EDITING LIFE

ENGINEERED CAR-T THERAPIES

A NEW PARADIGM IN ONCOLOGY

35th Annual J.P. Morgan
Healthcare Conference

JANUARY 2017

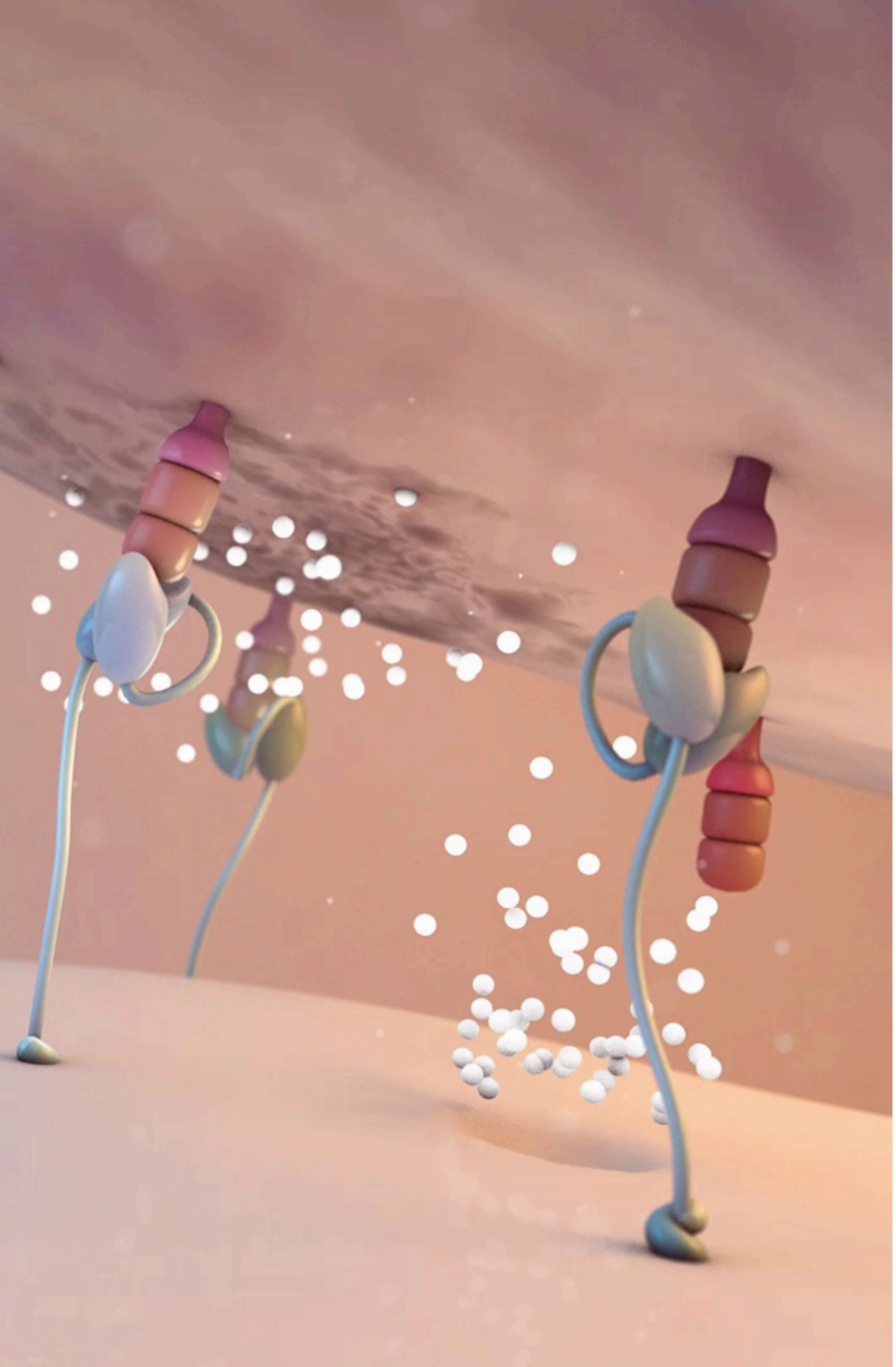
FORWARD LOOKING STATEMENTS

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 OF NOT OBTAINING REGULATORY APPROVAL TO COMMENCE CLINICAL TRIALS ON THE 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 RISKS FACTORS THAT MAY AFFECT COMPANY BUSINESS AND FINANCIAL PERFORMANCE, IS INCLUDED IN FILINGS CELLECTIS MAKES WITH THE SECURITY 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.



GENE EDITED ALLOGENEIC UCARTs

Entering clinical development

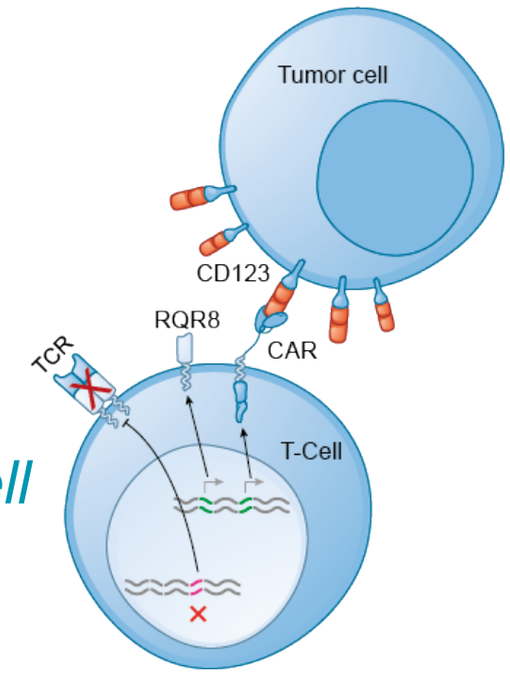
Entering Clinical Development

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*
  - 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*



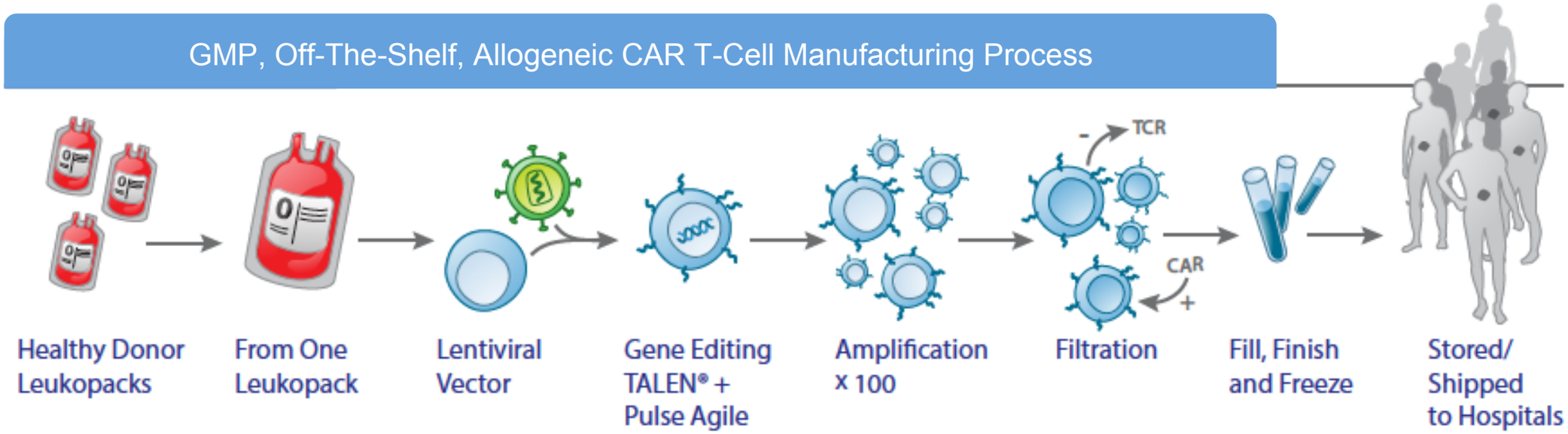
  - BPDCN Phase 1 trial at MD Anderson

    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

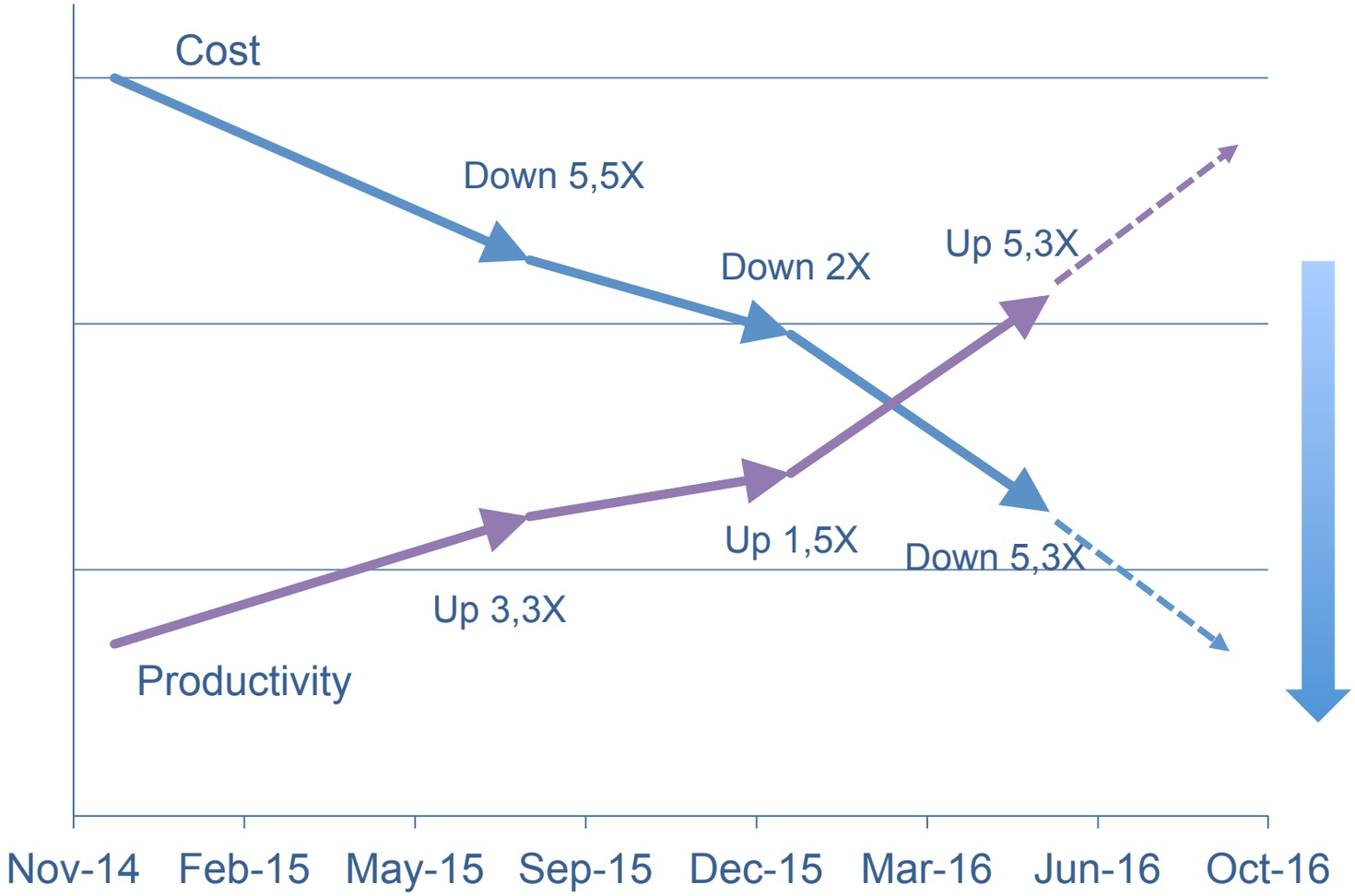
- ✓ Succeeded in producing UCART19 in Q4 2015
- ✓ Succeeded in producing UCART123 in Q4 2016
- ✓ Initiated technology transfer for UCARTCS1 in Q4 2016



