

# NEXT-GENERATION CAR T-CELLS AGAINST CANCER

*Gene-Edited Off-The-Shelf Immunotherapies*

# 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 Collectis 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.

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A stylized illustration of a cell on a dark blue background. The cell is represented by a white outline of a circle with a smaller dashed circle inside. Several blue and yellow structures, resembling CARs (Chimeric Antigen Receptors), are attached to the cell's surface. Some are pointing towards the center, while others are pointing outwards. The overall style is clean and modern, using simple lines and a limited color palette of blue, yellow, and white.

*Translate ground-breaking gene-editing and CAR T-cell technology into game changing therapies, bringing hope to patients with high unmet needs*

# OUR VISION

*Transform cell therapies through gene-editing, creating readily available pharmaceutical-grade products for broad patient populations*

# OUR STRATEGY

*Enable a paradigm shift in medically relevant targets in hematological malignancies and expand into solid tumors.*

*Explore and offer treatments for other therapeutic areas driven by the broad potential of our technology.*

# Investment Highlights



## First Company to Turn Gene-Editing into a Therapeutic Success

*In June 2015, the 1<sup>st</sup> infant ALL patient was treated with Celsis' gene-edited allogeneic CAR T-cells*

## Three Allogeneic CAR T-Cell Programs with IND approved by FDA

*UCART19 (ALL) – March 2017*

*UCART123 (AML, BPDCN) – July 2017*

*UCART22 (ALL) – May 2018*

## Inventing 21<sup>st</sup> Century Cell Manufacturing

*Building best-in-class Commercial cGMP facility for Gene-Edited Cell Therapy*

## Leading Gene-Editing Platform

*Proprietary TALEN<sup>®</sup> gene-editing platform*

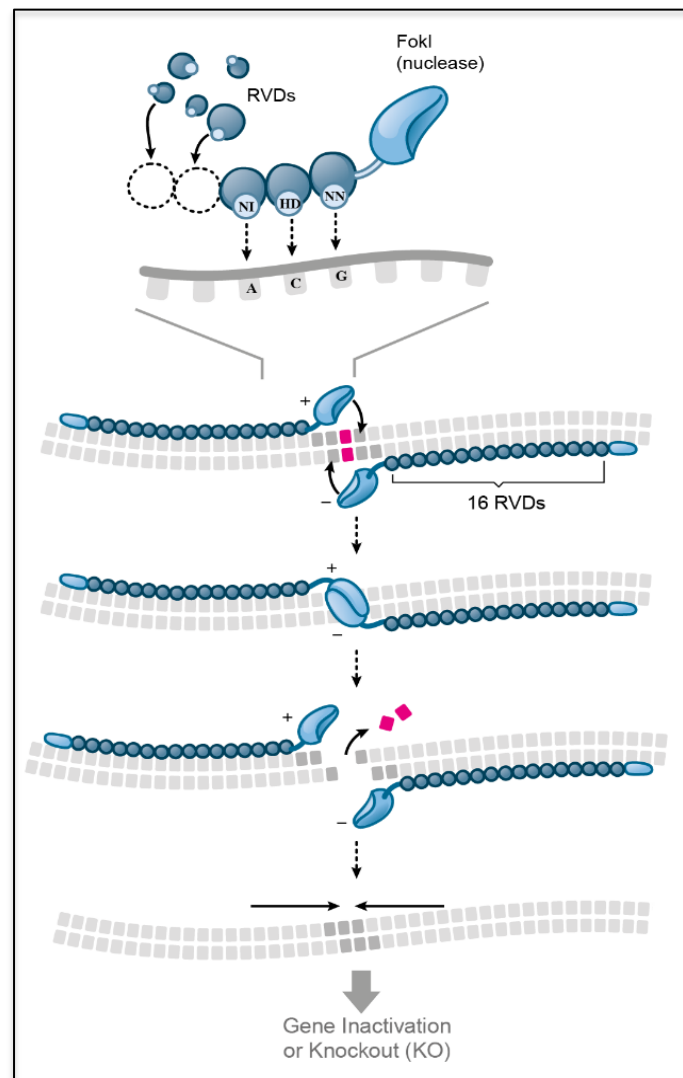
*Technologies approved by FDA and EMA for several clinical trials*

*Industry-leading precision and multiplexing gene editing capacity*

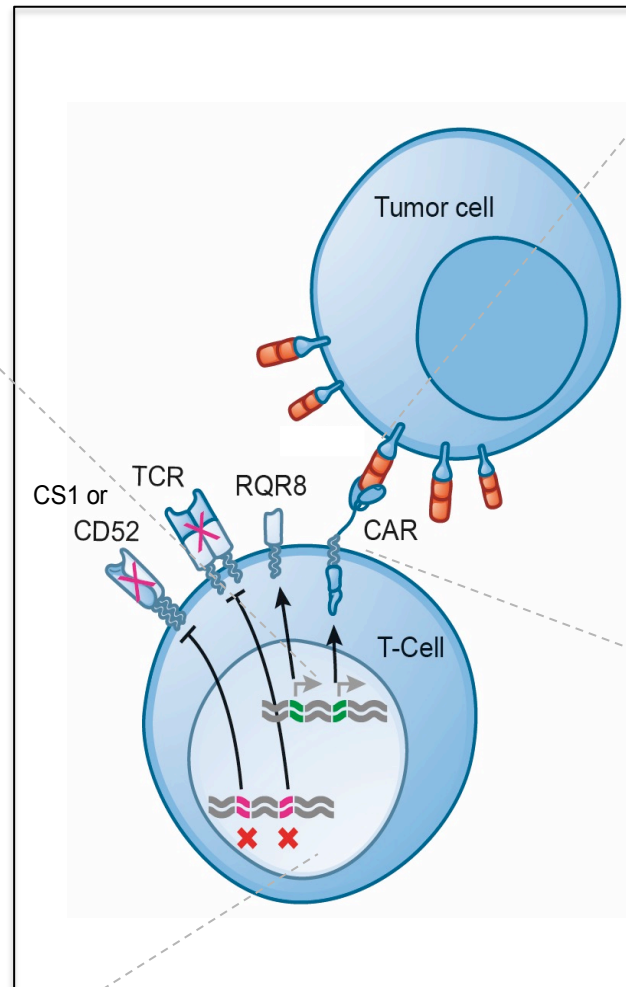
*Broad intellectual property portfolio, built on 18 years of experience*

