GENE EDITED CAR-T THERAPIES

THE PARADIGM IN ONCOLOGY

Cellectis, May 2018

Forward-looking Statements

THIS PRESENTATION CONTAINS “FORWARD-LOOKING” STATEMENTS THAT ARE BASED ON OUR MANAGEMENT’S CURRENT EXPECTATIONS AND ASSUMPTIONS AND ON INFORMATION CURRENTLY AVAILABLE TO MANAGEMENT.

FORWARD-LOOKING STATEMENTS INVOLVE KNOWN AND UNKNOWN RISKS, UNCERTAINTIES AND OTHER FACTORS THAT MAY CAUSE OUR ACTUAL RESULTS, PERFORMANCE OR ACHIEVEMENTS TO BE MATERIALLY DIFFERENT FROM ANY FUTURE RESULTS, PERFORMANCE OR ACHIEVEMENTS EXPRESSED OR IMPLIED BY THE FORWARD-LOOKING STATEMENTS.

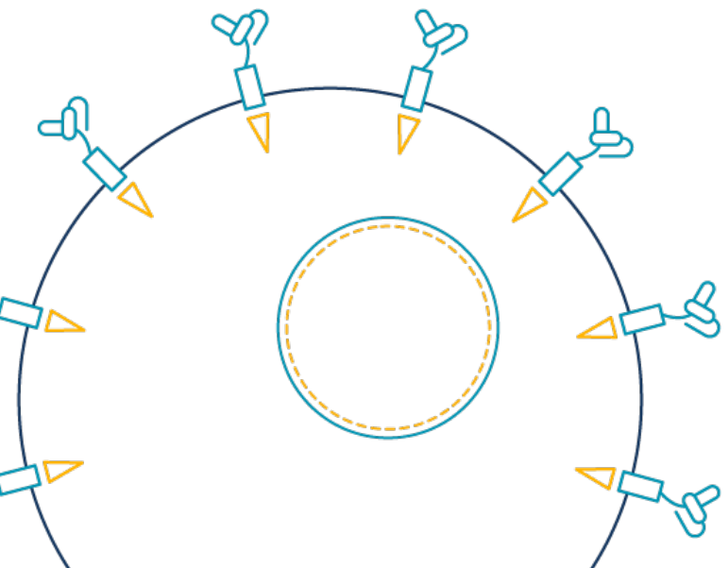
THE RISKS AND UNCERTAINTIES INCLUDE, BUT ARE NOT LIMITED TO THE RISK THAT THE PRELIMINARY RESULTS FROM OUR PRODUCT CANDIDATES WILL NOT CONTINUE OR BE REPEATED, THE RISK THAT OUR CLINICAL TRIALS WILL NOT BE SUCCESSFUL. THE RISK OF NOT OBTAINING REGULATORY APPROVAL TO COMMENCE CLINICAL TRIALS ON ADDITIONAL UCART PRODUCT CANDIDATES, THE RISK THAT ANY ONE OR MORE OF OUR PRODUCT CANDIDATES WILL NOT BE SUCCESSFULLY DEVELOPED AND COMMERCIALIZED. FURTHER INFORMATION ON THE RISK FACTORS THAT MAY AFFECT COMPANY BUSINESS AND FINANCIAL PERFORMANCE, IS INCLUDED OUR ANNUAL REPORT ON FORM 20-F AND OTHER FILINGS CELLECTIS MAKES WITH THE SECURITIES AND EXCHANGE COMMISSION FROM TIME TO TIME AND ITS FINANCIAL REPORTS.

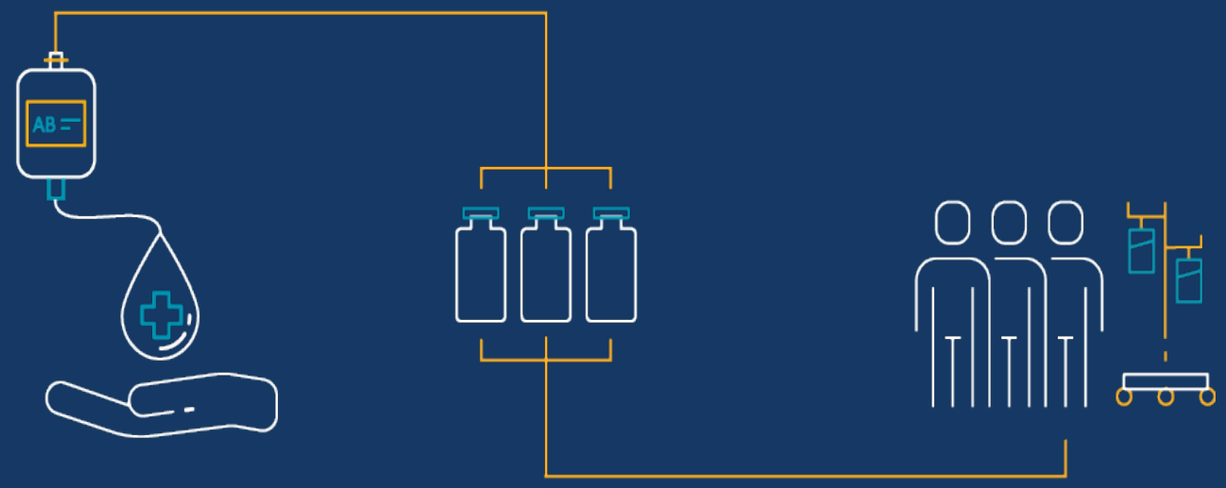
EXCEPT AS REQUIRED BY LAW, WE ASSUME NO OBLIGATION TO UPDATE THESE FORWARD-LOOKING STATEMENTS PUBLICLY, OR TO UPDATE THE REASONS ACTUAL RESULTS COULD DIFFER MATERIALLY FROM THOSE ANTICIPATED IN THE FORWARD-LOOKING STATEMENTS, EVEN IF NEW INFORMATION BECOMES AVAILABLE IN THE FUTURE.

1. Proof Of Concept For Off-the-shelf CAR T Shows Clear Viability

The “Off-The-Shelf” CAR-T Concept

- **ASH 2017: CAR-T in the spotlight**
  - CAR-Ts are here to stay
  - First FDA approved autologous CAR-Ts on the market
  - Allogeneic CAR-T concept validated
  - First market challenges for autologous CAR-Ts





- **Allogeneic CAR-Ts: major uncertainties lifted**
  - ✓ **Industrialized manufacturing process**
  - ✓ High-precision TALEN® gene editing used in clinical trial in US and EU
  - ✓ **No significant GvHD**
  - ✓ Allogeneic CAR-T **engraft and expand**
  - ✓ **Efficacy** on par with autologous CAR-T

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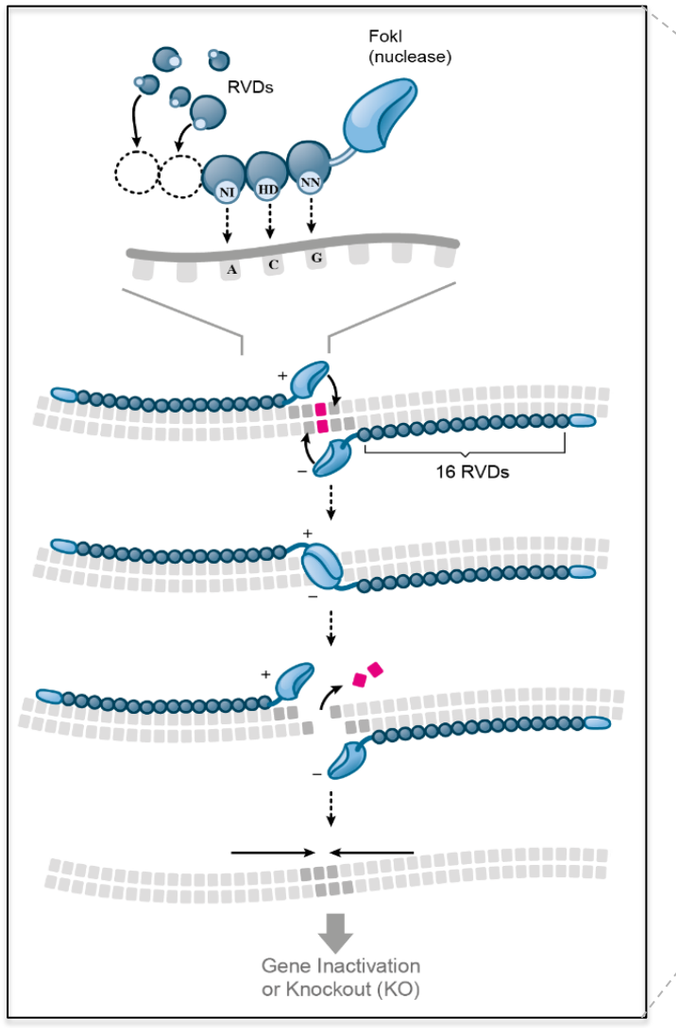
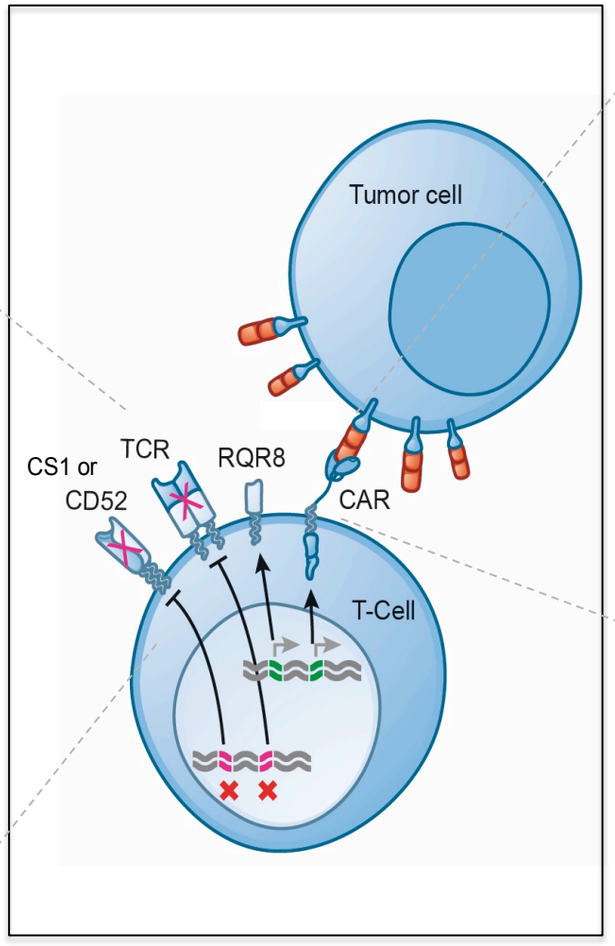
How it works