>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



>20x Increase in **Productivity**

>50x Decrease in **Cost**

UCART123
< $4000/dose*

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

Entering Clinical Development

Selecting the best gene editing technology for patients

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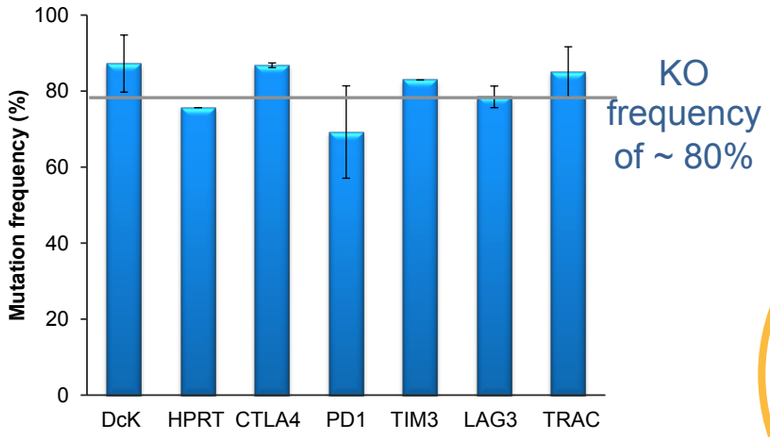
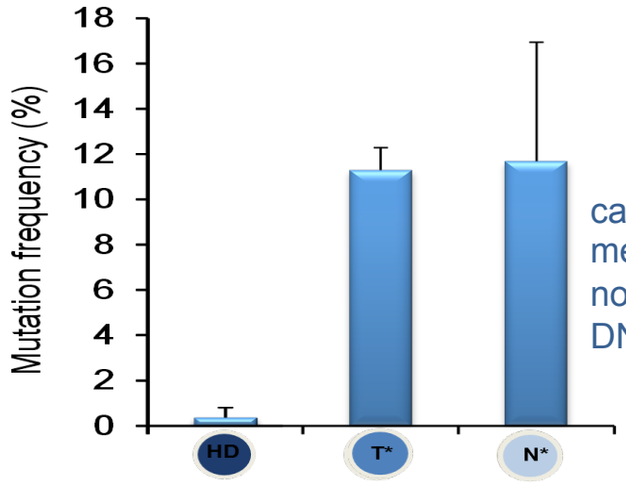
TALEN® are highly **Active**



KO frequency of ~ 80%

The power of protein/DNA interactions

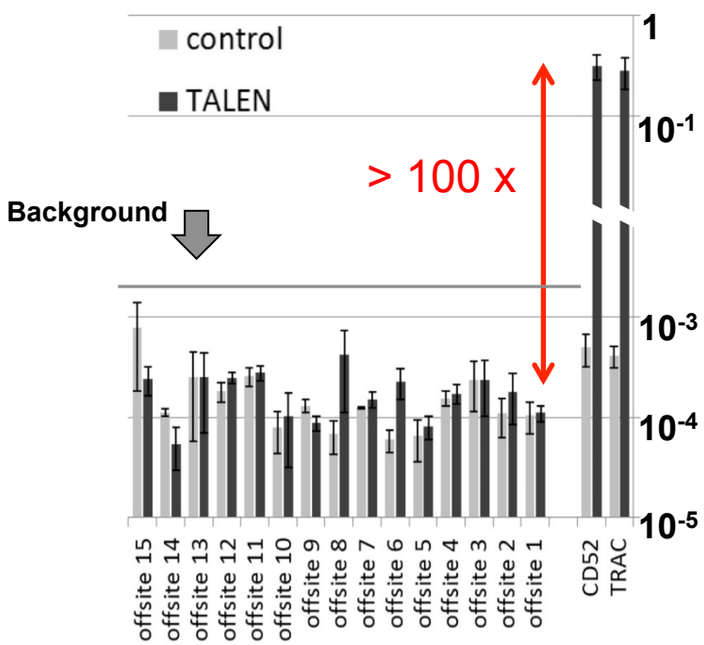
TALEN® are **Accurate** at **6** bps



can discriminate methylated or non methylated DNA

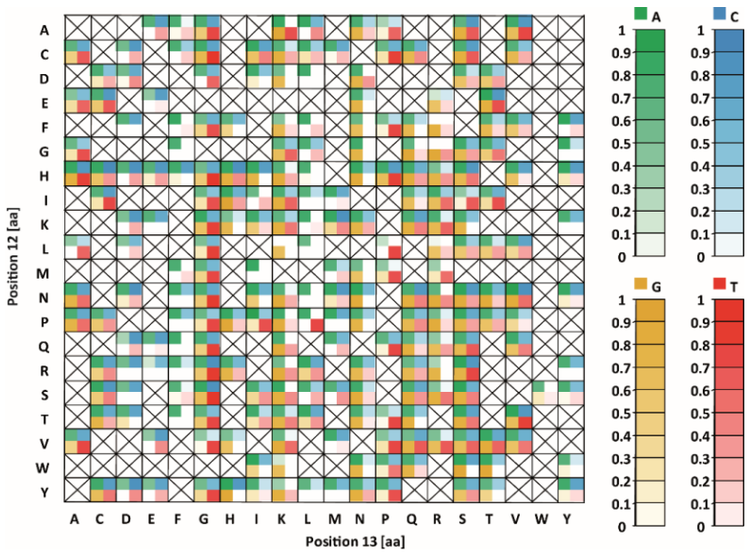
TALEN® are highly **Specific**

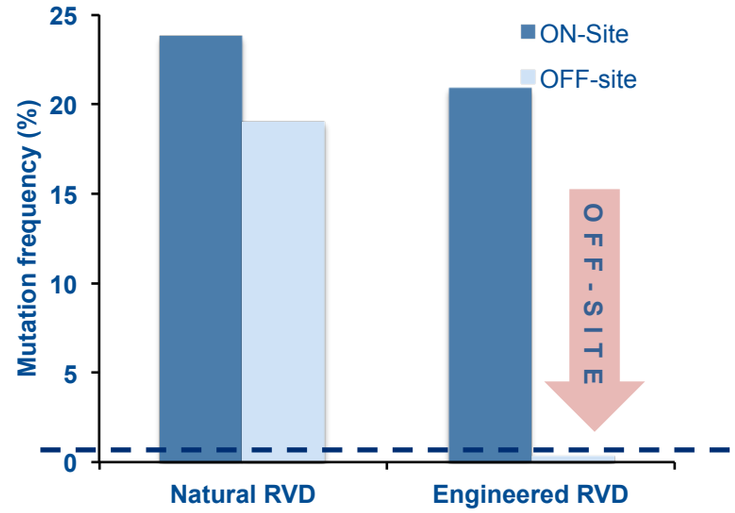
Poirot et al (Cancer Research 2015)



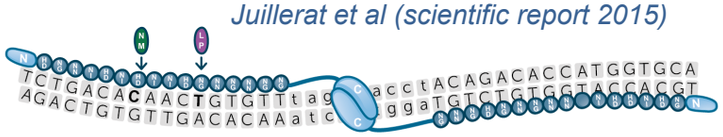
TALEN® are highly **Plastic**

to discriminate between ON and OFF-site





Juillerat et al (scientific report 2015)



Entering Clinical Development

An integrated Gene Edited Cell Therapy Platform

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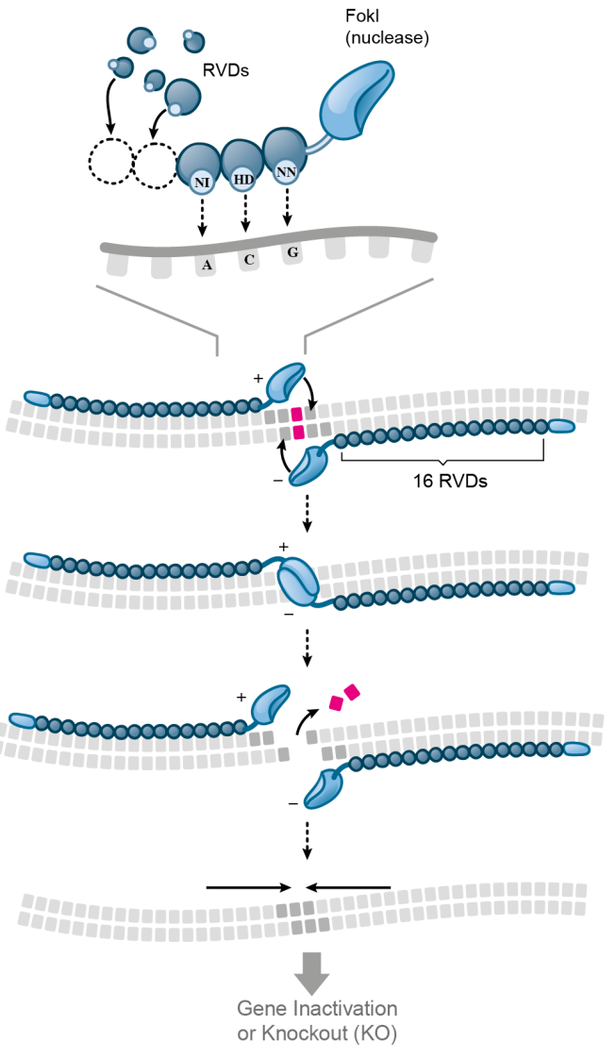
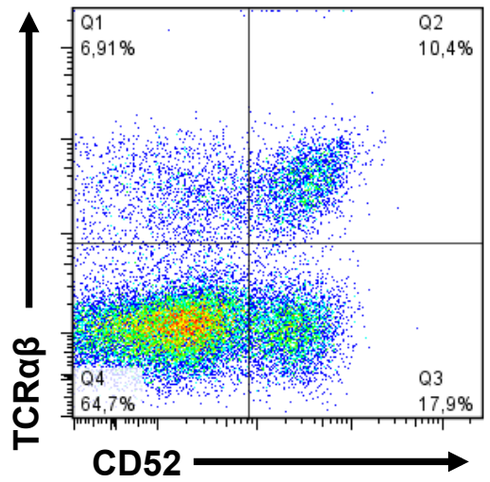
TALEN® Gene Editing



CytoPulse Electroporation

High Cell Transduction
High Gene Editing Rate
High Cell Survival

TRAC & CD52 TALEN® mRNA



High Yield & Quality Cell Therapy products

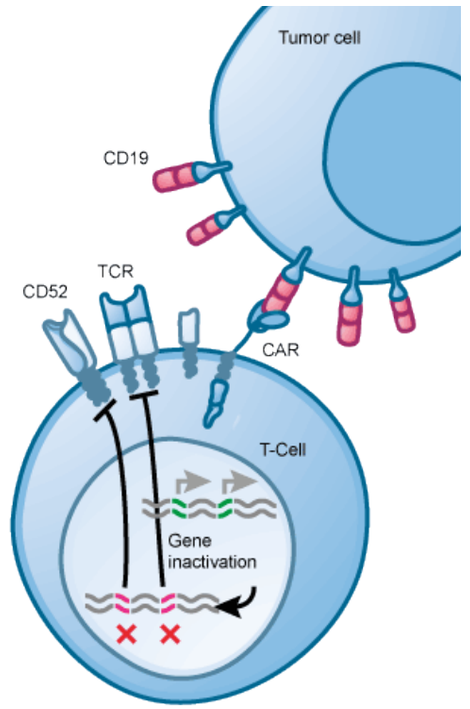
Licensed from UMN in 2011

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 all other countries
- Phase 1 Pediatric ALL (PALL)
  - Started June 2016 at UCL, UK
- Phase 1 Adult ALL (CALM)
  - Started July 2016 at KCL, UK
  - Pre-IND meeting in October 2016
  - RAC meeting in December 2016



