitoring will occur throughout the ELI-002-201 trial (see Section 12.2.1.3).

It is expected that ELI-002 7P based upon its demonstrated mechanism of action, will likely evoke immunological response leading to clinical benefit among protocol subjects.

4.6.4. Trial Rationale

KRAS is mutated in one quarter of human solid tumors, including the vast majority of pancreatic cancers, and substantial portions of colorectal, non-small cell lung, and other solid tumors. KRAS is a validated oncogene that when mutated drives tumor growth and maintenance. Enhancing the T-cell immune response to tumors by utilizing the targeted KRAS ELI-002 7P product candidate has the potential to improve the outcomes of subjects who have undergone resection surgery and/or who have MRD following locoregional therapy, a clinical setting with the highest ratio of ELI-002 7P induced T cells to target tumor cells. For example, the pancreatic population selected for this trial is comprised of subjects who have already received chemotherapy/ chemoradiation (in the neoadjuvant and/or adjuvant setting) as well as pancreatectomy with an R0 (no residual tumor cells observed) or R1 (microscopic residual tumor cells observed) outcome, yet 90% relapse despite locoregional treatment [Chawla and Ferrone, 2019]. The subset of this population with persistent ctDNA post-surgery have a particularly poor prognosis with an expected median RFS of only 5 months [Groot et al., 2019]. The selection of cancer patients after completion of locoregional treatment has several potential advantages:

- Maximization of the effector T-cell:target tumor cell ratio by minimization of tumor burden by successful prior therapy
- Maximization of T-cell trafficking potential because the fibrous stromal present in advanced tumors that can exclude T-cells has not yet formed
- Clinical settings where cytotoxic chemotherapy is not utilized, preserving the full potential of induced T-cells to persist and traffic

Rationale for a single, 2-phase trial design: ELI-002-201 is a single trial with 2 segments, Phase 1 and Phase 2.

The Phase 1 portion of the study includes a safety evaluation of the RP2D Amph-CpG-7909, established in protocol ELI-002-001, under IND 26909, when admixed with two Amph-Peptides 7P doses, 4.9 mg and 1.4 mg (Phase 1A). Phase 1A is planned to enroll approximately 12 subjects, 6 subjects at each Amph-Peptide 7P dose (designated Cohort 1) with mutant KRAS (mKRAS)/mutant NRAS (mNRAS) solid tumors (PDAC, CRC, and NSCLC). Following IDMC review of the Phase 1A safety data, if the IDMC recommends on a dose level to proceed to Phase 2, Phase 1A enrollment of PDAC subjects may continue at this dose level until Phase 2 is opened to enrollment. Phase 1B (Cohort 2, CRC) may be opened to enrollment by Elicio either concurrent or subsequent to Phase 2. If Cohort 2 is opened this will be documented in a study memo sent to all clinical sites and maybe submitted to IRBs, per IRB guidance.

If 2 or more of the 6 subjects in Phase 1A (Cohort 1) at either of the Amph-Peptides 7P dose levels experience a dose-limiting toxicity (DLT; see definition in Section 6.7.3) in the first 28 days following ELI-002 7P administration (ie, the DLT observation period), then, prior to opening Phase 1B/Phase 2 to enrollment, the independent data monitoring committee (IDMC) in

partnership with the Sponsor, will review the data and may recommend a change in the ELI-002 7P dose (ie RP2D−1 of Amph-CpG-7909 or an updated dose level of Amph-Peptides 7P), and if so, an additional 6 subjects will be enrolled in Phase 1A at the changed dose level. An additional 6 subjects at the RP2D−1 may also be added if further characterization of the Phase 2 dose is required. Following IDMC review of the Phase 1A safety data, if the IDMC recommends on a dose level to proceed to Phase 2, Phase 1A enrollment of PDAC subjects may continue at this dose level until Phase 2 is opened to enrollment.

The Phase 2 portion of the study (Cohorts 3A, 3B and 3C) will proceed contingent on the observation of antitumor activity with ELI-002 during the clinical development program. In Phase 2, approximately 135 subjects with PDAC will be randomized 2:1 to ELI-002 7P or SOC (observation), respectively. Subjects randomized to ELI-002 7P will receive SC injections of ELI-002 7P during the Immunization Period and the Booster Period. Subjects randomized to SOC (observation) will be able to cross over to ELI-002 7P treatment following confirmed disease progression.

Randomization in Phase 2 will be stratified according to the following:

- Nodal status: node negative versus node positive (0 versus 1)

Subject replacement: In Phase 1A, if any of the first 12 subjects discontinue for any reason other than toxicity prior to completing 28 days of ELI-002 7P therapy, a replacement subject will be added to the cohort until 12 subjects (6 per Amph-Peptide 7P dose, depending on whether the 1.4 mg dose is evaluated) complete 28 days of ELI-002 7P therapy. In Phase 2, once a subject is randomized, they will not be replaced for any reason.

4.6.5. Rationale for Endpoints

The safety and tolerability endpoints to characterize the incidence of AEs and clinically significant changes in laboratory tests and vital signs are standard endpoints that are used in many trials of immune-therapy agents including with CAR T cells that exhibit similar mechanism of action to ELI-002 7P. For example, CD19 CAR T cells were initially evaluated with the standard 3+3 design [Lee et al., 2015] as were BCMA CAR T cells [Raje, 2019]. Important immune related adverse events (irAEs) may occur late with immune-oncology products. For example, the median time to onset of irAEs when the checkpoint inhibitor nivolumab was administered in 576 subjects with advanced metastatic melanoma was 5.0 weeks for skin toxicities and 15.0 weeks for renal toxicities [Weber et al., 2017].

The MRD response to treatment with ELI-002 7P can be assessed through clearance or reduction of ctDNA. Emerging data using the ctDNA assay have shown a high median lead time for ctDNA changes relative to radiographic relapse and very high positive predictive value in colorectal and NSCLC [Abbosh et al., 2017; Reinert et al., 2019] resulting in FDA Breakthrough Device Designations in 2019 and 2021. In the event that ctDNA is not detectable, serum tumor biomarkers (such as CA19-9 and CEA) may be used to assess the MRD response to treatment (see Section 5.2).

The median DFS and median OS will provide preliminary data that may show a trend for a dose response in an outcome measure suitable to support the design of pivotal trials in the adjuvant setting. For example, DFS has been used as the primary endpoint supporting the approval of adjuvant breast cancer hormonal therapy, adjuvant chemotherapy for CRC, and adjuvant

chemotherapy for breast cancer [Guidance for Industry, Clinical Trial Endpoints, 2018], and OS may be suitable in populations where there is a short interval between progression and death.

Efficacy biomarkers CEA and CA19-9 will also be characterized where appropriate. In addition, exploratory objectives are included to document that ELI-002 induces the intended immune responses. T cell responses in PBMCs will be assessed by immune assays such as IFNγ, Fluorospot, intracellular cytokine staining (ICS), and/or dextramers. Tumor biopsy assessments may include gene expression and/or immunofluorescence to examine immune cell infiltration and tumor microenvironment phenotype.

In Phase 1A, patient reported outcomes (PROs) will be characterized to explore the potential symptomatic benefit of immunotherapy in protocol population. The PROs used are European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ)-C30 for general health, and for specific tumor types, QLQ-PAN26 for pancreatic, or QLQ-CR29 for colorectal.

4.6.6. Rationale for Dose Selection

The dose of Amph-Peptide for this study is based on prior clinical experience with both KRAS peptides and CpG-7909 and is supported by nonclinical data. In prior vaccine trials with mKRAS peptides, doses of peptides ranging from 100 to 5000 µg have been used, both as single peptides and in combination. Therefore the 700 µg per Amph-Peptide, 4900 µg total Amph-Peptide 7P, the highest dose in this study is within the range previously evaluated in other clinical trials. In addition, recent preclinical murine data suggest the potential for increased immunogenicity with lower Amph-Peptide doses. Therefore, a dose of 200 µg per Amph-Peptide, ie, 1400 µg total Amph-Peptides 7P, will also be evaluated in the Phase 1A portion of this study. This lower dose level (ie, 200 µg per Amph-Peptide, or 1400 µg total Amph-Peptides 7P) will evaluate the same total dose of peptide (1400 µg) as was used in Study ELI-002-001 with Amph-Peptides 2P at 700 µg per peptide.

Although other adjuvants were used in the previously conducted KRAS vaccine clinical trials, soluble CpG-7909 has been administered SC in other trials in cancer subjects at total doses up to at least 40 mg and on a body weight basis as high as 0.48 mg/kg [Melisi et al., 2014]. The dose-ranging Study No. 2795-001 (Section 4.4.1.1) also strongly supports the dose for this trial.

The administration of 48 µg Amph-Peptide with either 5 or 25 µg Adjuvant was well tolerated in the rodent Study No. 2795-002 (Section 4.4.1.2) with a dose-dependent reduced incidence and severity of local irritation and limited associated effects. Therefore, the NOAEL was 48 µg Amph-Peptide/25 µg Adjuvant.

The planned Amph-CpG-7909 dose for this study is the RP2D that was identified in Study ELI-002-001 under IND 26909.

5. TRIAL OBJECTIVES

5.1. Phase 1 Primary Objectives

The primary objectives of Phase 1 are:

- To assess the safety and tolerability of ELI-002 7P as adjuvant therapy for subjects with KRAS/NRAS mutated solid tumors who have MRD identified using either ctDNA or a serum tumor biomarker

5.2. Phase 1 Secondary Objective

The secondary objective of Phase 1 is:

- To assess ctDNA reduction and clearance, defined as reduction or clearance of ctDNA compared to baseline, or if ctDNA was not detectable at baseline, serum tumor biomarker (such as CA19-9 and CEA) reduction and clearance compared to baseline

5.3. Phase 1 Exploratory Objectives

The exploratory objectives of Phase 1 are:

- To report the median DFS (per investigator) and the median OS
- To assess the change relative to baseline in:
  - Phase 1A only: Serum cytokines interleukin (IL)-2, IFNγ, IL-6, IL-10, and tumor necrosis factor alpha (TNFα)
  - PROs: EORTC QLQ-C30 and QLQ-PAN26, or QLQ-CR29
  - To evaluate the immunogenicity of ELI-002 7P. T cell responses to ELI-002 7P will be assessed using assays such as ICS, Fluorospot, and/or dextramer^{+} T cells for subjects with HLA alleles for which dextramer/s is/are available
  - Biomarker levels (ctDNA, CA19-9, and CEA)
  - To evaluate tumor-infiltrating T cell and the tumor microenvironment after dosing with ELI-002 7P
- To correlate biomarker data to clinical safety and efficacy (DFS, OS)

5.4. Phase 2 Primary Objective

The primary objective of Phase 2 is:

- To compare ELI-002 7P versus standard of care (SOC; observation) in DFS (per investigator)

5.5. Phase 2 Secondary Objectives

The secondary objectives of Phase 2 are:

- To compare OS between subjects randomized to ELI-002 7P versus SOC (observation)
- To compare ctDNA reduction and clearance, defined as reduction or clearance in ctDNA compared to baseline, or if ctDNA was not detectable at baseline, serum tumor biomarker (such as CA19-9 and CEA) reduction and clearance compared to baseline in subjects randomized to ELI-002 7P versus SOC (observation)
- To assess the safety and tolerability of ELI-002 7P

5.6. Phase 2 Exploratory Objectives

The exploratory objectives of Phase 2 are:

- To assess objective response rate (irORR) in subjects who crossover to ELI-002 7P from observation after relapse according to Immune Response Evaluation Criteria in Solid Tumors (iRECIST)
- To assess the change relative to baseline in:
  - To evaluate the immunogenicity of ELI-002 7P. T cell responses to ELI-002 7P will be assessed using assays such as ICS, Fluorospot, and/or dextramer^{+} T cells for subjects with HLA alleles for which dextramer/s is/are available
  - Biomarker levels (ctDNA, CA19-9, and CEA)
  - To evaluate tumor-infiltrating T cells and the tumor microenvironment after dosing with ELI-002 7P

6. INVESTIGATIONAL PLAN

6.1. Overall Trial Design

ELI-002-201 is an open-label, Phase 1/2 trial of ELI-002 7P immunotherapy as adjuvant treatment for subjects with KRAS/NRAS mutated PDAC and other solid tumors who are at high risk for relapse (ie, presence of isolated tumor cells in the subject's body, in which the primary tumor has been removed and is currently without clinical signs of disease). High relapse risk is defined by either a ctDNA-positive result or an elevated serum tumor biomarker (such as CA19-9 or CEA). The design of the trial is outlined in Figure 2 and Figure 3.

This protocol builds on the experience obtained with a related product, ELI-002 2P (with Amph-Peptides G12D and G12R), which was studied in protocol ELI-002-001 under IND 26909. Study ELI-002-001 evaluated escalating doses of the adjuvant Amph-CpG-7909 when admixed with a fixed dose of Amph-Peptides 2P (1.4 mg [700 µg of each peptide]). Therefore, the dose carried forward into this protocol will be the RP2D of Amph-CpG-7909, determined to be 10.0 mg. This Amph-CpG-7909 RP2D will be evaluated in Phase 1A with two dose levels of Amph-Peptides 7P (G12D, G12R, G12V, G12A, G12C, G12S, G13D): 4.9 mg total (700 µg of each peptide) and 1.4 mg total (200 µg of each peptide).

Phase 1A is planned to enroll approximately 12 subjects, 6 subjects at each Amph-Peptide 7P dose (designated Cohort 1) with mutant KRAS (mKRAS)/mutant NRAS (mNRAS) solid tumors (PDAC, and CRC) Enrollment in the Phase 2 randomized cohorts (Cohorts 3A, and 3B) is contingent on confirmation of safety of the RP2D in Phase 1A, Cohort 1. Phase 1B (Cohort 2, CRC) may be opened to enrollment by Elicio either concurrent or subsequent to Phase 2. If Cohort 2 is opened this will be documented in a study memo sent to all clinical sites and maybe submitted to IRBs, per IRB guidance (see Figure 2).

The Phase 2 portion of the study (Cohorts 3A, 3B and 3C) will proceed contingent on the observation of antitumor activity with ELI-002 during the clinical development programs. In Phase 2, approximately 135 subjects with PDAC will be randomized 2:1 to ELI-002 7P or SOC (observation), respectively. Subjects randomized to ELI-002 7P will receive SC injections of ELI-002 7P during the Immunization Period and the Booster Period. Subjects randomized to SOC (observation) be able to cross over to ELI-002 7P treatment following confirmed disease progression.

Randomization in Phase 2 will be stratified according to the following:

- Nodal status: node negative versus node positive (0 versus 1)

The trial will consist of:

- A Screening Period in which study specific procedures, including eligibility determination, will begin at Visit 1, following locoregional therapy.
- An Immunization Period which will consist of 6 SC injections: 4 weekly injections (Visit 2 to Visit 5) followed by 2 injections every 2 weeks at Visit 6 and Visit 7, if assigned to a treatment cohort.
- A No Dosing 2-Month Period in which subjects will continue to be observed and evaluated.

- A Booster Period, consisting of 4 weekly injections (Visit 10 to Visit 13), in which eligible subjects will receive further lymph node antigen exposure, if assigned to a treatment cohort. A Booster Period is provided as further lymph node antigen exposure may be required to maintain effective levels of antigen-specific T cells. All subjects will receive booster doses unless they have unresolved toxicity.
- A Follow-up Period which will provide continued safety and efficacy data.

All subjects will be observed for safety and tolerability. Radiographic imaging with contrast will occur at screening, approximately 3 months after the first dose, and at additional timepoints as indicated in the Schedules of Assessments: Table 9, Table 11, and Table 12; and Table 15, Table 16, Table 17, and Table 18 for subjects randomized to observation only.

The central laboratory will confirm if at least 1 of the 7 mutant KRAS/NRAS alleles targeted by ELI 002 Amph-Peptides 7P (G12D, V, R, S, A, C, G13D) is present, and for Phase 1 only, there must be positive ctDNA or serum biomarker results (such as CA19-9 and CEA) from samples taken ≥21 days after resection or the last administration of adjuvant therapy (whichever comes last in the specific subject's treatment plan). KRAS data is required to determine a subject's eligibility and inclusion into all cohorts in the trial. Results confirming ctDNA positivity and/or serum biomarker elevation are required to determine a subject's eligibility and inclusion into Phase 1 of the trial.

Immunologic biomarkers of response may include HLA typing, serum cytokines, ICS, Fluorospot, and dextramer^{+} T cells for subjects with appropriate HLA alleles will be determined when matching dextramer/s is/are available. Tumor biopsy assessments may include gene expression and/or immunofluorescence to examine immune cell infiltration and tumor microenvironment phenotype.

Local laboratories will be utilized for tumor biomarkers (CA19-9 and CEA) and all other safety laboratory tests.

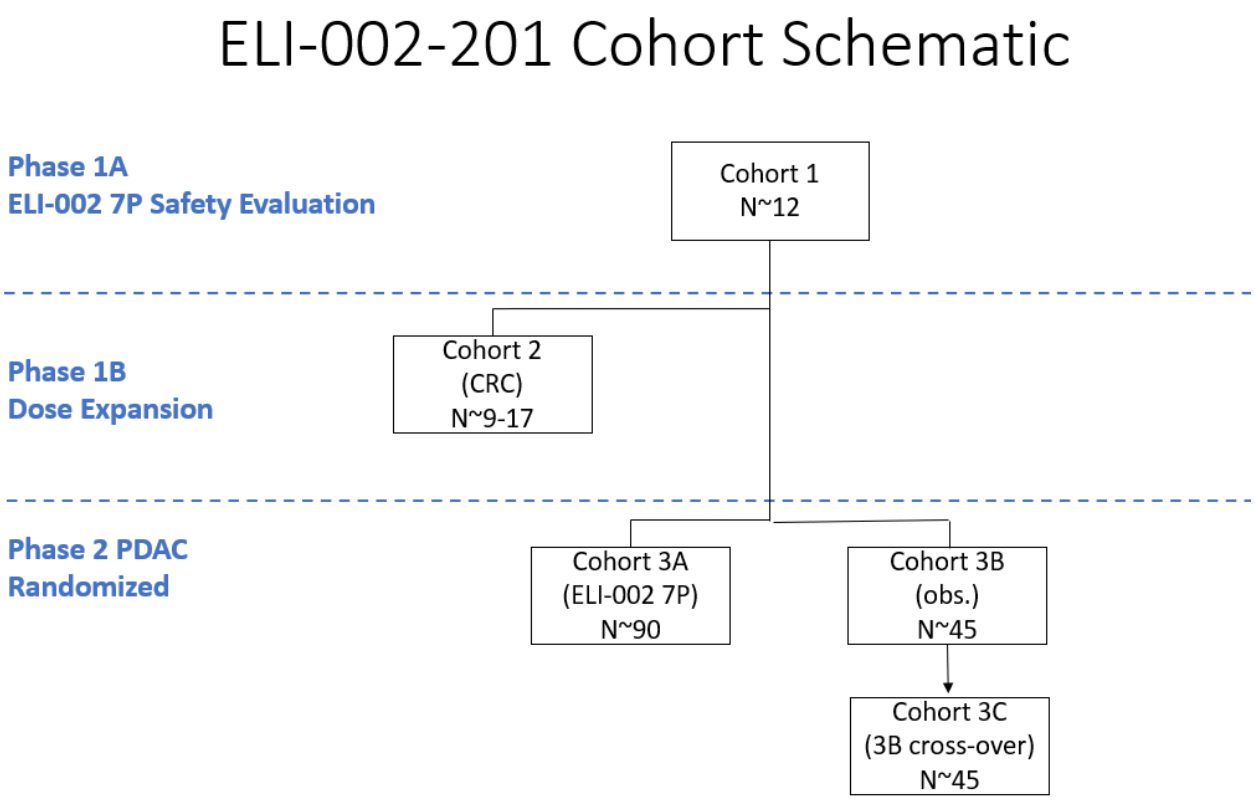
Central laboratories will be utilized for ctDNA analysis, HLA typing, PBMC isolation, tumor microenvironment and T-cell infiltration, and immunogenicity assessment (such as Fluorospot, ICS, and/or T cell dextramer testing) as detailed in the central laboratory manual.

While HLA testing will be performed prior to first dose at Visit 2, cohorts will be enrolled regardless of the subject HLA subtype.

Discontinuation of Trial Treatment or Crossover from SOC (Observation) to ELI-002 7P

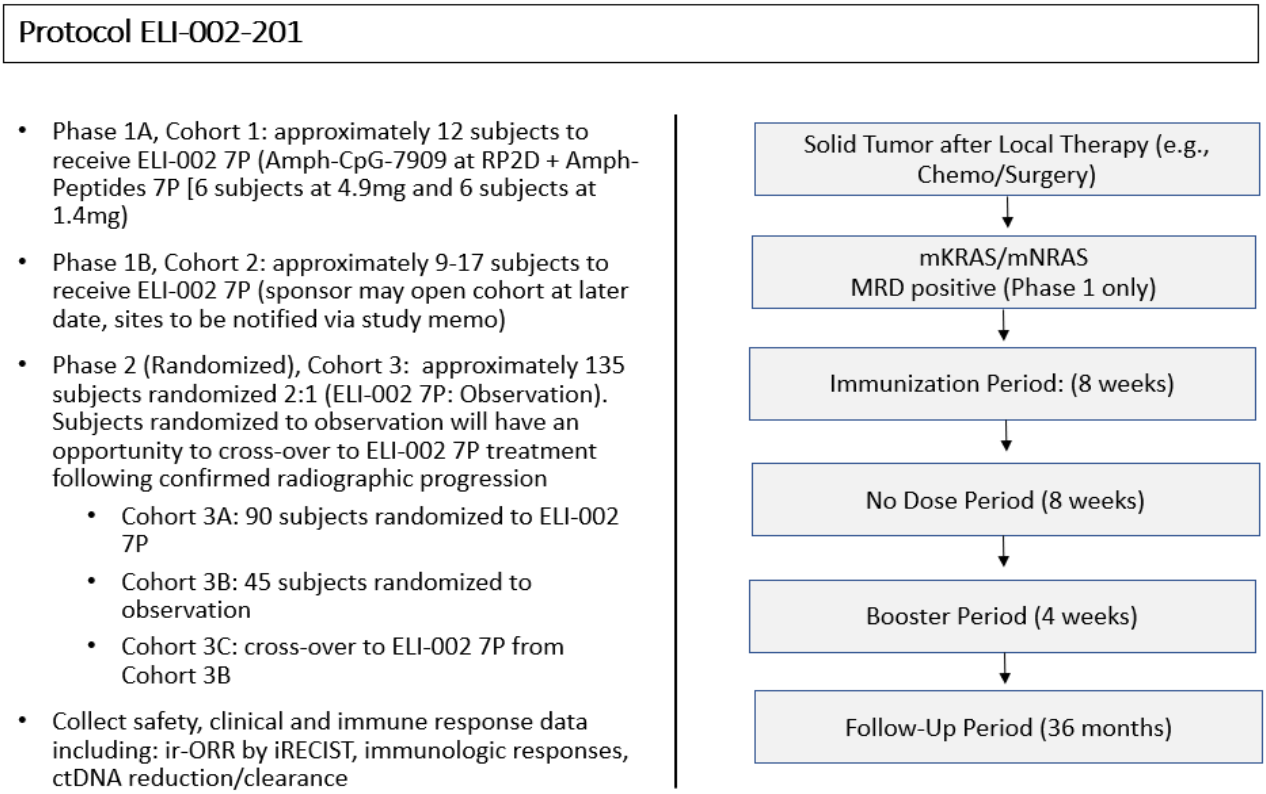
Subjects receiving ELI-002 7P (ie, all cohorts except Cohort 3B) with confirmed radiographic relapse (using iRECIST criteria; not judged as pseudoprogression) during treatment with ELI-002 7P may discontinue trial treatment or could continue treatment for clinical benefit per Section 6.1.2. Discussion should take place with Elicio Clinical prior to early treatment discontinuation to ensure potential pseudoprogression is considered. In Phase 2, subjects randomized to SOC (observation) in Cohort 3B will be eligible to crossover to intervention (ELI-002 7P) after confirmed relapse is documented using iRECIST criteria up through the time that the last subject from Cohorts 3A and 3B completes the study, and regardless of their election to crossover or not, they will continue to be followed for OS. For subjects who cross over, response to treatment will be characterized using iRECIST criteria.

Figure 2: ELI-002 Trial Cohort Schematic



CRC=colorectal cancer; PDAC=pancreatic ductal adenocarcinoma

Figure 3: Protocol ELI-002-201: Phase 1/2 Trial Design



ctDNA=circulating tumor deoxyribonucleic acid; iRECIST=Immune Response Evaluation Criteria in Solid Tumors; mKRAS=mutant Kirsten rat sarcoma; mNRAS=mutant neuroblastoma ras viral oncogene homolog; MRD=minimal residual disease; irORR=objective response rate; RP2D=recommended Phase 2 dose

6.1.1. Criteria for Booster and Additional Booster Vaccines

Accumulating clinical evidence indicates some subjects treated with an immunotherapy, such as ELI-002 7P, may be assessed as having disease progression by conventional response criteria before demonstrating clinical objective responses and/or stable disease [Wolchok et al, 2009]. Such pseudoprogression has been observed in the ELI-002-001 trial. Two hypotheses have been suggested to explain this phenomenon. The first is that enhanced inflammation within the lesions could lead to an increase in the lesion size which would appear as enlarged index lesions and therefore as newly visible small non-index lesions. Over time, both the malignant and inflammatory portions of the lesion(s) may then decrease leading to overt signs of clinical improvement. The second hypothesis is that, in some subjects, the speed of the lesion growth may initially outpace the anti-tumor immune activity of the therapy. With sufficient time, the anti-tumor activity will dominate and become clinically apparent.

All subjects free of unequivocal radiographic progression will receive booster doses unless they have unresolved toxicity. For subjects which have encountered signs of toxicity, the investigator must consult with the sponsor's medical monitor who must agree with resuming the subsequent booster vaccinations (see Section 6.7.1).

Subjects who remain in the trial until the end of the required Booster Period may be eligible to enroll in a separate extension protocol to continue to receive further lymph node antigen exposure to maintain effective levels of antigen-specific T-cells.

6.1.2. Criteria for Treatment with ELI-002 7P After Disease Progression

A subset of patients treated with immunotherapy can derive clinical benefit despite initial evidence of confirmed progressive disease. For example, on the Keynote-042 study, a group of NSCLC patients who progressed on checkpoint inhibitor therapy benefitted from continued anti-PD-1 therapy after progression. Therefore, Phase 1 subjects enrolled, and Phase 2 subjects randomized to ELI-002 7P treatment, who experience iRECIST confirmed progressive disease (iCPD) during the study treatment period will be permitted to continue ELI-002 7P treatment until the second progression is observed, provided that the subject has not completed the treatment period and the following criteria are met:

- The investigator determines that the use of ELI-002 7P is an appropriate treatment for the current clinical situation
- The subject tolerates ELI-002 7P and has stable performance status.

Subsequent imaging should be within 12 weeks of the initial assessment of iRECIST progression.

Other anti-tumor therapy should be considered at this time, as appropriate; if other anti-tumor therapy is commenced, ELI-002 7P treatment must be discontinued.

Subjects should continue with assessments according to the study schedule of events.

6.1.3. Screening for Human Leukocyte Antigen Subtypes

High-resolution HLA information can be helpful in analyzing immune responses. Therefore, high-resolution (ie, DNA based) HLA typing will be collected via blood sample for all subjects at pre-dose Visit 2 using the central laboratory. Cohorts will be enrolled regardless of the subject's HLA type.

6.1.4. Schedule of Assessments for ELI-002 7P Treated Subjects

The schedules of assessments are provided in Table 7 through Table 12.

Table 7: Schedule of Assessments: Screening and Observation

Assessment	Screening Period
Visit	**Visit 1**
Window (± days)	**Days −56 to −1**
Written informed consent [1]	X
Tumor tissue and blood sample for next generation sequencing[2]	X
Pregnancy testing (urine)	X
Demographics (including sex, age, race and ethnicity)	X
Height/weight	X
Record medical and medication history, including cancer history/prior treatments and current medications	X
Review of eligibility criteria[3]	X
Physical examination[4]	X
Vital signs	X
Electrocardiogram	X
ECOG[5]	X
CT with contrast[6]	X
Clinical laboratory (local laboratory) including IL-6 and HbA1c[7]	X
Serum CEA/CA19-9 (local laboratory)[8]	X
Virology – including hepatitis C and COVID-19 viral tests (local laboratory)[9]	X
ctDNA (central laboratory)[10]	X
Leukapheresis-PBMC collection for immunogenicity testing (central laboratory)[11]	X
Tumor sample from prior surgical resection, where available (central laboratory)[12]	X
Adverse events	X

CT=computed tomography; ctDNA=circulating tumor deoxyribonucleic acid; ECOG=Eastern Cooperative Oncology Group; HbA1c=hemoglobin A1c; IL-6=interleukin 6; PBMC=peripheral blood mononuclear cell

1. The ICF has no expiration and can be signed at any time during or after the prior treatment (including surgery/resection). The screening window (56 days) begins when the first screening procedure is performed.
2. Once a subject has consented, a retrospective tumor tissue sample taken during surgical resection will be requisitioned. A blood sample will also be collected, per the study Lab Manual. Tumor DNA will be sequenced to guide ctDNA testing in subsequent blood samples and baseline tumor gene

expression will be assessed. The somatic DNA from the blood sample will serve as a control to ensure only tumor-specific DNA is included in the selection for ctDNA testing. If a subject does not have acceptable tumor sample to undergo testing, upon approval from Elicio the site may use the central lab for plasma-based ctDNA analysis.

3. See Inclusion and Exclusion Criteria in Section 7.1 and Section 7.2, respectively.
4. Physical examinations per standard of care (see Section 12.1.3).
5. To be eligible, ECOG performance status must be 0 to 1 (see Section 12.1.5)
6. To be eligible, post-operative CT must be negative for radiographic recurrent disease. CT imaging assessments will occur within 60 days of the first dose. For subjects with IV contrast allergy/intolerance, MRI may be performed.
7. See inclusion criterion #8 regarding laboratory values in Section 7.1. Safety laboratories should include complete blood count with differential; hematology to include parameters listed in Section 12.1.6.1; chemistry to include parameters listed in Section 12.1.6.2.
8. See inclusion criterion #4 (Section 7.1) for serum biomarker values (CA19-9 [PDAC], CEA [PDAC/CRC]) for Phase 1 eligibility. Biomarker values must be obtained ≥21 days post-surgery or last administration of adjuvant therapy, whichever comes last in the specific subject's treatment plan. In Phase 2, two serum biomarker values (at least 1 week apart) will be required in order to assess if the subject is biomarker evaluable for the protocol specified safety review.
9. Samples such as swabs, saliva, or others as appropriate may be used for COVID-19 viral testing according to the locally available assay.
10. See inclusion criterion #3 and #4 in Section 7.1. Blood will be collected for ctDNA analysis at a central laboratory. Phase 1 eligibility requires that subjects must be MRD positive, as measured by ctDNA blood test, persisting ≥21 days post-surgery or after last administration of adjuvant treatment (whichever is last in the specific subject treatment plan) with 1 of the7 ELI-002-specific mKRAS/mNRAS alleles. Details for blood collection are provided in the Central Laboratory Manual.
11. The leukapheresis sample must be collected once eligibility has been confirmed and prior to the first dose of ELI-002 7P. The PBMCs may be used for immunogenicity and/or biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.
12. The tumor sample from prior surgical resection (when available) must be collected once eligibility has been confirmed and prior to the first dose of ELI-002 7P. The sample will be used as a baseline in evaluating tumor-infiltrating T cells, the tumor microenvironment and may also be used for biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.

Table 8: Schedule of Assessments: Immunization Period

Assessment	Immunization Period						
Visit	**Visit 2**		**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**
Week (± days)	**Week 1/Day 0 Baseline (prior to dosing)**	**Week 1/Day 0 (±3 days)**	**Week 2 (±3 days)**	**Week 3 (±3 days)**	**Week 4 (±3 days)**	**Week 6 (±3 days)**	**Week 8 (±3 days)**
Dose #	—	**Dose 1**	**Dose 2**	**Dose 3**	**Dose 4**	**Dose 5**	**Dose 6**
Review medical history[1]	X						
Review cancer history/prior treatments	X						
Physical examination[2]	X		X	X	X	X	X
Vital signs	X		X	X	X	X	X
Weight	X		X	X	X	X	X
ECG	X						
ECOG	X		X	X	X	X	X
Concomitant medications	X		X	X	X	X	X
Clinical laboratory (local laboratory)[3]	X		X	X	X	X	X
ctDNA (central laboratory)[4]	X					X	
Whole blood-PBMC collection for immunogenicity testing (central laboratory)[3]						X	
High Resolution HLA typing (central laboratory)[5]	X						
Randomization (Phase 2 only)	X						
Trial drug administration for those randomized to ELI-002 7P[6]		X	X	X	X	X	X
Adverse events[7]	X	X	X	X	X	X	X
Reactogenicity diary[8]		X	X	X	X	X	X

CA=carbohydrate antigen; CBC=complete blood count; CEA=carcinoembryonic antigen; CRC=colorectal cancer; CT=computed tomography; ctDNA=circulating tumor deoxyribonucleic acid; ECG=electrocardiogram; ECOG=Eastern Cooperative Oncology Group: HLA=human leukocyte antigen; mKRAS=mutant Kirsten rat sarcoma; mNRAS=mutant neuroblastoma ras viral oncogene homolog; MRD=minimal residual disease; PBMC=peripheral blood mononuclear cell; PDAC=pancreatic ductal adenocarcinoma

1. Subjects must have recovered from surgery without any ongoing medical/surgical issues. See Inclusion and Exclusion Criteria in Section 7.1 and Section 7.2, respectively.
2. Physical examinations per standard of care (see Section 12.1.3).
3. Safety laboratories should include CBC with differential; hematology to include parameters listed in Section 12.1.6.1; chemistry to include parameters listed in Section 12.1.6.2. The PBMCs may be used for immunogenicity and/or biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.
4. ctDNA blood testing will occur at a central laboratory. Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date. Details for blood collection are

provided in the Central Laboratory Manual

5. High resolution HLA will be performed for all subjects, prior to first dose at Visit 2. Cohorts will be enrolled regardless of the HLA subtype (see Section 6.1.3 for details). Details for blood collection are provided in the Central Laboratory Manual. Subjects randomized to SOC in Phase 2 of the study and who decide to crossover to ELI-002 7P intervention after documented relapse do not need to have HLA repeated prior to dosing.
6. ELI-002 7P administration for those subjects in Phase 1, and those randomized (or who crossover) to ELI-002 7P in Phase 2. Subjects must be observed for safety for at least 1-hour post-dose.
7. Check for signs of toxicity. See Section 6.7 for instructions regarding signs of toxicity and for criteria for stopping treatment administration.
8. Sites will observe subjects for at least 1 hour post-dose for reactogenicity. Subjects will be provided with a paper reactogenicity diary at the end of the visit. They will be instructed to fill out the diary each day, for 7 days, at the same time per the instructions on the study template. See Section 12.2.1.3 for details. Subjects will return the completed diary at the next scheduled visit. The site staff will review the diary with the subject and file in the subject study records. This completed diary will be used as source data for eCRF data entry.

