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EDITING LIFE

ENGINEERED CAR-T THERAPIES

A NEW PARADIGM IN ONCOLOGY

March 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.

The Cellectis Group

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

- 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

Cellectis is…

TRANSFORMING

CAR T Immunotherapy into a pharmaceutical product

Cost effective, high yield, controllable cell properties, potential front-line therapy

CREATING

First ever, off-the-shelf, gene-edited CAR T-Cells used in humans

First patient treated in phase 1 trial of UCART19 in B-ALL*

TRANSLATING

Clinical success of autologous CARTs in off-the-shelf therapies

Next generation, commercially viable, universal treatment option

LEADING

Best in class gene-editing and electroporation platform

To-date unmatched gene editing efficiency and precision with TALEN®

SERVING

Worldwide patient population with unmet medical needs

Potentially increasing patient access and targetable tumor types

* Exclusively licensed to Servier

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						

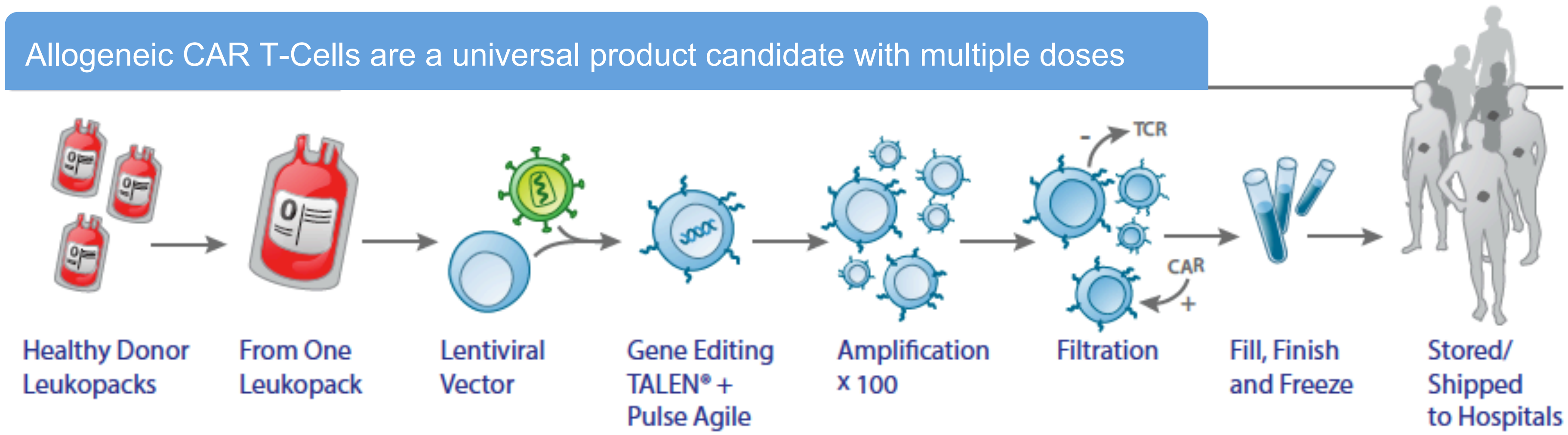
* or European equivalent

** Under exclusive licensed to Servier and joint clinical development program between Servier and Pfizer

Disruptive Innovation

Patient-Oriented Therapeutic Proposal

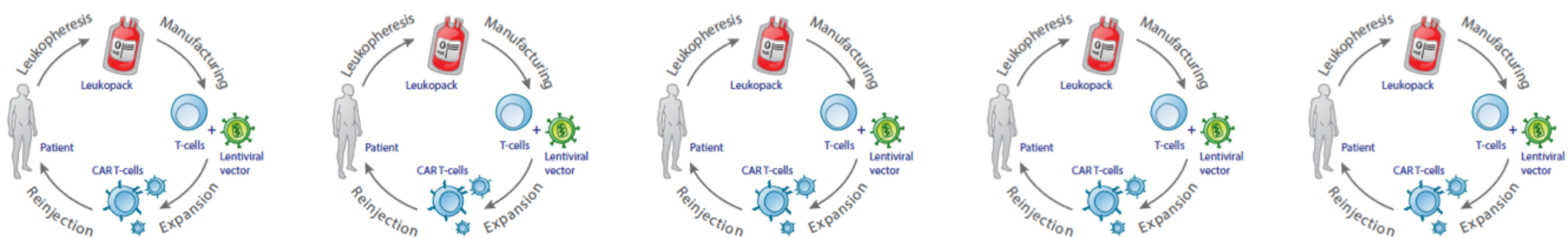
Allogeneic CAR T-Cells are a universal product candidate with multiple doses