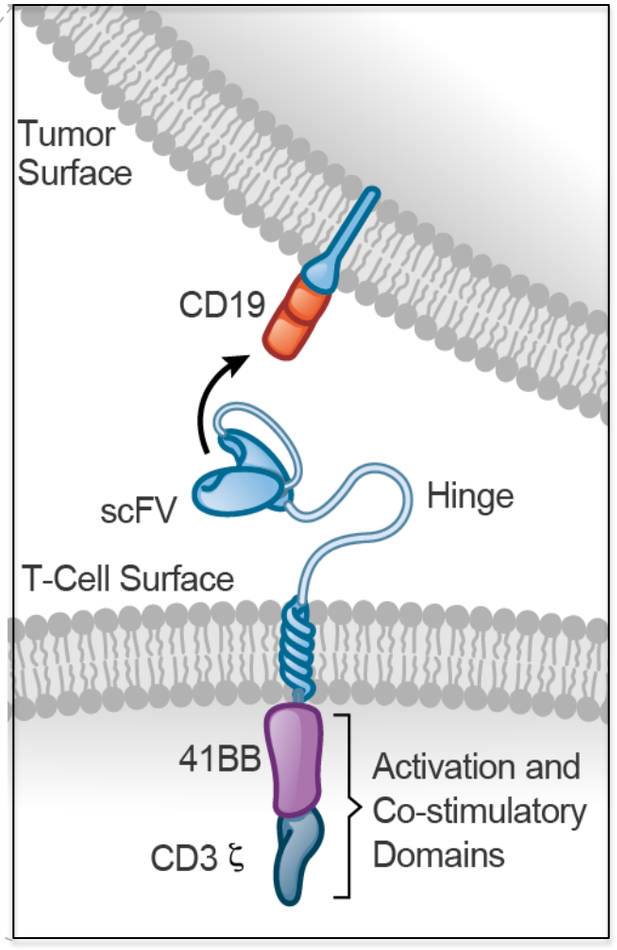
Allogeneic CAR T Cells Through Gene Editing



Gene Editing
TALEN® Nuclease



Allogeneic
CAR T Cell



Chimeric Antigen Receptor
Tumor Recognition

The Benefits Of UCARTs

UCARTs = Cellectis' "Off-The-Shelf" or Allogeneic CAR T Cells

Market access

- Ability to manufacture large amounts of product in advance
- Easily available in large number of hospitals

Cost of treatment

- Possibility to lower the price range of CART therapies to other IO standard
- No additional cost linked to "segment of one" supply chain

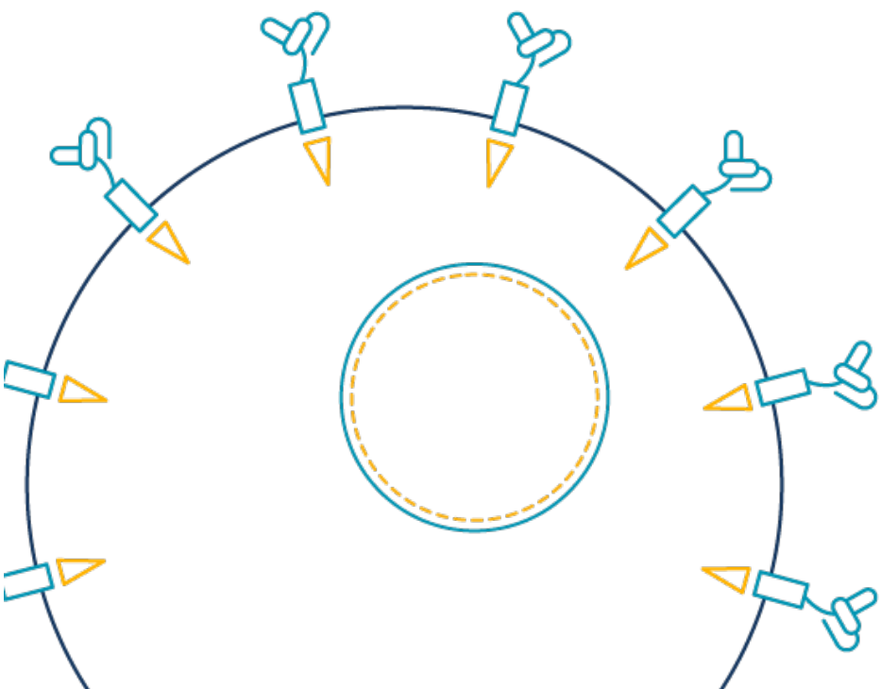
Ability to re-dose

- Possibility to re-dose with same antigen
- Combine different antigen targeting CARTs
- No issue of long term persistence and related side effects

Leading Alliance with Allogene

Bringing Allogeneic CAR T Immunotherapies to Patients

A Biotechnology Company led by Former Kite Executives



- Pioneers of autologous and allogeneic fields joining forces to **accelerate**
- Allogene was formed with one of the **largest Series A financings in biotechnology** of $300m
  - Co-founded and led by former executives of Kite Pharma
  - Investor consortium includes TPG, Vida Ventures, BellCo Capital, the University of California Office of the Chief Investment Officer and Pfizer
- Collaboration on 15 targets, including the 1st allogeneic **BCMA & EGFRvIII** CART programs
- Up to **$2.8bn** in total aggregated milestones and tiered royalties
- Pfizer will hold a 25% ownership stake in Allogene and would continue to have an 8% ownership stake in Cellectis

2. Cellectis Is The Leading Allogeneic CAR T Company

Rich Allogeneic CAR-T Pipeline

Addressing Unmet Medical Need With Proven Targets

Program	Indication	Product development	Preclinical	Manu-facturing	Filing[1]	Phase I	Ph II	Ph III
UCART19[2] (Servier / Allogene)	ALL (PALL)							
	ALL (CALM)							
UCART123	AML R/R							
	AML high risk 1st line							
	BPDCN							
	Pediatric leukemia							
	Hodgkin's disease							
UCART22	B-ALL							
	B-NHL							
UCARTCS1	MULTIPLE MYELOMA							

- **Already 2 UCART programs in clinic: UCART19 & UCART123**
- **IND filed for UCART22**
- **Manufacturing of UCARTCS1 ongoing**
- **Rich pipeline, with proven targets**