Table 9: Schedule of Assessments: No Dosing 2-Month Period

Assessment	No Dosing 2-Month Period	
Visit	**Visit 8**	**Visit 9**
Week (± days)	**Week 10 (±3 days)**	**Week 14 (±3 days)**
Physical examination[1]	X	X
Vital signs	X	X
Weight	X	X
Changes in concomitant medications	X	X
CT with contrast[2]		X
Clinical laboratory (local laboratories)[3]	X	X
ctDNA (central laboratory)[4]	X	
Leukapheresis-PBMC collection for immunogenicity testing (central laboratory)[5]	X	
Whole blood-PBMC collection for immunogenicity testing (central laboratory)[6]		X
Serum CEA/CA19-9 (local laboratories)[3]		X
Standard of care biopsy (central laboratory)[7]		X
Adverse events	X	X

CA=carbohydrate antigen; CBC=complete blood count; CEA=carcinoembryonic antigen; CRC=colorectal cancer; CT=computed tomography; ctDNA=circulating tumor deoxyribonucleic acid; IV=intravenous; mKRAS=mutant Kirsten rat sarcoma; mNRAS=mutant neuroblastoma ras viral oncogene homolog; MRI=magnetic resonance imaging; PBMC=peripheral blood mononuclear cell

1. Physical examinations per standard of care (see Section 12.1.3).
2. A visit window of ±14 days is permitted for imaging assessments. For subjects with IV contrast allergy/intolerance, MRI may be performed. The same modality used for the screening imaging should be used for all subsequent on-study imaging.
3. Safety laboratories should include CBC with differential: hematology to include parameters listed in Section 12.1.6.1; chemistry to include parameters listed in Section 12.1.6.2. Serum biomarkers CA19-9 [PDAC], CEA [PDAC/CRC].
4. ctDNA blood testing will occur at a central laboratory. Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date. Details for blood collection are provided in the Central Laboratory Manual
5. The leukapheresis sample may be collected between −7 days and +3 days from Visit 8. The PBMCs may be used for immunogenicity and/or biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.
6. The PBMCs may be used for immunogenicity and/or biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.
7. Post-Visit 2 standard of care biopsy to be obtained if new lesions are observed on radiographic imaging and when the investigator judges that tissue can be safely obtained. The sample will be collected within +30 days of the radiographic evidence of new lesions. The sample will be used in evaluating tumor-infiltrating T cells, the tumor microenvironment and may also be used for biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.

Table 10: Schedule of Assessments: Booster Period

Assessment	Booster Period			
Visit	**Visit 10**	**Visit 11**	**Visit 12**	**Visit 13/ End of Treatment**
Week (± days)	**Week 17 (±3 days)**	**Week 18 (±3 days)**	**Week 19 (±3 days)**	**Week 20 (±3 days)**
Dose #	**Dose 7**	**Dose 8**	**Dose 9**	**Dose 10**
Physical examination[1]	X	X	X	X
Vital signs	X	X	X	X
Weight	X	X	X	X
ECOG	X	X	X	X
Concomitant medications	X	X	X	X
Clinical laboratory (local laboratory)[2]	X	X	X	X
ctDNA (central laboratory)[3]	X			X
Trial drug administration for those randomized to ELI-002 7P[4]	X	X	X	X
Adverse events[5]	X	X	X	X
Reactogenicity diary[6]	X	X	X	X

CA=carbohydrate antigen; CBC=complete blood count; CEA=carcinoembryonic antigen; CRC=colorectal cancer; ctDNA=circulating tumor deoxyribonucleic acid; ECOG=Eastern Cooperative Oncology Group; IV=intravenous; mKRAS=mutant Kirsten rat sarcoma; mNRAS=mutant neuroblastoma ras viral oncogene homolog; MRI=magnetic resonance imaging; PBMC=peripheral blood mononuclear cell; PDAC=pancreatic ductal adenocarcinoma

1. Physical examinations per standard of care (see Section 12.1.3).
2. Safety laboratories should include CBC with differential: hematology to include parameters listed in Section 12.1.6.1; chemistry to include parameters listed in Section 12.1.6.2.
3. ctDNA blood testing will occur at a central laboratory. Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date. Details for blood collection are provided in the Central Laboratory Manual
4. ELI-002 7P administration for those subjects in Phase 1, and those randomized (or who crossover) to ELI-002 7P in Phase 2. Subjects must be observed for safety for at least 1-hour post-dose.
5. Check for signs of toxicity. See Section 6.7 for instructions regarding signs of toxicity and for criteria for stopping treatment administration.
6. Sites will observe subjects for at least 1 hour post-dose for reactogenicity. Subjects will be provided with a paper reactogenicity diary at the end of the visit. They will be instructed to fill out the diary each day, for 7 days, at the same time per the instructions on the study template. See Section 12.2.1.3 for details. Subjects will return the completed diary at the next scheduled visit. The site staff will review the diary with the subject and file in the subject study records. This completed diary will be used as source data for eCRF data entry.

Table 11: Schedule of Assessments: Follow-up Period (Year 1 to Year 2)

Assessment	Follow-up Period								
Visit	**Visit 14**	**Visit 15**	**Visit 16**	**Visit 17**	**Visit 18**	**Visit 19**	**Visit 20**	**Visit 21**	**Visit 22[1]**
Week (± days)	**Week 22 (±3 days)**	**Week 26 (±7 days)**	**Week 34 (±14 days)**	**Week 46 (±14 days)**	**Week 58 (±14 days)**	**Week 70 (±14 days)**	**Week 82 (±14 days)**	**Week 94 (±14 days)**	**Week 102 (±14 days)**
Physical examination[2]					X				
Vital signs	X	X	X	X	X	X	X	X	X
Weight	X	X	X	X	X	X	X	X	X
ECOG	X	X	X	X	X	X	X	X	X
CT with contrast[3]		X		X	X	X	X	X	X
Clinical laboratory (local laboratory)[4]	X								
ctDNA (central laboratory)[5]		X		X		X			X
Whole blood-PBMC collection for immunogenicity testing (central laboratory)[6]	X			X		X			
Serum CEA/CA19-9 (local laboratory)[4]		X		X	X	X	X	X	X
Standard of care biopsy (central laboratory)[7]		X		X	X	X	X	X	X
Adverse events[8]	X	X	X	X	X	X	X	X	X

CA=carbohydrate antigen; CBC=complete blood count; CEA=carcinoembryonic antigen; CRC=colorectal cancer; CT=computed tomography; ctDNA=circulating tumor deoxyribonucleic acid; ECOG=Eastern Cooperative Oncology Group; MRI=magnetic resonance imaging; PBMC=peripheral blood mononuclear cell; PDAC=pancreatic ductal adenocarcinoma

1. All enrolled subjects should be followed in the Follow-Up period for overall survival and disease status. As part of the study sites may conduct searches of public records, such as those establishing survival status, to obtain survival data as needed (ie: subject lost to follow-up, withdraws from study, etc.).
2. Physical examination per standard of care (see Section 12.1.3).
3. A visit window of ±14 days is permitted for imaging assessments during the Follow-up Period. For subjects with IV contrast allergy/intolerance, MRI may be performed. The same modality used for the screening imaging should be used for all subsequent on-study imaging. If a subject has had confirmed radiographic progression via iRECIST and has initiated subsequent therapy, further imaging is not required. If a subject has not yet had iCPD prior to subsequent therapy, continue with scans until iCPD is confirmed.
4. Safety laboratories should include CBC with differential: hematology to include parameters listed in Section 12.1.6.1; chemistry to include parameters listed in Section 12.1.6.2. Serum biomarkers CA19-9 [PDAC], CEA [PDAC/CRC] - if a subject has had confirmed radiographic progression via iRECIST and has initiated subsequent therapy, further serum biomarker testing is not required. If a subject has not yet had iCPD prior to subsequent therapy, continue with serum biomarker collection until iCPD is confirmed.
5. ctDNA blood testing will occur at a central laboratory. Details for blood collection are provided in the Central Laboratory Manual. If a subject has had confirmed radiographic progression via iRECIST and has initiated subsequent therapy, further ctDNA collection is not required. If a subject has not yet had iCPD prior to subsequent therapy, continue with ctDNA collection until iCPD is confirmed. Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were

both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date.

6. The PBMCs may be used for immunogenicity and/or biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.
7. Post-Visit 2 standard of care biopsy to be obtained if new lesions are observed on radiographic imaging and when the investigator judges that tissue can be safely obtained. The sample will be collected within +30 days of the radiographic evidence of new lesions and will be used to evaluate tumor-infiltrating T cells, the tumor microenvironment and maybe biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.
8. Long-term observation for post-dose vaccination adverse events will be recorded for any new events that occur up to 30 days post Visit 13/last dose. Any event that occurs during this timeframe will continue to be followed until the event returns to baseline or the subject discontinues from the study.

Table 12: Schedule of Assessments: Follow-up Period (Year 2 to Year 3)

Assessment	Follow-up Period			
Visit	**Visit 23**	**Visit 24**	**Visit 25**	**Visit 26/ End of Study[1]**
Week (± days)	**Week 114 (±14 days)**	**Week 126 (±14 days)**	**Week 138 (±14 days)**	**Week 150 (±14 days)**
ECOG	X	X	X	X
CT with contrast[2]	X	X	X	X
ctDNA (central laboratory)[4]		X		X
Serum CEA/CA19-9 (local laboratory)[3]	X	X	X	X
Standard of care biopsy (central laboratory)[5]	X	X	X	X
Adverse events[6]	X	X	X	X

CA=carbohydrate antigen; CBC=complete blood count; CEA=carcinoembryonic antigen; CRC=colorectal cancer; CT=computed tomography; ctDNA=circulating tumor deoxyribonucleic acid; ECOG=Eastern Cooperative Oncology Group; MRI=magnetic resonance imaging; PBMC=peripheral blood mononuclear cell; PDAC=pancreatic ductal adenocarcinoma

1. All enrolled subjects should be followed in the Follow-Up period for overall survival and disease status. As part of the study sites may conduct searches of public records, such as those establishing survival status, to obtain survival data as needed (ie: subject lost to follow-up, withdraws from study, etc.).
2. A visit window of ±14 days is permitted for imaging assessments during the Follow-up Period. For subjects with IV contrast allergy/intolerance, MRI may be performed. The same modality used for the screening imaging should be used for all subsequent on-study imaging. If a subject has had confirmed radiographic progression via iRECIST and has initiated subsequent therapy, further imaging is not required. If a subject has not yet had iCPD prior to subsequent therapy, continue with scans until iCPD is confirmed.
3. Serum biomarkers CA19-9 [PDAC], CEA [PDAC/CRC] If a subject has had confirmed radiographic progression via iRECIST and has initiated subsequent therapy, further serum biomarker testing is not required. If a subject has not yet had iCPD prior to subsequent therapy, continue with serum biomarker collection until iCPD is confirmed.
4. ctDNA blood testing will occur at a central laboratory. Details for blood collection are provided in the Central Laboratory Manual. If a subject has had confirmed radiographic progression via iRECIST and has initiated subsequent therapy, further ctDNA collection is not required. If a subject has not yet had iCPD prior to subsequent therapy, continue with ctDNA collection until iCPD is confirmed. Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date.
5. Post-Visit 2 standard of care biopsy to be obtained if new lesions are observed on radiographic imaging and when the investigator judges that tissue can be safely obtained. The sample will be collected within +30 days of the radiographic evidence of new lesions. The sample will be used in evaluating tumor-infiltrating T cells, the tumor microenvironment and may also be used for biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.
6. Long-term observation for post-dose vaccination adverse events will be recorded will be recorded if an adverse event began within 30 days of last dose of treatment and continues in the follow-up period.

6.1.5. Schedule of Assessments for Standard of Care/Observation Subjects

The schedules of assessments are provided in Table 13 through Table 18.

Table 13: Schedule of Assessments: Screening and Observation

Assessment	Screening Period
Visit	**Visit 1**
Window (± days)	**Days −56 to −1**
Written informed consent [1]	X
Tumor tissue and blood sample for next generation sequencing[2]	X
Pregnancy testing (urine)	X
Demographics (including sex, age, race and ethnicity)	X
Height/weight	X
Record medical and medication history, including cancer history/prior treatments and current medications	X
Review of eligibility criteria[3]	X
Physical examination[4]	X
Vital signs	X
Electrocardiogram	X
ECOG[5]	X
CT with contrast[6]	X
Clinical laboratory (local laboratory) including IL-6 and HbA1c[7]	X
Serum CEA/CA19-9 (local laboratory)[8]	X
Virology – including hepatitis C and COVID-19 viral tests (local laboratory)[9]	X
ctDNA (central laboratory)[10]	X
Leukapheresis PBMC collection for immunogenicity testing (central lab) [11]	X
Tumor sample from prior surgical resection, where available (central laboratory)[12]	X
Adverse events	X

CT=computed tomography; ctDNA=circulating tumor deoxyribonucleic acid; ECOG=Eastern Cooperative Oncology Group; HbA1c=hemoglobin A1c; IL-6=interleukin 6; PBMC=peripheral blood mononuclear cell

1. The ICF has no expiration and can be signed at any time during or after the prior treatment (including surgery/resection). The screening window (56 days) begins when the first screening procedure is performed.
2. Once a subject has consented, a retrospective tumor tissue sample taken during surgical resection will be requisitioned. A fresh 6 mL blood sample will also be collected, per the study Lab Manual. Tumor DNA will be sequenced to guide ctDNA testing in subsequent blood samples and baseline tumor gene

expression will be assessed. The somatic DNA from the blood sample will serve as a control to ensure only tumor-specific DNA is included in the selection for ctDNA testing. If a subject does not have acceptable tumor sample to undergo testing, upon approval from Elicio the site may use the central lab for plasma-based ctDNA analysis.

3. See Inclusion and Exclusion Criteria in Section 7.1 and Section 7.2, respectively.
4. Physical examinations per standard of care (see Section 12.1.3).
5. To be eligible, ECOG performance status must be 0 to 1 (see Section 12.1.5)
6. To be eligible, post-operative CT must be negative for radiographic recurrent disease. CT imaging assessments will occur within 60 days of the first dose. For subjects with IV contrast allergy/intolerance, MRI may be performed.
7. See inclusion criterion #8 regarding laboratory values in Section 7.1. Safety laboratories should include complete blood count with differential: hematology to include parameters listed in Section 12.1.6.1; chemistry to include parameters listed in Section 12.1.6.2; serum IL-6 must be <500 pg/mL (inclusion criterion #8.h)
8. See inclusion criterion #4 (Section 7.1) regarding serum biomarker values (CA19-9 [PDAC], CEA [PDAC/CRC]) for Phase 1 eligibility. Biomarker values must be obtained ≥21 days post-surgery or last administration of adjuvant therapy, whichever comes last in the specific subject's treatment plan. In Phase 2, two serum biomarker values (at least 1 week apart) will be required in order to assess if the subject is biomarker evaluable for the protocol specified safety review.
9. Samples such as swabs, saliva, or others as appropriate may be used for COVID-19 viral testing according to the locally available assay.
10. See inclusion criterion #3 and #4 in Section 7.1. Blood will be collected for ctDNA analysis at a central laboratory. Details for blood collection are provided in the Central Laboratory Manual.
11. For subjects randomized to observation (SOC, Cohort 3B), the leukapheresis can be done at Visit 2, to accommodate the subject's schedule. The PBMCs may be used for immunogenicity and/or biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.
12. The tumor sample from prior surgical resection (when available) must be collected once eligibility has been confirmed and prior to the first dose of ELI-002 7P. The sample will be used as a baseline in evaluating tumor-infiltrating T cells, the tumor microenvironment and may also be used for biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.

Table 14: Schedule of Assessments: Immunization Period

Assessment	Immunization Period					
Visit	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**
Week (± days)	**Week 1/Day 0 Baseline (prior to dosing)**	**Week 2 (±3 days)**	**Week 3 (±3 days)**	**Week 4 (±3 days)**	**Week 6 (±3 days)**	**Week 8 (±3 days)**
Review medical history[1]	X					
Review cancer history/prior treatments	X					
Physical examination[2]	X				X	
Vital signs	X				X	
Weight	X				X	
ECG	X					
ECOG	X				X	
Concomitant medications	X	X	X	X	X	X
Clinical laboratory (local laboratory)[3]	X				X	
ctDNA (central laboratory)[4]	X				X	
High Resolution HLA typing (central laboratory)[5]	X					
Randomization (Phase 2 only)	X					
Adverse events[6]	X	X	X	X	X	X

CA=carbohydrate antigen; CBC=complete blood count; CEA=carcinoembryonic antigen; CRC=colorectal cancer; CT=computed tomography; ctDNA=circulating tumor deoxyribonucleic acid; ECG=electrocardiogram; ECOG=Eastern Cooperative Oncology Group: HLA=human leukocyte antigen; mKRAS=mutant Kirsten rat sarcoma; mNRAS=mutant neuroblastoma ras viral oncogene homolog; MRD=minimal residual disease; PBMC=peripheral blood mononuclear cell; PDAC=pancreatic ductal adenocarcinoma

1. Subjects must have recovered from surgery without any ongoing medical/surgical issues. See Inclusion and Exclusion Criteria in Section 7.1 and Section 7.2, respectively.
2. Physical examinations per standard of care (see Section 12.1.3).
3. Safety laboratories should include CBC with differential: hematology to include parameters listed in Section 12.1.6.1; chemistry to include parameters listed in Section 12.1.6.2.
4. ctDNA blood testing will occur at a central laboratory. Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date. Details for blood collection are provided in the Central Laboratory Manual
5. High resolution HLA will be performed for all subjects, prior to first dose at Visit 2. Cohorts will be enrolled regardless of the HLA subtype (see Section 6.1.3 for details). Details for blood collection are provided in the Central Laboratory Manual. Subjects randomized to SOC in Phase 2 of the study and who decide to crossover to ELI-002 7P intervention after documented relapse do not need to have HLA repeated prior to dosing.
6. Check for adverse events

Table 15: Schedule of Assessments: No Dosing 2-Month Period

Assessment	No Dosing 2-Month Period	
Visit	**Visit 8**	**Visit 9**
Week (± days)	**Week 10 (±3 days)**	**Week 14 (±3 days)**
Physical examination[1]	X	X
Vital signs	X	X
Weight	X	X
Changes in concomitant medications	X	X
CT with contrast[2]		X
Clinical laboratory (local laboratories)[3]	X	X
ctDNA (central laboratory)[4]	X	
Serum CEA/CA19-9 (local laboratories)[3]		X
Standard of care biopsy (central laboratory)[5]		X
Adverse events	X	X

CA=carbohydrate antigen; CBC=complete blood count; CEA=carcinoembryonic antigen; CRC=colorectal cancer; CT=computed tomography; ctDNA=circulating tumor deoxyribonucleic acid; IV=intravenous; mKRAS=mutant Kirsten rat sarcoma; mNRAS=mutant neuroblastoma ras viral oncogene homolog; MRI=magnetic resonance imaging; PBMC=peripheral blood mononuclear cell

1. Physical examinations per standard of care (see Section 12.1.3).
2. A visit window of ±14 days is permitted for imaging assessments. For subjects with IV contrast allergy/intolerance, MRI may be performed. The same modality used for the screening imaging should be used for all subsequent on-study imaging.
3. Safety laboratories should include CBC with differential: hematology to include parameters listed in Section 12.1.6.1; chemistry to include parameters listed in Section 12.1.6.2. Determine serum biomarker values (CA19-9 [PDAC], CEA [PDAC/CRC]).
4. ctDNA blood testing will occur at a central laboratory. Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date. Details for blood collection are provided in the Central Laboratory Manual
5. Post-Visit 2 standard of care biopsy to be obtained if new lesions are observed on radiographic imaging and when the investigator judges that tissue can be safely obtained. The sample will be collected within +30 days of the radiographic evidence of new lesions. The sample will be used in evaluating tumor-infiltrating T cells, the tumor microenvironment and may also be used for biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.

Table 16: Schedule of Assessments: Booster Period

Assessment	Booster Period			
Visit	**Visit 10**	**Visit 11**	**Visit 12**	**Visit 13/ End of Treatment**
Week (± days)	**Week 17 (±3 days)**	**Week 18 (±3 days)**	**Week 19 (±3 days)**	**Week 20 (±3 days)**
Physical examination[1]	X			X
Vital signs	X			X
Weight	X			X
ECOG	X			X
Concomitant medications	X	X	X	X
Clinical laboratory (local laboratory)[2]	X			X
ctDNA (central laboratory)[3]	X			X
Adverse events[4]	X	X	X	X

CA=carbohydrate antigen; CBC=complete blood count; CEA=carcinoembryonic antigen; CRC=colorectal cancer; ctDNA=circulating tumor deoxyribonucleic acid; ECOG=Eastern Cooperative Oncology Group; IV=intravenous; mKRAS=mutant Kirsten rat sarcoma; mNRAS=mutant neuroblastoma ras viral oncogene homolog; MRI=magnetic resonance imaging; PBMC=peripheral blood mononuclear cell; PDAC=pancreatic ductal adenocarcinoma

1. Physical examinations per standard of care (see Section 12.1.3).
2. Safety laboratories should include CBC with differential: hematology to include parameters listed in Section 12.1.6.1; chemistry to include parameters listed in Section 12.1.6.2.
3. ctDNA blood testing will occur at a central laboratory. Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date. Details for blood collection are provided in the Central Laboratory Manual
4. Check for adverse events.

Table 17: Schedule of Assessments: Follow-up Period (Year 1 to Year 2)

Assessment	Follow-up Period								
Visit	**Visit 14**	**Visit 15**	**Visit 16**	**Visit 17**	**Visit 18**	**Visit 19**	**Visit 20**	**Visit 21**	**Visit 22[1]**
Week (± days)	**Week 22 (±3 days)**	**Week 26 (±7 days)**	**Week 34 (±14 days)**	**Week 46 (±14 days)**	**Week 58 (±14 days)**	**Week 70 (±14 days)**	**Week 82 (±14 days)**	**Week 94 (±14 days)**	**Week 102 (±14 days)**
Physical examination[2]					X				
Vital signs					X				
Weight					X				
ECOG	X	X		X	X	X	X	X	X
CT with contrast[3]		X		X	X	X	X	X	X
Clinical laboratory (local laboratory)[4]	X								
ctDNA (central laboratory)[5]		X		X		X			X
Serum CEA/CA19-9 (local laboratory)[4]		X		X	X	X	X	X	X
Standard of care biopsy (central laboratory)[6]		X		X	X	X	X	X	X
Adverse events[7]	X	X	X	X	X	X	X	X	X

CA=carbohydrate antigen; CBC=complete blood count; CEA=carcinoembryonic antigen; CRC=colorectal cancer; CT=computed tomography; ctDNA=circulating tumor deoxyribonucleic acid; ECOG=Eastern Cooperative Oncology Group; MRI=magnetic resonance imaging; PBMC=peripheral blood mononuclear cell; PDAC=pancreatic ductal adenocarcinoma

1. All enrolled subjects should be followed in the Follow-Up period for overall survival and disease status. As part of the study sites may conduct searches of public records, such as those establishing survival status, to obtain survival data as needed (ie: subject lost to follow-up, withdraws from study, etc.).
2. Physical examination per standard of care (see Section 12.1.3).
3. A visit window of ±14 days is permitted for imaging assessments during the Follow-up Period. For subjects with IV contrast allergy/intolerance, MRI may be performed. The same modality used for the screening imaging should be used for all subsequent on-study imaging. If a subject has had confirmed radiographic progression via iRECIST and has initiated subsequent therapy, further imaging is not required. If a subject has not yet had iCPD prior to subsequent therapy, continue with scans until iCPD is confirmed.
4. Safety laboratories should include CBC with differential: hematology to include parameters listed in Section 12.1.6.1; chemistry to include parameters listed in Section 12.1.6.2. Serum biomarkers CA19-9 [PDAC], CEA [PDAC/CRC] - If a subject has had confirmed radiographic progression via iRECIST and has initiated subsequent therapy, further serum biomarker testing is not required. If a subject has not yet had iCPD prior to subsequent therapy, continue with serum biomarker collection until iCPD is confirmed.
5. ctDNA blood testing will occur at a central laboratory. Details for blood collection are provided in the Central Laboratory Manual. If a subject has had confirmed radiographic progression via iRECIST and has initiated subsequent therapy, further ctDNA collection is not required. If a subject has not yet had iCPD prior to subsequent therapy, continue with ctDNA collection until iCPD is observed. Subjects that were ctDNA negative at baseline (ie: Screening and

Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date.

6. Post-Visit 2 standard of care biopsy to be obtained if new lesions are observed on radiographic imaging and when the investigator judges that tissue can be safely obtained. The sample will be collected within +30 days of the radiographic evidence of new lesions and will be used to evaluate tumor-infiltrating T cells, the tumor microenvironment and maybe biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.
7. Long-term observation for post-dose vaccination adverse events will be recorded for any new events that occur up to 30 days post Visit 13/last dose. Any event that occurs during this timeframe will continue to be followed until the event returns to baseline or the subject discontinues from the study.

Table 18: Schedule of Assessments: Follow-up Period (Year 2 to Year 3)

Assessment	**Follow-up Period**			
Visit	**Visit 23**	**Visit 24**	**Visit 25**	**Visit 26/ End of Study[1]**
Week (± days)	**Week 114 (±14 days)**	**Week 126 (±14 days)**	**Week 138 (±14 days)**	**Week 150 (±14 days)**
ECOG	X	X	X	X
CT with contrast[2]	X	X	X	X
ctDNA (central laboratory)[3]		X		X
Serum CEA/CA19-9 (local laboratory)[4]	X	X	X	X
Standard of care biopsy (central laboratory)[5]	X	X	X	X
Adverse events[6]	X	X	X	X

CA=carbohydrate antigen; CBC=complete blood count; CEA=carcinoembryonic antigen; CRC=colorectal cancer; CT=computed tomography; ctDNA=circulating tumor deoxyribonucleic acid; ECOG=Eastern Cooperative Oncology Group; MRI=magnetic resonance imaging; PBMC=peripheral blood mononuclear cell; PDAC=pancreatic ductal adenocarcinoma

1. All enrolled subjects should be followed in the Follow-Up period for overall survival and disease status. As part of the study sites may conduct searches of public records, such as those establishing survival status, to obtain survival data as needed (ie: subject lost to follow-up, withdraws from study, etc.).
2. A visit window of ±14 days is permitted for imaging assessments during the Follow-up Period. For subjects with IV contrast allergy/intolerance, MRI may be performed. The same modality used for the screening imaging should be used for all subsequent on-study imaging. If a subject has had subsequent therapy, further imaging is not required.
3. ctDNA blood testing will occur at a central laboratory. Details for blood collection are provided in the Central Laboratory Manual. If a subject has had confirmed radiographic progression via iRECIST and has initiated subsequent therapy, further ctDNA collection is not required. If a subject has not yet had iCPD prior to subsequent therapy, continue with serum biomarker collection until iCPD is confirmed. Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date.
4. If a subject has not yet had iCPD prior to subsequent therapy, continue with serum biomarker collection until iCPD is confirmed.
5. Post-Visit 2 standard of care biopsy to be obtained if new lesions are observed on radiographic imaging and when the investigator judges that tissue can be safely obtained. The sample will be collected within +30 days of the radiographic evidence of new lesions. The sample will be used in evaluating tumor-infiltrating T cells, the tumor microenvironment and may also be used for biomarker genetic sequencing. Details for central laboratory sample collections are provided in the Central Laboratory Manual.
6. Long-term observation for post-dose vaccination adverse events will be recorded will be recorded if an adverse event began within 30 days of last dose of treatment and continues in the follow-up period.

6.1.6. Risk Determination for Investigational In Vitro Diagnostics

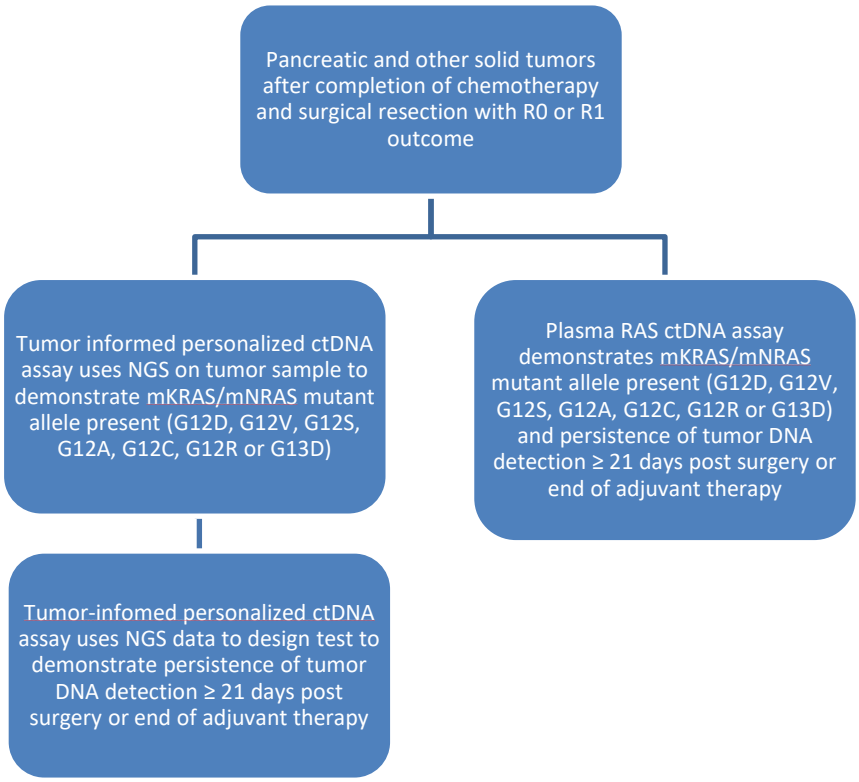
Protocol ELI-002-201 incorporates 2 different investigational in vitro diagnostics (IVDs). Only one IVD will be used for each subject's enrollment, based on ability to access acceptable tumor sample and/or upon Elicio instruction.

1. Plasma RAS ctDNA assay: This approach requires a single ctDNA assay to monitor both KRAS mutation and MRD status performed at a central laboratory under CLIA requirements.
2. A tissue-informed personalized ctDNA assay will be used. This approach requires two assays, a tissue based next generation sequencing, or NGS test (KRAS mutation) followed by a personalized ctDNA assay (MRD status). Both assays are performed at central laboratories under CLIA and CAP requirements.

For the plasma RAS ctDNA assay, to determine eligibility, subjects will have their blood tested to confirm the presence of at least 1 of the mKRAS/mNRAS alleles targeted by ELI-002 7P and the detection of ctDNA in plasma in a single assay (see Figure 4).

For the tumor-informed personalized ctDNA assay, to determine eligibility, subjects will have their tumor specimen assayed using NGS to confirm presence of at least 1 of the mKRAS/mNRAS alleles targeted by ELI-002 7P. Next, the NGS data will be used to identify subject-specific somatic variants and design a personalized assay, per subject, for the detection of ctDNA in plasma (see Figure 4).

Figure 4: Flow Diagram of Eligibility Determination for Protocol ELI-002-201



In the event of insufficient tumor sample to permit NGS and negative ctDNA status on plasma RAS ctDNA assay, screening subjects may enroll if a historical FDA approved KRAS mutation test confirms presence of at least 1 of the 7 mKRAS/mNRAS alleles targeted by ELI-002 7P.

Subjects eligible to participate must have at least 1 of the mKRAS/mNRAS alleles targeted by ELI-002 7P. Subjects participating in Phase 1 must in addition have either detectable ctDNA or a successively rising serum tumor biomarker (CA19-9 or CEA) or individual serum tumor biomarker above a threshold associated with relapse, in samples taken ≥21 days after surgery or after the last administration of adjuvant therapy, whichever comes last in the subject's treatment plan. The ctDNA status is determined by the investigational IVDs.

Elicio considers the use of ctDNA investigational IVDs in Protocol ELI-002-201 to be a nonsignificant risk. The planned administration of ELI-002 7P occurs after standard surgery and neoadjuvant and/or adjuvant chemotherapy and before relapse characterized by the re-emergence of clinical or radiographic symptoms. As there is no standard of care treatment in this space, a false positive or false negative will not result in a substitution or omission of standard treatment.

6.1.6.1. Description of the IVDs

6.1.6.1.1. Plasma RAS ctDNA Assay

The plasma ctDNA assay was designed to deliver a clinical grade, ultra-sensitive liquid biopsy solution for the identification of gene mutations in KRAS and ctDNA detection. This test is intended for the detection of ctDNA isolated from plasma. The plasma ctDNA assay will identify

subjects who are positive for any of the specific mutations within the KRAS or NRAS genes that are targeted by the ELI-002 product candidate. In addition, the plasma ctDNA assay will inform the presence or absence of ctDNA. Unlike the tumor-informed personalized assay, tumor tissue is not required for KRAS mutation identification; instead, a single plasma sample will inform both KRAS mutation type and ctDNA positivity (MRD).

