



# ENGINEERED CAR-T THERAPIES

A NEW PARADIGM IN ONCOLOGY

FEBRUARY 2017

# FORWARD LOOKING STATEMENTS



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# GENE EDITED ALLOGENEIC UCARTs

Entering clinical development



# Entering Clinical Development

## UCART123 in AML & BPDCN

### UCART123 product candidate is ready to enter clinical trials

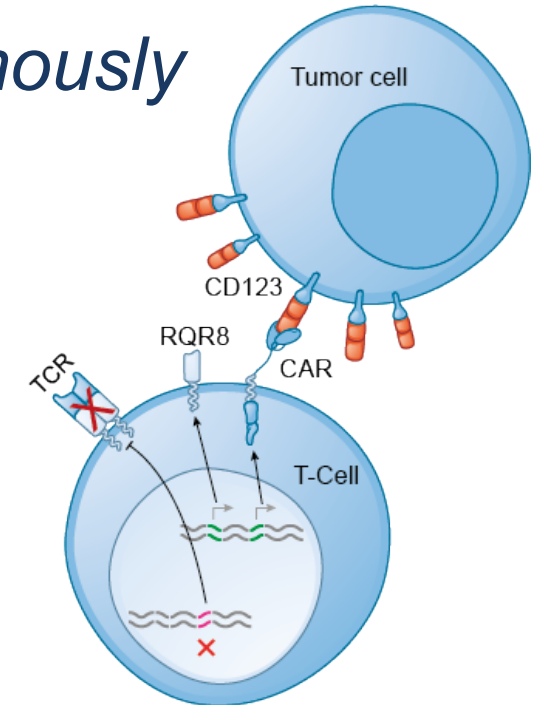
- ✓ *NIH Recombinant DNA Advisory Committee (RAC) unanimously approved proposed clinical trial protocols*
- ✓ *IND has been filed in December 2016*
- ✓ *FDA gave the green light for both Phase I studies early February 2017*

- **AML Phase 1 trial at Weill-Cornell**

PI: Pr. Gail Roboz, *Professor Of Medicine and Director Of Clinical and Translational Leukemia program at Weill Cornell Medical College, New York Presbyterian Hospital*

- **BPDCN Phase 1 trial at MD Anderson**

PI: Dr. Naveen Pemmaraju, *Assistant Professor, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center*

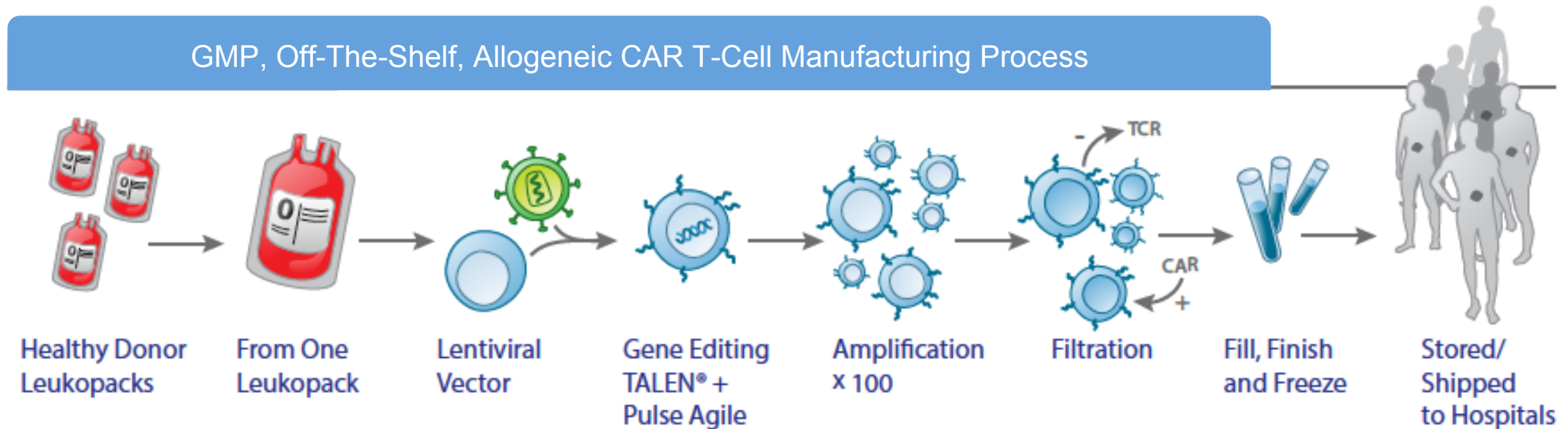




# Entering Clinical Development

## A Rolling GMP Manufacturing Process

- ✓ Succeeded in producing UCART19 in Q4 2015
- ✓ Succeeded in producing UCART123 in Q4 2016
- ✓ Initiated technology transfer for UCARTCS1 in Q4 2016



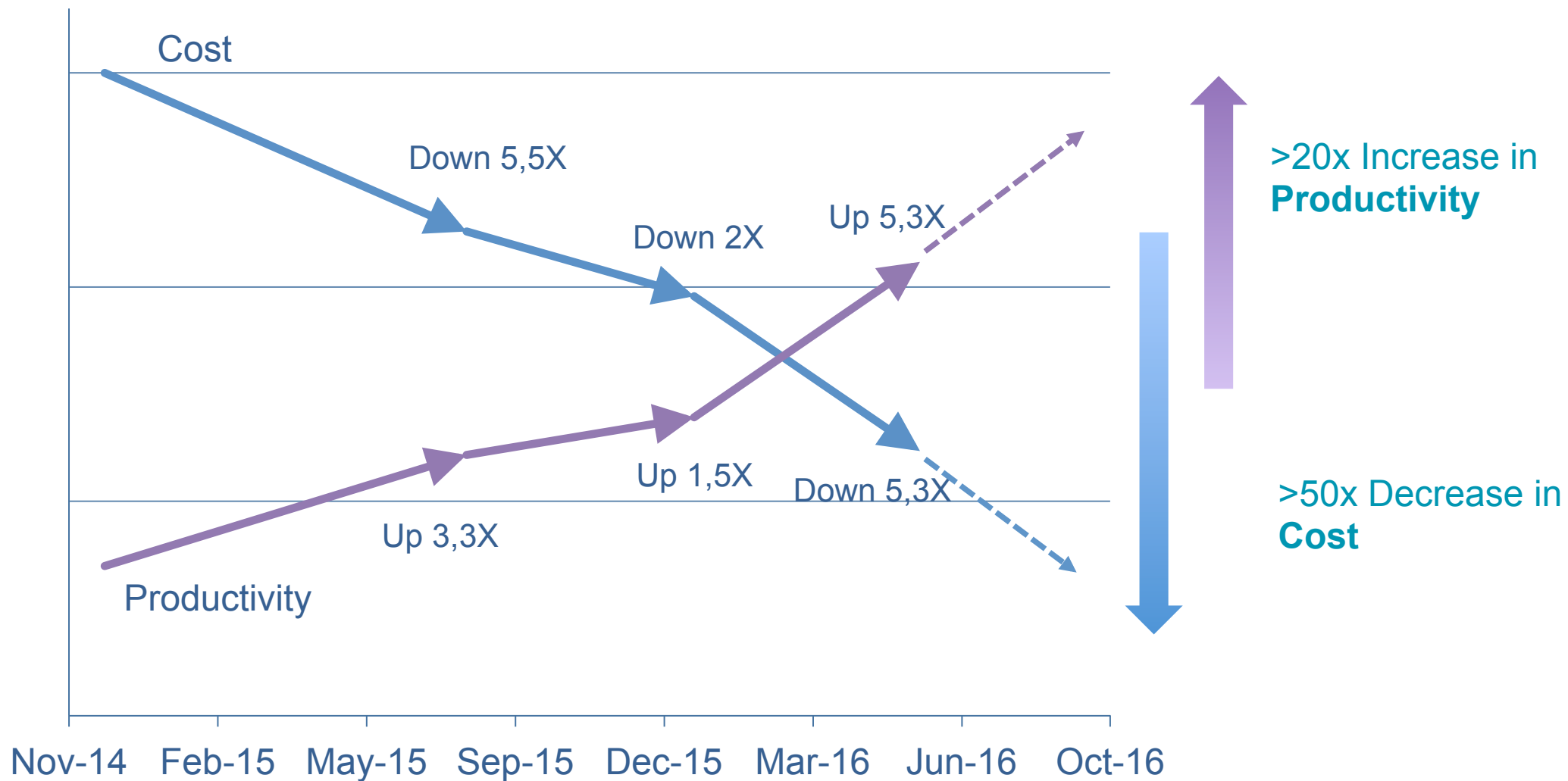
>100's of frozen doses per manufacturing campaign  
Vials are frozen, shipped and stored



# Entering Clinical Development

## Increasing Yields, Decreasing CoGs

- Worldwide, immediate access to patients
- CoGs already decreased by a factor of 5x