# The Allogeneic CAR T-Cell Concept

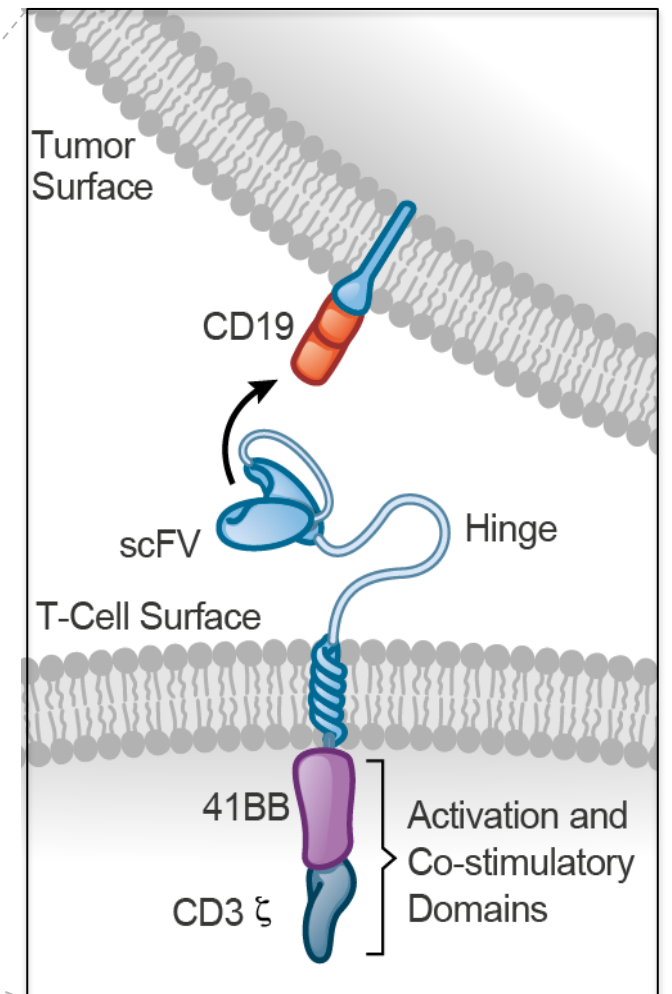
*How it works*



**Gene Editing**  
**TALEN® Nuclease**



**Allogeneic**  
**CAR T-cell**

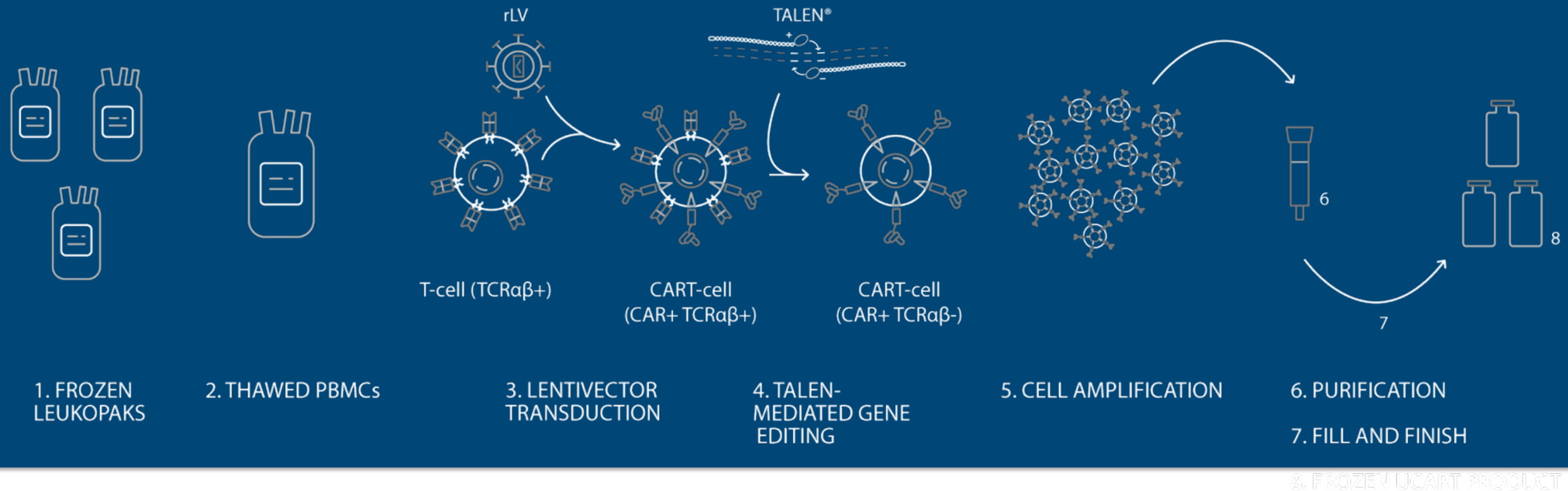


**Chimeric Antigen Receptor**  
**Tumor Recognition**

# GMP Manufacturing



## Integrated System for Gene-Editing And CAR T-Cell Manufacturing



- Industry-leading experience in allogeneic CAR-T manufacturing
- Successful GMP manufacturing of UCART19, UCART123, UCART22
- GMP manufacturing of UCARTCS1 in progress
- Full QC system in place, cleared for clinical trials in the EU and by the FDA

# Key Differentiating Objectives of UCARTs



*UCARTs = Cellestis' Allogeneic CAR T-Cells*

## Market access

- Easily and readily available at hospitals
- Potential to address large patient population (broader than autologous CAR T-cells)
- Enables a fast and dynamic medical footprint in underserved geographical regions

## Cost of treatment

- Possibility to lower the price of CAR T-cell therapies
- Scalable business model

## Ability to re-dose

- Possibility to re-dose / re-challenge with same antigen targeting CAR T-cells
- Possibility to combine different antigen targeting CAR T-cells

# A Powerhouse in Allogeneic CAR T-Cells



## Strategic Alliance With Leading Cell Therapy Team

The leader in allogeneic CAR T-cells:



In collaboration with Kite Pharma's former leadership team:



Expanding the clinical development in collaboration with:



### Economics to Cellecctis:

UCART19 (Allogene/Servier):

- \$350M in development milestones
- Royalties on sales

15 Licensed Programs (Allogene):

- \$185M in development milestones per program
- Royalties on sales

> \$3bn in potential total milestone payments

With equity investments by leading pharma partners:



The success of our Partners is the success of Cellecctis



# Pipeline



*Rich allogeneic CAR T-Cell pipeline with multiple shots on goal*

INDICATION	PROGRAM	TARGET	PRE-CLINICAL	PHASE 1	PHASE 2	ANTICIPATED MILESTONES
ALL	UCART19 <sup>1</sup>	CD19				<i>Initiate potential registration trials in ALL in 2H 2019 <sup>3</sup></i>
ALL	UCART22	CD22				<i>Initiate Ph1 trials in 2H 2018</i>
NHL	UCART22	CD22				
NHL	ALLO-501 <sup>1</sup>	CD19				<i>File IND in 1H 2019 <sup>3</sup></i>
AML	UCART123	CD123				<i>Initiate potential expansion trials in AML in 2H 2019</i>
BPDCN	UCART123	CD123				
AML	UCART CLL1	CLL1				
AML	ALLO-819 <sup>2</sup>	FLT3				
MM	UCART CS1	CS1				<i>File IND in 1H 2019</i>
MM	ALLO-715 <sup>2</sup>	BCMA				<i>File IND in 2019 <sup>3</sup></i>
MM	UCART 38	CD38				

<sup>1</sup> UCART19 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene

<sup>2</sup> Product candidate is exclusively licensed to Allogene

<sup>3</sup> According to Allogene investor presentation

Proprietary Development Program  
 Licensed Development Program

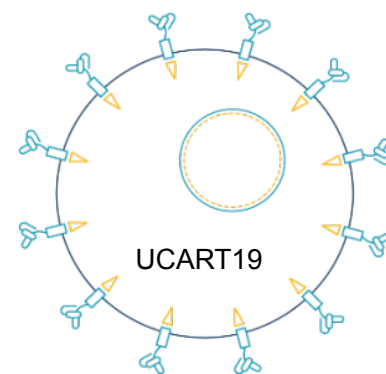
# UCART Targeting Rationale



*A summary of our most advanced CAR T-cell product candidates*

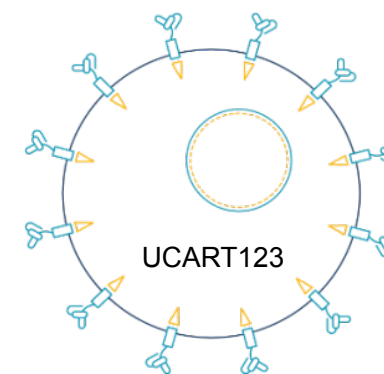
## CD19<sup>1</sup> in ALL

- High expression in ALL / DLBCL / NHL patients
- Well proven CAR T-cell target
- Allogeneic proof-of-concept



## CD123 in AML

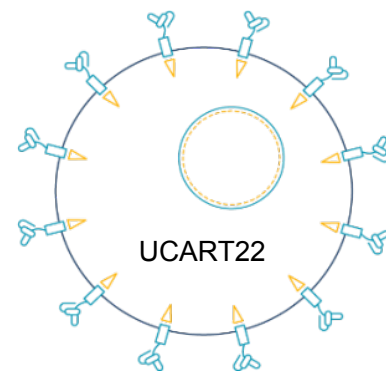
- High expression on blasts in majority of AML patients
- High relapse rate and poor overall survival in R/R patients



- TCR gene disruption using TALEN<sup>®</sup> to avoid GvHD
- Suicide gene is included for safety

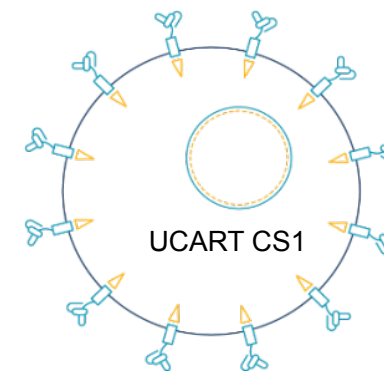
## CD22 in ALL

- High number of patients relapse after CD19- CAR T-cell treatment
- CD22 expression frequently maintained in CD19-negative blasts



## CS1 in Multiple Myeloma

- Well proven mAb target with elotuzumab (BMS/Abbvie)
- CS1 (SLAMF7) is highly expressed on MM cancer cells



<sup>1</sup>UCART19 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene

# UCART19<sup>1</sup>



## *Initial Proof Of Concept In Relapsed / Refractory ALL Patients*

### **Product Objectives**

- Ready-to-use, off-the-shelf therapy
- Single healthy donor cell batch can be used to treat multiple patients

### **Development Status**

- Phase I trials started in 2016 in EU, in 2017 in the US
- Phase II planned for 2019
- Multiple recruiting centers (EU and the US)
- Enrolled patients failed >5 lines of treatment

### **Results to date**

- Comparable results to early Phase I results from autologous CAR T-cell trials
- Some patients received a second dose of UCART19

<sup>1</sup> UCART19 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene.

