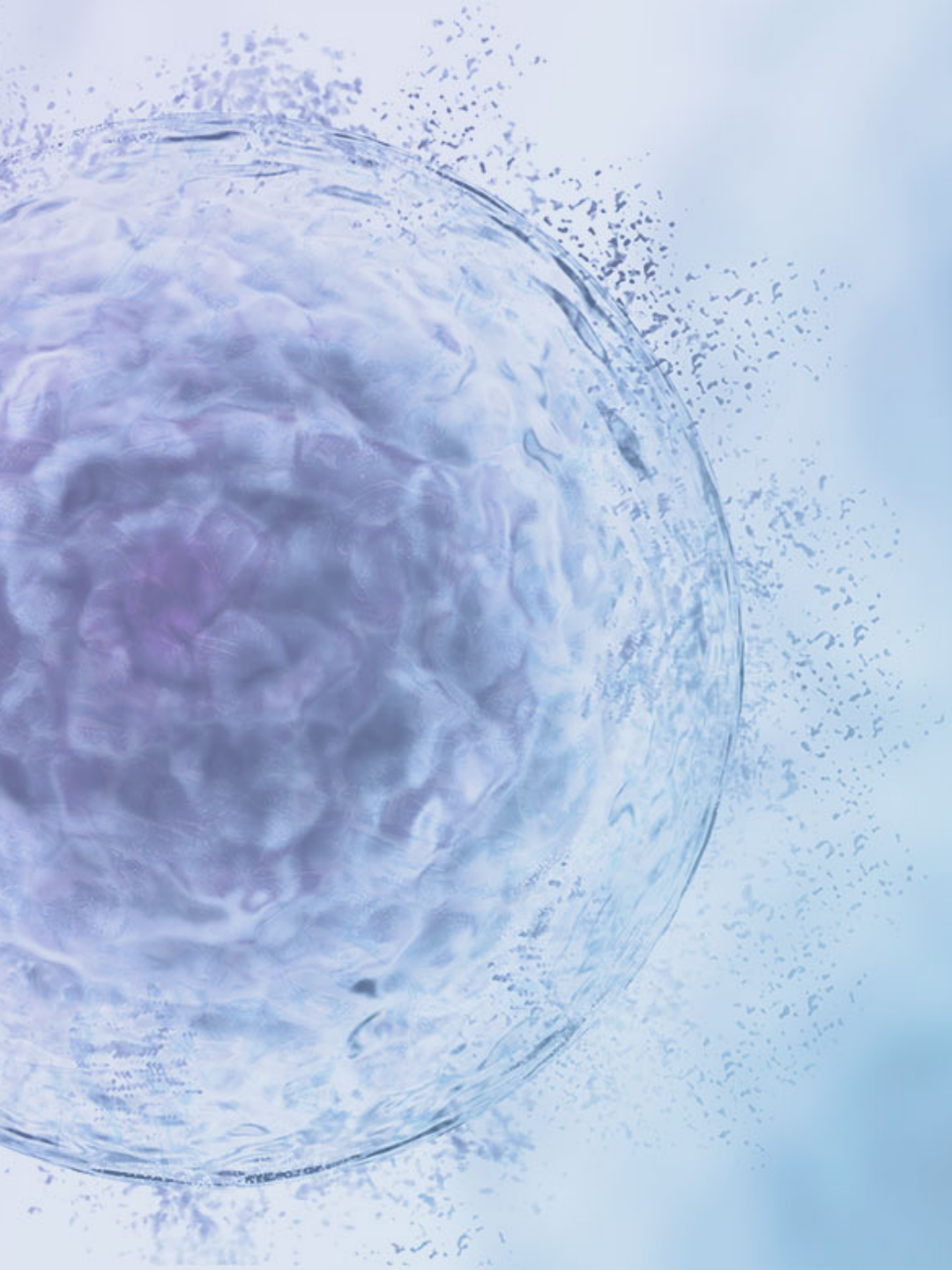
elicera
THERAPEUTICS

Fighting cancer with next generation of cell and gene therapies and a universally compatible CAR T-cell enhancement technology platform

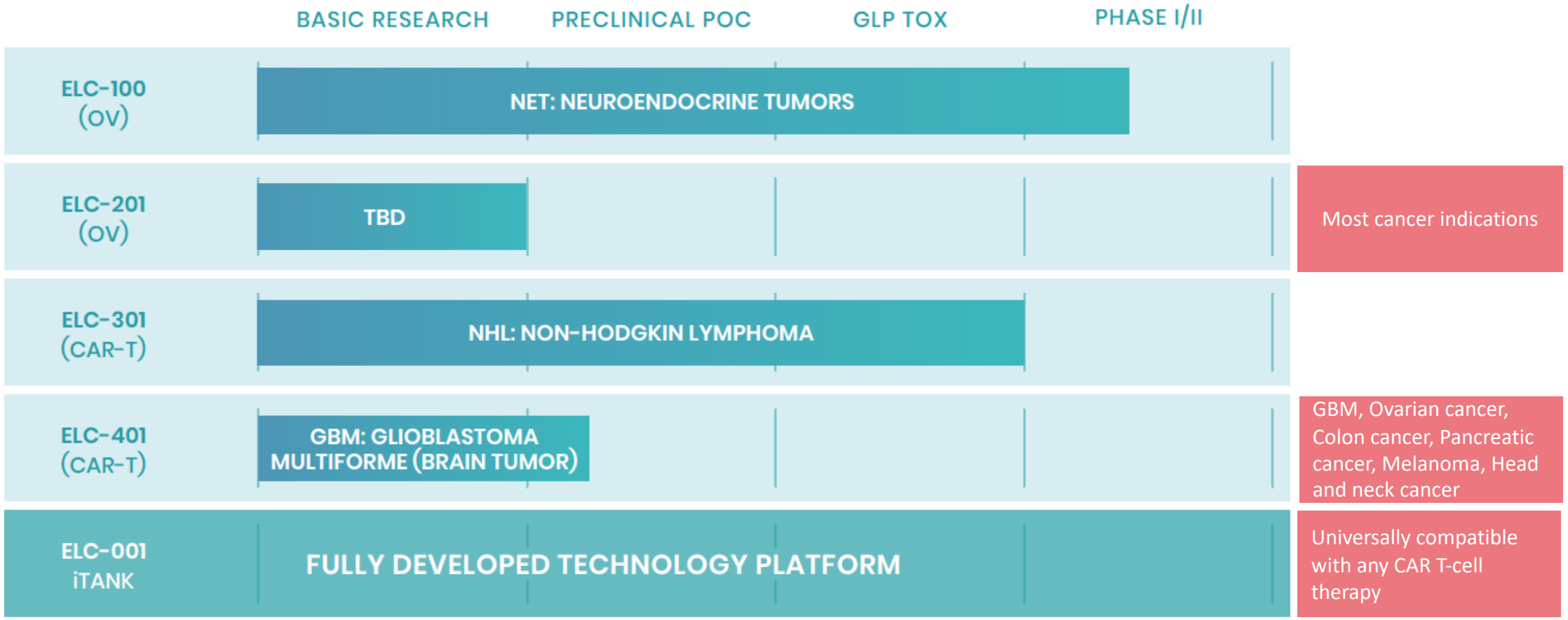
October, 2022



Elicera Therapeutics

- **Armed CAR T-cells (4th generation):**
  - ELC-301: B-cell malignancies
  - ELC-401: IL13Ra2, solid tumors
- **Oncolytic viruses/OV:**
  - ELC-100: Clinical study in neuroendocrine tumors
  - ELC-201: Next generation OV, armed with iTANK and 4-1BBL, any tumor
- **iTANK: Universal CAR T-cell enhancement technology platform:**
  - Proof-of-concept data published in **Nature Biomedical Engineering** in April 2022
- **Ongoing clinical study in with oncolytic virus**
- **Fully financed upcoming clinical phase I/II-study** in B-cell lymphoma with **CAR T-cell** therapy, ELC-301 thanks to **2,5 million Euro grant from the EIC Accelerator Fund** in June 2022

Broad pipeline of next generation cell- and gene therapies enhanced with Elicera's technology platform (iTANK*) with potential for further expansion

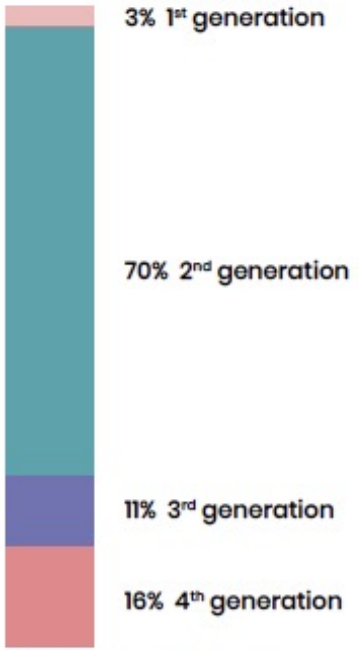


*immunoTherapies Activated with NAP for efficient Killing – PoC-data published in Nature Biomedical Engineering in April 2022