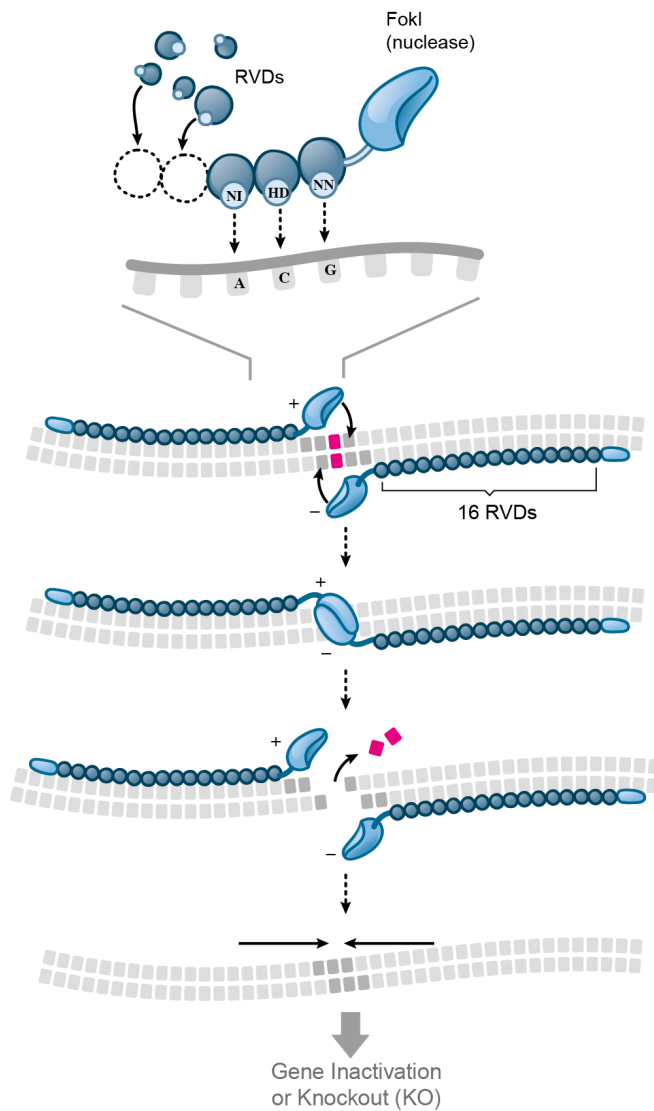
**UCART123**  
**< \$4000/dose\***

\* Anticipated CoGs based on current conditions and an effective dose at 6.25E5 UCART vialled cells/kg

# Entering Clinical Development

## An integrated Gene Edited Cell Therapy Platform

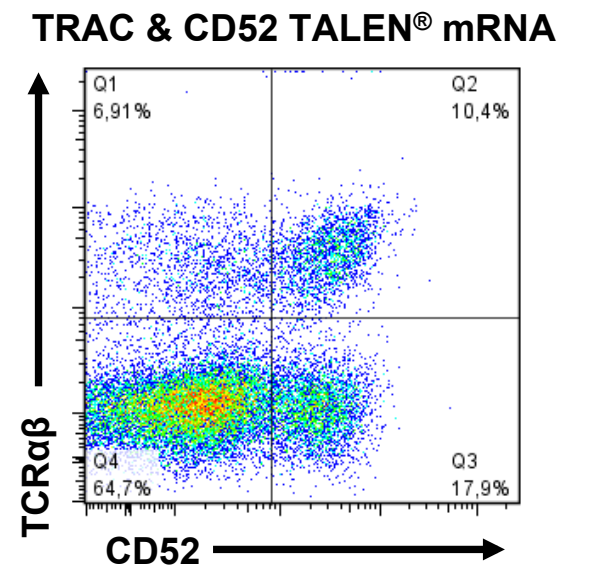
### TALEN® Gene Editing



### CytoPulse Electroporation



High Cell Transduction  
High Gene Editing Rate  
High Cell Survival



High Yield & Quality  
Cell Therapy products



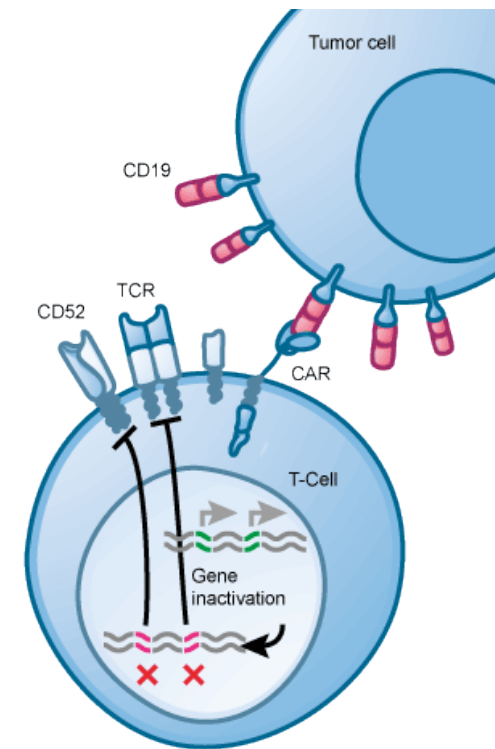
Licensed from UMN in 2011

Asset acquired in 2010

# Entering Clinical Development

## UCART19 as Proof of Concept

- Servier acquired exclusive rights to UCART19 from Cellectis (November 2015)
- Joint clinical development program between Servier and Pfizer
- Servier has granted Pfizer exclusive rights to develop and commercialize UCART19 in the US
- Servier retains exclusive rights for UCART 19 for Ex-US
- Phase 1 Pediatric ALL (PALL)
  - Started June 2016 at University College London (UCL), UK
- Phase 1 Adult ALL (CALM)
  - Started July 2016 at King's College London (KCL), UK
  - Pre-IND meeting in October 2016 for expansion into the US
  - RAC meeting in December 2016





# Entering Clinical Development

## UCART19\* Preliminary Data



### In Relapsed/Refractory ALL Patients

Data Presented at the RAC meeting on December the 14<sup>th</sup> 2016

Study	Age	Relevant Non-Hematologic AE	Status
Compassionate Use	11 months**	• Grade 2 Skin GvHD	Alive, MRD-, 18+ Months
	16 months***	• Grade 1 Suspected Skin GvHD	Alive, MRD-, 12+ Months
	44 years	• Grade 1 CRS	Died, Progressive Disease
PALL Study (pediatric ALL patients)	4.8 years	• Grade 3 CRS • Grade 1 Suspected Skin GvHD • Grade 1 Neurological	Alive, 6+ Months, Relapsed
	2.7 years	• Grade 2 CRS • Grade 1 Neurological	Alive, MRD-, 4+ Months
CALM Study	42 years	• Grade 2 CRS	Alive, MRD-, 4+ Months
(adult ALL patients)	18 years	• Grade 4 CRS	Died, Cause Under Investigation

\* Exclusively licensed to Servier

\*\* Qasim W et al., ASH 2015

\*\*\*Qasim W et al., ASGCT 2016

# UCART123

Our lead product candidate in  
AML & BPDCN

# UCART123

## CD123 (IL-3R $\alpha$ ), a High-Value Target

### *Acute Myeloid Leukemia (AML)*

#### ➤ *Phase 1 dose escalation at Weill-Cornell; IND cleared 2/2017*

- 19,950 new cases of AML in the US in 2016 were diagnosed with 10,430 deaths
- Five-year survival 15-70%; relapse rate 33-78%, depending on age and subtype
- No major advances in the treatment of AML in 30 years
- Trial in the setting of relapsed/refractory AML and 1<sup>st</sup> line high risk AML
- Orphan Drug Designation potential

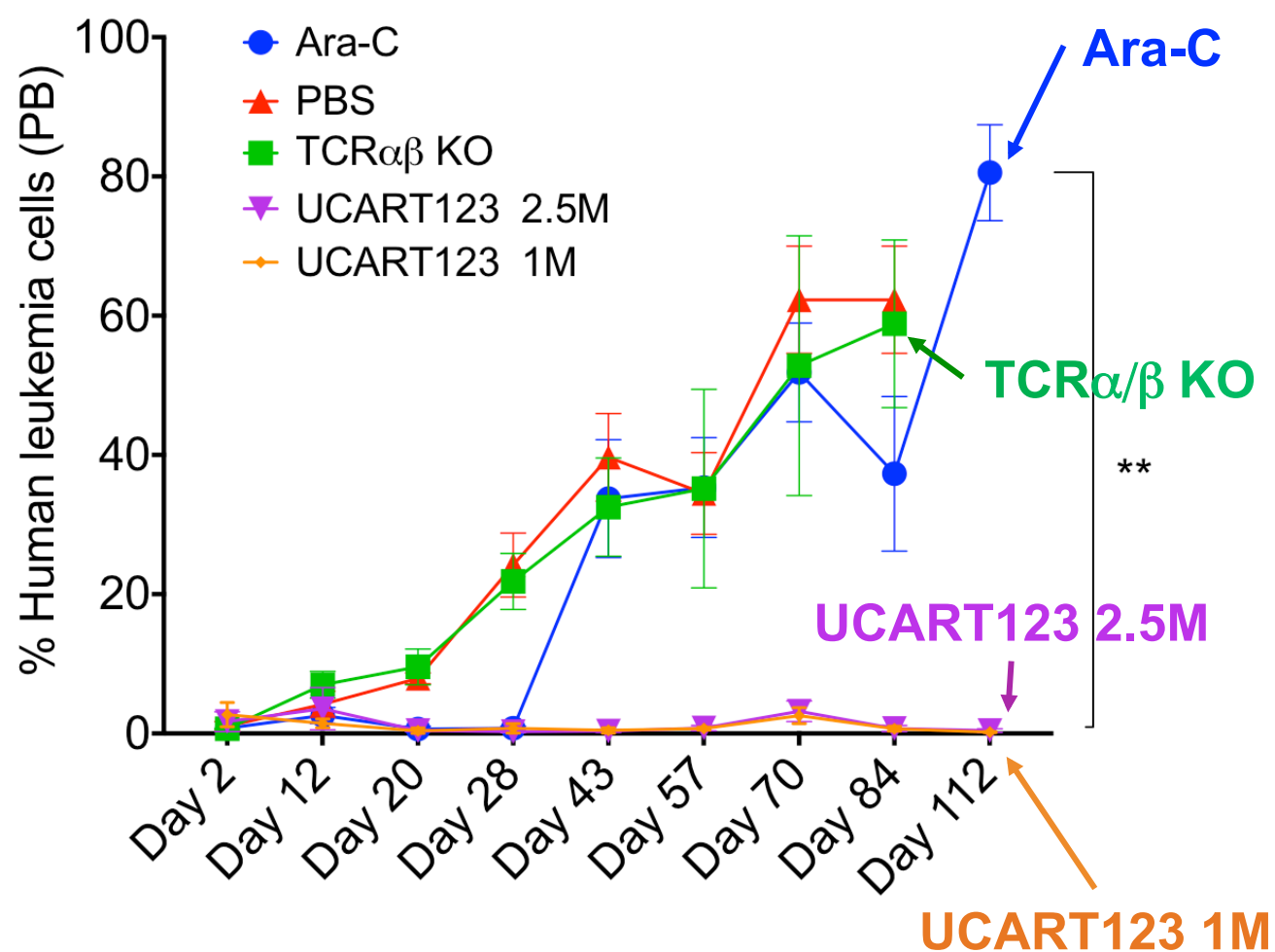
### *Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)*