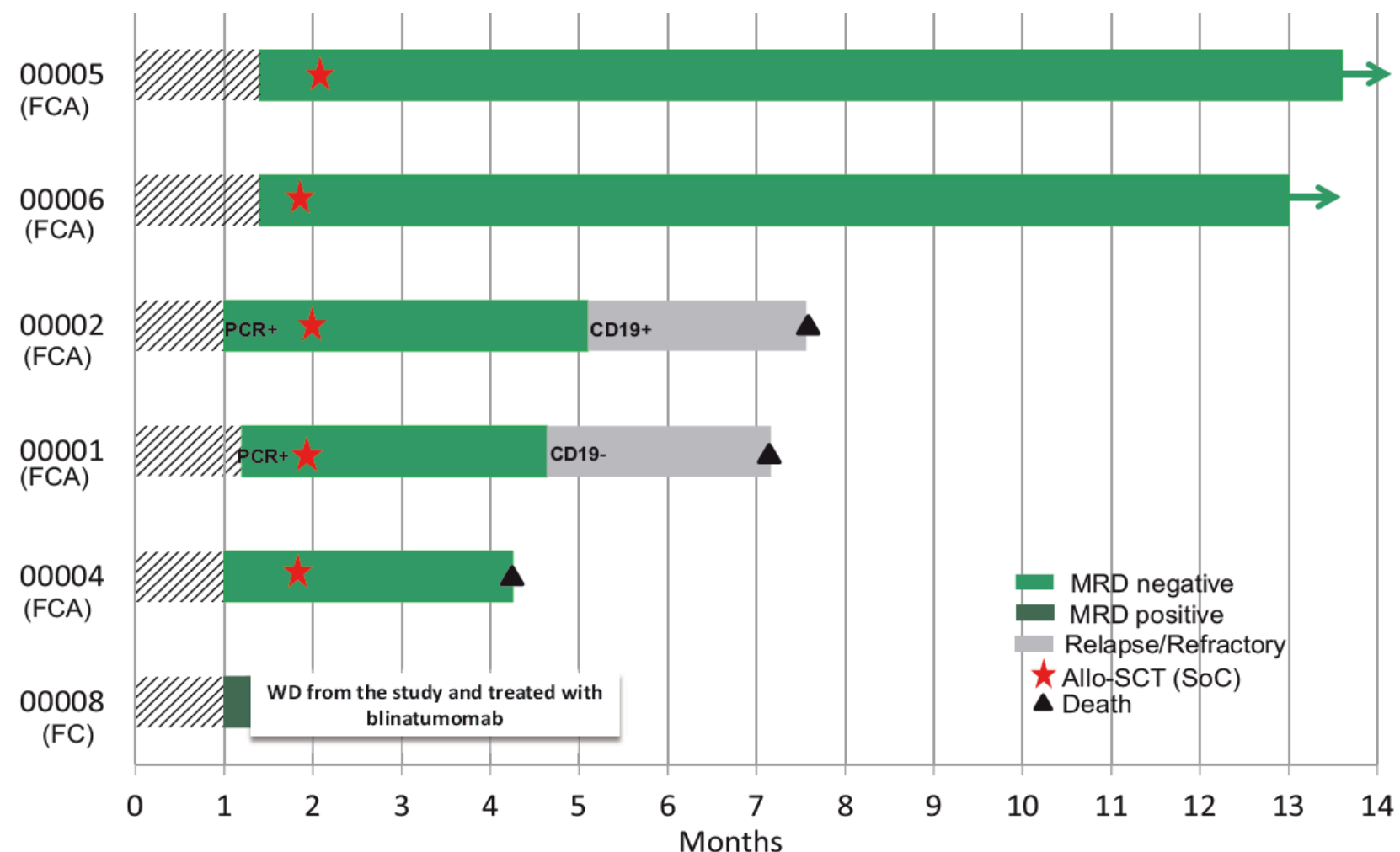
# UCART19<sup>1</sup> – Ph 1 R/R Pediatric ALL Study



Presentation at 23<sup>rd</sup> Congress of EHA, June 14-17, 2018

- All patients completed the 28-day evaluation period and were evaluable for anti-leukemic activity
- 5/6 pts had achieved complete remission with incomplete blood count recovery and were MRD<sup>2</sup> negative (<0.01%) by flow cytometry or qPCR
- To date UCART19 related toxicities have been manageable

UCART19 Anti-Leukemic Activity (EHA 2018 Poster #PF175<sup>3</sup>)



<sup>1</sup> UCART19 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene.

<sup>2</sup> MRD: Molecular Residual Disease

<sup>3</sup>Poster #PF175 "Phase I study of UCART19, an allogeneic anti-CD19 CAR T-cell product, in high risk pediatric patients with CD19+ relapsed/refractory (R/R) B-cell ALL: Preliminary results of PALL study" presented at 23rd EHA Congress, June 14-17, 2018, Stockholm

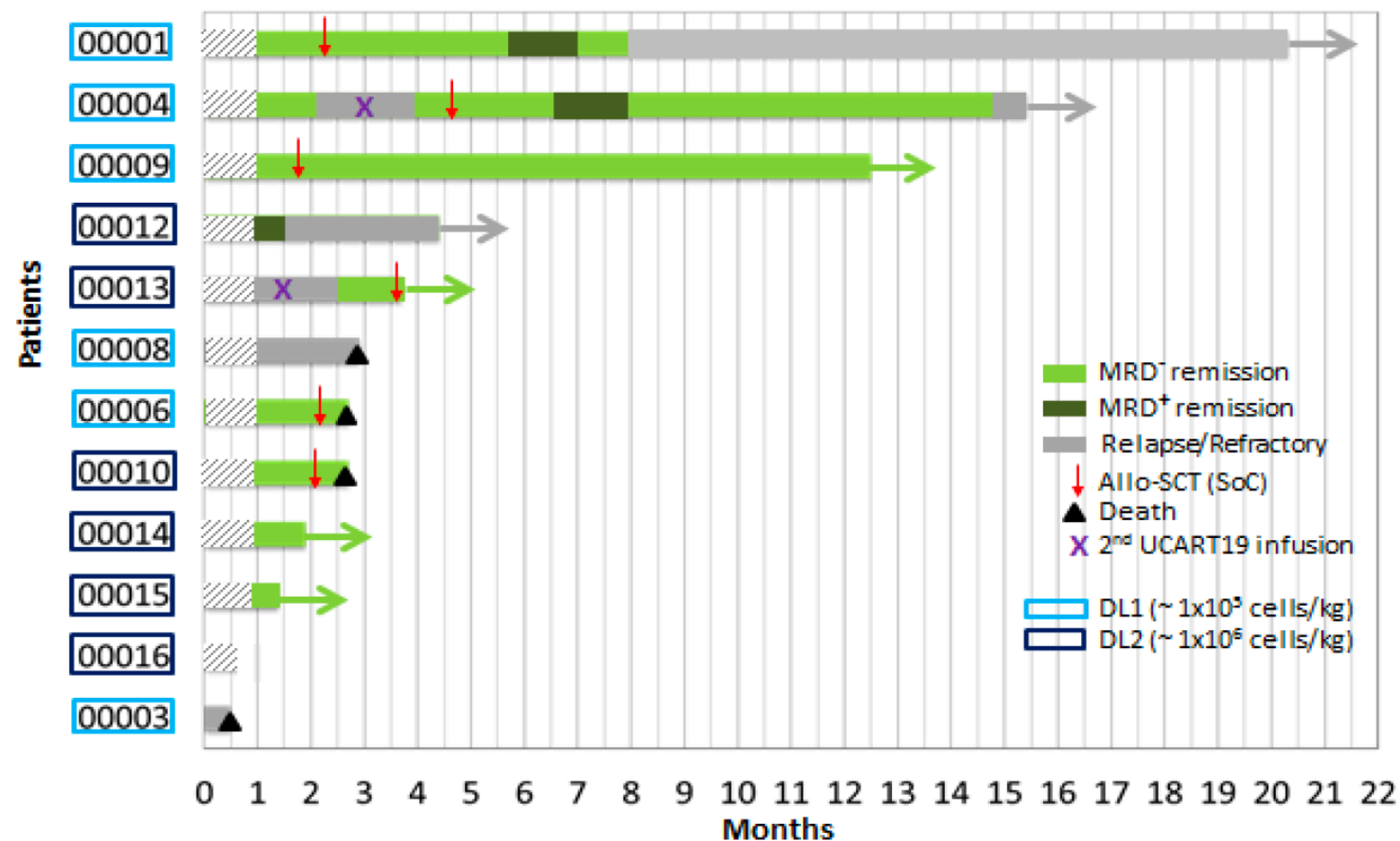
# UCART19<sup>1</sup> – Ph 1 R/R Adult ALL Study



Presentation at 23<sup>rd</sup> Congress of EHA, June 14-17, 2018

- 10/12 patients were evaluable for anti-leukemic activity at day 28 post UCART19 infusion
- At day 28, 8/10 evaluable patients achieved a complete remission (CR), including 7 patients in MRD- CR
- Two patients have been re-dosed with UCART19 following a first dose. Both patients achieved MRD- CR at day 28 following the second dose.

UCART19 Anti-Leukemic Activity (EHA 2018 Poster #PF178<sup>2</sup>)



<sup>1</sup>UCART19 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene.