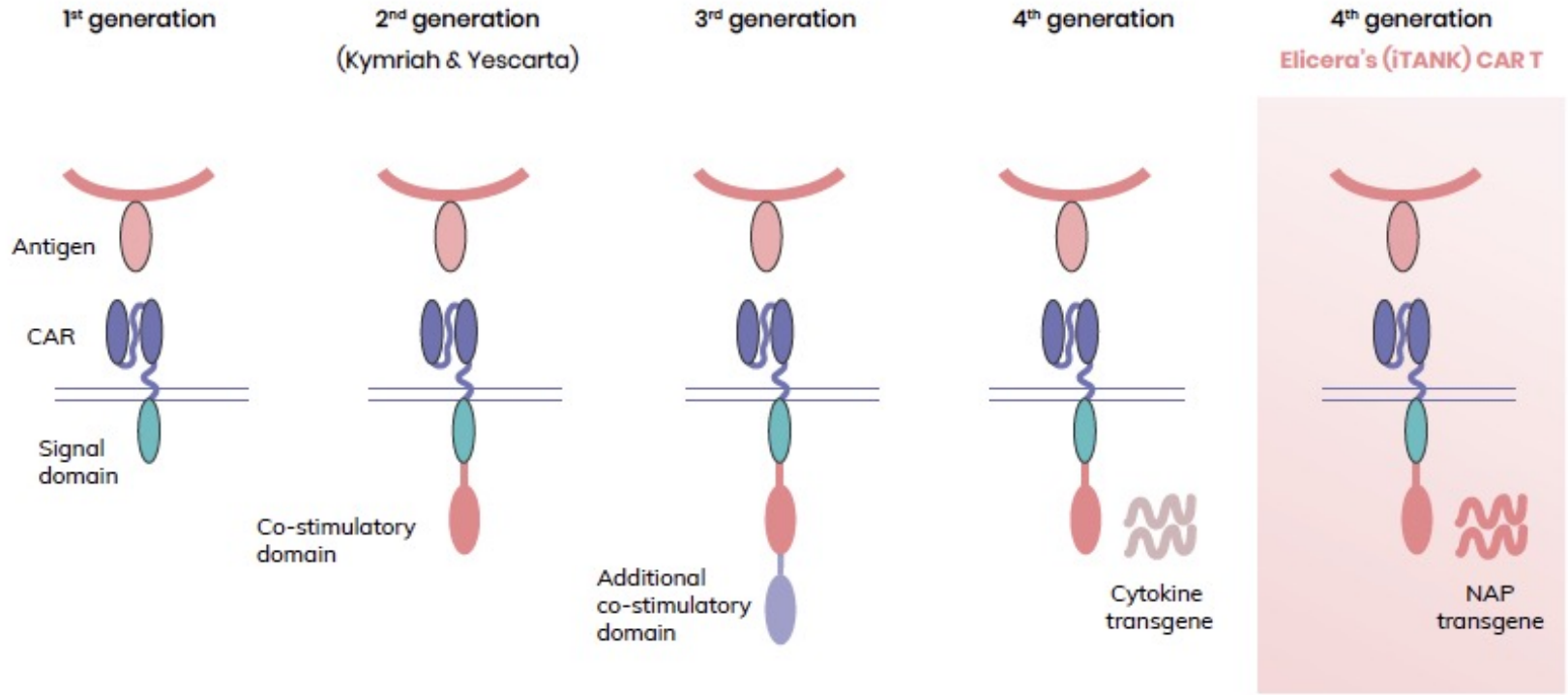
Partnering ambitions

- **iTANK**
  - Non-exclusive licenses of the iTANK-platform
  - Co-development of iTANK-armed CAR T-cells
- **Oncolytic viruses**
  - Licensing of ELC-100 and/or ELC-201
  - Combination studies for ELC-100 in neuroendocrine tumors: checkpoint inhibitors, TKIs, etc
- **CAR T-cells**
  - Licensing of ELC-301 and/or ELC-401

iTANK sets Elicera apart in the CAR T-cell field



CAR-T Therapies Market
(2nd Edition): Roots Analysis

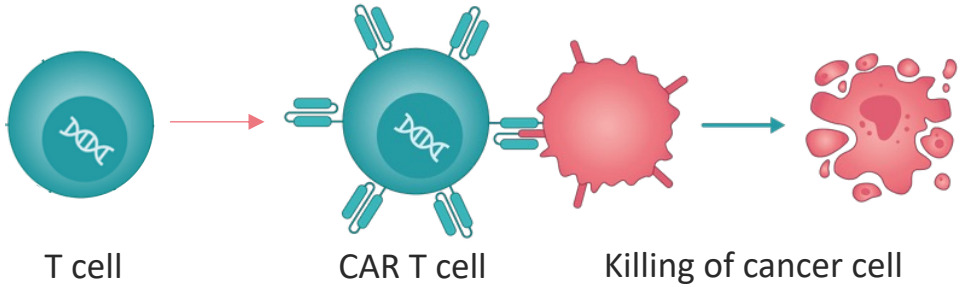


Proliferation	Insufficient	Improved	Improved +	Improved +	Improved +
T cell survival/ongoing response	Brief	Extended	Extended	Extended +	Extended +
Immune activation	Insufficient	Improved	Improved	Improved +	Improved +++

iTANK*: Universal CAR T-cell enhancing technology that can help meet two major challenges in solid tumors

Liquid tumor CAR T

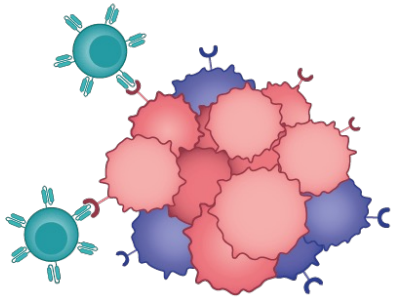
- **Homogeneous target antigen expression**
- **No immunosuppressive tumor microenvironment**



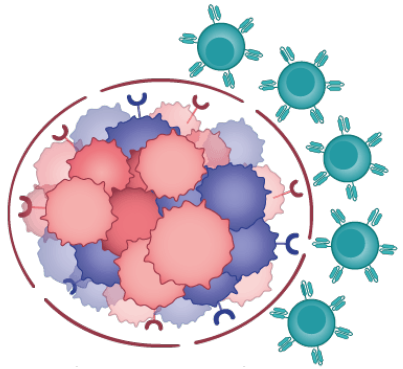
Solid tumor CAR T

- **Heterogenous target antigen expression**
- **Highly immunosuppressive tumor microenvironment**

1) Only kills a “portion”



2) Can NOT “penetrate”



*immunoTherapies Activated with NAP for efficient Killing – PoC-data published in Nature Biomedical Engineering in April 2022

iTANK generates a parallel attack on tumor cells on multiple antigen targets

CAR-T cells therapies are highly promising treatments, yet the efficacy is still not satisfactory in solid tumors, mainly due to two major challenges

Challenge 1:

Heterogenous antigen expression on tumor cells increases the risk of antigen-escape and the formation of CAR T-cell resistant tumors

iTANK solution 1:

iTANK leads to activation of endogenous killer T-cells against the whole repertoire of tumor-associated antigens

iTANK counteracts the hostile tumor microenovironment in solid tumors

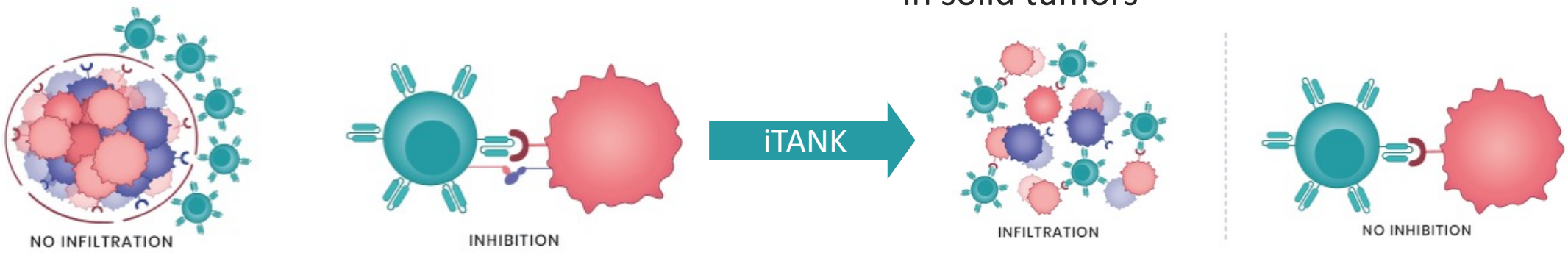
CAR-T cells therapies are highly promising treatments, yet the efficacy is still not satisfactory in solid tumors, mainly due to two major challenges

Challenge 2:

Hostile tumor microenvironment down-regulates the function of CAR T-cells

iTANK solution 2:

iTANK creates a pro-inflammatory environment that strengthens the function of the CAR T-cell and combats the otherwise hostile microenvironment in solid tumors



Nature Biomedical Engineering* (impact factor 25,7) published PoC-data on the mode-of-action on 4 April

Unique mode-of-action

- Creates a **parallel multi-targeted attack** on cancer cells by activation of killer T-cells
- Combats immunosuppressive tumor microenvironment and creates an **immunologically hot tumor**
- Makes **CAR T-cells stronger**

Universal

- Can be **applied to arm any CAR T-cell** regardless of choice of target or type of indication to treat

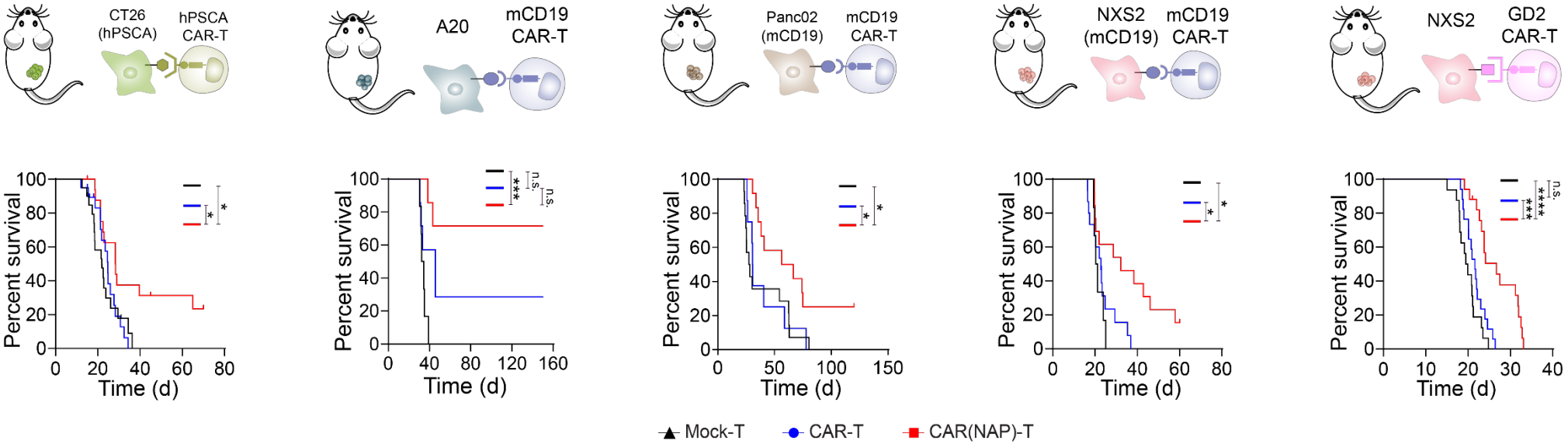
Safety

- **No added toxicity**

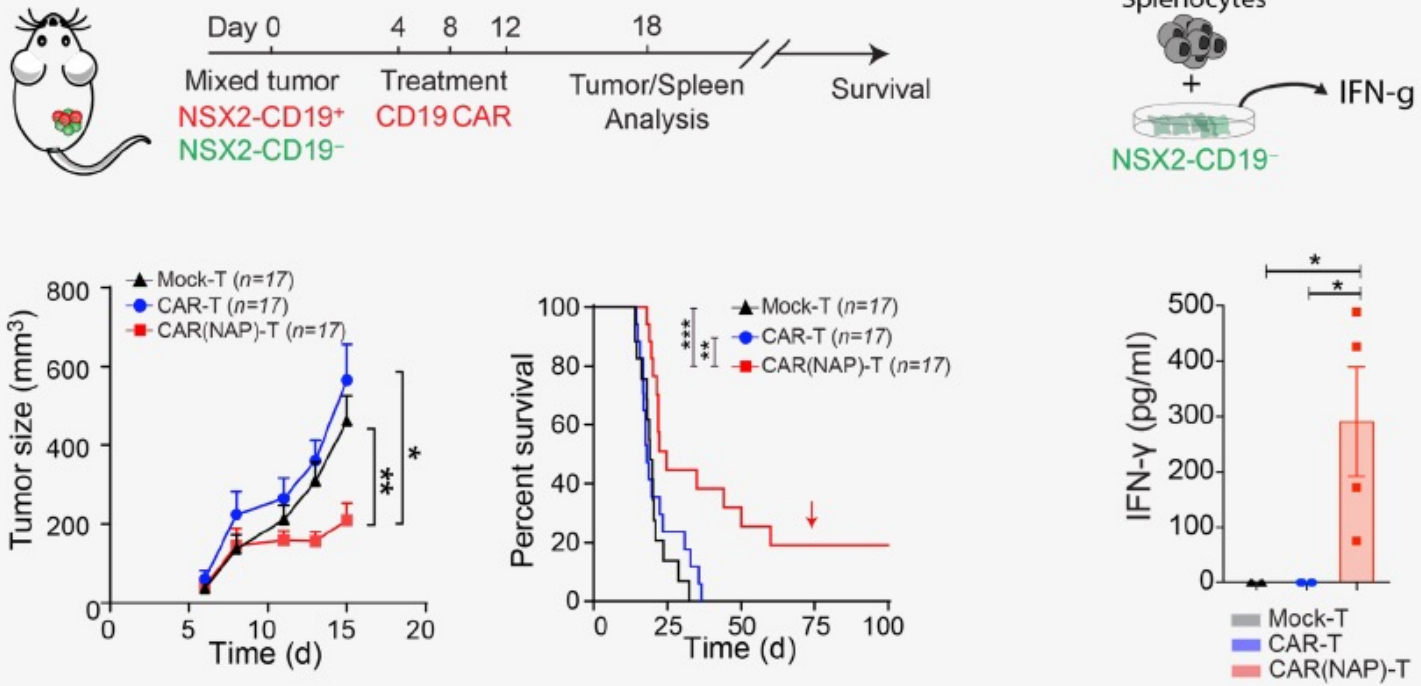
*https://www.nature.com/articles/s41551-022-00875-5

Preclinical data show that iTANK is universally compatible with other CAR T-cell therapies giving many opportunities for partnering

Different Tumors	Colon cancer	Lymphoma	Pancreatic cancer	Neuroblastoma
Different Mouse	Balb/c		A/J	C57bl/6
Different CAR	PSCA	CD19		GD2



iTANK induces bystander immune response



Mice harboring mixed tumors (1:1 mixture of CD19+ and CD19- tumor cells) were treated with either conventional CAR-T or iTANK-armed CAR(NAP)-T.

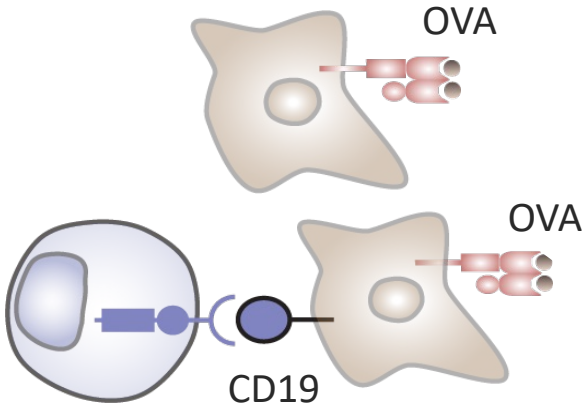
CAR(NAP)-T showed enhanced tumor growth inhibition, and prolonged mice survival.

Survived mice are able to reject CD19-negative tumor re-challenge, indicating the establishment of bystander immunity.

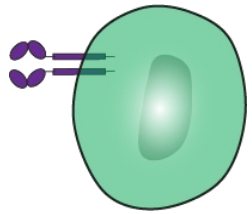
Endogenous T cells (splenocytes) from survived mice are able to recognize and react against CD19-negative tumor cells, confirming the establishment of bystander immunity.