#### ➤ *Phase 1 dose escalation at MD Anderson; IND cleared 2/2017*

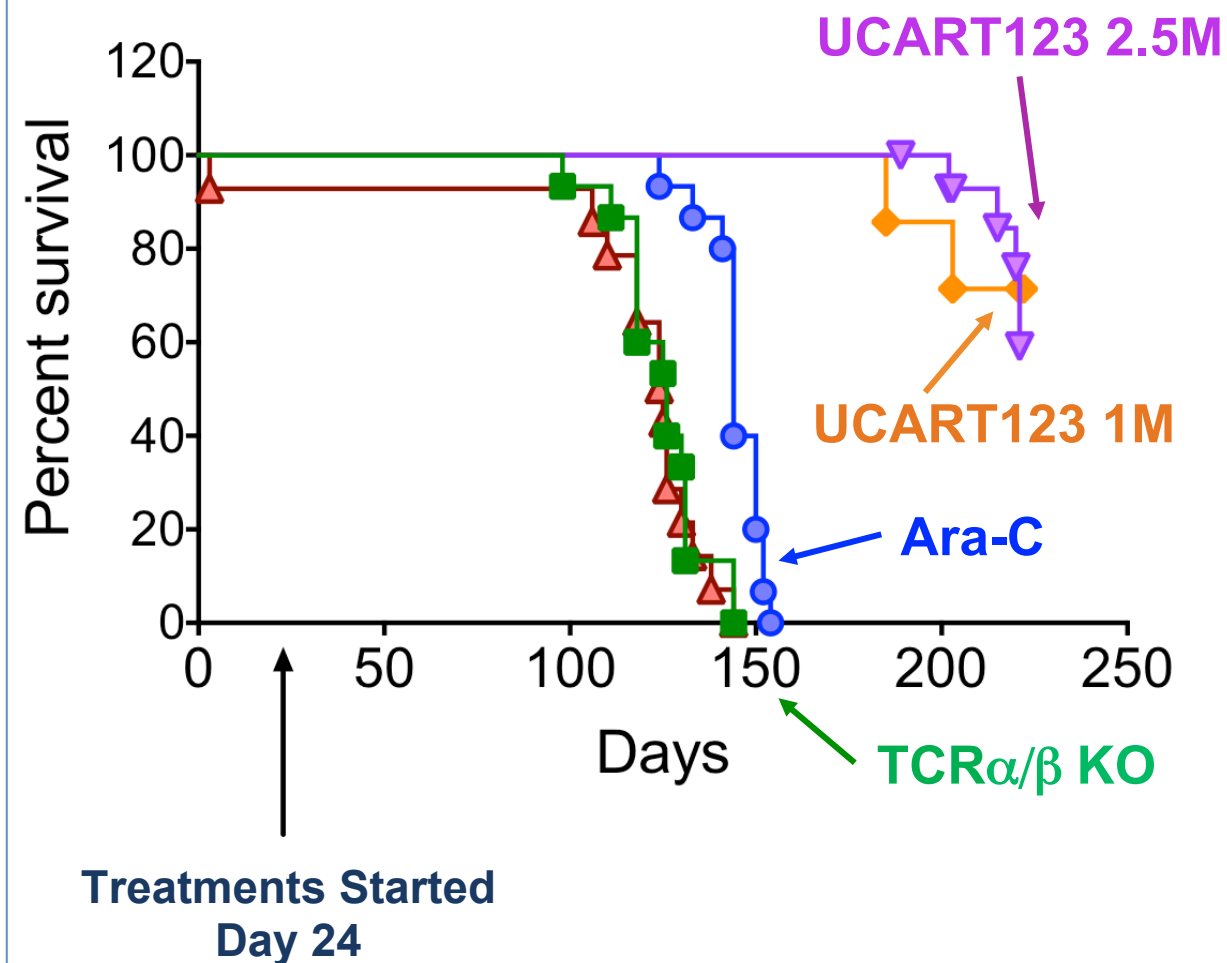
- Rare disease involving bone marrow, skin, lymph nodes with no standard of care
- In the US, a few hundred cases are diagnosed per year
- Classified under Myeloid Neoplasms and Acute Leukemia (WHO classification 2016)
- Orphan Drug Designation potential

➤ UCART123 significantly decreases tumor burden and improves survival

### Peripheral Blood Evaluation



### Overall Survival





# UCART123

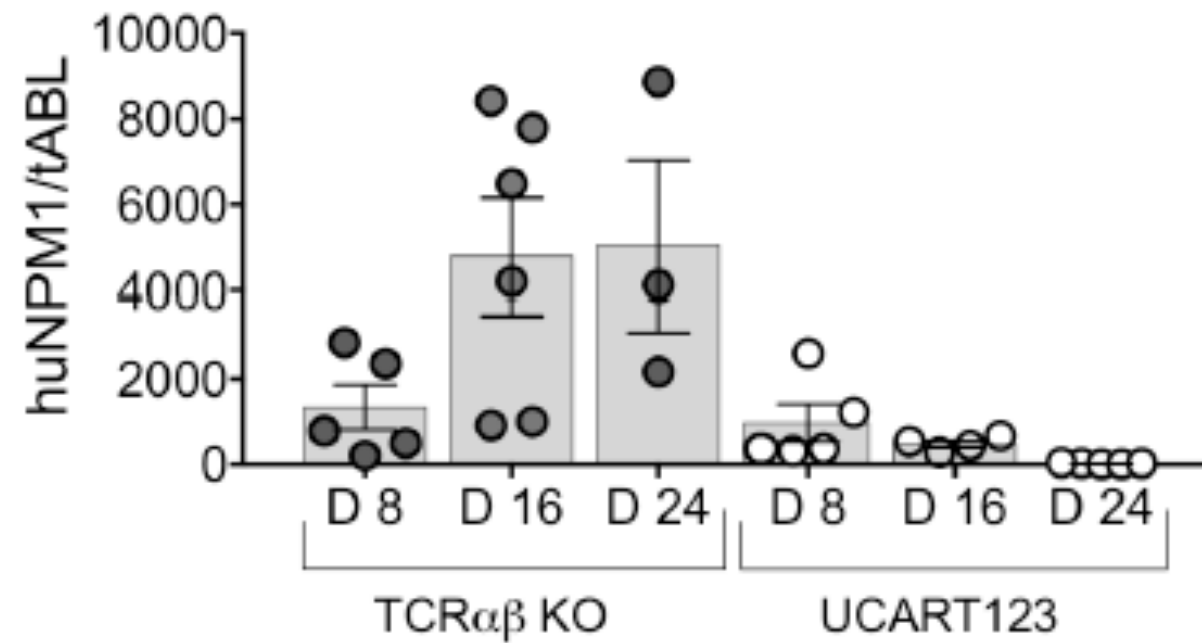
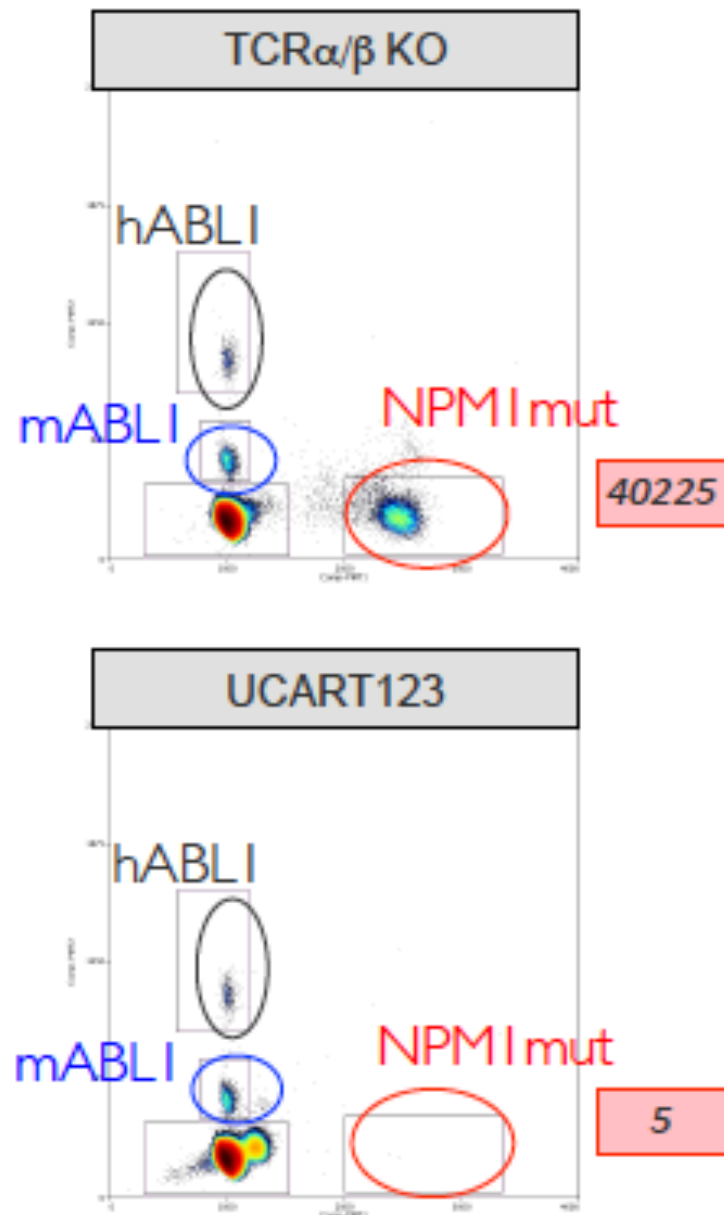
## Encouraging Preclinical Efficacy Data