<sup>2</sup>Poster #PF178 “Phase I study of UCART19, an allogeneic anti-CD19 CAR T-cell product, in high risk adult patients with CD19+ relapsed/refractory (R/R) B-cell ALL: Preliminary results of phase I CALM study” presented at 23<sup>rd</sup> EHA Congress, June 14-17, 2018, Stockholm

# UCART123



## Targeting AML and BPDCN

### Unmet Medical Need

- Current chemotherapeutics fail to eliminate leukemia stem cells (LSC)
- Newly approved therapies have shown limited benefit over standard of care

### Pre-Clinical Data

- Significant improvement compared to Cytarabine standard-of-care (Ara-C)
- Encouraging results with CD123 target in autologous CAR T-cell approaches (City of Hope trials presented at ASH 2017)

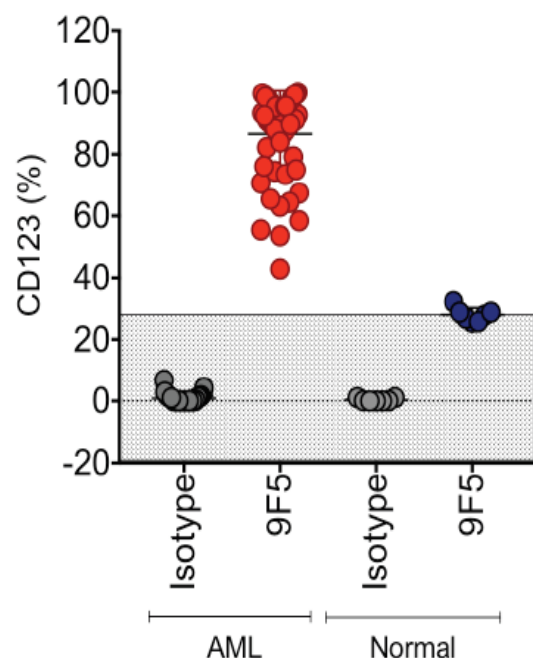


**Weill Cornell  
Medicine**

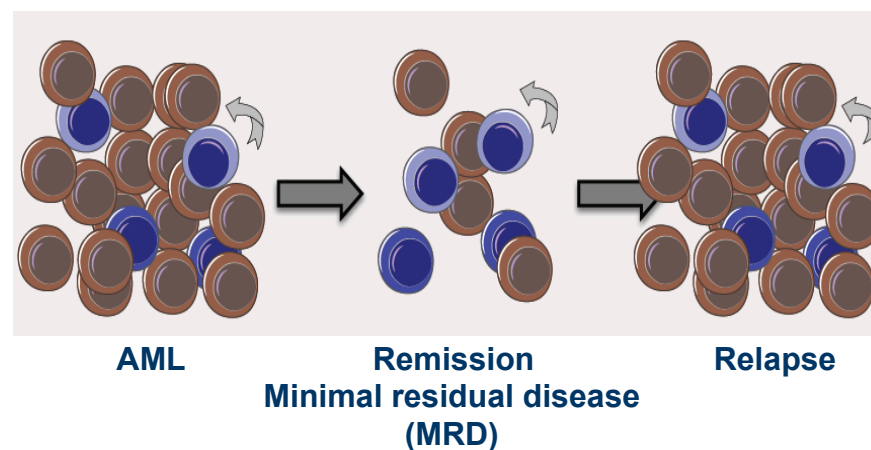
THE UNIVERSITY OF TEXAS  
**MD Anderson  
Cancer Center**

Making Cancer History®

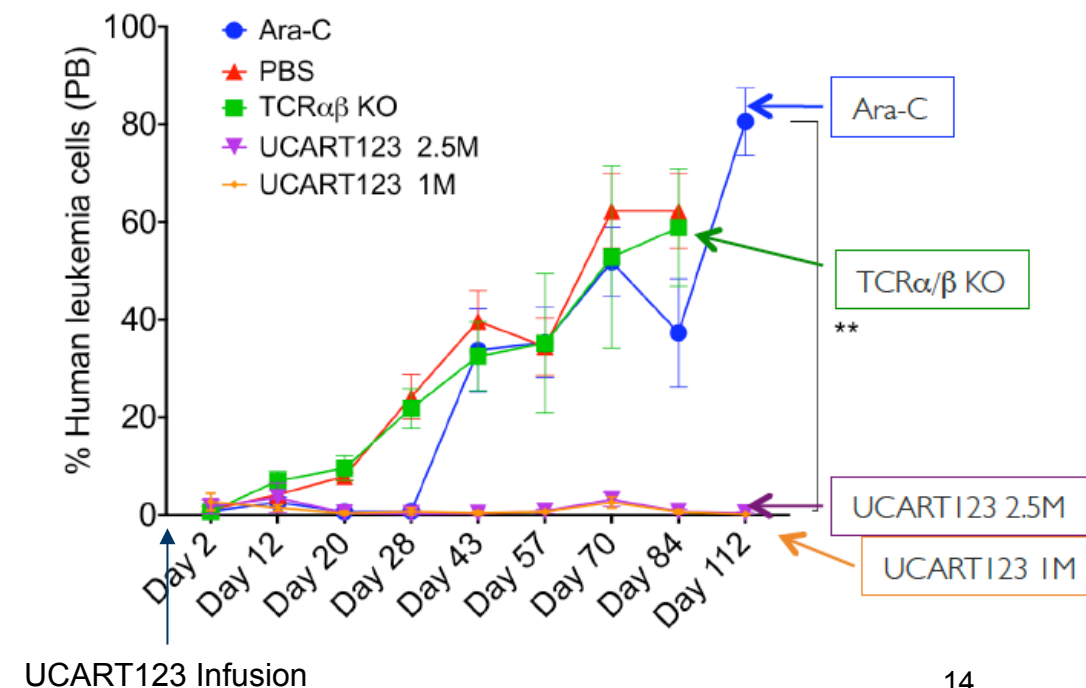
### CD123 Expression



### Failure to eliminate leukemia stem cells



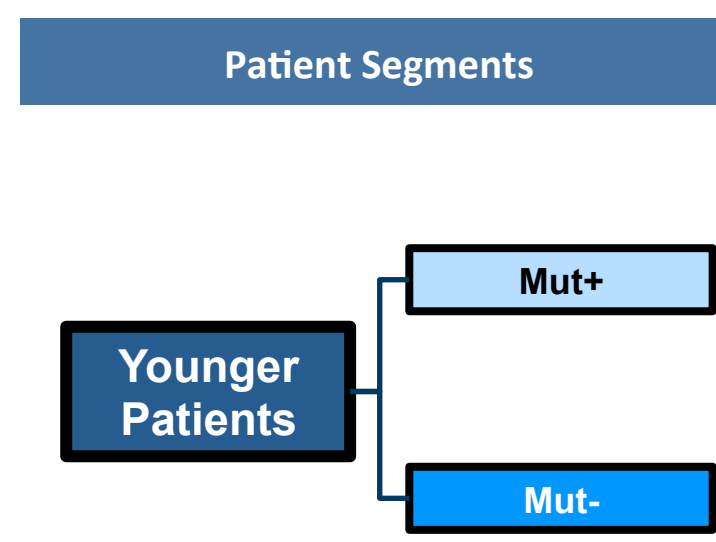
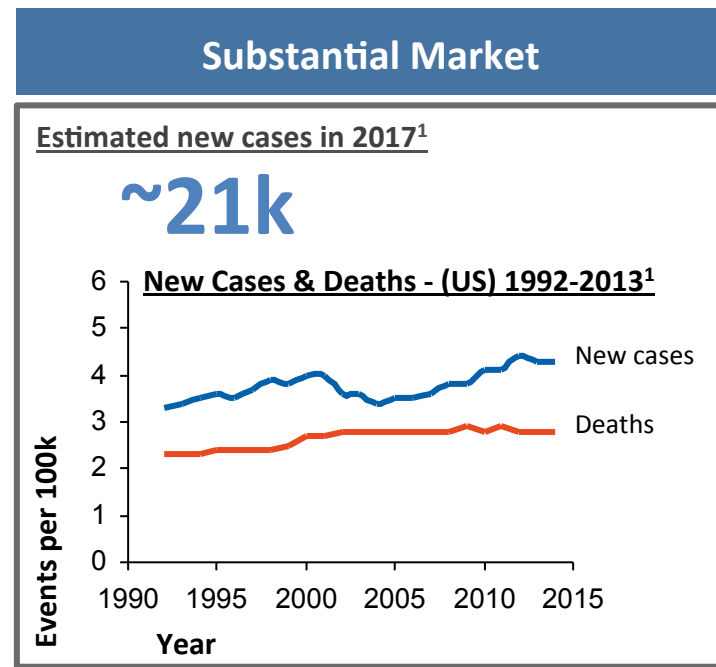
### Peripheral Blood Evaluation