Entering Clinical Development

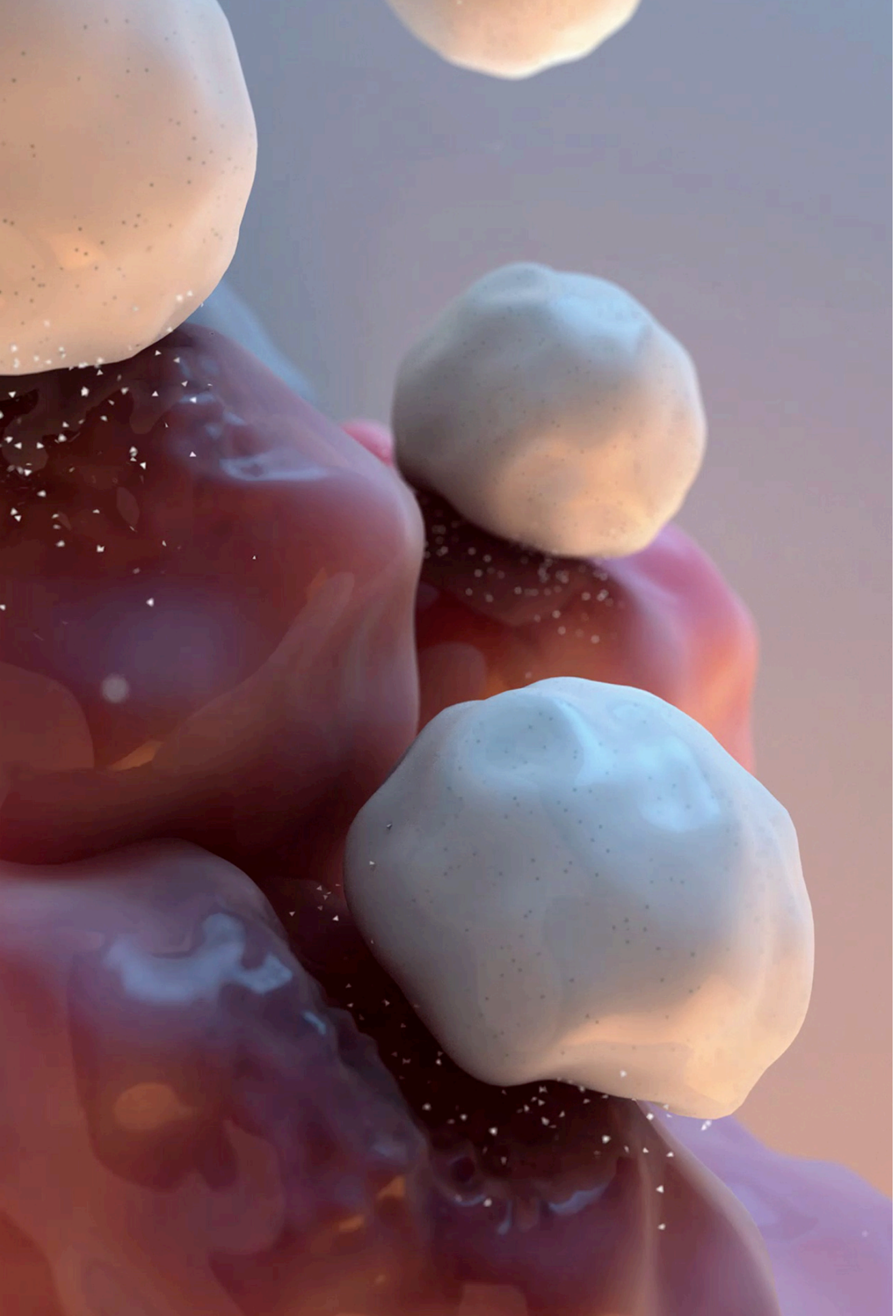
UCART19 Preliminary Data*

In Relapsed/Refractory ALL Patients

Data Presented at the RAC meeting on December the 14th 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 (adult ALL patients)	42 years	• Grade 2 CRS	Alive, MRD-, 4+ Months
	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



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UCART123

A lead product candidate in AML & BPDCN

UCART123

CD123 (IL-3Rα), a High-Value Target

Acute Myeloid Leukemia (AML)

➢ ***Phase 1 dose escalation at Weill-Cornell; IND filed 12/2016***

- 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 1st line high risk AML
- Orphan Drug Designation potential

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

➢ ***Phase 1 dose escalation at MD Anderson; IND filed 12/2016***

- 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

Encouraging Preclinical Efficacy Data

Weill Cornell Medicine

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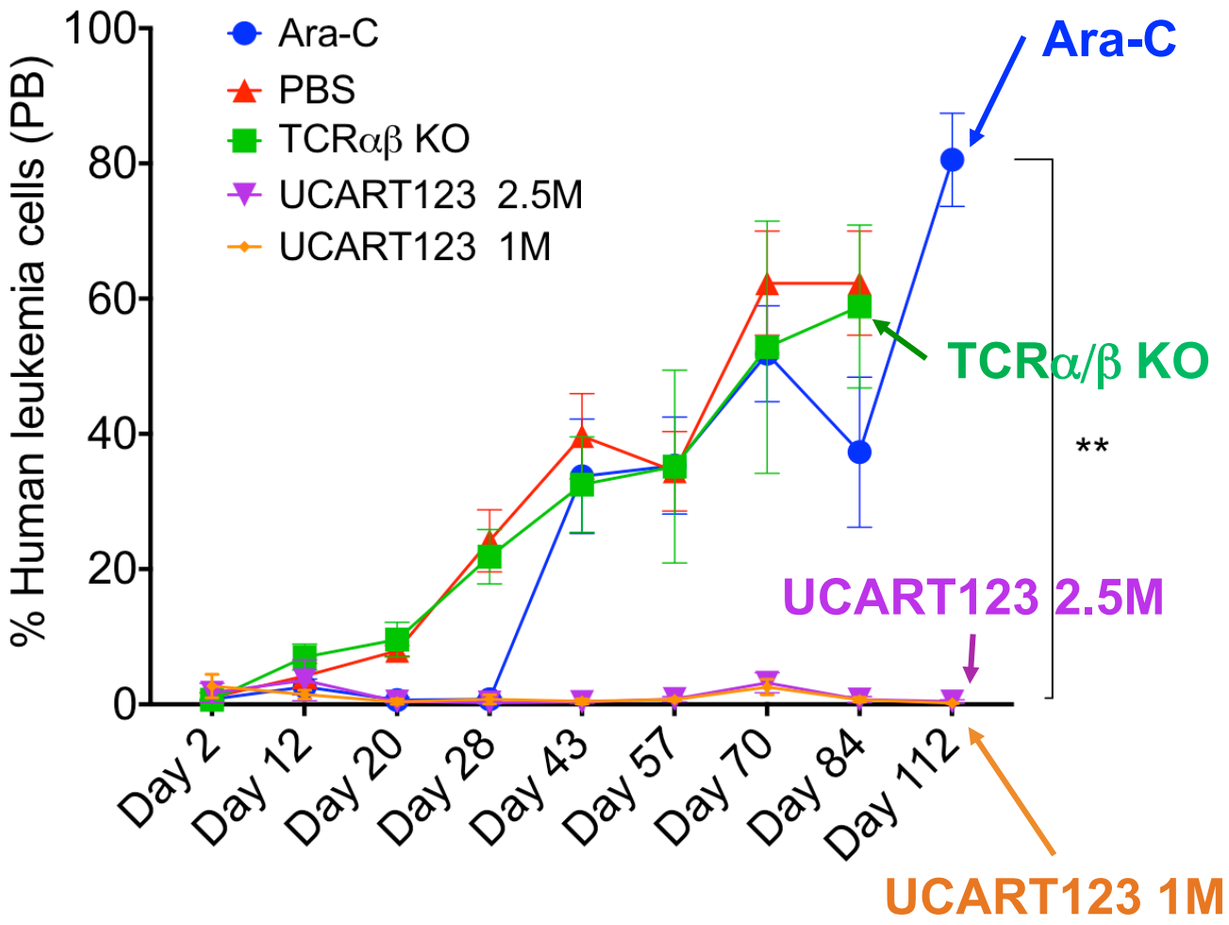
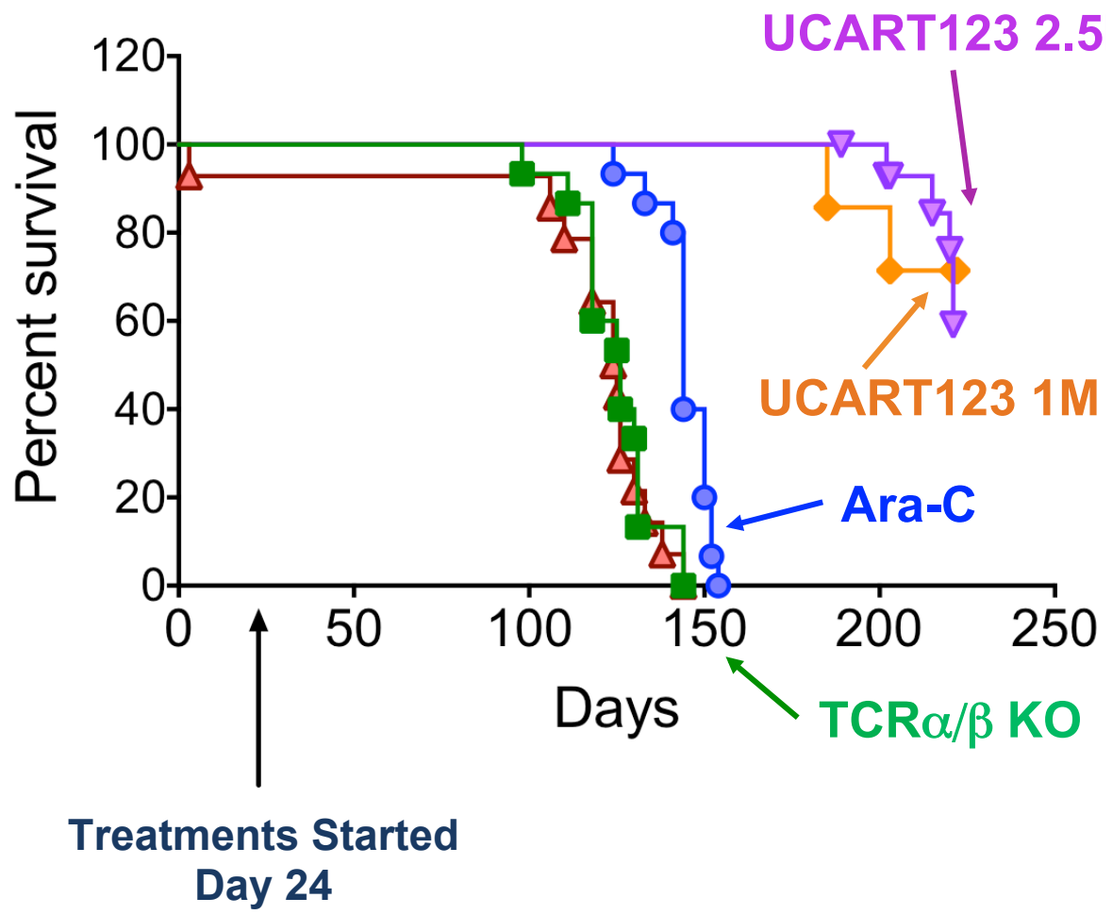
UCART123 Significantly Decreases Tumor Burden and Improves Survival