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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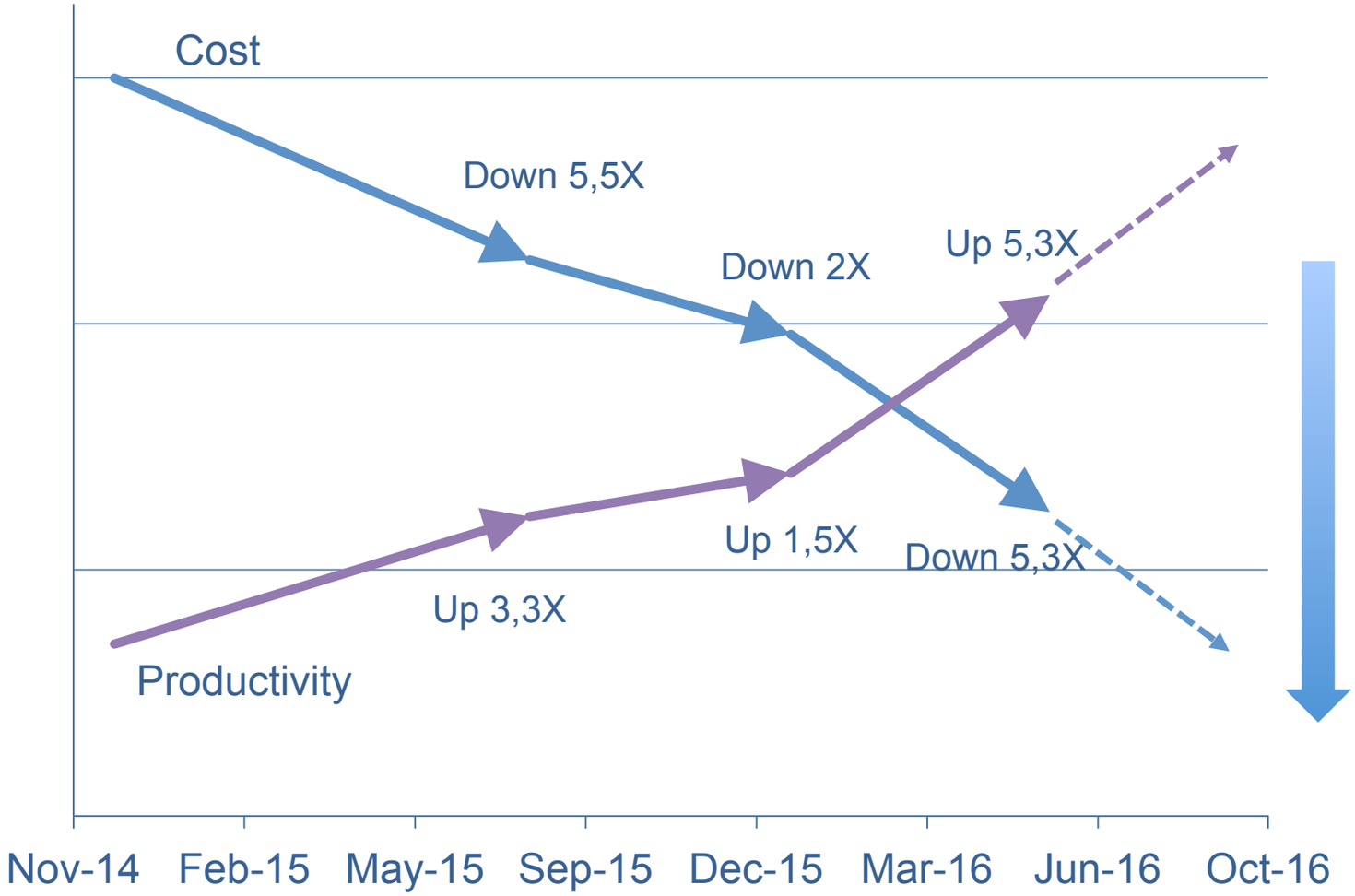
Entering Clinical Development

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**

Unmet Medical Need
in Clinical Oncology

2016 US Estimate	Incidence	Annual Death
ALL*	6,590	1,430
CLL*	18,960	4,660
AML*	20,830	10,460
BPDCN**	Estimated < 1% of all hematologic malignancies	Reported Overall Survival in one group 12-16 months
MYELOMA*	30,330	12,650
NON HODGKIN LYMPHOMA*	72,580	20,150