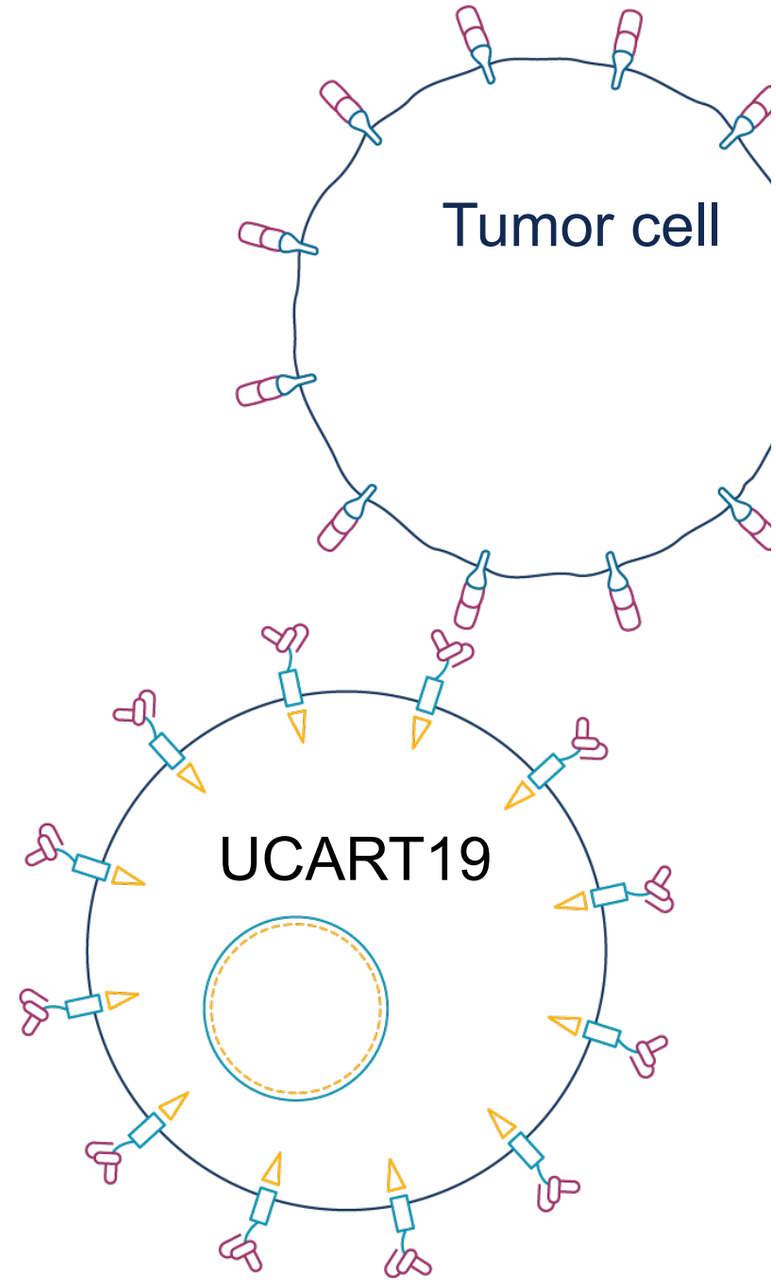
[1] *Or European equivalent.*

[2] *UCART19 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene.*

UCART19[1]

Initial Proof Of Concept In ALL Patients

- 1st patient dosed in June 2015 (compassionate)
- Phase I trials started in June 2016 in EU, in 2017 in the US
- Multiple recruiting centers (EU and US)
- 17 patients treated disclosed (9 adults and 8 pediatric)[2]
- Patients failed >5 lines of treatment, including autologous CAR-T



[1] *UCART19 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene.*
[2] *Including compassionate.*

UCART19 Early Clinical Data

Interim Ph1 Dose Escalation In Pediatric & Adult All Patients

- Dose-escalation trial ongoing, with starting doses 100-1000x lower than currently approved autologous CAR T doses
- Results already in line with early autologous CAR-T Phase I results published in past years

	Lymphodepletion & Patient Age	Disease Status Before Treatment	Dose Level (CAR-T Cells/ kg)	CR/CRi	Adverse Event > Grade 3	Relapse Follow up
SERVIER & KCL (PALL) ASH 2017	**CFA 6 m to 17 y**	**5/8 with >4 lines of treatment; All patients were ineligible for or had failed autologous CAR T treatment; 1/8 with >50% BM blasts**	**1.1 to 2.3x10^6**	**90% (7/8)[1] CR or CRi**	**CRS 14% (1/8) NT 0% (0/8)**	**29% (2/8) at 5 m 1 CD19- and 1 CD19+**
SERVIER & KCL (CALM) ASH 2017	**CFA >16y**	**5/9 with >4 lines of treatment; 7/9 with prior allo-SCT and in relapse; 2/9 with >85% BM blasts**	**1x10^5 to 1x10^6**	**70% (6/9)[1] CR or CRi**	**CRS 14% (1/7) NT 0% (0/7)**	**25% (1/4) at 6 m CD19+**

[1] *Including 2 patients in compassionate use.*

C: Cyclophosphamide; CF: Cyclophosphamide and Fludarabine; CFA: Cyclophosphamide, Fludarabine and Alemtuzumab; CE: Cyclophosphamide and Etoposide; CEVD: Cyclophosphamide, Etoposide, Vincristine, Dexamethasone; CDVP: Cyclophosphamide, Daunorubicin, Vincristine, Prednisone Minimal disease < 5% blasts, morphologic disease ≥ 5% blasts

CRi: Complete Remission with Incomplete Hematopoietic Recovery

UCART123 in AML and BPDCN

Product Attributes And Pre-clinical Data

Weill Cornell Medicine

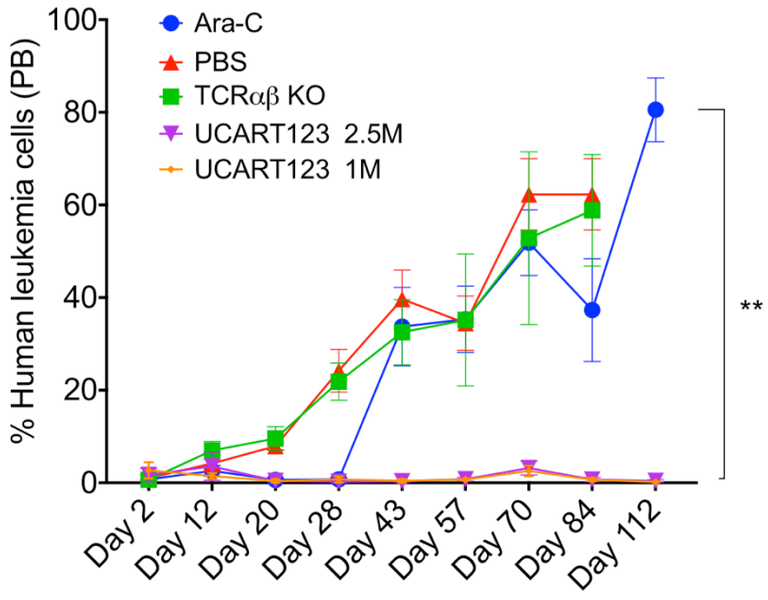
UCART123 attributes

- Overexpressed in myeloid leukemias
- Anti-CD123 CAR expression to redirect T-cells to tumor antigens
- Suicide gene for safety
- TCR disruption to avoid GvHD

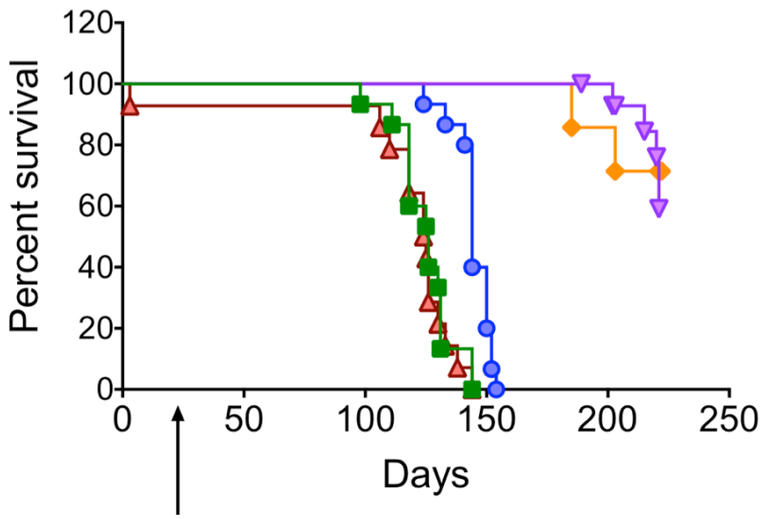
Encouraging pre-clinical efficacy data

- Significant improvement compared to Cytarabine standard-of-care (Ara-C)
- Encouraging results with CD123 target in autologous CAR-T approaches

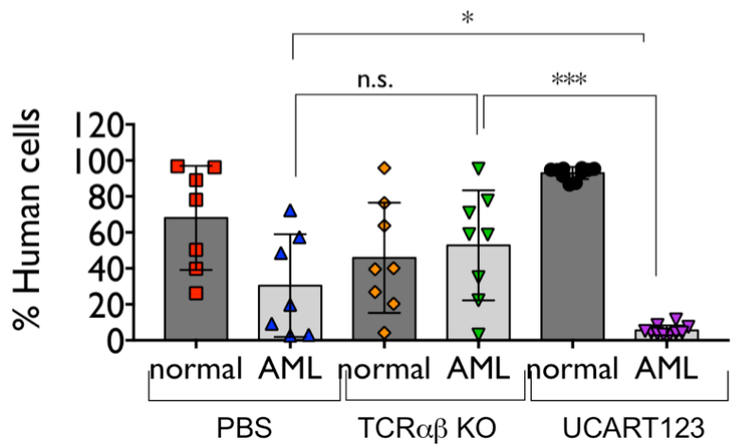
Peripheral Blood Evaluation



Overall Survival



Bone Marrow at Day 36



UCART123 Dosing Schedule

First wholly-controlled CAR-T in the clinic

- AML Ph 1 dose escalation trial ongoing at Weill Cornell
- First patient dosed in June 2017
- Expansion to other centres in 2018

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Weill Cornell Medicine

Dose Escalation Phase (R/R AML)

DL3 N=3	1.25x10^6/kg
DL2 N=3	1.25x10^5/kg
DL1 new start dose N=3	6.25x10^4/kg
DL-1	1.25x10^4/kg