Peripheral Blood Evaluation



Overall Survival



In collaboration with Dr. Monica Guzman, Cornell-Weill

UCART123

Encouraging Preclinical Efficacy Data

Weill Cornell Medicine

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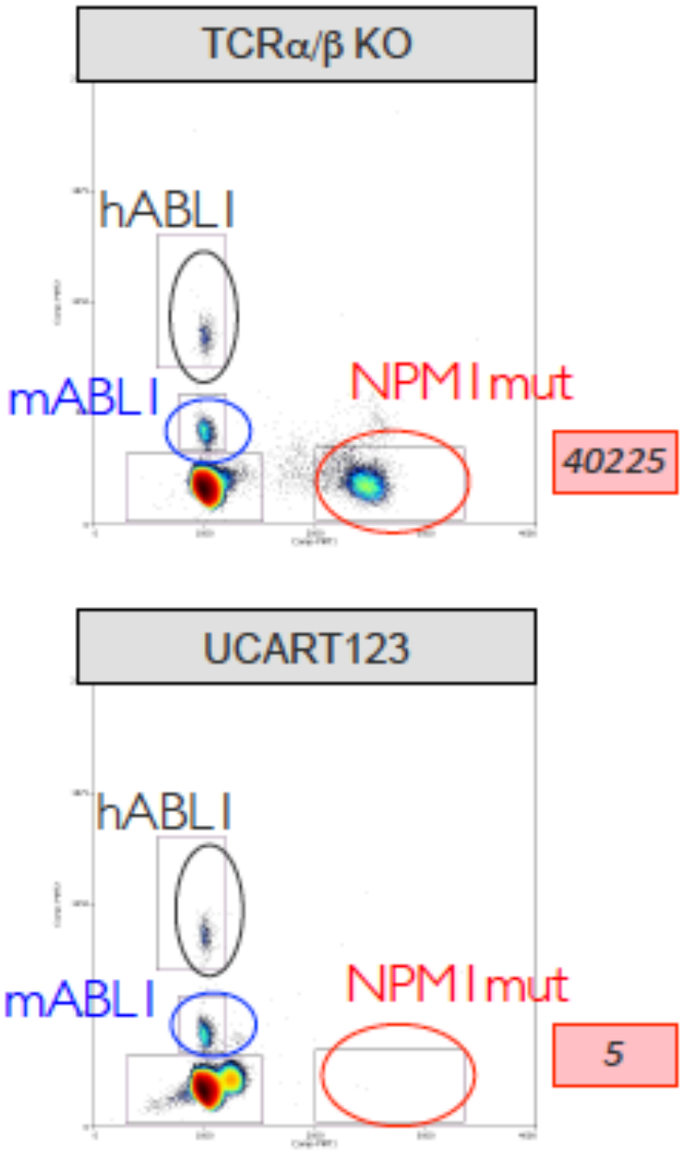
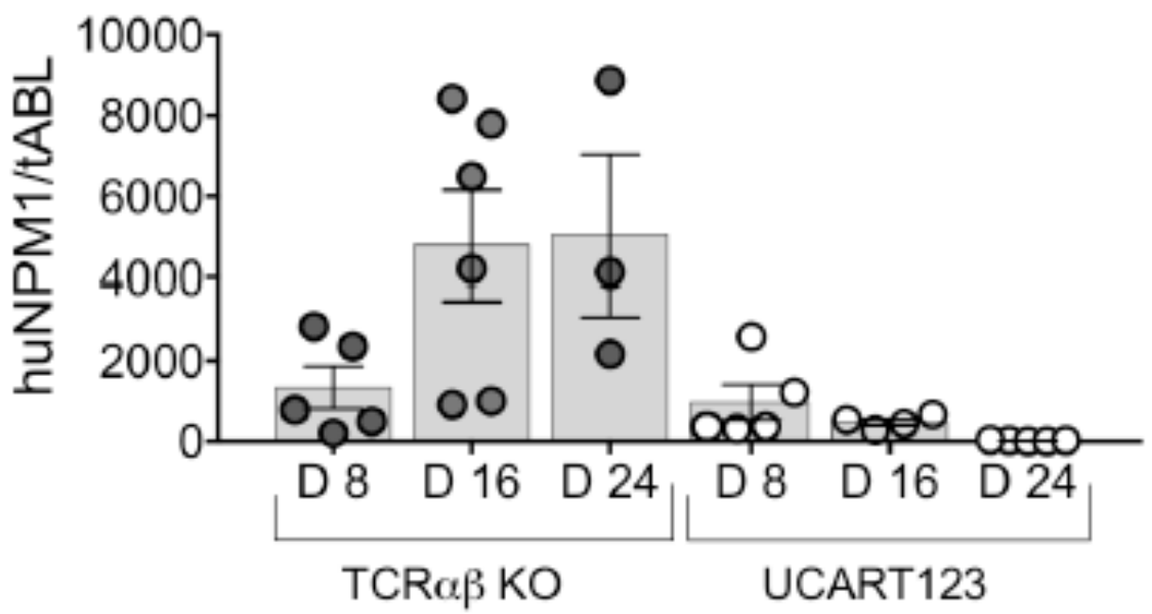
Animals treated with UCART123 achieves molecular remission

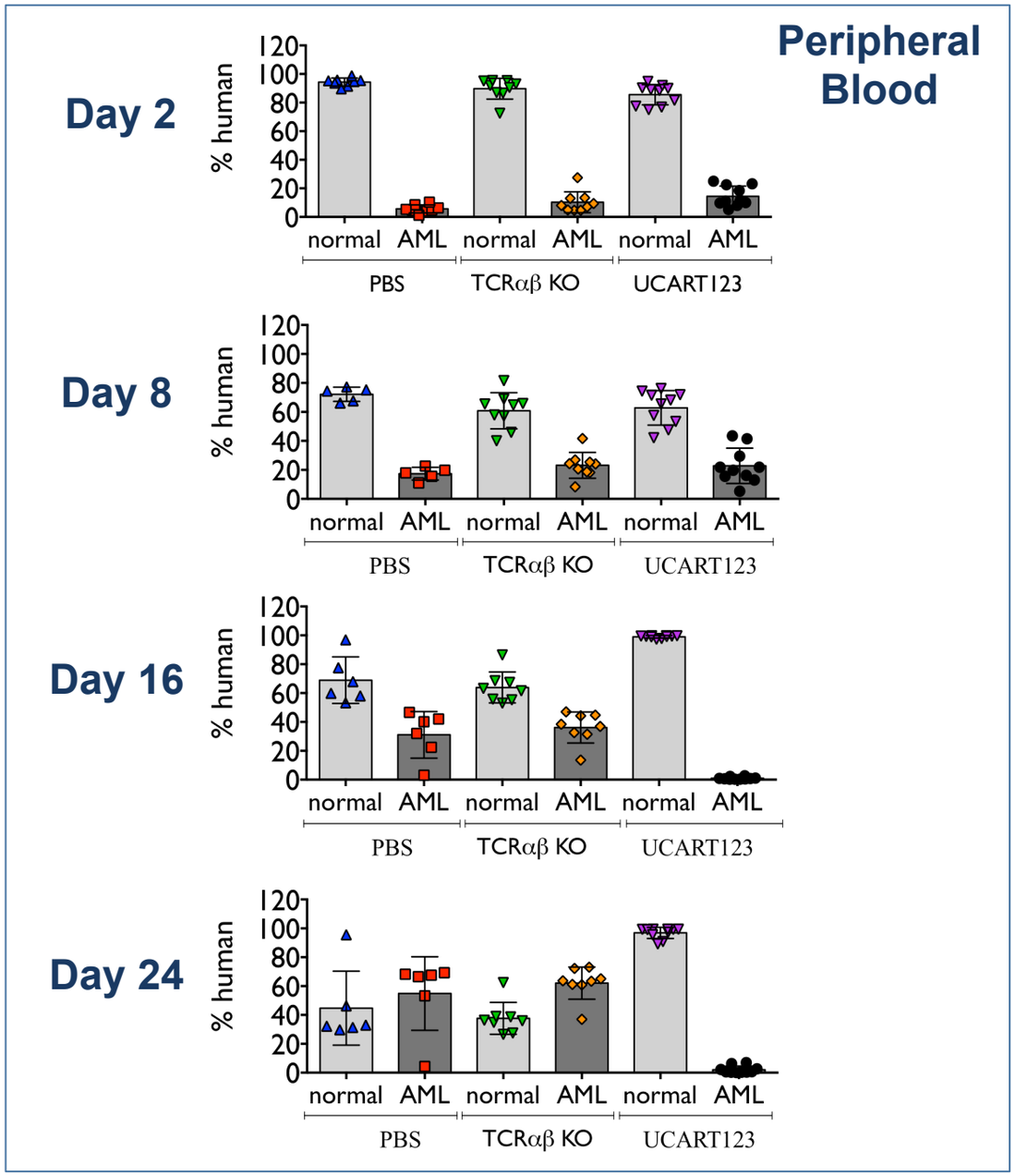


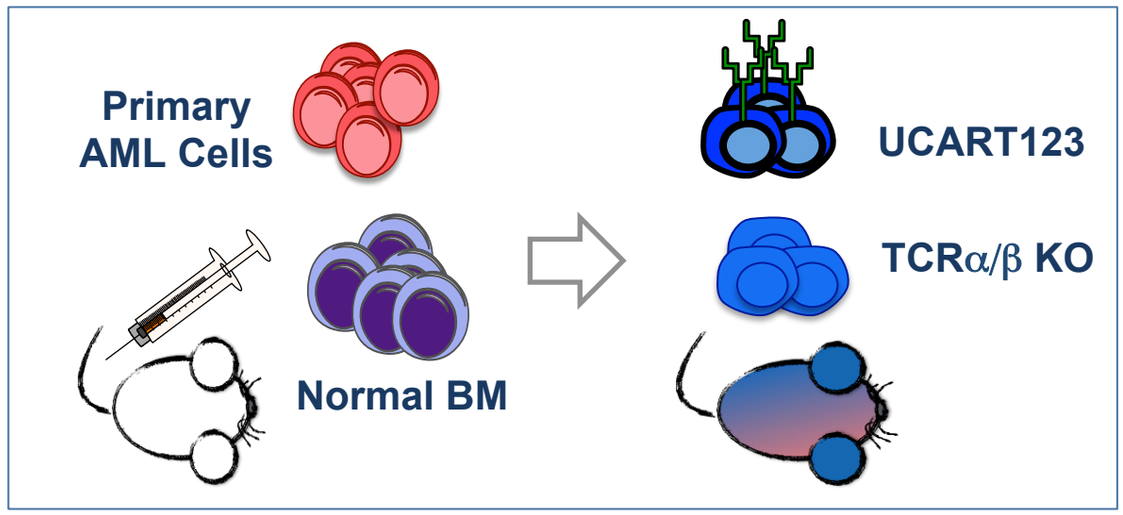


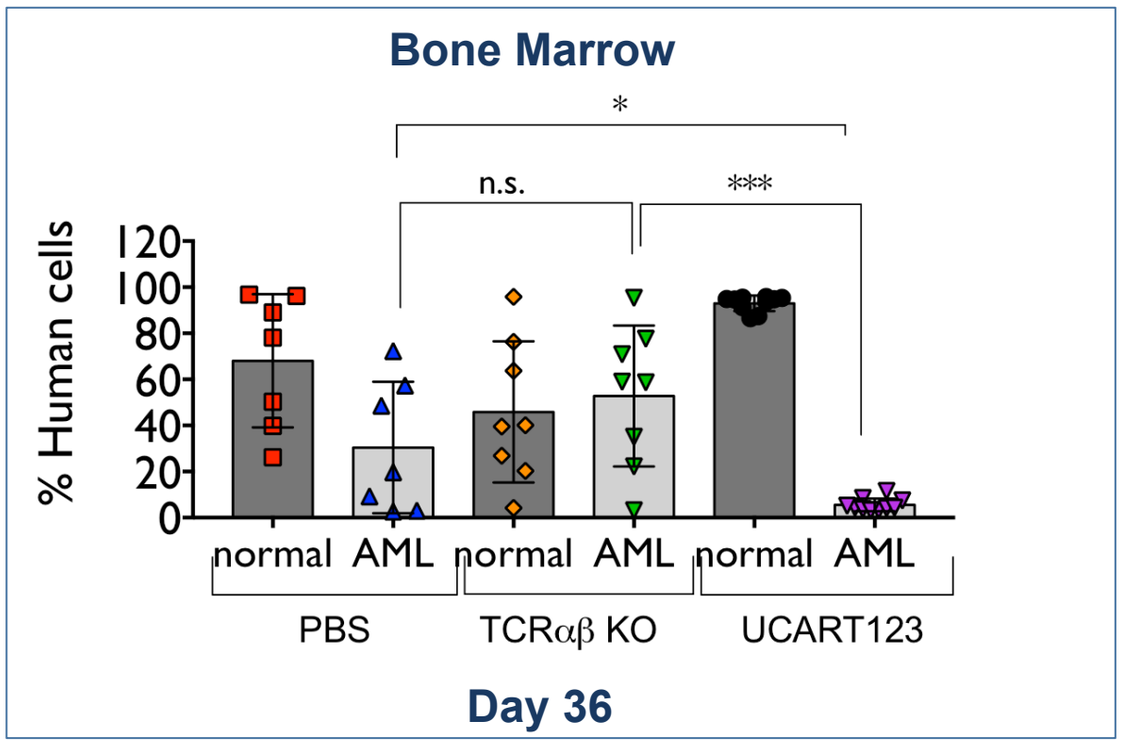
In collaboration with Dr. Monica Guzman, Cornell-Weill