CAR(NAP)-T cells induce bystander immunity with epitope spreading to counteract antigen heterogeneity

Tumor cells expressing both CD19 (CAR-targeted antigen) and OVA (passenger antigen)



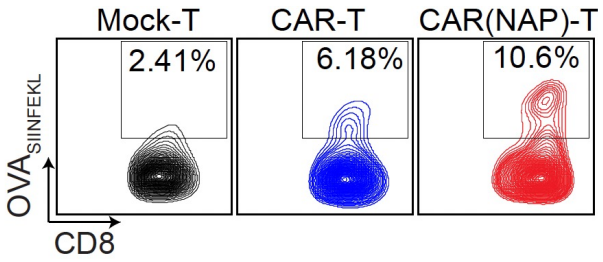
CD19 CAR(NAP)-T cell

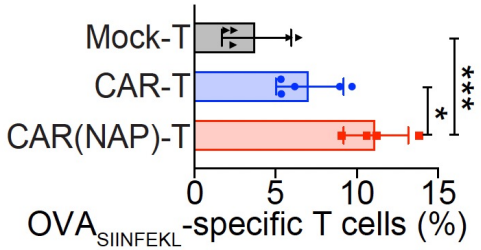


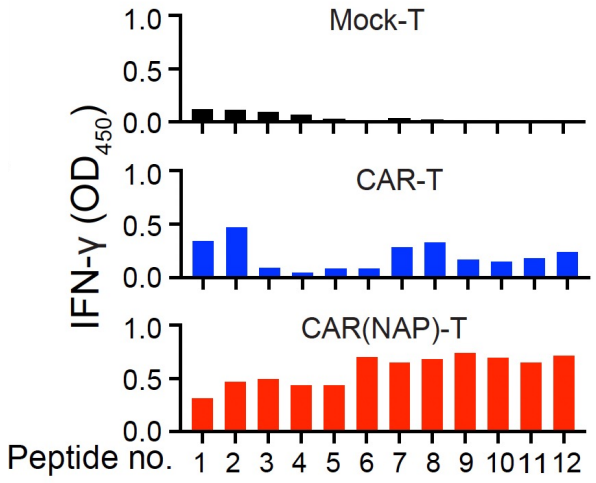
Activation of T cells (epitope spreading)

C57Bl/6

A/J



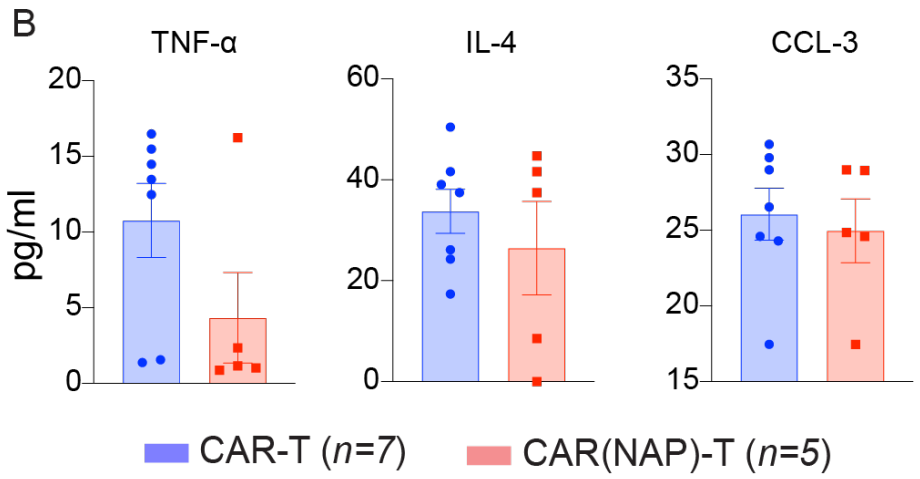




Jin C. *et al.*, Nat. Biomed. Eng., 2022

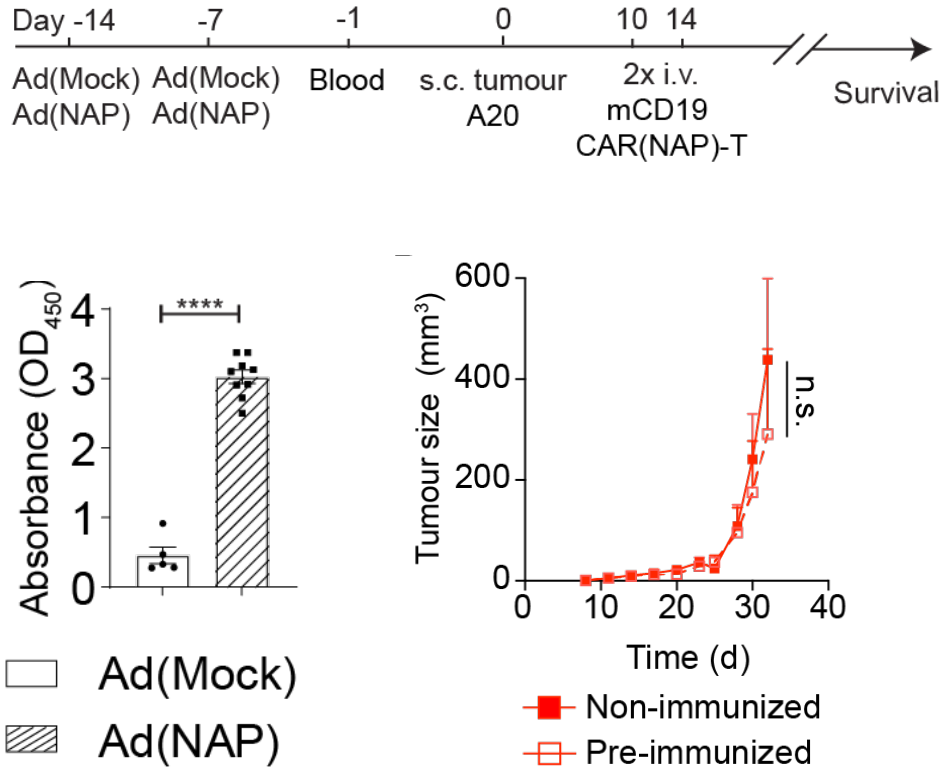
CAR(NAP)-T does not show elevated toxicity

No elevated CRS compared to conventional CAR-T

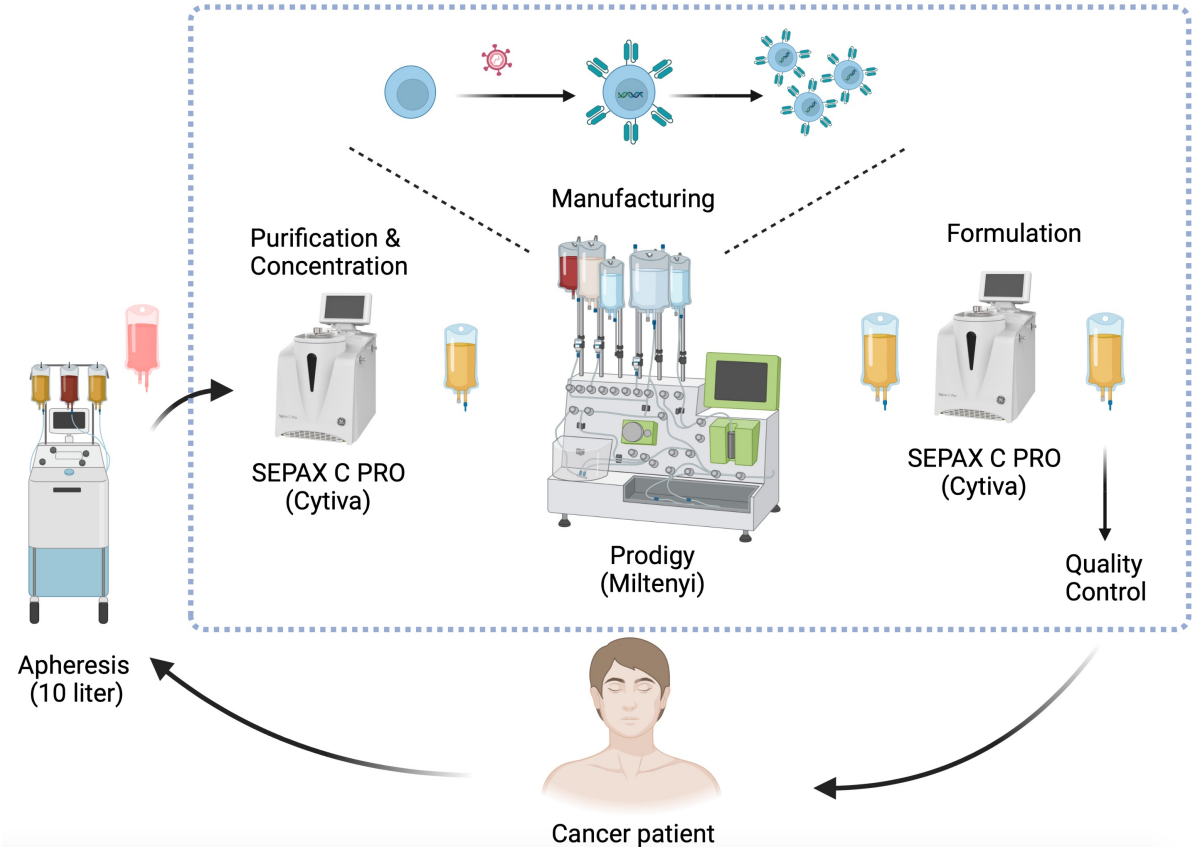


	IFN-γ	IL-10	CCL4	IFN-α	CXCL10	IL-6	VEGF	CCL2	GM-CSF
CAR T-cells	<0.24	<0.24	<4.26	<0.24	<0.94	<12.05	<0.24	<0.24	<2.54
CAR(NAP) T-cells	<0.24	<0.24	<4.26	<0.24	<0.94	<12.05	<0.24	<0.24	<2.54

