



COMMITMENT TO A CURE

Collectis Innovation Days Episode 2

collectis.com



FORWARD-LOOKING STATEMENTS

This presentation contains “forward-looking” statements within the meaning of applicable securities laws, including the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by words such as “at this time,” “anticipate,” “believe,” “expect,” “on track,” “plan,” “scheduled,” and “will,” or the negative of these and similar expressions.

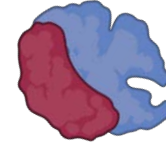
These forward-looking statements, which are based on our management’s current expectations and assumptions and on information currently available to management, include statements about our research and development projects and priorities, our pre-clinical project development efforts, the timing and progress of clinical trials (including with respect to patient enrollment and follow-up), the timing of our presentation of data, the adequacy of our supply of clinical vials, the timing of completion of construction of our Raleigh, North Carolina manufacturing facility, and operational capabilities at our manufacturing facilities, and the sufficiency of cash to fund operations.

These forward-looking statements are made in light of information currently available to us and are subject to numerous risks and uncertainties, including with respect to the numerous risks associated with biopharmaceutical product candidate development as well as the duration and severity of the COVID-19 pandemic and governmental and regulatory measures implemented in response to the evolving situation.

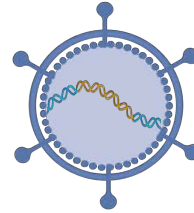
With respect to our cash runway, our operating plans, including product development plans, may change as a result of various factors, including factors currently unknown to us. Furthermore, many other important factors, including those described in our Annual Report on Form 20-F and the financial report (including the management report) for the year ended December 31, 2020 and subsequent filings Cellectis makes with the Securities Exchange Commission from time to time, as well as other known and unknown risks and uncertainties may adversely affect such forward-looking statements and cause our actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

Protein engineering 21 years



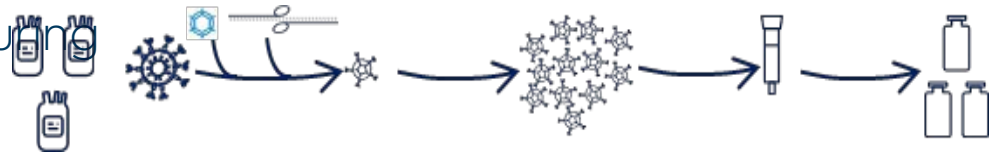
Vectorization
10 years



Proprietary electroporation technologies (devices, buffers)
11 years



Cell and Gene therapy manufacturing
8 years



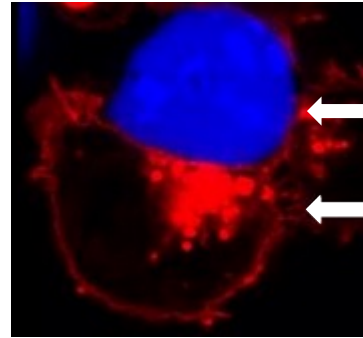
UCART20x22

First Allogeneic Dual CAR T-cells product candidate for B-cell Malignancies*



* UCART20x22 product candidate is under pre-clinical development

Strong Contact Between CAR T-cells And Tumor Cells

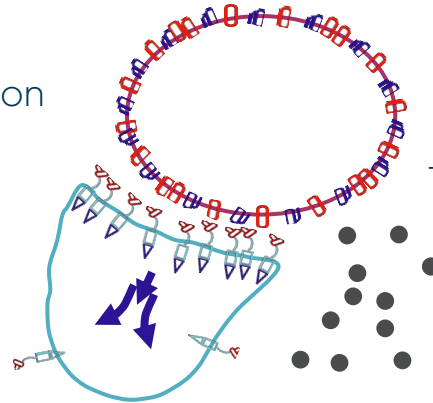


Nalm6 (Tumor antigen - CD19)

CART19

Ruella M et al. *J Clin Invest.* 2016;126(10)

Synapse formation

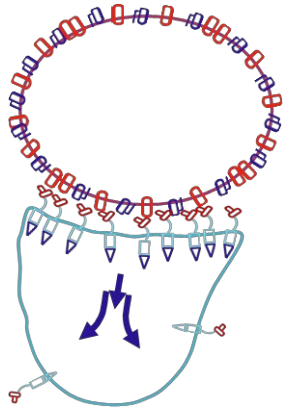


Tumor killing

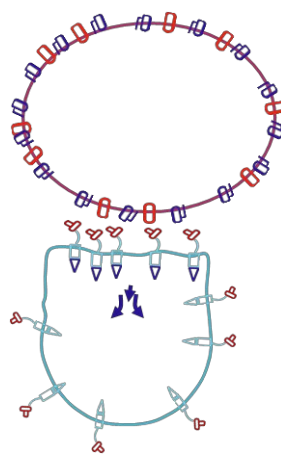
* UCART20x22
product candidate is
under pre-clinical
development

Antigen Modulation and/or Loss vs CAR T-cell Activity

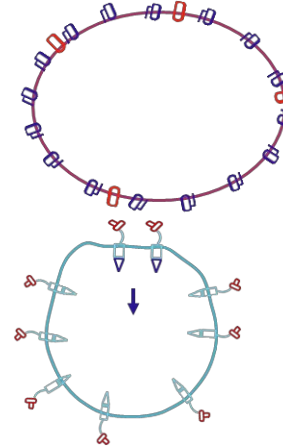
Strong kill



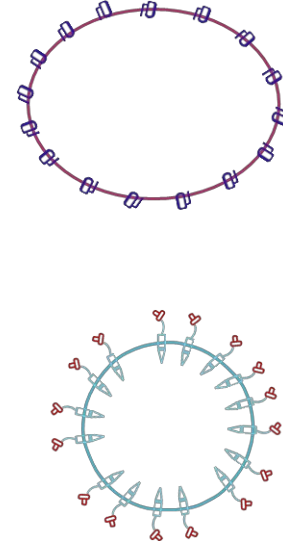
Kill



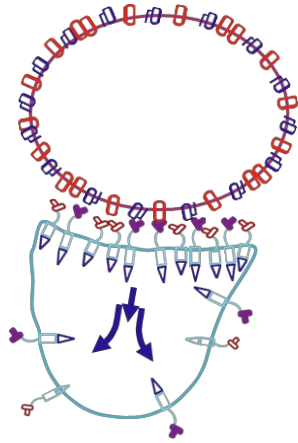
Impaired kill



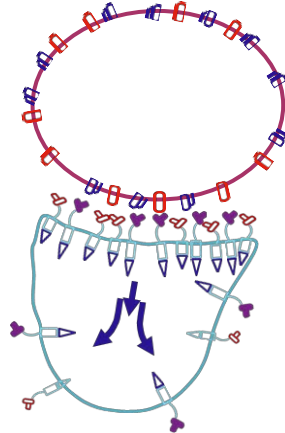
No activity,
Escape



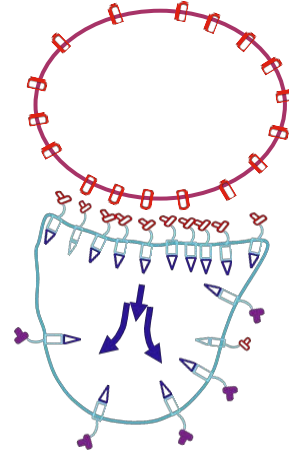
Dual CAR T-cells to Strengthen Response



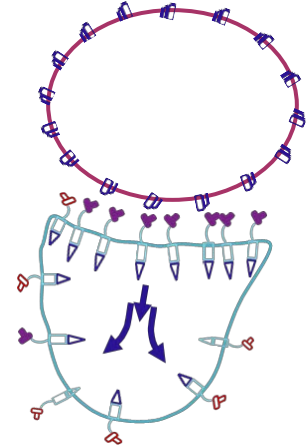
Strong kill



Strong kill

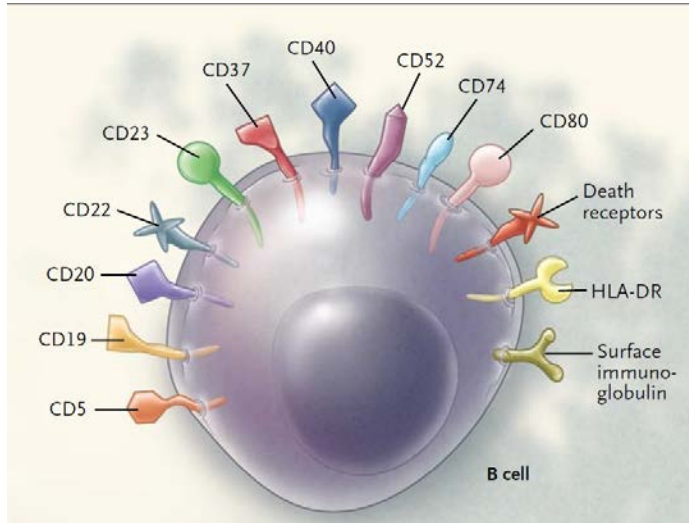


Strong kill

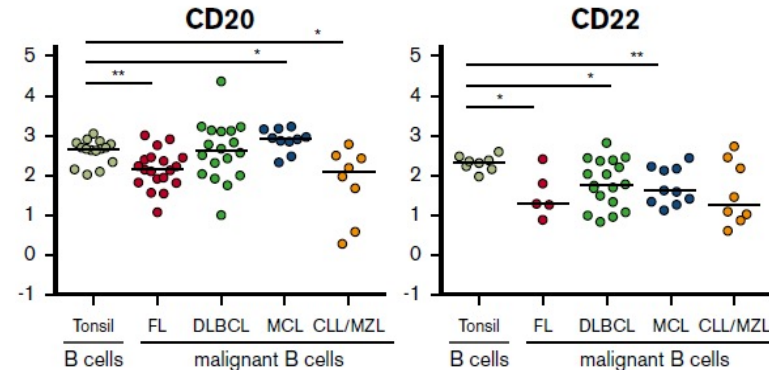
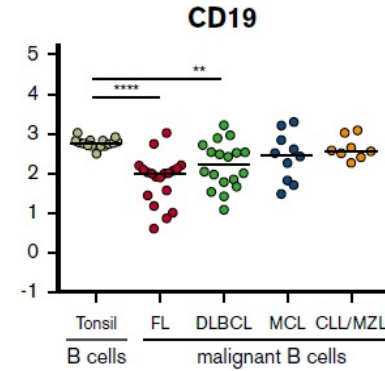


Strong kill

CD20 and CD22 are Expressed in Multiple B-cell Malignancies

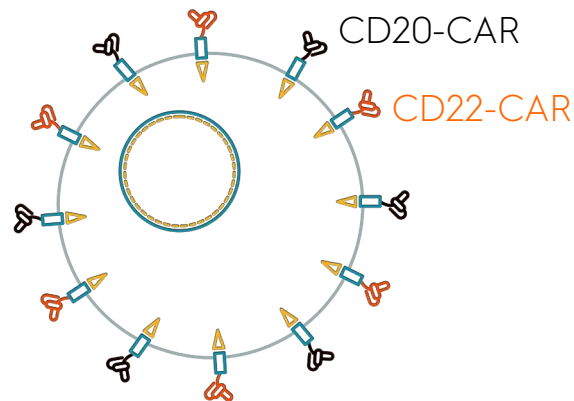


Cheson et al. NEJM, 359; 613-626



Koksai H et al. 2019. Blood Advances 3(8):1230-1243

UCART20x22 – a Dual-Targeted CAR T-cell product candidate for Lymphoma

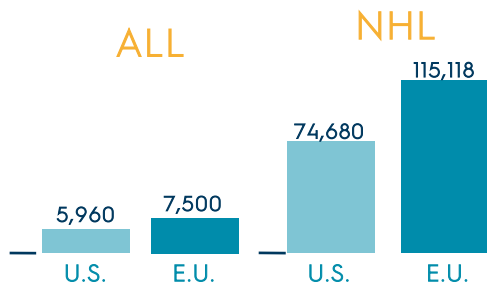


- Alternative to single target: CD19
- **CD22** and **CD20**, both validated targets in B cell malignancies
- Expected to prevent target escape and strengthen contact

TALEN® attributes:

TALEN® for TRAC and CD52 KO, same as UCART22 and UCART123

Incidence rates per year



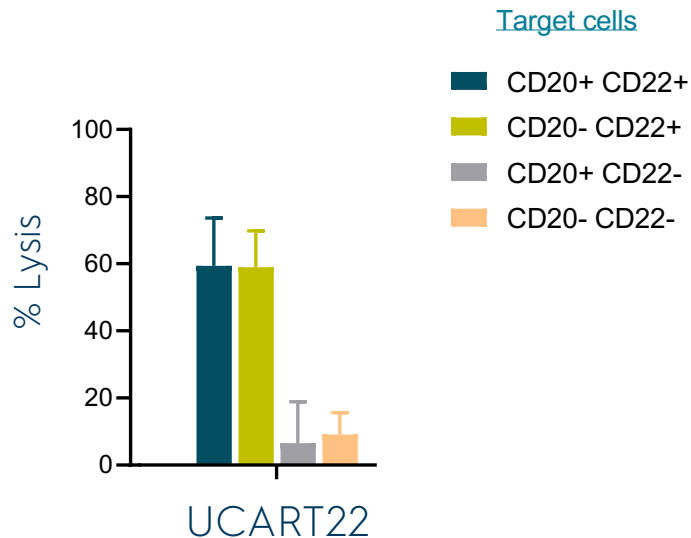
CD22 expressed in
>90% B-ALL

CD20 expressed
in >90% NHL
>50% B-ALL

* UCART20x22 product candidate is under pre-clinical development

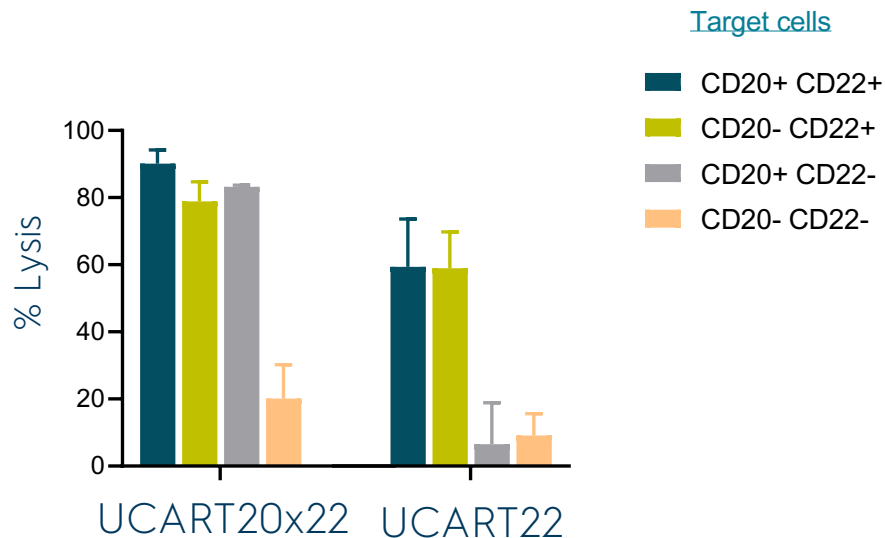
Dual CAR T-cells: Robust Activity Against Multiple Antigen Combinations

In vitro tumor cell killing

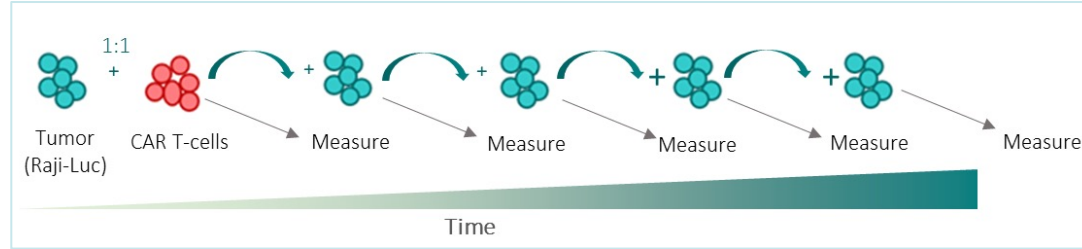


Dual CAR T-cells: Robust Activity Against Multiple Antigen Combinations

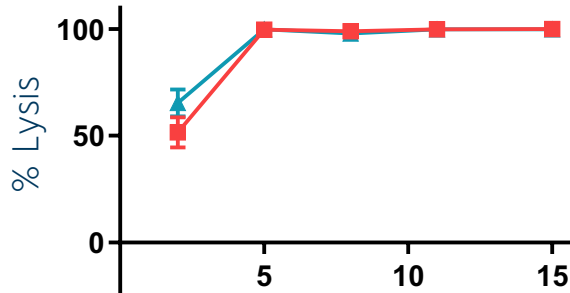
In vitro tumor cell killing



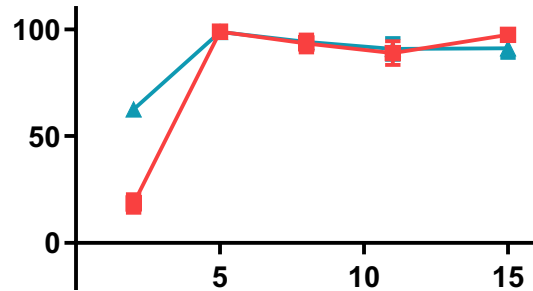
Persistent Activity Against CD22+ and CD20+ Tumor Cells