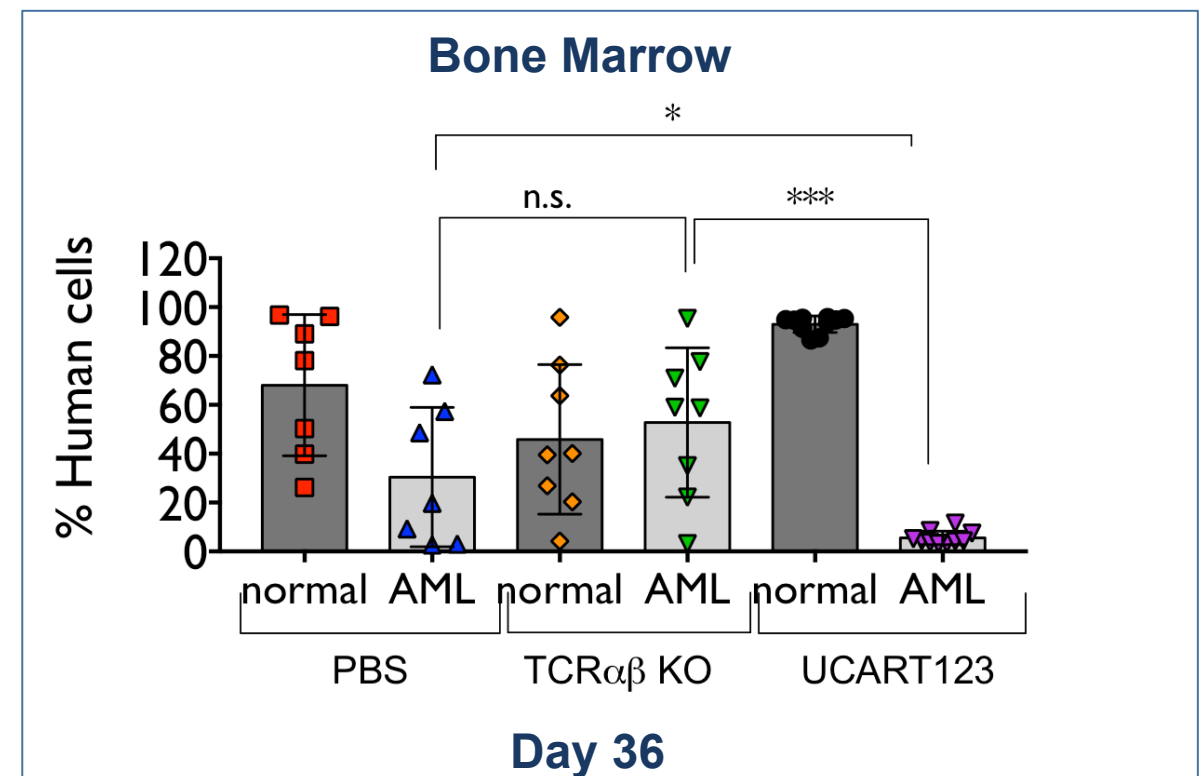
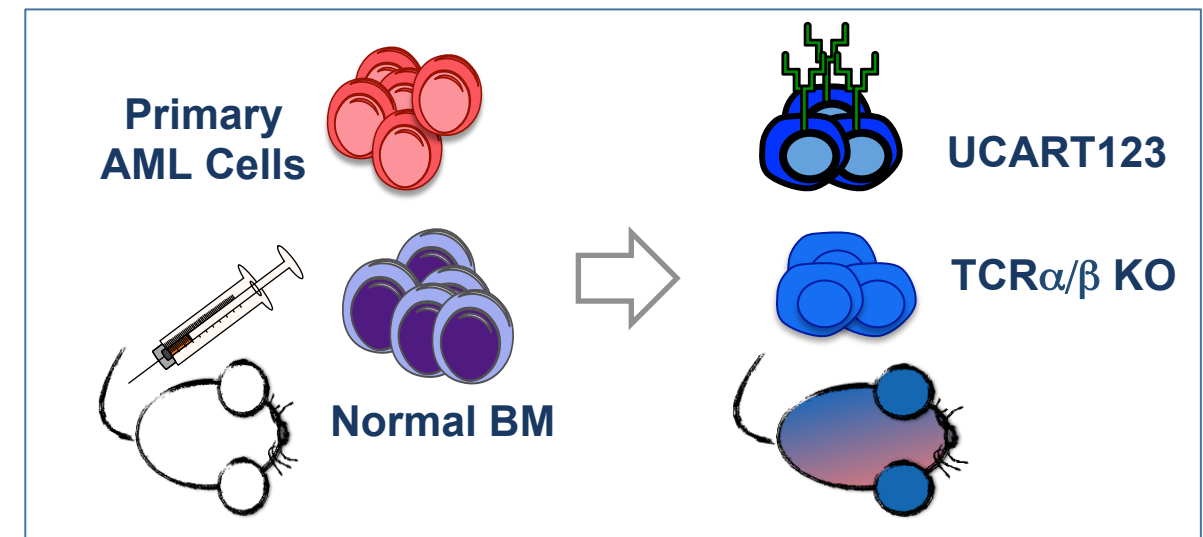
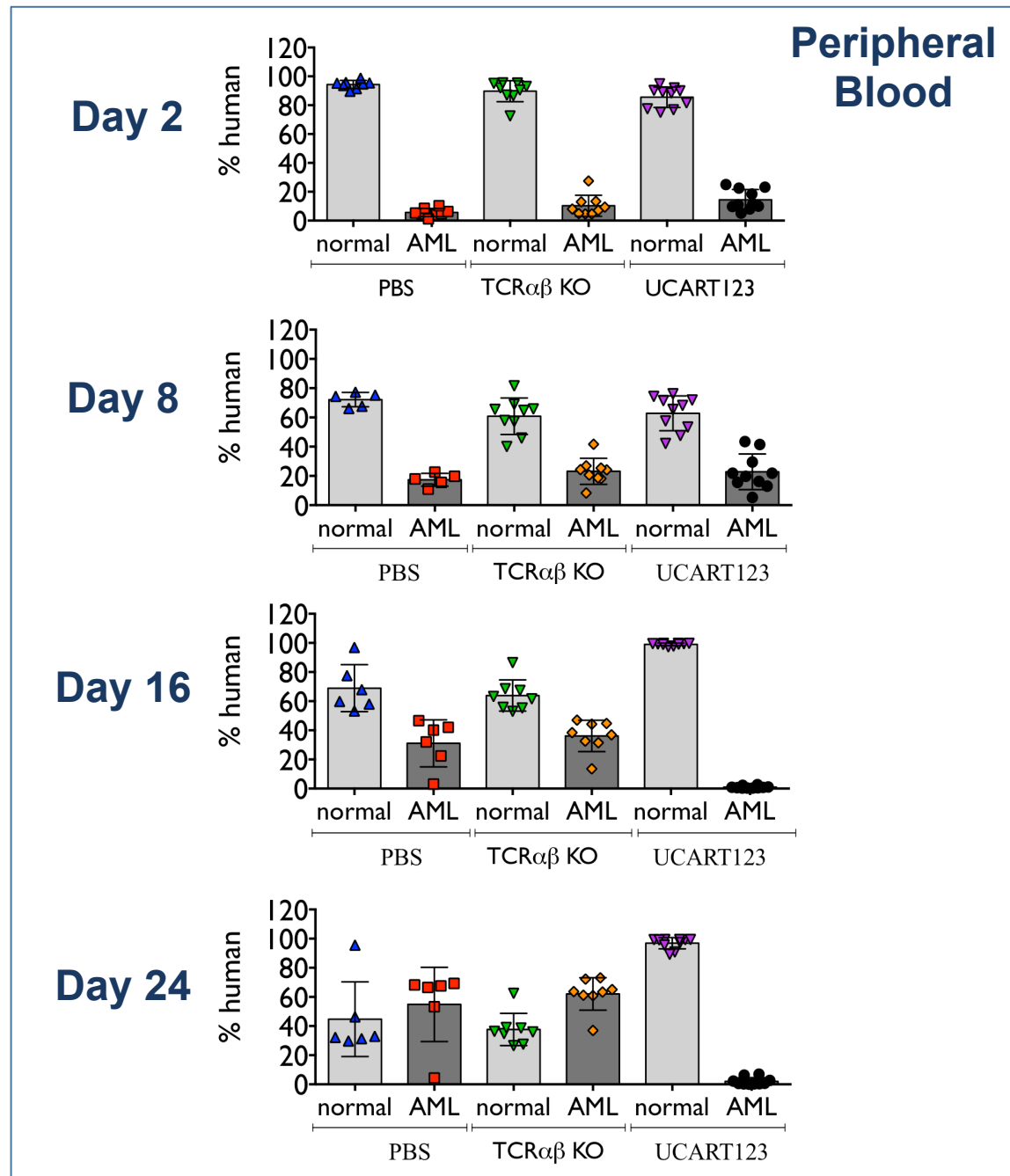
Weill Cornell  
Medicine