3 Patients Treated at the RP2D (Recommended Phase II Dose)

Total Dose Escalation N= 9-12 pts

Expansion Phase

- **RR AML N=18-37**
- **Untreated AML ELN Adverse Genetic Group N=46-107**

Total Phase I Expansion N=64-144

In collaboration with Cornell-Weill

UCART22

Product Attributes And Pre-clinical Data

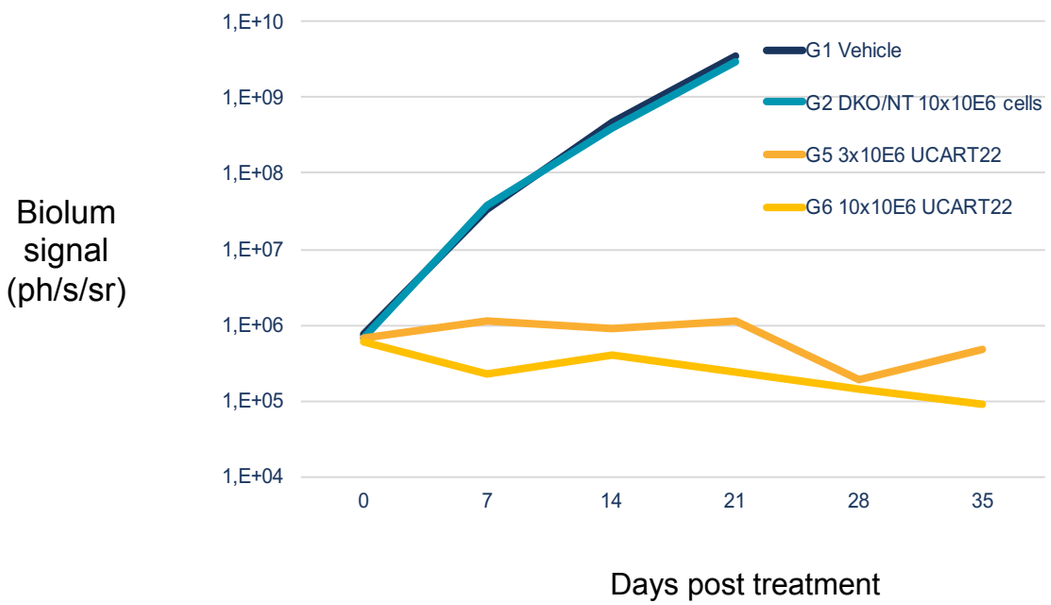
UCART 22 Rationale

- Both CD22 and CD19 are expressed on various B-cells
- CD22 expression frequently maintained in CD19-negative blasts1

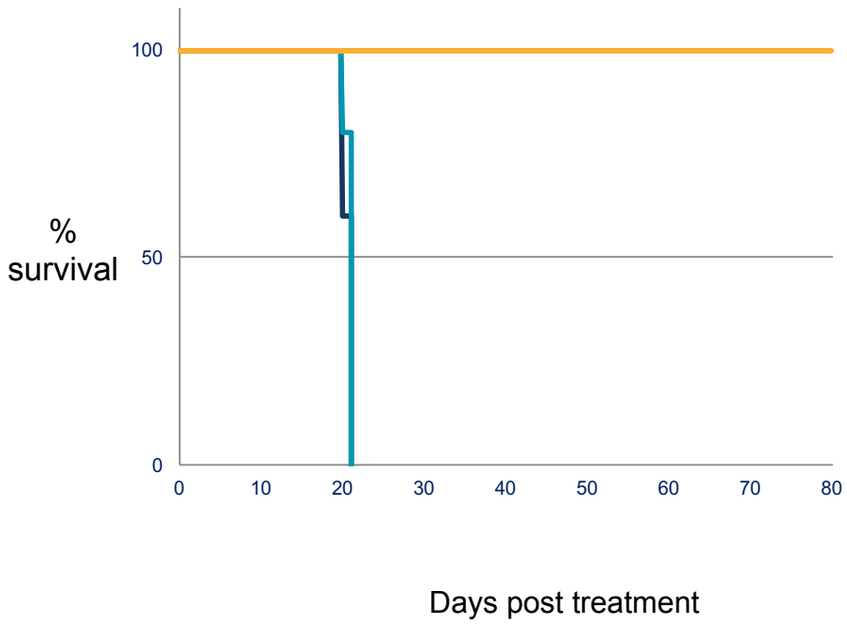
Strong anti-tumour activity

- UCART22 is highly efficient at eradicating tumors *in vivo*
- UCART22 cells result in increased mice survival

CD22+ Cell Line Show no Tumor Progression



Survival Curves



UCART22

Objective for patient enrolment

- Relapsed / refractory adult ALL patients first
- Potential to expand to pediatric patients
- Focus on patients who have relapsed after CD19 directed CAR T treatment
- Enrolment also open to CD19 treatment naïve patients
- Looking for strong expression of CD22 (Higher than 2000 CD22 antigens per cell)
- No Alemtuzumab pre-treatment – only in case there is no CAR T cell expansion
- First dose cohort starting at 1x10^5 cells per Kg
- Age limit is 65 years
- Allows for patients that have received 1 bone marrow transplant
- Transplant after UCART22 treatment not a requirement

UCARTCS1

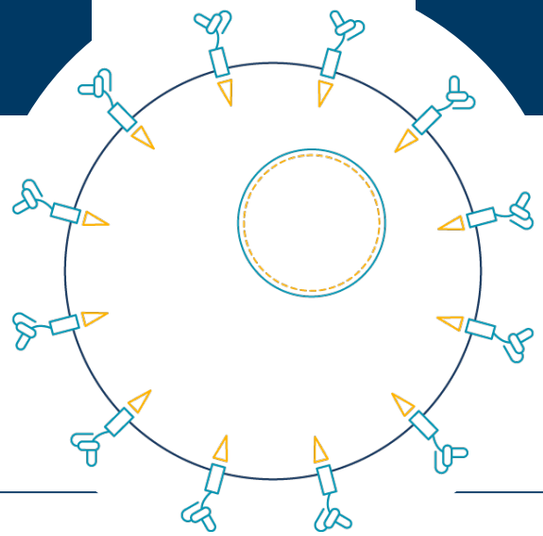
Targeting Multiple Myeloma

Unmet Medical Need

- > 30,000 patients / year in the US
- High relapse rate, median OS of 9 months

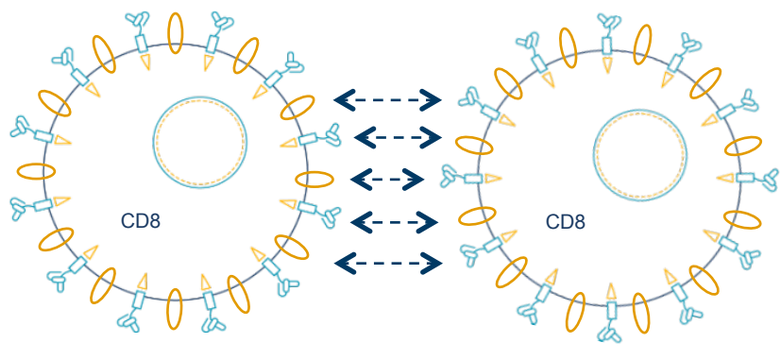
Target Antigen

- Well proven target with Elotuzumab (BMS/ Abbvie) as PoC
- CS1 (SLAMF7) is highly expressed on MM cancer cells
- CS1 is expressed on CD8 T-cells



UCARTCS1 Attributes

- Pre-clinical data shows high efficacy of re-dosing strategies
- Suicide gene is included for safety
- TCR gene disruption using TALEN® to avoid GvHD
- CS1 gene is disabled by TALEN® to prevent CAR T-cell cross-reactivity (CS1 is naturally expressed on CD8+ T-cells)