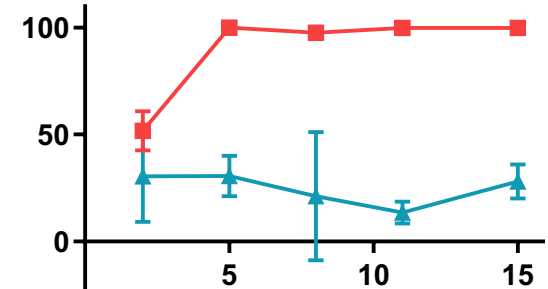
CD20+CD22+
Raji cells



CD20-CD22+
Raji cells



CD20+CD22-
Raji cells



In vitro serial killing assay

■ UCART20x22

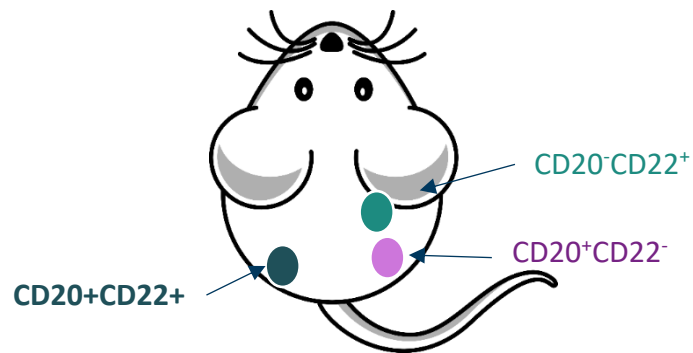
▲ UCART22

CD22 "negative" tumor cells are killed by UCART20x22, not by UCART22

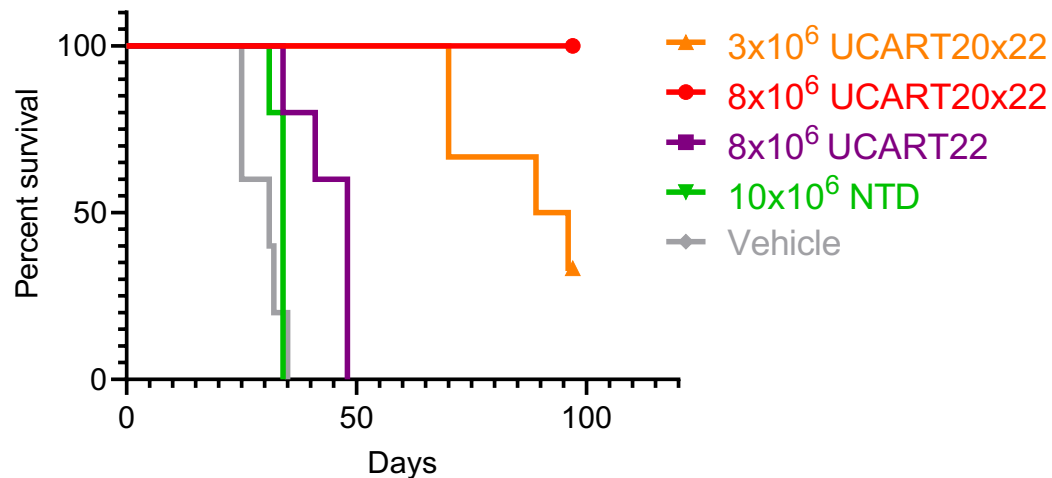
* UCART20x22 product candidate is under pre-clinical development



Efficient Activity *in vivo* Against Multiple Antigen Combinations

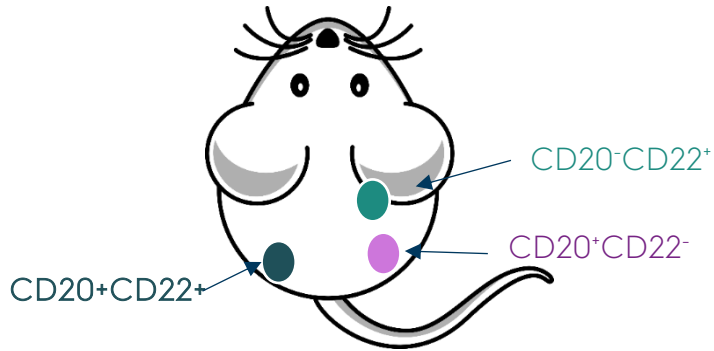


Growth of each tumor followed independently

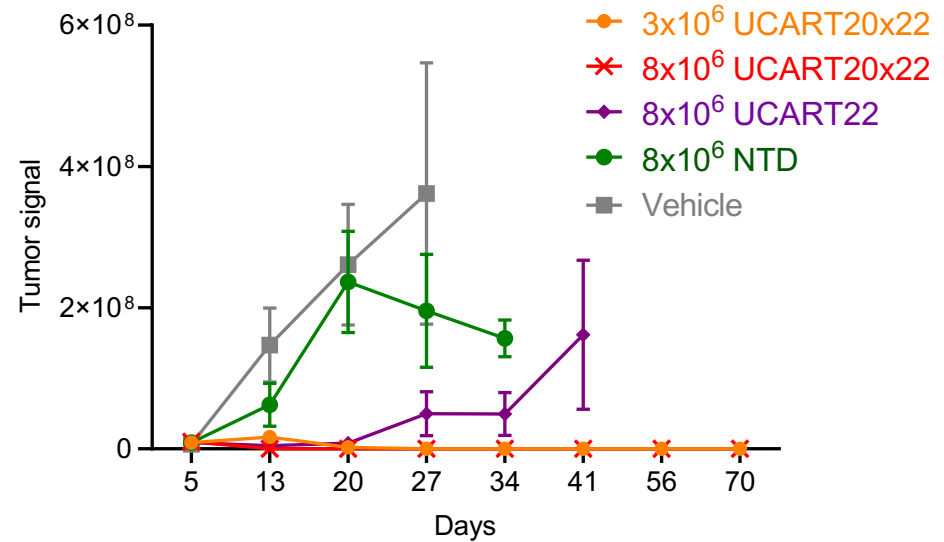


Efficient Activity *in vivo* Against Multiple Antigen Combinations

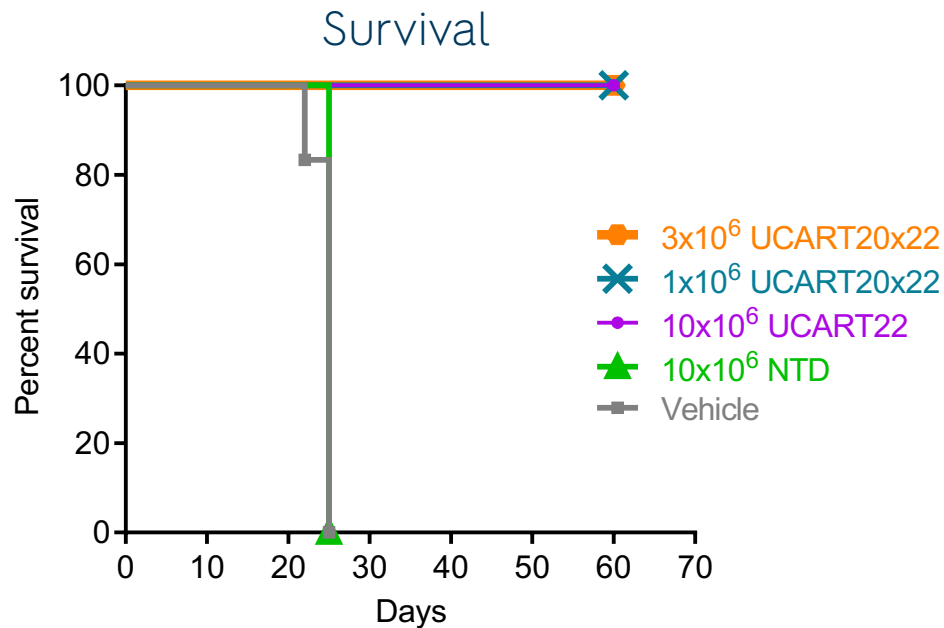
Focus on CD20+ CD22+ tumor



Growth of each tumor followed independently



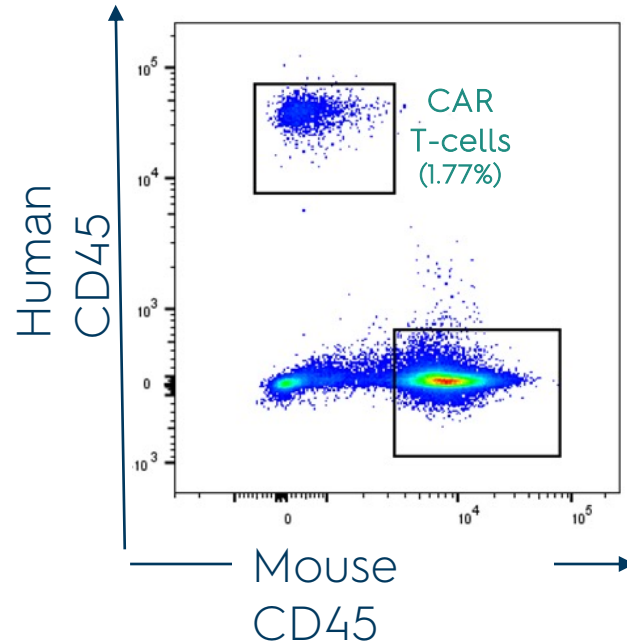
Strong *in vivo* Activity for Lymphoma Treatment



Efficient activity *in vivo* at low CAR T-cell doses in disseminated lymphoma model

Dual CAR T-cells: Long Persistence In The Bone Marrow

Persistence in bone marrow



UCART20x22 – First Allogeneic Dual CAR T-cells product candidate, with strong potential

First of its kind in the
allogeneic CAR T-cell
space

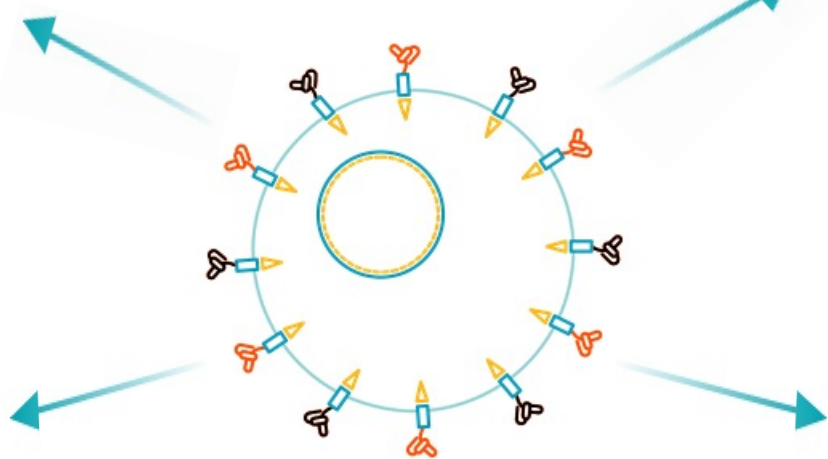
Strong *in vitro* and *in vivo*
preclinical results

Large market

Lymphoma, Leukemia,
CD22- and CD19-
relapses

ALL > 11,000 US/EU

NHL > 200,000 US/EU



Fast development
to the **clinic**

Manufacturing ready
Regulatory ready



* UCART20x22 product candidate is under pre-clinical development

SOLID TUMOR

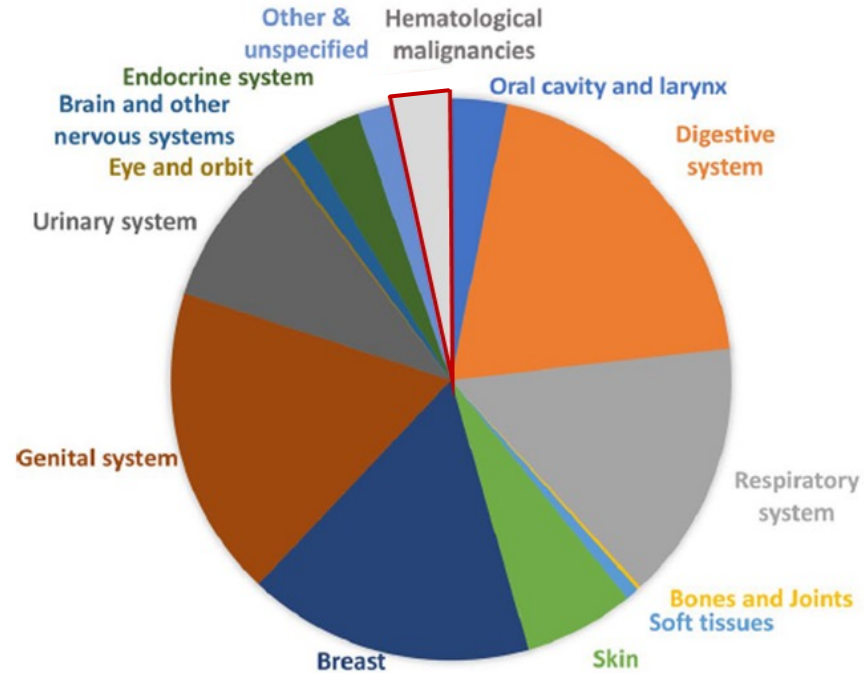
UCARTMESO PRODUCT CANDIDATE FOR MESOTHELIOMA AND PANCREATIC CANCER*



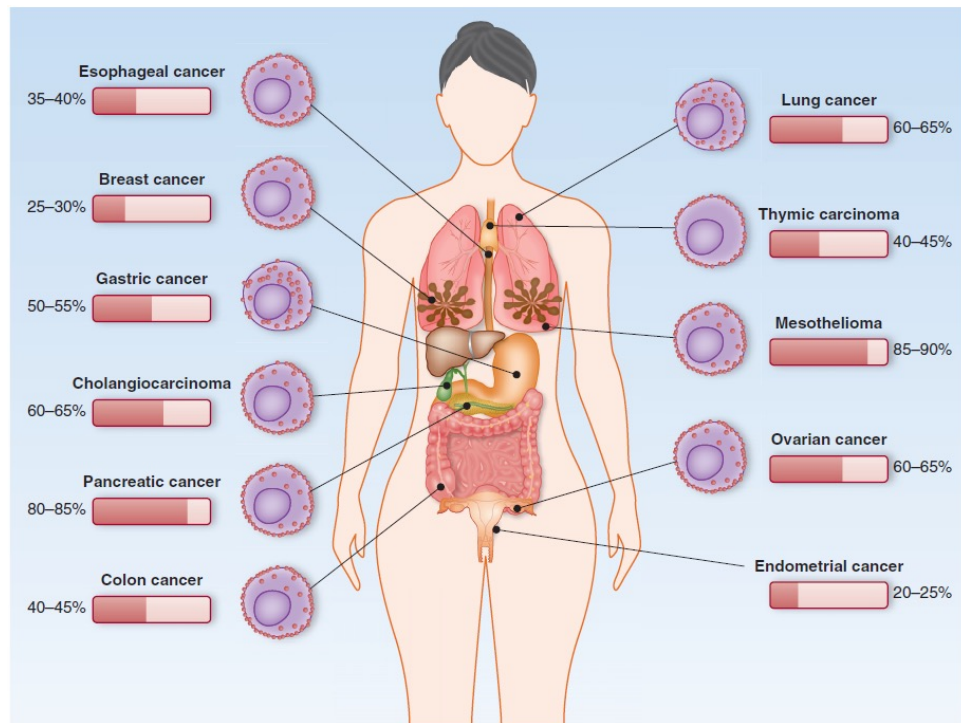
* UCARTMESO product candidate is under pre-clinical development

Medical Need for Solid Tumors

NEW CASES IN US 2019 - PER ORGAN CLASS

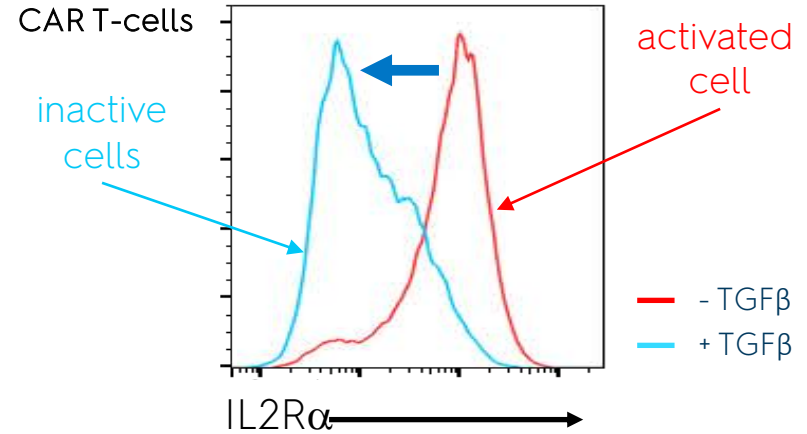
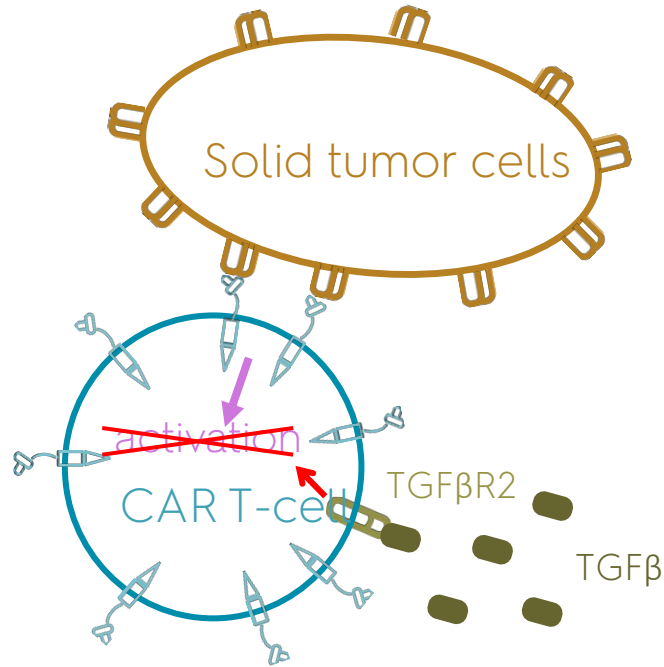