- Animals treated with UCART123 achieve molecular remission



➤ UCART123 preferentially eliminates AML cells over normal hematopoietic cells

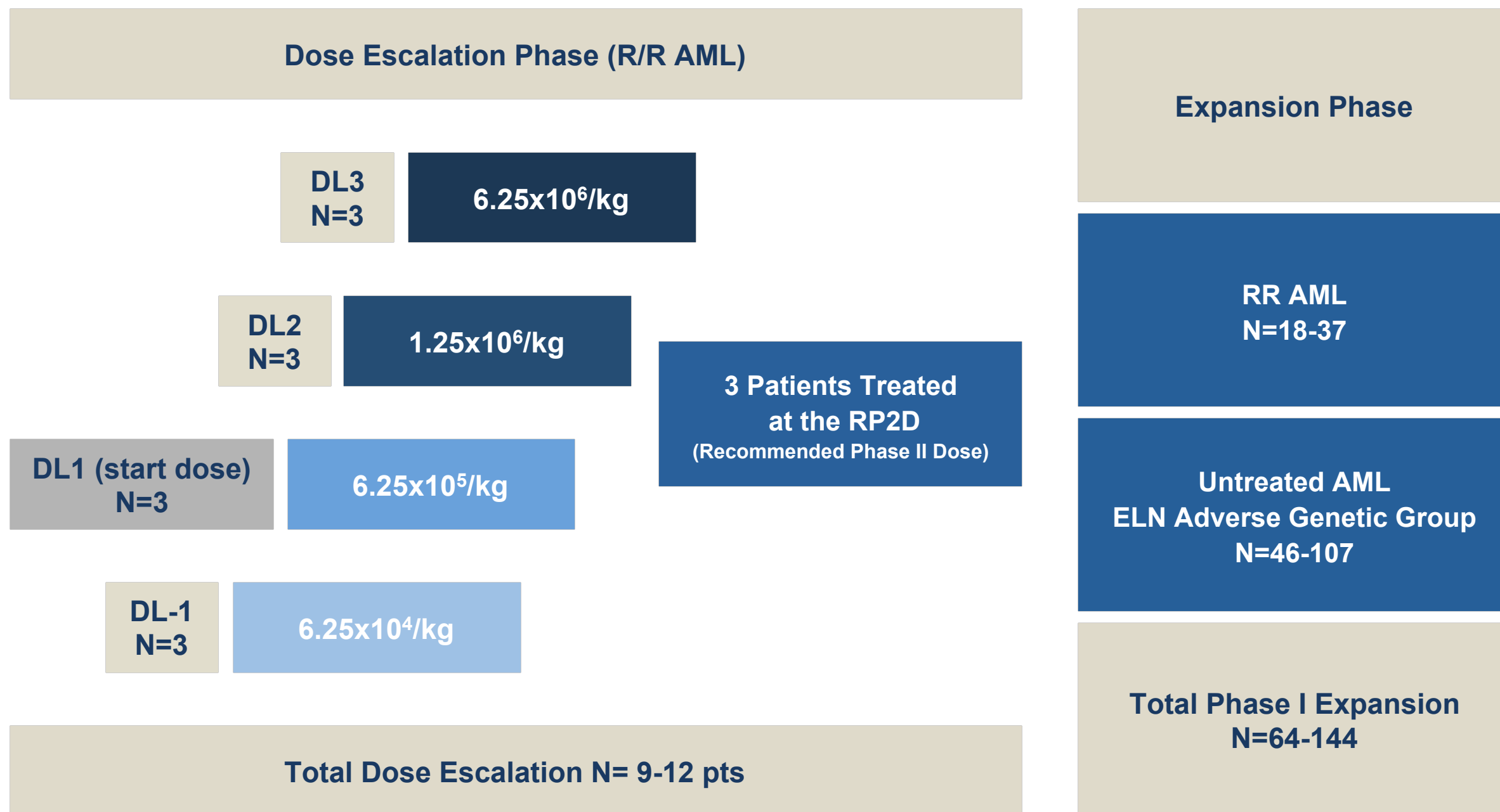


# UCART123

## Study Design for AML

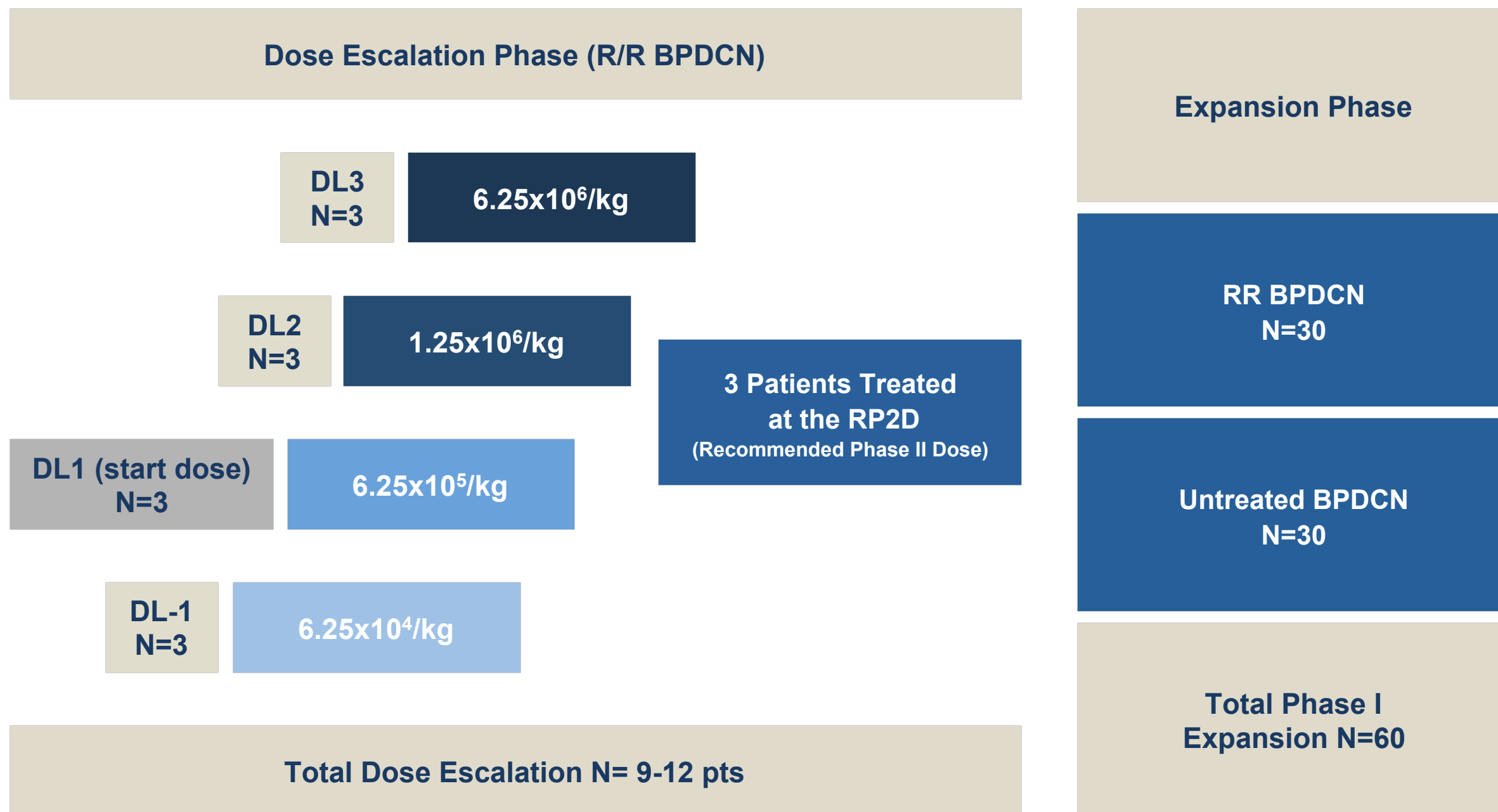


**Weill Cornell  
Medicine**



# UCART123

## Study Design for BPDCN





### Preclinical Proof of Concept UCART123

- *In vitro* and *in vivo* development finalized

completed November 2016



### Manufacturing UCART123

- High yield, high potency cGMP batches

achieved November 2016



### NIH RAC meeting

- Unanimous positive recommendation by the RAC

held December 2016



### IND for both indications

- AML Cornell-Weill
- BPDCN MD Anderson

cleared February 2017



### Phase 1

- First patient enrollment

expected Q2 2017

### Potential clinical developments

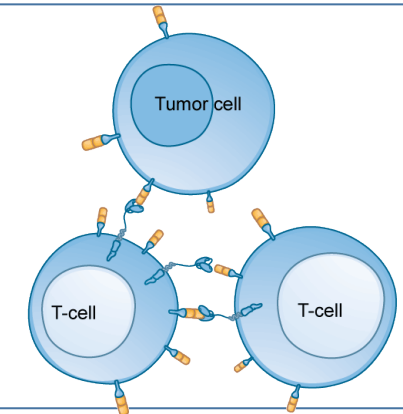
- CD19 negative Relapse Acute Lymphoid Leukemia (B-ALL)
- Myelodysplastic Syndromes (MDS)
- Chronic Myeloid Leukemia (CML)
- Hodgkin's Lymphoma (HL)
- Hairy Cell Leukemia (HCL)
- Systemic Mastocytosis

### Taking Gene-Edited CARTs one step ahead

#### *Targets expressed on T-Cells Surface*

Gene must be KO from T-Cells to prevent cross T-Cell reaction (self killing)

- CS-1 : Mab PoC → Elotuzumab
- CD38: Mab PoC → Daratumumab



#### *Targets expressed on vital tissues*

Long term persistence can lead the non reconstitution of tissue

- CD123 is expressed on bone marrow stem cells, a long term persistence of anti-CD123 CART could be toxic and lead to durable aplasia

#### *New CART dosing after relapse with an initial CART treatment*

Alternate CART treatment could be used as a salvage therapy

- Relapsing CD19 negative patient could potentially be treated with UCART22

# UCART Pipeline

Addressing a large tumor spectrum

Program	Indication	Product development	Preclinical	Manufacturing	IND Filing*	Phase I	Phase II
UCART19**	ALL (PALL)	█	█	█	█	█	█
	ALL (CALM)	█	█	█	█	█	█
UCART123	AML	█	█	█	█	█	█
	BPDCN	█	█	█	█	█	█
	CML	█	█	█	█	█	█
	HL	█	█	█	█	█	█
	HCL	█	█	█	█	█	█
	MDS	█	█	█	█	█	█
UCARTCS1	MULTIPLE MYELOMA	█	█	█	█	█	█
UCART22	B-ALL	█	█	█	█	█	█