# AML – an overview

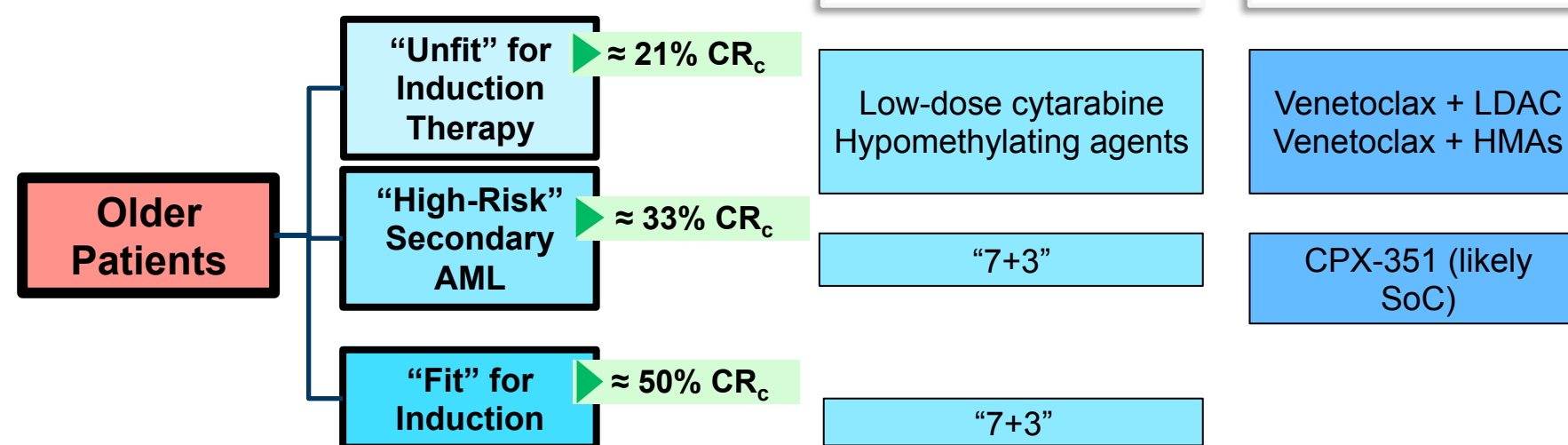
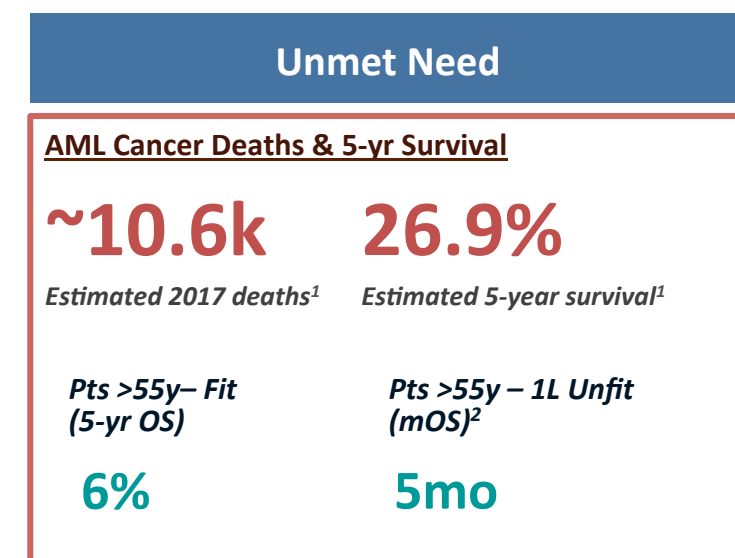


High unmet medical need remains clinical reality



With Rydapt and Idhifa approvals, AML market is becoming increasingly **fragmented by mutation status**  
 FLT3-mut.30% of cases, IDH1-mut 7.3%, IDH2-mut 8.7%

**Epigenetic dysregulation** is a hallmark of AML regardless of FLT3 or IDH mutation status.  
 Hypomethylating agents are a standard in AML care, especially in patients unfit for 7+3 and in the r/r setting



1) SEER; 2) ASH Conference 2016 Abstract #102; Dillman et al (1991) Blood; Stone et al (2015) Blood; Stein and Tallman (2016) Blood; Ravandi et al (2016) Cancer; Tefferi and Letendre (2012) JCO; Borate et al (2015) Cancer; Stone et al (2012) Leukemia, Heiblig et al (2016) Medit. J. Hematol Infect Dis.; Burnett et al (2007) Cancer; Lin et al (2016) ASCO Abstract #7007; Pollyea et al (2016) ASCO Abstract #7009; Lancet et al (2016) ASCO Abstract #7000; Stone et al (2015) JCO, European Hematology Association 2017 Abstract S473

# UCART123 Dosing Schedule

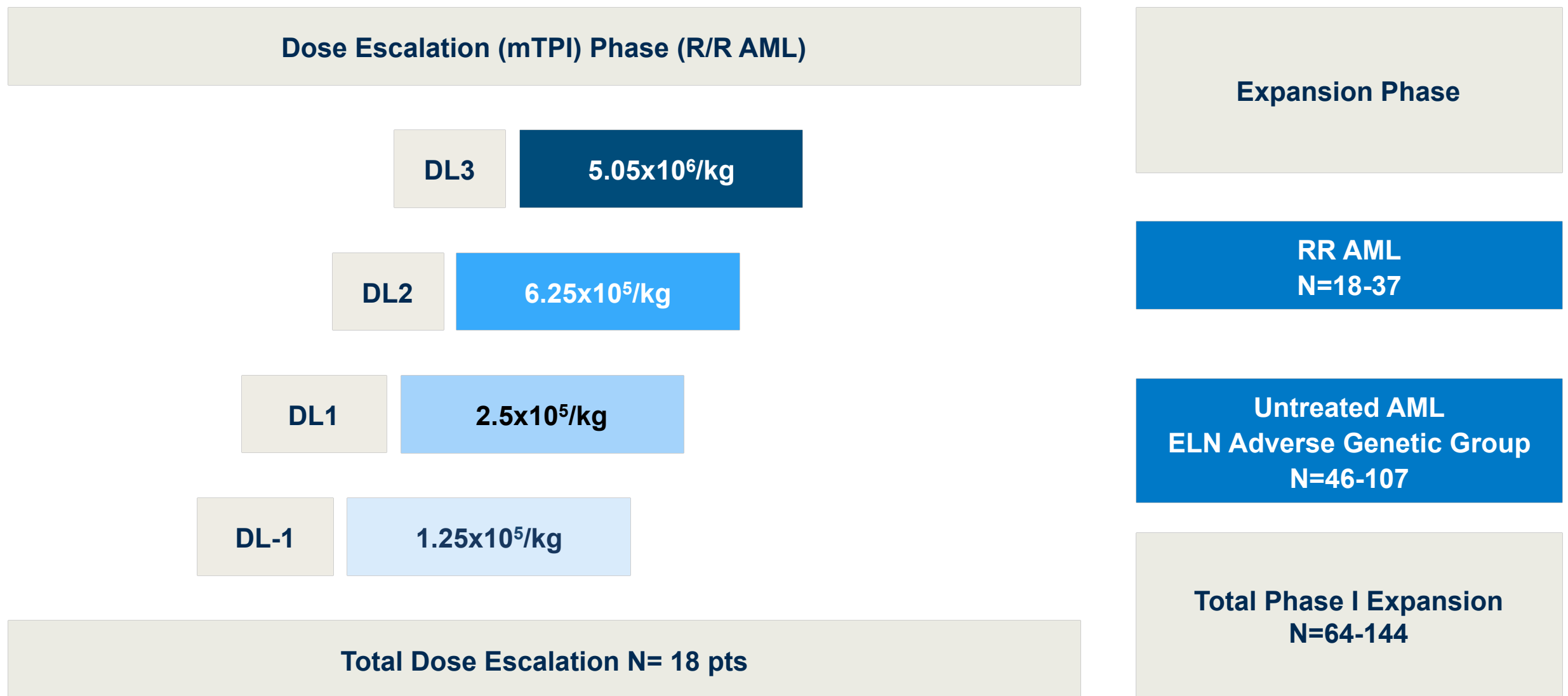
## First Wholly-Controlled CAR T-Cell Program In The Clinic

- AML Phase 1 dose-escalation trial ongoing at Weill Cornell & MD Anderson Cancer Center
- First patient dosed in June 2017



**Weill Cornell  
Medicine**

THE UNIVERSITY OF TEXAS  
**MDAnderson  
Cancer Center**  
Making Cancer History®



Clinical research coordinated by principal investigator Prof. Gail J. Roboz, MD, at Weill Cornell



# UCART22

## Targeting R/R ALL



### Unmet Medical Need

- Proven target for ALL and potentially NHL
- No solution for relapsed patients after CD-19 directed CAR T-cell treatment
- Loss of CD-19 antigen requires new CAR T-cell target