6.1.6.1.2. Tumor-informed Personalized ctDNA Assay

The tumor informed personalized ctDNA assay is composed of two parts: NGS from tumor DNA to identify tumor-specific mutations and a plasma-based ctDNA assay to detect ctDNA. The NGS test is a CAP- and CLIA-validated laboratory developed test. The assay compares the exome sequence of tumor and germline DNA, facilitating identification of tumor-specific DNA alterations. The NGS test will identify subjects who are positive for any of the specific mutations (e.g., G12D, G12R, G12V, G12A, G12C, G12S, G13D) within the KRAS or NRAS genes targeted by ELI-002 7P. In addition, the NGS data will serve as the input for subject specific personalized MRD ctDNA assay. Tumor tissue and matched normal blood is required for the NGS portion of the tumor-informed ctDNA assay.

The standard MRD assay is based on tracking driver clonal/truncal mutations that occur early in tumor initiation. This ctDNA tracks a subset of these early clonal variants to detect residual ctDNA with significantly increased sensitivity using an error-corrected next generation sequencing methodology. The presence of ctDNA indicates MRD and changing levels of ctDNA may predict response to treatment. A plasma sample is required for the MRD portion of the tumor-informed ctDNA assay.

6.1.6.2. Applying the IVD Results in the Clinical Trial

Study ELI-002-201 will evaluate ELI-002 as adjuvant therapy for subjects with mKRAS/mNRAS^{+} solid tumors who have no standard available treatment. These subjects have undergone surgical resection and may have MRD as determined by detectable ctDNA. MRD will be defined as the presence of ctDNA in the subject's body, in which the primary tumor has been removed and the subject is currently without clinical signs of disease. The mKRAS/mNRAS^{+} status will be confirmed from plasma RAS ctDNA samples or by NGS from tumor samples versus normal germline, and ctDNA status will be determined by either the plasma RAS or tumor-informed ctDNA assays at screening. The status of mKRAS/mNRAS (and MRD for Phase 1 subjects) will be used to assess a subject's eligibility for enrollment.

The prevalence of mutations in KRAS and NRAS to be evaluated by the IVDs is reviewed in detail in protocol Section 4.1. The prevalence of NRAS mutations is highest in CRC among tumor types included in this study, while KRAS mutations are found across all histologies.

6.2. Endpoints

6.2.1. Phase 1 Primary Endpoints

The primary endpoints of Phase 1 are:

- To evaluate safety as assessed by the incidence of AEs and clinically significant changes in laboratory tests and vital signs

6.2.2. Phase 1 Secondary Endpoint

The secondary endpoint of Phase 1 is:

- To report the proportion of subjects with ctDNA reduction or clearance, defined as reduction or clearance of ctDNA from baseline, or if ctDNA was not detectable at baseline, serum tumor biomarker (such as CA19-9 and CEA) reduction and clearance compared to baseline

6.2.3. Phase 1 Exploratory Endpoints

The exploratory endpoints of Phase 1 are:

- Median DFS (per investigator) and median OS
- Duration of biomarker (ctDNA or serum tumor biomarker) reduction or clearance, defined as the time from the date of the first decreased and/or negative biomarker to the earliest date of any of the following events:
  - Subsequent increased/positive biomarker
  - Subsequent disease relapse
  - Death due to any cause
- Change relative to baseline in:
  - Phase 1A only: Serum cytokines IL-2, IFNγ, IL-6, IL-10, and TNFα
  - PROs: EORTC QLQ-C30 and QLQ-PAN26, or QLQ-CR29
  - Immunogenicity of ELI-002 7P determined by magnitude of response and fold-change from baseline using assays such as ICS, Fluorospot, and/or dextramer+ T cells for subjects with HLA alleles for which dextramer/s is/are available
  - Biomarker levels (ctDNA, CA19-9, and CEA)
  - Immune cell infiltrate and tumor microenvironment if standard-of-care biopsies are obtained to confirm new lesions

6.2.4. Phase 2 Primary Endpoints

The primary endpoint of Phase 2 is:

- DFS (per investigator)

6.2.5. Phase 2 Secondary Endpoints

The secondary endpoints of Phase 2 are:

- 1-year DFS rate
- OS

- BRR - Proportion of subjects with biomarker response (ctDNA or serum tumor biomarker) reduction and clearance, defined as reduction or clearance in biomarker compared to baseline
- Safety as assessed by the incidence of AEs and clinically significant changes in laboratory tests and vital signs

6.2.6. Phase 2 Exploratory Endpoints

The exploratory endpoints of Phase 2 are:

- irORR in subjects who crossover to ELI-002 7P from observation after relapse according to iRECIST
- Change relative to baseline in:
  - Immunogenicity of ELI-002 7P determined by the magnitude of response and the fold-change from baseline, using assays such as ICS, Fluorospot, and/or dextramer^{+} T cells for subjects with HLA alleles for which dextramer/s is/are available
  - Biomarker levels
  - Immune cell infiltrate and tumor microenvironment if standard-of-care biopsies are obtained to confirm new lesions

6.3. Number of Subjects

Approximately 164 subjects will be enrolled in this trial: approximately 12 subjects in Phase 1A, up to 17 subjects in Phase 1B (if Elicio opens this cohort), and 135 subjects in Phase 2.

6.4. Treatment Assignment

Phase 1A: Approximately 12 subjects (Cohort 1) are planned to receive SC injections of ELI-002 7P during the Immunization Period and the Booster Period.

Phase 1B: Approximately 9-17 subjects (Cohort 2) will receive SC injections of ELI-002 7P during the Immunization Period and the Booster Period. Phase 1B (Cohort 2, CRC) may be opened to enrollment by Elicio either concurrent or subsequent to Phase 2. If Cohort 2 is opened this will be documented in a study memo sent to all clinical sites and maybe submitted to IRBs, per IRB guidance.

Phase 2: Approximately 135 subjects (PDAC Cohort) will be randomized 2:1 to ELI-002 7P versus SOC (observation), respectively. Subjects randomized to ELI-002 7P (Cohort 3A) will receive SC injections of ELI-002 7P during the Immunization Period and the Booster Period. Subjects randomized to SOC (observation; Cohort 3B) will have the same safety and efficacy evaluations and follow the same assessment schedule as subjects randomized to ELI-002 7P. In Phase 2, subjects randomized to SOC (observation) will be eligible to cross over to intervention (ELI-002 7P, Cohort 3C) after confirmed progressive disease via iRECIST is documented.

6.5. Dose Adjustment Criteria

An IDMC will have the authority to assess and recommend dosing changes (ie, dose reductions) due to safety concerns.

There are no PK assessments in this protocol, therefore, there will be no consideration for PK criteria for adjustment or stopping of doses.

6.6. Safety Criteria for Temporarily or Permanently Stopping the Trial

The sponsor's medical monitor will be continuously monitoring the safety of subjects. In addition, the cumulative safety will be reviewed by the IDMC at the following anticipated key time points:

- After the 12th subject in Phase 1A
- After the approximately 20 biomarker evaluable subject completes Visit 7 in Phase 2
- After approximately 71 DFS events have occurred in Phase 2
- Ad hoc as necessary

The trial may be temporarily or permanently stopped by the sponsor, if any subject death occurs attributed to administration of ELI-002 7P (ie, if there is Grade 5 toxicity that is definitely, probably, or possibly attributed to trial treatment).

Any potential re-initiation of the trial will be discussed by the Sponsor, with the support of the IDMC and in consultation with the FDA, if necessary.

6.7. Management of Study Drug-Related Events

6.7.1. Temporarily Suspending Treatment Administration

In the event the ELI-002 7P dose is held, the other visit procedures should continue to be performed for that visit (with the exception of dosing and the reactogenicity diary). If a dose is missed for reasons other than toxicity, the subject may receive a make-up dose following approval from the Elicio medical monitor; dosing would then continue per the protocol dosing schedule. If a dose is missed due to toxicity, the subject should not receive any make-up dose and will remain on the original protocol schedule (ie, their next dose will be at the next protocol-specified dose if they meet the criteria for dosing). Treatment administration will be resumed as soon as the subject's condition allows or at the investigator's discretion after Sponsor approval.

6.7.2. Permanent Stopping Treatment Administration

If a subject meets any of the following conditions, the subject will be required to discontinue the trial treatment administration but should continue other trial-related procedures as specified for the follow-up period of the study. (See Section 7.4 for more information on procedures for subjects withdrawn from trial treatment.)

1. Any intolerable AE, at the investigator's discretion
2. During study treatment:

- Any investigational product use other than ELI-002 7P
- Other anti-cancer treatment

3. Non-compliance with trial treatments/procedures. If a subject misses ≥2 trial visits without underlying toxicity, the subject should be re-instructed regarding dosing and follow up and continue trial participation. If a subject continues to miss trial visits without toxicity and despite re-instruction, they should be discontinued from the trial treatment phase but follow up data should be collected as possible.
4. The subject requests to be withdrawn from the trial treatment

For subjects whose treatment is discontinued prematurely, the procedures outlined for End-of-Treatment/Visit 13 (Table 10 or Table 16 for subjects in the Observation Cohort) will be carried out and, if possible, prior to the initiation of any other anti-cancer treatment. These subjects should then enter the Follow-up Period, where procedures listed in Table 11 (or Table 17 for subjects in the Observation Cohort) and Table 12 (or Table 18 for subjects in the Observation Cohort) will be performed. In the event that a subject will not continue to be evaluated in the Follow-up Period, the End-of-Study visit (Visit 26) should be scheduled and all procedures performed.

6.7.3. Dose-limiting Toxicity Guidelines

In Phase 1A (first 12 subjects enrolled), a DLT will be defined as any event at least possibly related to ELI-002 7P as follows:

a. Any Grade ≥ 3 non-hematologic toxicity except asymptomatic laboratory abnormalities (see Section 12.2.1.1)
b. Any Grade ≥ 3 toxicity involving major organ systems for greater than 72 hours and occurring within 28 days of SC administration
c. Grade 3 CRS that does not resolve to ≤ Grade 2 within 7 days
d. Any Grade 4 CRS that does not improve to < Grade 2 within 72 hours
e. Any Grade ≥ 3 autoimmune disorder
f. Any Grade ≥ 3 rash that does not resolve to ≤ Grade 1 within 7 days with appropriate treatment

The DLT observation period will be 28 days following the first SC administration of ELI-002 7P.

Grade 3 maculo-papular or acneiform rashes are commonly observed after SC delivery of therapeutic cancer vaccines and are not dose-limiting. Management of maculo-papular or acneiform rashes is provided in Section 6.8.2.

6.8. Management of Risks and Toxicities

6.8.1. Management of On-target Off-tumor Toxicity

Examples of on-target off-tumor toxicities have been observed in different immunotherapies where these events were not expected from pre-clinical data. It is difficult to anticipate all “autoimmune

inflammation" that theoretically may be induced by an on-target off-tumor effect of ELI-002 7P. Any observed treatment-emergent autoimmune events must be followed closely. The exact diagnostic and the therapeutic approach to be followed will be left to the investigator's discretion who can contact at any time the Sponsor Medical Monitor. The Sponsor may discuss any specific case with the IDMC members to evaluate appropriate therapeutic action.

6.8.2. Management of Maculo-Papular or Acneiform Rashes, Injection Site Reactions

For routine injection site reactions manifested as maculo-papular or acneiform rashes, erythema, induration, pruritis and pain, topical application of cool compresses, or antihistamines may be used. If needed, systemic antihistamines and antipyretics may be added. Injection site reactions following administration of products containing oligonucleotides, including CpG oligonucleotides, are common and are generally managed conservatively with application of cold compresses and alternation of the site of injection [van Meer et al., 2016]; rarely, ulceration requires administration of systemic anti-inflammatory agents such as colchicine.

7. SELECTION AND WITHDRAWAL OF SUBJECTS

7.1. Subject Inclusion Criteria

Subjects must meet the following criteria on screening examination to be eligible to participate in the trial. The American Joint Committee on Cancer (AJCC) staging criteria (8th edition) should be used for all tumor types:

1. Male or female subjects aged ≥18 years
2. Histologically or cytologically confirmed diagnosis of solid tumor
3. Laboratory value that demonstrates at least 1 of the 7 mKRAS/NRAS alleles (eg, G12D, G12V, G12S, G12A, G12C, G12R or G13D) targeted by ELI-002 7P
4. For phase 1 subjects only: high relapse risk, as evidenced by biomarker data with the last value obtained ≥21 days after surgery or last administration of adjuvant therapy, whichever comes last in the specific subject's treatment plan (values must not be attributable to a non-cancer condition, such as pancreatitis, peritonitis, postoperative leak/fistula, or biliary obstruction) as follows:
    a. ctDNA blood test positive, or
    b. successive rising values (≥1 week apart) in a serum tumor biomarker (such as CA19-9 and CEA), or
    c. individual biomarker values CA19-9 ≥90 U/mL, or CEA ≥15 ng/mL
5. If subject has PDAC:
    a. Up front resectable (ie, resectable or borderline resectable) stage I, II, or III disease per current AJCC staging criteria, with radiographic NED (no evidence of disease) status and enroll within 6 months following completion of locoregional treatment (defined as date of resection for subjects that received total neoadjuvant treatment or date of last dose of treatment for those that received peri-operative or adjuvant treatment). Equivocal radiographic findings (eg, subcentimeter lesions, potential resolving soft tissue changes) are acceptable
    b. Prior treatment with a SOC chemotherapy or chemotherapy/chemoradiation (eg, FOLFIRINOX, gemcitabine/nab-paclitaxel, or 5-FU/capecitabine) according to NCCN pancreatic cancer guidelines and administered in neoadjuvant and/or adjuvant setting
    c. Successful surgical resection (use of microwave ablation [eg, Nanoknife®] is permitted): complete resection (R0) or with microscopic residual disease (R1)
6. If subject has CRC:
    a. Stage IV oligometastatic disease per current AJCC staging criteria, with radiographic NED status and enroll within 6 months following locoregional treatment (defined as date of resection for subjects that received neoadjuvant treatment or date of last dose of treatment for those that received peri-operative or adjuvant treatment). Equivocal radiographic findings (eg, subcentimeter lesions, potential resolving soft tissue changes) are acceptable

b. Prior treatment with standard of care chemotherapy (eg, FOLFOX, CAPEOX) according to NCCN colon cancer guidelines and administered in neoadjuvant and/or adjuvant setting
c. If the subject has rectal cancer, prior treatment with standard of care chemoradiation (eg, 5-FU or capecitabine- based) according to NCCN rectal cancer guidelines and administered in the neoadjuvant or adjuvant setting, or as total neoadjuvant therapy
d. Successful surgical resection of primary tumor and oligometastatic lesion(s) (use of microwave ablation [eg, Nanoknife®] is permitted): complete resection (R0) or with microscopic residual disease (R1)

7. Screening CT is negative for recurrent disease
8. Laboratory values must be:
   a. Absolute lymphocyte count ≥1.0 x 10^9/L (or if the pre-cytotoxic therapy values were less than 1.0 x 10^9/L, a return to that baseline level or above)
   b. Platelets ≥100 x 10^9/L
   c. Hemoglobin ≥9 g/dL
   d. Total bilirubin ≤1.5 x ULN, unless subject has documented Gilbert's syndrome
   e. Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≤2.5 x ULN (except for non-alcoholic fatty liver disease where AST or ALT ≤5 x ULN is acceptable)
   f. Creatinine <1.5 mg/dL (or if creatinine ≥1.5 mg/dL, the creatinine clearance calculated by the Cockcroft-Gault formula must be ≥60 mL/min)
   g. Albumin ≥2.5 g/dL
   h. Serum IL-6 <500 pg/mL
9. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
10. Subjects have recovered from prior surgery, chemotherapy, or radiation without any ongoing medical/surgical issues (excluding resolved, low grade, or chronic stable findings such as neuropathy, impaired hearing, or reproductive changes)
11. Women of childbearing potential and men with a female partner of childbearing potential must be willing to use effective methods of contraception during trial participation and for 30 days after the last dose of trial drug to prevent pregnancy as follows:
    a. Women: willing to use contraceptives with a failure rate <1% per year when used consistently and correctly, eg, combined oral contraceptives, barrier methods, approved contraceptive implant, long- term injectable contraception, or intrauterine device, sexual abstinence, or a vasectomized partner

       Definitions that meet the criteria to not be considered of childbearing potential:

       – Women >1 year postmenopausal (defined as 1 year or longer since last menstrual period) AND >55 years of age
       – Postmenopausal women (as defined above) and <55 years of age with a negative pregnancy test within 1 week of first dose
       – Women who were surgically sterilized at least 3 months prior to enrollment

b. Men: willing to use an acceptable method of birth control, eg, condom with spermicide. In addition, men must refrain from donating sperm.

12. Able to provide written (signed) informed consent to participate in the trial prior to any trial specific screening procedures

7.2. Subject Exclusion Criteria

Subjects must not meet any of the following criteria on screening examination to be eligible to participate in the trial:

1. Has received an anti-tumor therapy including investigational drug within 4 weeks prior to trial drug administration
2. Is currently receiving any agent with a known effect on the immune system, unless at dose levels that are not immunosuppressive (eg, inhaled corticosteroids at doses used for the treatment of asthma) (see Section 8.1.1)
3. Has previously received HB-700, ELI-002 or other cancer vaccine
4. Has any other serious illnesses or medical conditions such as, but not limited to:
   a. Any uncontrolled infection
   b. Uncontrolled cardiac failure classification III or IV (New York Heart Association)
   c. Myocardial infarction ≤6 months prior to enrollment
   d. Serious or uncontrolled cardiac arrhythmia, unstable angina
   e. History of or active auto-immune disease (excluding mild conditions, such as vitiligo, type 1 diabetes, psoriasis)
   f. History of or active interstitial lung disease/pneumonitis requiring treatment with systemic steroids
   g. Prior organ transplant
5. Has received prior checkpoint inhibition (ie: anti-PD-1, anti-PD-L1, anti-CTLA4)
6. Known history of positive tests for human immunodeficiency virus/acquired immune deficiency syndrome (HIV)/AIDS or hepatitis B
7. Hepatitis C subjects are excluded unless they have had a sustained virologic response to direct-acting antiviral therapy; such subjects must have an undetectable hepatitis C virus RNA at screening
8. Active severe acute respiratory syndrome (SARS)-CoV-2. Testing is not required in the absence of symptoms. If symptoms are present, dosing should not proceed until a return to baseline.
9. Pregnant or lactating females
10. Women of childbearing potential who have a confirmed positive pregnancy test result at Baseline. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required.
11. Had any other malignancies within the last 3 years where, in the investigator's judgement, there is anticipation that the subject would need treatment for the other malignancy in the next 2 years, except for endocrine therapy for early-stage tumors.

12. Known malignant brain lesion(s).
13. Pancreatic neuroendocrine tumor, pancreatic ampullary tumor, or germline BRCA 1/2
14. If a subject has pancreatic cancer:
    a. Any tumor mutation where specific therapy is approved, and the subject is able to receive the approved therapy (except in cases where the subject cannot receive the approved therapy, such as due to a contraindication)
15. If subject has CRC:
    a. Prior immunotherapy as part of their adjuvant regimen
    b. Mismatch repair defective (MSI+)
    c. Any tumor mutation where specific therapy is approved, and the subject is able to receive the approved therapy

7.3. Phase 2 Subject Crossover Eligibility Criteria

Once a subject randomized to the observation cohort (Cohort 3B) is determined to have confirmed radiographic progression via iRECIST, they may be able to cross over to ELI-002 7P treatment (Cohort 3C), following confirmation of iCPD with Elicio. Crossover to Cohort 3C can occur up through the time that the last subject from Cohorts 3A and 3B completes the study (a study memo will be released to all active sites when this happens). At that time and prior to beginning dosing at Visit 2, the subject will be assessed and must meet all the criteria below:

1. Laboratory values must be:
    a. Absolute lymphocyte count ≥1.0 x 10^9/L (or if the pre-cytotoxic therapy values were less than 1.0 x 10^9/L, a return to that baseline level or above)
    b. Platelets ≥100 x 10^9/L
    c. Hemoglobin ≥9 g/dL
    d. Total bilirubin ≤1.5 x ULN, unless subject has documented Gilbert's syndrome
    e. AST or ALT ≤2.5 x ULN (except for non-alcoholic fatty liver disease where AST or ALT ≤5 x ULN is acceptable)
    f. Creatinine <1.5 mg/dL (or if creatinine ≥1.5 mg/dL, the creatinine clearance calculated by the Cockcroft-Gault formula must be ≥60 mL/min)
    g. Albumin ≥2.5 g/dL
    h. Serum IL-6 <500 pg/mL
2. ECOG performance status of ≤2
3. Men and women of childbearing potential must be willing to use effective methods of contraception during trial participation and for 30 days after the last dose of trial drug to prevent pregnancy as follows:
    a. Women: willing to use contraceptives with a failure rate <1% per year (eg, combined oral contraceptives, barrier methods, approved contraceptive implant, long-term injectable contraception, or intrauterine device)

       Definitions that meet the criteria to not be considered of childbearing potential:

- Women >1 years postmenopausal (defined as 1 year or longer since last menstrual period) AND >55 years of age.
- Postmenopausal women (as defined above) and <55 years of age with a negative pregnancy test within 1 week of first dose.
- Women who were surgically sterilized at least 3 months prior to enrollment.

b. Men: willing to use an acceptable method of birth control (eg, condom with spermicide). In addition, men must refrain from donating sperm.

4. Must not have discontinued early from Cohort 3B
5. Must not have received any intervening anti-tumor therapy including investigational drug prior to crossover to Cohort 3C (ELI-002 7P treatment)
6. Must not currently be receiving any agent with a known effect on the immune system, unless at dose levels that are not immunosuppressive (eg, inhaled corticosteroids at doses used for the treatment of asthma) (see Section 8.1.1)
7. No other serious illnesses or medical conditions such as, but not limited to:
   a. Any uncontrolled infection
   b. Uncontrolled cardiac failure classification III or IV (New York Heart Association)
   c. Myocardial infarction ≤6 months prior to enrollment
   d. Serious or uncontrolled cardiac arrhythmia, unstable angina
   e. History of or active auto-immune disease (excluding mild conditions, such as vitiligo, type 1 diabetes, psoriasis)
   f. History of or active interstitial lung disease/pneumonitis requiring treatment with systemic steroids
   g. Prior organ transplant
8. Must not have active SARS-CoV-2. Testing is not required in the absence of symptoms. If symptoms are present, dosing should not proceed until a return to baseline.
9. If the subject is female, must not be pregnant or lactating
10. Must not have known malignant brain lesion(s)

7.4. Subject Withdrawal Criteria

A subject may voluntarily withdraw or be withdrawn from the trial at any time for reasons including, but not limited to, the following:

- The subject wishes to withdraw from further participation.
- The subject is significantly noncompliant with the protocol.
- Continuation in the trial would be detrimental to the subject's safety in the opinion of the investigator.

Any subject who wishes to withdraw from the trial may do so at any time without it affecting their medical care. The investigator may withdraw a subject from the trial at any time if it is felt to be in the best interest of the subject.

If a subject is discontinued prematurely from further treatment, the investigator must provide an explanation in the subject source records, as well as the eCRF and perform all End of Treatment evaluations according to Visit 13 in Table 10 (or Table 16 for subjects in the Observation Cohort). These subjects should then enter the Follow-up Period, where procedures listed in Table 11 and Table 12 (or Table 17 and Table 18 for subjects in the Observation Cohort) will be performed. In the event that a subject will not continue to be evaluated in the Follow-up Period, the End-of-Study visit should be scheduled, and all procedures performed.

In the event that a subject does not return for the Follow-up evaluations, the investigator must make every effort to contact the subject to review all AEs and to determine the reason for dropping out (see Section 7.4.2).

In the event that a subject discontinues prematurely due to an AE or SAE assessed to be study drug-related, the event should be followed until it resolves (returned to normal or baseline values), stabilizes, or is judged by the investigator to be no longer clinically significant. Follow-up of an AE may also be continued at the request of the Sponsor Medical Monitor.

7.4.1. Subject Replacement

In Phase 1A, if any of the first 12 subjects discontinue for any reason other than toxicity prior to completing 28 days of ELI-002 7P therapy, a replacement subject will be added to the cohort until 6 subjects at each peptide dose complete 28 days of ELI-002 7P therapy. In Phase 2, once a subject is randomized, they will not be replaced for any reason.

7.4.2. Subjects Lost to Follow-up

If a subject is lost to follow-up, every attempt must be made to contact the subject and to determine the reason for dropping out. If the subject cannot be reached after three documented attempts over a reasonable amount of time, a certified letter must be sent to the subject asking them to contact the trial center for follow-up. Only after all the above documented attempts will a subject be considered lost to follow up.

8. TREATMENT OF SUBJECTS

8.1. Concomitant Medications

Subjects should receive medication appropriate to their health condition during the entire trial. All concomitant medications during the length of the trial, including screening, will be documented in the subject source record and in the appropriate electronic case report form (eCRF) page.

8.1.1. Prohibited Concomitant Medications

The following concomitant medications should not be used during study drug administration and are criteria for permanent stopping of the trial treatment administration for an individual subject

- Growth factors (except erythropoietin). The effect of growth factor administration on expansion and persistence of ELI-002 is unknown.
- Corticosteroids and other immunosuppressive agents except as needed for management of safety events. Systemic immunosuppressive agents should not be used during the trial, except if needed for counteracting an AE. However, the use of corticosteroids for anti-allergic reaction/symptoms (eg, pre/post tumor imaging [contrast product]) is allowed, topical and inhaled steroids is permitted.
- Complementary or alternative medicine use intended for anti-cancer effect (general supplements, such as for joint health, will be permitted)
- Cytotoxic agents and any other cancer therapy
- Investigational products/devices

8.2. Treatment Compliance

All subjects are expected to be fully complaint throughout the trial (see Section 6.7.2).

Subjects will receive SC injections of ELI-002 7P by qualified site staff who are under the supervision of the investigator or designee.

Treatment administration will be recorded on the eCRF.

8.3. Randomization and Blinding

ELI-002-201 is an open-label trial with a single arm for Phase 1A (Cohort 1) and 1B (Cohort 2) and 1 randomized cohort for Phase 2 (Cohort 3). Treatment will not be blinded.

In Phase 2 of the trial, approximately 135 subjects will be randomized 2:1 to ELI-002 7P or SOC (observation) (PDAC Cohort 3) via web-based technology (see Section 13.3 for further details regarding randomization).

Randomization, as well as vial dispensing for treatment preparation, will be managed by an interactive voice/web response system (IxRS). Please refer to the ELI-002-201 Investigational Product Manual (IPM) for more details.

9. TRIAL DRUG MATERIALS AND MANAGEMENT

9.1. Trial Drug

ELI-002 is an investigational product consisting of 2 drug products:

1. A mixture of lipid-conjugated peptide-based antigens (amphiphilic peptides, referred to as Amph-Peptides). During the study, the Amph-Peptide mixture (Amph-Peptides 7P) will be comprised of 7 Amph modified KRAS peptides (G12D, G12R, G12V, G12A, G12C, G12S, G13D).
2. A lipid-conjugated immune-stimulatory oligonucleotide (Amph-CpG-7909)

The ELI-002 7P admixture is prepared by combining the separately provided products in a diluent prior to dosing. The KRAS Amph-Peptides are provided in 5.0 mM, pH 4.5 acetate buffer in a 2-mL glass vial. The Amph-CpG-7909 is provided in water for injection in a 2-mL glass vial. These 2 drug products will then be provided to the clinical pharmacy for combination with 10X phosphate buffered saline (PBS) for administration to the subject as a drug product admixture. For further details, refer to the IPM.

The IPM will provide instructions for the admixing procedure as well as storage instructions.

9.2. Trial Drug Packaging and Labeling

The ELI-002 7P study product will be provided in 2 separate kits comprised of 10 vials of ELI-002 Amph-CpG-7909 and 10 vials of ELI-002 Amph-Peptides 7P. In addition, kits containing 10 vials of 10X PBS will be provided to sites. Each vial is for single use only and is labeled according to local regulatory requirements. ELI-002 7P is for SC injection.

9.3. Trial Drug Storage

The Amph-Peptides 7P contains a mixture of 7 KRAS Amph-Peptide drug substances. The Amph-Peptides 7P is provided as a clear, colorless to slightly yellow, sterile frozen liquid. The recommended storage condition is Freezer Storage at −25°C to −10°C. For further details please refer to the IPM.

The Amph-CpG-7909 drug product is a clear, colorless, sterile liquid fill for injection and the adjuvant will be produced by admixing with the Amph-Peptides 7P drug product. The intended storage condition is Freezer Storage at −25°C to −10°C. For further details please refer to the IPM.

9.4. Trial Drug Preparation

For details and instruction on preparation of study drug, please see the ELI-002-201 IPM.

9.5. Administration and Dosage

Subjects in Phase 1 and those subject randomized to Cohort 3A, or in the crossover cohort, Cohort 3C, will receive SC injections of ELI-002 7P during the Immunization Period at Visit 2 through Visit 7 (Table 8). Two months after the Immunization Period, subjects being treated with

ELI-002 7P will receive SC injections of ELI-002 7P during the Booster Period at Visit 10 through Visit 13 (Table 10).

The cohorts planned are as shown in Table 19.

Table 19: Phase 1 and Phase 2 Cohorts and Doses

Cohort	Tumor Type	Treatment
Phase 1A: ELI-002 7P Safety Evaluation		
1	mKRAS/mNRAS solid tumors	ELI-002 7P
Phase 1B: Dose Expansion Cohort		
2	CRC	ELI-002 7P
Phase 2: Randomized Cohorts		
3A	PDAC	ELI-002 7P
3B	PDAC	Observation
3C	PDAC	ELI-002 7P (crossover)

CRC=colorectal cancer; mKRAS=mutant Kirsten rat sarcoma; mNRAS=mutant neuroblastoma ras viral oncogene homolog; PDAC=pancreatic ductal adenocarcinoma

9.6. Trial Drug Accountability

The investigator is responsible for trial drug accountability, reconciliation, and record maintenance. Drug accountability records will be maintained during the trial, including the amount of trial drug received from the Sponsor (or Sponsor's designee), the amount distributed to each subject, and the amount of used/unused drug destroyed at the site or returned to the Sponsor for destruction.

The trial center will maintain a log of all trial drug prepared and administered to subjects, as well as destruction of used/unused vials. Administration of the drug product admix (the test article) will occur during the Immunization Period and the Booster Period, according to the Schedule of Assessments (Table 8 and Table 10, respectively).

Trial center personnel should refer to the ELI-002-201 IPM for instructions regarding disposal of any trial drug or used trial drug packaging.

9.7. Trial Drug Handling and Disposal

All used and unused trial drug supplies must remain stored at the clinical site in a secure location and within appropriate temperature conditions up until receiving instructions for destruction. Disposal of trial drug will be conducted in compliance with all applicable laws and regulations.

10. TIMING OF TRIAL PROCEDURES

10.1. Screening and Observation Period

Visit 1, the screening procedures, should occur between 1 and 56 days after signing the informed consent form. Subjects will provide written informed consent before any trial-related procedures are performed.

- Once a subject has consented among the first procedures will be:
  - A retrospective tumor tissue sample from the prior surgery will be requisitioned for NGS. Tumor DNA will be sequenced to guide ctDNA testing in subsequent blood samples and baseline tumor gene expression will be assessed (Table 7 and Table 13)
  - A blood sample will be collected and shipped per screening timelines provided by Elicio and the study Lab Manual. The somatic DNA from the blood sample will serve as a control to ensure only tumor-specific DNA is included for ctDNA testing
- Collect a urine sample for a pregnancy test for women of childbearing potential (local laboratory). If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required.
- Record demographic information (including sex, age, race and ethnicity).
- Record height and weight.
- Record medical and medication history, including cancer history/prior treatments and current medications.
- Review available eligibility criteria. While mKRAS/mNRAS and (for Phase 1 only) MRD results may not yet be available, the expectation is that these will be reviewed, and full eligibility determined, prior to leukapheresis and Visit 2.
- Perform a complete PE (see Section 12.1.3).
- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate). Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures should be performed during this 3-minute period.
- Perform a 12-lead ECG (to be reviewed by a cardiologist or clinical investigator according to institutional guidelines and practice).
- Perform an ECOG Scale of Performance Status. To be eligible, ECOG performance status must be 0 to 1.
- Perform a CT with contrast within 60 days of anticipated first ELI-002 7P dose. For subjects with IV contrast allergy/intolerance, MRI may be performed. The same modality should be used for all imaging throughout the trial.

- Collect a blood sample for clinical laboratory assessments, including the hepatitis C antibody test, HbA1c (Phase 2 subjects only) and serum IL-6 test (local laboratory; see Section 12.1.6).
- Collect a sample appropriate for the available test method for active COVID-19 infection (local laboratory), if needed per exclusion criterion #8.
- Collect a blood sample for ctDNA test ≥21 days post-surgery or after last administration of adjuvant treatment, whichever is last in the specific subject treatment plan (to be performed at a central laboratory).
- Collect blood sample(s) for serum tumor biomarker (local laboratory; Table 7 and Table 13). Biomarker values must be obtained ≥21 days post-surgery or after the last administration of adjuvant therapy, whichever comes last in the specific subject's treatment plan. In Phase 2, two serum biomarker values (at least one week apart) will be required in order to assess if the subject is biomarker evaluable for the protocol specified safety review. For definition of serum biomarker evaluable, please refer to inclusion criterion #4.
- Collect a leukapheresis for immunogenicity assessment (central laboratory). The leukapheresis must be collected once eligibility has been confirmed and prior to the first dose of ELI-002 7P. For subjects randomized to observation (SOC, Cohort 3B), the leukapheresis can be done at Visit 2, to accommodate subject schedule.
- Record any pre-treatment SAEs that have occurred.

10.1.1. Rescreening

Subjects are allowed to rescreen for the trial. No screening procedures will need to be repeated as long as the screening CT/MRI scan was performed ≤60 days from the time of the anticipated first dose of trial drug. If the CT/MRI scan was performed >60 days from the anticipated first dose, then it will need to be repeated and reviewed, to ensure that the subject is "negative for recurrent disease", per the protocol inclusion criteria.

Other screening evaluations can be repeated as deemed appropriate and necessary by the investigator.