Preformed NAP antibody do not affect CAR(NAP)-T



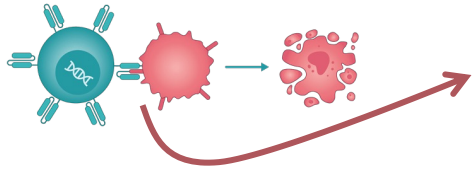
CAR-T Manufacturing process development



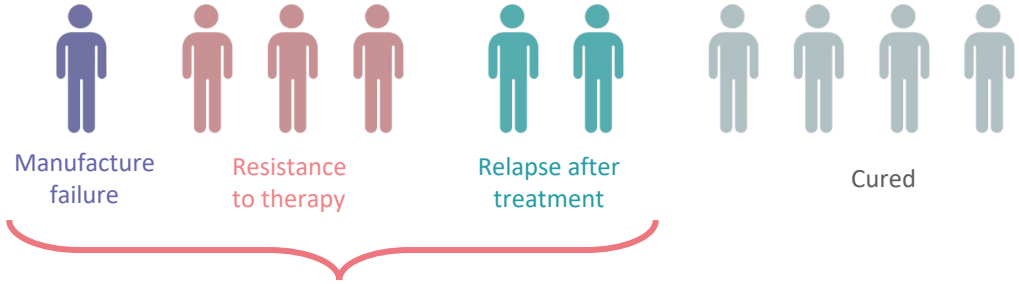
	Median time (Days) From Leukapheresis to CAR-T release/ From enrollment to CAR-T infusion
BELINDA	28/52 (Kymriah, Novartis)
ZUMA-7	13/29 (Yescarta, Gilead)
Elicera	**10/23**

ELC-301: fully funded lymphoma clinical ph I/II-study

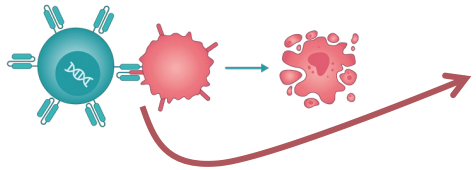
Current approved CAR-T therapy on lymphoma patients



Recognize CD19

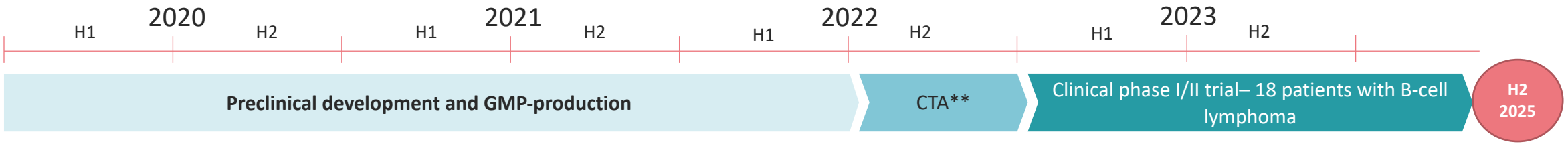


ELC-301 solution:



Recognize CD20

- iTANK armed
- Improved/automated manufacture



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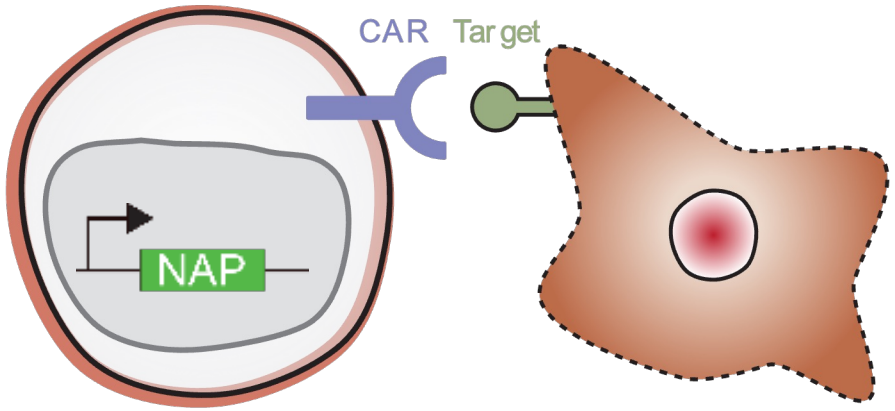
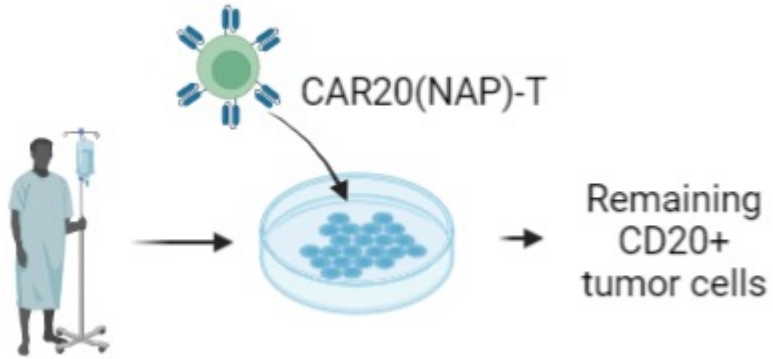
* Nature Medicine, Review article 2019: https://doi.org/10.1038/s41591-019-0564-6

**CTA: Clinical Trial Application

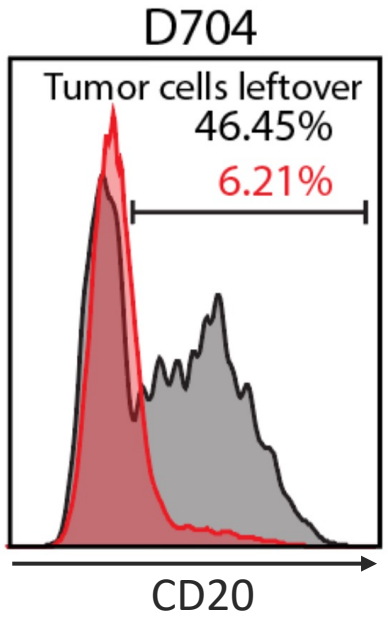
CAR20(NAP)-T: r/r B cell lymphoma

Targeting CD20, scFv derived from Rituximab





Relapsed after R-CHOP

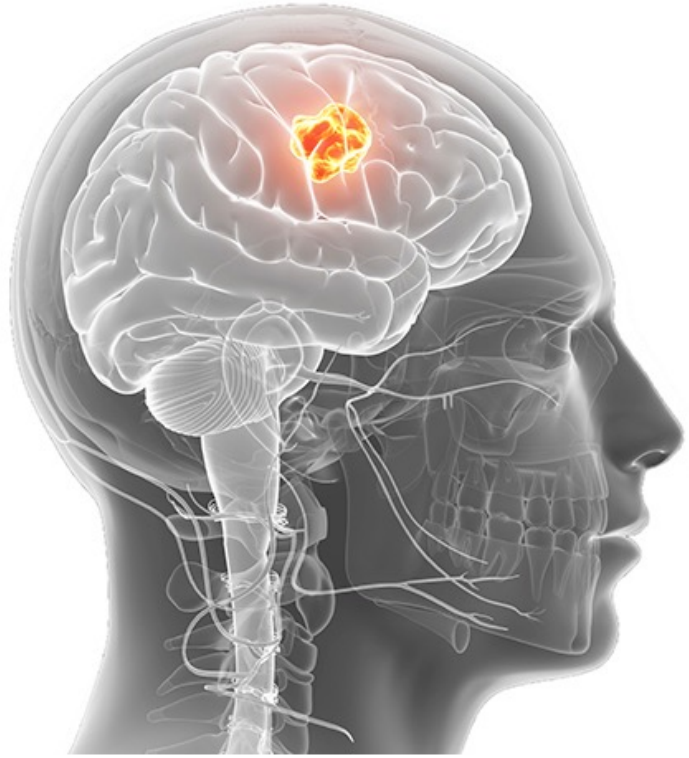


Before / After

Sarén T. *et al.*, unpublished, PLEASE DO NOT POST

ELC-401: CAR T-cell for treatment of a selection of solid tumors

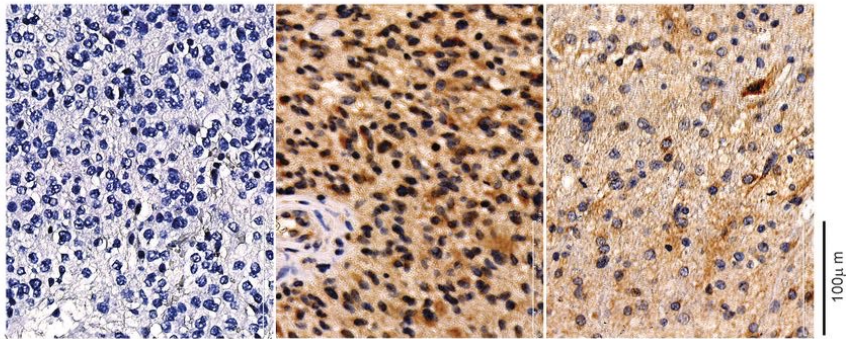
- ELC-401 targets IL13Ra2, which is overexpressed in glioblastoma (brain cancer) and potentially in a number of **other solid tumors, such as:**
  - **colon cancer**
  - **pancreatic cancer**
  - **ovarian cancer**
  - **head and neck cancer**
  - **melanoma**
- Initial focus on patients with glioblastoma, ≈30 000 patients yearly
- GBM: 5-year survival below 5%
- Competitor has shown complete response seen in a patient treated with IL13Ra2 CAR T-cell. However, the tumor grew back, negative for IL13Ra2 stressing that bystander immunity must be achieved to cure glioblastoma patients