Mesothelin is an Attractive Solid Tumor Target

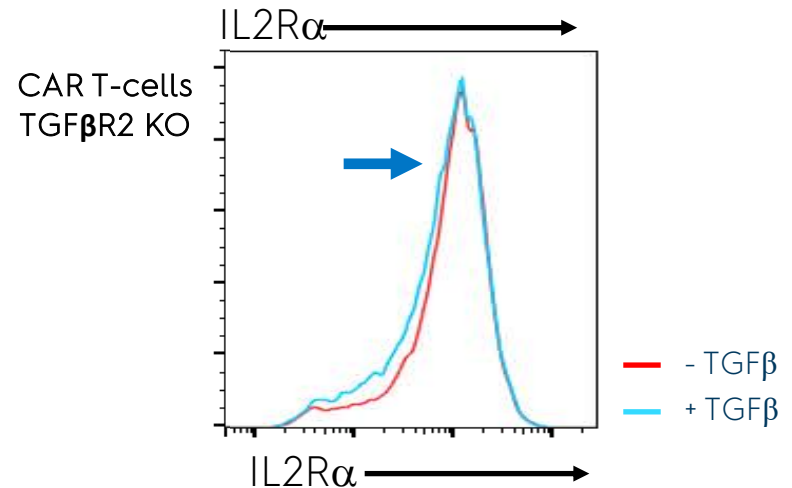
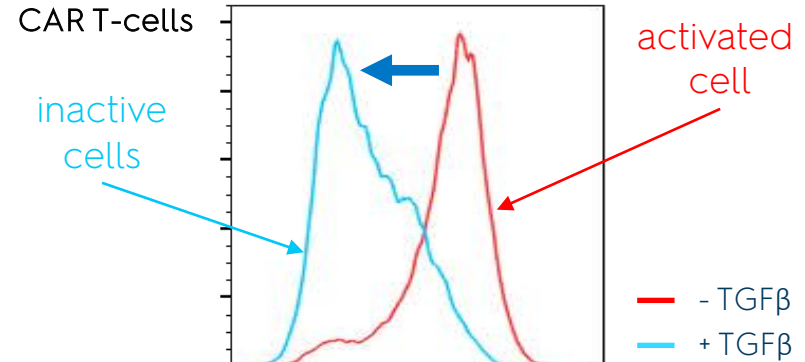
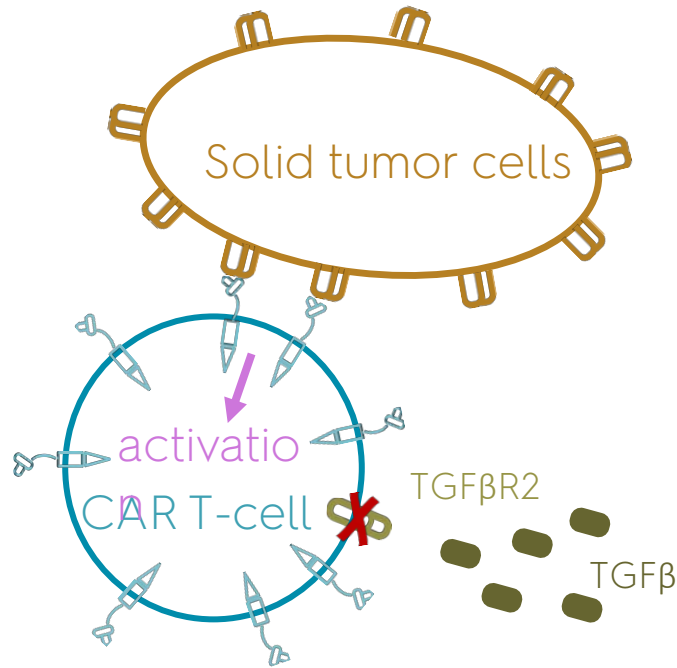


- ✓ Mesothelin is a tumor-associated antigen broadly overexpressed on various malignant tumor cells
- ✓ Mesothelin is one of the most studied target for solid tumor treatment
- ✓ Promising preliminary clinical results were obtained with mesothelin-targeted agents

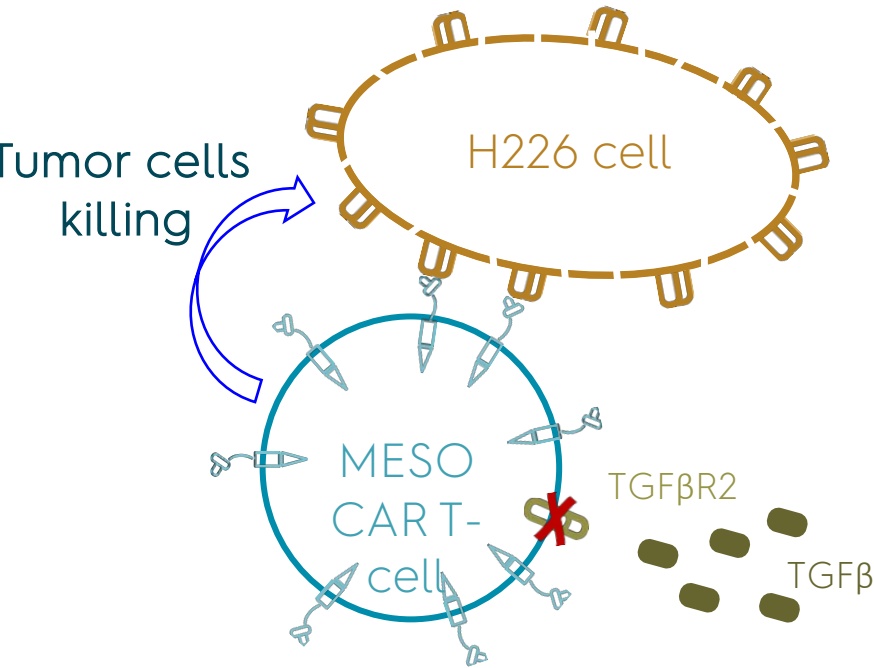
TGF β Impairs CAR T-cell Activity in Solid Tumors



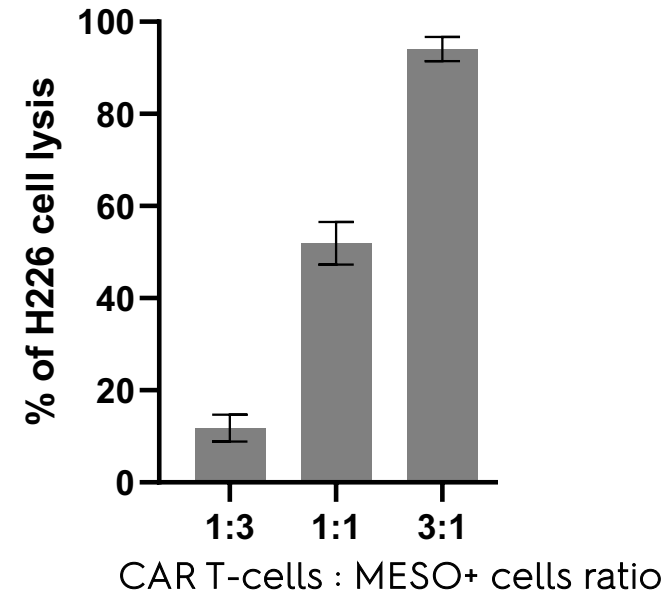
TGFbR2-Edited CAR T-cells are Resistant To TGFb Inhibitory Effect



TGF β R2-Edited MESO CAR T-cells Product Candidate Displays High Anti-Tumor Activity *in vitro* and *in vivo*

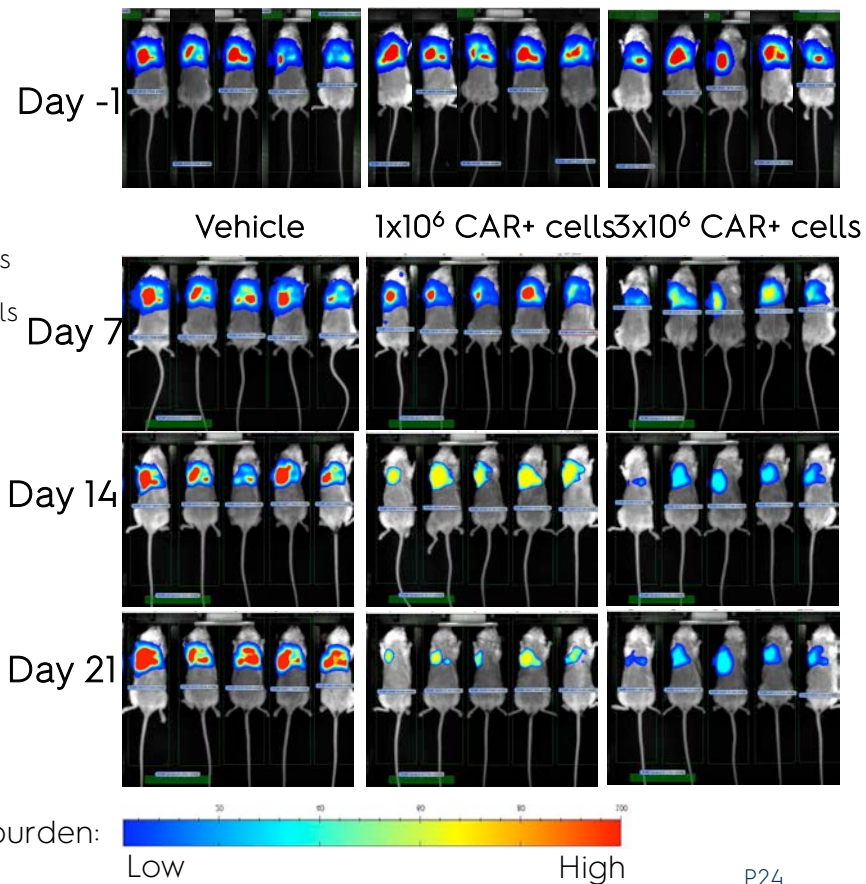
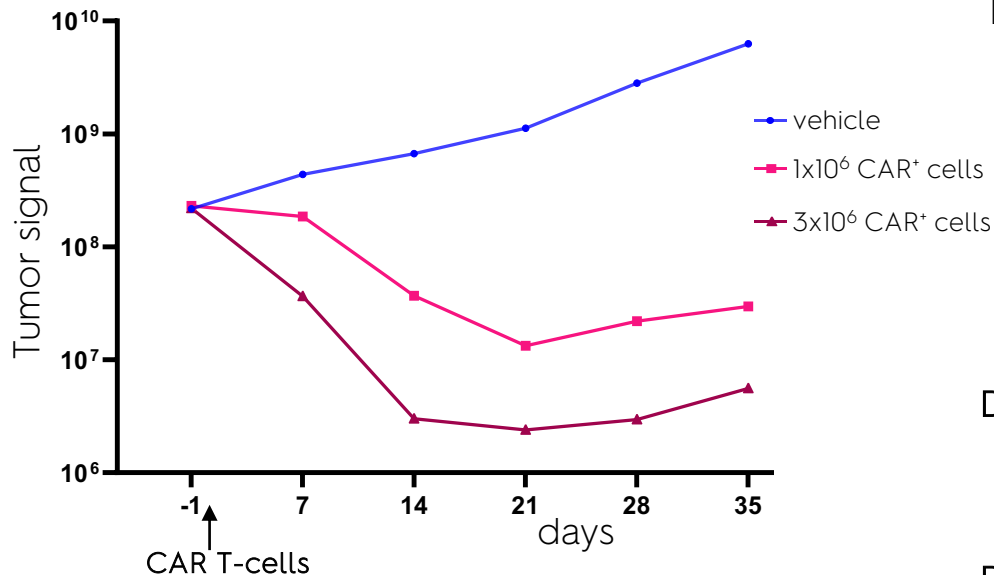


In vitro Killing of MESO+ cells



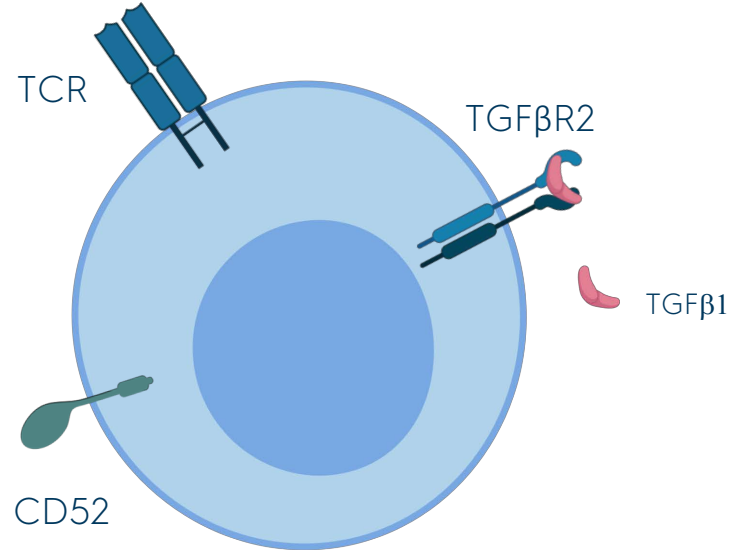
TGF β R2-Edited MESO CAR T-cells Product Candidate Displays High Anti-Tumor Activity *in vitro* and *in vivo*

In vivo Killing of MESO+ cells

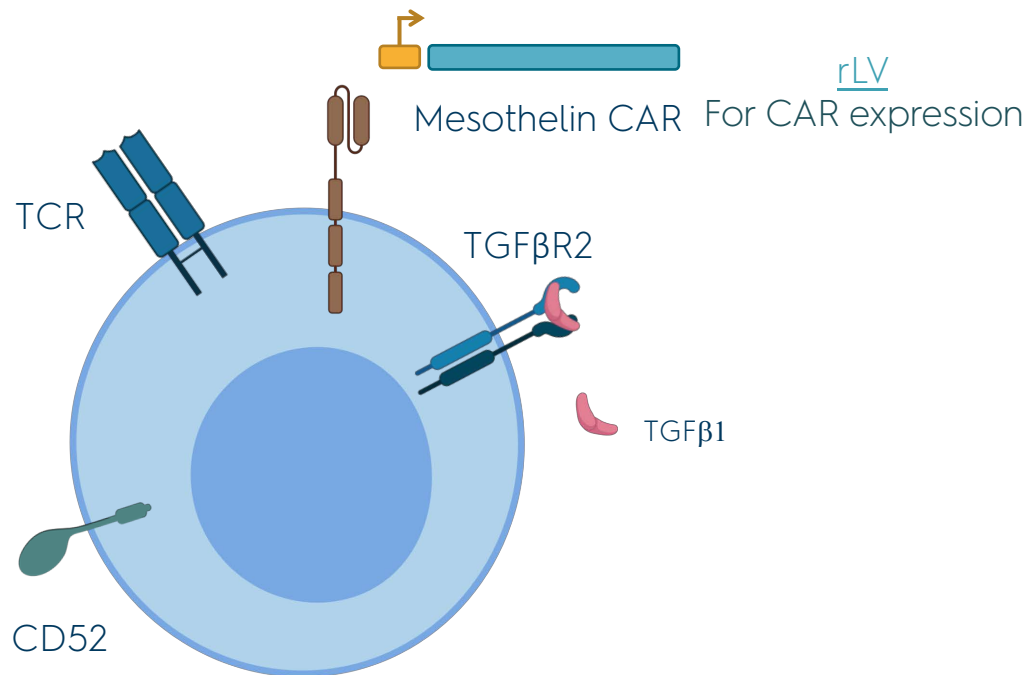


* UCARTMESO product candidate is under pre-clinical development

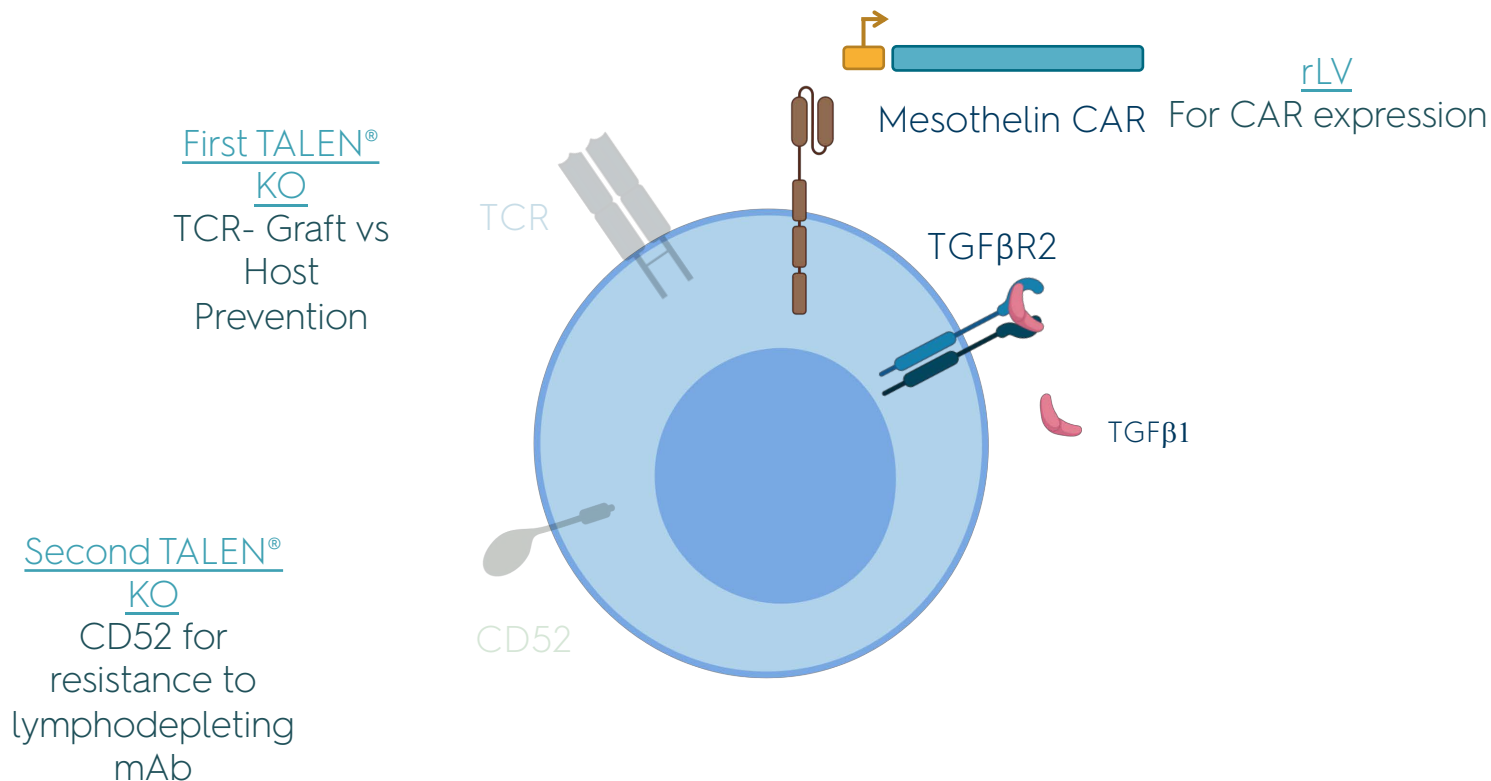
UCARTMESO – Allogeneic CAR T-cells Product Candidate in Solid Tumors