10.2. Immunization Period

During the Immunization Period, subjects enrolled in Phase 1, and those either randomized to Cohort 3A or those who have crossed over to Cohort 3C will receive 4 weekly SC doses followed by 2 biweekly doses (Table 8). Subjects in Phase 2 randomized to Cohort 3B (observation) will have procedures as outlined below, without ELI-002 7P treatment (Table 14).

All laboratory samples should be taken prior to dosing on any study visit that includes dosing.

At **Visit 2 (Baseline, Week 1/Day 0) prior to trial drug administration,** the following visit procedures will include:

- Record any change in medical history since the previous visit. Subjects must have recovered from surgery without any ongoing medical/surgical issues.

- Record any change in cancer history and prior treatments since the previous visit.
- Perform a physical exam (PE) (see Section 12.1.3).
- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate).
- Record weight.
- Perform a 12-lead ECG (to be reviewed by a cardiologist or clinical investigator according to institutional guidelines and practice).
- Confirm ECOG Scale of Performance Status is 0 or 1.
- Record any change in concomitant medications since the previous visit.
- Collect a blood sample for clinical laboratory assessments(local laboratory; see Section 12.1.6).
- Collect a blood sample for ctDNA (to be performed at a central laboratory).
- Collect a blood sample for high resolution HLA typing (central laboratory).
- Record any pre-treatment SAEs that have occurred since the previous visit.
- Randomization of subjects in Phase 2 only: ELI-002 7P or SOC (observation)
- **Dose 1**: Trial drug administration for subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P. Subjects must be observed by study staff for at least 1-hour post-dose.

After dose administration the following procedures will occur:

- Subjects in Phase 1 and those in Phase 2 who are randomized (or cross-over) to ELI-002 7P will be provided with the reactogenicity diary to complete for 7 days following the dose. Subjects will be instructed how to complete the diary and to return the completed form at their next visit.

At **Visit 3 (Week 2)**, the following visit procedures will include:

- Perform a PE (see Section 12.1.3). This is not required for those subjects randomized to observation (Cohort 3B).
- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate). Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures were performed during this 3-minute period. This is not required for those subjects randomized to observation (Cohort 3B).
- Record weight. This is not required for those subjects randomized to observation (Cohort 3B).
- Confirm ECOG Scale of Performance Status. This is not required for those subjects randomized to observation (Cohort 3B).
- Record any change in concomitant medications since the previous visit.

- All laboratory samples should be taken prior to dosing on any study visit that has dosing.
  - Collect a blood sample for clinical laboratory assessments (local laboratory; see Section 12.1.6). This is not required for those subjects randomized to observation (Cohort 3B).
- Record any AEs since last visit.
- **Dose 2:** Trial drug administration for subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P. Subjects must be observed by study staff for at least 1-hour post-dose.
- Subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P will be provided with the reactogenicity diary to complete for 7-days following the dose. Subjects will be instructed how to complete the diary and to return the completed form at their next visit.

At **Visit 4 (Week 3)**, the following visit procedures will include:

- Perform a PE (see Section 12.1.3). This is not required for those subjects randomized to observation (Cohort 3B).
- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate). Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures were performed during this 3-minute period. This is not required for those subjects randomized to observation (Cohort 3B).
- Record weight. This is not required for those subjects randomized to observation (Cohort 3B).
- Confirm ECOG Scale of Performance Status. This is not required for those subjects randomized to observation (Cohort 3B).
- Record any change in concomitant medications since the previous visit.
- All laboratory samples should be taken prior to dosing on any study visit that has dosing.
  - Collect a blood sample for clinical laboratory assessments(local laboratory; see Section 12.1.6). This is not required for those subjects randomized to observation (Cohort 3B).
- Record any AEs since last visit.
- **Dose 3**: Trial drug administration for subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P. Subjects must be observed for safety for at least 1-hour post-dose.
- Subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P will be provided with the reactogenicity diary to complete for 7-days following the dose. Subjects will be instructed how to complete the diary and to return the completed form at their next visit.

At **Visit 5 (Week 4)**, the following visit procedures will include:

- Perform a PE (see Section 12.1.3). This is not required for those subjects randomized to observation (Cohort 3B).
- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate). Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures were performed during this 3-minute period. This is not required for those subjects randomized to observation (Cohort 3B).
- Record weight. This is not required for those subjects randomized to observation (Cohort 3B).
- Confirm ECOG Scale of Performance Status. This is not required for those subjects randomized to observation (Cohort 3B).
- Record any change in concomitant medications since the previous visit.
- All laboratory samples should be taken prior to dosing on any study visit that has dosing.
  - Collect a blood sample for clinical laboratory assessments(local laboratory; see Section 12.1.6). This is not required for those subjects randomized to observation (Cohort 3B).
- Record any AEs since last visit.
- **Dose 4**: Trial drug administration for subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P. Subjects must be observed for safety for at least 1-hour post-dose.
- Subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P will be provided with the reactogenicity diary to complete for 7-days following the dose. Subjects will be instructed how to complete the diary and to return the completed form at their next visit.

At **Visit 6 (Week 6)**, the following visit procedures will include:

- Perform a PE (see Section 12.1.3).
- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate). Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures were performed during this 3-minute period.
- Record weight.
- Confirm ECOG Scale of Performance Status.
- Record any change in concomitant medications since the previous visit.
- All laboratory samples should be taken prior to dosing on any study visit that has dosing.
  - Collect a blood sample for clinical laboratory assessments(local laboratory; see Section 12.1.6).

  - Collect a whole blood sample for immunogenicity testing (central laboratory). Following the 16th subject being enrolled into Cohort 3B (observation), all subsequent observation cohort subjects will not require PBMC collection. The date of the 16th subject being enrolled is documented in a study level memo for site reference.
  - Collect a blood sample for ctDNA. Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date.
- Record any AEs since last visit.
- **Dose 5**: Trial drug administration for subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P. Subjects must be observed for safety for at least 1-hour post-dose.
- Subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P will be provided with the reactogenicity diary to complete for 7-days following the dose. Subjects will be instructed how to complete the diary and to return the completed form at their next visit.

At **Visit 7 (Week 8)**, the following visit procedures will include:

- Perform a PE (see Section 12.1.3). This is not required for those subjects randomized to observation (Cohort 3B).
- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate). Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures were performed during this 3-minute period. This is not required for those subjects randomized to observation (Cohort 3B).
- Record weight. This is not required for those subjects randomized to observation (Cohort 3B).
- Confirm ECOG Scale of Performance Status. This is not required for those subjects randomized to observation (Cohort 3B).
- Record any change in concomitant medications since the previous visit.
- All laboratory samples should be taken prior to dosing on any study visit that has dosing.
  - Collect a blood sample for clinical laboratory assessments(local laboratory; see Section 12.1.6). This is not required for those subjects randomized to observation (Cohort 3B).
- Record any AEs since last visit.
- **Dose 6**: Trial drug administration for subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P. Subjects must be observed for safety for at least 1-hour post-dose.

- Subjects will be provided with the reactogenicity diary to complete for 7-days following the dose. Subjects will be instructed how to complete the diary and to return the completed form at their next visit.

10.3. No Dosing 2-Month Period

After the Immunization Period, subjects will be observed during a No Dosing 2-Month Period (Table 9 and Table 15).

At **Visit 8 (Week 10),** the following visit procedures will include:

- Perform a PE (see Section 12.1.3).
- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate). Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures were performed during this 3-minute period.
- Record weight.
- Record any change in concomitant medications since the previous visit.
- Collect a blood sample for clinical laboratory assessments (local laboratory; see Section 12.1.6).
- Collect leukapheresis for immunogenicity assessments (central laboratory). This procedure may be performed -7 days to +3 days from Visit 8. Following the 16th subject being enrolled into Cohort 3B (observation), all subsequent observation cohort subjects will not require PBMC collection. The date of the 16th subject being enrolled is documented in a study level memo for site reference.
- Collect a blood sample for ctDNA (to be performed at a central laboratory). Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date.
- Record any AEs since last visit.

At **Visit 9 (Week 14)**, the following visit procedures will include:

- Perform a PE (see Section 12.1.3).
- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate). Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures were performed during this 3-minute period.
- Record weight.
- Record any change in concomitant medications since the previous visit.
- Perform a CT with contrast. For subjects with IV contrast allergy/intolerance, MRI may be performed. The same modality as the screening imaging assessment should be used throughout the trial.

- Collect a blood sample for clinical laboratory assessments (local laboratory; see Section 12.1.6).
  - Collect a serum sample for CA19-9/CEA for appropriate tumor type (local laboratory).
  - Collect a whole blood sample for immunogenicity testing (central laboratory). Following the 16th subject being enrolled into Cohort 3B (observation), all subsequent observation cohort subjects will not require PBMC collection. The date of the 16th subject being enrolled is documented in a study level memo for site reference.
- Record any AEs since last visit.

10.4. Booster Period

During the Booster Period, eligible subjects enrolled in Phase 1, and those either randomized to Cohort 3A or those who have crossed over to Cohort 3C will receive booster vaccinations, consisting of 4 weekly doses (Table 10). Subjects in Phase 2 randomized to Cohort 3B (observation) will have procedures as outlined below, without ELI-002 7P treatment (Table 16).

At **Visit 10 (Week 17)**, the following visit procedures will include:

- Perform a PE (see Section 12.1.3).
- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate). Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures were performed during this 3-minute period.
- Record weight.
- Confirm ECOG Scale of Performance Status.
- Record any change in concomitant medications since the previous visit.
- All laboratory samples should be taken prior to dosing on any study visit that has dosing.
  - Collect a blood sample for clinical laboratory assessments (local laboratory; see Section 12.1.6).
  - Collect a blood sample for ctDNA (to be performed at a central laboratory). Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date.
- Record any AEs since last visit.
- **Dose 7**: Trial drug administration for subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P. Subjects must be observed for safety for at least 1-hour post-dose.
- Subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P will be provided with the reactogenicity diary to complete for 7-days

following the dose. Subjects will be instructed how to complete the diary and to return the completed form at their next visit.

At **Visit 11 (Week 18)**, the following visit procedures will include:

- Perform a PE (see Section 12.1.3). This is not required for those subjects randomized to observation (Cohort 3B).
- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate). Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures were performed during this 3-minute period. This is not required for those subjects randomized to observation (Cohort 3B).
- Record weight. This is not required for those subjects randomized to observation (Cohort 3B).
- Confirm ECOG Scale of Performance Status. This is not required for those subjects randomized to observation (Cohort 3B).
- Record any change in concomitant medications since the previous visit.
- All laboratory samples should be taken prior to dosing on any study visit that has dosing.
  - Collect a blood sample for clinical laboratory assessments (local laboratory; see Section 12.1.6). This is not required for those subjects randomized to observation (Cohort 3B).
- Record any AEs since last visit.
- **Dose 8**: Trial drug administration for subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P. Subjects must be observed for safety for at least 1-hour post-dose.
- Subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P will be provided with the reactogenicity diary to complete for 7-days following the dose. Subjects will be instructed how to complete the diary and to return the completed form at their next visit.

At **Visit 12 (Week 19)**, the following visit procedures will include:

- Perform a PE (see Section 12.1.3). This is not required for those subjects randomized to observation (Cohort 3B).
- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate). Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures were performed during this 3-minute period. This is not required for those subjects randomized to observation (Cohort 3B).
- Record weight. This is not required for those subjects randomized to observation (Cohort 3B).
- Confirm ECOG Scale of Performance Status. This is not required for those subjects randomized to observation (Cohort 3B).

- Record any change in concomitant medications since the previous visit.
- All laboratory samples should be taken prior to dosing on any study visit that has dosing.
  - Collect a blood sample for clinical laboratory assessments (local laboratory; see Section 12.1.6). This is not required for those subjects randomized to observation (Cohort 3B).
- Record any AEs since last visit.
- **Dose 9**: Trial drug administration for subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P. Subjects must be observed for safety for at least 1-hour post-dose.
- Subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P will be provided with the reactogenicity diary to complete for 7-days following the dose. Subjects will be instructed how to complete the diary and to return the completed form at their next visit.

At **Visit 13/ End of Treatment (Week 20)**, this visit is to be performed when the subject completes the treatment period or if they discontinue treatment early and prior to entering the follow up period of the study. The visit procedures will include:

- Perform a PE (see Section 12.1.3).
- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate). Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures were performed during this 3-minute period.
- Record weight.
- Confirm ECOG Scale of Performance Status.
- Record any change in concomitant medications since the previous visit.
- All laboratory samples should be taken prior to dosing on any study visit that has dosing.
  - Collect a blood sample for clinical laboratory assessments (local laboratory; see Section 12.1.6).
  - Collect a blood sample for ctDNA (to be performed at a central laboratory). Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date.
- Record any AEs since last visit.
- **Dose 10**: Trial drug administration for subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P. Subjects must be observed for safety for at least 1-hour post-dose.

- Subjects in Phase 1 and those in Phase 2 who are randomized (or who crossover) to ELI-002 7P will be provided with the reactogenicity diary to complete for 7-days following the dose. Subjects will be instructed how to complete the diary and to return the completed form at their next visit.

10.5. Follow-up Period

A Follow-up Period will provide safety and efficacy data (Table 11 and Table 12, and Table 17 and Table 18 for subjects in the Observation Cohort). Visit 22/End of Study visit will be scheduled for subjects who complete the study or for any subject who discontinues from the study early.

At every visit during the Follow-up Period, **Visit 14 (Week 22), Visit 15 (Week 26), Visit 16 (Week 34), Visit 17 (Week 46), Visit 18 (Week 58), Visit 19 (Week 70), Visit 20 (Week 82), Visit 21 (Week 94), Visit 22 (Week 102)**, **Visit 23 (Week 114), Visit 24 (Week 126), Visit 25 (Week 138) and Visit 26/End of Study (Week 150)** the following visit procedures will include:

- Confirm ECOG Scale of Performance Status.
  - **Visit 16 only**: This is not required for those subjects randomized to observation (Cohort 3B).
- Record any AEs since last visit. Check for signs of toxicity.

At **Visit 14 (Week 22), Visit 15 (Week 26), Visit 16 (Week 34), Visit 17 (Week 46), Visit 18 (Week 58), Visit 19 (Week 70), Visit 20 (Week 82), Visit 21 (Week 94), Visit 22 (Week 102)**, the following visit procedures will include:

- Record vital signs (blood pressure, pulse rate, body temperature, and respiratory rate). Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures were performed during this 3-minute period.
  - **Visits 14 to 17 and Visits 19 to 22**: This is not required for those subjects randomized to observation (Cohort 3B). This is only required at Visit 18 for Cohort 3B subjects.
- Record weight
  - **Visits 14 to17 and Visits 19 to 22**: This is not required for those subjects randomized to observation (Cohort 3B). This is only required at Visit 18 for Cohort 3B subjects.

In addition, the following assessments will be conducted at the designated Follow-up visits:

At **Visit 14 (Week 22),** the following visit procedures will include

- Collect a blood sample for clinical laboratory assessments (local laboratory; see Section 12.1.6).

At **Visit 15 (Week 26), Visit 17 (Week 46), Visit 19 (Week 70), Visit 22 (Week 102), Visit 24 (Week 126), and Visit 26/End of Study (Week 150)** the following visit procedures will include:

- Collect a blood sample for ctDNA (central laboratory). If a subject has had confirmed radiographic progression via iRECIST and has initiated subsequent therapy, further ctDNA collection is not required. If a subject has not yet had iCPD prior to subsequent therapy, continue ctDNA collection until iCPD is confirmed. Subjects that were ctDNA negative at baseline (ie: Screening and Visit 2 results were both negative) will not have additional ctDNA sample collections as of 26 January 2026, also documented in a study level memo with the same date.

At **Visit 14 (Week 22), Visit 17 (Week 46), and Visit 19 (Week 70)** the following visit procedures will include:

- Collect a whole blood sample for immunogenicity testing (central laboratory). Following the 16th subject being enrolled into Cohort 3B (observation), all subsequent observation cohort subjects will not require PBMC collection. The date of the 16th subject being enrolled is documented in a study level memo for site reference.

At **Visit 15 (Week 26), Visit 17 (Week 46), Visit 18 (Week 58), Visit 19 (Week 70), Visit 20 (Week 82), Visit 21 (Week 94), Visit 22 (Week 102), Visit 23 (Week 114), Visit 24 (Week 126), Visit 25 (Week 138) and Visit 26/End of Study (Week 150)** the following visit procedures will include:

- Perform a CT (±14 days) with contrast. For subjects with IV contrast allergy/intolerance, MRI may be performed. The same modality as the screening imaging assessment should be used throughout the trial. If a subject has had confirmed radiographic progression via iRECIST and has initiated subsequent therapy, further imaging is not required. If a subject has not yet had iCPD prior to subsequent therapy, continue with scans until iCPD is confirmed.
- Collect a serum sample for CA19-9/CEA for appropriate tumor type (local laboratory). If a subject has had confirmed radiographic progression via iRECIST and has initiated subsequent therapy, further serum biomarker testing is not required. If a subject has not yet had iCPD prior to subsequent therapy, continue with serum biomarker collection until iCPD is confirmed.

At **Visit 18 (Week 58),** the following visit procedures will include:

- Perform a PE, (see Section 12.1.3).

10.6. Crossover from SOC (Observation) to ELI-002

In Phase 2, subjects randomized to SOC (observation, Cohort 3B) will be eligible to cross over to intervention (ELI-002) after confirmed radiographic progression is documented and confirmed with Elicio. Crossover to Cohort 3C can occur up through the time that the last subject from Cohorts 3A and 3B completes the study (a study memo will be released to all active sites when this happens). Prior to receiving the first dose of ELI-002 these subjects will be assessed and must meet all the criteria as outlined in Section 7.3. At the time of crossover, the last scan performed on Cohort 3B (observation), identifying progression, will be used for the baseline for crossover (Cohort 3C). This scan will need to be reviewed via iRECIST again, this time for the Cohort 3C baseline and recording of Target and/or Non-Target Lesions.

Regardless of their election to cross over or not, subjects will continue to be followed for OS. The irORR using iRECIST criteria will be characterized for any crossover subjects.

Subjects who crossover from SOC (observation) to ELI-002 will follow the visit procedures as outlined in Table 8, Table 9, and Table 10 corresponding to the Immunization Period (Section 10.2), the No Dosing 2-Month Period (Section 10.3), and the Booster Period (Section 10.4), respectively.

11. CLINICAL ACTIVITY, IMMUNE ASSESSMENTS, AND SUBJECT REPORTED OUTCOMES

Clinical activity, immune assessments, and PROs will be collected according to the Schedule of Assessments (in Table 7 through Table 12, and Table 13 through Table 18 for subjects in the Observation Cohort).

For radiographic assessments, DFS and 1-year DFS rate will be assessed through radiographic imaging with contrast as assessed by the site investigators using iRECIST criteria [Seymour et al., 2017]; subjects will be followed for OS. Unscheduled CT or MRI imaging may be performed at any time, if the investigator determines that there are clinical signs of disease progression.

In addition, biomarker response rate will be based on the percentage of subjects achieving biomarker reduction or clearance, as measured by the absence or decrease of ctDNA from baseline and the duration of ctDNA reduction and/or clearance, or if ctDNA was not detectable at baseline, serum tumor biomarker (such as CA19-9 and CEA) reduction and clearance compared to baseline will be recorded. T cell responses in PBMCs will be assessed by immune assays such as IFNγ Fluorospot, ICS, and/or dextramers. Tumor biopsy assessments may include gene expression and/or immunofluorescence to examine immune cell infiltration and tumor microenvironment phenotype. Serum cytokine, CEA and CA19-9 levels will also be examined where applicable.

Immune responses will be correlated to clinical efficacy parameters.

11.1. Mixed Response/Tumor Flare

Pseudoprogression (tumor flare) may be observed with immunotherapy; therefore, subjects should remain on-study following observation of unconfirmed progression until the next protocol scheduled scan, or until a biopsy confirms progression, per iRECIST guidelines. In the event a biopsy is performed, CD3 staining for T cell infiltration will be performed locally to aid in the assessment for pseudoprogression versus tumor progression. If tissue is sufficient, a tissue sample will be sent to the central lab to be used in evaluating tumor-infiltrating T cells, the tumor microenvironment and may also be used for biomarker genetic sequencing. For crossover subjects, mixed response may be observed. Mixed response is defined as growth and/or appearance of new lesions with disease control noted in remaining sites. In accordance with the iRECIST guidelines [Seymour et al., 2017], treatment with ELI-002 7P may continue until confirmatory imaging is obtained when a subject has a mixed response, or when a standard of care biopsy has confirmed disease status (see Section 11.2).

11.2. Immunogenicity

Subjects will have leukapheresis and blood samples drawn to evaluate the immunogenicity of ELI-002 7P. T cell responses in PBMCs will be assessed by immune assays such as IFNγ Fluorospot, ICS, and/or dextramers. CEA and CA19-9 levels will also be examined.

HLA Typing: High resolution HLA typing will be used to identify certain individual variations in the immune system. Cohorts will be enrolled regardless of the HLA subtype.

Cellular immune response: The cellular immune response to ELI-002 will be monitored by examining T cell responses using immune assays such as Fluorospot and ICS. The Fluorospot

assay enumerates the release of cytokines such as IFNγ in human PBMCs following KRAS peptide stimulation. The ICS assay is a flow cytometry-based assay that can detect cytokine production by CD4+ and CD8+ T cells to the KRAS peptides. For both assays, PBMCs will be stimulated individually with mKRAS peptide pools to determine the frequency of KRAS-specific T cells per subject and timepoint. Dextramers are fluorescently labeled HLA multimers that can detect antigen-specific T cells. In subjects with HLA alleles for which dextramer(s) are available, the frequency of KRAS-specific T cells can be monitored in PBMCs before and after vaccination.

Full details of the leukapheresis or phlebotomy procedure to obtain PBMCs will be provided in the Central Laboratory Manual.

Standard of Care Biopsies: Tumor specimens will be collected at screening following confirmation of subject eligibility from prior surgical resection (when available); tumor specimens will also be collected post-Visit 2 from biopsies if performed as standard of care (ie, following observation of new lesions on radiographic imaging and investigator assessment that tissue can be safely obtained). Formalin-fixed paraffin-embedded sections will be requested for central lab analysis to examine tumor-infiltrating T cells and the tumor microenvironment. Potential assays may include in situ gene expression and/or immunofluorescence. Subjects initially randomized to observation (Cohort 3B) who cross-over to treatment (Cohort 3C) will also have another biopsy taken at the time of unconfirmed progression on treatment if the investigator assesses the tissue can be safely obtained.

11.3. ctDNA Levels

Levels of ctDNA (mean tumor molecules/mL or mutant molecules) will be assessed using a ctDNA assay (central laboratory) in anticoagulated peripheral whole blood at indicated timepoints post vaccination. The ctDNA fold change from baseline will be calculated at each timepoint.

For Phase 1, if a subject is MRD^- by ctDNA at screening (and not otherwise eligible via serum tumor biomarkers such as CA19-9 and CEA), sites may continue to monitor ctDNA levels per their standard of care testing and rescreen if the subject becomes MRD^+ by ctDNA analysis. It is recommended that the time between ctDNA screening tests be ≥90 days.

11.4. Future Use of Biospecimens

Subject coded study information, as well as residual samples and scans being collected for study specified analyses may also be used for future additional unanticipated medical and/or scientific research projects relating to the diseases being studied, or similar diseases, or further development of ELI-002 7P (at all times in compliance with applicable laws and regulations). The subject-coded study data may also be reanalyzed at a later date, combined with data from other studies, or used for other research purposes related to this study, including:

- Reviewing the safety and effectiveness of ELI-002 7P
- Conducting performance reviews of the study
- Improving the design of future studies for the treatment of similar diseases

- Further development of ELI-002 7P and other potential new products or therapies for treatment of similar diseases

12. ASSESSMENT OF SAFETY

12.1. Safety Parameters

12.1.1. Demographics and Medical History

Demographic variables will include age, gender, and race/ethnicity. Medical and medication history, including cancer history/prior treatments, current medications (prescription, herbal and dietary supplements, over-the-counter medications, and topical treatments), and diseases will be assessed at screening and recorded in the source documents and the eCRF.

Weight and height will be collected during the Screening Period and weight will collected throughout the trial according to the Schedule of Assessments (Table 7 through Table 11 and Table 13 through Table 17 for subjects in the Observation Cohort).

12.1.2. Vital Signs

Vital signs will be collected throughout the trial according to the Schedule of Assessments (Table 7 through Table 11 and Table 13 through Table 17 for subjects in the Observation Cohort) and will include blood pressure, pulse rate, body temperature, and respiratory rate. Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures were performed during this 3-minute period.

12.1.3. Physical Examinations

Physical examination will be performed at screening and at specified times during the trial (Table 7 through Table 11 and Table 13 through Table 17 for subjects in the Observation Cohort) based on standard of care.

12.1.4. Electrocardiogram

A resting 12-lead ECG will be performed according to the Schedule of Assessments (Table 7 and Table 8 and Table 13 and Table 14 for subjects in the Observation Cohort) and reviewed by a cardiologist or clinical investigator, per institutional guidelines and practice.

12.1.5. Eastern Cooperative Oncology Group

The ECOG Scale of Performance Status describes a subject's level of functioning in terms of their ability to care for themselves, daily activity, and physical ability (walking, working, etc.).

Eligibility for this trial requires a subject's ECOG performance status to be 0 to 1. The ECOG assessment will be performed according to the Schedule of Assessments (Table 7, Table 8, Table 10, Table 11, and Table 12, and Table 13, Table 14, Table 16, Table 17, and Table 18 for subjects in the Observation Cohort).

12.1.6. Laboratory Assessments

Laboratory values will be collected according to the Schedule of Assessments (Table 7 through Table 11, and Table 13 through Table 17 for subjects in the Observation Cohort). A central clinical laboratory will be utilized as noted in Section 6.1, but local clinical laboratories will be used for safety assessments and serum tumor biomarkers.

The results of clinical laboratory tests conducted during screening for the trial will be assessed by the investigator to determine each subject's appropriateness for trial participation.

For the remainder of the trial, the investigator will review laboratory values that are outside the normal reference ranges to determine whether the values are clinically significant. Clinically significant changes will be followed until the parameter returns to Baseline or until the investigator determines that follow-up is no longer medically necessary. Clinically significant values will be documented as Adverse Events as described in Section 12.2.1.1. Unscheduled re-tests may be performed as needed through the Follow-up Visit.

12.1.6.1. Hematology

The following hematology parameters will be assessed:

- White blood cell count
- Absolute and % Neutrophils
- Absolute and % Lymphocytes
- Absolute and % Monocytes
- Absolute and % Eosinophils
- Red blood cell count
- Hematocrit
- Hemoglobin
- Platelet Count
- Absolute and % Basophils

12.1.6.2. Blood Chemistry

The following blood chemistry parameters will be assessed:

- Sodium
- Potassium
- Magnesium
- Chloride
- Creatinine
- Calcium
- Phosphate
- Glucose
- HbA1c (Phase 2 screening only)
- Bilirubin (total)
- Protein (total)
- Albumin
- Uric acid
- AST
- ALT
- Alkaline phosphatase
- Bicarbonate (if not available, then CO_2)

12.1.6.3. IL-6 at Screening

Determination of serum IL-6 will be performed at screening according to the Schedules of Assessments (Table 7 and Table 13).

12.1.6.4. Viral Laboratory at Screening

The following viral parameters will be assessed at screening only:

- Hepatitis C antibody test (for all subjects screened)/Hepatitis C RNA (for those subjects who are hepatitis C positive with sustained response to treatment); see exclusion criterion #7
- COVID-19 active infection

12.1.6.5. Pregnancy Screen

A urine pregnancy test will be performed according to the Schedule of Assessments (Table 7) for women of childbearing potential. Childbearing status for all women will be recorded in the source documents and in the eCRF.

Definitions that meet the criteria to not be considered of childbearing potential:

- Women >1 years postmenopausal (defined as 1 year or longer since last menstrual period) AND >55 years of age
- Postmenopausal women (as defined above) and <55 years of age with a negative pregnancy test within 1 week of first dose
- Women who were surgically sterilized at least 3 months prior to enrollment

A positive pregnancy test will exclude the subject from participation in the trial. Any clinically abnormal or inconclusive test will be repeated.

12.2. Adverse and Serious Adverse Events

12.2.1. Definition of Adverse Events

12.2.1.1. Adverse Event

An AE is the development of an undesirable medical condition or the deterioration of a pre-existing medical condition following or during exposure to a pharmaceutical product, whether or not considered study-drug related. An AE can be any unfavorable and unintended sign, symptom of disease temporally associated with the use of study drug, without any judgement about causality (see current ICH guidelines).

In this study, investigators should report AEs based on CTCAE v5.0 criteria. Treatment-emergent AEs (TEAEs) are defined as events not present prior to the initiation of study drug or any event already present that worsens in either intensity of frequency following exposure to study treatment. AEs must be recorded in the eCRF and on forms as provided by Elicio.

An AE does not include the following:

- Medical or surgical procedures (eg, surgery, endoscopy, dental extraction, transfusion); the condition that necessitates the procedure is the AE
- Any pre-existing disease or condition, or laboratory or ECG abnormality, which is present prior to the start of the study medication and that does not worsen

- Laboratory or ECG abnormalities without clinical significance (ie, those which do not require medical intervention or that do not result in discontinuation or interruption of the study drug)
- Situations where an adverse medical event has not occurred (ie, hospitalization for elective surgery, social admission)
- Overdose of study medication or any concomitant medication without any signs or symptoms, unless the subject is hospitalized for observation

The time period for collecting and documenting AEs for each subject begins from the time the subject is from Visit 2 (ie, first dose of study drug for those receiving treatment, all cohorts except Cohort 3B) through 30 days after the end of study treatment administration.

Adverse event term clarification: neither death nor disease progression is an appropriate event term. The event term should be what caused the death or the event that was related to disease progression that met the criteria for an SAE or AE in the judgement of the investigator.

12.2.1.2. Serious Adverse Event

An SAE is an AE occurring during any trial phase (ie, screening, treatment, or follow-up), and at any dose of the investigational product, that fulfils one or more of the following:

- Results in death
- It is immediately life-threatening
- It requires inpatient hospitalization or prolongation of existing hospitalization
- It results in persistent or significant disability or incapacity
- Results in a congenital abnormality or birth defect
- It is an important medical event that may jeopardize the subject or may require medical intervention to prevent one of the outcomes listed above.

The time period for collecting and documenting SAEs for each subject begins from the time the subject provides informed consent through 30 days after the end of study treatment administration.

12.2.1.3. Reactogenicity to the Vaccine

Injection site reactions, skin rash, and pruritis will not be considered safety events and should be recorded in the subject diary and eCRF for reactogenicity. (See Section 6.8.2 for toxicity management and Section 12.2.1.2 for SAE definition.) Severe skin rashes such as Steven-Johnson Syndrome or toxic epidermal necrolysis (TEN) will be considered a DLT (in Phase 1A) and should be reported on the eCRF as safety events including SAE as appropriate if observed at any time during the reactogenicity monitoring period. Reactogenicity monitoring will include subject's reactogenicity to the trial drug (vaccine). This will be captured at several time points as follows:

- 1-hour post ELI-002 dose administration (subjects will be observed in the clinic for at least 1-hour after each dose for all symptoms including temperature and as documented on the subject reactogenicity diary template)
- 1-week post ELI-002 dose administration (subjects will record daily observations in diary)
- Any unresolved reactogenicity event should be followed until resolution.

12.3. Relationship to Trial Drug

An investigator who is qualified in medicine must make the determination of relationship to the investigational product for each AE (Unrelated, Possibly Related, or Related). The investigator should decide whether, in his or her medical judgement, there is a reasonable possibility that the event may have been caused by the investigational product.

Unrelated: The AE is definitely not associated with the study drug administration and is judged related to causes other than the study drug.

Possibly Related (Suspected Adverse Reaction [SAR]): A causal relationship between treatment with the study drug and the AE is at least a reasonable possibility, ie, the relationship cannot be ruled out. This implies a lesser degree of certainty about causality than a related AE. Additional evidence to suggest a SAR includes:

- Occurrence of uncommon AEs that are known to be strongly associated with drug exposure (eg, anaphylaxis, angioedema, blood dyscrasias, rhabdomyolysis, hepatic injury, Stevens-Johnson Syndrome)
- Occurrence of AEs that are uncommon in the study population, but not commonly associated with drug exposure (eg, intussusception in healthy infants)

Related (Adverse Reaction): A causal relationship between the study drug administration and the AE is definite.

If the relationship between the AE/SAE and the investigational product is determined to be "possible" the event will be considered to be related to the investigational product for the purposes of expedited regulatory reporting.

12.4. Severity of Adverse Events

The CTCAE Version 5 displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline:

- **Grade 1** Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
- **Grade 2** Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living (such as preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.)

- **Grade 3** Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living (such as bathing, dressing, and undressing, feeding self, using the toilet, taking medications, and not bedridden)
- **Grade 4** Life-threatening consequences; urgent intervention indicated
- **Grade 5** Death related to AE.

12.5. Recording Adverse Events

Adverse events spontaneously reported by the subject and/or in response to an open question from the trial personnel or revealed by observation will be recorded during the trial at the investigational trial center. Treatment emergent AEs (TEAEs) are defined as events not present prior to the initiation of study drug or any event already present that worsens in either intensity of frequency following exposure to study treatment. AEs must be recorded in the eCRF and/or on forms as provided by Elicio. The AE term should be reported in standard medical terminology when possible. For each AE, the investigator will evaluate and report the onset (date and time), resolution (date and time), severity, causality, action taken, outcome, and whether or not it caused the subject to discontinue the trial.

Severity will be assessed according to CTCAE v5.0. For AEs not described in the consensus criteria, the following scale will be used:

- Mild (awareness of sign or symptom, but easily tolerated. Concomitant prescription medications are not ordinarily needed for relief of symptoms)
- Moderate (discomfort sufficient to cause interference with normal activities. Concomitant prescription medications/treatment(s) may be needed for relief of symptoms)
- Severe (incapacitating, with inability to perform normal activities. Requires interruption or discontinuation of study medication. Systemic drug therapy or other treatment is needed)

Reactogenicity will be assessed according to the toxicity grading scale for local reactions for preventive vaccines (see Section 12.2.1.3).