*GBM: Glioblastoma Multiforme/Brain cancer

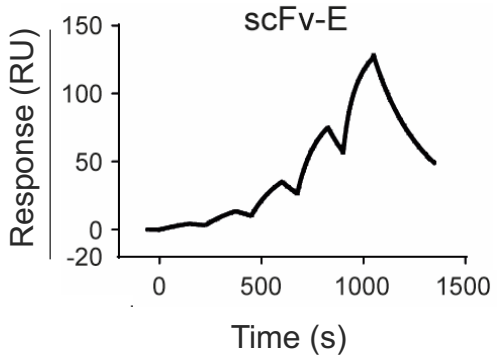
CARIL13Rα2(NAP)-T: Glioblastoma

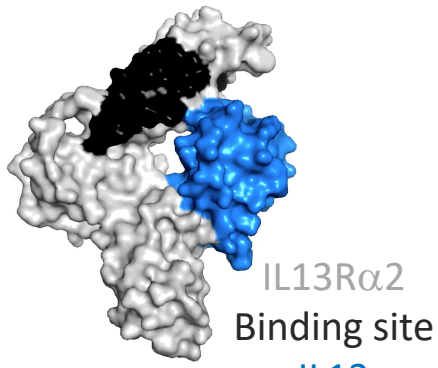
Heterogenous IL13Rα2 expression in glioblastoma



Brown CE et al., Clin Cancer Res 2015

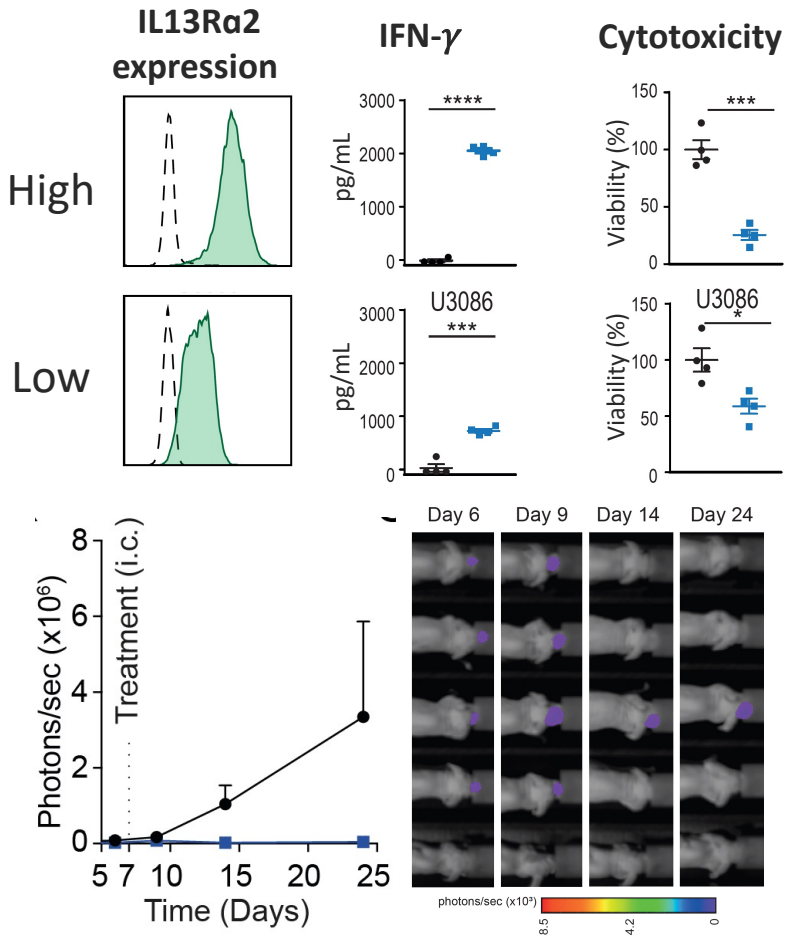
Binding of our CAR-T to IL13Rα2



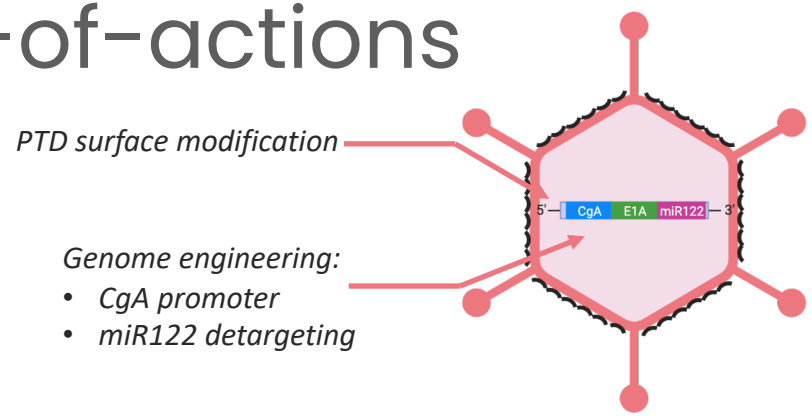


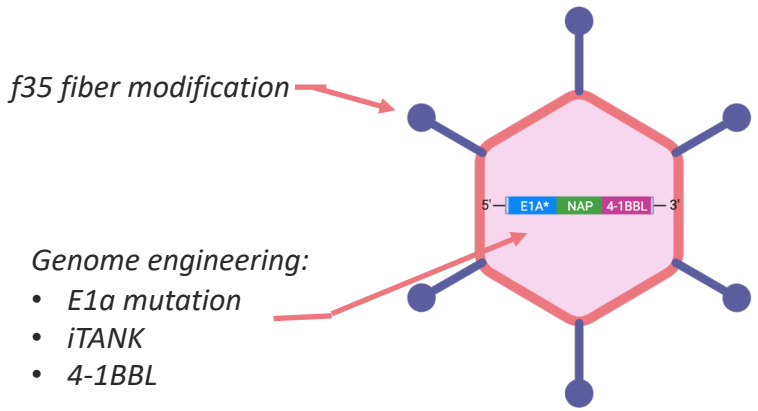
IL13Rα2
Binding site
IL13

CAR-T cell targeting IL13Rα2



Two oncolytic viruses under development, ELC-100 in NET and ELC-201 in any cancers, with three combined mode-of-actions

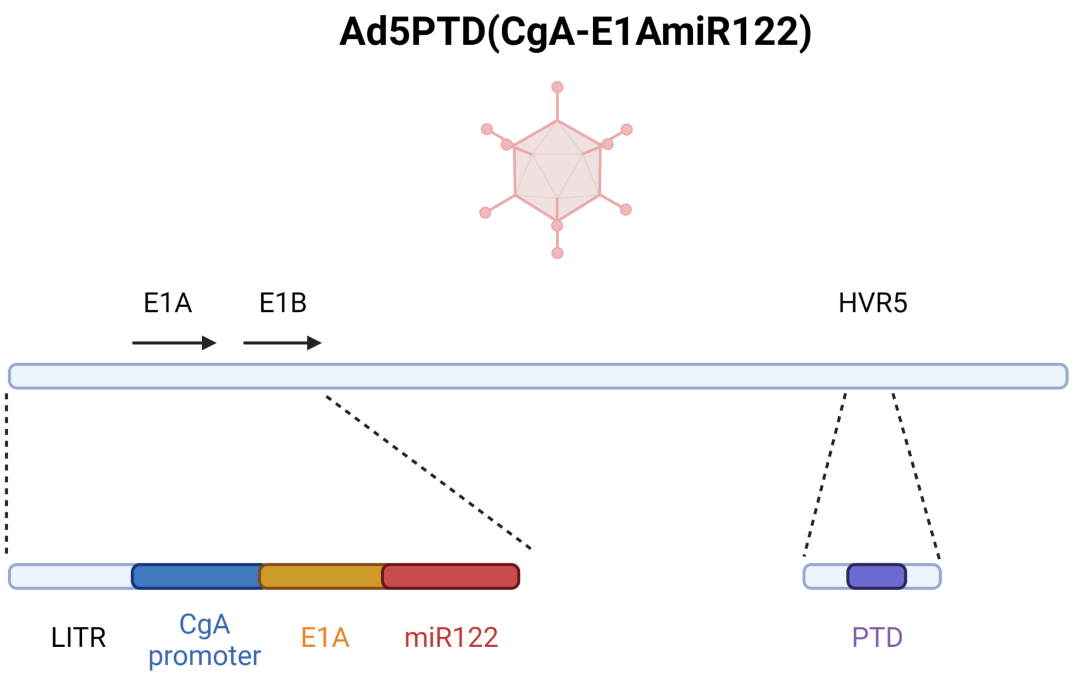




	ELC-100	ELC-201
Virus	Adenovirus serotype 5	Adenovirus serotype 5
Infectivity enhancement	PTD	f35
Tumor restriction	neuroendocrine specificity (CgA promoter)	Multiple cancers (E1A mutation)
Other safety	E1B deletion and Reduced liver tox (miR122 de-targeting)	E1B deletion
Immune stimulation	native	iTANK
T cell direct stimulation	native	4-1BBL