	B-NHL	█	█	█	█	█	█
	B-CLL	█	█	█	█	█	█
UCART38	MULTIPLE MYELOMA	█	█	█	█	█	█
	T-CELL ALL	█	█	█	█	█	█
	NHL	█	█	█	█	█	█
	MCL	█	█	█	█	█	█

\* or European equivalent

\*\* Joint clinical development program between Servier and Pfizer



- Collaboration on 15 targets: 1<sup>st</sup> allogeneic BCMA CART
- 4 years exclusivity on CARTs in human oncology
- \$2.8B in total aggregated milestones
- Tiered Royalties on net sales



- Collaboration on 5 targets including UCART19
- UCART19 pediatric and adult trials ongoing in the UK
- \$974M in aggregate total milestones
- Tiered Royalties on net sales





## Weill Cornell Medicine

- Development of UCART123 for AML
- New York-Presbyterian Hospital was ranked in 2016 as New York's No. 1 hospital for the 16th year in a row, and No. 6 ranked hospital in the United States.

THE UNIVERSITY OF TEXAS

## MD Anderson Cancer Center

Making Cancer History®



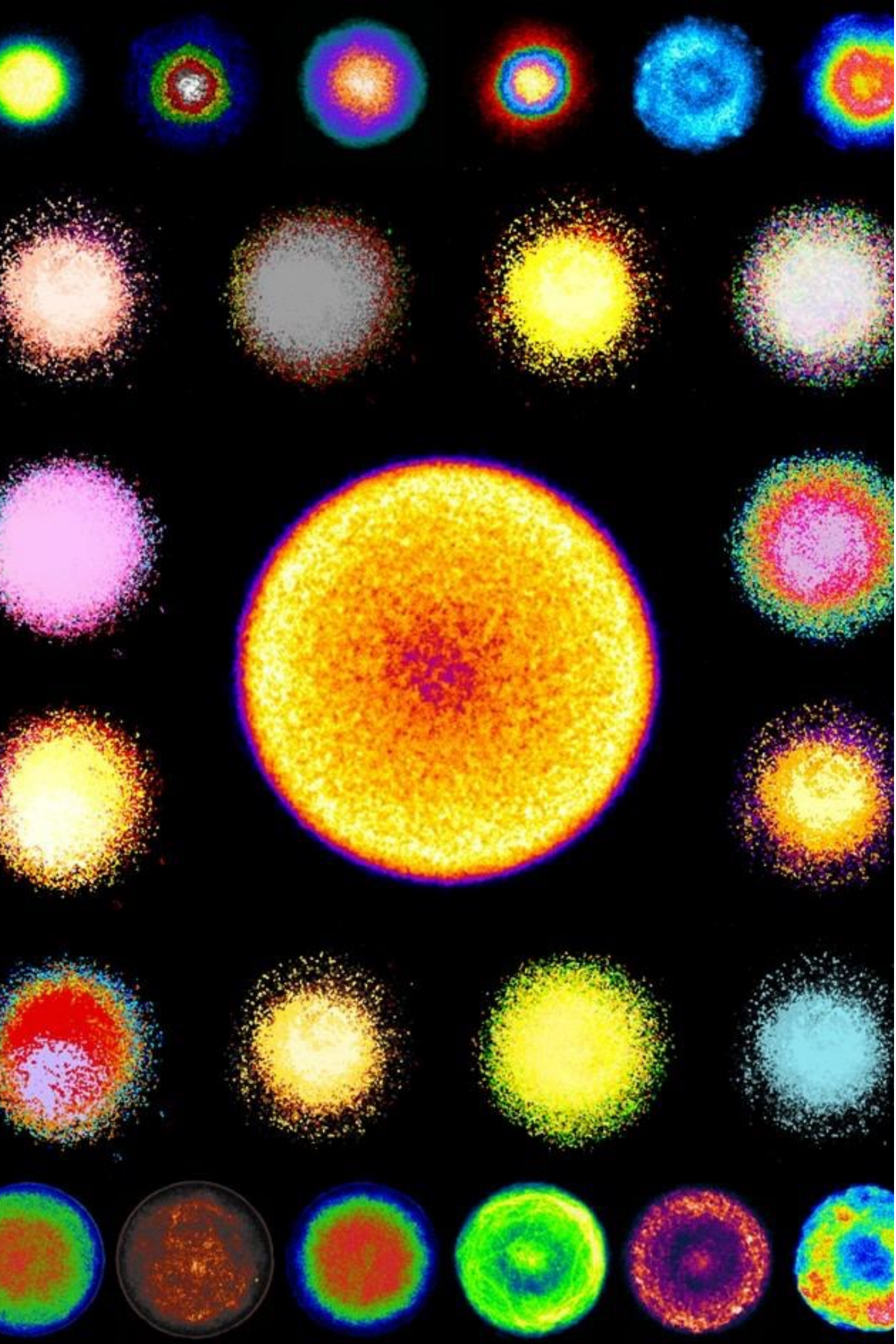
- Development of UCARTCS1 for Multiple Myeloma, UCART22 for ALL, UCART38 in for T-Cell ALL and UCART123 for BPDCN
- MD Anderson is ranked the No. 1 hospital for cancer care in the nation by U.S. News & World Report's "Best Hospitals" survey



- Phase 1 clinical trial of Servier UCART19 in pediatric patients
- Great Ormond Street Hospital, London is ranked among the best hospitals in the UK and top ranking in the world



- Phase 1 clinical trial of Servier UCART19 in adult patients
- King's is one of the world's most prestigious research universities, ranked 21st in the world in 2016/17



# THE PRODUCT CHALLENGE

From process to products



# The Power of Off-the-Shelf CARTs

## Why choosing allogeneic CAR T-Cell products?

Potential to:

1. Immediately available to the patient
2. Patients do not have to provide raw materials
3. Ease of use for physicians
4. If lost, vial can be replaced by a new one
5. Shipped Worldwide, ahead of time
6. Competitive CoGs and logistics costs
7. No compromise on performance
8. Can be dosed and re-dosed



**Allogeneic CARTs:  
Potential to become frozen pharmaceuticals**

# The Power of Off-the-Shelf CARTs

Why choosing allogeneic CAR T-Cell products?