It is important to distinguish between serious and severe AEs. Severity is a measure of intensity whereas seriousness is defined by the criteria under Section 12.2.1.2. An AE of severe intensity may not be considered serious.

12.6. Pregnancy

Should a pregnancy occur within 30 days of the last ELI-002 7P dose in a female subject, or in the partner of a male subject, it must be reported on Elicio's paper pregnancy form. Neither pregnancy itself nor an induced elective abortion to terminate a pregnancy for non-medical reasons is considered an AE. However, an induced therapeutic abortion to terminate a pregnancy due to complications or other medical reasons will be recorded as an SAE. The underlying medical reason for this procedure should be recorded as the AE term. Pregnancy outcomes considered to be SAEs are:

- Spontaneous abortion (miscarriage)
- Stillbirth
- Induced therapeutic abortion to terminate pregnancy due to complications or other medical reasons
- Neonatal death; this includes all neonatal deaths that occur within 1 month of the expected birthdate (ie, either before or after the expected birth date)
- Infant death occurring 1 month after birth, if the investigator assesses the death as possibly related to in utero exposure to study treatment
- Congenital anomaly (in live birth or aborted fetus)

If the subject has signed the pregnancy informed consent, the outcome of all pregnancies (spontaneous miscarriage, elective termination, normal birth or congenital abnormality) must be followed up and documented even if the subject was discontinued from the trial.

12.7. Reporting Adverse Events

All AEs and SAEs will be reported on the appropriate eCRF pages and on forms as provided by Elicio, which will also be the reporting mechanism to Elicio safety/pharmacovigilance. All AEs (related and unrelated) will be recorded from first dose administration until 30 days after the end of study treatment administration. All SAEs (related and unrelated) will be recorded from the signing of the ICF until 30 days after the end of study treatment administration. All SAEs must be reported to Elicio or their designee within 1 business day of the first awareness of the event. The investigator must verify the accuracy of the information recorded on the SAE pages with the corresponding source documents.

Additional follow-up information, if required or available, should all be sent to Elicio or its designee within one business day of receipt and this should be completed on a follow-up SAE form, as well as documented with the original SAE source information and kept with the appropriate section of the subject source records.

Elicio is responsible for notifying the relevant regulatory authorities of certain events. It is the PI's responsibility to notify the Institutional Review Board (IRB) of all SAEs that occur at his or her trial center in accordance with local IRB requirements. Investigators will also be notified of all unexpected, serious, drug-related events (Suspected Unexpected Serious Adverse Reaction [SUSAR] Reports) that occur during the clinical trial. Each trial center is responsible for notifying its IRB of these additional SAEs in accordance with local requirements. If the clinical site submits to a central IRB, SUSAR reports will be submitted by Elicio or its designee.

12.8. Extension Protocol

Subjects who remain in the trial until the end of the required Booster Period may be eligible to enroll in a separate Extension protocol to continue to receive further mKRAS/mNRAS lymph node immunotherapy to maintain effective levels of antigen-specific T-cells.

13. STATISTICS

ELI-002-201 is an open-label, Phase 1/2 trial of ELI-002 7P (with Amph-Peptides G12D, G12R, G12V, G12A, G12C, G12S, and G13D) immunotherapy as adjuvant treatment for subjects with KRAS/ NRAS mutated solid tumors who are at high risk for relapse. This protocol builds on the experience obtained with a related product, ELI-002 2P (with Amph-Peptides G12D and G12R), which was studied in protocol ELI-002-001 under IND 26909.

A Phase 1A safety evaluation cohort will confirm the safety of the RP2D Amph-CpG-7909 and Amph-Peptides 7P doses, then a Phase 2 cohort will assess the safety and efficacy in pancreatic cancer subjects randomized to ELI-002 7P versus standard of care (observation). If the Phase 1B cohort is opened (Cohort 2), it will assess safety and preliminary evidence of antitumor activity in CRC subjects.

13.1. General Statistical Considerations

All statistical analyses will be performed using SAS statistical software (Version 9.3 or later), unless otherwise noted. Medical History and AEs will be coding using MedDRA.

Unless otherwise specified, all continuous endpoints will be summarized using descriptive statistics, which will include the number of subjects (n), mean, standard deviation, median, minimum and maximum. All categorical variables will be summarized using frequencies and percentages. The baseline measurement will be the last value on or before the date of first study treatment. Nominal p-values may be computed for secondary or exploratory efficacy analyses as a descriptive measure of strength of results rather than for formal tests of hypotheses. No formal tests of hypotheses are planned for safety analyses.

13.2. Sample Size

For Phase 1A, approximately 12 subjects' safety evaluation is empiric and will achieve the protocol objective of confirming the safety of the RP2D of Amph-CpG-7909 and Amph-Peptides 7P doses.

For Phase 1B Cohort 2 (CRC), BOP2 design assumes a null hypothesis of biomarker (ctDNA or serum tumor biomarker) response (reduction/clearance) rate ≤ 0.05 and the alternate hypothesis of biomarker response rate ≥ 0.3. The BOP2 is designed with 90% power to reject the null hypothesis that the true ctDNA response rate is ≤ 0.05 with a sample size of 17 subjects. An interim analysis for go/no-go decision for expansion to a sample size of 17 subjects will occur after 9 biomarker evaluable subjects are available and have been on study for at least 28 days. If ≥ 1 biomarker response is observed, then the Phase 1B cohort will continue to enroll until it reaches 17 subjects with the criteria $\geq 3/17$ biomarker responses to reject the null hypothesis at alpha=0.05 (1-sided). Enrollment will stop if there are 0 responses observed in the first 9 subjects (ie, no-go).

For Phase 2 (PDAC), the sample size of approximately 135 subjects will be randomized 2:1 to receive ELI-002 7P or SOC (observation), respectively. Randomization will be stratified by nodal status (N0 vs. N1). Assuming the true HR is 0.53 (median DFS [per investigator] of 7 months vs. 13.2 months), a 2-sided alpha of 0.10 (or equivalently 1-sided alpha 0.05), and a power of 80%, approximately 71 total number of DFS events will be required to detect the

hypothesized HR of 0.53. One interim analysis and one final analysis is planned. A safety evaluation is also planned when approximately 20 biomarker evaluable subjects are available who had been on study for at least 28 days. See Section 13.7 for further details on interim analysis.

13.3. Randomization

In Phase 2, subjects will be randomized 2:1 to ELI-002 7P or SOC (observation) using IxRS technology after subject eligibility is confirmed during screening. Randomization in Phase 2 will be stratified according to the following:

- Nodal status: node negative versus node positive (0 versus 1)

13.4. Analysis Population

The following populations will be used for data analyses and presentations.

13.4.1. Full Analysis Set (FAS) / Intention-to-Treat (ITT)

For Phase 1, the Full Analysis Set (FAS) will include all subjects who received any amount of vaccine. Actual treatment received will be used for FAS.

For Phase 2, the Intention-to-treat (ITT) Set includes all subjects randomized to ELI-002 7P or SOC (observation). The ITT set will be the primary set for the analysis of efficacy unless otherwise specified.

Additional exploratory analyses may be performed for the subjects treated in the Phase 1 cohorts where biomarker (ctDNA, or if ctDNA was not detected at baseline, serum tumor biomarker) clearance/reduction is observed.

The FAS and ITT sets will be used for summaries of subject demographics and baseline characteristics.

13.4.2. Safety Analysis Set

The Safety Analysis Set (SAF, defined as any subjects receiving any amount of vaccine in Phase 1 and for Phase 2, subjects received any amount of vaccine or observation study treatment and will be used for the safety evaluation (AEs, clinical laboratory assessments, vital signs, ECGs, ECOG, PEs). No data will be imputed for the safety analysis set unless otherwise specified. Actual treatment received will be used for the Safety Analysis Set.

13.4.3. Per Protocol Set

The Per Protocol Analysis Set will include all ITT subjects who have no major protocol deviations. The exclusion list for this set will be identified prior to database lock. Analysis with this analysis set will be conducted if warranted.

13.4.4. PD/Biomarker Evaluable Set (BES)

All Phase 1 subjects (FAS) who receive any amount of trial treatment and all Phase 2 subjects who are randomized (ITT), with the additional requirement that relevant blood sampling data at

the appropriate assessment time point(s) must be available for inclusion in the analysis for the corresponding parameter.

For all Phase 2 subjects who are randomized (ITT), the additional requirement that relevant blood sampling data at the appropriate assessment time point(s), including baseline, must be available for inclusion in the analysis for the corresponding parameter (immunogenicity, serum tumor biomarker CA19-9/CEA, ctDNA). Unscheduled post-baseline biomarker tests will be included in the analysis. Further, subjects evaluated for serum tumor biomarker (CA19-9 or CEA) must meet the criteria that,

1. Successive rising values, at least 1 week apart, at baseline, or
2. Baseline biomarker values CA19-9 ≥90 U/mL or CEA ≥15 ng/mL

13.5. Missing Data

In the case of DFS (per investigator), duration of biomarker reduction/clearance, or OS analyses, missing data will be handled using censoring at the date of last tumor assessment, last date of recoded reduction/clearance, or date last known to be alive, respectively. Further details on the censoring rules will be provided in the Statistical Analysis Plan (SAP).

13.6. Statistical Analyses

Continuous variables of efficacy endpoints will be summarized using descriptive statistics while categorical variables will be presented using counts and percentage of subjects. Kaplan-Meier (KM) estimates of the median and other quantiles, as well as individual time points (for time to event endpoints) will also be provided as appropriate. KM plots will be presented as applicable. Unless otherwise specified, the full analysis sets (FAS and ITT) will be the primary analysis sets for all efficacy endpoints for the respective phase of the study.

13.6.1. Efficacy Analysis

13.6.1.1. Disease-free Survival (DFS)

For Phase 2, DFS is defined as time from randomization to cancer recurrence or death due to any cause, whichever occur first. DFS (in months) is calculated as:

[(date of recurrence/death – date of randomization) + 1)]/30.4375

Disease-free survival will be censored on the date of the last evaluable CT scan on study for subjects who do not have recurrence and who did not die while on study. Subjects without any post baseline CT scans will have their DFS time censored on the date of randomization. Subjects who withdraw from the study (including withdrawal of consent and lost to follow-up) will be censored at the date of the last CT scan or last date known to be alive. For disease recurrence documented by CT between scheduled evaluations, the actual date of the scan will be used. For death or recurrence after no more than 1 missed evaluation, the date of the event will be the date of recurrence or death, whichever occurs first. For death or recurrence after more than 1 missed evaluation, DFS will be censored at the last evaluable disease assessment. Further details will be provided in the SAP.

The median DFS will be estimated using the Kaplan-Meier method. The number of subjects with events (recurrence/death), the number of subjects censored, and the reason for censoring will be presented. In addition to the KM estimates, hazard ratio (HR) and its associated 95% confidence interval will be calculated using the Cox proportional hazards model with the stratified log-rank test used to compare between the treatment arms (ELI-002 7P vs. SOC); unstratified log-rank test will also be performed.

A 1-year DFS rate will also be presented along with the statistical test.

For Phase 1, the computation of the endpoint will start at first dose instead of at randomization and will be presented by cohort and overall (pooled across all cohorts).

13.6.1.2. Overall Survival (OS)

For Phase 2, the OS (in months) is defined as time from randomization to death due to any cause.

[(date of death or last known alive – date of randomization) + 1)]/30.4375

Subjects who are lost to follow-up or do not have a date of death at the time of data cut-off will be censored at the last date that they were known to be alive.

The summary for OS will be presented similarly to that of DFS.

For Phase 1, the computation of the endpoint will start at first dose instead of at randomization and will be presented by cohort. No HR will be presented for the Phase 1 study.

13.6.1.3. Biomarker Response Rate (BRR)

For Phase 2, the biomarker response rate is defined as the percent of subjects whose biomarker resulted in either a decline or clearance of the biomarker. A negative percentage change from baseline would be considered a decline, while a clearance would require a -100% change from baseline. A Chi-square test will be performed to compare between the two treatment arms; Fisher's exact test may be performed if warranted.

13.6.1.4. Objective Response Rate (irORR)

For Phase 2, the irORR is defined as the percentage of subjects achieved iCR or iPR per investigator's assessment according to iRECIST. A Chi-square test will be used to compare between the treatment arms; Fisher's exact test may be performed if warranted.

The irORR in subjects who crossover to ELI-002 7P (Cohort 3C) from observation arm after confirmed disease progression according to iRECIST, will be analyzed if warranted.

13.6.1.5. Duration of Biomarker Response (DBR)

For Phase 2, analysis of duration of biomarker response will be conducted (if warranted) using the Kaplan-Meier method to estimate the distribution; the 2-sided 95% CIs will be estimated using the Brookmeyer-Crowley method. The hazard ratio (HR) and its associated 95% confidence interval will be calculated using the Cox proportional hazards model with the unstratified log-rank test used to compare between the treatment arms. The Kaplan-Meier plot will be presented. Further details will be provided in the Statistical Analysis Plan (SAP).

13.6.1.6. Multiplicity Adjustment

Treatment arms will be compared for each of the following secondary endpoints using Holm's procedure [Holm 1979] to control the family-wise error rate:

1. 1-year DFS rate
2. OS
3. BRR

All confidence intervals will be two-sided 95% confidence intervals and inferential statistical analyses will be evaluated with an overall significance level of alpha 0.05 (two-sided).

13.6.2. Safety Analysis

All summaries of safety data will be conducted for the safety analysis sets (SAF) using actual treatment received. Safety measurements will include:

- AEs
- Clinical laboratory evaluations
- Vital sign measurement
- Physical examinations
- 12-lead ECG
- ECOG performance status.

No statistical tests will be performed on the above safety endpoints.

13.7. Interim Analyses

Phase 1A: If 2 or more of the 6 subjects in Phase 1A (Cohort 1) at each peptide dose experience a DLT in the first 28 days following ELI-002 7P administration, then, prior to opening Phase 1B/Phase 2 to enrollment, the IDMC will review the events and may recommend a change in the ELI-002 7P dose (ie, RP2D−1 of Amph-CpG-7909 or an updated dose level of Amph-Peptides 7P), and if so, an additional 6 subjects will be enrolled in Phase 1A at the changed dose level. An additional 6 subjects at the RP2D−1 may also be added in the event that further characterization of the Phase 2 dose is required. In partnership with the Sponsor and following IDMC review of the Phase 1A safety data, if the IDMC recommends a dose level to proceed to Phase 2, Phase 1A enrollment of PDAC subjects may continue at this dose level until Phase 2 is opened to enrollment.

Phase 1B: If Elicio opens the Phase 1B expansion cohort (Cohort 2, CRC), an interim analysis to determine further expansion of the cohort to the final analysis is to be conducted (see Section 13.2 for details).

The analyses will be performed by the CRO and reviewed by the IDMC, who will make recommendations to the Sponsor regarding future state of the trial.

Phase 2: A safety evaluation is planned when approximately 20 biomarker evaluable subjects who had been on study for at least 28 days are available for review by the IDMC. This will

include a review of the limited biomarker data for consistency with the data observed in the similar patient population treated with study treatment ELI-002 2P conducted in Study ELI-002-001. There will be no hypothesis testing, therefore, no alpha adjustment is planned.

One interim analysis on the primary endpoint of DFS is planned when approximately 67% of the total events are observed. The efficacy boundaries are constructed using the O'Brien-Fleming boundaries as implemented by the Lan-deMets alpha spending function. The interim analysis also includes a non-binding futility analysis constructed using a Rho spending function with parameter of 4. At 67% of the total events, the efficacy alpha spend is 0.0171 (1-sided). The actual alpha spend will be adjusted based on the actual observed number of DFS events at the time of analysis.

A final analysis of the DFS endpoint will be conducted when the total number of events (71 events) is observed. Similarly, the alpha adjustment will be made accordingly.

Safety monitoring will occur continuously in the trial. Safety tables will be produced at the efficacy interim analysis to allow the IDMC to comprehensively evaluate the risk-benefit profile.

14. DATA INTEGRITY AND QUALITY ASSURANCE

14.1. Data Management and Case Report Forms

Elicio and/or its designee will be responsible for the processing and quality control of the data. Data management will be performed as described in the sponsor's and/or designee's standard operating procedures (SOPs) for clinical studies and the study Data Management Plan. Adverse events will be coded using MedDRA and medications will be coded using the World Health Organization Drug Dictionary (WHO Drug).

The handling of data, including data quality control, will comply with regulatory guidelines (ie, current ICH E6) and the sponsor and/or designee SOPs.

The eCRF will be provided by the sponsor or its designee and should be completed in accordance with applicable study guidelines and within the timeframe specified. Each eCRF should be filled out completely by the investigator or designee as stated on the Delegation of Authority Log. All data entry in the eCRF must have corresponding source documentation located in the subject study records.

All data will be stored in a validated database that is 21 CFR Part 11 compliant. The principal investigator is responsible for ensuring the timely completion of eCRFs. The principal investigator (or sub-investigator) must review, sign and date the eCRFs at the time of study completion to attest to the accuracy and completeness of the study data at the clinical site.

14.2. Source Documentation

Source documents are defined as documentation of the observations and activities of a clinical study. Source documents may include, but are not limited to, study progress notes, email correspondence, subject QLQs (or PROs), subject diaries, laboratory data and pathology and/or imaging reports. All source documents for this study will be maintained by the investigator and made available to the sponsor, the sponsor designee and regulatory authorities. The signed informed consent document and statement of consent will be maintained in the subject study records, and a copy of the informed consent will be provided to the subject.

14.3. Study Drug Accountability

At all times, a record of the study drug inventory and study drug accountability must be maintained. Inventory and accountability records must be readily available to the study monitor, the sponsor and any regulatory authority. The investigator, in conjunction with the site pharmacy or study drug preparation lab, is responsible for ensuring accountability of all used and unused study drug.

At the end of the trial, and following study monitor verification of drug accountability, Elicio or its designee will provide instruction for the destruction of unused study drug supplies remaining at the clinical site. During the conduct of the study, used vials may be destroyed on-site if Elicio has approved the destruction policy and only after the study monitor has verified drug accountability. If study drug destruction by the clinical site is approved by Elicio or its designee, the investigator must ensure that all study drug is destroyed in compliance with institutional

policy, applicable local regulations, as well as 21 CFR 312.59 and current ICH E6 guidelines pertaining to drug destruction. All destruction at the clinical site must be adequately documented.

14.4. Laboratory Assessments

Local laboratories will be responsible to analyze safety laboratory tests and serum tumor biomarkers for this study. All local laboratory results will be captured on eCRFs. Central labs will be used for the analysis of HLA typing, pharmacodynamic and immunology assays, as well as specialty biomarkers.

14.5. Trial Monitoring

During the trial, Elicio and/or its designee will perform periodic monitoring visits to ensure that the protocol and ICH/GCP are being followed in the conduct of the study. Study monitoring will be performed in accordance with ICH/GCP, the sponsor and/or its designee's SOPs, the study protocol and study plans, as well as applicable local regulations. The monitor will maintain current personal knowledge of the study through observation, review of study records and source documentation, as well as discussion on the conduct of the study with the investigator and site staff. The monitor will review all study source documents to ensure that the eCRFs are completed and accurate.

The monitor, Elicio representatives and regulatory authorities will be given direct access to all study related documentation (such as medical charts/records, laboratory reports, diagnostic reports, study drug logs), study staff training documentation and institutional SOPs to verify study conduct. This verification may continue following completion of the study. It is important that the investigator and study staff are available during the monitoring visit and that sufficient time is devoted to items requiring follow up or resolution.

14.6. Protocol Deviations

A deviation from the protocol is a departure from the procedures and/or processes approved by the sponsor and the IRB and agreed to by the principal investigator.

Protocol deviations will be reported to the sponsor or its designee as they occur or are discovered and must be documented as appropriate in the study source record. In addition, protocol deviations will be reported to the IRB per the individual IRB guidelines. The monitor will document deviations discovered throughout the course of monitoring visits and review of the eCRFs. These deviations, and any necessary corrective actions, will be reviewed and discussed with the sponsor and the investigators as applicable.

14.7. Audits and Inspections

During and/or after the completion of the study, authorized representatives of Elicio, a regulatory authority, or an IRB may visit the trial center to perform audits or inspections, including source data verification. The purpose of an audit or inspection, which is independent from routine monitoring, is to systematically and independently evaluate all trial-related activities and documents to determine whether these activities were conducted, according to the protocol, GCP and current ICH guidelines, and applicable regulatory requirements.

The investigators accept that by endorsing the protocol signature page that the sponsor, IRB or regulatory authorities may conduct an inspection to verify compliance to the protocol and GCP/ICH guidelines. Representatives of the sponsor, IRB or regulatory authority will be permitted direct access to source documents. It is important that the investigator and study staff are available during the inspection or audit and that sufficient time is given to addressing any questions or items that require resolution.

If a regulatory authority or IRB notifies the clinical site of an inspection related to the study, the investigator will immediately notify the sponsor. The investigator agrees to cooperate with Elicio or its designees, when possible, to be present at the inspection. The investigator also agrees to promptly provide the sponsor with copies of inspection findings. Before submitting a response to regulatory authorities, the investigator will give Elicio and/or its designees the opportunity to review the response and provide feedback.

14.8. Institutional Review Board and Other Committees

14.8.1. Institutional Review Board

Federal regulations and ICH guidelines require that IRB approval be obtained prior to participation of human subjects in research studies. Prior to the study start, the protocol, IB, informed consent form (ICF) and any other relevant documents must be approved by an IRB. IRB approvals, and all materials approved by the IRB for this trial must be maintained by the investigator and made available for inspection. Copies of all IRB approvals should be forwarded to Elicio or its designee.

The investigator is responsible for informing the IRB of any amendment to the protocol in accordance with local requirements. In addition, the IRB must approve all advertising used to recruit subjects for the trial. The protocol must be re-approved by the IRB upon receipt of amendments and annually, as local regulations require.

The investigator is also responsible for providing the IRB with reports of any SUSAR (suspected unexpected serious adverse reaction) from any other site or trial conducted with ELI-002 7P. Elicio or its designee will provide this information to each participating site.

Progress reports and notifications of SUSARs will be provided to the IRB according to local regulations and guidelines.

If the clinical site submits to a central IRB, Elicio or its designee will submit the protocol, amendments, and any required safety notifications on the site's behalf to the central IRB.

14.8.2. Independent Data Monitoring Committees

The IDMC is anticipated to meet to review safety from Phase 1A and Phase 2; the IDMC will advise on interim safety and efficacy aspects of the trial as required. Refer to the IDMC charter for details.

During Phase 1A (Cohort 1), if 2 or more of the 6 subjects experience a DLT in the first 28 days (except laboratory abnormalities that are not clinically significant), then the IDMC will review and may recommend a reduction in the ELI-002 7P dose (ie, RP2D−1) and an additional 6 subjects will be added to Phase 1A at the reduced dose level. An additional 6 subjects at the

RP2D−1 may also be added if further characterization of the Phase 2 dose is required. The IDMC will review prior to activating Phase 1B/Phase 2 enrollment. Following IDMC review of the Phase 1A safety data, if the IDMC decides on a dose level to proceed to Phase 2, Phase 1A enrollment of PDAC subjects may continue at this dose level until Phase 2 is opened to enrollment. Phase 1B (Cohort 2, CRC) may be opened to enrollment by Elicio either concurrent or subsequent to Phase 2. If Cohort 2 is opened this will be documented in a study memo sent to all clinical sites and maybe submitted to IRBs, per IRB guidance.

A trial memo will be sent to all study sites following IDMC review of safety and efficacy data with any changes to the planned dosing.

15. ETHICS

15.1. Ethical Conduct of the Trial

The trial will be performed in accordance with the protocol, legal and regulatory requirements, and the general principals in the Declaration of Helsinki, International Ethical Guidelines for Biomedical Research Involving Human Subjects, and ICH Guidelines for GCP.

15.2. Written Informed Consent

A written informed consent form in compliance with 21 CFR Part 50 will be obtained from each subject prior to the subject entering the study or performance of any study specific procedures. The investigator at each center will ensure that the IRB approved consent form is used to provide the subject full and adequate oral and written information about the nature, purpose, possible risk, the possibility of disease progression or recurrence, and benefit of the trial. Subjects must also be notified that they are free to discontinue from the trial at any time. The subject should be given the opportunity to ask questions and allowed time to consider the information provided.

Remote/electronic consent procedures may be used following sponsor review of the process.

The investigator must maintain the signed Informed Consent Form in the subject study record, along with documentation of the informed consent process (ie, statement of consent). A copy of the signed Informed Consent Form must be given to the subject. If the ICF is revised during the study, the subject must sign the revised consent form.

16. DATA HANDLING AND RECORDKEEPING

16.1. Retention of Records

The investigator must maintain all documentation relating to the trial (defined as all essential documents in ICH/GCP) for at least a period of 2 years after the last marketing application approval, or if not approved 2 years following the discontinuance of the study; or in accordance with local requirements (if longer). If it becomes necessary for Elicio or the Regulatory Authority to review any documentation relating to the trial, the investigator must permit access to such records.

The clinical site will provide details of storage location for all study related documentation to the sponsor or its designee both during and after the study.

17. PUBLICATION POLICY

Elicio encourages publication of results obtained during the conduct of the sponsored clinical trial, whether the results are positive or negative. To ensure against inadvertent disclosure of confidential information or unprotected inventions, the investigator and/or institution will provide Elicio the proposed publication at least thirty (30) days prior to disclosure so that Elicio has an opportunity to review prior to the submission or other disclosure. Upon the request of Elicio, Institution and Investigator will remove all confidential information of sponsor other than study data from such proposed publication. In addition, if any patent action is required to protect intellectual property rights or other proprietary rights contained in any proposed publication, the investigator and/or institution will delay the proposed publication for an additional 60 days to allow sponsor to obtain such protection.

If the site is part of a multicenter study, the first publication will be jointly authored by all clinical trial sites and any subsequent publications by the investigator will reference the first publication. Authorship will be determined by the sponsor and investigators according to the ethical standards concerning publication and authorship, including Section II – "Ethical considerations in the Conduct and Reporting of Research" of the requirements for submission to biomedical journals set by the International Committee of Medical Journal Editors. Subject identity will remain anonymous in any presentation or reporting of the trial. At least 2 sponsor representatives will also be included as co-authors on the first publication of the multicenter results to allow recognition of the sponsor's involvement in the design, clinical operation, and management of the study. If a joint manuscript is not submitted within 18 months of study completion the investigator is free to publish separately, following all other requirements in this section.

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19. APPENDICES

19.1. ECOG Performance Status Scale

The ECOG Performance Status Scale is provided in Table 20.

Table 20: ECOG Performance Status Scale

GRADE	ECOG PERFORMANCE STATUS
0	Normal activity. Fully active, able to carry on all pre-disease performance without restriction.
1	Symptoms, but ambulatory. Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature (eg, light housework, office work).
2	In bed <50% of the time. Ambulatory and capable of all self-care, but unable to carry out any work activities. Up and about more than 50% of waking hours.
3	In bed >50% of the time. Capable of only limited self-care, confined to bed or chair more than 50% of waking hours.
4	100% bedridden. Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair.
5	Dead

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Phase 2 Statistical Analysis Plan (SAP2)

Customer Name: Elicio Therapeutics, Inc.

Protocol Number: ELI-002-201

Protocol Title: First in Human Phase 1/2 Trial of ELI-002 7P Immunotherapy as Treatment for Subjects with Kirsten Rat Sarcoma (KRAS)/Neuroblastoma RAS viral oncogene homolog (NRAS) Mutated Pancreatic Ductal Adenocarcinoma (PDAC) and Other Solid Tumors

Protocol Version and Date: Version 8.0 06-Feb-2026

Syneos Health Project Code: 7039255

Author: [redacted], Principal Biostatistician

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APPROVALS

ATTESTATION AND APPROVALS		
Attestation: I confirm that I have reviewed this document and agree with the content.		
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TABLE OF CONTENTS

Version History **2**

APPROVALS **3**

TABLE OF CONTENTS **4**

1. GLOSSARY OF ABBREVIATIONS **7**

2. PURPOSE **9**

2.1. Responsibilities 10

2.2. Timings of Analyses 10

3. STUDY OBJECTIVES AND ASSOCIATED ENDPOINTS **11**

3.1. Phase 2 Primary Objective and Associated Endpoint 11

3.2. Phase 2 Secondary Objectives and Associated Endpoints 11

3.3. Phase 2 Exploratory Objectives and Endpoints 11

4. STUDY DETAILS AND PLAN **13**

4.1. Brief Description 13

4.2. Subject Replacement 14

4.3. Inclusion and Exclusion Criteria 14

4.4. Determination of Sample Size 14

4.5. Treatment Assignment and Blinding 14

4.6. Study Procedures and Flowchart 15

5. ENDPOINTS **16**

5.1. Phase 2 Primary Endpoint 16

5.2. Phase 2 Secondary Endpoints 16

5.3. Phase 2 Exploratory Endpoints 16

6. ANALYSIS SETS **17**

6.1. Intent-to-Treat Set (ITT) 17

6.2. Safety Analysis Set (SAF) 17

6.3. Per Protocol Analysis Set (PPS) 17

6.4. Pharmacodynamical (PD)/Biomarker Evaluable Set (BES) 17

7. GENERAL ASPECTS FOR STATISTICAL ANALYSIS **18**

7.1. Statistical and Analytical Issues 18

7.2. Key Definitions 18

7.2.1. Study Period and Cohort 20

This document is confidential.

7.2.2. Definition of Study Periods for Analysis in Phase 2 21
7.3. Missing Data (Non-Efficacy) and Missing dates 23
7.4. Visit Windows 26
7.5. Pooling of Centers 27

8. DEMOGRAPHIC, OTHER BASELINE CHARACTERISTICS AND MEDICATION 28
8.1. Subject Disposition and Withdrawals 28
8.1.1. Subject Enrollment 28
8.1.2. Subject Disposition 28
8.2. Demographic and Baseline Characteristics 29
8.3. Baseline Mutational Status and Biomarkers 30
8.4. Protocol Deviations 30
8.5. Medical History and Concomitant Diseases 31
8.6. Medication 31
8.6.1. Prior Anti-Cancer Therapies 31
8.6.2. Prior and Concomitant Medications 31
8.6.3. Subsequent Anti-Cancer Therapies 32
8.7. Treatment Exposure and Compliance 32
8.7.1. Method of Administration 32
8.7.2. Treatment Exposure 33

9. EFFICACY 34
9.1. Multiple Comparisons and Multiplicity 34
9.2. Disease-Free Survival (DFS) 34
9.3. Overall Survival (OS) 40
9.4. Biomarker Response Rate (BRR) 41
9.4.1. Proportion of Subjects Who Have Reduction or Clearance (Responders vs. Non-Responders) 41
9.4.2. Duration of Biomarker Response (DBR) 42
9.4.3. Summary of Percent Change from Baseline by Visit 44
9.5. Best Overall Response (ir-BOR) and Objective Response Rate (ir-ORR) 45
9.6. Duration of Response (ir-BOR) 45

10. SAFETY 46
10.1. Adverse Events 46
10.2. Reactogenicity to the Vaccine 48
10.3. Laboratory Evaluations 48

This document is confidential.

10.4. Vital Signs 50
10.5. Electrocardiogram (ECG) 51
10.6. Physical Examination 51
10.7. Eastern Cooperative Oncology Group (ECOG) 51

11. EXPLORATORY ANALYSIS 52
11.1. Patient Reported Outcomes (PROs) 52
11.2. EORTC QLQ-C30 52
11.3. Tumor Type-specific PRO QLQ-PAN26 54

12. INTERIM ANALYSES 56

13. CHANGES FROM ANALYSIS PLANNED IN PROTOCOL 57

14. REFERENCE LIST 58

15. LIST OF TABLES, FIGURES AND LISTINGS 1
15.1. Index of Tables and Figures 1
15.2. Index of Listings 12

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1. GLOSSARY OF ABBREVIATIONS

Abbreviation	Description
ADaM	Analysis data model
AE	Adverse event
ATC	Anatomical Therapeutic Chemical
BES	Pharmacodynamical/Biomarker Evaluable Set
BOR	Best Overall Response
BRR	Biomarker response rate
CA19-9	Cancer antigen19-9
CEA	Carcinoembryonic antigen
CI	Confidence interval
CRC	Colorectal carcinoma
CRF	Case report form
CSR	Clinical Study Report
CT	Computed tomography
CTCAE	Common Terminology Criteria for Adverse Events, Version 5.0
ctDNA	Circulating tumor deoxyribonucleic acid
DBR	Duration of Biomarker Response
DFS	Disease-Free Survival
DNA	Deoxyribonucleic acid
DOR	Duration of Response
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case report form
EORTC	European Organization for Research and Treatment of Cancer
HLA	Human Leukocyte Antigen
HRQOL	Health Related Quality of Life
ICH	International Conference on Harmonization
ICS	Intracellular cytokine staining
IDMC	Independent data monitoring committee
IRB	Institutional review board
ir-BOR	iRECIST Best Overall Response
ir-DOR	iRECIST Duration of Response
ir-ORR	iRECIST Objective Response Rate
ITT	Intent-to-Treat
iUPD	Immune Unconfirmed Progressive Disease
iRECIST	Immune Response Evaluation Criteria in Solid Tumors
KRAS	Kirsten rat sarcoma viral oncogene homolog
LOD	Limit of detection
LLOQ	Lower limit of quantitation
MedDRA	Medical Dictionary for Regulatory Activities

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Abbreviation	Description
mKRAS	Mutant Kirsten rat sarcoma
MMRS	Mixed Effect Model for Repeated Measurement
mNRAS	Mutant neuroblastoma ras viral oncogene homolog
MRD	Minimal residual disease
MTM	Mean tumor molecules
NRAS	Neuroblastoma rat sarcoma viral oncogene homolog
ORR	Objective response rate
OS	Overall survival
PD	Progressive disease
PDAC	Pancreatic ductal adenocarcinoma
PDNC	Protocol Deviation and Non-Compliance
PE	Physical Exam
PPS	Per-Protocol analysis set
PR	PR interval
PROs	Patient reported outcomes
PT	Preferred term
QLQ	Quality of Life Questionnaire
QLQ-C30	Quality of Life Questionnaire for cancer
QLQ-PAN26	Quality of Life Questionnaire for Pancreatic Cancer
QoL	Quality of life
QTc	Corrected QT interval
QTcB	Bazett correction of QT interval
QTcF	Fridericia correction of QT interval
RFS	Relapse-free survival
RP2D	Recommended Phase 2 dose
SAE	Serious adverse event
SAF	Safety Analysis Set
SAP	Statistical Analysis Plan
SC	Subcutaneous
SOC	System organ class or standard of care
TEAE	Treatment-emergent adverse event
TNFα	Tumor necrosis factor alpha
TNM	TNM Classification of Malignant Tumors
ULN	Upper limit of normal
ULOQ	Upper limit of quantification
WHO	World Health Organization

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2. PURPOSE

This document outlines the statistical methods to be implemented during the analyses of data collected within the scope of Elicio Therapeutics, Inc. Study, ELI-002-201. The purpose of this statistical analysis plan (SAP) is to provide specific guidelines for the statistical analyses. Any deviations from this plan will be documented in the clinical study report (CSR).