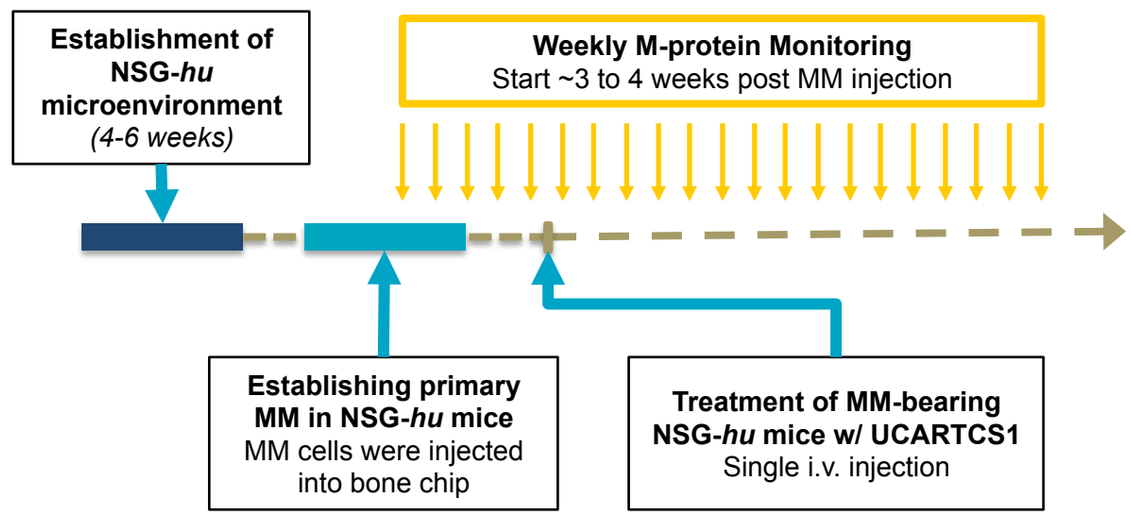
UCARTCS1

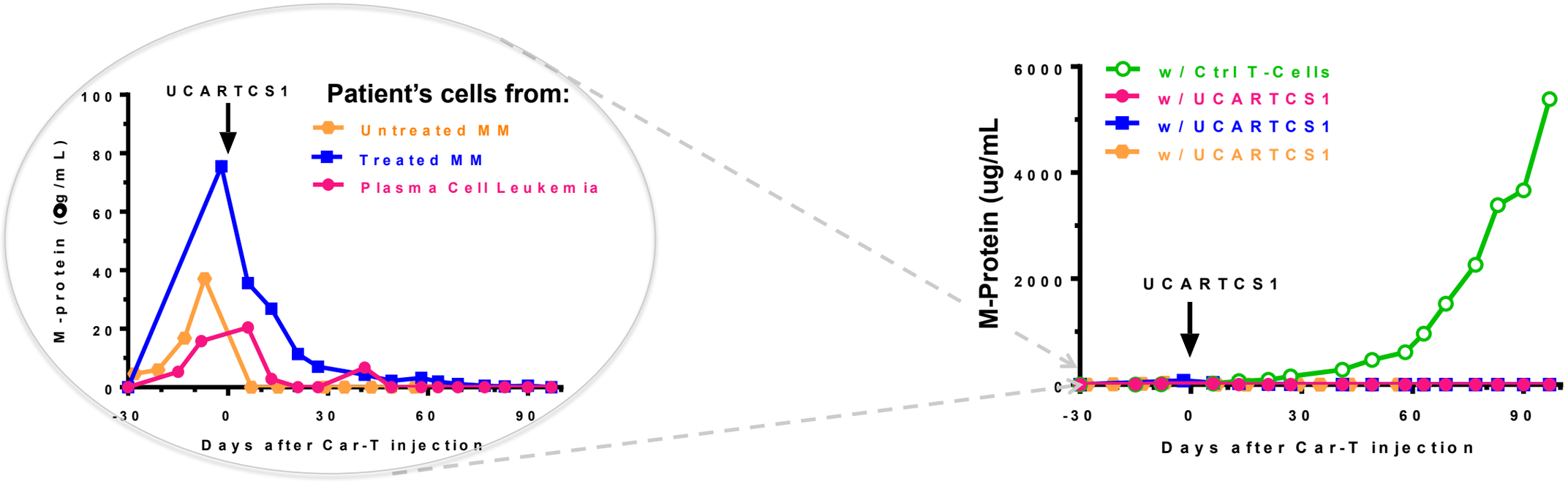
In vivo activity against primary myeloma tumor cells

MD Anderson Cancer Center

- UCARTCS1 exhibits durable in vivo efficacy in high-risk MM in PDX-MM models

PDX-MM models





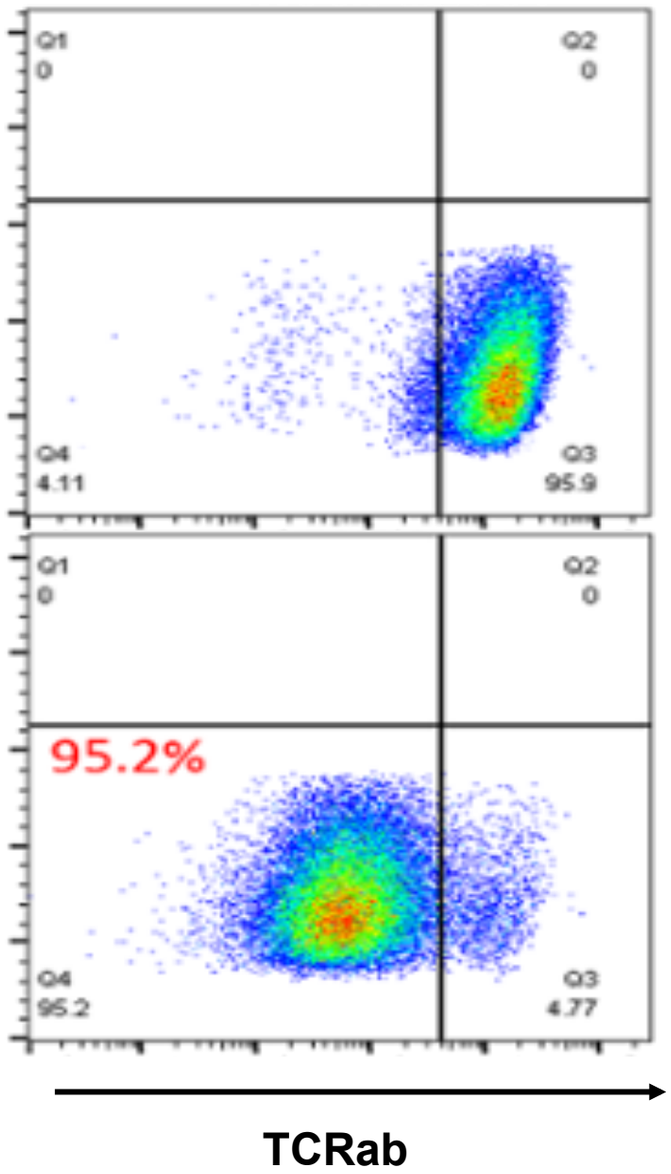
Jin He, Jing Yang, and Sattva Neelapu

3. Cellectis Is Built On A Leading Gene Editing Platform – TALEN®

TALEN® High Yield Gene Editing

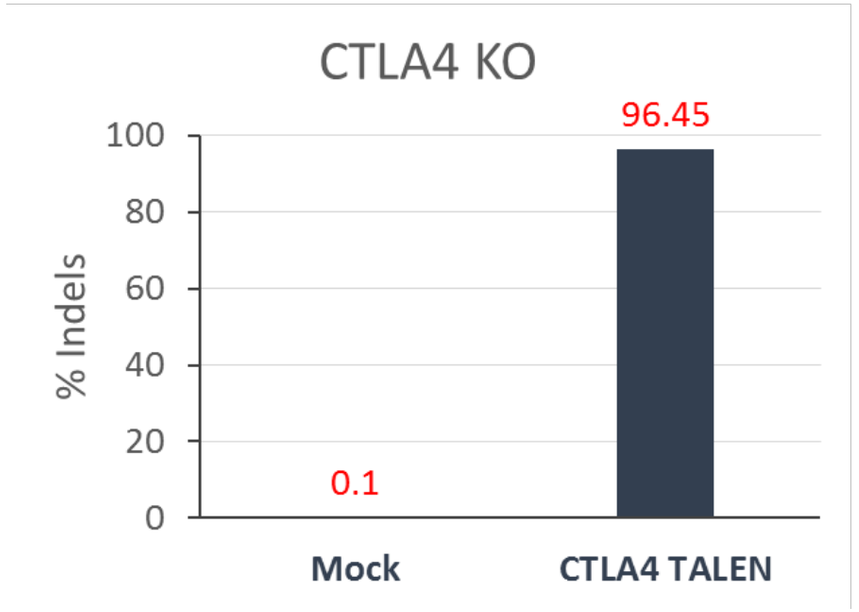
Consistent Single Knock Out Efficiencies Of Over 95%