## Cellectis' chartered course

- Early in CAR-T competition (back in 2011)
- Autologous therapies are not our primary strategy
- 1<sup>st</sup> injection in patients in 2015
- Questions at the time:
  - Early rejection?
  - Persistence?
  - Underperformance?
  - GvHD?
- TALEN<sup>®</sup> is setting a precedent for gene editing for patients

Today we lead the way in Allogeneic CARTs



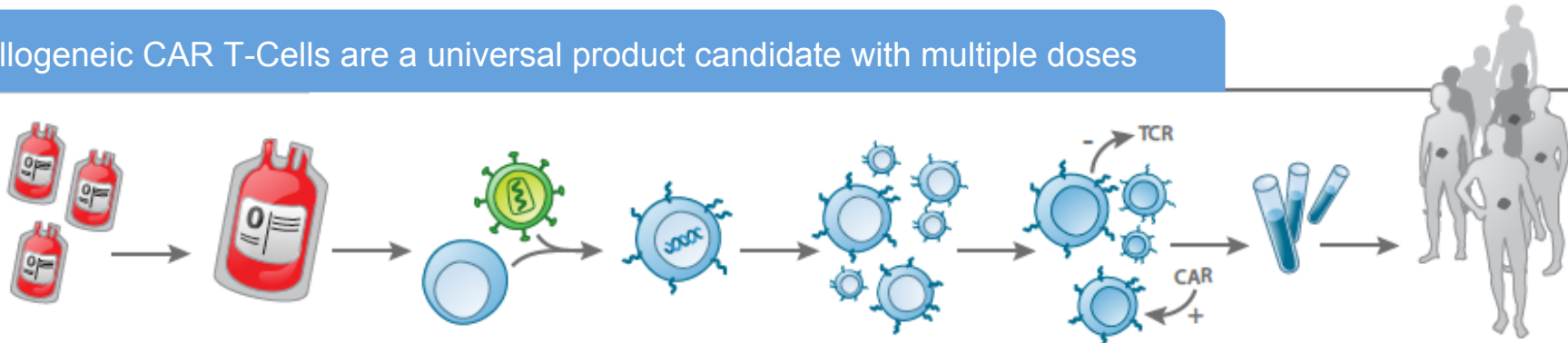
# DISRUPTIVE INNOVATION

How Cellectis is shaping Cell  
Therapies with Breakthrough  
Innovations

# Disruptive Innovation

## Patient-Oriented Therapeutic Proposal

Allogeneic CAR T-Cells are a universal product candidate with multiple doses

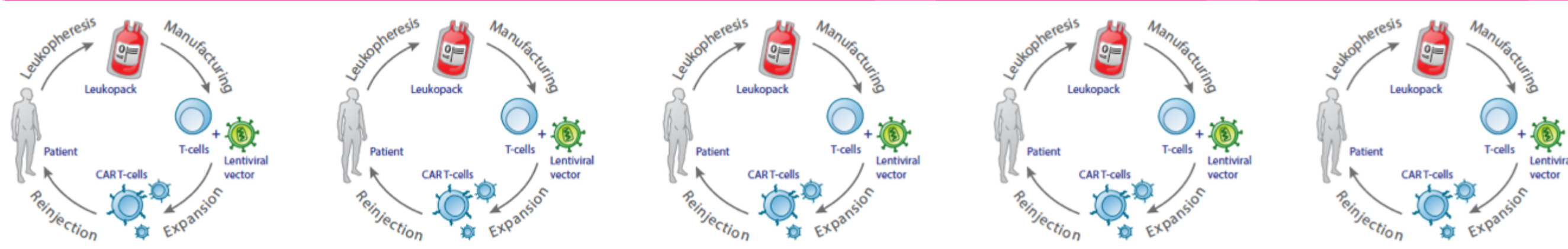


One Leukopack can yield 100s of doses



Product vs. Service

Autologous CAR T-Cells are a personalized therapeutic procedure



1 PROCEDURE  
BENEFITS  
1 PATIENT

1 PROCEDURE  
BENEFITS  
1 PATIENT

1 PROCEDURE  
BENEFITS  
1 PATIENT

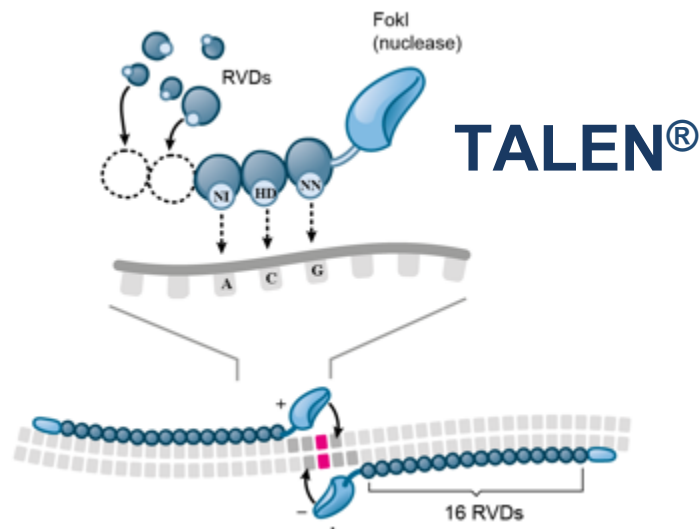
1 PROCEDURE  
BENEFITS  
1 PATIENT

1 PROCEDURE  
BENEFITS  
1 PATIENT

# Disruptive innovation

Three technological pillars for manufacturing allo-CART

## High Quality Gene Editing



## Efficient Electroporation

### PulseAgile

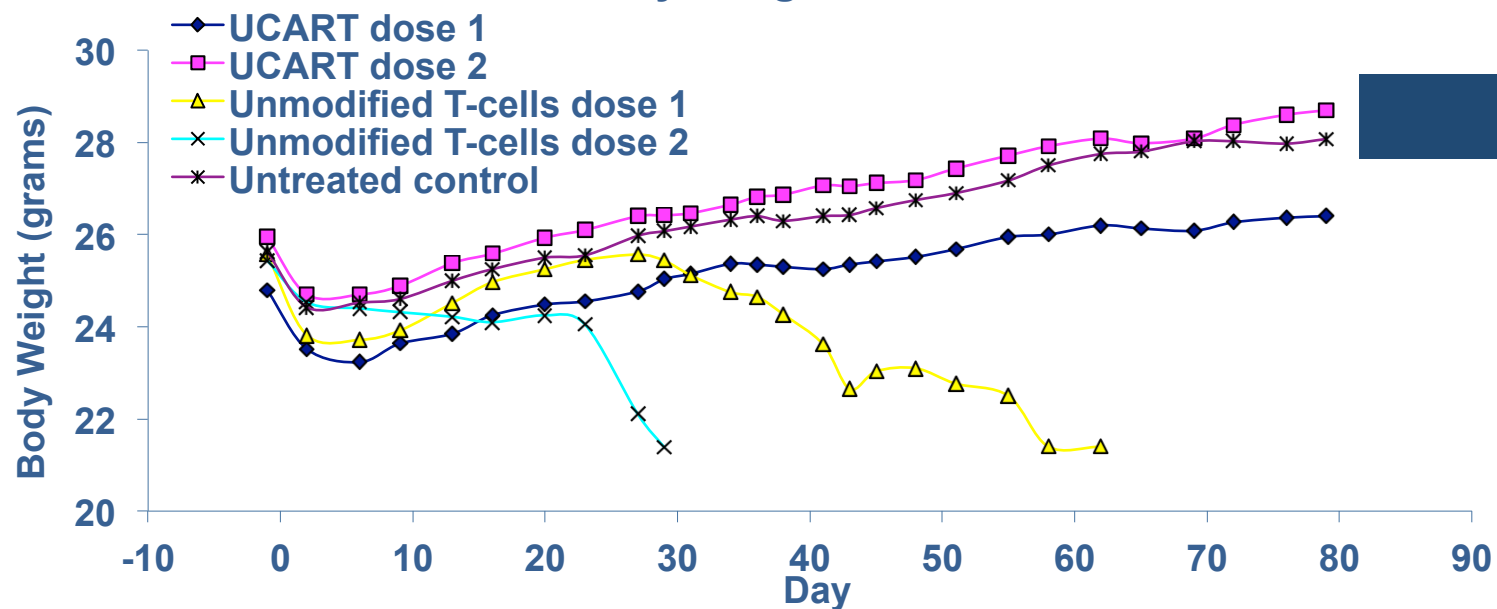


## TCR negative Filtration

### CliniMACS®



## Body Weight Curves



No GvHD

Allogeneic T-Cells

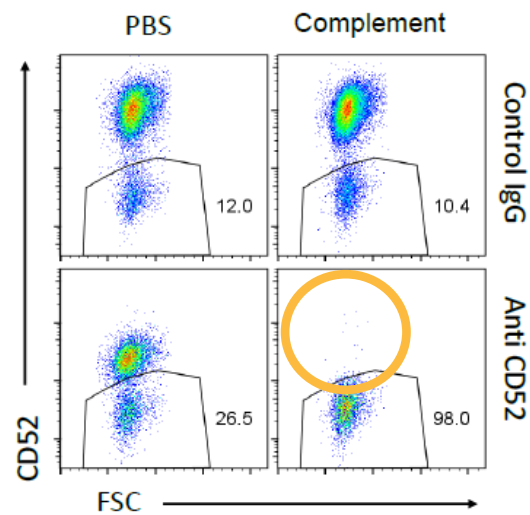
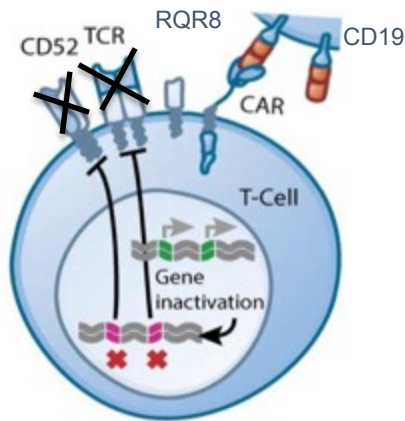