This SAP2 is dedicated to the Phase 2 portion of the protocol. A separate SAP1 was prepared for the Phase 1 portion of the protocol.

ELI-002-201 is an open-label, Phase 1/2 trial of ELI-002 7P immunotherapy as adjuvant treatment for subjects with Kirsten Rat Sarcoma (KRAS)/neuroblastoma RAS viral oncogene homolog (NRAS) mutated pancreatic ductal adenocarcinoma (PDAC) and other solid tumors who are at high risk for relapse.

ELI-002 7P is a structurally novel amphiphilic therapeutic vaccine being studied as adjuvant treatment of minimal residual disease (MRD) in the Phase 1 subjects with KRAS viral oncogene homolog mutated PDAC and other KRAS mutated solid tumors who have previously had locoregional therapy, while the Phase 2 subjects do not require MRD positivity for eligibility into the study.

ELI-002 7P targets mutant KRAS (mKRAS)-driven malignancies expressing the most common oncogenic mutant forms of KRAS. Upon subcutaneous (SC) injection, the components of the vaccine are drained from the peripheral tissues into the lymph nodes.

ELI-002 7P is well suited to pancreatic cancer since it covers common mutations in KRAS that are present in the majority of pancreatic adenocarcinoma cases. Enhancing the T-cell immune response to PDAC by utilizing the targeted KRAS ELI-002 product candidate has the potential to improve the outcomes of subjects who have undergone pancreatic resection surgery.

In this protocol, ELI-002-201, the safety and efficacy of ELI-002 7P (Amph-CpG-7909 admixed with Amph-Peptides 7P) will be evaluated in subjects with KRAS/neuroblastoma RAS viral oncogene homolog (NRAS) mutated solid tumors who have MRD; Phase 2 subjects do not require MRD positivity for eligibility into the study). Specifically, the ELI-002 7P admixture will consist of Amph-CpG-7909 at the recommended Phase 2 dose (RP2D; determined in Study ELI-002-001 to be 10.0 mg). This Amph-CpG-7909 RP2D will be evaluated in Phase 1A with two dose levels of Amph-Peptides 7P (G12D, G12R, G12V, G12A, G12C, G12S, and G13D): 4.9 mg of total 7 Amph-Peptides (700 μg of each peptide) and 1.4 mg total (200 μg of each peptide). Following IDMC review of the Phase 1A safety data, if the IDMC recommends on a dose level to proceed to Phase 2, Phase 1A enrollment of PDAC subjects may continue at this

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dose level until Phase 2 is opened to enrollment. A Phase 1B (Cohort 2, CRC) may be opened to enrollment by Elicio either concurrent or subsequent to Phase 2.

2.1. Responsibilities

Syneos Health will perform the statistical analyses and is responsible for the production and quality control of all tables, figures and listings (TFLs).

2.2. Timings of Analyses

For Phase 2, a safety evaluation is planned when approximately 20 biomarker evaluable subjects observed for at least 28 days are available for review by the IDMC. This will include a review of the limited biomarker data for consistency with the data observed in the similar patient population treated with study treatment ELI-002 2P conducted in Study ELI-002-001. There will be no hypothesis testing at this safety evaluation; consequently, no type I error (alpha) is spent at this review.

One interim analysis on the primary endpoint of DFS is planned when approximately 67 percent of the total DFS events are observed. Complete details are provided in Section 12.

At the time that approximately 71 DFS events have occurred, a final primary analysis of the DFS endpoint will be performed using the methods described in Section 9.2.

Because this is a non-registrational Phase 2 trial, separate analysis of key secondary and safety endpoints (including OS) may be performed later after additional follow up has accrued and at the discretion of the Sponsor. The database will be locked at this point.

Safety monitoring will occur continuously in the trial. Safety tables will be produced at the DFS interim analysis to allow the IDMC to comprehensively evaluate the risk benefit profile.

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3. STUDY OBJECTIVES AND ASSOCIATED ENDPOINTS

3.1. Phase 2 Primary Objective and Associated Endpoint

Primary Objective	Primary Endpoint
To compare ELI-002 7P versus standard of care (SOC; observation) in Disease-Free Survival (DFS) (per investigator)	DFS

3.2. Phase 2 Secondary Objectives and Associated Endpoints

Secondary Objective	Secondary Endpoint
To compare overall survival (OS) between subjects randomized to ELI-002 7P versus SOC (observation)	OS
To assess 6, 12, and 18 month DFS and OS rates	DFS6, DFS12, DFS18, OS6, OS12, OS18
To compare circulating tumor deoxyribonucleic acid (ctDNA) reduction and clearance, or if ctDNA was not detectable at baseline, serum tumor biomarker (such as Cancer antigen 19-9 (CA19-9) and Carcinoembryonic antigen (CEA)) reduction and clearance compared to baseline in subjects randomized to ELI-002 7P versus SOC (observation)	The secondary endpoint is called the biomarker response rate (ctDNA, CA19-9, CEA) and is referenced later in the document.
To assess the safety and tolerability of ELI-002 7P	Adverse events Reactogenicity to the vaccine Clinical Laboratories Vital Signs Electrocardiograms (ECG) Physical Exam Eastern Cooperative Oncology Group Performance Status

3.3. Phase 2 Exploratory Objectives and Endpoints

The exploratory objectives of Phase 2 are:

- To assess the change from baseline in:
  - To assess objective response rate (irORR) in subjects who cross over to ELI-002 7P from observation after relapse according to Immune Response Evaluation Criteria in Solid Tumors (iRECIST)

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- To evaluate the immunogenicity of ELI-002 7P. T cell responses to ELI-002 7P will be assessed using assays such as ICS, Fluorospot, and/or dextramer^{+} T cells for subjects with HLA alleles for which dextramer/s is/are available
- Biomarker levels (ctDNA, CA19-9, and CEA)
- To evaluate tumor-infiltrating T cells and the tumor microenvironment after dosing with ELI-002 7P

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4. STUDY DETAILS AND PLAN

4.1. Brief Description

The Phase 2 portion of the study (Cohorts 3A, 3B and 3C) will proceed contingent on the observation of antitumor activity with ELI-002 during the clinical development programs. In Phase 2, approximately 135 subjects with PDAC will be randomized 2:1 to ELI-002 7P or SOC (observation), respectively. Subjects randomized to ELI-002 7P will receive SC injections of ELI-002 7P during the Immunization Period and the Booster Period. These are Cohort 3A subjects. Subjects randomized to SOC (observation) will be able to cross over to ELI-002 7P treatment following confirmed disease progression.

Cohort 3B are the subjects randomized to SOC and includes all time up to the optional cross over to ELI-002 7P. Cohort 3C is the period of time after cross over from SOC to ELI-002 7P for subjects randomized to SOC.

Randomization in Phase 2 will be stratified according to the nodal status: node negative versus node positive (0 versus 1).

The trial will consist of:

- A Screening Period in which study specific procedures, including eligibility determination, will begin at Visit 1, following locoregional therapy.
- An Immunization Period which will consist of 6 SC injections: 4 weekly injections (Visit 2 to Visit 5) followed by 2 injections every 2 weeks at Visit 6 and Visit 7, if assigned to the ELI-002 7P treatment arm.
- A No Dosing 2-Month Period in which subjects will continue to be observed and evaluated.
- A Booster Period, consisting of 4 weekly injections (Visit 10 to Visit 13), in which eligible subjects will receive further lymph node antigen exposure, if assigned to the ELI-002 7P treatment arm. A Booster Period is provided as further lymph node antigen exposure may be required to maintain effective levels of antigen-specific T cells. All subjects will receive booster doses unless they have unresolved toxicity.
- A Follow-up Period which will provide continued safety and efficacy data

All subjects will be observed for safety and tolerability. Radiographic imaging with contrast will be performed at screening, approximately every 3 months after the first dose, and at additional timepoints as described in the Schedules of Assessment; for subjects randomized to observation only.

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4.2. Subject Replacement

There are no planned subject replacements in Phase 2.

4.3. Inclusion and Exclusion Criteria

Refer to Protocol Section 7.1 and Section 7.2 for more information on Inclusion and Exclusion criteria.

4.4. Determination of Sample Size

For Phase 2 (PDAC), the sample size of approximately 135 subjects will be randomized 2:1 to receive ELI-002 7P or SOC (observation), respectively. Randomization will be stratified by nodal status (N0 vs. N1). Assuming the true HR is 0.53 (median DFS of 7 months vs. 13.2 months), a 2-sided alpha of 0.10 (or equivalently 1-sided alpha 0.050), and a power of 80%, approximately 71 total number of DFS events will be required to detect the hypothesized HR of 0.53. One interim analysis and one final analysis is planned. A safety evaluation is also planned when approximately 20 biomarker evaluable subjects are available and have been on study for at least 28 days. Although the sample size calculation uses a conventional hypothesis testing framework, this non-registrational Phase 2 study will be interpreted primarily in terms of estimation of the DFS treatment effect. As described in Section 9.2, the decision as to whether the study is considered successful will be based on the totality of evidence on DFS (hazard ratio, confidence intervals, 1-year DFS rate and key subgroup results), together with the observed safety profile and biomarker data, rather than on any single p-value.

4.5. Treatment Assignment and Blinding

In Phase 2, approximately 135 subjects with PDAC will be randomized 2:1 to ELI-002 7P or SOC (observation), respectively. Randomization in Phase 2 will be stratified according to the nodal status: node negative versus node positive (0 versus 1).

Subjects randomized to SOC (observation) will be able to cross over to ELI-002 7P treatment following confirmed disease progression.

Elicio contracted with the vendor Almac to produce the randomization schedule and the assignment of treatments were managed by Almac.

The study is open-label.

If a subject meets any of the following conditions, the subject will be required to discontinue study drug administration but should continue other trial related procedures as specified for the follow-up period of the study.

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1. Any intolerable AE, at the investigator's discretion
2. During study treatment:
    a. Any investigational product use other than ELI-002 7P
    b. Other anti-cancer treatment

3. Non-compliance with trial treatments/procedures. If a subject misses ≥ 2 trial visits without underlying toxicity, the subject should be re-instructed regarding dosing and follow up and continue trial participation. If a subject continues to miss trial visits without toxicity and despite re-instruction, they should be discontinued from the trial treatment phase but follow up data should be collected as possible.
4. The subject requests to be withdrawn from the trial treatment

4.6. Study Procedures and Flowchart

The total duration of participation for each subject is approximately 3 years, and includes a Screening Period, an Immunization Period, a No Dosing 2-Month Period, a Booster Period, and a Follow-up Period. Subjects who cross over after observation in the Phase 2 portion of the study will be followed for a minimum of 1 year after the final administration of ELI-002 7P.

The design of the Phase 1/2 trial is outlined in the Cohort Schematic in the SAP Section 7.2.1.

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5. ENDPOINTS

5.1. Phase 2 Primary Endpoint

The primary endpoint of Phase 2 is:

- DFS (per investigator)

5.2. Phase 2 Secondary Endpoints

The secondary endpoints of Phase 2 are:

- 1-year DFS rate
- OS
- Biomarker response rate (BRR) – Proportion of subjects with biomarker response (ctDNA or serum tumor biomarker), defined as reduction or clearance in biomarker compared to baseline
- Safety as assessed by the incidence of AEs and clinically significant changes in laboratory tests and vital signs

5.3. Phase 2 Exploratory Endpoints

The exploratory endpoints of Phase 2 are:

- irORR in subjects who cross over to ELI-002 7P from observation after relapse according to iRECIST
- Change relative to baseline in:
    - Immunogenicity of ELI-002 7P determined by the magnitude of response and the fold-change from baseline, using assays such as ICS, Fluorospot, and/or dextramer^{+} T cells for subjects with HLA alleles for which dextramer/s is/are available
    - Biomarker levels
    - Immune cell infiltrate and tumor microenvironment if standard-of-care biopsies are obtained to confirm new lesions

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6. ANALYSIS SETS

The following analysis sets will be evaluated and used for presentation of the data.

6.1. Intent-to-Treat Set (ITT)

For Phase 2, the Intention-to-treat (ITT) Set includes all subjects randomized to ELI-002 7P or SOC (observation). The ITT Set will be the primary set for the analysis of efficacy unless otherwise specified.
The planned, randomized treatment will be used for the summaries. The ITT set will also be used for summaries of subject demographics and baseline characteristics.

6.2. Safety Analysis Set (SAF)

For Phase 2, the Safety Analysis Set (SAF) includes subjects who received any amount of vaccine or observation study treatment. This population will be used for the safety evaluations (AEs, clinical laboratory assessments, vital signs, ECGs, PEs). No data will be imputed for the safety analysis sets unless otherwise specified. Refer to Section 7.3 for imputation rules. Actual treatment received will be used for the Safety Analysis Set.

6.3. Per Protocol Analysis Set (PPS)

The Per Protocol Analysis Set will include all ITT subjects who have no major protocol deviations. The exclusion list for this set will be identified prior to database lock. Analysis with this analysis set will be conducted if warranted.

6.4. Pharmacodynamical (PD)/Biomarker Evaluable Set (BES)

For all Phase 2 subjects who are randomized (ITT), the additional requirement that relevant blood sampling data at the appropriate assessment time point(s), including baseline, must be available for inclusion in the analysis for the corresponding parameter (immunogenicity, serum tumor biomarker CA19-9/CEA, ctDNA). Unscheduled post-baseline biomarker tests will be included in the analysis. Further, subjects evaluated for serum tumor biomarker response (ctDNA, CA19-9 or CEA) must meet one of the criteria that,

1. Successive rising values, at least 1 week apart, at baseline, or
2. Baseline biomarker values CA19-9 ≥90 U/mL or CEA ≥15 ng/mL, or
3. ctDNA detected at baseline

The BES will be used for all biomarker analyses.

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7. GENERAL ASPECTS FOR STATISTICAL ANALYSIS

7.1. Statistical and Analytical Issues

Statistical analyses will be carried out by using SAS Version 9.4 or higher.

Any deviations from the planned analysis as described in this SAP will be justified and recorded in the clinical study report. This SAP (including any subsequent amendments) will be finalized and approved by the Sponsor and the responsible statistician prior to database lock for the Phase 2 primary DFS analysis.

Any post hoc analyses or changes made after database lock will be clearly identified and justified in the clinical study report.

Tabulations will be produced for appropriate demographic, baseline, safety, and efficacy parameters. Continuous variables will be summarized by reporting the number of observations, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized using frequency tables showing the number and percentage of subjects within a particular category, where the denominator is the number of non-missing values within the category at applicable time point (unless otherwise specified).

7.2. Key Definitions

Date of First Treatment:

This date of first treatment will be applied for the determination of period of occurrence / usage of adverse events, concomitant medications, and for the determination of study day for safety endpoints.

- For subjects randomized to the ELI-002 7P, the date of first treatment will be the date of first vaccination (scheduled for Visit 2).
- For subjects randomized to the SOC treatment arm, the date of Visit 2 will be the date of first treatment.
- For subjects in the SOC treatment arm who cross over to ELI-002 7P, the date of first ELI-002 7P administration will be the first treatment date in the crossover period.

Date of Last Treatment

- For subjects randomized to the ELI-002 7P, the date of last treatment will be the date of last vaccination administration in either the immunization or booster time periods.
- For subjects randomized to the SOC treatment arm, the date of last treatment will be the date of the last study visit up to and including Visit 13 (Week 20/End of Treatment), if

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the subject did not cross over to ELI-002 7P, or minimum of the date of last visit up to and including Visit 13 (Week 20/End of Treatment) or the day before first ELI-002 7P administration, if the subject crossed over to ELI-002 7P.

- For subjects in the SOC treatment arm who cross over to ELI-002 7P, the date of last treatment in the cross over period will be the date of last ELI-002 7P administration.

Calculation of Study Day:

The calculation of study day will depend on the endpoint being summarized.

For baseline characteristics, medical history, prior and concomitant treatments, and efficacy endpoints, study day will be calculated relative to the randomization date.

- Pre-randomization and post-randomization study days are numbered relative to the date of randomization, which is designated as Day 1. The preceding day is Day -1, the day before that is Day -2, etc.
- Study day will be calculated relative to the date of randomization. If an assessment date is on or after date of randomization, then study day will be calculated as assessment date – randomization date + 1. If an assessment date is prior to the date of randomization, then study day will be calculated as assessment date – date of randomization.

For safety endpoints, study day will be calculated relative to the first treatment date.

- Pre-randomization and post-randomization study days are numbered relative to the date of first treatment, which is designated as Day 1. The preceding day is Day -1, the day before that is Day -2, etc.
- Study day will be calculated relative to the date of first treatment. Note, for SOC subjects, the date of first treatment is the Visit 2 date. If an assessment date is on or after date of first treatment, then study day will be calculated as assessment date – first treatment date + 1. If an assessment date is prior to the date of first treatment, then study day will be calculated as assessment date – first treatment.

Baseline

Baseline will be defined as the last evaluable/non-missing observation/assessment prior to the date/time of Day 1.

Time-to-event data will be summarized using the Kaplan-Meier method; statistical testing of the time-to-event endpoint will be made using the log-rank test.

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Adverse events (AEs) will be recorded and graded using Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.

AEs and medical history will be coded for summarization using the Medical Dictionary for Regulatory Activities (MedDRA® Version 28.0). Medications will be coded using the World Health Organization (WHO) Drug Dictionary (WHODD B3G Mar 2025).

By-subject data listings will be produced for data collected throughout the study (e.g., CRF, lab). All data listings that contain an evaluation date will also display the relative study day.

7.2.1. Study Period and Cohort

Summaries will be provided by treatment arm. Note that Cohort 3C will consist of subjects who were randomized to the SOC arm and had confirmed progression and may cross over to receive ELI-002 7P treatment. The total column will include subjects randomized to ELI-002 7P and SOC only.

Refer to Section 4.1 or Cohort information. Presentations for analyses in this SAP can be categorized into three different types of summaries.

Table 1: Presentation for Phase 2

ELI-002 7P N=xx n (%)	SOC N=xx n (%)	Total N=xx n (%)	SOC crossover to ELI-002 7P N=xx (n (%)

This will be used for disposition, demographics, deviations, baseline characteristics, prior treatments, and concomitant therapies.

The second type of summary will be used for efficacy analyses. See Section 9 of the SAP for handling rules for the endpoints.

Table 2: Presentation for Phase 2

ELI-002 7P N=xx n (%)	SOC N=xx n (%)

For Adverse event summaries and selected concomitant treatment columns, an additional column will be added, as described in Table 3.

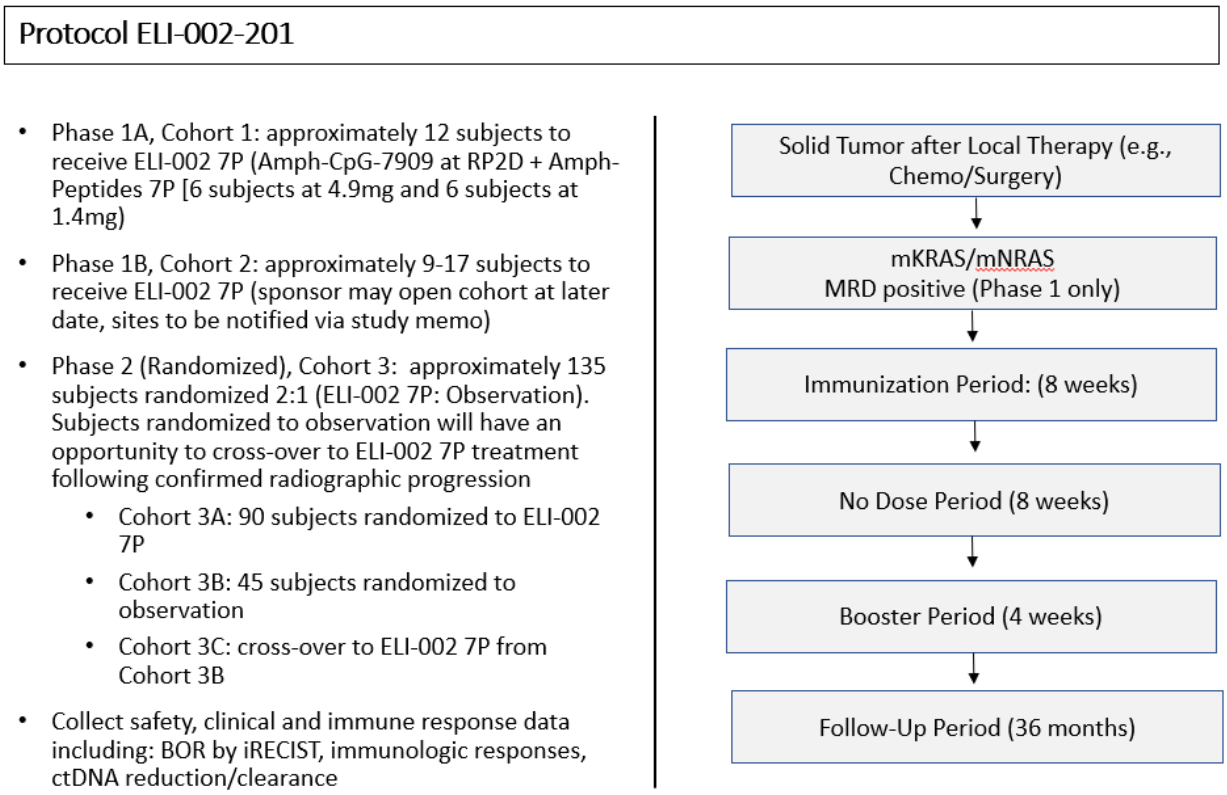
Table 3: Presentation for Phase 2

ELI-002 7P N=xx n (%)	SOC N=xx n (%)	SOC crossover to ELI-002 7P N=xx (n (%)

Summary data in the SOC column includes data up to the time of cross over if the subject crossed over, while summary data in the "SOC crossover to ELI-002 7P" column includes data starting from the date of first treatment in the crossover period.

7.2.2. Definition of Study Periods for Analysis in Phase 2

The following diagram is from Protocol Section 6.1 Figure 3 describes the study periods in the study.



For determination of study periods, the following definitions will be used for Cohorts 3A and 3B. For subjects in Cohort 3B who opt to crossover to ELI-002 7P, visits after crossover will be described as crossover visits.

Table 4: Study Phase for Randomized Subjects (Prior to Crossover)

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Study Phase	Starting Date	Ending Date
Screening Period	Date of Informed Consent	Day before Date of randomization; Note the definition of baseline values in Section 7.2.
Immunization Period	Date of Randomization	Last Visit Date Among Visit 3 (Week 2) – Visit 7 (Week 8)
No Dose Period	Day after Last Visit in Immunization Period	Day Before Date of Visit 10 (Week 17)
Booster Period	Date of Visit 10 (Week 17)	Date of Last Visit Among Visit 10 – Visit 13 (Week 20)
Follow-up Period	Day after Last Visit in Booster Period	Study Discontinuation

For the Cohort 3B subjects who opted to crossover to ELI-002 7P, periods will be defined relative to the first ELI-002 7P vaccination date.

Table 5: Study Phase for Subjects Who Crossover to ELI-002 7P

Period	Starting Date	Ending Date
Crossover Immunization Period	Date of First ELI-002 7P vaccination	Date of Last Vaccination among Vaccinations 1 - 6
Crossover No Dose Period	Day after Last Vaccination in Crossover Immunization Period	Day Before Vaccination 7
Crossover Booster Period	Date of Vaccination 7	Date of Last Vaccination among Vaccination 7 – 10
Crossover Follow-up Period	Day after Last Visit in Crossover Booster Period	Study Discontinuation

7.2.2.1. *Repeated or Unscheduled Assessments*

It is possible that repeat or unscheduled assessments are made for safety or efficacy endpoints (e.g., ctDNA, biomarkers, radiographic scans, clinical laboratory tests, vital signs, ECGs, etc.). It is also possible that multiple measurements are available within the same window for summary, whether they are scheduled or not. In this case, the following rules should be applied for statistical summary unless otherwise specified:

- If a subject has repeated assessments before randomization (date of first treatment for safety endpoints), then the results from the final assessment made prior to randomization (date of first treatment for safety endpoints) will be used as baseline assessment..

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- If unscheduled values (radiographic scans, ctDNA, CA19-9, or CEA) are collected, those values will be included in the analysis as follows:
    - If the unscheduled scans are performed earlier than the scheduled visit, the progression (PD) or disease relapse found earlier at the unscheduled visit will be presented at that unscheduled visit date.
    - Unscheduled ctDNA, CA19-9, and CEA collections will be considered in the same manner as scheduled collections.

All end of study assessment visits will be identified in the CRF. All assessments will be presented in the subject data listings.

7.3. Missing Data (Non-Efficacy) and Missing dates

The following rules will be applied to impute missing start and stop dates in appropriate datatypes (e.g., AEs or concomitant medications)

Start Date

Missing Day Only

- If the month and year of the incomplete date are the same as the month and year of the first dose date, then the day of the first dose date will be assigned to the missing day.
- If either the year is before the year of the first dose date or if years are the same, but the month is before the month of the first dose date, then the last day of the month will be assigned to the missing day.
- If either the year is after the year of the first dose date or if both years are the same, but the month is after the month of the first dose date, then the first day of the month will be assigned to the missing day.

Missing Month Only

- If month is missing only, then the day will be treated as also missing and both month and day will be replaced according to the below procedure for missing day and month.

Missing Day and Month

- If the year of the incomplete date is the same as the year of the first dose date, then the day and month of the first dose date will be assigned to the missing fields.
- If the year of the incomplete date is not the same as the year of the first dose date, then January 1 will be assigned to the missing fields.

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If the stop date is complete and the imputed start date is after the stop date, then the start date will be imputed using the stop date.

Stop Date

Missing Day Only

- If the month and year of the incomplete date are the same as the month and year of the last visit date, then the day of the last visit date will be assigned to the missing day.
- If either the year is before the year of the last visit date or if both years are the same, but the month is before the month of the last visit date, then the last day of the month will be assigned to the missing day.
- If either the year is after the year of the last visit date or if both years are the same, but the month is after the month of the last visit date, then the first day of the month will be assigned to the missing day.

Missing Month Only

- If month is missing only, then the day will be treated as missing and both month and day will be replaced according to the below procedure for missing day and month.

Missing Day and Month

- If the year of the incomplete date is the same as the year of the last visit date, then the day and month of the last visit date will be assigned to the missing fields.
- If the year of the incomplete date is before the year of the last visit date, then December 31 will be assigned to the missing fields.
- If the year of the incomplete date is after the year of the last visit date, then Jan 1 will be assigned to the missing fields.

Imputed Start date and Stop date

- If the imputed stop date is before the imputed start date, the stop date will be set as the imputed start date.
- No imputation will be performed for medication with completely missing start dates. Medications with completely missing start dates will be listed in both prior medications and concomitant medications.

If the start date is complete and the imputed stop date is before the start date, then the stop date will be imputed using the start date.

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Missing Values for Subsequent Cancer Treatment:

The following rules will be applied to impute missing start date of the subsequent cancer treatment.

If the start date is completely missing, given that the patient did receive the anti-cancer therapy, the start date will be set to last dose date of study drug + 1.

Missing Day Only

- If the month and year of the incomplete date are the same as the month and year of the last dose date, then the last dose date + 1 will be assigned to the missing day.
- If the month and year of the incomplete date are after the month and year of the last dose date, then the first day of the month will be assigned to the missing day.

Missing Month Only

- If month is missing only, then the day will be set as missing and treated as missing Day and Month. The day will be treated as also missing and both month and day will be replaced according to the below procedure.

Missing Day and Month

- If the year of the incomplete date is the same as the year of the last dose date, then the last dose date + 1 will be assigned to the missing day and month.
- If the year of the incomplete date is after the year of the last dose date, then Jan 1 will be assigned to the missing day and month.

All data recorded on the CRF will be included in data listings that will accompany the clinical study report (CSR).

Laboratory Tests Results

If the reported value for a clinical laboratory test, with the exception of Biomarker and ctDNA parameters, cannot be used in a statistical summary and analysis due to, for example, a character string being reported for a numerical value, an imputed value may be used in the statistical analysis according to the conventions described below.

- A character field represents a value below a number, e.g., <XX, where XX is the lower limit of quantification (LLOQ) or the limit of detection (LOD), the imputed value will be calculated as half of the numerical cut-off, i.e. XX/2.

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- A character field represents a value greater than a number, e.g., >XX, where XX is the upper limit of quantification (ULOQ), the imputed value will be calculated as XX.

Biomarker and ctDNA Results

- For the ctDNA and biomarker parameters (CEA and CA19-9), values that are below LLOQ, will be imputed as a value of 0.

Details of the imputation algorithm will be provided in the analysis data model (ADaM) specifications document after reviewing the dry run lab listing prior to database lock.

Actual values as recorded in the database (i.e., the character field) will be presented in data listings.

7.4. Visit Windows

All data will be tabulated per the evaluation visit as recorded on the eCRF, even if the assessment is outside of the visit window. The repeated assessments will be included in analysis as described below and in the data listings.

It is possible that repeat or unscheduled assessments are made for safety or efficacy endpoints (e.g., ctDNA, biomarkers, radiographic scans, clinical laboratory tests, vital signs, ECGs, etc.). It is also possible that multiple measurements are available within the same window for summary, whether they are scheduled or not. In this case, the following rules should be applied for statistical summary unless otherwise specified:

- If a subject has repeated assessments before randomization (date of first treatment for safety endpoints), then the results from the final assessment made prior to randomization (date of first treatment for safety endpoints) will be used as baseline assessment.
- If unscheduled values (radiographic scans, ctDNA, CA19-9, or CEA) are collected, those values will be included in the analysis as follows:
    - If the unscheduled scans are performed earlier than the scheduled visit, the progression (PD) or disease relapse found earlier at the unscheduled visit will be presented at that unscheduled visit date.
    - Unscheduled ctDNA, CA19-9, and CEA collections will be considered in the same manner as scheduled collections.

All end of study assessment visits will be identified in the CRF. All assessments will be presented in the subject data listings.

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7.5. Pooling of Centers

No pooling of sites will be performed as no by-site analyses are planned for this study.

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8. DEMOGRAPHIC, OTHER BASELINE CHARACTERISTICS AND MEDICATION

8.1. Subject Disposition and Withdrawals

8.1.1. Subject Enrollment

Subject enrollment will be presented by randomized treatment and overall, for Phase 2, using all Phase 2 subjects. Subjects will be considered to have completed the study if the End of Study eCRF indicates completed study. Tabulation will include the following:

- Number of screened subjects
- Number of screen failed subjects
- Number (%) in each analysis set (ITT, Safety, Per Protocol, Pharmacodynamic/Biomarker Evaluable)
    - For ITT subjects excluded from the Per Protocol Set, the classification of major deviations leading to exclusion will be added.
    - For ITT subjects excluded from the BES set, the reason for exclusion will be summarized:
- Subjects excluded from the various analysis sets will be listed by treatment arm.

8.1.2. Subject Disposition

Subject disposition will be based on the ITT Set. Summaries will be done by treatment arm.

- Number (%) of subjects in each study period (Immunization period, No Dosing 2-Month Period, Booster Period, Follow-up Period Year 1 – Year 2, Follow-up Period Year 2-Year 3.
- Number (%) of subjects ongoing in the study
- Number (%) of subjects completing the treatment period.
- Number (%) of subjects who discontinued treatment and reason for discontinuation of study treatment
- Number (%) of subjects completing the study
- Number (%) of subjects who discontinued from the study and reason(s) for discontinuation of study
- Subjects who discontinue from the treatment or study will be listed by treatment arm with reason for treatment/study discontinuation.
- Subjects who crossed over from SOC to ELI-002 7P will be classified as terminated SOC Treatment and terminated study for their original treatment arm with termination reason as “Cross-over to ELI-002 7P”

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8.2. Demographic and Baseline Characteristics

Demographics and baseline characteristics will be presented by treatment arm and overall, for Phase 2 subjects. In addition, all demographic and baseline characteristics will be provided in listings.

The ITT set will be used for the summary of demographics and baseline characteristics.

The following variables will be summarized for demographics using both continuous and categorical descriptive statistics:

- Age (years) as collected in CRF
- Age group, defined as <65 years, ≥65 years, <75 years, ≥75 years
- Sex
- Female of child-bearing potential, categorized as Yes, No:
    - (i) Post-menopausal (1 year or longer since last menstrual period) and > 55 years of age
    - (ii) Post-menopausal (1 year or longer since last menstrual period) and ≤ 55 years of age with a negative pregnancy test within 1 week of first dose
    - (iii) Surgically sterilized at least 3 months prior to enrollment
- Race
- Ethnicity
- Height (cm)
- Weight (kg)

Note: Age (years) will be obtained from CRF. If weight is collected in pounds (lb), this will be converted to kilograms (kg) by multiplying by 0.4535.