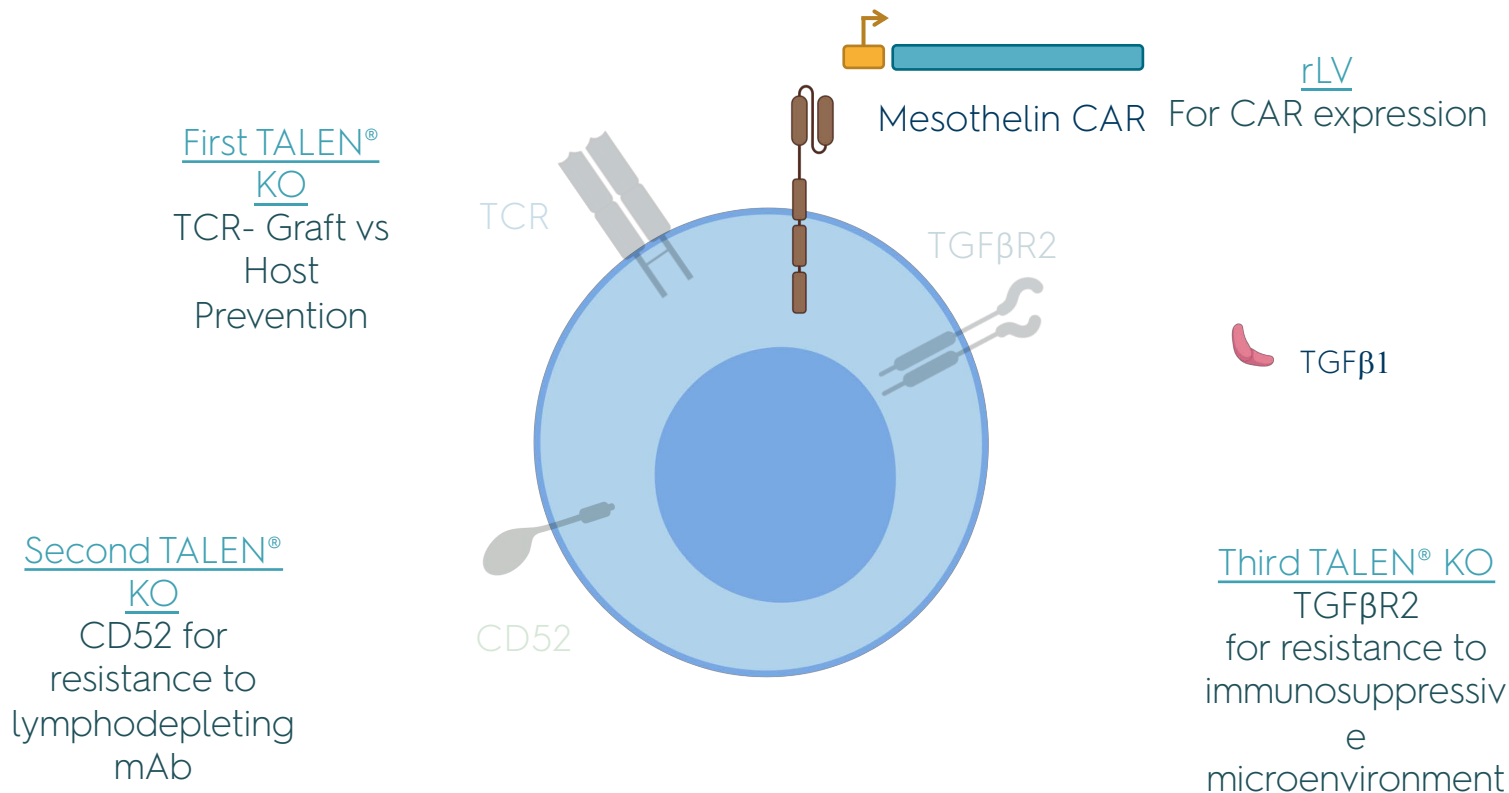
UCARTMESO – Allogeneic CAR T-cells Product Candidate in Solid Tumors



UCARTMESO – Allogeneic CAR T-cells Product Candidate in Solid Tumors



UCARTMESO – Allogeneic CAR T-cells Product Candidate in Solid Tumors



- TALEN[®] gene editing unlocks CAR T-cell activation in TGF β -enriched environment
- TGF β R2-edited MESO CAR T-cells show potent anti-tumor activity
- Targeting TGF β signaling could be beneficial for multiple solid tumors