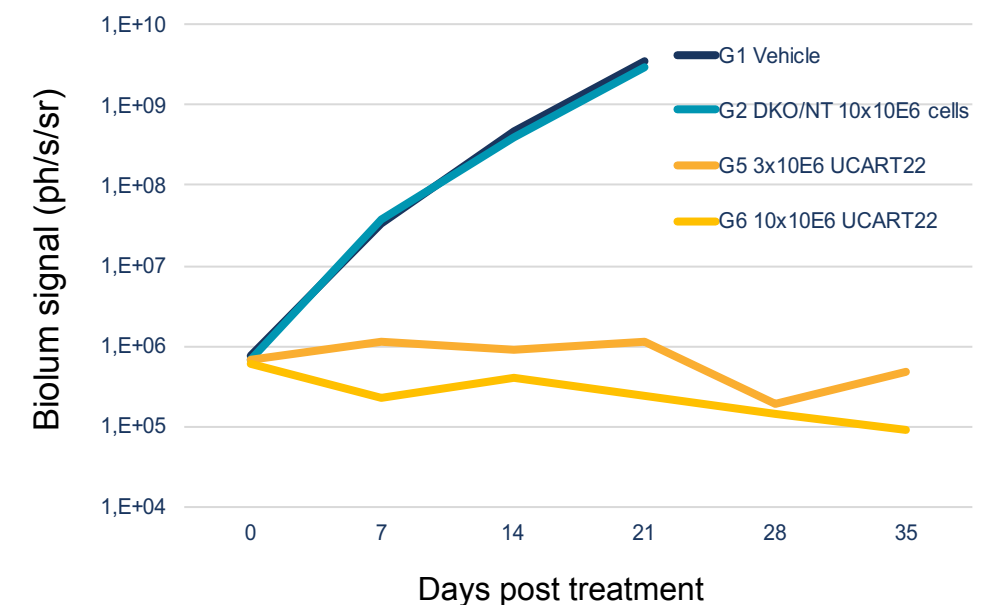
### Pre-Clinical Data

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

### Enrolment Strategy

- Relapsed / refractory adult ALL patients first
- Enrolment open to CD19 treatment naïve patients
- Open also to anti-CD19 pre-treated relapsing patients
- Selection of strong CD22 expressing B-malignant cells (>2,000 CD22/cell)
- First dose cohort starting at  $1 \times 10^5$  UCART22 cells per kg
- Age limit is 65 years
- Transplant after UCART22 treatment not a requirement

### CD22+ Cell Line Show no Tumor Progression



# UCARTCS1

## Targeting Multiple Myeloma



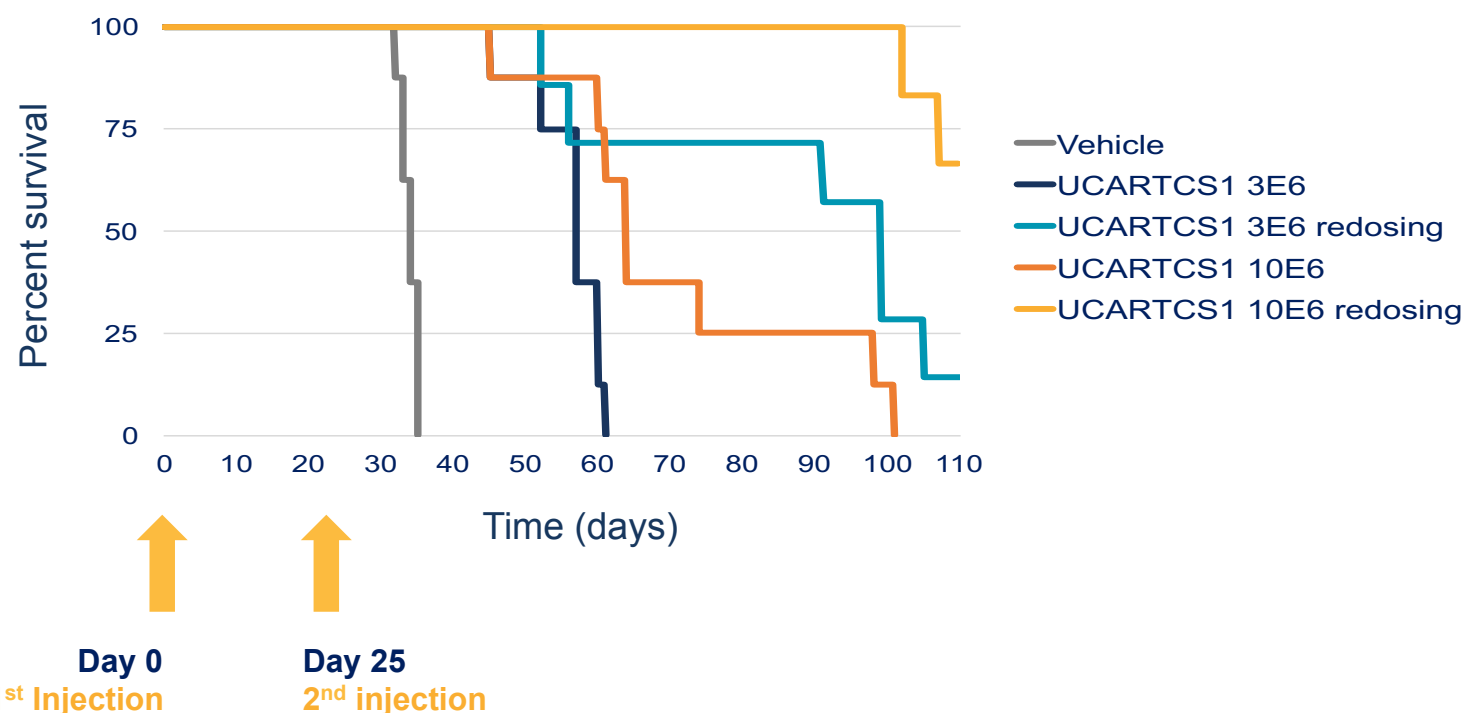
### Unmet Medical Need

- > 30,000 patients / year in the US
- High relapse rate, median OS of 9 months
- Autologous BCMA-targeted CAR T-cell therapies show high relapse rate
- Need for potential multiple dosing strategy

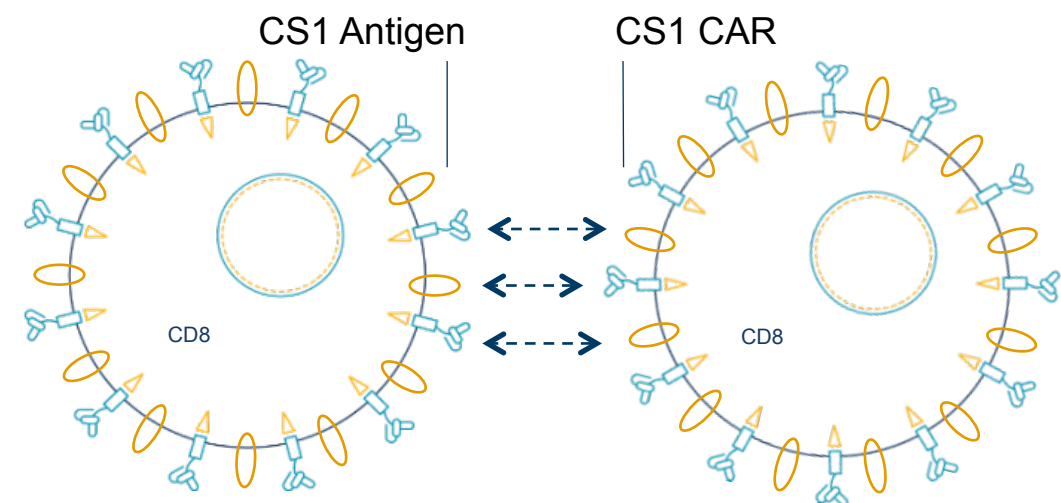
### Pre-Clinical Data

- Strong anti-tumor effect in mice
- Mice injected with two consecutive doses of UCARTCS1 show longer survival than single dose injected mice
- Total number of cells of two doses is lower than single dose

Two consecutive doses vs single dose of UCART CS1 :