The following variables will be summarized for baseline characteristics using both continuous and categorical descriptive statistics:

- Time since initial study disease diagnosis (months)
- Study disease diagnosis
- Stage at screening
- TNM Stage at screening: PDAC T (T1, T2, T3, T4)
- TNM Stage at screening: PDAC N (N0, N1, N2)
- TNM Stage at screening: PDAC M (M0, M1)
- Did the subject have a resection? (Yes/No)
- If yes, Outcome of resection
- Time since resection (months)

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Time since initial study disease diagnosis (months) = (date of first treatment – date of screening disease diagnosis)/30.4375. Missing data imputation is described earlier in Section 7.3.

Time since initial cancer diagnosis, calculated as the date of informed consent signature minus date of initial diagnosis.

Time since resection (months) = (date of first treatment date - date of resection)/30.4375. For subjects who crossed over from SOC to ELI-002 7P, the time since initial resection will be calculated relative to the randomization in the study.

8.3. Baseline Mutational Status and Biomarkers

The following variables for baseline mutational status and biomarkers will be listed and summarized using descriptive statistics. The ITT Set will be used for the summary.

- KRAS mutation
- NRAS mutation
- Missing both mutation status (for subjects without a sample for both KRAS and NRAS mutations)
- Gene mutation detected (G12A, G12C, G12D, G12R, G12S, G12V, G13D)
- ctDNA blood test (positive vs. negative vs. missing)
- ctDNA quantity (MTM/mL)
- Subjects with elevated baseline CA19-9 ≥ 90 U/mL
- Subjects with elevated baseline CEA ≥15 ng/mL
- Subjects with successive rising values of CA19-9 or CEA

8.4. Protocol Deviations

The list of protocol deviations will be finalized per the protocol deviation and non-compliance (PDNC) management plan and will be reviewed by the Sponsor Medical Monitor and the study statistician and finalized before database lock.

Major protocol deviations will result in the removal of a subject from the PPS. Other deviations/scenarios may arise during the pre-lock data review that will be documented and reported.

The summary of major deviations will be done using the ITT set. Deviations will be summarized according to their randomized treatment. The number and percentage of subjects with a major deviation by type of deviation category will be presented by treatment arm (including the crossover period) and overall, for Phase 2 on all enrolled Phase 2 subjects. In addition, all minor and major protocol deviations will be provided in a by-subject listing.

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8.5. Medical History and Concomitant Diseases

Medical history will be coded using MedDRA and will be presented in a data listing by treatment arms and subject. Medical history will be presented for the ITT Set.

8.6. Medication

8.6.1. Prior Anti-Cancer Therapies

Descriptive summaries of prior treatments will be presented for the ITT Set by treatment arm and overall:

- Prior Anti-Cancer Systemic Therapies (systemic therapy line, type, WHO Drug ATC 2 term, Preferred Name, intent, best response, reason for discontinuation, progressing during or after)
- Prior Anti-Cancer Chemotherapies (number of therapies, WHO preferred name, intent, best response, reason for discontinuation, progressing during or after)
- Prior Anti-Cancer Regimens for Pancreatic Cancer (combinations of medications used in a single treatment regimen by preferred names)
- Prior Anti-Cancer Radiotherapy (treatment site, type, intent, settings, unit, and best response)
- Prior Anti-Cancer Surgeries and Procedures (anatomical location and complete removal status)

Anti-cancer medications taken after the last study treatment will be considered as subsequent therapy (therapy being administered specifically for the cancer being studied) medications. Prior anti-cancer therapies and subsequent anti-cancer therapies will be summarized for the ITT Set.

8.6.2. Prior and Concomitant Medications

Prior medication is defined as any medication started prior to the date of randomization. Concomitant medications are defined as any medication taken between the date of randomization and the date of last study treatment, as well as any medication started before the date of randomization and ongoing or ended after the date of randomization. Using these definitions, a medication started prior to randomization and after randomization will be counted in both prior and concomitant medications.

Missing data imputation is described earlier in Section 7.3.

Prior and concomitant medications will be coded using the WHO Drug Dictionary, and subject incidence will be tabulated by Anatomic Therapeutic Class (ATC2) and preferred term, by

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treatment arm. Prior medications and concomitant medications will be presented for the SAF Analysis Set.

Subjects will be counted only once for each ATC level 2 or preferred term if they have multiple records of the same ATC level 2 or preferred term in the database. All prior and concomitant medications will be included in a by-subject data listing for Phase 2.

8.6.3. Subsequent Anti-Cancer Therapies

Summaries of subsequent anti-cancer therapies will be presented by treatment arm using the ITT Set. The number of subjects and percentage who used subsequent therapies will be summarized by treatment arm. The type of anti-cancer therapy used and best response to these anti-cancer therapies will be summarized.

8.7. Treatment Exposure and Compliance

Subjects randomized to the ELI-002 7P are planned to receive SC injections of ELI-002 7P during the Immunization Period and the Booster Period.

8.7.1. Method of Administration

The ELI-002 7P mixture is prepared by combining the separately provided products (ELI-002 Amph-CpG-7909 and ELI-002 Amph-Peptides 7P) in a diluent (10X PBS) prior to dosing. The KRAS Amph-Peptides are provided in 5.0mM, pH 4.5 acetate buffer in a 2-mL glass vial. The Amph-CpG-7909 is provided in water for injection in a 2-mL glass vial. Description of the treatment is shown in Table 6.

Table 6: Description of study treatment

Name	Product Physical Description
ELI-002 Amph-Peptides 7P (Concentration: 4.9 mg/mL)	2 mL glass vial containing 1.4mL for SC injection
ELI-002 Amph-CpG-7909 Vials (Concentration: 5.0 mg/mL)	2 mL glass vial containing 0.70 mL for SC injection

For each subject dose, one vial of Amph-Peptides 7P and four vials of Amph-CpG-7909 will be used. One vial of 10X PBS will be needed.

Subjects will receive SC injections of ELI-002 7P during the Immunization Period at Visit 2 through Visit 7 (see protocol Table 8). For the immunization period, the first 4 doses are weekly, followed by 2 bi-weekly doses. Two months after the Immunization Period, subjects will receive SC injections of ELI-002 7P during the Booster Period at Visit 10 through Visit 13 (End of Treatment) (see protocol Table 10). During the Booster Period, 4 weekly doses will be

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administered. There are four SC injections per dose, one in each upper arm and one in each upper thigh.

The planned cohorts are as shown in Table 7.

Table 7: Phase 2 Randomized Cohorts

Phase	Cohort	Tumor Type	Treatment
Phase 2: Randomized Cohorts	3A	PDAC	ELI-002 7P
Phase 2: Randomized Cohorts	3B	PDAC	SOC/Observation
Phase 2: Randomized Cohorts	3C	PDAC	ELI-002 7P (crossover)

PDAC=pancreatic ductal adenocarcinoma

8.7.2. Treatment Exposure

The following characteristics of treatment exposure will be summarized.

Assigned ELI-002 7P dose: For Phase 2, this is assigned to be 4.9 mg for all treated subjects.

The number of injections administered (noting that at each vaccination visit, the dosage is separated into 4 different syringes. The dosage per injection is assigned ELI-002 7P dose / 4.

Expected cumulative dosage = number of injections administered multiplied by (assigned ELI-002 7P dose) / 4.

Dose intensity = Expected cumulative dose / planned dosage for a subject receiving a full 10-vaccination course of treatment (i.e. 10 vaccination visit = 40 injections * (assigned ELI-002 7P dose / 4).

Relative dose intensity = Dose intensity * 100%.

Duration of treatment (weeks) = Duration of treatment (weeks) is defined as (last injection date – first injection date + 1)/7, this duration also includes dose interruptions or missed doses. For subjects on SOC who cross over to ELI-002 7P, the first injection will be after disease progression during their time on SOC.

Study drug exposure will be summarized descriptively.

These analyses will be presented by treatment arm (ELI-002 7P and crossover ELI-002 7P for Phase 2). All dosing data will be presented in a by-subject data listing for each phase.

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9. EFFICACY

Planned interim and final analyses of efficacy endpoints are described in Section 12 of this SAP.

Efficacy analyses are included under the primary, secondary, and exploratory objectives for Phase 2. The ITT Set will be used for presentation of DFS and OS. The BES will be used for biomarker response rate (reduction or clearance) and duration of biomarker reduction or clearance analyses.

9.1. Multiple Comparisons and Multiplicity

Treatment arms will be compared for each of the following secondary endpoints using the Holm's procedure to control the family-wise error rate:

1.) 1-year DFS rate

2.) OS

3.) Biomarker response rate (BRR)

All confidence intervals will be two-sided 95% confidence intervals and inferential statistical analyses will be evaluated with an overall significance level of alpha = 0.05 (two-sided) unless otherwise specified.

9.2. Disease-Free Survival (DFS)

In Phase 2, DFS is defined as time from randomization to cancer recurrence or death due to any cause, which ever occur first. Cancer recurrence is defined as a confirmed disease progression (per iRECIST) on the response CRF. Scans and disease recurrence dates after the initiation of subsequent anticancer therapies will not be included in the determination of DFS (see exceptions in the censoring rule below Table 8).

For the primary analysis, DFS will be defined as the time from the date of randomization to the earliest of: (1) disease recurrence (iCPD per investigator assessment using iRECIST), or (2) death due to any cause. Subjects will continue to be followed for disease recurrence and survival after the start of any subsequent anti-cancer therapy. If no disease recurrence or death is observed, DFS will be censored at the date of the last evaluable CT/MRI assessment without documented progression (iUPD or absence of progression), including assessments obtained after initiation of subsequent anti-cancer therapy.

Censoring rules for DFS are provided in the following table. An alternate (sensitivity) analysis for DFS will be provided.

Table 8: Censoring Rules for Primary Analysis of DFS

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Primary Analysis		
Situation	**Event or censored date**	**Event or censored**
Censoring Rules for DFS		
No subsequent anti-cancer therapy initiated or **lost to follow up/withdrawal of consent for follow up**:		
1. Death or recurrence **(iCPD)**	1. Date of recurrence **(iCPD)** or death, whichever occurs first 2. If recurrence (iCPD) occurred after iUPD, the event date is the date of the last iUPD prior to the iCPD 3. Note that if recurrence (iCPD) occurred after Absence of Progression with no prior iUPD, the event date is the date of iCPD	1. Event
2. No recurrence or death	2. Date of last evaluation CT/MRI visit, without documentation of recurrence of disease (iUPD or absence of progression)	2. Censored
Note that per protocol, death information is permitted to be collected and entered in the database. The date of death, if present in the database, will be used as an event date.		
Subsequent anti-cancer therapies initiated:		
1. Death or recurrence **(iCPD)** after no more than 1 consecutive missed **CT/MRI** evaluation (i.e., ≤182 days (24 weeks + 2 weeks) after start of subsequent anti-cancer therapies	1. Date of recurrence **(iCPD)** or death, whichever occurs first, according to the following: a. If death occurs without recurrence, then event is the date of death b. If recurrence occurs prior to death, then the date of last evaluable CT/ MRI visit, without documentation of recurrence of disease **(iUPD or absence of progression)**, that is done before the start of subsequent anti-cancer therapy	1. Event
2. No recurrence or death after no more than 1	2. Date of last evaluable CT/ MRI visit, without documentation of recurrence of	2. Censored

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Primary Analysis		
Situation	**Event or censored date**	**Event or censored**
consecutive missed **CT/MRI** evaluation (ie, ≤182 days (≤24 weeks + 2 weeks) after start of subsequent anti-cancer therapy	disease **(iUPD or absence of progression)** that is done before the start of subsequent anti-cancer therapy	
NOTE: If the study allows subjects to crossover to receive ELI-002, the event/censor will be handled similar to the rule for subsequent anti-cancer therapies initiated		
Incomplete or no baseline assessment	Date of randomization or start of treatment (censored on Day 1)	Censored
No post baseline CT/MRI scans	Date of randomization or start of treatment (censored on Day 1)	Censored
Treatment discontinuation for undocumented progression or for toxicity	Date of last evaluation CT/MRI visit, without documentation of recurrence of disease (iUPD or absence of progression)	Censored

Note regarding more than 1 consecutive missed CT/MRI scans: per protocol, scans are scheduled every 12 weeks (84 days). If the difference between the current scan and the previous scan is > 24 weeks + 2 weeks allowable window = 182 days, the subject will have been considered to have missed more than 1 consecutive CT/MRI scans.

A sensitivity analysis of DFS will be completed that ignores the censoring rules regarding start of subsequent anti-cancer therapy, see Table 9. That is, all assessments including those after the start of subsequent anti-cancer therapies will be used. DFS (in months) is calculated as: [(event date or censoring date – date of randomization + 1)] / 30.4375.

Table 9: Censoring Rules for Sensitivity Analysis of DFS

Primary Analysis		
Situation	**Event or censored date**	**Event or censored**
Censoring Rules for DFS		
No subsequent anti-cancer therapy initiated or **lost to**		

Primary Analysis		
Situation	**Event or censored date**	**Event or censored**
follow up/withdrawal of consent for follow up:		
1. Death or recurrence **(iCPD)**	1. Date of recurrence **(iCPD)** or death, whichever occurs first 2. If recurrence (iCPD) occurred after iUPD, the event date is the date of the last iUPD prior to the iCPD 3. Note that if recurrence (iCPD) occurred after Absence of Progression with no prior iUPD, the event date is the date of iCPD	1. Event
2. No recurrence or death	2. Date of last evaluation CT/MRI visit, without documentation of recurrence of disease (iUPD or absence of progression)	2. Censored
Note that per protocol, death information is permitted to be collected and entered in the database. The date of death, if present in the database, will be used as an event date.		
Subsequent anti-cancer therapies initiated:		
1. Death or recurrence **(iCPD)** after no more than 1 consecutive missed **CT/MRI** evaluation (i.e., ≤182 days (24 weeks + 2 weeks)	1. Date of recurrence **(iCPD)** or death, whichever occurs first, according to the following: a. If death occurs without recurrence, then event is the date of death b. If recurrence occurs prior to death, then the date of last evaluable CT/ MRI visit, without documentation of recurrence of disease **(iUPD or absence of progression)**	1. Event
2. No recurrence or death after no more than 1 consecutive missed **CT/MRI** evaluation	2. Date of last evaluable CT/ MRI visit, without documentation of recurrence of disease **(iUPD or absence of progression)**	2. Censored

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Primary Analysis		
Situation	**Event or censored date**	**Event or censored**
Incomplete or no baseline assessment	Date of randomization or start of treatment (censored on Day 1)	Censored
No post baseline CT/MRI scans	Date of randomization or start of treatment (censored on Day 1)	Censored
Treatment discontinuation for undocumented progression or for toxicity	Date of last evaluation CT/MRI visit, without documentation of recurrence of disease (iUPD or absence of progression)	Censored

Note regarding more than 1 consecutive missed CT/MRI scans: per protocol, scans are scheduled every 12 weeks (84 days). If the difference between the current scan and the previous scan is > 24 weeks + 2 weeks allowable window = 182 days, the subject will have been considered to have missed more than 1 consecutive CT/MRI scans.

Summaries will be provided for the ITT Set; analysis based on the PPS may be conducted if warranted.

The median DFS will be estimated using the Kaplan-Meier method. The number of subjects with events (recurrence / death) and the number of subjects censored and the reason of censoring will be presented.

A stratified log-rank test for treatment difference with baseline nodal status as stratification factor will be performed using SAS PROC LIFETEST. A Cox proportional hazards model stratified by baseline nodal status using SAS PROC PHREG will be used to obtain the hazard ratio and its associated 95% confidence interval for hazard ratio. The SOC arm will be used as the reference arm. An unstratified log-rank test for treatment difference will also be carried out as supportive analysis using PROC LIFETEST. Hazard ratios for the unstratified analysis will be calculated using PROC PHREG.

DFS rate at 6, 12, 18 months (additional milestone timepoint may be added if warranted) and confidence intervals (CI) using the method of Brookmeyer-Crowley method will be presented in the tables.

The difference in the DFS rate at 1 year (12 months) will be tested using the complementary log-log method (cloglog) method described in Klein JP (2007).

A Kaplan-Meier plot by treatment arm will be provided. The stratified hazard ratio, corresponding 95% confidence interval and corresponding log rank pvalue will be displayed on the Kaplan-Meier figure. A forest plot for DFS showing unstratified hazard ratios, corresponding

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95% confidence intervals, and corresponding logrank pvalue will be generated. Subgroups to be considered for the forest plot include:

- Age: < 65 years vs. ≥ 65 years
- Sex: Male vs. Female
- Baseline ECOG performance status: 0 vs. 1
- Nodal status at randomization: N0 vs. all others
- Pathologic stage at resection: Stage I vs. all others
- Pathologic stage at resection: Stage I and IIa vs. Stage IIb and III
- Pathologic stage at resection: Stage 1 vs. Stage IIa, IIb, Stage III
- Resection Margin: R0 vs. R1
- Biomarker responder (ctDNA or serum biomarker): Yes vs. No
- Baseline ctDNA status: Negative/missing vs. Positive
- Splenectomy performed: No vs. Yes
- Prior radiation: Yes vs. No
- Prior systemic chemotherapy regimen for PDAC: FOLFIRINOX-based vs. gemcitabine-based + all others
- Prior systemic therapy: Adjuvant vs. all others
- Prior systemic therapy: Neoadjuvant vs. all others
- Prior systemic therapy: Perioperative (both adjuvant and neoadjuvant) vs. all others
- KRAS Mutation: G12D vs. all others
- KRAS Mutation: G12R vs. all others
- KRAS Mutation: G12V vs. all others
- MRD Status – Positive vs. Negative
    - MRD Positive will include subjects who have:
        - Baseline ctDNA positive, or
        - Successive rising CA19-9 or CEA at baseline, or
        - Baseline CA19-9 ≥ 90 U/mL, or
        - Baseline CEA ≥ 15 ng/mL
    - MRD Negative – Includes other subjects.

Note that the subgroup of "ctDNA Negative" includes subjects with negative or had missing ctDNA values. Further subgroups based on the T-cell sample results collected per protocol may be added if warranted.

A table will be presented for DFS using RECIST criteria. For RECIST criteria, overall responses of Unconfirmed PD (iUPD) and Confirmed PD (iCPD) will be considered as disease progressions. A listing of subjects' DFS status will be generated.

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Because this is a non-registrational, proof of concept Phase 2 study, the primary objective is to estimate the magnitude and precision of the DFS treatment effect rather than to formally confirm a hypothesis. The study will be considered to have met its primary objective if the point estimate of the DFS hazard ratio for ELI-002 7P versus SOC is consistent with a clinically meaningful benefit (for example, hazard ratio less than or equal to 0.70 corresponding to an approximately 4 to 6 month improvement in median DFS) and the upper bound of the 2-sided 80 percent confidence interval is less than 1.0, with supportive trends in the landmark DFS rate and key MRD related and biomarker subgroups. Nominal p values from the log rank tests will be provided to characterize the strength of evidence but will not alone determine study success.

9.3. Overall Survival (OS)

In Phase 2, the OS (in months) is defined as time from randomization to death due to any cause.

OS (months) = [(date of death or last known alive – date of randomization + 1)] / 30.4375.

Censoring rules for OS are provided in Table 10.

Summaries will be provided for the ITT Set; An analysis based on the PPS may be conducted if warranted. Given the optional cross over from SOC to ELI-002 7P upon disease recurrence, the randomized comparison of OS is expected to be confounded, and at the time of the primary DFS analysis the number of deaths is anticipated to be limited. Accordingly, OS analyses will be descriptive and exploratory; no formal success criterion is defined based on OS and no type I error is allocated to OS. The stratified hazard ratio with corresponding 95 percent confidence interval and the log rank pvalue will be displayed on the OS Kaplan Meier figure. Unstratified hazard ratios, corresponding 95% confidence intervals, and corresponding p-values will be shown in the forest plot, but these will be interpreted descriptively in the context of DFS, safety, and biomarker results.

Subjects who do not experience death will be censored at the last date they were known to be alive. For subjects in the SOC arm, the last known alive date or death dates may include dates after the subject has crossed over from SOC to ELI-002 7P.

Table 10: Event or Censoring for OS Analyses

Case Scenario	Event/Censor (Event or Censoring Description)	Event or Censoring Date
No post-baseline assessments data	Censored	Date of first treatment with duration of 1 day

Death occurs during the treatment or after treatment	Event (death)	Date of death (Collected in CRF or obtained from public records)
Subjects who are still alive at the time of data cut-off	Censored (ongoing without event)	Date of the last date alive (Programming will search across all data domain for the last date of alive)

If death occurs during the treatment or after follow-up period, the OS will be analyzed as an event. As part of the study, sites may conduct searches of public records, such as those establishing survival status, to obtain survival data as needed (i.e., subject lost to follow-up, withdraws from study etc.). Subjects who have died based on the quarterly survival review after completion of study will have their date of death incorporated into this analysis.

Median OS will be estimated using the Kaplan-Meier method. The OS rate at 6, 12, 18 months (additional milestone timepoint may be added if warranted) and CI using the method of Brookmeyer-Crowley method will be presented in the tables. Number of subjects with events (death) will be presented by treatment group. The median survival time (in months) and quartile estimates (in months) will be presented by treatment arm.

Reason for censoring in OS will be presented in a separate table:

- No evaluable post-baseline assessments
- No death/ subject still alive (obtained from published sources or available data)

A stratified log-rank test with baseline nodal status as stratification factor will be performed using SAS PROC LIFETEST. A Cox proportional hazards model stratified by baseline nodal status to obtain the stratified hazard ratio and its associated 95% confidence interval for hazard ratio using SAS PROC PHREG will be used. The SOC arm will be used as the reference arm. An unstratified log-rank test will also be carried out as supportive analysis using PROC LIFETEST. Hazard ratios for the unstratified analysis will be calculated using PROC PHREG.

A Kaplan-Meier plot by treatment arm will be provided. A forest plot for OS showing unstratified hazard ratios, corresponding 95% CI and logrank p-value will be generated using the same subgroups described in Section 9.2.

9.4. Biomarker Response Rate (BRR)

9.4.1. Proportion of Subjects Who Have Reduction or Clearance (Responders vs. Non-Responders)

The biomarker response (i.e., reduction or clearance) will be summarized for subjects in the BES. Biomarker response will be defined as any subject with a reduction or clearance of

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biomarker (ctDNA or serum tumor biomarker) compared with baseline [Tie et al., 2019]. The serum tumor biomarkers used in this analysis are CEA and CA19 9-AG. Baseline values of ctDNA, CEA, or CA19 9-AG that are below the limit of quantification will be set to 0, according to the rules in the data imputation Section 7.1.4. When one of these markers are set to 0 at baseline, by definition, that marker cannot be used to determine biomarker reduction of clearance.

A reduction is defined as the percent change from baseline of the on-study ctDNA, or CA19-9, or CEA that achieved any decrease (i.e., a negative percent change from baseline).

Clearance is defined as the percent change from baseline of the on-study ctDNA, or CA19-9, or CEA that achieved -100%.

Subjects who do not attain a reduction or clearance of biomarker for any reason will be counted as non-responders in the analysis of BRR.

Comparison of biomarker response rate (reduction or clearance) between treatment arms (ELI-002 7P and SOC) will be performed using the Chi-square test. A Fisher's Exact test may be performed if warranted. The reduction or clearance of biomarker will also be presented with a by-subject listing. A waterfall plot and/or swimmer plot may be generated.

9.4.2. Duration of Biomarker Response (DBR)

The duration of biomarker response (i.e., reduction or clearance) will be reported for subjects in the BES who meet the biomarker reduction or clearance definitions.

Analyses of duration of biomarker response will be conducted using the Kaplan-Meier method to estimate the distribution; the 2-sided 95% CIs will be estimated using the method of Brookmeyer-Crowley. Event-free rates at 6, 12, and 18 months (additional milestone timepoint may be added if warranted) will be presented. The hazard ratio (HR) and its associated 95% confidence interval will be calculated using the Cox proportional hazards model with the unstratified log-rank test used to compare between the treatment arms. The Kaplan-Meier plot will be presented.

The derivation of the endpoint is as follows:

1. The start date and end date of biomarker reduction or clearance can be any of ctDNA, or CA19-9, or CEA.
2. Once the first documentation of reduction or clearance is identified according to any one of the 3 biomarkers, the same biomarker will be used to determine the end of reduction or clearance. E.g., if CA19-9 was used as the first documentation of clearance, then CA19-9 throughout the study will be used to determine the end of biomarker clearance. A similar

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rule is applied for biomarker reduction. If two or more of the biomarker ctDNA values showed reduction or clearance on the same date, the following preference order will be used. ctDNA will be chosen first, then CA19-9, and then CEA.

3. Clearance
    a. The start date of biomarker clearance is the date of the first documentation of -100% in the percent change from baseline of on-study ctDNA, or CA19-9, or CEA. If two or more of the biomarkers had -100% reduction on the same date, the order of preference in the biomarker is as described above.
    b. A subsequent increase that is confirmed by a second increase at least 1 week apart compared to the first documented clearance (as noted in 3a above) in the percent change from baseline of the ctDNA, or CA19-9, or CEA would result in an end of the biomarker clearance. Also refer to 2 above. The end date will be the date of the first subsequent increase.
    c. Additional notes
        i. If the ctDNA, or CA19-9, or CEA at subsequent increase is below the lower limit of normal (LLN), it is considered undetectable and will assume a value of zero.
        ii. The second increase may be above or below the first subsequent increase as long as it is above the first documented clearance can be used to confirm the end of the biomarker clearance.
        iii. If the increase cannot be confirmed by a second increase, then the potential end date of the biomarker clearance will proceed to the next increase and so on.
4. Reduction
    a. The start date of biomarker reduction is the date of the first documentation of reduction in the percent change from baseline of on-study ctDNA, or CA19-9, or CEA. If two or more of the biomarker values showed the same magnitude of reduction on the same date, the order of preference in the biomarker is as described above.

    b. A subsequent increase that is confirmed by a second increase at least 1 week apart (i.e., at more than 7 days between collections) compared to the first documented reduction (as noted in 4a. above) in the percent change from baseline of the ctDNA, or CA19-9, or CEA would result in an end of the biomarker reduction. Also refer to 2 above. The end date will be the date of the first subsequent increase.

    c. Additional notes

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i. If the ctDNA, or CA19-9, or CEA at subsequent increase is below the lower limit of normal (LLN), it is undetectable and will be set to zero.

ii. The second increase may be above or below the first subsequent increase as long as it is above the first documented reduction.

iii. If the increase cannot be confirmed by a second increase, then the potential end date of biomarker reduction will proceed to the next increase and so on.

5. Handling of a patient experienced reduction follow-by clearance(s) throughout the study

    a. If a patient first achieved a reduction follow-by clearance(s) in the percent change from baseline of ctDNA, or CA19-9, or CEA, the first documented date of reduction will be the start date for the calculation of the duration of biomarker reduction/clearance. The end date of the duration will follow 4b above.

    b. Note that the scenario of achieving clearance follow-by reduction would simply be that described in 3 above.

6. Handling of a patient who has only one post-baseline ctDNA, or CA19-9, or CEA, and a reduction or clearance was achieved.

    a. The patient who achieved a clearance or a reduction as described in 3 and 4 respectively, and the patient had no other data available, the patient will be censored on "Day 1" (i.e., end date – start date +1).

7. Analysis of duration of biomarker reduction/clearance

    a. The analysis of the duration of biomarker reduction/clearance will be conducted only on the subset of patients who have met the definitions described in 3, 4 and 5 above.

    b. Finally, the duration will 'start' on the first documentation of biomarker reduction/clearance and 'end' on the earliest of biomarker end date, disease recurrence, or death, whichever occurs first. Note that 'end' can be either censor or event.

9.4.3. Summary of Percent Change from Baseline by Visit

For ctDNA and serum biomarkers (CA-19-9 and CEA), observed values and percent change from baseline (CFB) values will be summarized for subjects in the BES by visit and by treatment arm for each parameter. The summary at an analysis visit will not be presented when > 90% of the subjects in either of the treatment arm have missing data at the analysis visit.

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A boxplot by visit for each biomarker (ctDNA, CA19-9, CEA) parameters will be generated summarizing the values for the BES.

9.5. Best Overall Response (ir-BOR) and Objective Response Rate (ir-ORR)

Assessments or overall response made after initiation of subsequent anti-cancer therapies will not be considered in the summarizations.

Best Overall Response (ir-BOR) will be defined using the investigator's overall response assessments collected post-baseline. Responses will be scored as follows: iCR – Complete Response, iPR = Partial Response, Stable Disease, Absence of Progression, iUPD – Unconfirmed Progressive Disease, iCPD = Confirmed Progressive Disease, Not Evaluable, and Not Assessed.

Objective Response Rate (ir-ORR) is defined as a subject achieving a best overall response (ir-BOR) of iCR or iPR per investigator's assessment according to iRECIST.

For subjects randomized to SOC, the ir-BOR and ir-ORR will be based on overall assessments prior to the crossover from SOC to ELI-002 7P. Subjects without a post-baseline overall assessment prior to subsequent anti-cancer therapy will be considered non-responders in the ORR analysis.

For the ITT Set, the objective response rate (ir-ORR) for ELI-002 7P and SOC will be summarized. Comparisons will be performed using Chi-Square test. A Fisher's Exact test may be used in the event that the cell counts are low. The odds ratio (OR) will be calculated with OR>1.0 favors ELI-002 7P over SOC.

9.6. Duration of Response (ir-BOR)

If there are sufficient responses observed, the duration of response may also be performed.

The ir-DOR is defined as time from first documented iCR or iPR to iCPD or death, whichever occurs first. The Kaplan-Meier method will be used in this analysis. Subjects who did not have a documented iCPD or death after first documented iCR or iPR will be censored at the date of the last completed CT/MRI Scan. The 2-sided 95% CIs will be estimated using the method of Brookmeyer-Crowley. Event-free rates at 6, 12, and 18 months (additional milestone timepoint may be added if warranted) will be presented. The hazard ratio (HR) and its associated 95% confidence interval will be calculated using the Cox proportional hazards model with the unstratified log-rank test used to compare between the treatment arms. The Kaplan-Meier plot will be presented.

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10. SAFETY

All safety analyses will be performed using the SAF Analysis Set. All safety analyses will be summarized by treatment arm. Safety measurements will include AEs and reactogenicity.

No statistical tests will be performed on the safety endpoints.

10.1. Adverse Events

Adverse events (AEs) will be graded (1- 5) according to the NCI CTCAE Version 5.0 criteria), AEs will be coded using the MedDRA coding system and displayed in tables and data listings by system organ class (SOC) and preferred term (PT).

The time period for collecting and documenting AEs for each subject begins from the time the subject is in Visit 2 (i.e., first dose of study drug) through 30 days after the end of the study treatment period.

The time period for collecting and documenting serious adverse events (SAEs) for each subject begins from the time the subject provides informed consent through 30 days after the last dose of study treatment administration.

Analyses of AEs will be performed for those events that are considered treatment-emergent, where treatment-emergent AEs (TEAEs) are defined as events not present prior to initiation of study treatment or any event already present that worsens in either intensity following exposure to treatment. A condition present at baseline that worsens after initiation of study drug will be captured as an AE with the onset date as the date the event worsened. An AE that occurs more than 30 days after the last dose of treatment will not be counted as a treatment-emergent.

For the SOC crossover to ELI-002 7P treatment, TEAE will be summarized under the 'crossover' column of the table. The TEAEs will be defined as an event that was not present prior to the initiation of ELI-002 7P treatment or any event already present that worsens in either intensity or frequency following exposure to ELI-002 7P treatment.

A treatment-related adverse events (TRAE) is defined as an AE with Related or Possibly Related AE. An AE with missing relatedness will be considered Related.

An SAE is an AE occurring during any trial phase (i.e., screening, treatment, or follow-up), and at any dose of the study drug, that fulfills one or more of the following:

- Results in death
- It is immediately life-threatening

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- It requires inpatient hospitalization or prolongation of existing hospitalization
- It results in persistent or significant disability or incapacity
- Results in a congenital abnormality or birth defect
- It is an important medical event that may jeopardize the subject or may require medical intervention to prevent one of the outcomes listed above.

Treatment-emergent adverse events are summarized by subject incidence rates; therefore, in any tabulation, a subject contributes only once to the count for a given SOC or PT (i.e., the most related occurrence or the most intense (highest grade) occurrence).

An overall TEAE incidence summary table will be produced and will include:

- Number and percentage of subjects reporting at least 1 TEAE
- Number and percentage of subjects reporting at least 1 TEAE of Grade 3 or higher
- Number and percentage of subjects reporting at least 1 Treatment-Related Adverse Events (TRAE)
- Number and percentage of subjects reporting at least 1 TRAE of Grade 3 or higher
- Number and percentage of subjects reporting at least 1 Treatment-Emergent Serious Adverse Events (TESAE)
- Number and percentage of subjects reporting at least 1 Treatment-Related Serious Adverse Events (TRSAE)
- Number and percentage of subjects reporting at least 1 TEAE leading to Dose Modification of Study Treatment
- Number and percentage of subjects reporting at least 1 TRAE leading to Dose Modification of Study Treatment
- Number and percentage of subjects reporting at least 1 TEAE leading to Withdrawal of Study Treatment
- Number and percentage of subjects reporting at least 1 TRAE leading to Withdrawal of Study Treatment
- Number and percentage of subjects reporting at least 1 TEAE leading to Death
- Number and percentage of subjects reporting at least 1 TEAE of Special Interest (AESI). AESIs will be defined by Elicio prior to database lock.

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All TEAE and TRAE related tables will be summarized by SOC and PT and sorted by decreasing frequency. Some TEAE and TRAE tables will be summarized by PT only. A summary of most frequently occurring TEAE and TRAEs by PT and maximum severity will be provided. The cutoff for determination of most frequent will be determined at the time of final analysis, based on the number of terms reported, but will default to terms that occurred in 5% or more of subjects in the SAF Analysis Set.

No formal hypothesis-testing analysis of AE incidence rates will be performed. All AEs occurring on-study will be provided in data listings. By-subject listings also will be provided for the following: SAEs, AEs leading to treatment discontinuation, and AEs leading to death, and death due to any reason.