UCART123
Safety

UCART123 Preferentially Eliminates AML Cells Over Normal Hematopoietic Cells







In collaboration with Dr. Monica Guzman, Cornell-Weill

UCART123

Study Design for AML

Dose Escalation Phase (R/R AML)

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

UCART123

Study Design for BPDCN

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

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Dose Escalation Phase (R/R BPDCN)

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

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

Total Dose Escalation N= 9-12 pts

Expansion Phase

RR BPDCN N=30

Untreated BPDCN N=30

Total Phase I Expansion N=60

In collaboration with MD Anderson

UCART123

Development plan

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

filed December 2016 ☑

Phase 1
- First patient

expected Q1 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

UCARTs

Expanding Tumor Target Space

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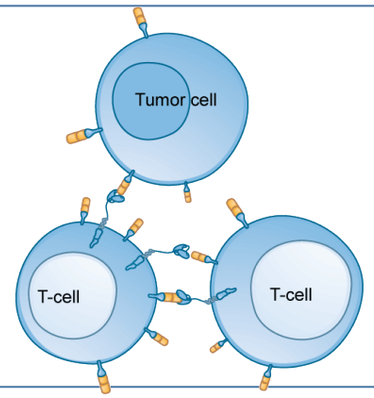
Taking Gene-Edited CARTs one step ahead

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 spectrum

Program	Indication	Product development	Preclinical	Manufactu-ring	IND Filling*	Phase I	Phase II
UCART19**	ALL (PALL)						
	ALL (CALM)						
UCART123	AML						
	BPDCN						
	CML						
	HL						
	HCL						
	MDS						
UCARTCS1	MULTIPLE MYELOMA						
	B-CLL						
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

Strategic Partners

- Collaboration on 15 targets: 1st 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

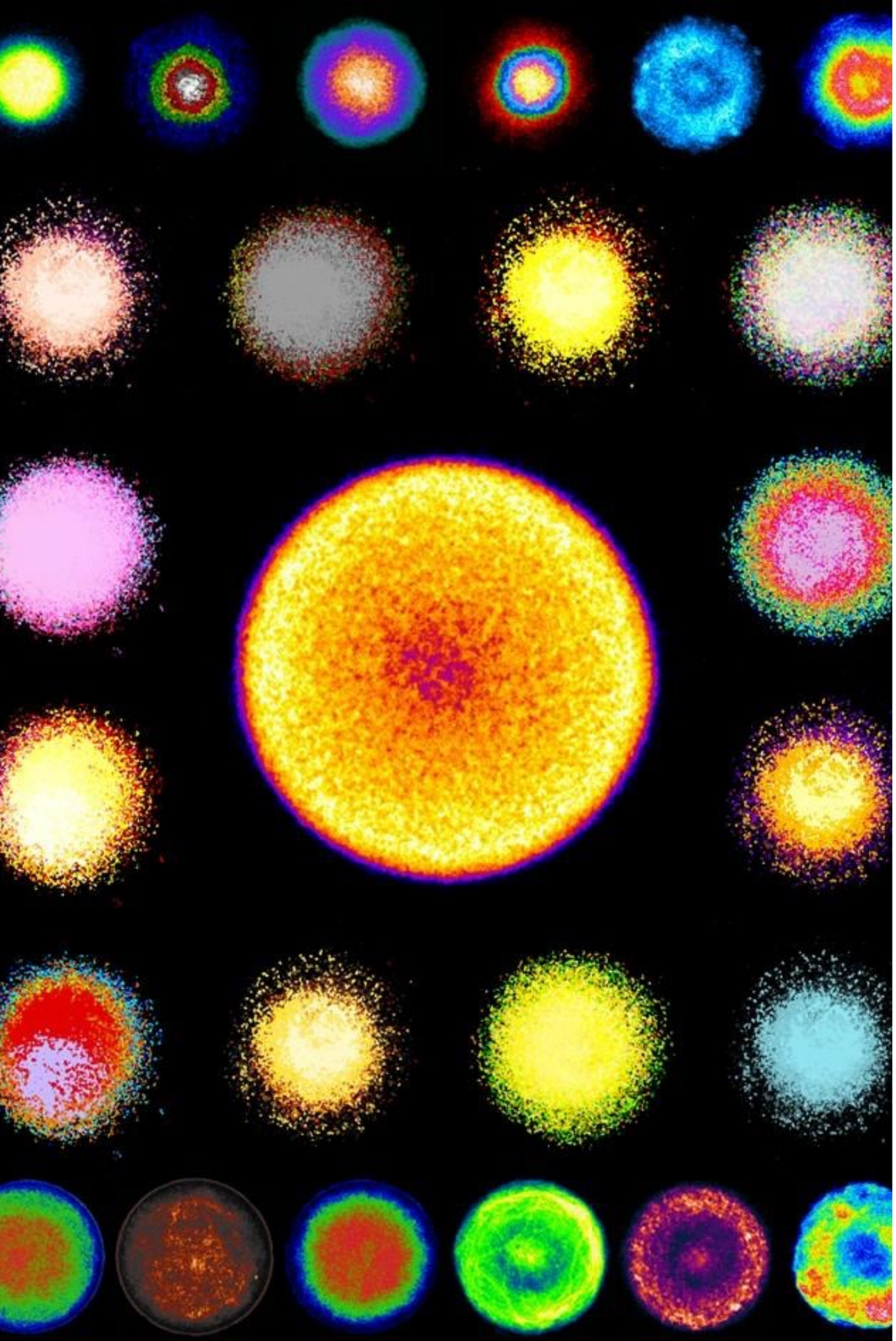
World Class Clinical Centers

- 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.

- 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 is not our primary strategy
- 1st injection in patients in 2015
- Question marks at the time:
  - Early rejection?
  - Persistence?
  - Underperformance?
  - GvHD?
- TALEN® is setting a precedent for gene editing for patient

Today we lead the way in Allogeneic CARTs

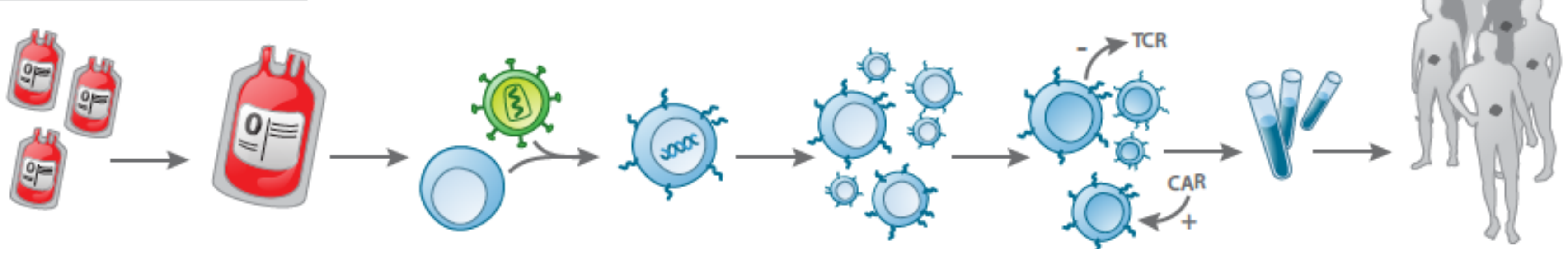
DISRUPTIVE INNOVATION

How Cellectis is shaping Cell Therapies with Breakthrough Innovations

Disruptive Innovation

Patient-Oriented Therapeutic Proposal

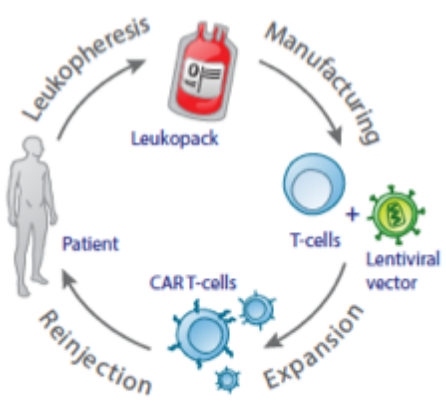
Allogeneic CAR T-Cells are a universal product candidate with multiple doses



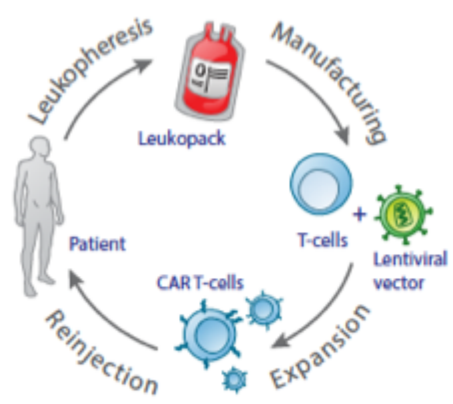
One Leukopack can yield **100s of doses**

Product vs. Service

Autologous CAR T-Cells are a personalized therapeutic procedure



1 PROCEDURE BENEFITS 1 PATIENT



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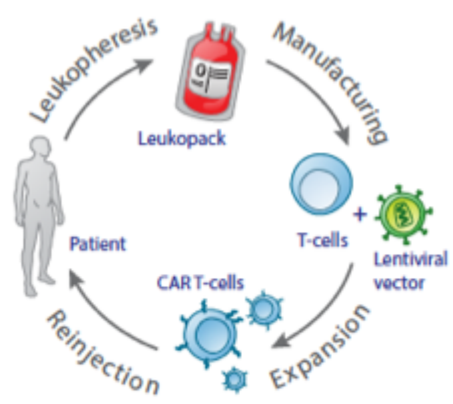

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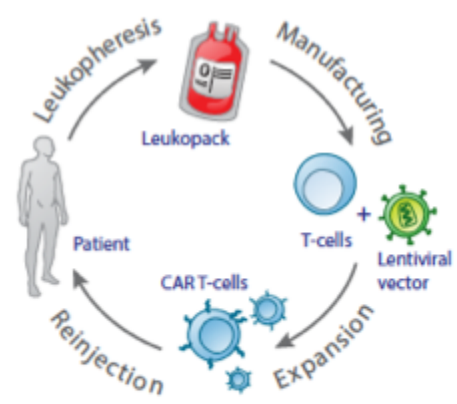