Knock-Out of CS1 on CAR T-Cells to disable cross-reaction

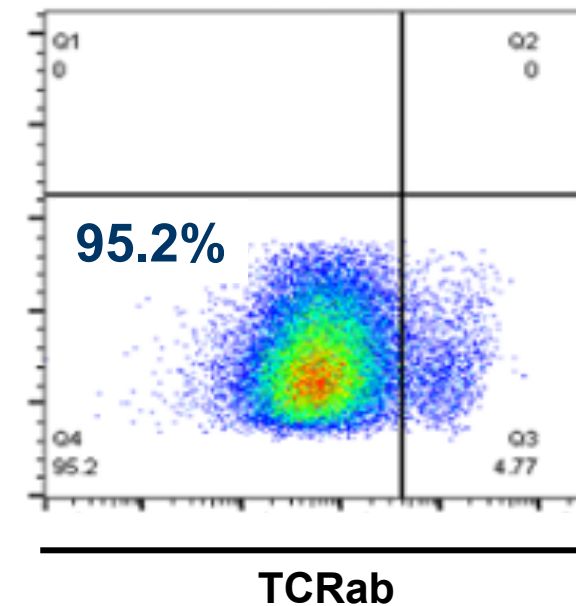


# Proprietary TALEN<sup>®</sup> Gene-Editing Platform

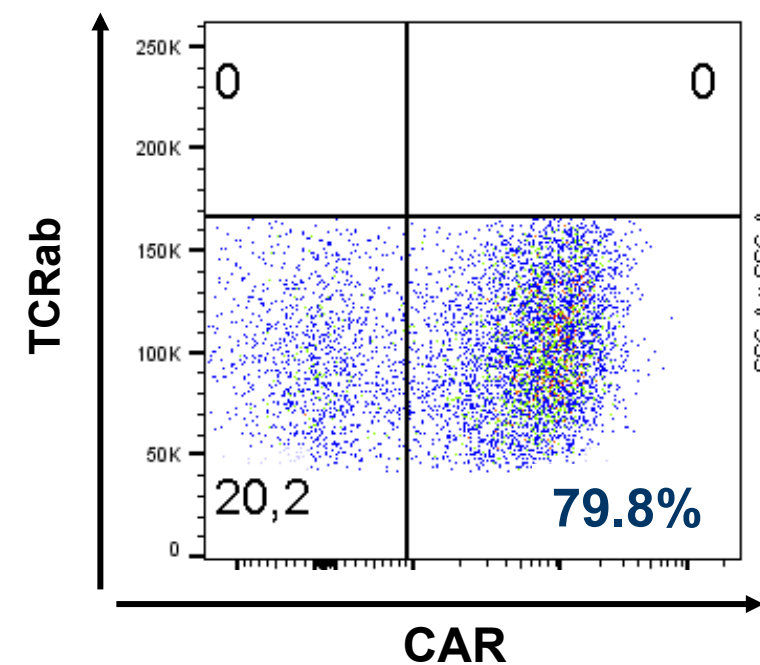


*High Knock-Out and Knock-In Efficiencies*

- **95.2% single targeted gene knock-out**
  - TRAC Knock-Out



- **~80% single gene integration**
  - CAR Knock-In at TRAC Locus

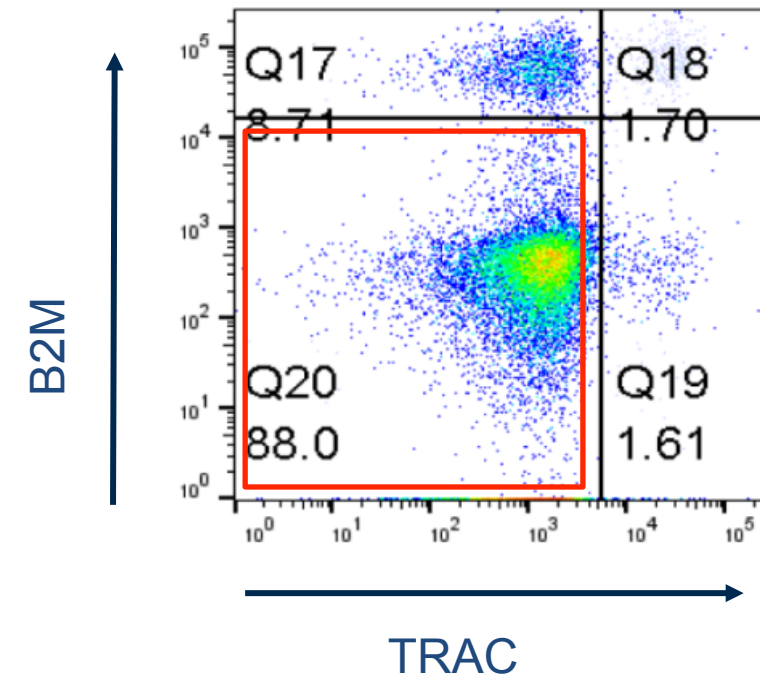


# TALEN<sup>®</sup> High Yield Multiplex Gene Editing

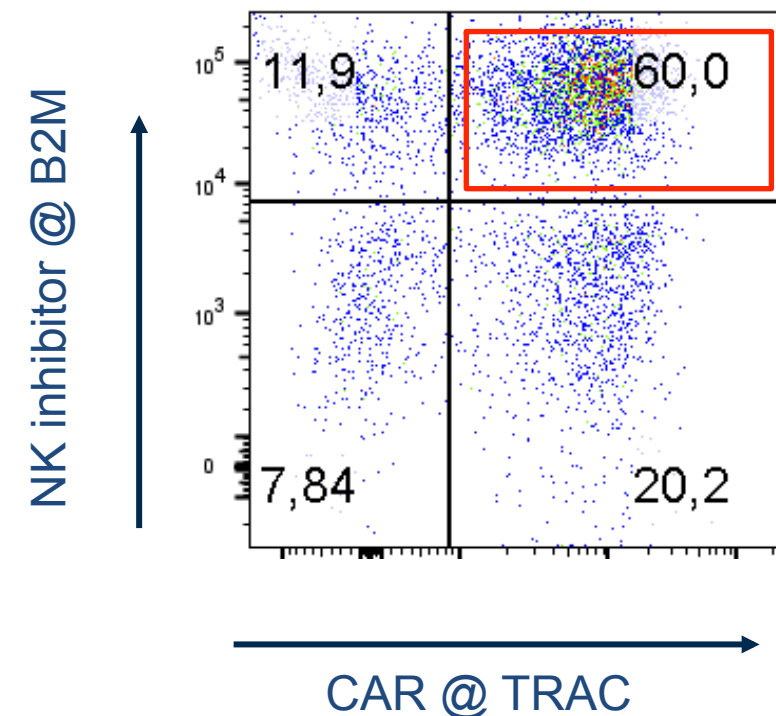


## Combining Knock-Out and/or Knock-In in T-Cells

- **88% double targeted gene knock-out**
  - TCR and B2M



- **60% double targeted gene insertion**
  - CAR insertion at TCR
  - NK inhibitor at B2M



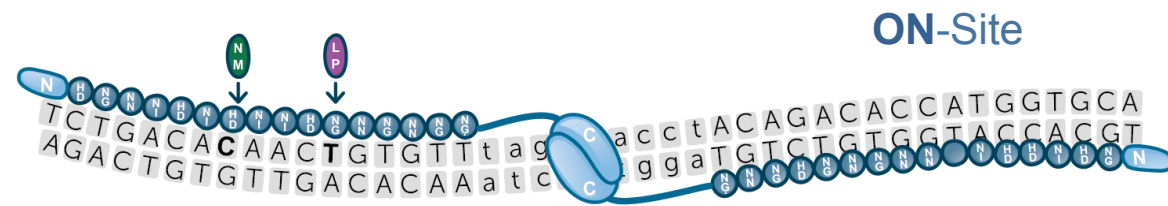
# Control of TALEN<sup>®</sup> Off-Target Effect



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



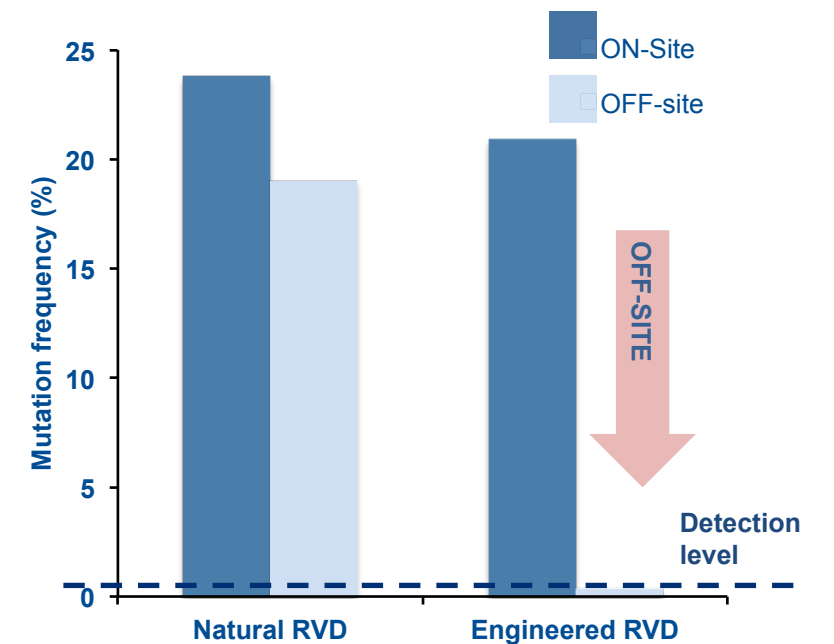
ON-Site

ON-site/OFF-site > 94 % identity

HBD



OFF-Site



Juillerat et al (scientific report 2015)