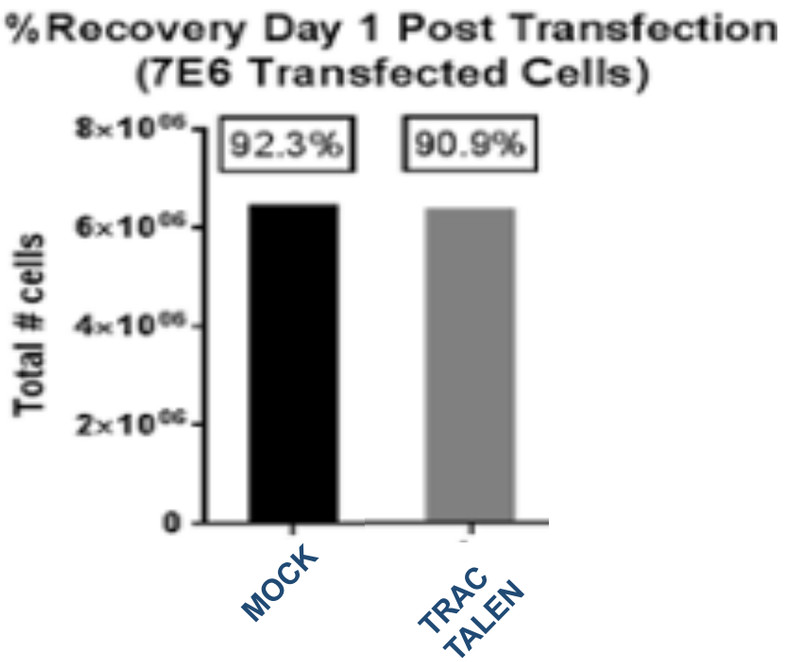
MOCK



TRAC TALEN

TCRab





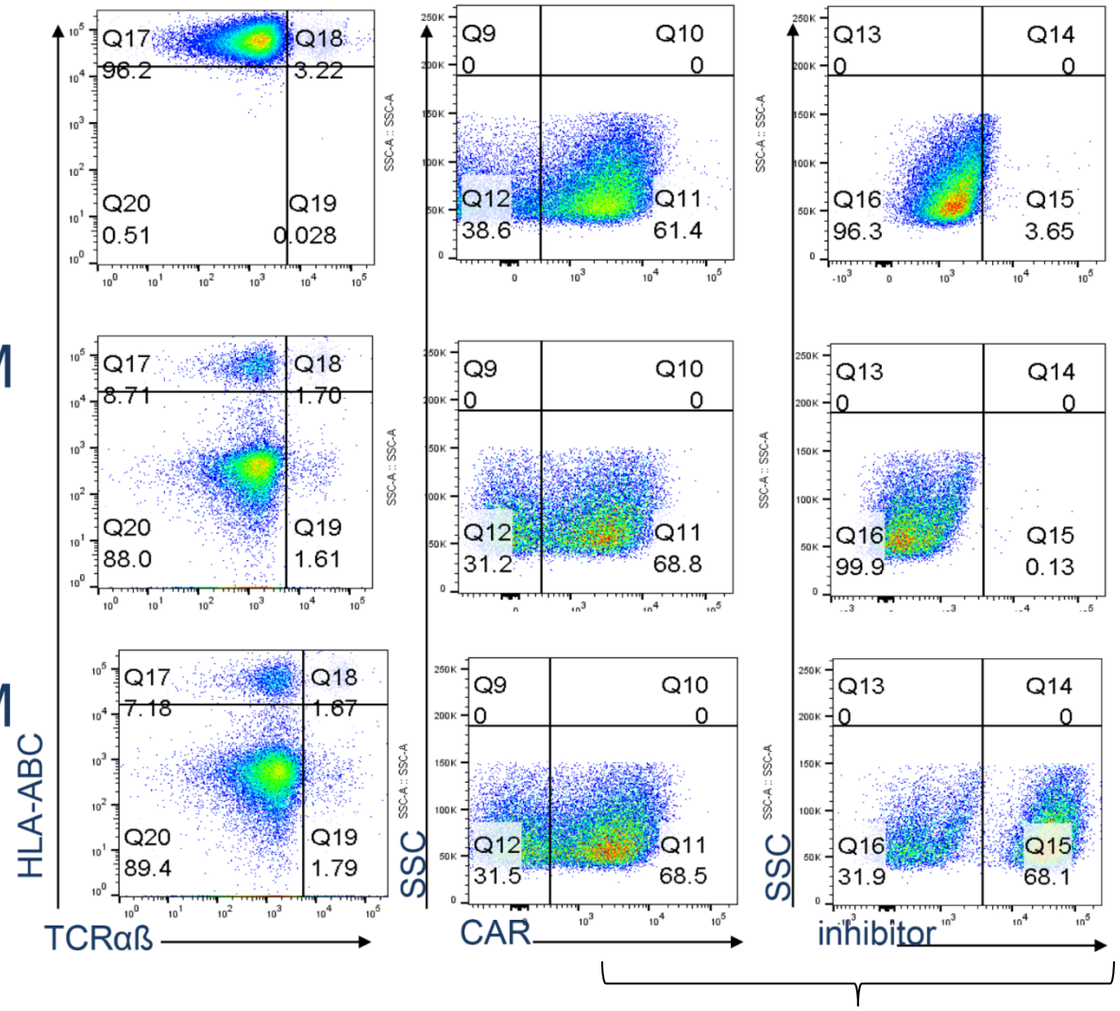
High Yield Multiplex Knockout and Knock-In

Combining B2M knockout and NK inhibition

Key Results

- **90% double knockout** of TCR and B2M in T-cells
- **61% efficiency single targeted insertion** (CAR) with **double knockout** (TCR, B2M)
- **42% double targeted insertion** (CAR, NK inhibitor) at TRAC and B2M locus with **double knockout** (TCR, B2M)