# Disruptive innovation

## Building more powerful T-Cells

### Mab-resistance

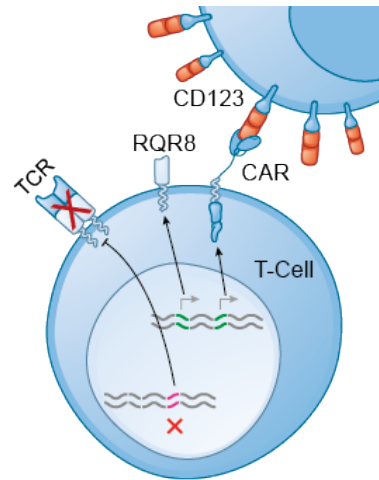
- CD52 KO for Alemtuzumab resistance



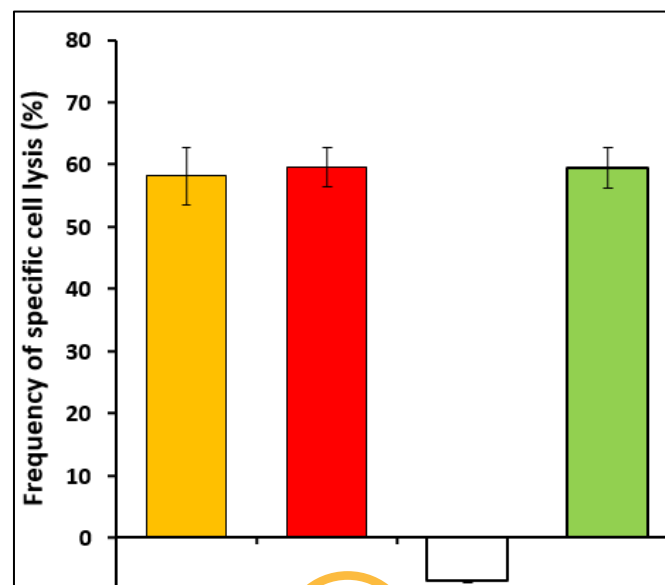
CD52-negative T-Cells are resistant to Campath  
 Poirot L *et al.* (2015) Cancer Res.

### Chemo-resistance

- dCK KO for Fludarabine, Clofarabine resistance



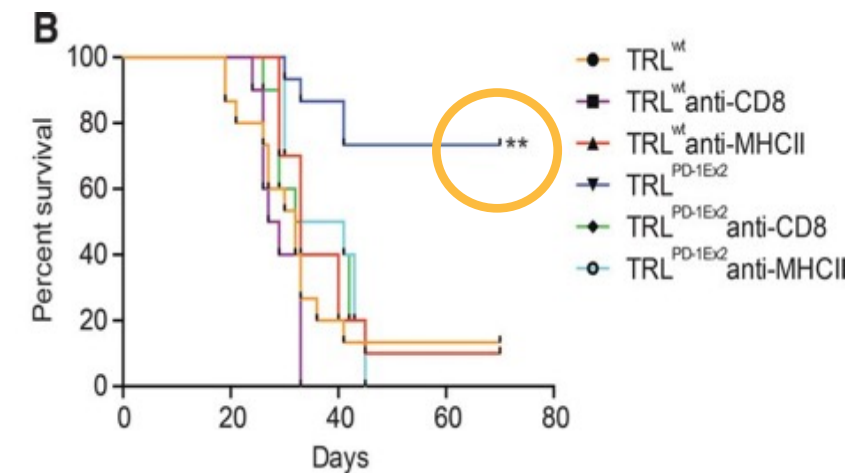
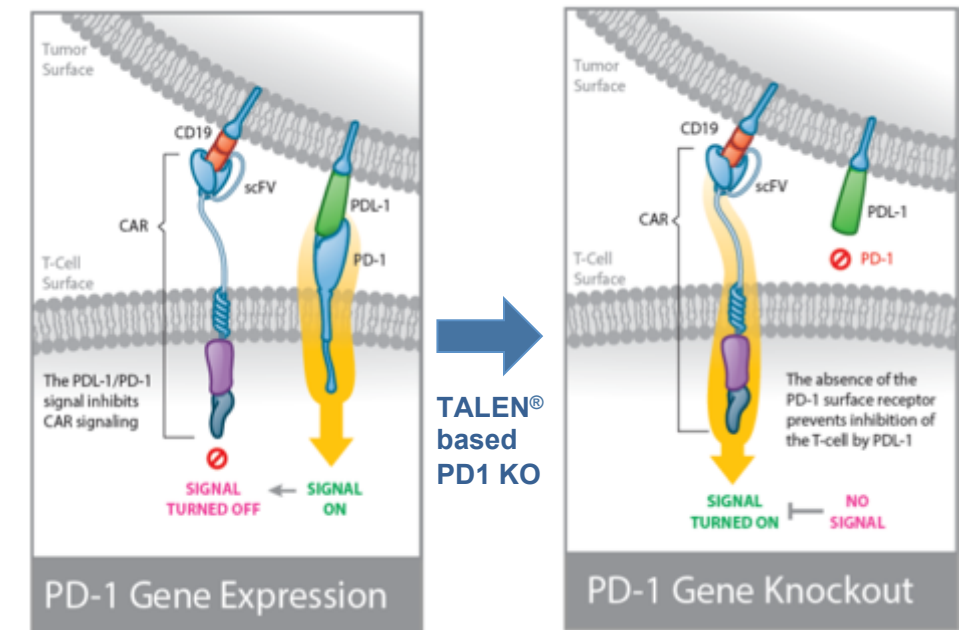
dCK-negative T-Cells are resistant to Clofarabine



Clofarabine	-	+	+	-
CAR	+	+	+	+
KO DCK/TCR	+	+	-	-

### PDL1-resistance

- PD1 KO to be insensitive to PDL1 inhibition



PD1-negative T-Cells have a higher efficacy on PDL1 tumor

Menger L *et al.* (2016) Cancer Res.



# TAKING THE LEAD

High performance gene  
editing technologies

# *Collectis expectations in 2017*

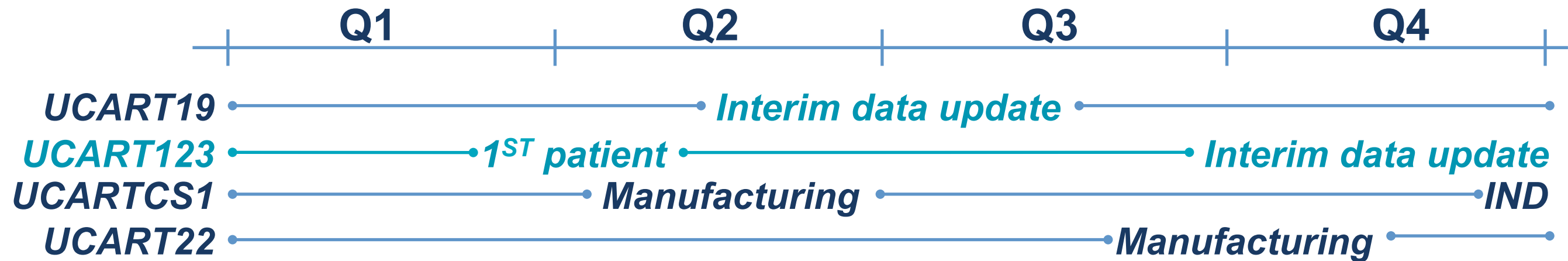
## *A Snapshot at CLLS*



- **UCART19** clinical trials ongoing
- **UCART123** clinical trials to start Q2 2017
- **UCARTCS1** manufacturing in Q2 and IND filing end of 2017
  
- UCART22, UCART38, UCARTCLL1 will follow
- Then potentially solid tumors
- Strong partnerships with Servier and Pfizer
- Exclusivity with Pfizer ends June 2018
  
- \$295M in cash at end of Q3-2016; Cash runway into 2019 for the Collectis Group, including Calyxt

# Cellectis expectations in 2017

## What to watch?



1. UCART123 clinical trial
2. More data on UCART19
3. Pfizer's INDs
4. Manufacturing of UCARTCS1
5. UCARTCS1 IND filing by end of 2017
6. Development of UCART22 and UCART38
7. New indications with Gene Editing
8. More disruptive innovations



- IMMUNO-ONCOLOGY / CAR T
- THERAPEUTIC GENE EDITING
- GENE THERAPY
- \$295M IN CASH END Q3-2016

- NASDAQ: #CLLS
- ALTERNEXT: #ALCLS
- 35.3M OUTSTANDING SHARES

100% owned



- BASED IN MINNESOTA
- INNOVATIVE CROPS
- CONSUMER FOCUS
- NON-REGULATED PRODUCTS
- HIGH VALUE ASSET

**GENE EDITING IS THE LINK**





THANK YOU

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