ELC-100: Product description

AdVince, also known as Ad5PTD(CgA-E1AmiR122), is a neuroendocrine-specific replicating oncolytic adenovirus designed to treat NETs (**especially liver metastases**)



Formulation: Ad5PTD(CgA-E1AmiR122) in concentration of 1 x 10^{10} – 1 x 10^{12} vp/vial is formulated in 20 mM Tris-HCl pH 8.0, 0.25 mM sodium chloride, 2.5% glycerol (w/v).

Primary packaging: 1.5 ml cryovials.

Storage: at -70 to -80°C.

Mode of administration: into hepatic artery as a 10 ml suspension in patients with NET liver metastases or directly into individual tumours.

ELC-100: Mode of action

- Virus replication (the pharmacological activity) of AdVince is under control of several genetic elements restricting viral replication and subsequent cell killing to preferably metastatic NET cells in the liver

- Developed from wild-type Human adenovirus serotype 5, with following modifications:

  - **CgA promoter** controls the E1A gene, ensure selectivity, virus can only replicate in neuroendocrine cells[1]
  - **miR122 detargeting**: degrade traces of E1A mRNA in healthy hepatocytes to reduce liver toxicity[2]
  - **Surface PTD modification**: enhance transduction efficacy[3]

[1]Leja J. et al. Clin. Can. Res. 2007; [2]Leja et al., PLoS ONE, 2010; [3]Yu, D., et al., J Virol, 2011.

ELC-100: Ongoing clinical phase I/II-study in neuroendocrine tumors/NET* initiated

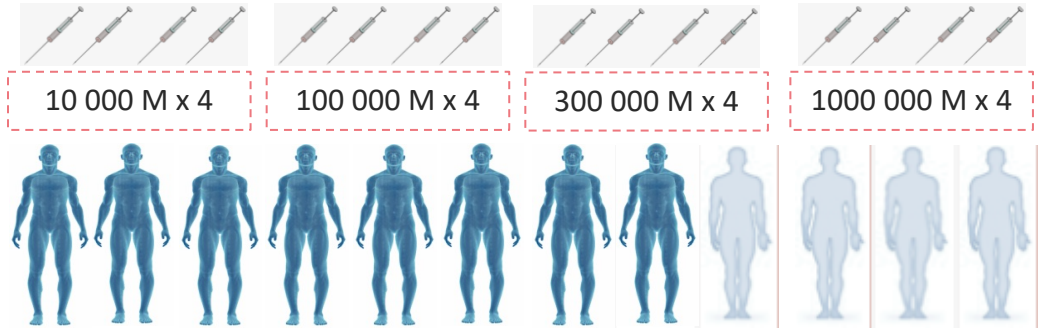
Phase I/II-study in NET
Step 1

- Step 1: dose escalation in 12 patients – 7 patients treated to date
- In collaboration with Uppsala University, sponsoring the study
- Partial response reported from a patient in lowest dose group

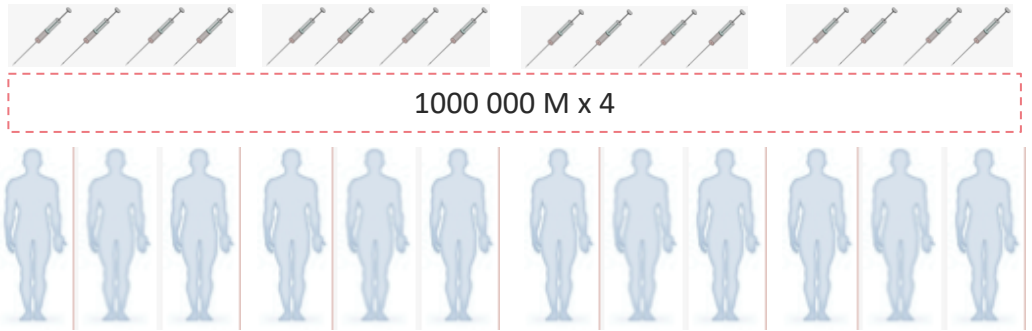
Phase I/II-study in NET
Step 2

- Step 2: maximal tolerable dose in 12 additional patients.
- Step 2 approved by MPA as monotherapy.
- Potential combination in step 2 with Keytruda

STEP 1 (expect completion in late 2023



STEP 2 (expected initiation in 2024 – PD1 combo?

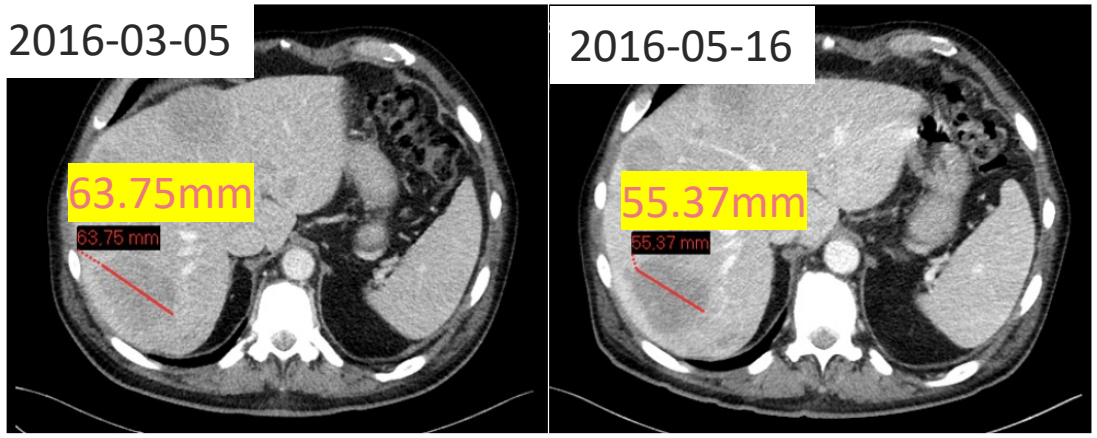


*NET: neuroendocrine tumors

Clinical efficacy of AdVince – Lung NET

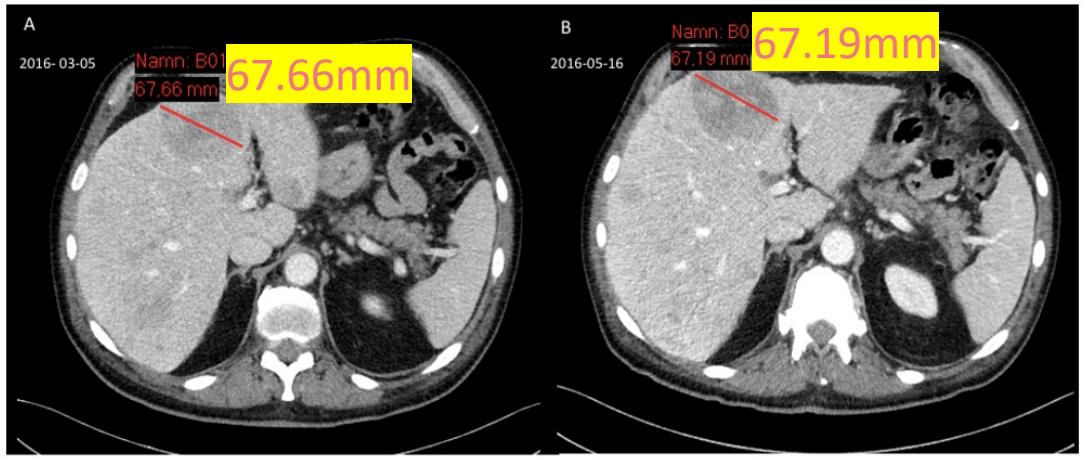
After 4 cycles of AdVince a shrinkage of one liver metastasis (Figure 1) and stabilization of another liver metastasis (Figure 2)

Figure 1. CT scans of the liver of patient #01 showing liver metastasis shrinkage



A. Baseline CT scan taken on March 5, 2016. Metastasis in the liver of 64 mm was observed; **B.** CT scan taken on May 16, 2016 after 4 cycles of AdVince. Tumour shrinkage from 64 mm to 55 mm is observed.