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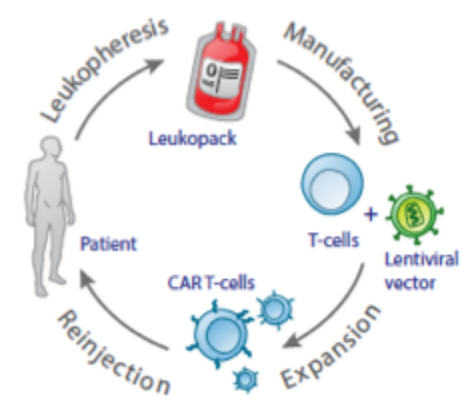

1 PROCEDURE BENEFITS 1 PATIENT

Disruptive innovation

Three technological pillars for manufacturing allo-CART

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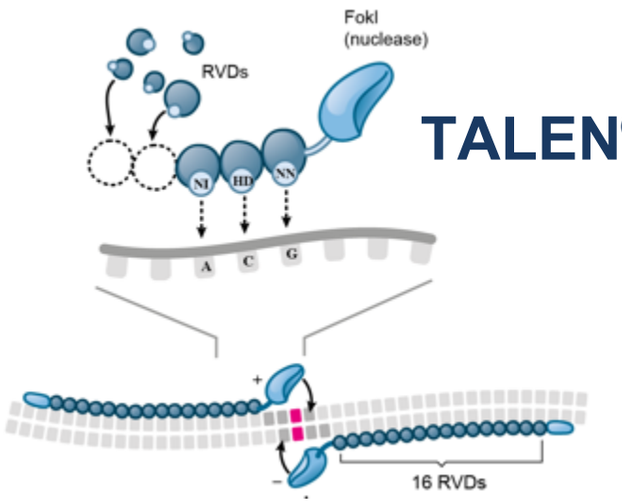
High Quality Gene Editing

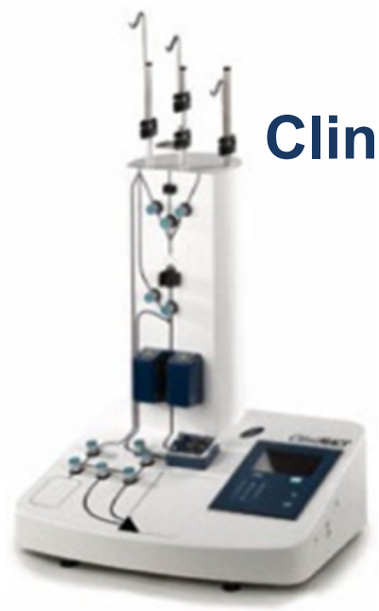


TALEN®

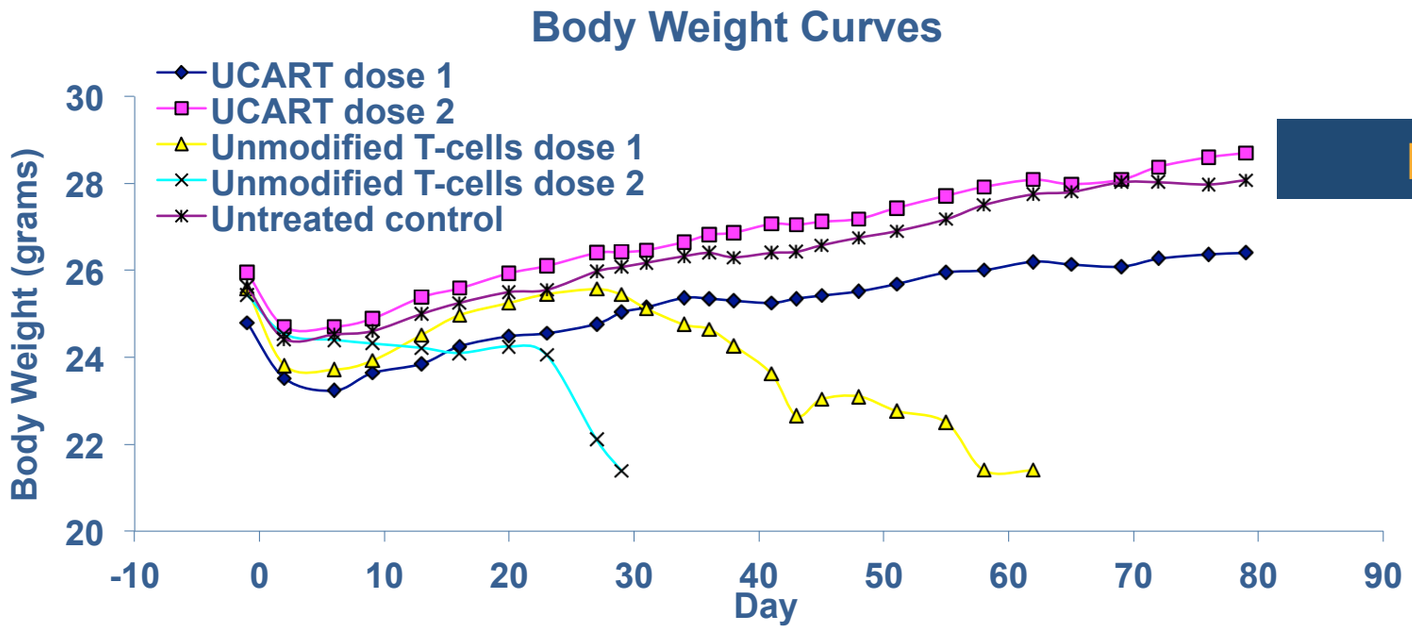
Efficient Electroporation

PulseAgile

TCR negative Filtration



CliniMACS®



No GvHD

Allogeneic T-Cells

Disruptive innovation

Building more powerful T-Cells

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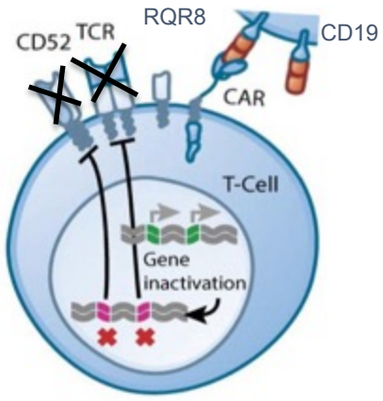
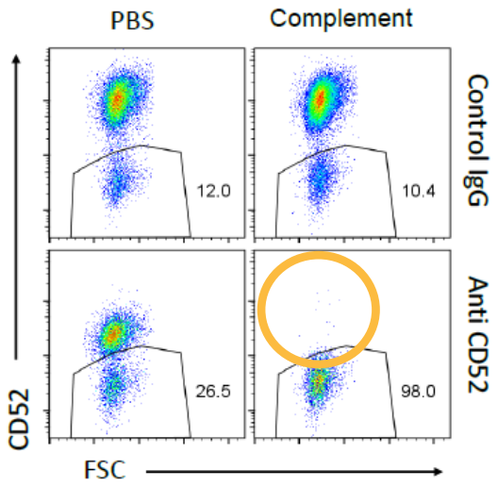
Mab-resistance

- **CD52 KO** for Alemtuzumab resistance



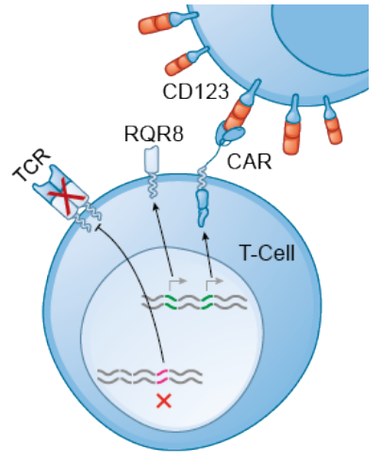


CD52-negative T-Cells are resistant to Campath

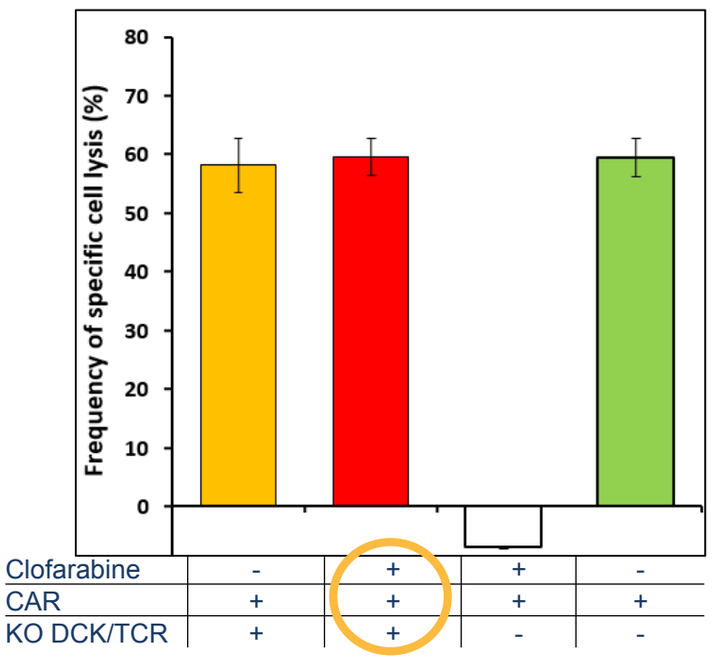
Poirot L *et al*. (2015) Cancer Res.

Chemo-resistance

- **dCK KO** for Fludarabine, Clofarabine resistance

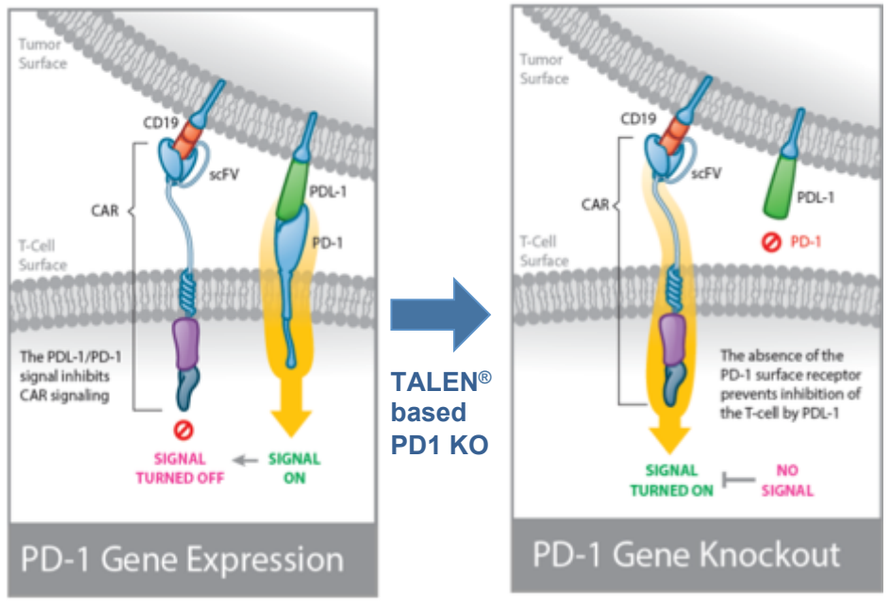


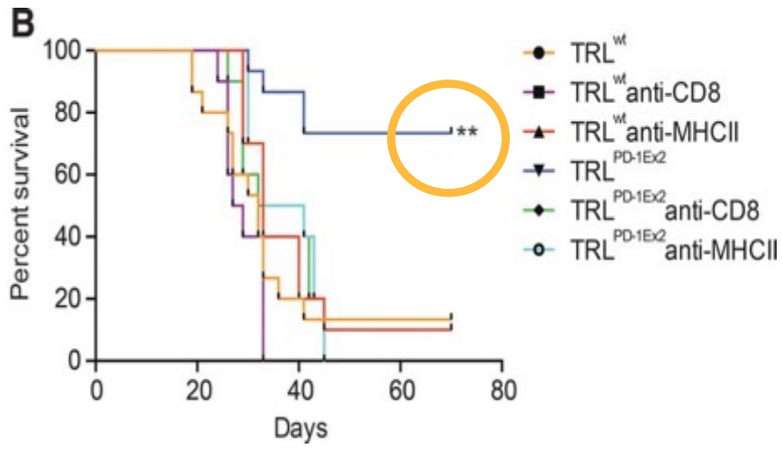
dCK-negative T-Cells are resistant to Clofarabine