10.2. Reactogenicity to the Vaccine

For subjects in the treatment arm ELI-002 7P, and subjects in the SOC treatment arm who crossed over to ELI-002 7P, injection site reactions, skin rash, and pruritus will not be considered safety events and should be recorded in the subject diary and eCRF for reactogenicity. Reactogenicity monitoring will include subject's reactogenicity to the study drug (vaccine). This will be captured at several time points as follows:

- 1-hour post ELI-002 dose administration (subjects will be observed in the clinic for at least 1-hour after each dose)
- 1-week post ELI-002 dose administration (subjects will record daily observations in diary)
- Any unresolved reactogenicity event should be followed until resolution.

Reactogenicity to the vaccine will be listed by subject. Reactogenicity to the vaccine will be presented for the SAF Analysis Set. Reactogenicity events will be summarized for the ELI-002 7P and the SOC crossover to ELI-002 7P treatment arms in Phase 2.

- Summary of Reactogenicity by type
- Summary of Reactogenicity by worst toxicity grade

10.3. Laboratory Evaluations

Laboratory values will be collected according to the Schedule of Assessments (Protocol Section 6.1.3 Table 7 - Table 12). Local laboratories will be utilized for serum cytokine testing, tumor biomarkers CA19-9/CEA (as appropriate per tumor type), and all other safety laboratory tests. Central laboratories will be utilized for WES and ctDNA analysis, HLA typing, tumor microenvironment and T-cell infiltration.

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Laboratory parameters will be summarized for the SAF Analysis Set. Immunogenicity assessment (such as Fluorospot, ICS, and/or T cell dextramer testing) statistical analysis will be provided in a separate addendum. Abnormalities in local laboratory values will be graded using CTCAE criteria.

The laboratory analytes presented in Table 11 below will be summarized in the tables and figures. All laboratory parameters will be presented in the listings.

Baseline values for each laboratory parameter reported in Table 11 will be descriptively summarized. Also shift tables with significant changes from baseline to maximum post baseline CTCAE grade will be provided by treatment arm. The worst post-baseline CTCAE grade will be summarized by treatment arm.

A boxplot by visit for each of the hematology and chemistry laboratory parameters will be generated summarizing the values for the SAF Analysis Set. The summary at an analysis visit will not be presented when > 90% of the subjects in either of the treatment arm have missing data at the analysis visit.

Table 11 Clinical Laboratory Parameters

Hematology Parameters
White Blood Cell Count
Absolute Neutrophils
Hematocrit
Absolute Lymphocyte
Hemoglobin
Platelet Count
Chemistry Parameters
Lactate dehydrogenase
Bilirubin (total)
Albumin
Uric Acid

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Alkaline Phosphatase
Aspartate Transaminase (AST)
Alanine Transaminase (ALT)
Ferritin
C-reactive protein
Coagulation Parameters
Prothrombin Time (PT)
Partial Thromboplastin Time (PTT)
International Normalized Ratio (INR)
Fibrinogen
D-dimer

10.4. Vital Signs

Vital signs will be collected throughout the trial according to the Schedule of Assessments and will include systolic and diastolic blood pressure, pulse rate, body temperature, and respiratory rate. Measurements will be obtained after 3 minutes in the sitting position. No other measurements or procedures are to be performed during this 3-minute period.

Vital signs will be summarized for the SAF Analysis Set.

The summary at an analysis visit will not be presented when > 90% of the subjects in either of the treatment arm have missing data at the analysis visit.

The actual value and change from baseline at each visit and at end of study will be descriptively summarized by visit/assessment for vital signs by treatment arm. A boxplot by visit for each of the vital sign parameters will be generated summarizing the values for the SAF Analysis Set.

Shift tables with significant changes from baseline (i.e. normal to abnormal non-clinically significant, normal to abnormal clinically significant, and abnormal non-clinically significant to abnormal clinically significant) will be provided by treatment arm.

Vital sign measurements will be presented for each subject in a data listing.

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10.5. Electrocardiogram (ECG)

ECG parameters (e.g., heart rate, QRS interval, RR interval, PR interval, QT interval, and QTc interval) will be collected at screening and prior to the first dose. QTc interval will be calculated using either Bazett [QTcB = QT/(RR)1/2] or Fridericia [QTcF = QT/(RR)1/3] corrections; and if RR is not available, it will be replaced with 60/HR in the correction formula. Electrocardiogram data will be presented for the SAF Analysis Set.

Electrocardiogram data will be only provided in a by-subject listing.

10.6. Physical Examination

Physical examinations will be performed at screening and at specified times during the trial (see Table 8 - Table 12 in the protocol) based on standard of care. Results of the body system will be collected, and may include general appearance, HEENT (head, eyes, ears, nose, throat), Respiratory (Lungs), Cardiovascular (Heart), Gastrointestinal, Renal/Genitourological, Dermatological (Skin), Lymphatic/Hematological, Musculoskeletal, Neurological, Metabolic/Endocrine and Lymph Nodes. Physical examination will be presented for the SAF Analysis Set. Physical examination will be provided in a by-subject listing.

10.7. Eastern Cooperative Oncology Group (ECOG)

The ECOG Performance Status describes a subject's level of functioning in terms of their ability to care for themselves, daily activity, and physical ability (walking, working, etc.).

Eligibility for this trial requires a subject's ECOG performance status to be 0 to 1 (see protocol Table 13).

The ECOG assessment will be performed according to the Schedule of Assessments (protocol Tables 7-12). ECOG assessment will be presented for the SAF Analysis Set. ECOG will be reported in a by-subject listing only.

A shift table for baseline ECOG status and worst post-baseline ECOG status will be summarized for the SAF Analysis Set.

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11. EXPLORATORY ANALYSIS

11.1. Patient Reported Outcomes (PROs)

For Phase 2, patient reported outcomes (PROs) will be assessed for EORTC QLQ-C30 and QLQ-PAN26. PROs will be administered to subjects according to the Schedule of Assessments and prior to other visit procedures (refer to Protocol sections: Table 8, Table 9, Table 10, Table 11, and Table 12). Verification of validation can be obtained through EORTC, and the list of questionnaires and the phase of validation can be found at the following site: https://qol.eortc.org/questionnaires/.

Per Protocol Version 7.0, the collection of patient reported outcomes (PRO) were removed from the study schedule of assessments. PRO questionnaire results collected prior to the implementation of Protocol Version 7.0 will have the subscale scores calculated. The rules for calculation of the subscale scores are described in Section 11.2 and Section 11.3. PRO data collected prior to the implementation of Protocol Version 7.0 will be listed but not summarized.

11.2. EORTC QLQ-C30

EORTC QLQ-C30 is a tool for assessing the QoL of cancer subjects participating in clinical trials. The EORTC QLQ-C30 contains both single-item and multi-item scales. Of the 30 items, 24 aggregate into nine multi-item scales representing various health-related quality of life (HRQoL) subscales/dimensions – Physical Functioning, Role Functioning, Emotional Functioning, Cognitive Functioning, Social Functioning, Fatigue Symptoms, Pain Symptoms, Nausea Symptoms, and Global Measure of Health Status. The remaining six single-item scales assess individual symptoms. High scores indicate better HRQoL for the global health status and functioning scales, while high scores indicate worse HRQoL for the symptom scales.

Scoring of the EORTC QLQ-C30 is performed according to the Scoring manual. All scales and single-item measures range in score from 0 to 100. Higher score for the functioning scales and global health status denotes a better level of functioning (i.e. a better state of the subject), while higher scores on the symptom and single-item scales indicate a higher level of symptoms (i.e. a worse state of the subject).

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Table 12: Scoring the EORTC QLQ-C30 Version 3.0

	Scale	Number of items	Item range*	**Version 3.0** Item numbers	Function scales
Global health status / QoL					
Global health status/QoL (revised)†	QL2	2	6	29, 30	
Functional scales					
Physical functioning (revised)†	PF2	5	3	1 to 5	F
Role functioning (revised)†	RF2	2	3	6, 7	F
Emotional functioning	EF	4	3	21 to 24	F
Cognitive functioning	CF	2	3	20, 25	F
Social functioning	SF	2	3	26, 27	F
Symptom scales / items					
Fatigue	FA	3	3	10, 12, 18	
Nausea and vomiting	NV	2	3	14, 15	
Pain	PA	2	3	9, 19	
Dyspnoea	DY	1	3	8	
Insomnia	SL	1	3	11	
Appetite loss	AP	1	3	13	
Constipation	CO	1	3	16	
Diarrhoea	DI	1	3	17	
Financial difficulties	FI	1	3	28	

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* *Item range* is the difference between the possible maximum and the minimum response to individual items; most items take values from 1 to 4, giving *range* = 3.
† (revised) scales are those that have been changed since version 1.0, and their short names are indicated in this manual by a suffix "2" – for example, PF2.

For all scales, the *RawScore*, *RS*, is the mean of the component items:

$$RawScore = RS = (I_1 + I_2 + ... + I_n)/n$$

Then for **Functional scales**:

$$Score = \left\{1 - \frac{(RS - 1)}{range}\right\} \times 100$$

and for **Symptom scales / items** and **Global health status / QoL:**

$$Score = \{(RS - 1)/range\} \times 100$$

Examples:

Emotional functioning

$$RawScore = (Q_{21} + Q_{22} + Q_{23} + Q_{24})/4$$
$$\text{EF } Score = \{1 - (RawScore - 1)/3\} \times 100$$

Fatigue

$$RawScore = (Q_{10} + Q_{12} + Q_{18})/3$$
$$\text{FA } Score = \{(RawScore - 1)/3\} \times 100$$

11.3. Tumor Type-specific PRO QLQ-PAN26

The Tumor type-specific PRO QLQ-PAN26: pancreatic cancer QLQ-C30 is intended to supplement the EORTC QLQ-C30 with questions appropriate for the symptoms experienced by subjects with pancreatic cancer. The QLQ-PAN26 consists of 26 questions relating to disease symptoms, treatment side effects and emotional issues specific to pancreatic cancer. All 26 questions are completed on a 4-point Likert scale ranging from '1=not at all' to 4='very much'. These scores are then converted into a range from 0-100 (higher scores= greater degree of symptoms or treatment side effects and emotional issues). QLQ-PAN26 score representing 7 health-related HRQoL subscales/dimensions – Pancreatic Pain (item 31, 33, 34 and 35), Digestive (item 36 and 37), Altered Bowel Habit (item 46 and 47), Hepatic (item 44 and 45), Body Image (item 48 and 49), Health care satisfaction (item 53 and 54), Sexuality (item 55 and 56).

Scoring of the PRO QLQ-PAN26 is performed according to the Scoring manual. All of the scales and single-item measures range in score from 0 to 100. Higher score for the functioning scales and global health status denotes a better level of functioning (i.e. a better state of the

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subject), while higher scores on the symptom and single-item scales indicate a higher level of symptoms (i.e. a worse state of the subject).

Table 13: Scoring the PRO QLQ-PAN26

	Scale	Number of items (n)	Item range*	QLQ-PAN26 item numbers ($I_1, I_2, \ldots, I_n$)	Reverse scoring items
Symptom scales / items					
Pancreatic pain	PP	4	3	31, 33 – 35	
Bloating	BF	1	3	32	
Digestive symptoms	DS	2	3	36, 37	
Taste	TA	1	3	38	
Indigestion	ID	1	3	39	
Flatulence	FL	1	3	40	
Weight loss	WL	1	3	41	
Weakness arms and legs	WE	1	3	42	
Dry mouth	DM	1	3	43	
Hepatic symptoms	LI	2	3	44, 45	
Altered bowel habit	BO	2	3	46, 47	
Body image	BI	2	3	48, 49	
Troubled with side-effects	SE	1	3	50	
Future Worries	FU	1	3	51	
Planning of activities	PL	1	3	52	
Functional scale					
Satisfaction with health care	SA	2	3	53, 54	53, 54
Sexuality	SX	2	3	55, 56	

* "Item range" is the difference between the possible maximum and the minimum response to individual items. All items are scored 1 to 4, giving range = 3.

For directions on missing data or more detailed information refer to PRO QLQ-PAN26 scoring manual.

12. INTERIM ANALYSES

For Phase 2, a safety evaluation is planned when approximately 20 biomarker evaluable subjects observed for at least 28 days are available for review by the IDMC. This will include a review of the limited biomarker data for consistency with the data observed in the similar patient population treated with study treatment ELI-002 2P conducted in Study ELI-002-001. There will be no hypothesis testing at this safety evaluation; consequently, no type I error (alpha) is spent at this review. One interim analysis on the primary endpoint of DFS is planned when approximately 67 percent of the total DFS events are observed. The efficacy boundaries are constructed using the O'Brien Fleming boundaries as implemented by the Lan DeMets alpha spending function. The interim analysis also includes a non-binding futility analysis constructed using a Rho spending function with parameter of 4. At 67 percent of the total DFS events, the planned efficacy alpha spend is 0.0038 (1 sided); the actual alpha spend will be adjusted based on the actual observed number of DFS events at the time of analysis. At the time that approximately 71 DFS events have occurred, a final primary analysis of the DFS endpoint will be performed using the methods described in Section 9.2. The Lan DeMets O'Brien Fleming spending function will be applied so that the cumulative 1-sided type I error for the primary DFS comparison across the interim and final analyses remains at 0.05. No alpha is spent on secondary or exploratory endpoints; p values for these endpoints will be reported descriptively.

Because this is a non-registrational Phase 2 trial, a separate final study analysis of key secondary and safety endpoints (including OS) may be performed at a later time point, after additional follow up has accrued and at the discretion of the Sponsor. At the time of the DFS primary analysis, OS is anticipated to be immature and subject to confounding due to optional cross over from SOC to ELI-002 7P; therefore, any OS results at that time will be descriptive and are not expected to provide definitive evidence of a survival benefit. A later descriptive analysis of secondary and safety endpoints is intended to provide more informative estimates once sufficient events and follow-up are available. Safety monitoring will occur continuously in the trial. Safety tables will be produced at the DFS interim analysis to allow the IDMC to comprehensively evaluate the risk benefit profile.

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13. CHANGES FROM ANALYSIS PLANNED IN PROTOCOL

There are no changes in methods described in Protocol Version 8.0.

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14. REFERENCE LIST

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15. LIST OF TABLES, FIGURES AND LISTINGS

15.1. Index of Tables and Figures

Number	Title	Analysis Set	IDMC/ Safety review (20 biomarker evaluable)	Interim Analysis/ IDMC (67% of events)	Interim Analysis/Elicio if positive results (immediate need)	Final Analysis/ CSR
		Section 14.1 Demographic Data				
Table 14.1.1.1	Subject Enrollment – Phase 2	All Subjects			X	X
Table 14.1.1.2	Subject Disposition – Phase 2	Intent-to-Treat Set	X	X	X	X
Table 14.1.2.1	Major Protocol Deviations - Phase 2	Intent-to-Treat Set			X	X
Table 14.1.3.1	Demographics - Phase 2	Intent-to-Treat Set	X	X	X	X
Table 14.1.3.2	Baseline Characteristics – Phase 2	Intent-to-Treat Set	X	X	X	X
Table 14.1.3.3	Baseline Mutational Status and Biomarkers – Phase 2	Intent-to-Treat Set	X	X	X	X
Table 14.1.3.4	Medical History - Phase 2	Intent-to-Treat Set			X	X
Table 14.1.4.1.1	Prior Anti-Cancer Systemic Therapy – Phase 2	Intent-to-Treat Set	X	X	X	X
Table 14.1.4.1.2	Prior Anti-Cancer Chemotherapies – Phase 2	Intent-to-Treat Set			X	X
Table 14.1.4.1.3	Prior Anti-Cancer Regimens for Pancreatic Cancer - Phase 2	Intent-to-Treat Set			X	X
Table 14.1.4.2	Prior Anti-Cancer Radiotherapy – Phase 2	Intent-to-Treat Set			X	X
Table 14.1.4.3	Prior Anti-Cancer Surgeries and Procedures – Phase 2	Intent-to-Treat Set	X	X	X	X
Table 14.1.5.1	Prior Medications (Non-Cancer) – Phase 2	Intent-to-Treat Set			X	X

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Number	Title	Analysis Set	IDMC/ Safety review (20 biomarker evaluable)	Interim Analysis/ IDMC (67% of events)	Interim Analysis/Elicio if positive results (immediate need)	Final Analysis/ CSR
Table 14.1.5.2	Concomitant Medications (Non-Cancer) – Phase 2	Intent-to-Treat Set			X	X
Table 14.1.6	Study Treatment Exposure and Compliance – Phase 2	Safety Analysis Set	X	X	X	X
		Section 14.2 Efficacy Data				
Table 14.2.1.1	Disease-Free Survival (DFS, iRECIST, Stratified Analysis) – Phase 2	Intent-to-Treat Set		X	X	X
Table 14.2.1.2	Disease-Free Survival (DFS, iRECIST, Unstratified Analysis) - Phase 2	Intent-to-Treat Set			X	X
Table 14.2.1.3	Disease-Free Survival by Subgroups (DFS, iRECIST, Unstratified Analysis) - Phase 2	Intent-to-Treat Set			X	X
Table 14.2.1.4	Disease-Free Survival (DFS, iRECIST, Stratified Analysis) – Sensitivity Analysis – Phase 2	Intent-to-Treat Set			X	X
Table 14.2.1.5	Disease-Free Survival (DFS, iRECIST, Unstratified Analysis) – Sensitivity Analysis - Phase 2	Intent-to-Treat Set			X	X
Table 14.2.1.6	Reason for Event/Censored in the Disease-Free Survival (DFS, iRECIST) Analysis – Phase 2	Intent-to-Treat Set			X	X
Table 14.2.1.7	Disease-Free Survival (DFS, RECIST, Stratified Analysis)– Phase 2	Intent-to-Treat Set			X	X

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Number	Title	Analysis Set	IDMC/ Safety review (20 biomarker evaluable)	Interim Analysis/ IDMC (67% of events)	Interim Analysis/Elicio if positive results (immediate need)	Final Analysis/ CSR
Table 14.2.1.8	Disease-Free Survival (DFS, RECIST, Unstratified Analysis)– Phase 2	Intent-to-Treat Set			X	X
Table 14.2.1.9	Reason for Event/Censored in the Disease-Free Survival (DFS, RECIST) Analysis — Phase 2	Intent-to-Treat Set			X	X
Table 14.2 1.10	1-Year Disease-Free Survival Rate (DFS, iRECIST, Stratified Analysis) - Phase 2	Intent-to-Treat Set			X	X
Table 14.2.1.11	1-Year Disease-Free Survival Rate (DFS, iRECIST, Stratified Analysis) – Sensitivity Analysis - Phase 2	Intent-to-Treat Set			X	X
Table 14.2.1.12	1-Year Disease-Free Survival (DFS, RECIST, Stratified Analysis)	Intent-to-Treat Set			X	X
Table 14.2.1.13	Overall Survival (OS, Stratified Analysis) - Phase 2	Intent-to-Treat Set		X	X	X
Table 14.2.1.14	Overall Survival (OS, Unstratified Analysis) - Phase 2	Intent-to-Treat Set			X	X
Table 14.2.1.15	Overall Survival by Subgroups (OS, Unstratified Analysis) – Phase 2	Intent-to-Treat Set			X	X
Table 14.2.1.16	Reason for Event/Censored in the Overall Survival (OS, Unstratified Analysis) – Phase 2	Intent-to-Treat Set			X	X
Table 14.2.1.17	Subsequent Anti-Cancer Therapies – Phase 2	Intent-to-Treat Set			X	X

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Number	Title	Analysis Set	IDMC/ Safety review (20 biomarker evaluable)	Interim Analysis/ IDMC (67% of events)	Interim Analysis/Elicio if positive results (immediate need)	Final Analysis/ CSR
Table 14.2.1.18	Subsequent Anti-Cancer Therapies Chemotherapies and Immunotherapies Details – Phase 2	Intent-to-Treat Set			X	X
Table 14.2.2.1	Best Biomarker Response (ctDNA or Serum Tumor Biomarker Reduction or Clearance) – Phase 2	Biomarker Evaluable Set	X	X	X	X
Table 14.2.2.2	Duration of Biomarker Response (ctDNA or Serum Tumor Biomarker Reduction or Clearance, DBR) (Unstratified Analysis) – Phase 2	Biomarker Evaluable Set			X	X
Table 14.2.2.3	Reason for Event/Censored in the Duration of Biomarker (ctDNA OR Serum Tumor Biomarker) Reduction/Clearance – Phase 2	Biomarker Evaluable Set			X	X
Table 14.2.3.1	Best Overall Response (ir-BOR) and Objective Response Rate (ir-ORR) – Phase 2	Intent-to-Treat Set			X	X
Table 14.2.3.2	Duration of Response (ir-DOR) (Unstratified Analysis) - Phase 2	Intent-to-Treat Set			X	X
	Section 14.3 Safety Data					
	Section 14.3.1 Displays of Adverse Events					
Table 14.3.1.1	Overall Summary of Treatment-Emergent Adverse Events – Phase 2	Safety Analysis Set			X	X
Table 14.3.1.2.1	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set		X	X	X

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Number	Title	Analysis Set	IDMC/ Safety review (20 biomarker evaluable)	Interim Analysis/ IDMC (67% of events)	Interim Analysis/Elicio if positive results (immediate need)	Final Analysis/ CSR
Table 14.3.1.2.2	Treatment-Emergent Adverse Events by Maximum Toxicity Grade by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set			X	X
Table 14.3.1.2.3	Grade 3 or Higher Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set			X	X
Table 14.3.1.3.1	Treatment-Emergent Adverse Events by Preferred Term – Phase 2	Safety Analysis Set		X	X	X
Table 14.3.1.3.2	Treatment-Emergent Adverse Events by Maximum Toxicity Grade and Preferred Term – Phase 2	Safety Analysis Set		X	X	X
Table 14.3.1.3.3	Most Frequent (>=5%) Treatment-Emergent Adverse Events by Maximum Toxicity Grade and Preferred Term – Phase 2	Safety Analysis Set		X	X	X
Table 14.3.1.3.4	Grade 3 or Higher Treatment-Emergent Adverse Events by Preferred Term – Phase 2	Safety Analysis Set			X	X
Table 14.3.1.4.1	Treatment-Emergent Related Adverse Events by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set	X	X	X	X
Table 14.3.1.4.2	Treatment-Emergent Related Adverse Events by Maximum Toxicity Grade by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set			X	X

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Number	Title	Analysis Set	IDMC/ Safety review (20 biomarker evaluable)	Interim Analysis/ IDMC (67% of events)	Interim Analysis/Elicio if positive results (immediate need)	Final Analysis/ CSR
Table 14.3.1.4.3	Grade 3 or Higher Treatment-Related Adverse Events by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set			X	X
Table 14.3.1.5.1	Treatment-Emergent Related Adverse Events by Preferred Term – Phase 2	Safety Analysis Set			X	X
Table 14.3.1.5.2	Treatment-Emergent Related Adverse Events by Maximum Toxicity Grade and Preferred Term – Phase 2	Safety Analysis Set	X	X	X	X
Table 14.3.1.5.3	Most Frequent (>= 5%) Treatment-Emergent Related Adverse Events by Maximum Toxicity Grade and Preferred Term – Phase 2	Safety Analysis Set			X	X
Table 14.3.1.5.4	Grade 3 or Higher Treatment-Emergent Related Adverse Events by Preferred Term – Phase 2	Safety Analysis Set			X	X
Table 14.3.1.6.1	Serious Adverse Events – Phase 2	Safety Analysis Set	X	X	X	X
Table 14.3.1.6.2	Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set	X	X	X	X
Table 14.3.1.6.3	Treatment-Related Serious Adverse Events by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set	X	X	X	X

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Number	Title	Analysis Set	IDMC/ Safety review (20 biomarker evaluable)	Interim Analysis/ IDMC (67% of events)	Interim Analysis/Elicio if positive results (immediate need)	Final Analysis/ CSR
Table 14.3.1.7.1	Treatment-Emergent Adverse Events Leading to Dose Modification by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set			X	X
Table 14.3.1.7.2	Treatment-Emergent Related Adverse Events Leading to Dose Modification by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set		X	X	X
Table 14.3.1.8.1	Treatment-Emergent Adverse Events Leading to Withdrawal of Study Treatment by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set	X		X	X
Table 14.3.1.8.2	Treatment-Emergent Related Adverse Events Leading to Withdrawal of Study Treatment by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set	X	X	X	X
Table 14.3.1.9.1	Treatment-Emergent Adverse Events Leading to Death by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set	X	X	X	X
Table 14.3.1.9.2	Treatment-Emergent Related Adverse Events Leading to Death by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set	X	X	X	X

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Number	Title	Analysis Set	IDMC/ Safety review (20 biomarker evaluable)	Interim Analysis/ IDMC (67% of events)	Interim Analysis/Elicio if positive results (immediate need)	Final Analysis/ CSR
Table 14.3.1.10	Adverse Events of Special Interest by System Organ Class and Preferred Term – Phase 2	Safety Analysis Set			X	X
Table 14.3.1.11	Deaths – Phase 2	Safety Analysis Set			X	X
	Section 14.3.5 Laboratory Parameters					
Table 14.3.5.1	Summary of Chemistry and Hematology Worst On-treatment CTCAE Grade – Phase 2	Safety Analysis Set	X	X	X	X
Table 14.3.5.2.1	Change from Baseline for Hematology Parameters by Visit – Phase 2	Safety Analysis Set			X	X
Table 14.3.5.2.2	Shift Summary of Hematology Results From Baseline to Maximum On-Study CTCAE Grade – Phase 2	Safety Analysis Set			X	X
Table 14.3.5.3.1	Change from Baseline for Chemistry Parameters by Visit – Phase 2	Safety Analysis Set			X	X
Table 14.3.5.3.2	Shift Summary of Chemistry Results From Baseline to Maximum On-study CTCAE Grade – Phase 2	Safety Analysis Set			X	X
Table 14.3.6.1.1	Change from Baseline for Vital Signs by Visit – Phase 2	Safety Analysis Set			X	X
Table 14.3.6.1.2	Shift Summary of Vital Signs Results from Baseline to Maximum On-Study Result – Phase 2	Safety Analysis Set			X	X

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Number	Title	Analysis Set	IDMC/ Safety review (20 biomarker evaluable)	Interim Analysis/ IDMC (67% of events)	Interim Analysis/Elicio if positive results (immediate need)	Final Analysis/ CSR
Table 14.3.7.1.1	Change from Baseline for Coagulation by Visit – Phase 2	Safety Analysis Set			X	X
Table 14.3.7.1.2	Shift Summary of Coagulation Results from Baseline to Maximum On-treatment Results – Phase 2	Safety Analysis Set			X	X
	Section 14.3.8 Reactogenicity					
Table 14.3.8.1.1	Summary of Subject Reactogenicity Diary - Phase 2	Safety Analysis Set	X	X	X	X
Table 14.3.8.1.2	Summary of Subject Reactogenicity Diary by Worst Toxicity Grade – Phase 2	Safety Analysis Set		X	X	X
	Section 14.3.9 ctDNA and Biomarkers					
Table 14.3.9.1	Percent Change from Baseline in Biomarker Level (ctDNA, CA19-9, and CEA) by Visit – Phase 2	Safety Analysis Set			X	X
Table 14.3.10.1	Change from Baseline in Immune Cell Infiltrate and Tumor Microenvironment by Visit – Phase 2	Biomarker Evaluable Set			X	X

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Number	Title	Analysis Set	IDMC/ Safety review (20 biomarker evaluable)	Interim Analysis/ IDMC (67% of events)	Interim Analysis/Elicio if positive results (immediate need)	Final Analysis/ CSR
Figure 14.2.1.19	Kaplan-Meier Plot of Disease-Free Survival (iRECIST, Stratified Analysis) – Phase 2	Intent-to-Treat Set		X	X	X
Figure 14.2.1.20	Forest Plot of Disease-Free Survival (iRECIST, Unstratified Analysis) – Phase 2	Intent-to-Treat Set			X	X
Figure 14.2.1.21	Kaplan-Meier Plot of Disease-Free Survival (Sensitivity Analysis) – Phase 2	Intent-to-Treat Set			X	X
Figure 14.2.1.22	Kaplan-Meier Plot of Overall Survival (Stratified Analysis) – Phase 2	Intent-to-Treat Set		X	X	X
Figure 14.2.1.23	Forest Plot of Overall Survival (Unstratified Analysis) - Phase 2	Intent-to-Treat Set			X	X
Figure 14.2.2.4	Kaplan-Meier Plot of Duration of Biomarker (ctDNA or Serum Tumor Biomarker) Response – Phase 2	Biomarker Evaluable Set			X	X
Figure 14.2.2.5	Waterfall Plot – Best Percentage Change in Biomarker Levels from Baseline by Subject – Phase 2	Biomarker Evaluable Set			X	X
Figure 14.2.3.5	Kaplan-Meier Plot of Duration of Response (ir-DOR) - Phase 2	Intent-to-Treat Set			X	X
Figure 14.3.5.4	Boxplot for Percentage Change from Baseline in Hematology Parameters by Visit – Phase 2	Safety Analysis Set	X	X	X	X
Figure 14.3.5.5	Boxplot for Percentage Change from Baseline in Chemistry Parameters by Visit – Phase 2	Safety Analysis Set	X	X	X	X

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Number	Title	Analysis Set	IDMC/ Safety review (20 biomarker evaluable)	Interim Analysis/ IDMC (67% of events)	Interim Analysis/Elicio if positive results (immediate need)	Final Analysis/ CSR
Figure 14.3.6.2	Boxplot for Percentage Change from Baseline in Vital Signs Parameters by Visit – Phase 2	Safety Analysis Set			X	X
Figure 14.3.9.2	Boxplot for Percentage Change from Baseline in Biomarker Parameters by Visit – Phase 2	Biomarker Evaluable Set			X	X

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15.2. Index of Listings

Number	Title	Analysis Set	IDMC/ Safety review (20 biomarker evaluable)	Interim Analysis/ IDMC (60% of events)	Interim Analysis/Elicio if positive results (immediate need)	Final Analysis/ CSR
Listing 16.2.1.1	Analysis Sets – Phase 2	All Subjects			X	X
Listing 16.2.1.2	Subject Disposition - Phase 2	All Subjects			X	X
Listing 16.2.2	Protocol Deviations - Phase 2	All Subjects			X	X
Listing 16.2.4.1.1	Demographics - Phase 2	All Subjects			X	X
Listing 16.2.4.1.2	Baseline Characteristics - Phase 2	All Subjects			X	X
Listing 16.2.4.1.3	Baseline Mutation Status - Phase 2	All Subjects			X	X
Listing 16.2.4.2	Inclusion/Exclusion - Phase 2	All Subjects			X	X
Listing 16.2.4.3	Medical History - Phase 2	Intent-to-Treat Set			X	X
Listing 16.2.4.4	Prior Anti-Cancer Systemic Therapies – Phase 2	Intent-to-Treat Set			X	X
Listing 16.2.4.5	Prior Cancer Surgery – Phase 2	Intent-to-Treat Set			X	X
Listing 16.2.4.6	Prior Radiation/Therapy for Cancer – Phase 2	Intent-to-Treat Set			X	X
Listing 16.2.4.7.1	Prior and Concomitant Medications (Non-Cancer) – Phase 2	Intent-to-Treat Set			X	X
Listing 16.2.4.7.2	Concomitant Medications (Non-Cancer) - Phase 2	Safety Analysis Set	X (for internal Clinician use)	X (for internal Clinician use)	X	X

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Listing 16.2.5.1	Study Drug Exposure and Compliance – Phase 2	Safety Analysis Set			X	X
Listing 16.2.5.2	Study Treatment Administration – ELI-002 7P Details– Phase 2	Safety Analysis Set			X	X
Listing 16.2.6.1.1	iRECIST Assessment – Phase 2	Intent-to-Treat Set			X	X
Listing 16.2.6.1.2	Disease-Free Survival – Phase 2	Intent-to-Treat Set			X	X
Listing 16.2.6.1.2.1	Disease-Free Survival (Sensitivity Analysis) – Phase 2	Intent-to-Treat Set			X	X
Listing 16.2.6.1.3	Overall Survival (OS) – Phase 2	Intent-to-Treat Set			X	X
Listing 16.2.6.1.4	Biomarker Reduction or Clearance and Duration of Biomarker Reduction or Clearance – Phase 2	Biomarker Evaluable Set			X	X
Listing 16.2.6.1.5	Subsequent Anti-Cancer Therapies – Phase 2	Intent-to-Treat Set			X	X
Listing 16.2.6.2	Listing of Deaths – Phase 2	Intent-to-Treat Set			X	X
Listing 16.2.7.1	Adverse Events – Phase 2	Safety Analysis Set	X	X	X	X
Listing 16.2.7.2	Serious Adverse Events - Phase 2	Safety Analysis Set			X	X
Listing 16.2.7.3	Adverse Events Leading to Treatment Discontinuation	Safety Analysis Set			X	X
Listing 16.2.8.1	Laboratory Assessment – Hematology - Phase 2	Safety Analysis Set	only upon request after IDMC meeting	only upon request after IDMC meeting	X	X
Listing 16.2.8.2	Laboratory Assessment – Chemistry - Phase 2	Safety Analysis Set	only upon request after	only upon	X	X

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			IDMC meeting	request after IDMC meeting		
Listing 16.2.8.3	Laboratory Assessment – Coagulation - Phase 2	Safety Analysis Set			X	X
Listing 16.2.8.4	Laboratory Assessment – Pregnancy Test - Phase 2	Safety Analysis Set			X	X
Listing 16.2.8.5	Biomarker (ctDNA, CA19-9, and CEA) - Phase 2	Biomarker Evaluable Set			X	X
Listing 16.2.9	Vital Signs – Phase 2	Safety Analysis Set			X	X
Listing 16.2.10	Physical Exam - Phase 2	Safety Analysis Set			X	X
Listing 16.2.11	Electrocardiogram Results – Phase 2	Safety Analysis Set			X	X
Listing 16.2.12	Performance Status (ECOG) – Phase 2	Safety Analysis Set			X	X
Listing 16.2.13.1	EORTC QLQ-C30 – Phase 2	Safety Analysis Set			X	X
Listing 16.2.13.2	EORTC QLQ-PAN26 – Phase 2	Safety Analysis Set			X	X
Listing 16.2.14	Reactogenicity to the Vaccine - Phase 2	Safety Analysis Set			X	X

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