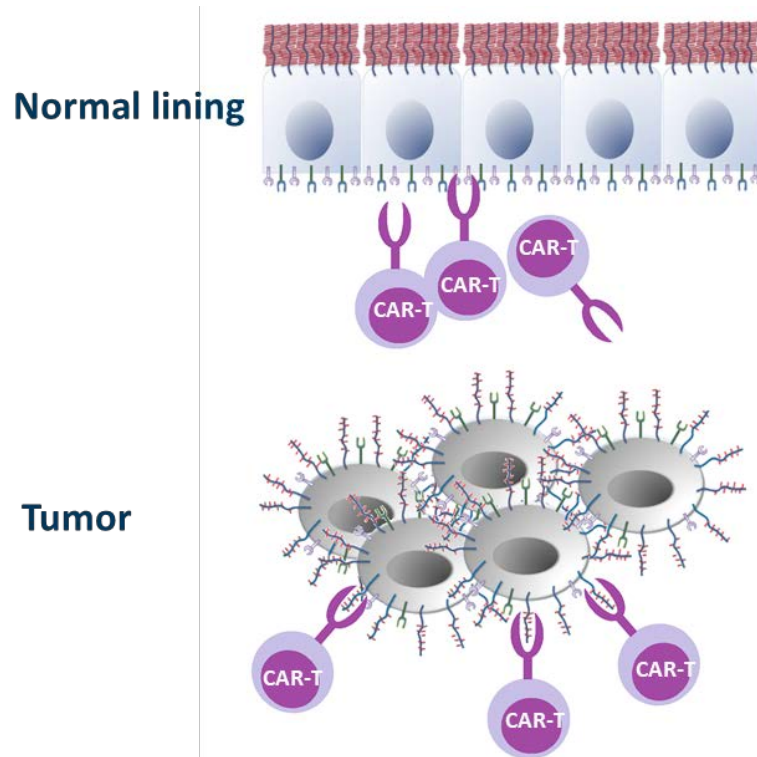
SOLID TUMOR PART II

SYNTHETIC BIOLOGY FOR TARGETING MUC1 IN TRIPLE NEGATIVE BREAST CANCER

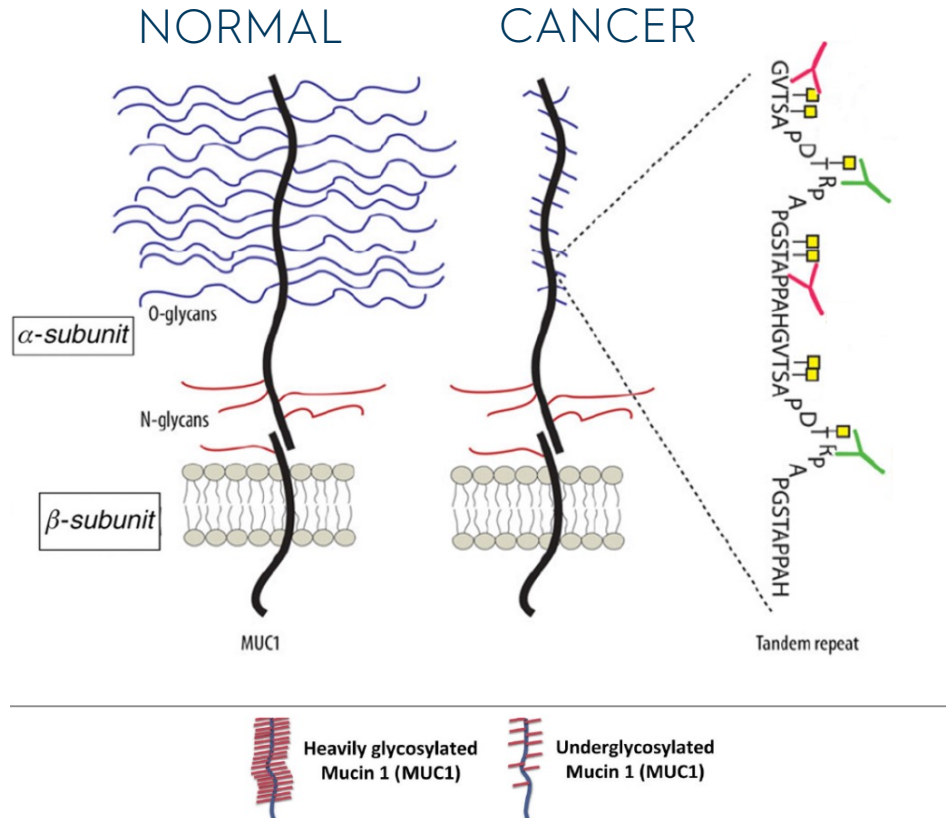


* UCARTMUC1 product candidate is under pre-clinical development

MUC1 on Healthy Epithelium is Exclusively on Apical Side

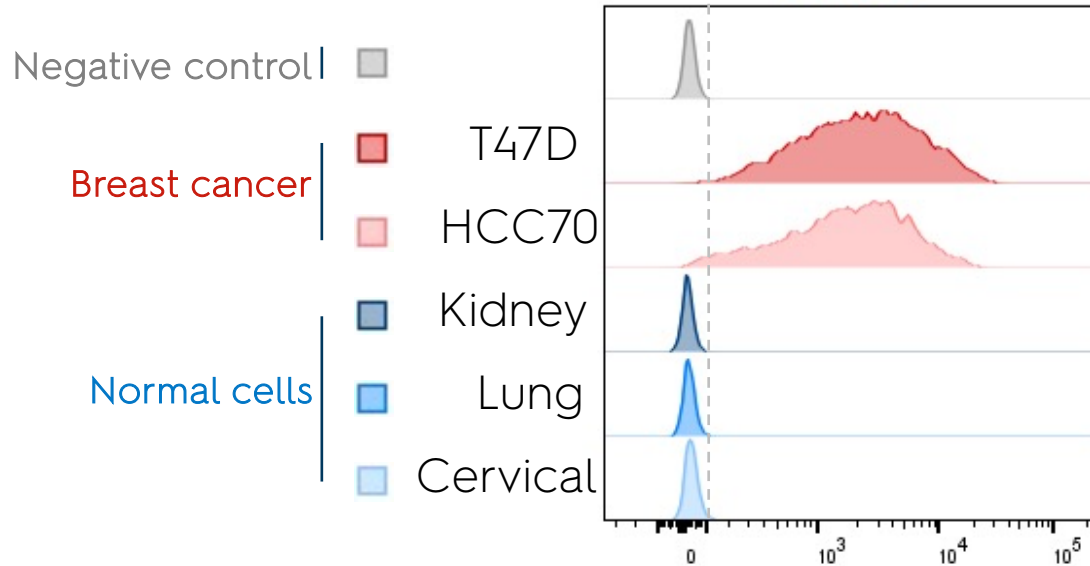


Cancer-Associated MUC1 is Under-Glycosylated

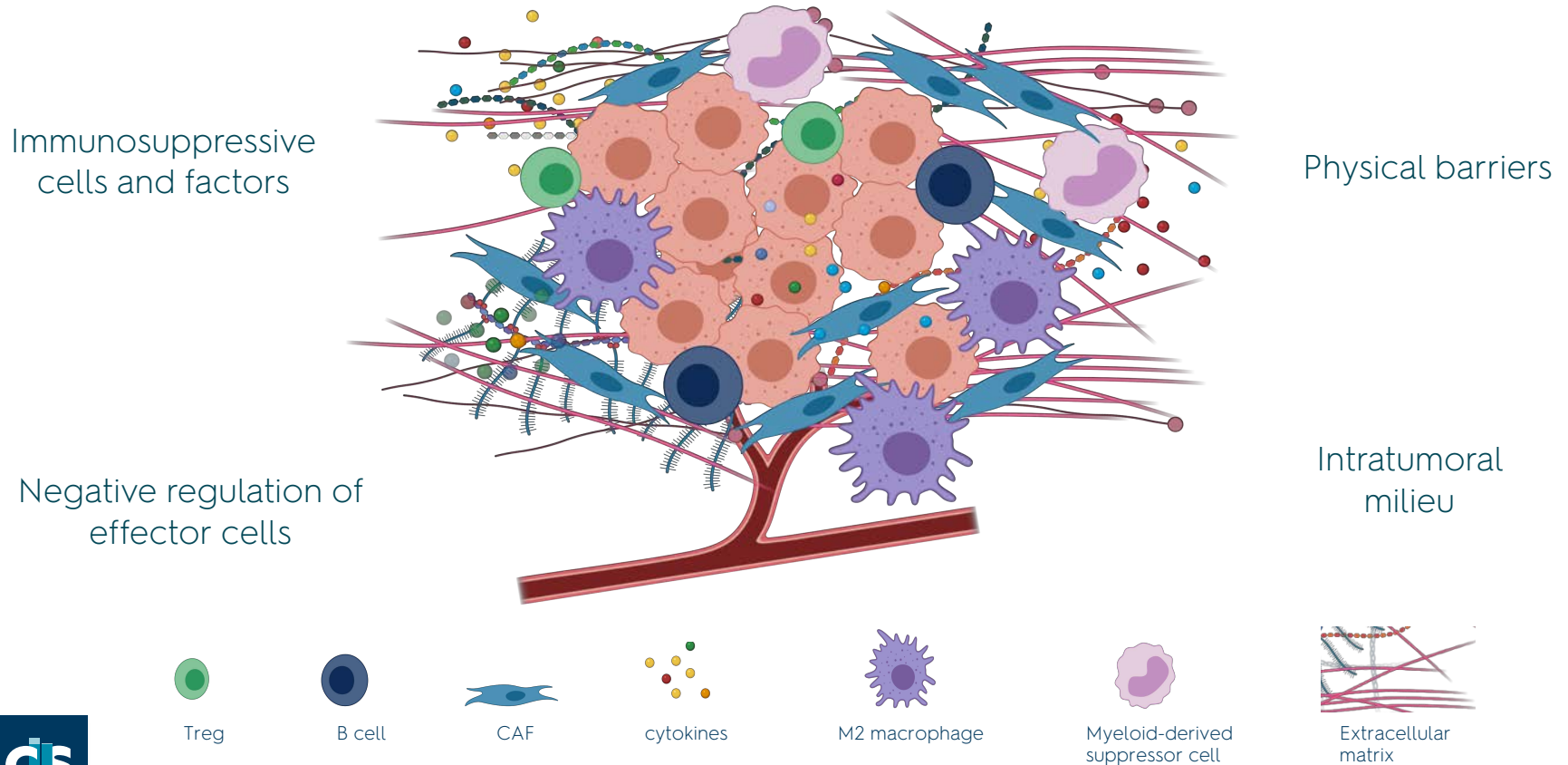


* UCARTMUC1 product candidate is under pre-clinical development

Our CAR Does not Recognize MUC1 on Healthy Tissues

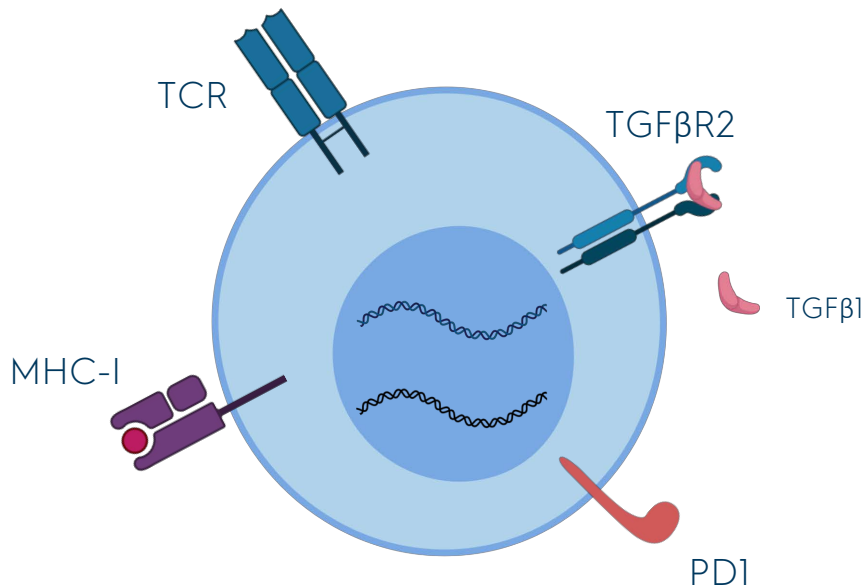


Outsmarting the Tumor With Gene Editing in CAR T-cells

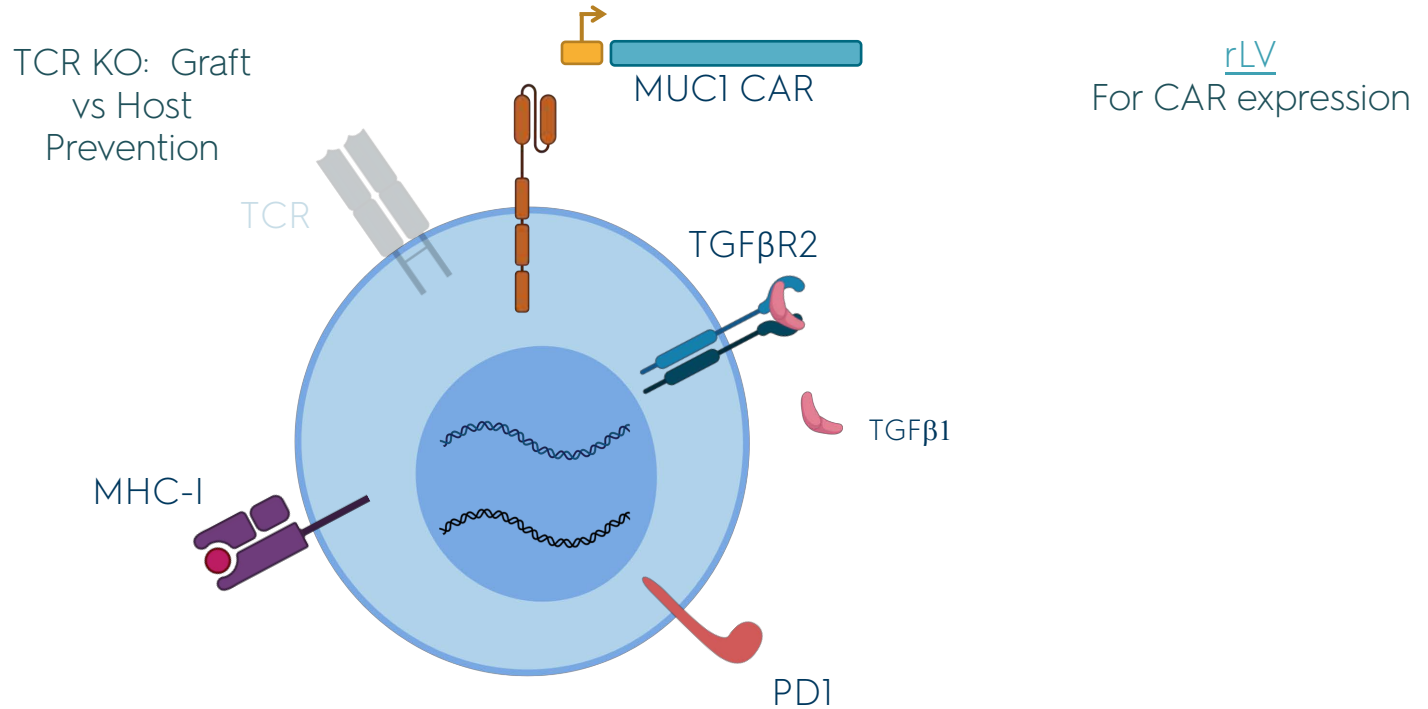


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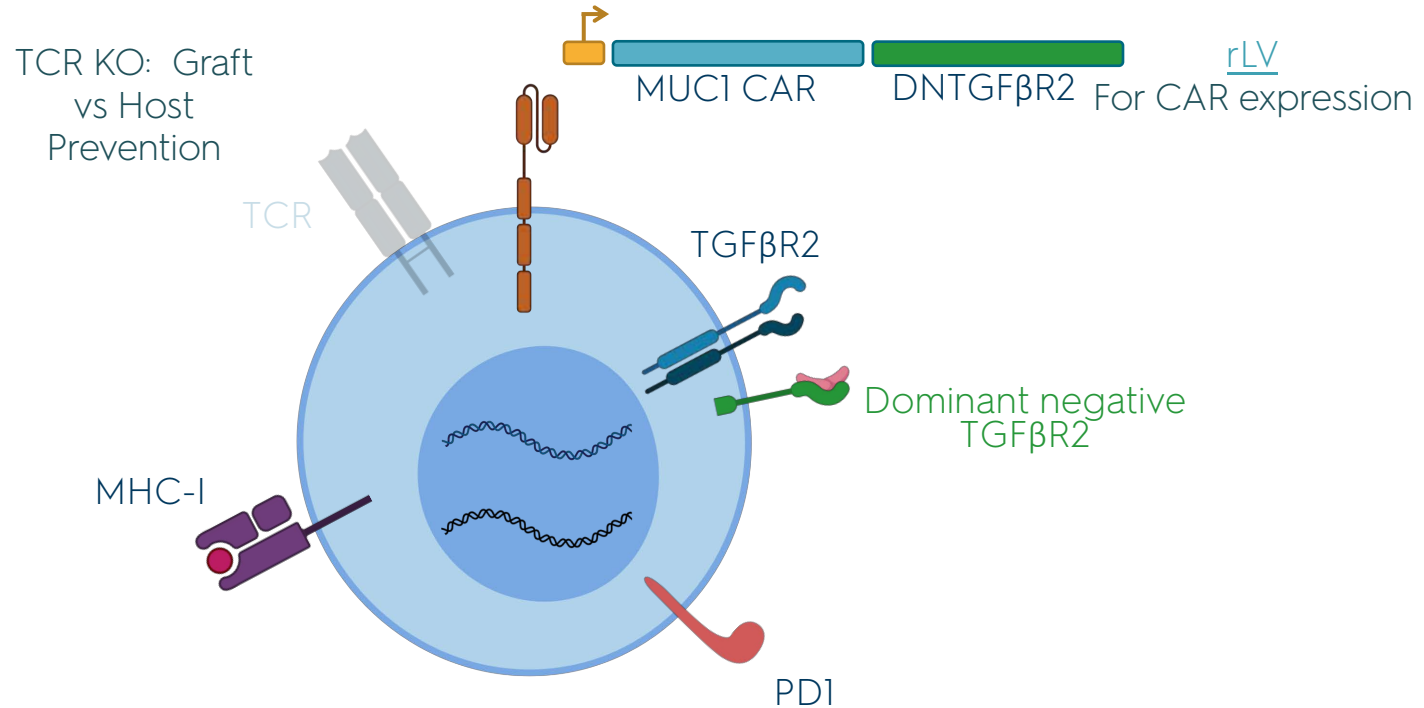
Next-gen CAR T-cells – UCARTMUC1 Product Candidate with Multiple Edits



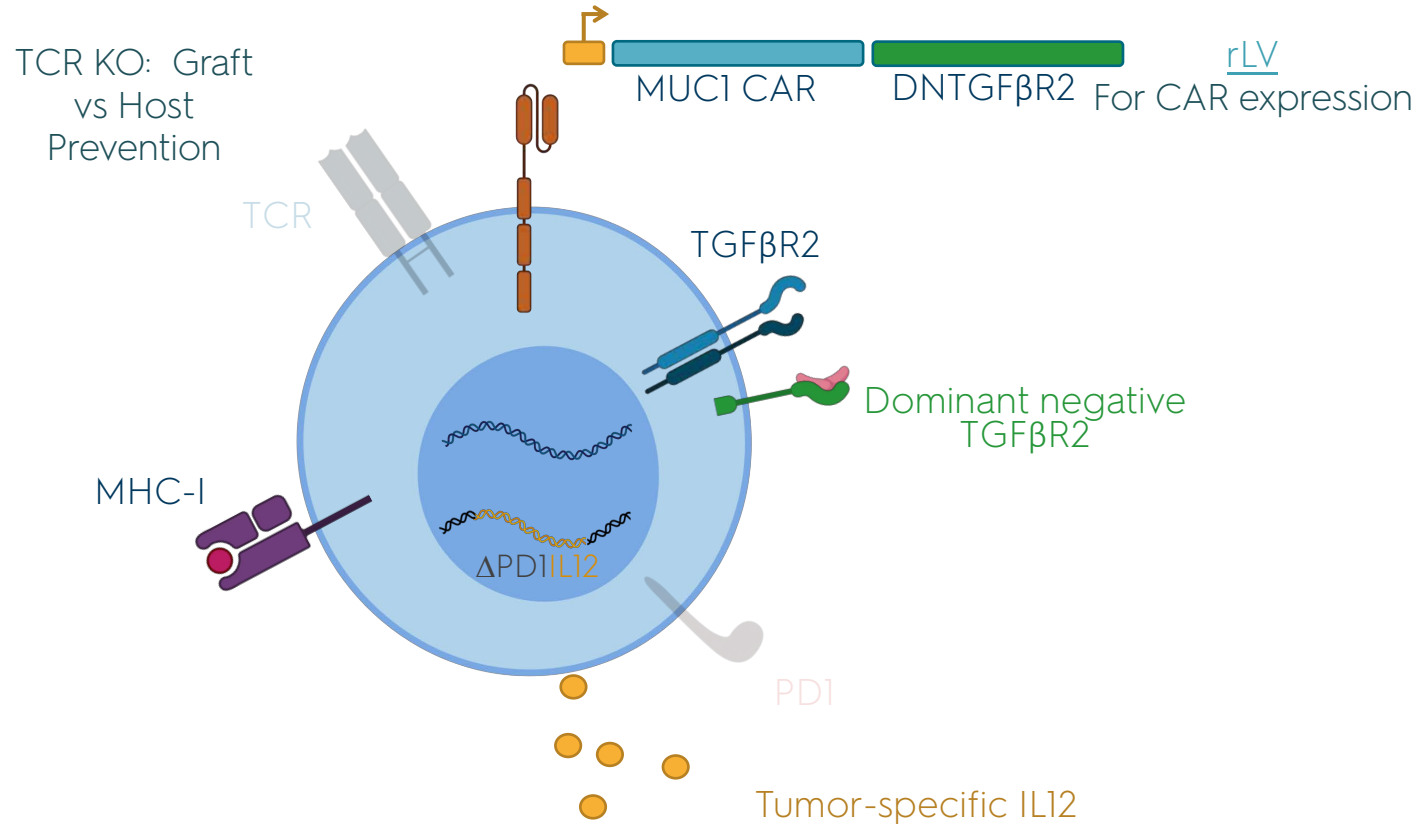
Next-gen CAR T-cells – UCARTMUC1 Product Candidate with Multiple Edits



Next-gen CAR T-cells – UCARTMUC1 Product Candidate with Multiple Edits

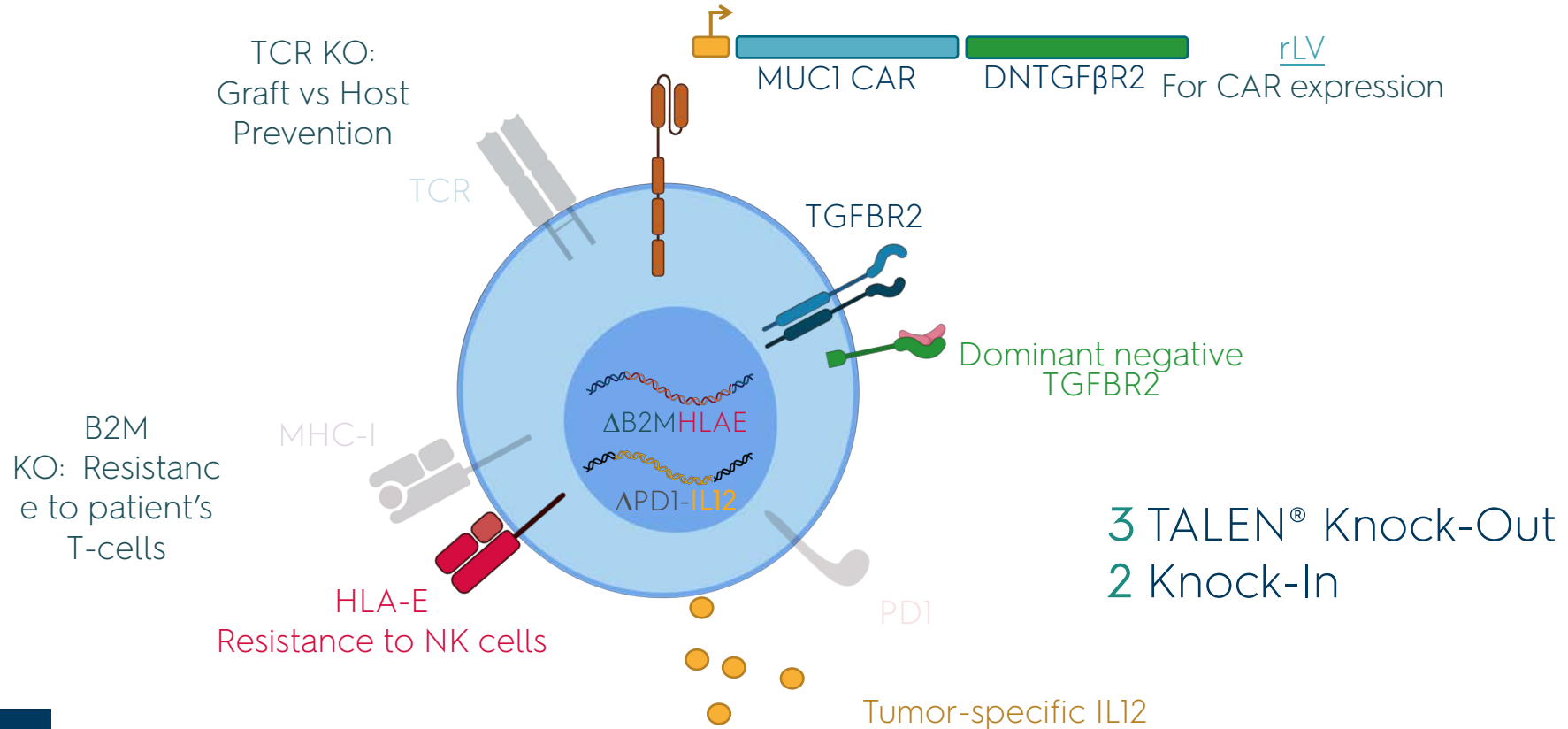


Next-gen CAR T-cells – UCARTMUC1 Product Candidate with Multiple Edits



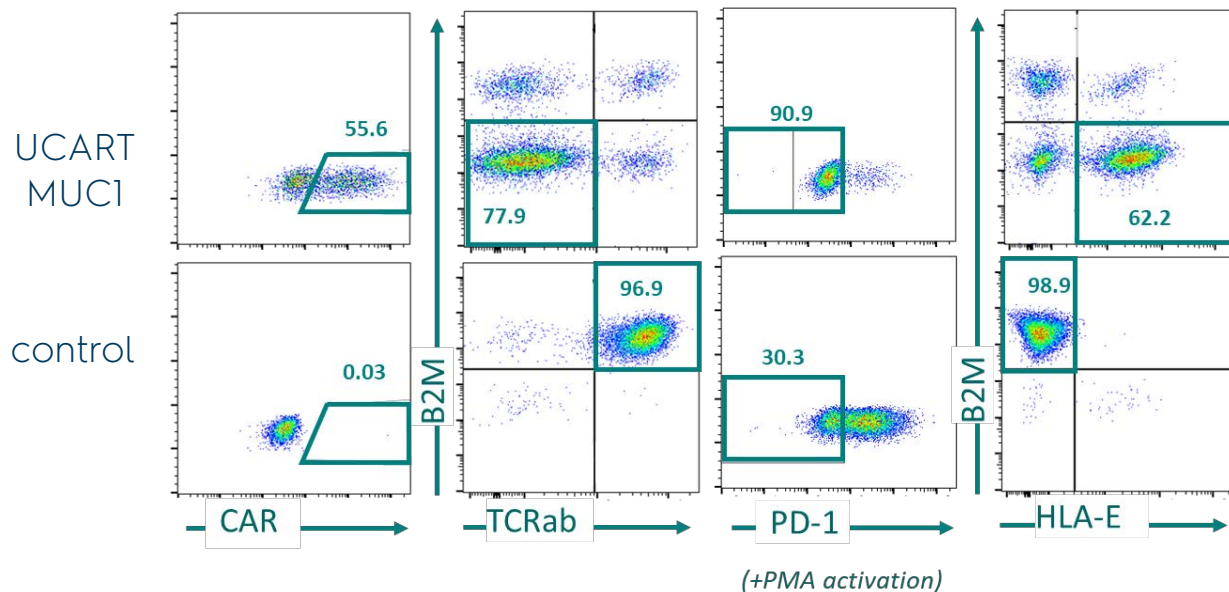
* UCARTMUC1 product candidate is under pre-clinical development

Next-gen CAR T-cells – UCARTMUC1Product Candidate with Multiple Edits



Synthetic Bio CAR T-cells First Engineering Results

Engineering efficiency in scalable process + rLV CAR-DNTGFβR2 transduction
+ Triple TALEN® transfection (TRAC/B2M/PD-1)
+ AAV-mediated KI of HLA-E

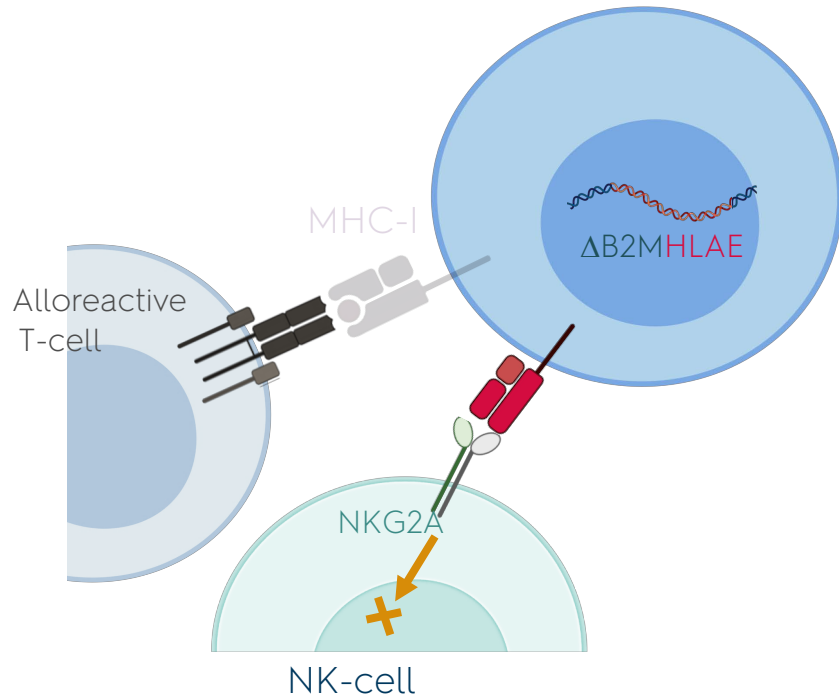


30% of cells are:

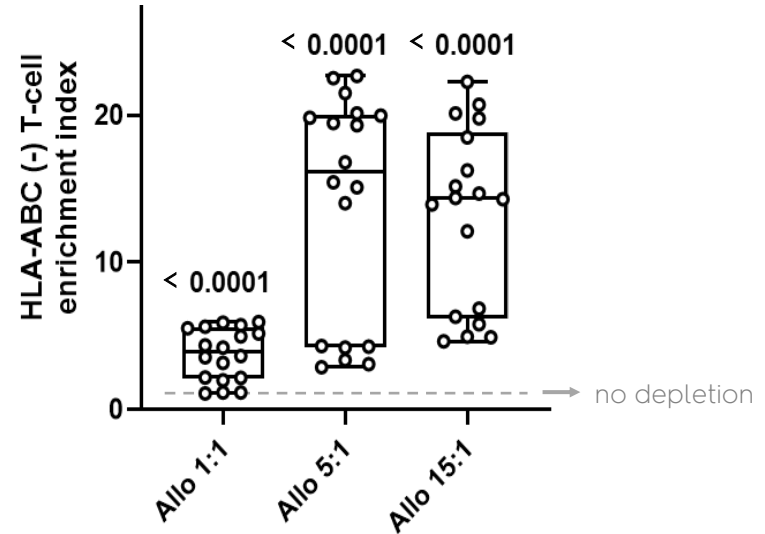
- CAR+
- Triple KO
- KI for HLA-E

* UCARTMUC1 product candidate is under pre-clinical development

Persistence: $\Delta B2M$ -HLA-E, a Stealth Scaffold



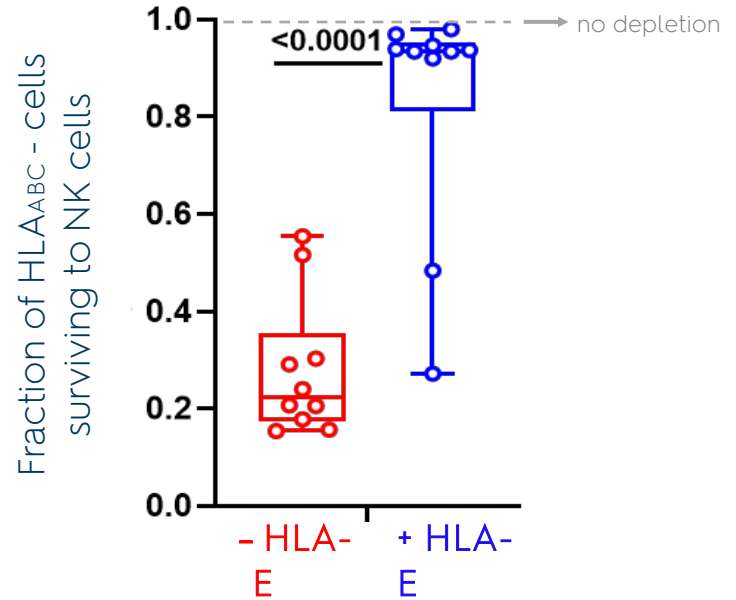
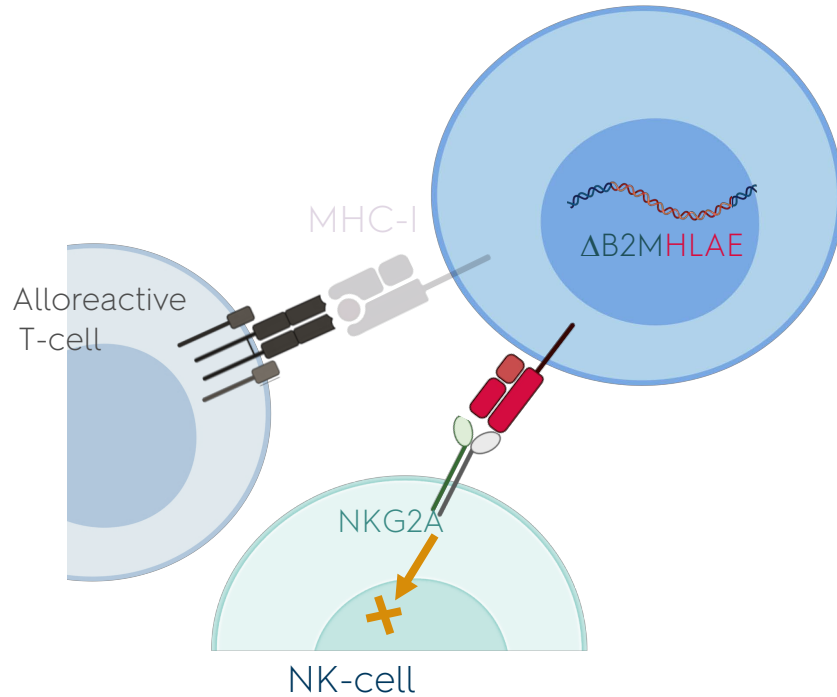
Enrichment of HLA_{ABC} - cells
over HLA_{ABC} + cells



B2M KO is designed to protect from alloreactive T-cells

* UCARTMUC1 product candidate is under pre-clinical development

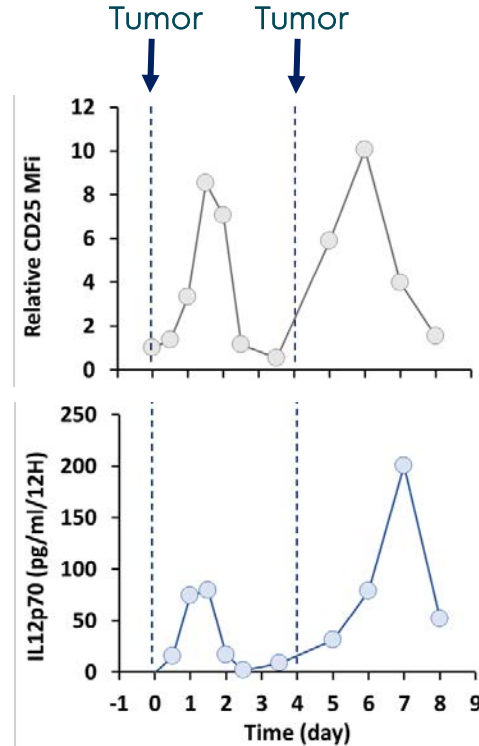
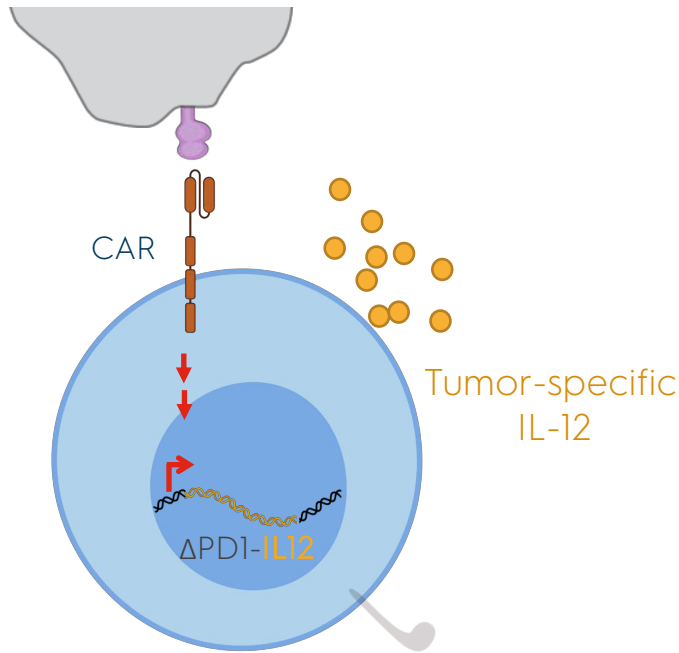
Persistence: Δ B2M-HLA-E, a Stealth Scaffold



HLA-E is designed to protect B2M KO cells from NK attack

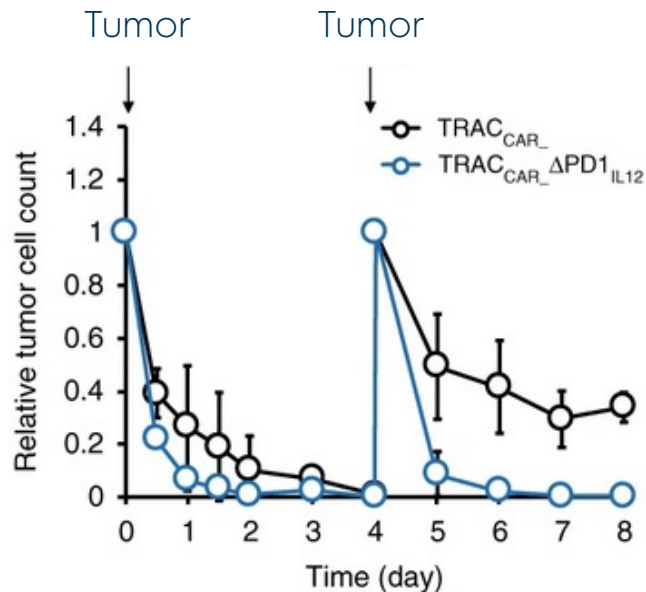
* UCARTMUC1 product candidate is under pre-clinical development

Potency: IL-12 Secretion Synchronized With Tumor Antigen Recognition

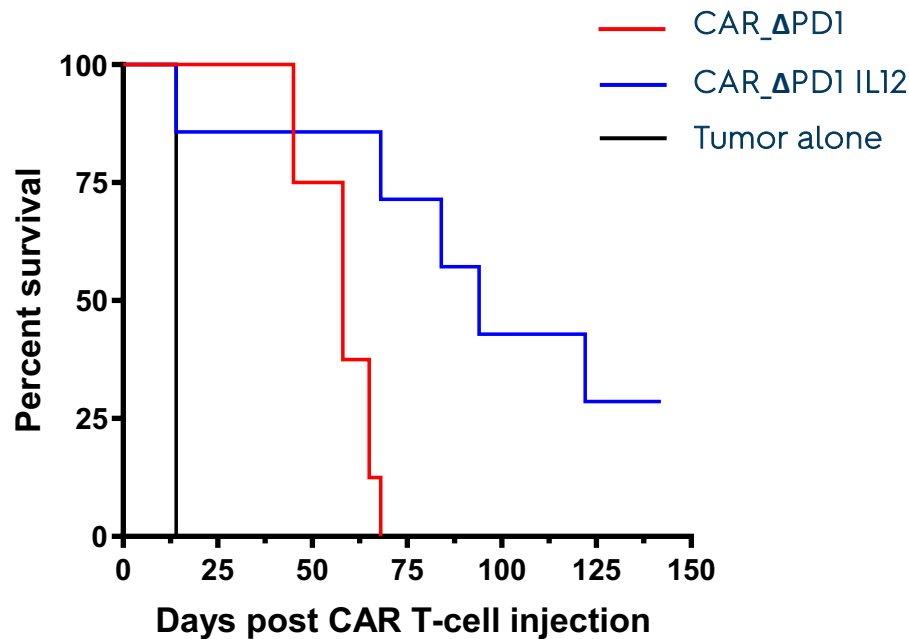


Sachdeva et al. Nature com, 2019

Smart CAR T-cells Enhance Antitumor Activity



In vitro assay



Disseminated model (*in vivo*)

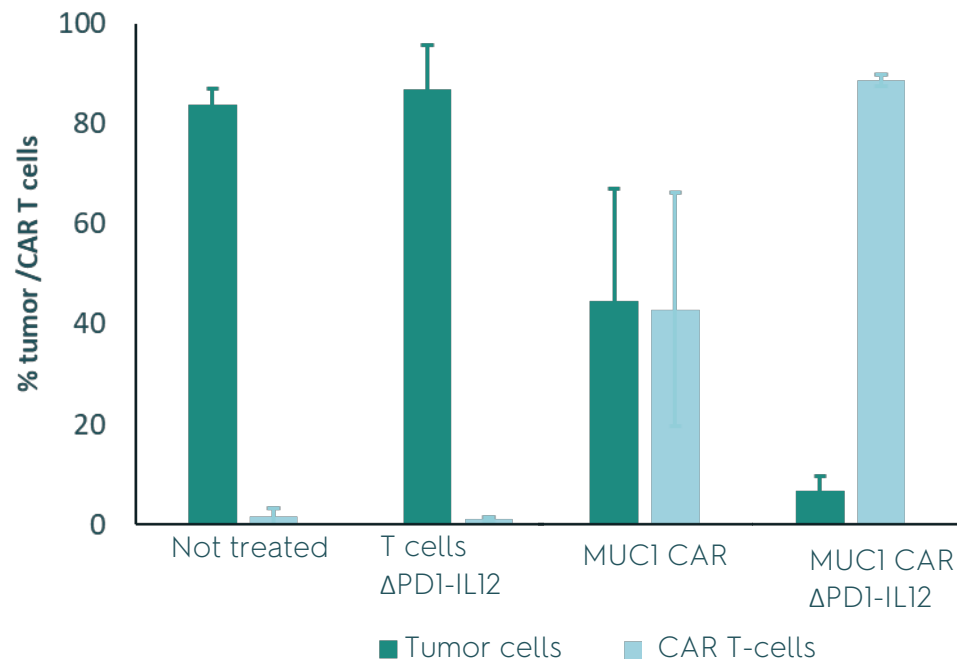
Sachdeva et al. Nature com, 2019

Inducible IL-12 secretion combined with PD1 Knock-Out enhances CAR-T response in a controlled manner

* UCARTMUC1 product candidate is under pre-clinical development

Strong *in vivo* Intratumoral UCARTMUC1 product Candidate Expansion Achieved With Δ PD1-IL12

Cancer cells vs. CAR T-cells within HCC70 tumors



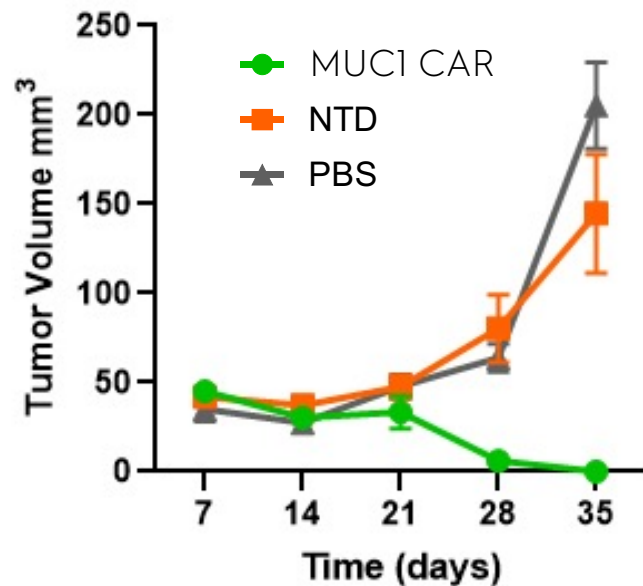
Inducible IL-12 is designed to allow for strong intratumoral expansion of UCARTMUC1 product candidate



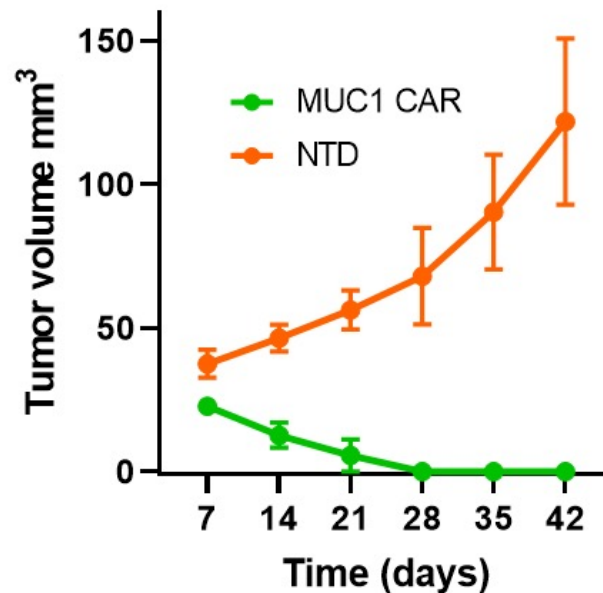
* UCARTMUC1 product candidate is under pre-clinical development