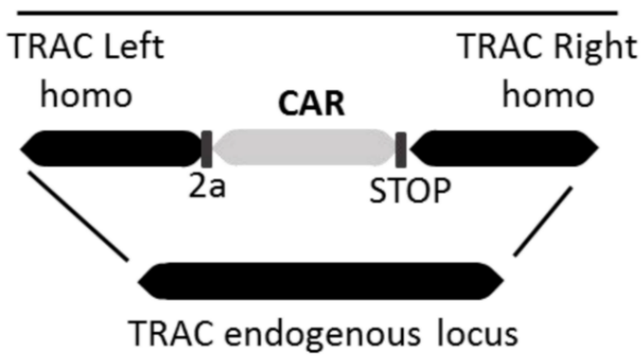
TRAC TALEN® + CAR

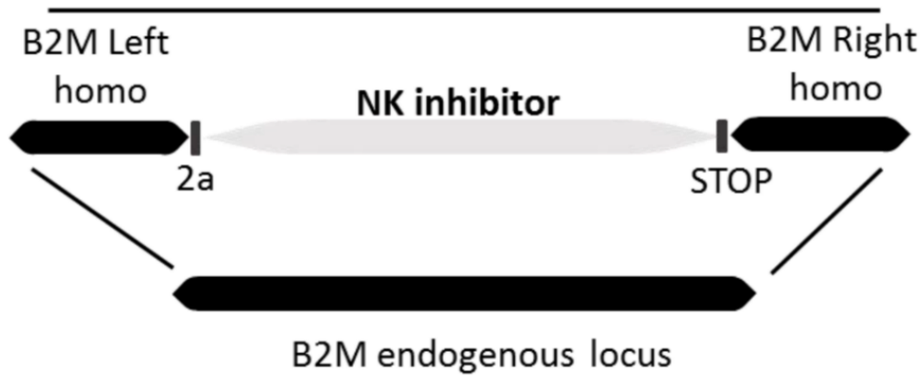


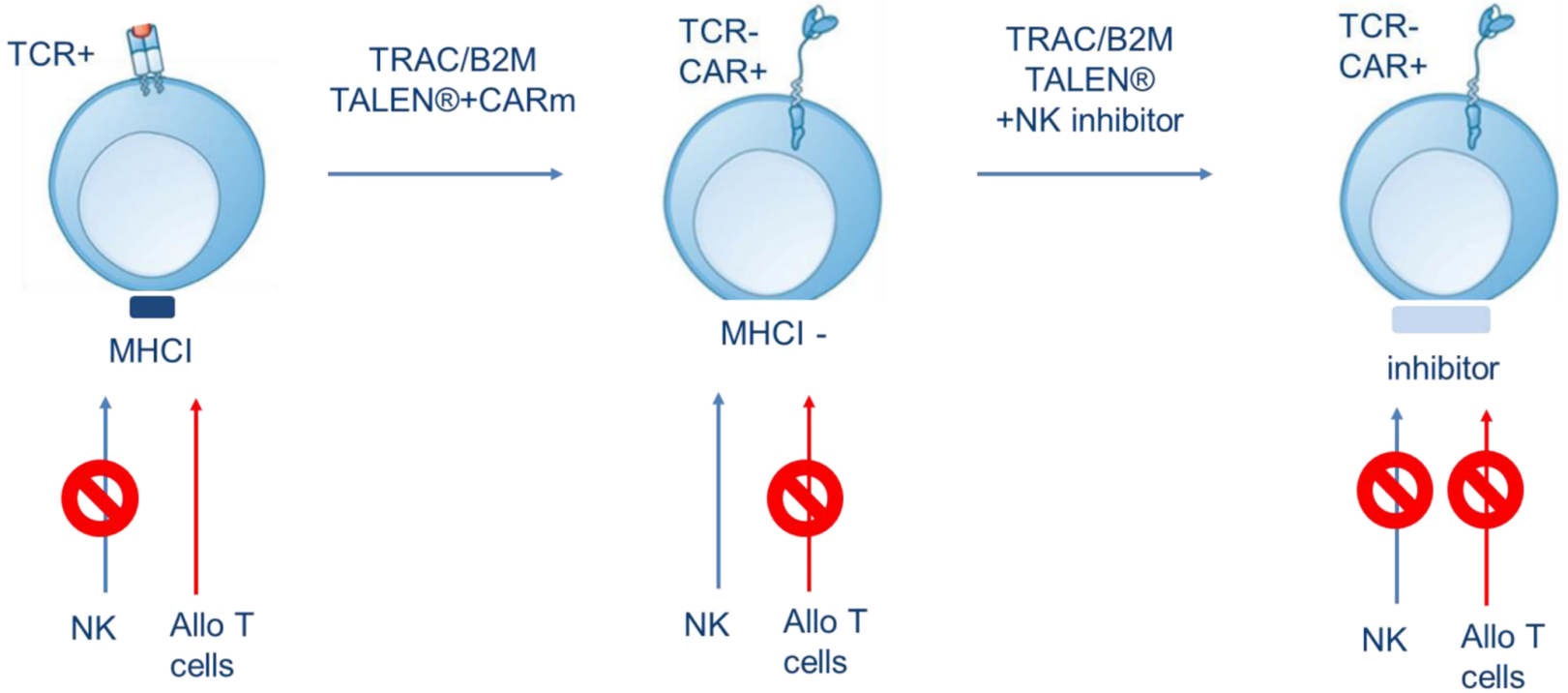
Gated on TCR-/HLA I- cells

Targeted Gene Integration

High Cell Viability And Engineered Persistence





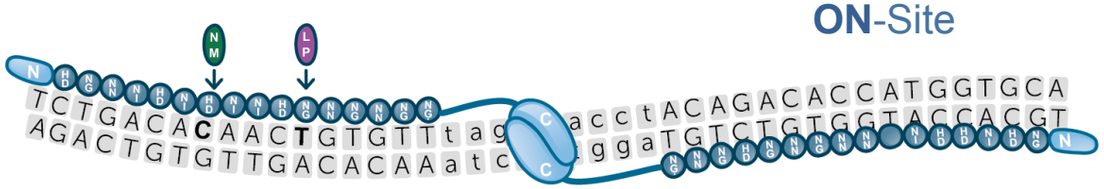


TALEN® Undetectable Off-Target Effect

Use of engineered RVDs to discriminate between ON and OFF-site

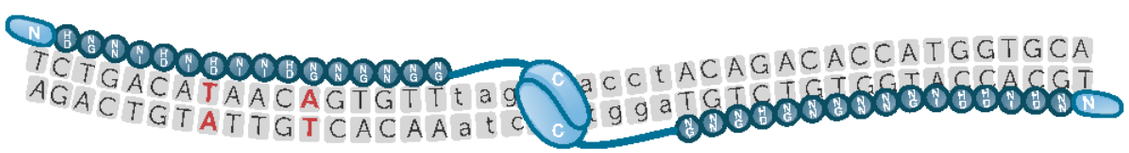
- Educated utilization of engineered RVDs to discriminate HBB loci preventing OFF-site cleavage

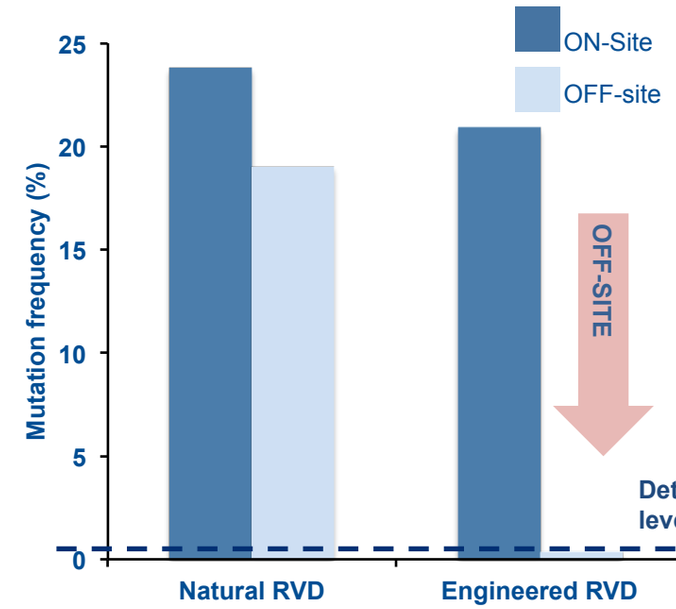
HBB



ON-site/OFF-site > 94 % identity

HBD

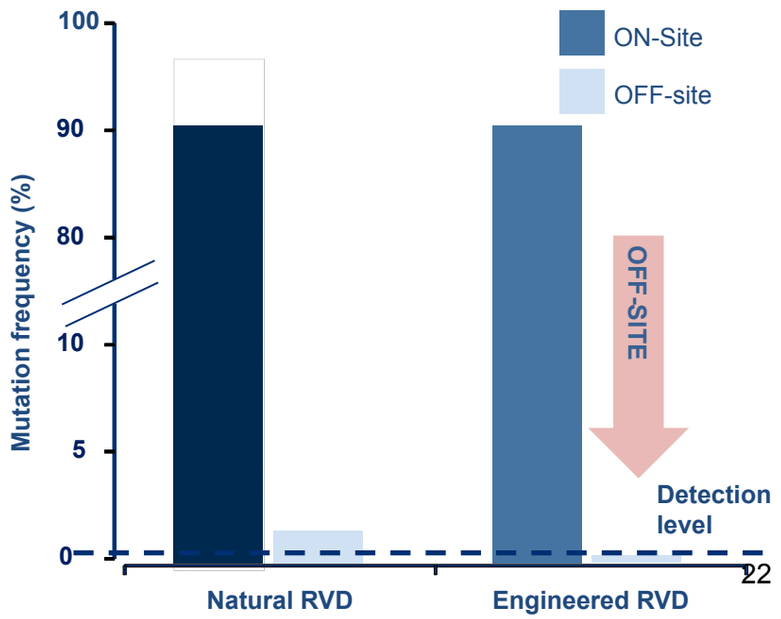




Juillerat et al (scientific report 2015)

PD1

Chr17 q24.1



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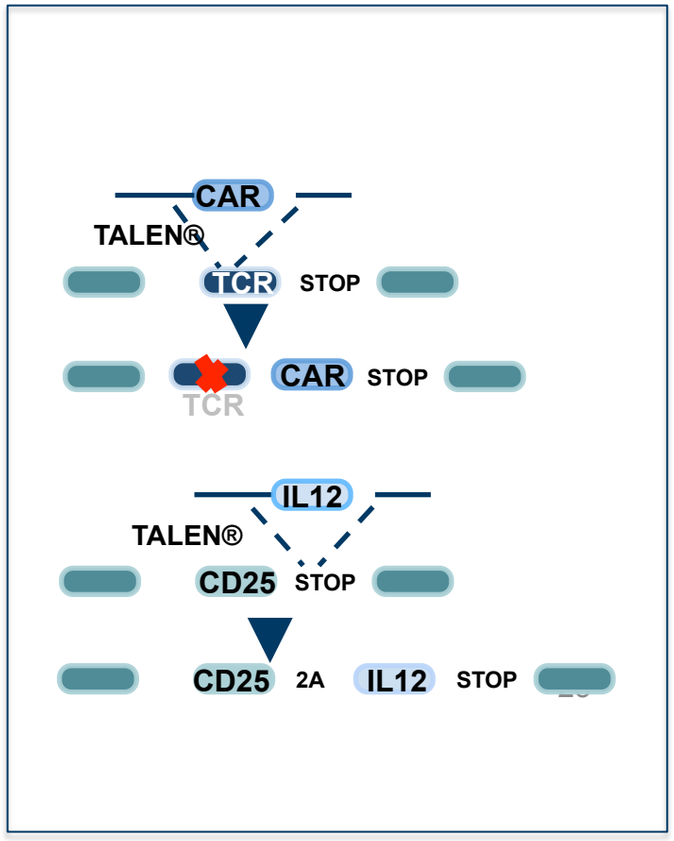
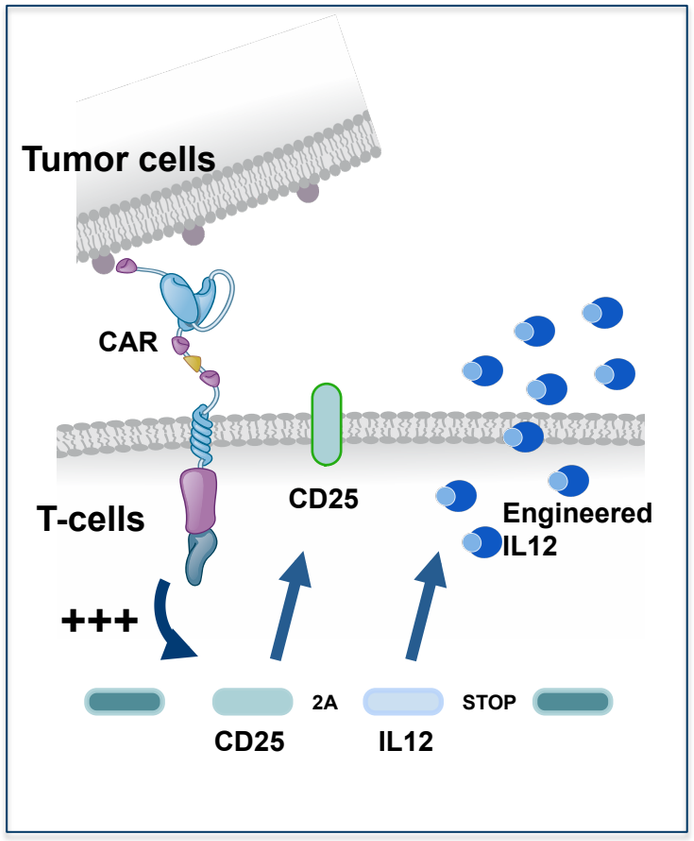
Next Gen. CARs To Target Solid Tumors

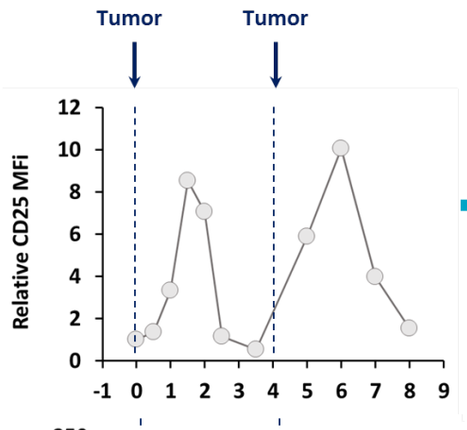
Synthetic Biology For High Performance UCARTs