PD1

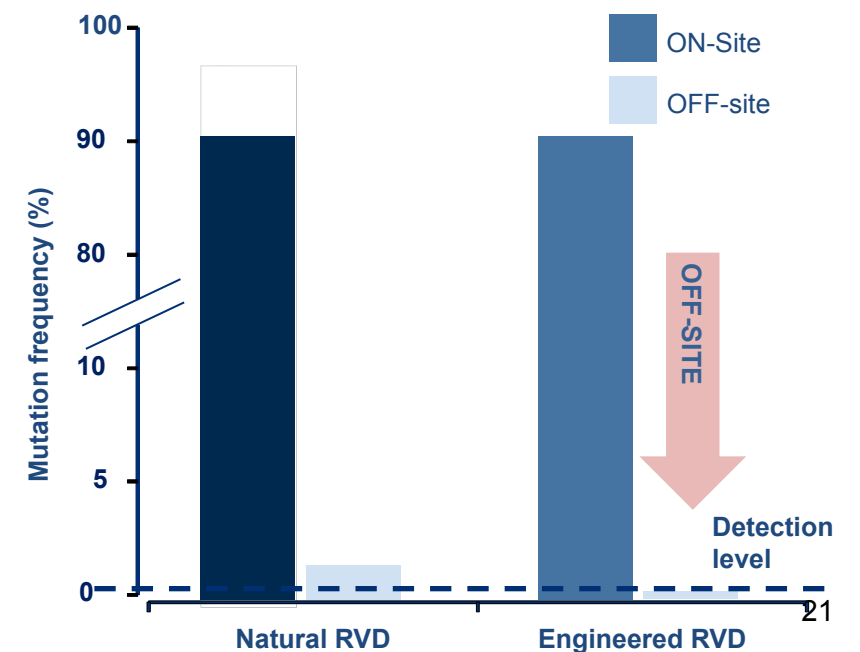


ON-Site

Chr17 q24.1



OFF-Site



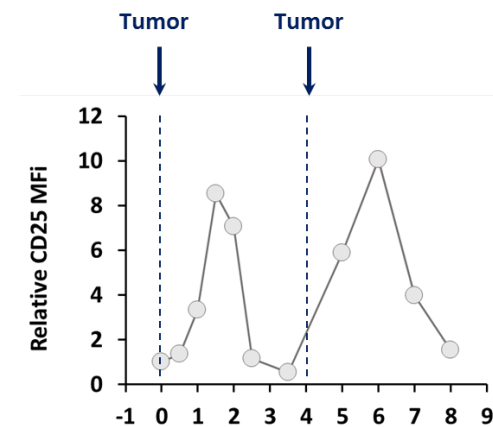
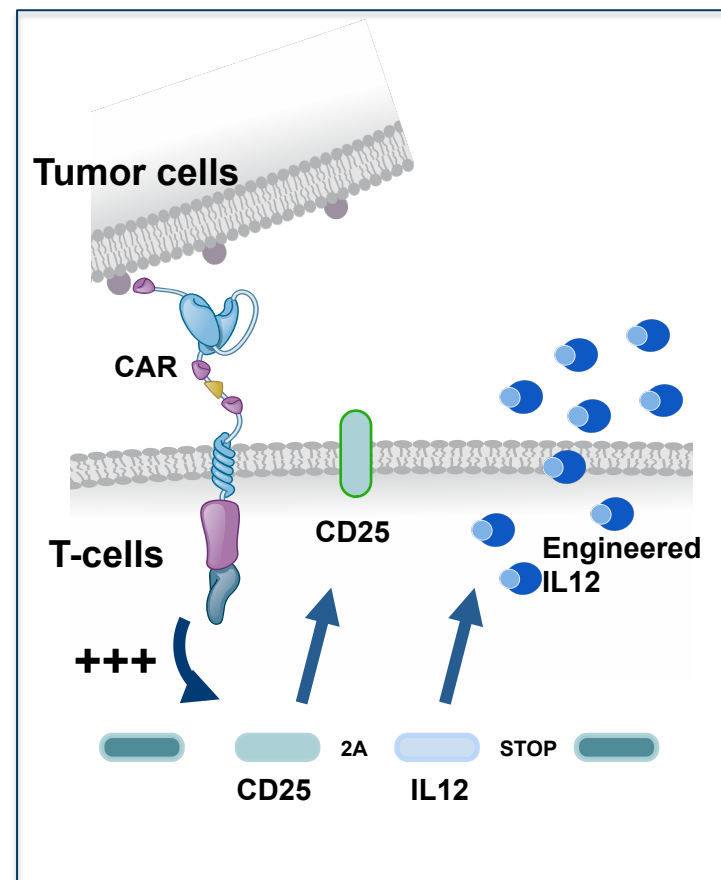
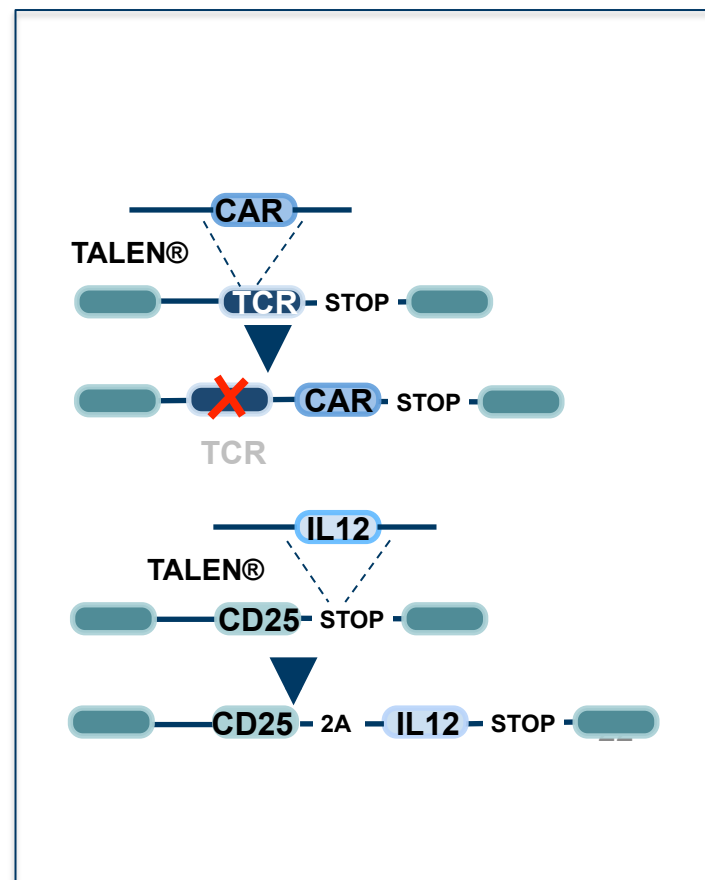
# Next Gen. CAR-T Cells Targeting Solid Tumors



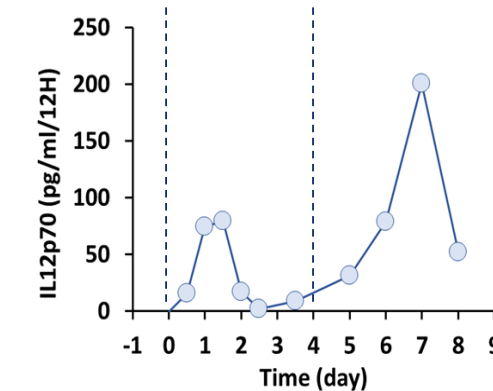
## Synthetic Biology For High Performance UCARTs

### Example of targeted integration at CD25 locus

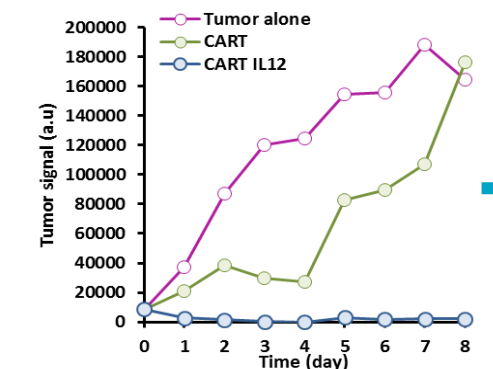
- IL12 contributes to anti tumor activity (Th1, NK, CD8)
- I.V. IL12 shows systemic adverse effects (BM, Liver, mucus membranes)
- Local On-Target IL12 secretion may avoid systemic toxicity



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

# The Collectis Group



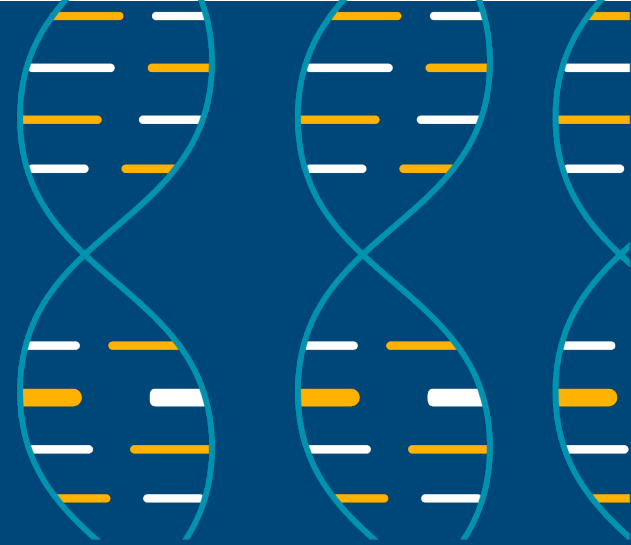
- NASDAQ: CLLS
- EURONEXT GROWTH: ALCLS
- 491M\$ cash as of June 30, 2018
- Expected to fund operations into 2022

70,2% ownership



- NASDAQ: CLXT
- 106M\$ cash as of June 30, 2018
- Based in Minnesota
- Consumer focus
- High value asset

• *Gene editing is the link* •



# THANK YOU



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