Strong *in vivo* Anti-Tumor Activity for UCARTMUC1 Product Candidate

Mammary fat pad tumor



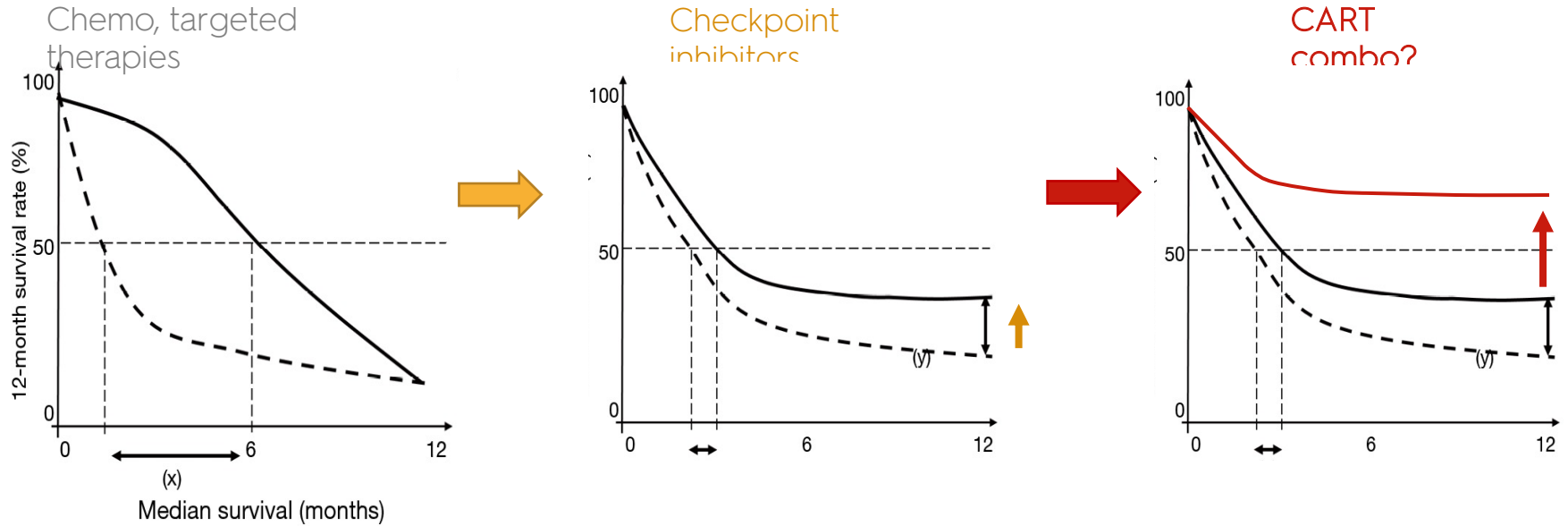
Subcutaneous tumor



- MUC1 is a promising target for Triple Negative Breast Cancer
- In diseases where targeting TGF β signalling is not enough, we develop strategies to increase potency
- TALEN[®] has the potential to allow highly efficient complex engineering:
 - Enhanced and controlled potency
 - Allogenic persistence

SOLID TUMOR PART III THE COMBO

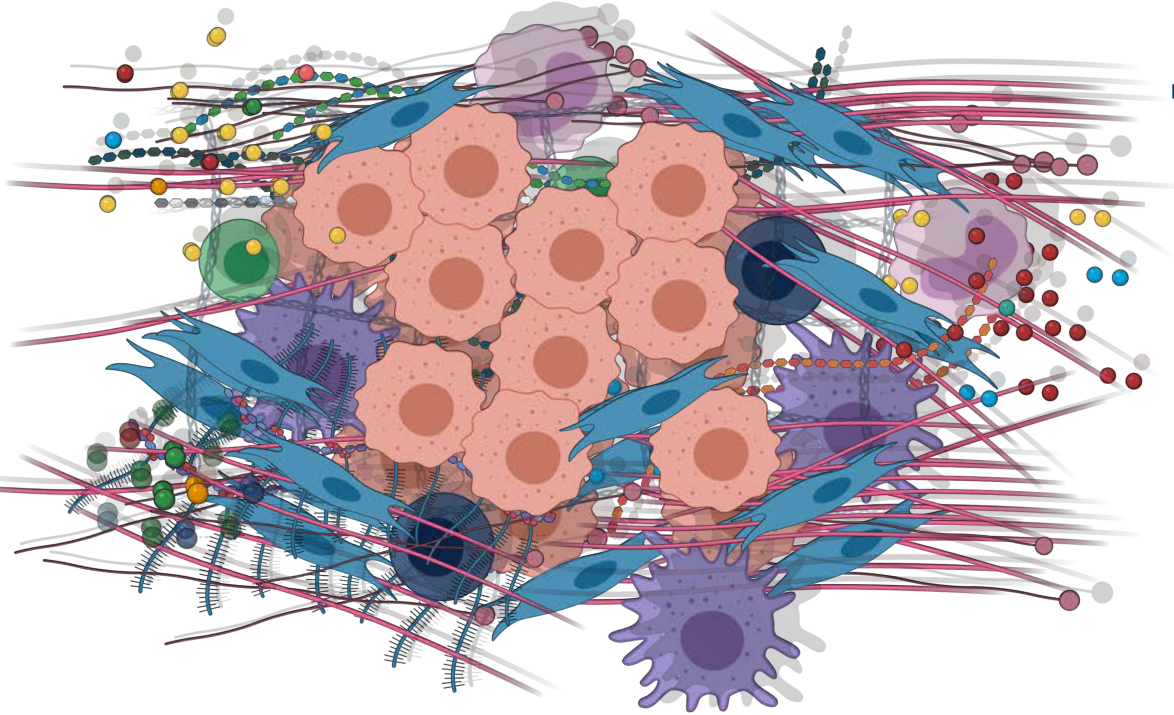
Using Allogeneic CAR T-cells to Continue the Immunotherapy Revolution



Checkpoint blockades hit a road-block

- Combining checkpoint blockers increases toxicity
- Poor response in cold tumors (low infiltration)

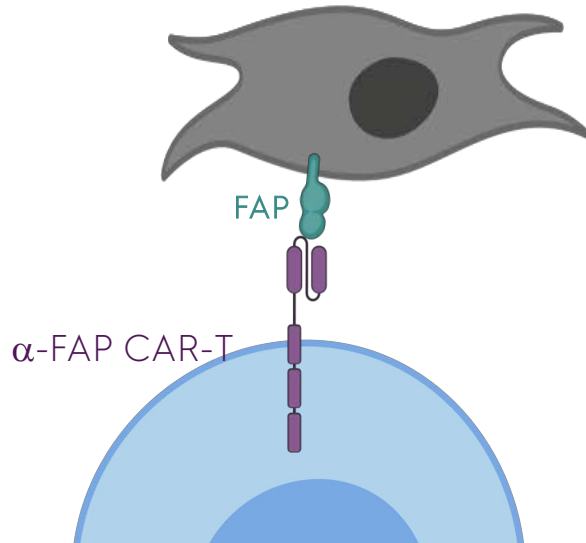
Overcoming 'Cold Tumor' Obstacle by Targeting CAFs



- ECM deposition forming physical barrier
- Cytokine secretion forming chemical barrier

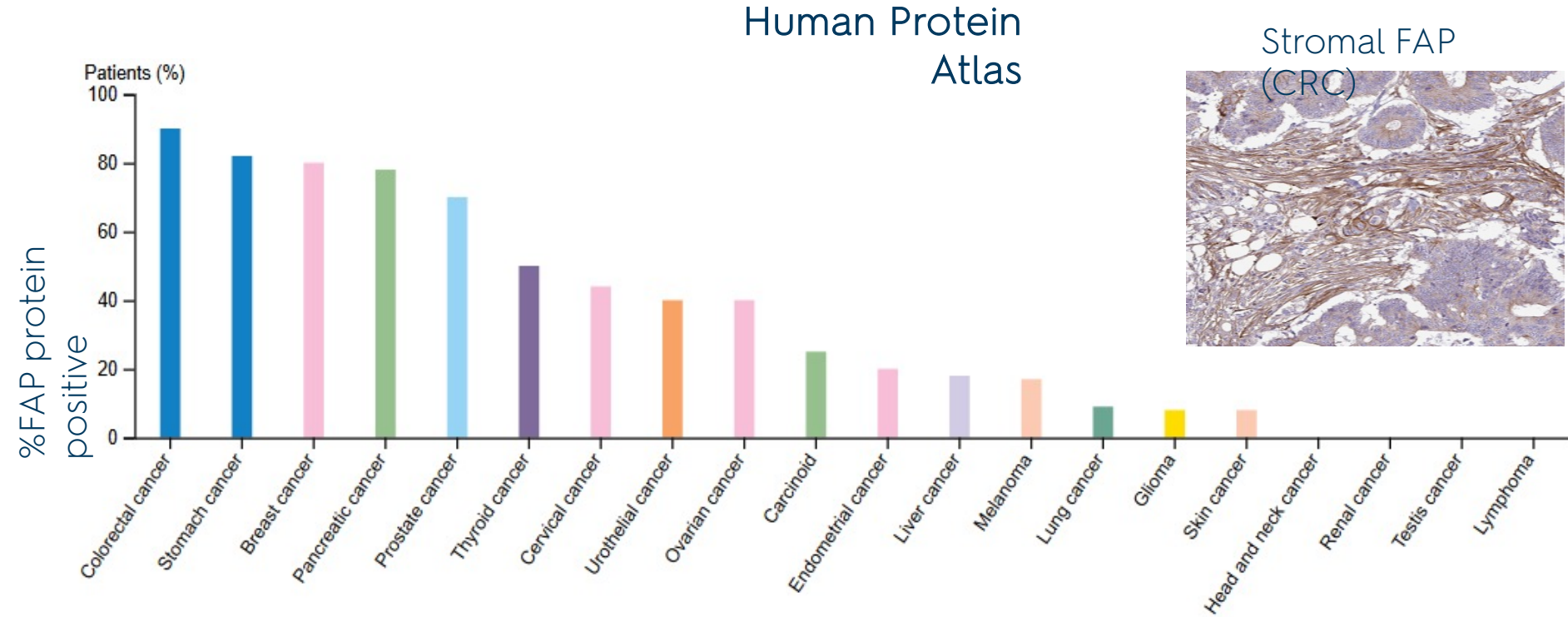
Targeting CAFs Using Anti-FAP CAR T-cells

Cancer-associated fibroblast



- Specific to Tumor Microenvironment
- Unique surface protein (FAP protein)
- High potential candidate for CAR T-cell therapy

Targeting CAFs Using Anti-FAP CAR T-cells



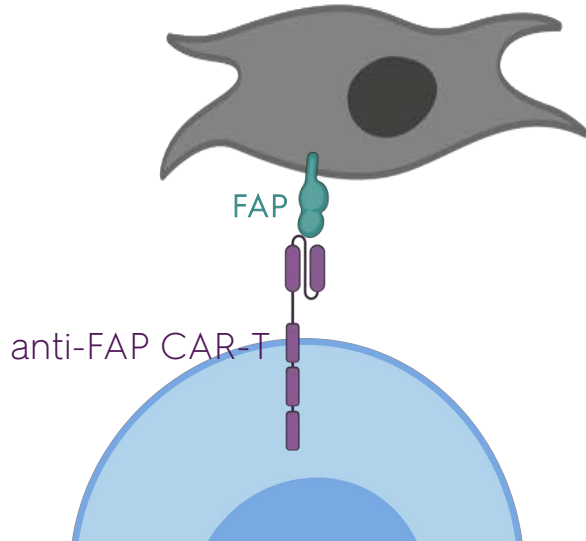
Wide array of applicable solid tumor indications



* UCARTFAP product candidate is under early stage of pre-clinical development

Anti-FAP CAR T-cells are Effective and Safe

Cancer-associated fibroblast



PRE-CLINICAL POC

anti-FAP CAR T-cells are an effective way of targeting CAFs and unlock CD8⁺ infiltration.

(Wang LS, Albeda SM et al., Canc Immunol Res, 2013)

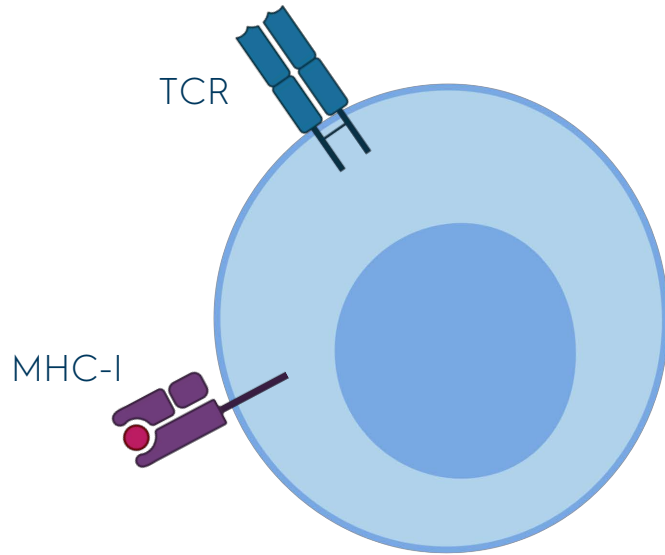
CLINICAL TRIAL (NCT01722149)*

No CAR T-cells toxicities (N=3 patients with malignant pleural mesothelioma (MPM))

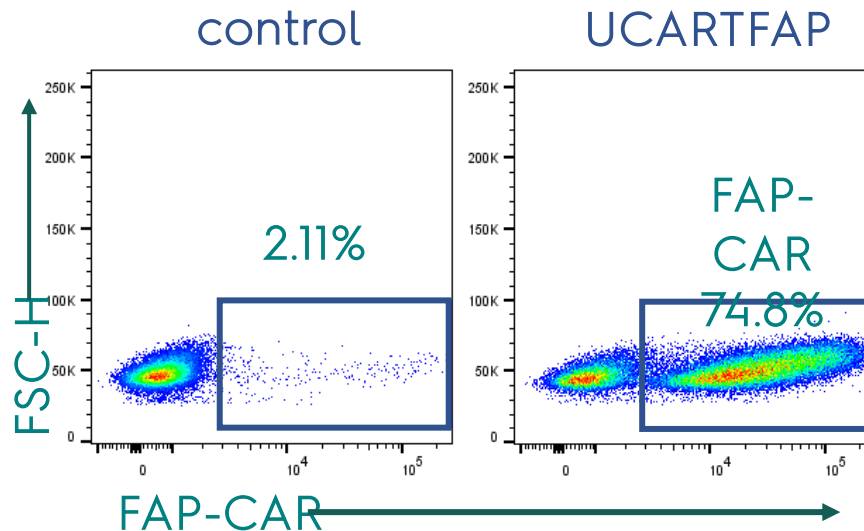
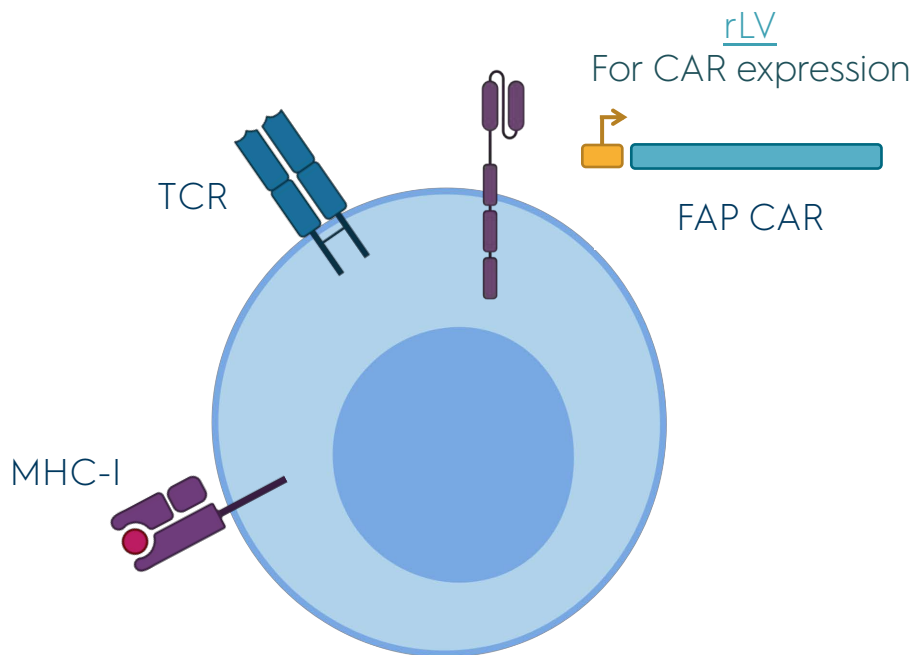
* Sponsored by University of Zurich

* UCARTFAP product candidate is under early stage of pre-clinical development

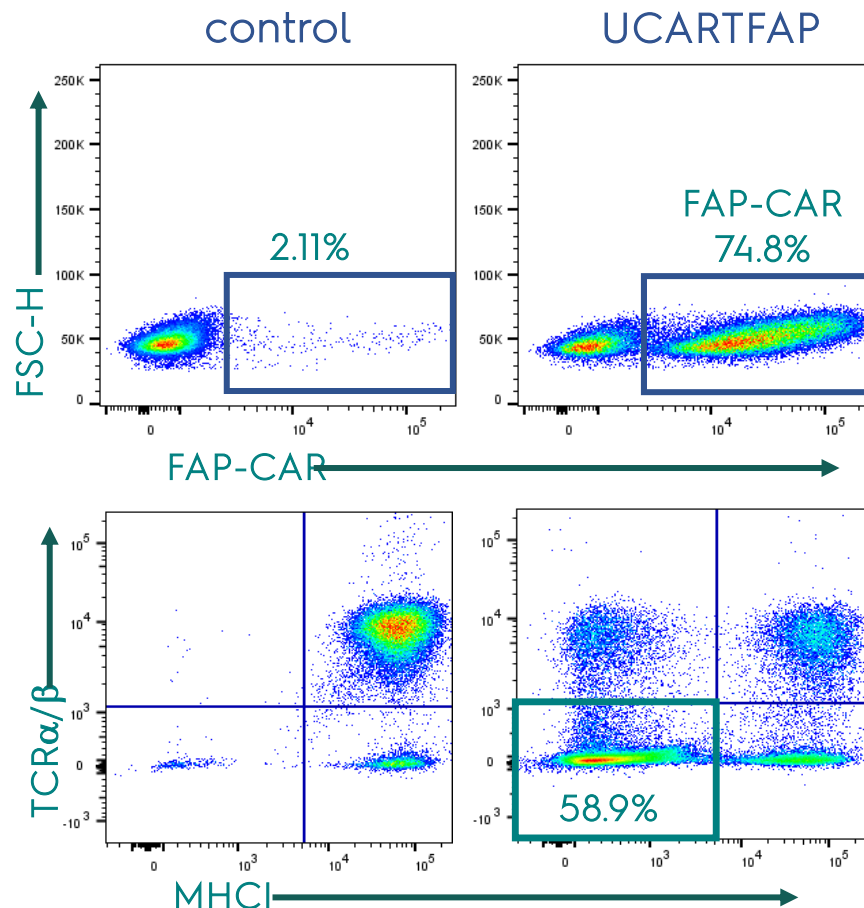
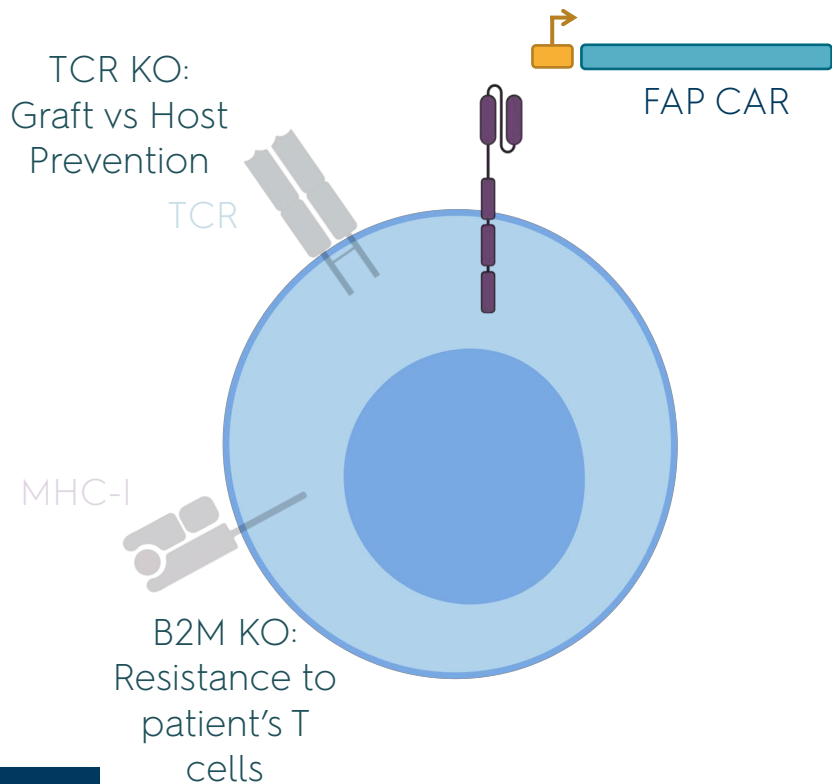
UCARTFAP: an Allogeneic CART Product Candidate for Combination Therapy of FAP⁺ Solid Tumors