PDL1-resistance

- **PD1 KO** to be insensitive to PDL1 inhibition





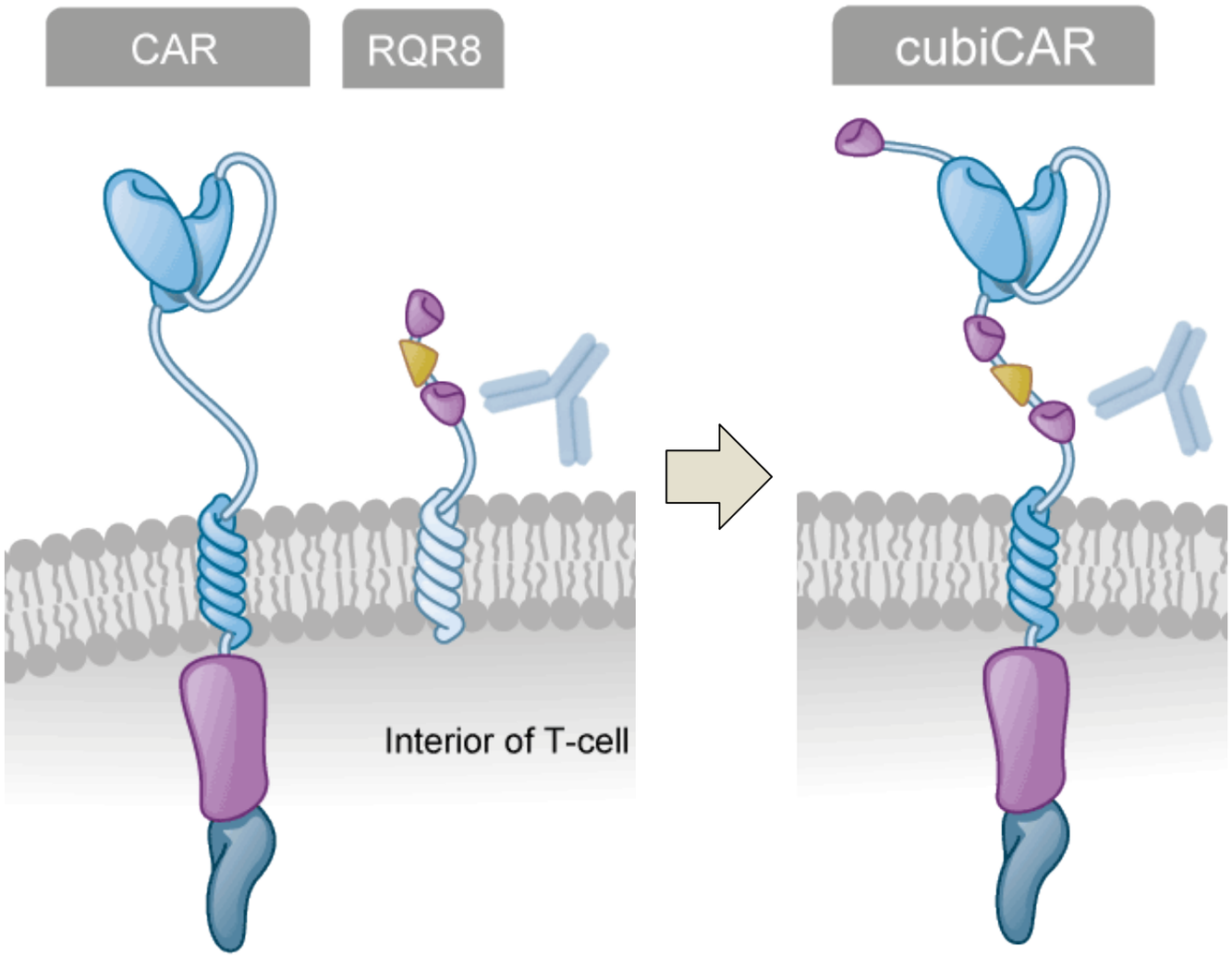
PD1-negative T-Cells have a higher efficacy on PDL1 tumor

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

Disruptive innovation

High Tech at the Service of Patients

A suicide switch embedded in the CAR molecule



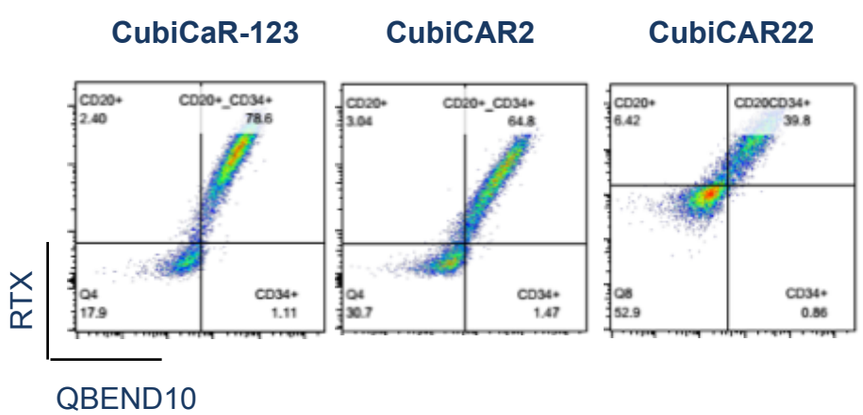
- ✓ Compact
- ✓ Specific cytotoxicity
- ✓ FDA-approved trigger molecule (Rituximab)