Example of targeted integration at CD25 locus

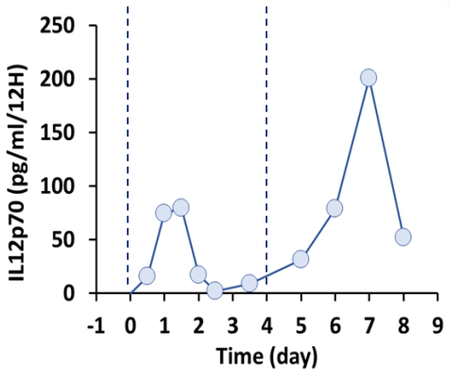
- IL12 contributes to anti tumor activity (Th1, NK, CD8)
- I.V. IL12 shows systemic adverse effects (BM, Liver, mucus membranes)
- Local On-Target IL12 secretion may avoid systemic toxicity



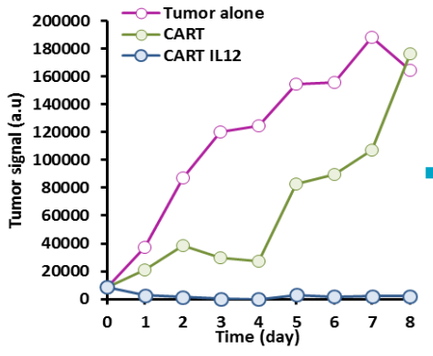




CD25 expression upon tumor engagement



Engineered IL-12 follows CD25 expression pattern upon tumor engagement.

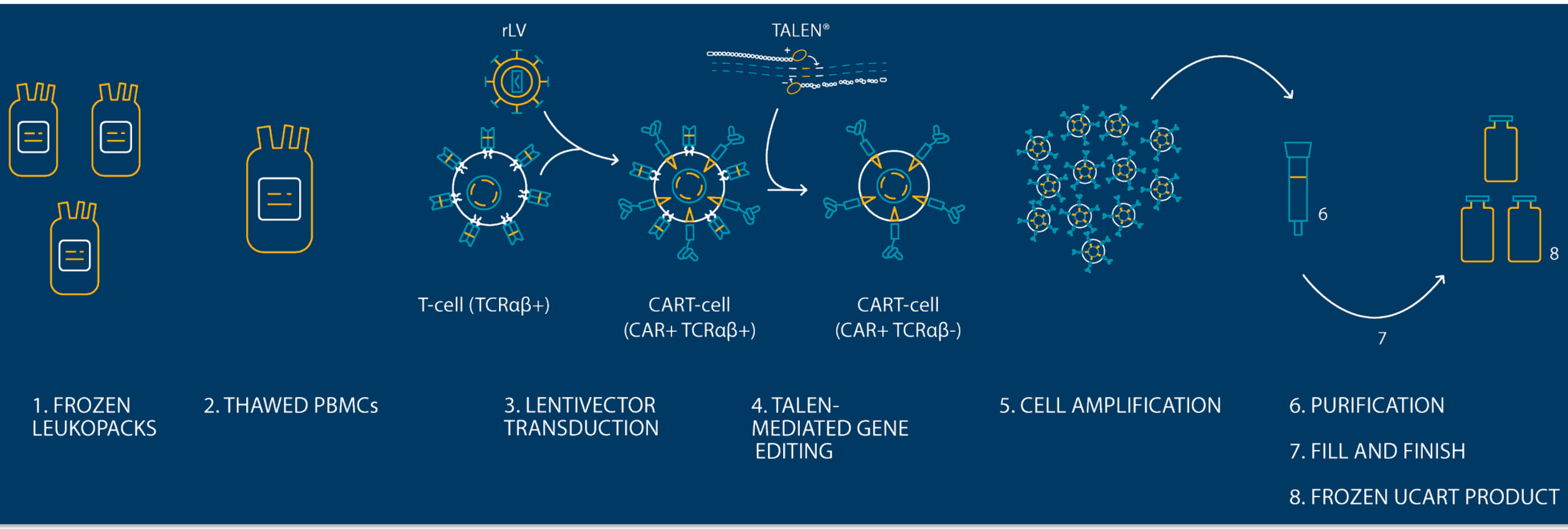


Tumor dependent expression of engineered IL-12 under the control of CD25 promoter significantly **improves tumor eradication.**

4. Acceleration And Building Commercial Manufacturing Capacity

Allogeneic CAR T – GMP Manufacturing

An integrated system combining gene editing and CAR T manufacturing



- Outsourced GMP manufacturing in place for UCART19, UCART123, UCART22, UCART CS1
- Full QC system in place, cleared for clinical trials
- In-house clinical supply facility by YE 2019
- In-house commercial supply facility by YE 2021

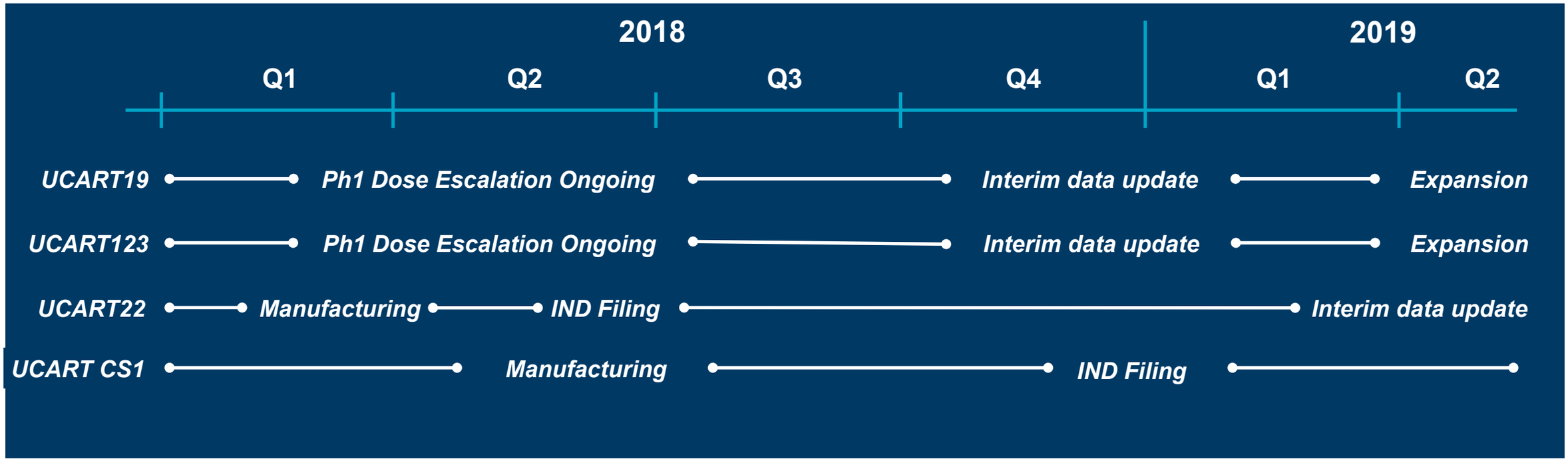
An Outstanding Experience in CAR T

Acceleration of timelines through previous proof-of-concept studies

- **UCART19 in ALL patients**
  - Phase I dose escalation studies ongoing
  - Expected to enter multi-centric Phase II studies in 2019
- **UCART123 in AML and BPDCN patients**
  - Clinical hold lifted in November 2017
  - Phase I dose escalation resumed in December 2017
- **UCART22 in ALL patients**
  - IND filed in May 2018
  - Built on experience of UCART19
- **UCARTCS1 in Multiple Myeloma**
  - Manufacturing and pre-clinical testing ongoing

Expected Milestone Timeline

Strong progress expected over the next 18 months



- **UCART19 in ALL patients** Phase 1 clinical trials ongoing; interim data was presented at ASH 2017
- **UCART123 in AML and BPDCN patients** Phase 1 clinical trials ongoing
- **UCART22** IND filed in May 2018
- **UCARTCS1** manufacturing ongoing
- **Cash Runway through 2021** providing funding through multiple data readouts

The Cellectis Group

~80% ownership

- NASDAQ: CLLS
- EURONEXT GROWTH: ALCLS
- $282M IN CASH AND EQUIVALENTS AS OF MARCH 31, 2018
- < $450M IN CASH AND EQUIVALENTS INCLUDING $190.5 M FOLLOW ON OFFERING
- IMMUNO-ONCOLOGY / CAR T
- THERAPEUTIC GENE EDITING
- GENE THERAPY

- NASDAQ: CLXT
- $50.7M IN CASH AND EQUIVALENTS AS OF MARCH 31, 2018
- BASED IN MINNESOTA
- CONSUMER FOCUS
- HIGH VALUE ASSET

Gene editing is the link

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THANK YOU

Cellectis S.A.
8, rue de la Croix Jarry
75013 Paris – France

Cellectis, Inc.
430 East 29th Street
10016 New York, NY – USA

investors@cellectis.com