UCARTFAP: an Allogeneic CART Product Candidate for the Treatment of FAP⁺ Solid Tumors

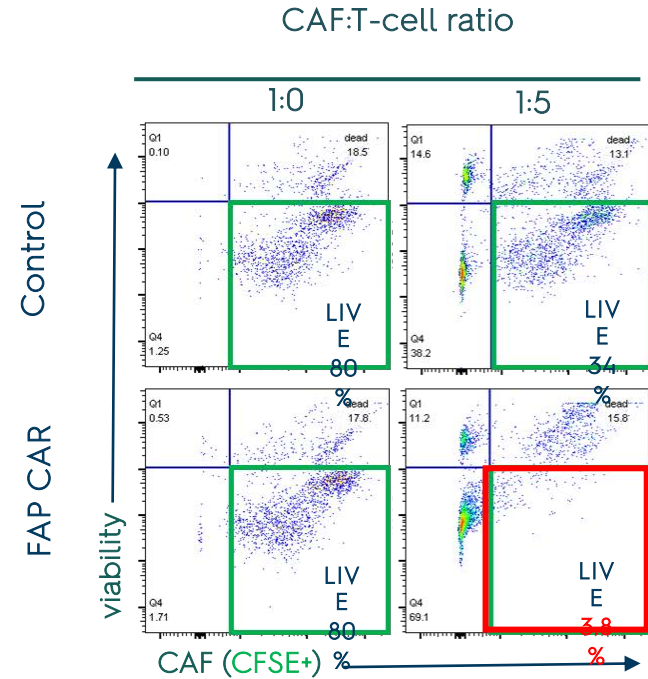
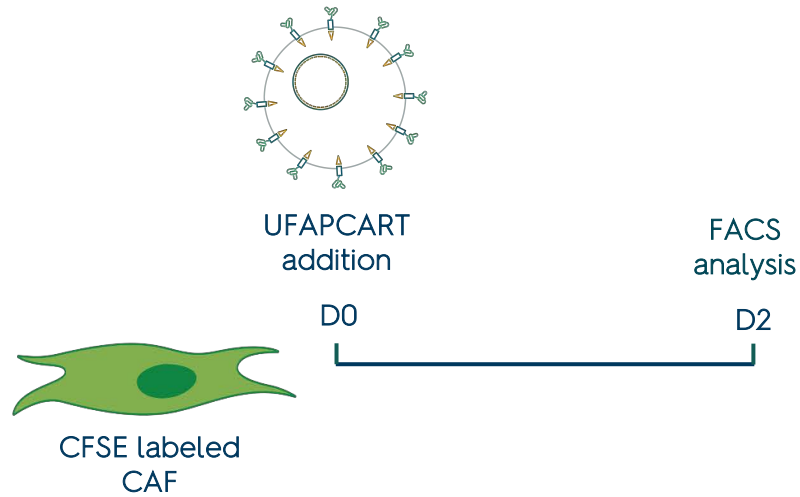


UCARTFAP: an Allogeneic CART Product Candidate for the Treatment of FAP⁺ Solid Tumors



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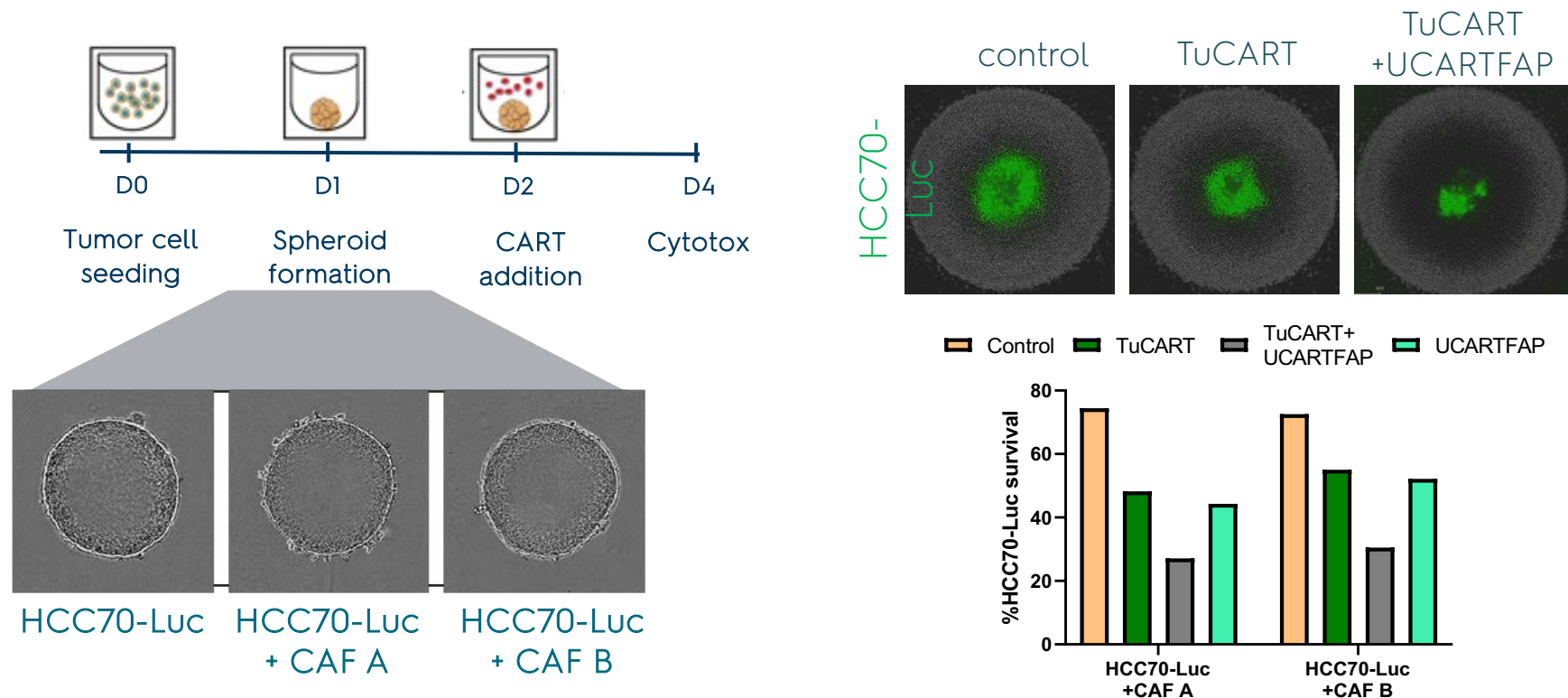
UCARTFAP Product Candidate Cytotoxicity Against CAF Cells



UCARTFAP product candidate has the potential to efficiently target patient cancer-associated fibroblasts

* UCARTFAP product candidate is under early stage of pre-clinical development

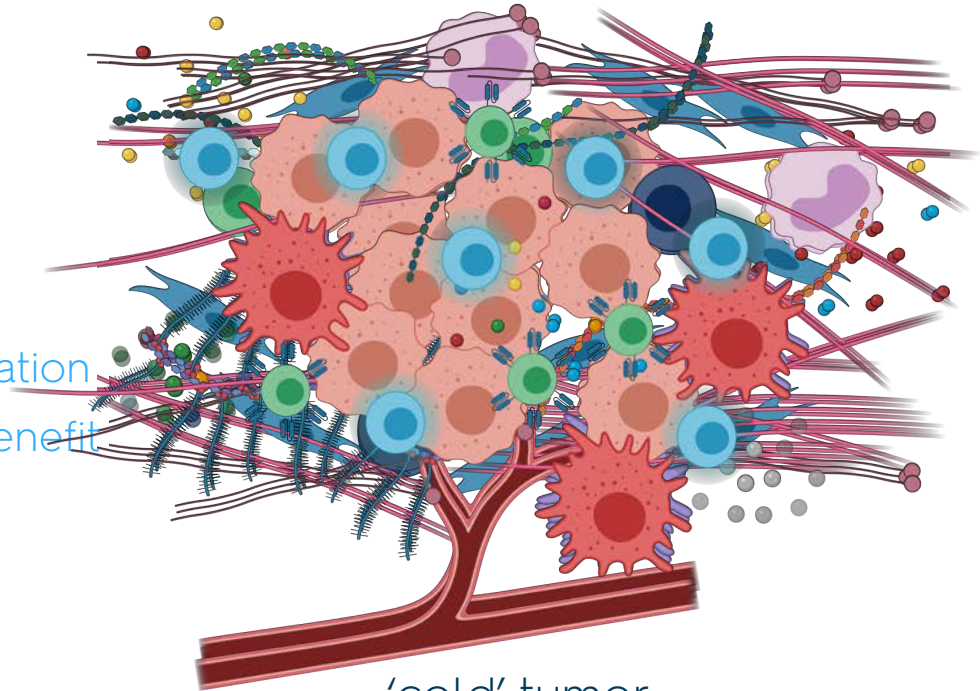
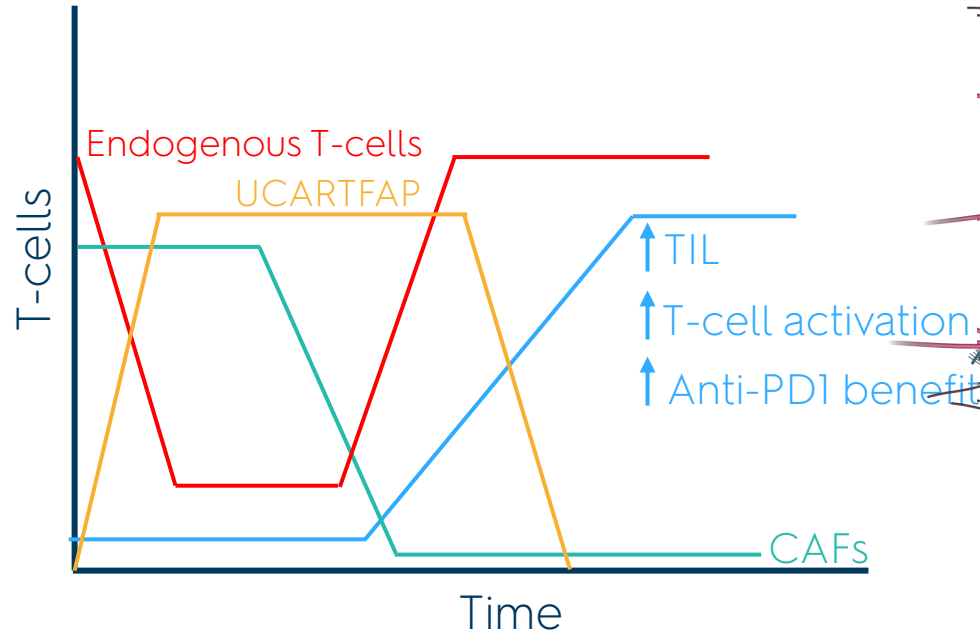
UCARTFAP Product Candidate Combination With Tumor-targeted CAR T-cells



UCARTFAP product candidate combination with TuCART has the potential to effectively kill breast tumor cells

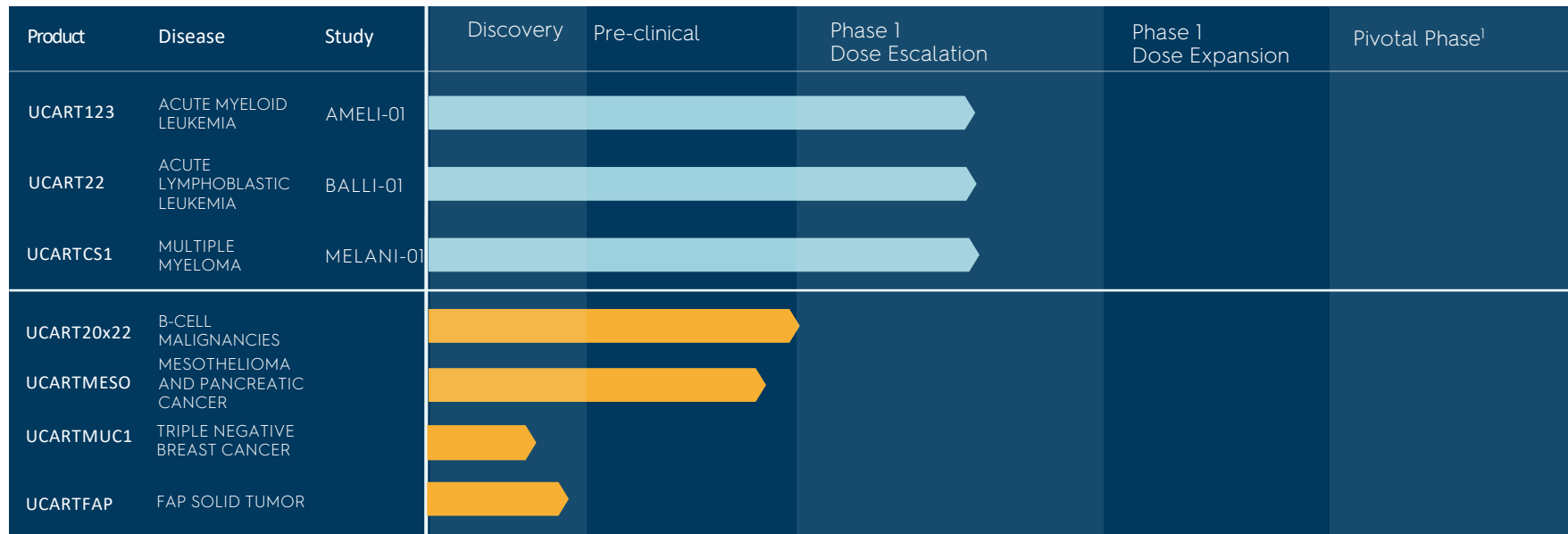
* UCARTFAP product candidate is under early stage of pre-clinical development

UCARTFAP Product Candidate : Combination Modality for T-cell Mediated Immunotherapies



'cold' tumor
'hot' (inflamed) tumor

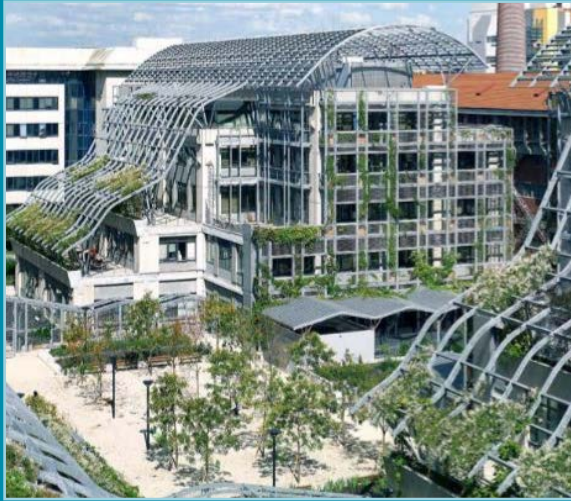
Pipeline Of Our Wholly-controlled Product Candidates



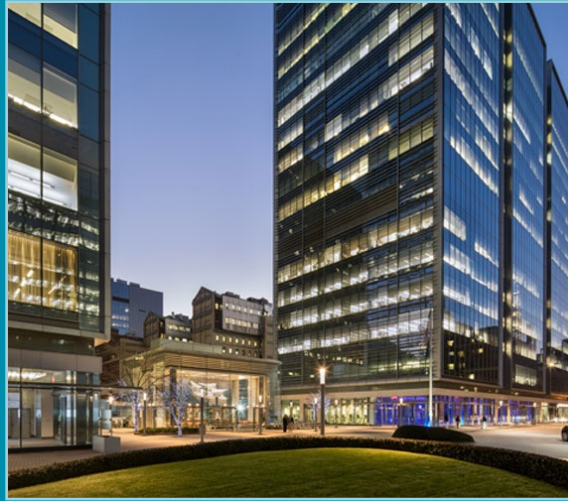
¹ We expect the pivotal phase to be the last clinical phase before commercialization

THANK YOU

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