Disruptive innovation

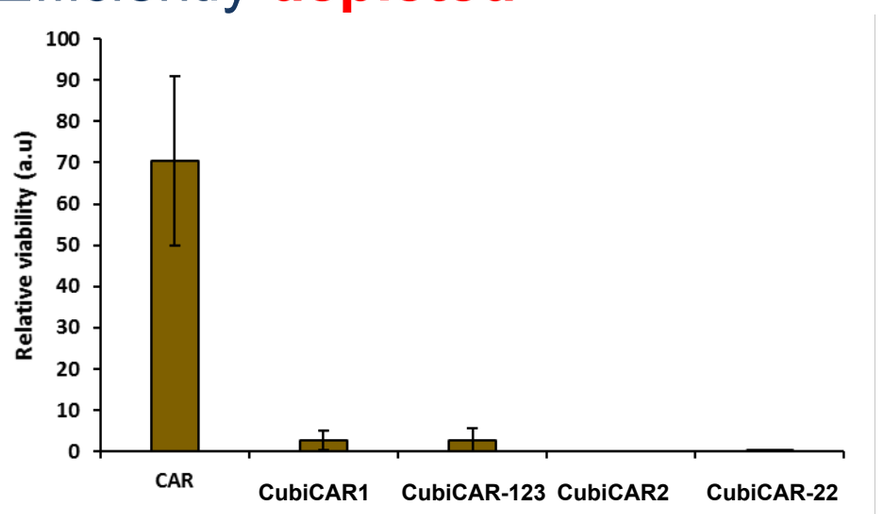
High Tech at Service of Patients

Transposable from one CART to another

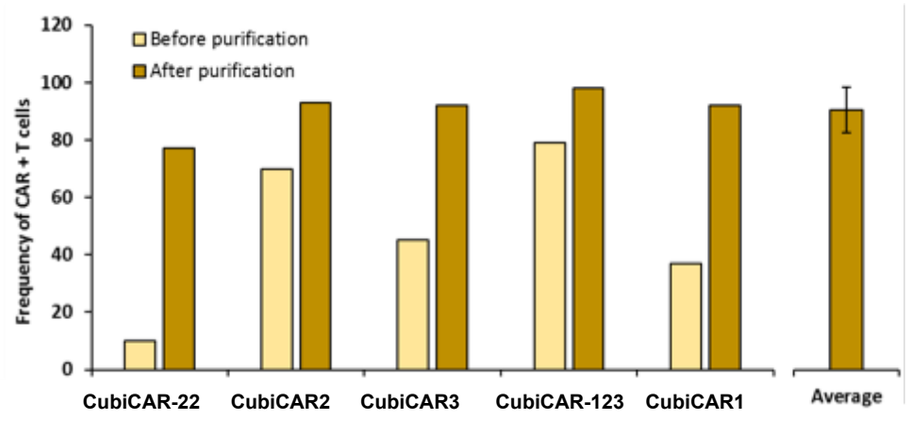
Expressed and **detected**



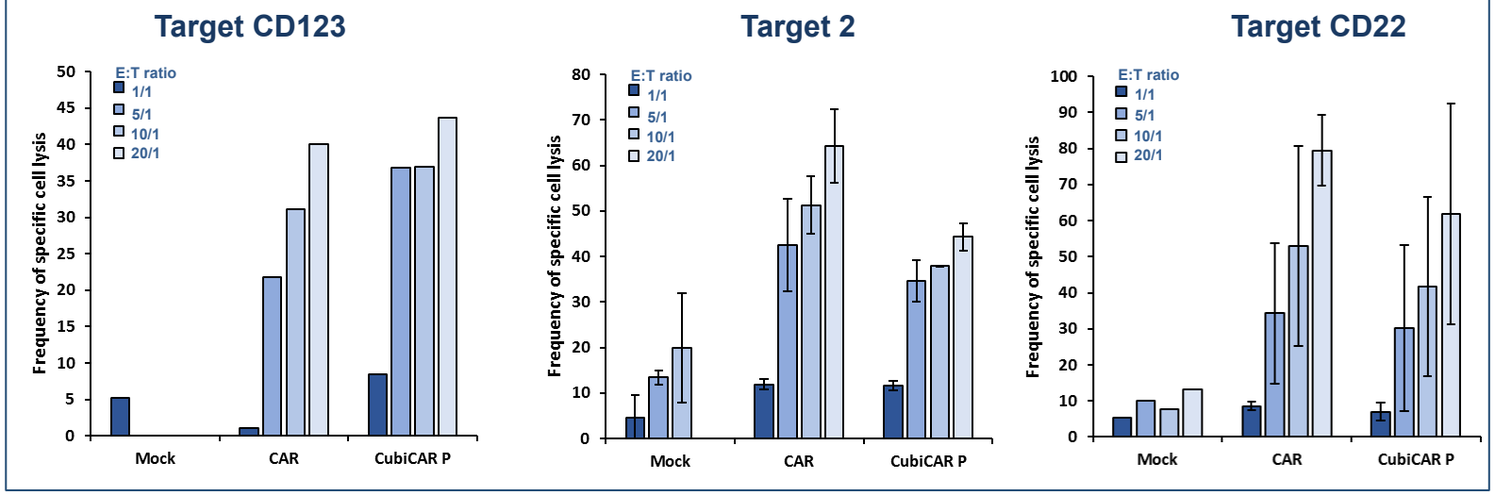
Efficiently **depleted**



Efficiently **purified**

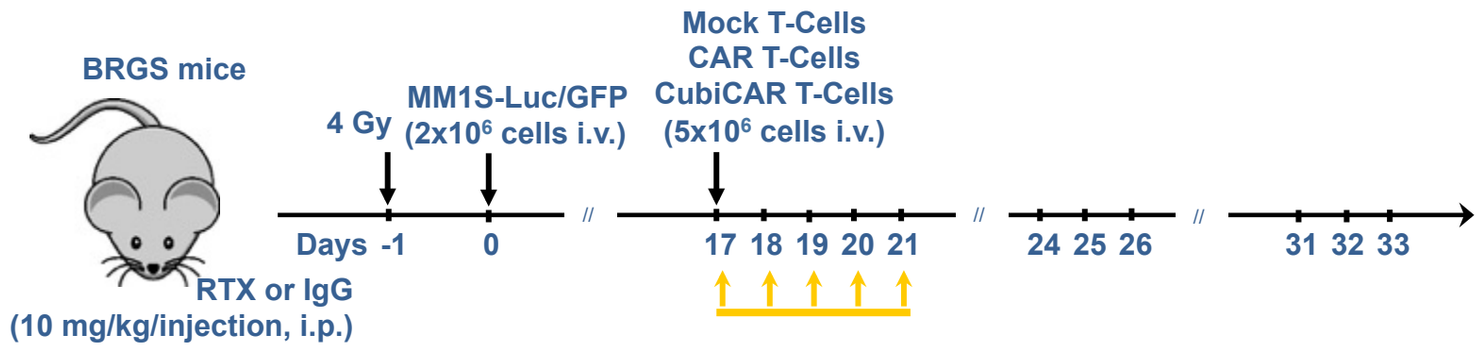


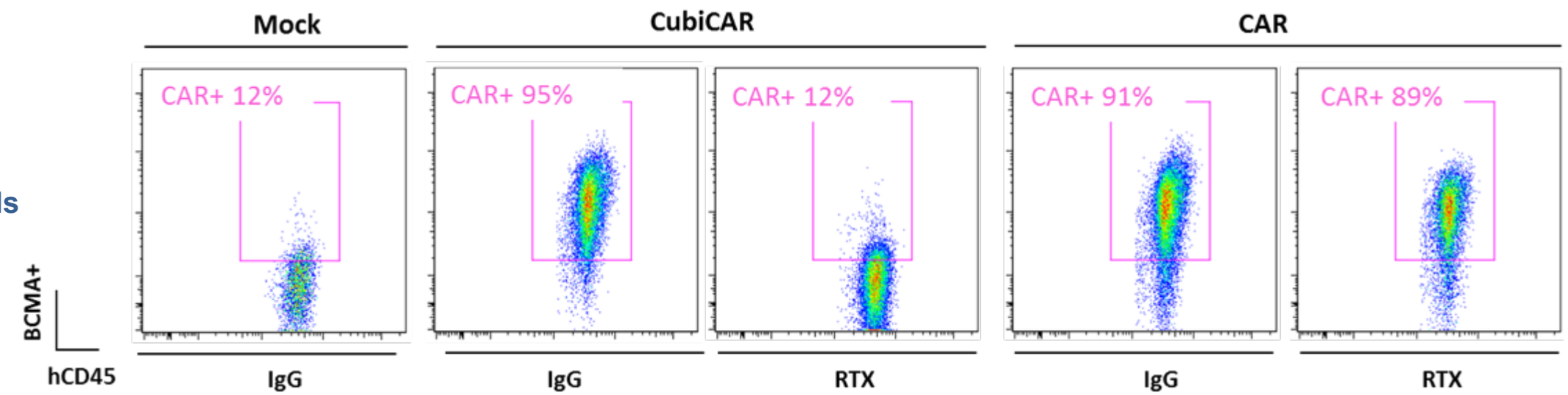
Display **antitumor activity**

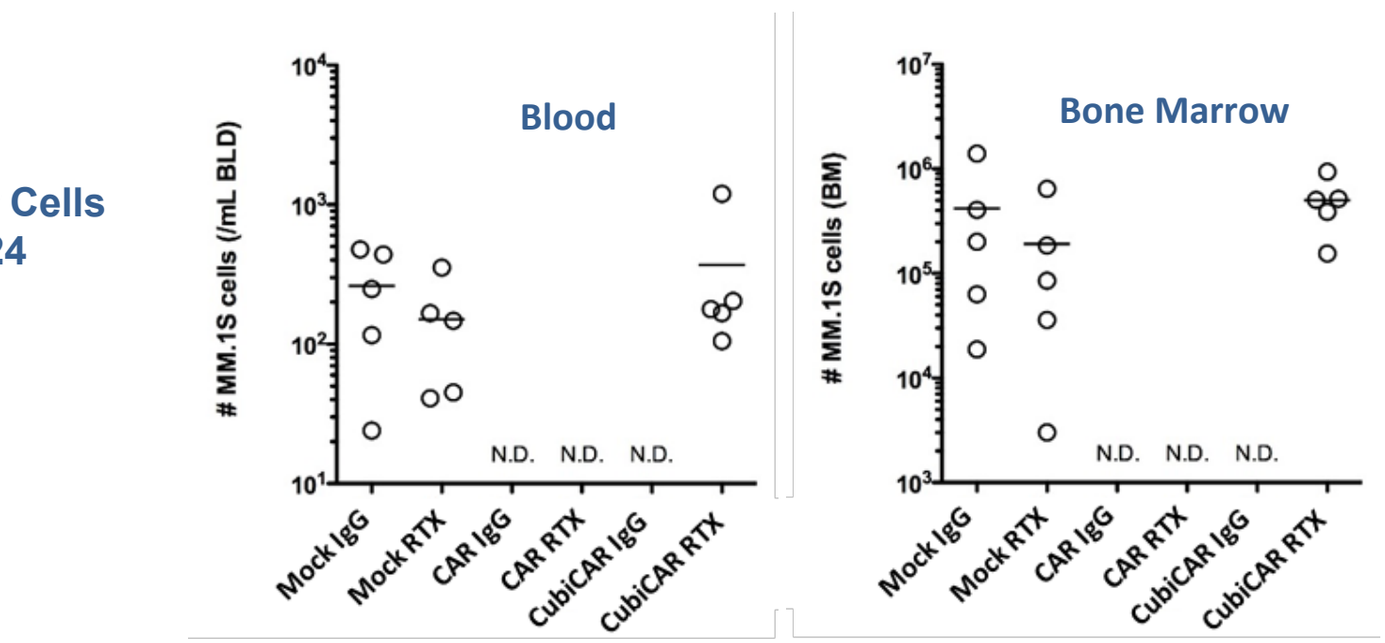


Disruptive innovation

Displays Antitumor Activity in vivo







CAR T-cells can be depleted *in vivo*

cellectis
EDITING LIFE

TAKING THE LEAD

High performance gene editing technologies

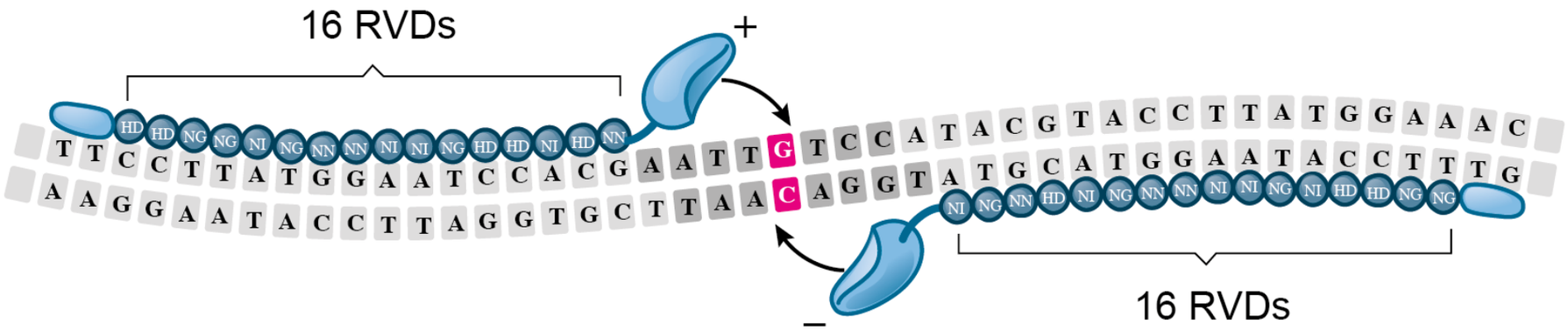
Therapeutic Cells Gene Edited

Performance above all

Best-in-class technologies for therapeutic

Strong know-how built on 17 years of experience in Gene Editing

N Terminal Repeat Variable Di-residues (RVD) Nuclease (FokI)



Highly active: >80% KO

Highly accurate : 6 bps

Low off-target

We take what we believe is best for patients

The Challenge of Therapeutic Gene Editing

INCREASED LEVELS OF DIFFICULTIES

Type of edit	Mix of transduced molecules	Location of the editing	Percentage of edited cells	Durability	Genomic off target	Tissue off target
Simple KO Double KO ~bps changes 1 or 2 alleles Insertions 1 or 2 alleles Replacements 1 or 2 alleles	DNA (size) RNA (size) Protein (size, charge, stability) Mixes DNA+RNA DNA+Protein RNA+Protein DNA+RNA +Protein	Liquid tissues Solid tissues *Ex vivo* *In vivo* Liver Eye Lung Muscle Brain Kidneys Etc.	Subpercent 1% 10% 50% 80% =100%	Somatic editing is OK Must hit renewable stem cells	Impacting cell quality *Allogeneic* *Autologous* Inducing cell defect Inducing cancer	Altering healthy tissues Destroying healthy tissues Inducing cancer

The Challenge of Therapeutic Gene Editing

INCREASED LEVELS OF DIFFICULTIES

Type of edit	Mix of transduced molecules	Location of the editing	Percentage of edited cells	Durability	Genomic off target	Tissue off target
Simple KO	DNA (size)	Liquid tissues	Subpercent	Somatic editing is OK	Impacting cell quality	Altering healthy tissues
Double KO	RNA (size)	Solid tissues	1%			
~bps changes 1 or 2 alleles	Protein (size, charge, stability)	*Ex vivo*	10%		*Allogeneic*	Destroying healthy tissues
		In vivo			*Autologous*	
Insertions 1 or 2 alleles	Mixes	Liver	50%	Must hit renewable stem cells	Inducing cell defect	
	DNA+RNA	Eye				
	DNA+Protein	Lung	80%			Inducing cancer
Replacements 1 or 2 alleles	RNA+Protein	Muscle			Inducing cancer	
	DNA+RNA +Protein	Brain				
		Kidneys				
		Etc.	=100%			

Cellectis expectations in 2017

A Snapshot at CLLS

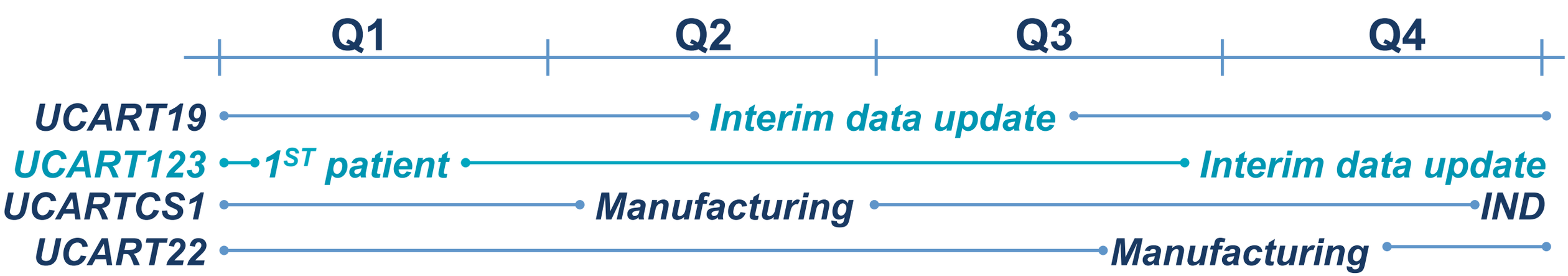
- **UCART19** clinical trials ongoing
- **UCART123** clinical trials to start early 2017
- **UCARTCS1** manufacturing in Q2 and IND filing end of 2017

- UCART22, UCART38, UCARTCLL1 will follow
- Then potentially solid tumors
- Strong partnerships with Servier and Pfizer
- Exclusivity with Pfizer ends June 2018

- Enough cash ($295M end of Q3-2016) until early 2019 for the Cellectis 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

The Cellectis Group

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

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

100% owned

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

GENE EDITING IS THE LINK

EDITING LIFE

THANK YOU

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