Figure 2. CT scans of the liver of patient #01 showing liver metastasis stabilisation



A. Baseline CT scan taken on March 5, 2016. Metastasis in the liver of 68 mm was observed; **B.** CT scan taken on May 16, 2016 after 4 cycles of AdVince. Tumour stabilisation is observed.

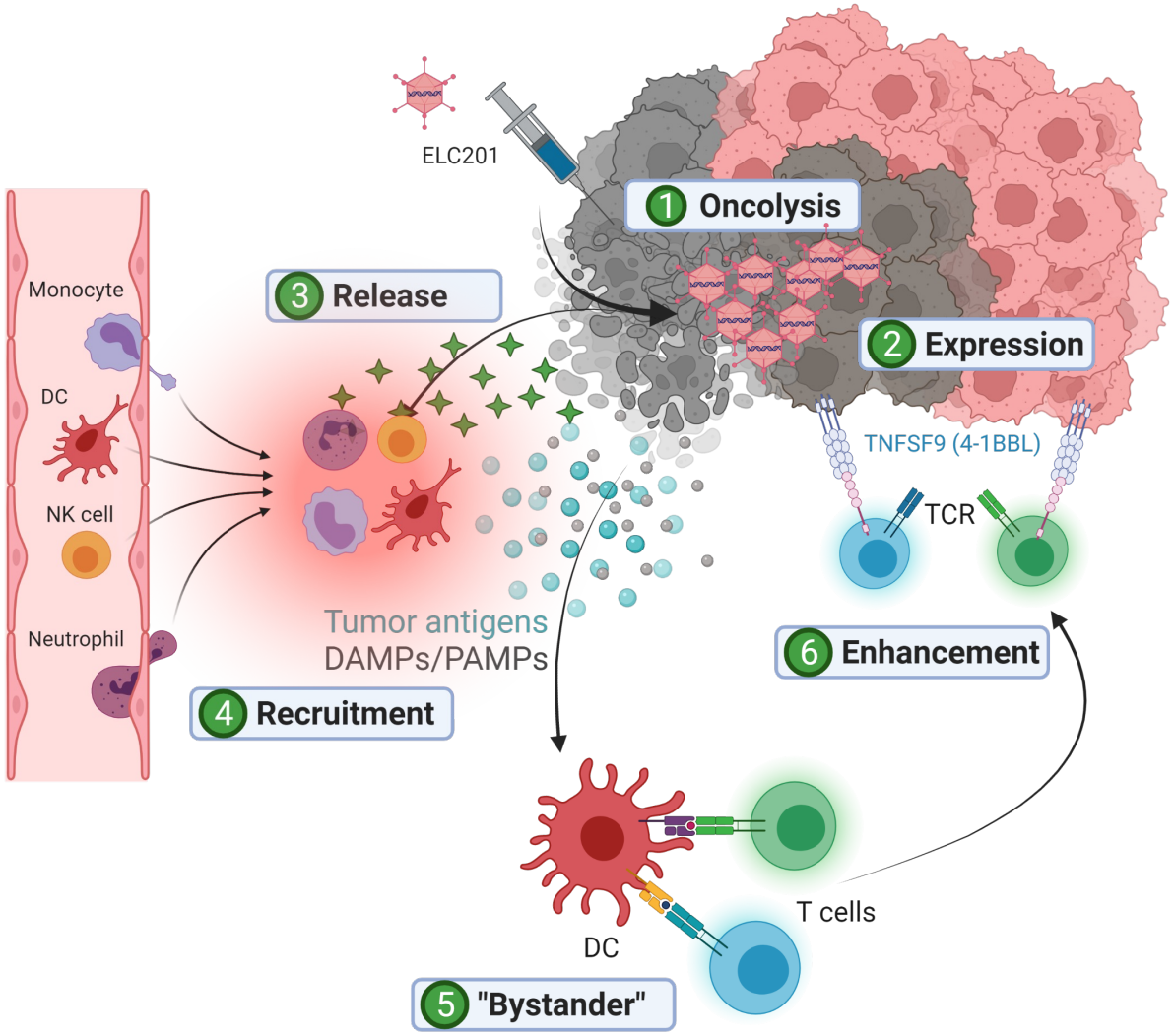
Results:

- Tumour volume shrinkage calculated as $V=4/3\pi r^3$ was **37 %**
- The response lasted for **8 months** (longer than mPFS of 3.9 months for placebo group in RADIANT-4 study for an earlier line of treatment [Afinitor (everolimus) SmPC)])
- Patient progressed but the Ki67 index was lower than prior to the treatment with AdVince
- Due to that, patient became eligible for a chemotherapy (streptozocine + 5FU) that he was not eligible prior to the treatment with AdVince

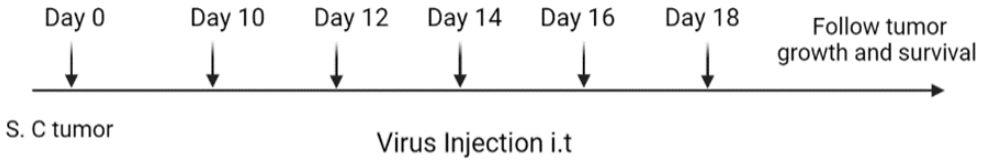
Conclusion:

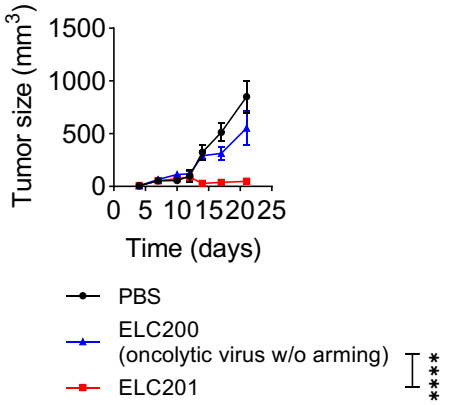
- Despite this response was seen in a patient with bronchial NET, this case **confirms clinically that AdVince,** Ad5PTD(CgA-E1AmiR122)**, targets liver metastases from neuroendocrine tumour as it was designed for**

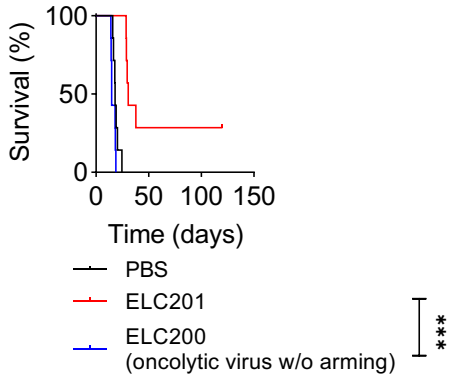
ELC-201 Mode of Action*



ELC-201 therapeutic efficacy







*Preclinical supports every step of the proposed mode of action. GMP production ongoing in preparation for clinical studies.

Thank you

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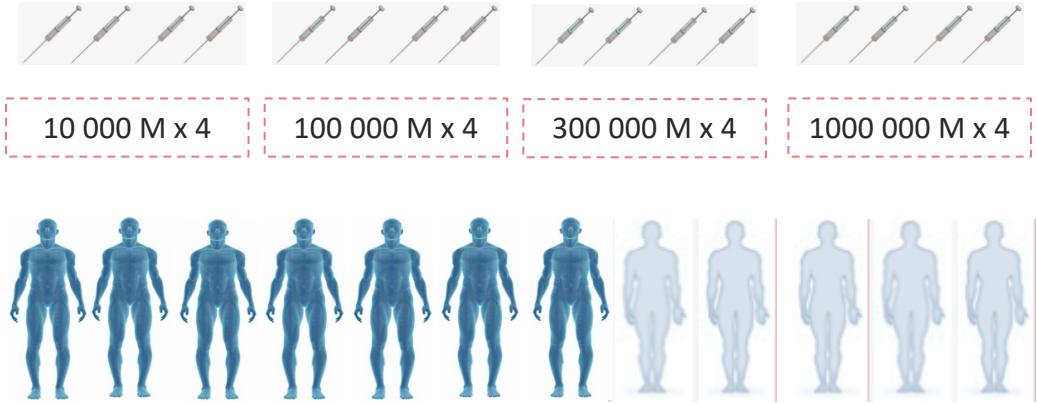
Ongoing clinical phase I/II trial in neuroendocrine tumors (NET)

- Step 1: dose escalation in 12 patients – 7 treated so far
- Step 2: maximal tolerable dose in 12 additional patients
- In collaboration with Uppsala University (sponsor) - reported promising efficacy data



Large donation from Vince Hamilton made it possible to start the study

*NET: Neuroendocrine tumors