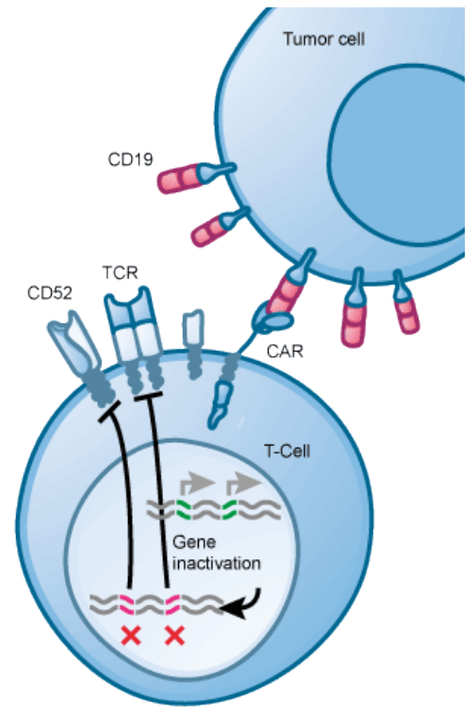
* National Cancer Institute (NCI), https://seer.cancer.gov

** Riaz et al, 2014

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) ongoing
  - Started June 2016 at University College London (UCL), UK
- Phase 1 Adult ALL (CALM) ongoing
  - Started July 2016 at King's College London (KCL), UK
- Pre-IND meeting in October 2016 for US expansion
  - 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

UCART123

CD123 (IL-3Rα), a High-Value Target for AML

Acute Myeloid Leukemia (AML)

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

- 20,830 new cases of AML in the US in 2016 were diagnosed with 10,460 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 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

Encouraging Preclinical Efficacy Data

Weill Cornell Medicine

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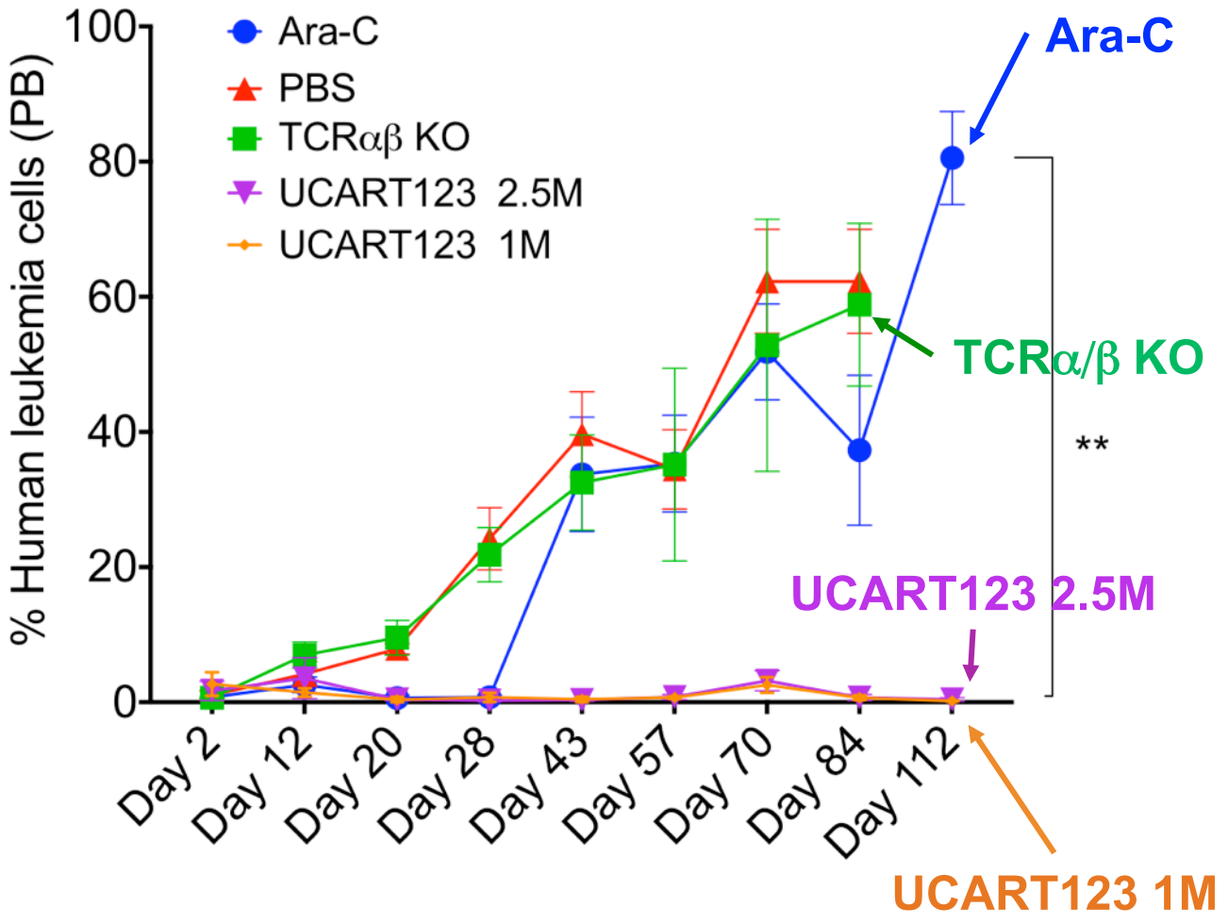
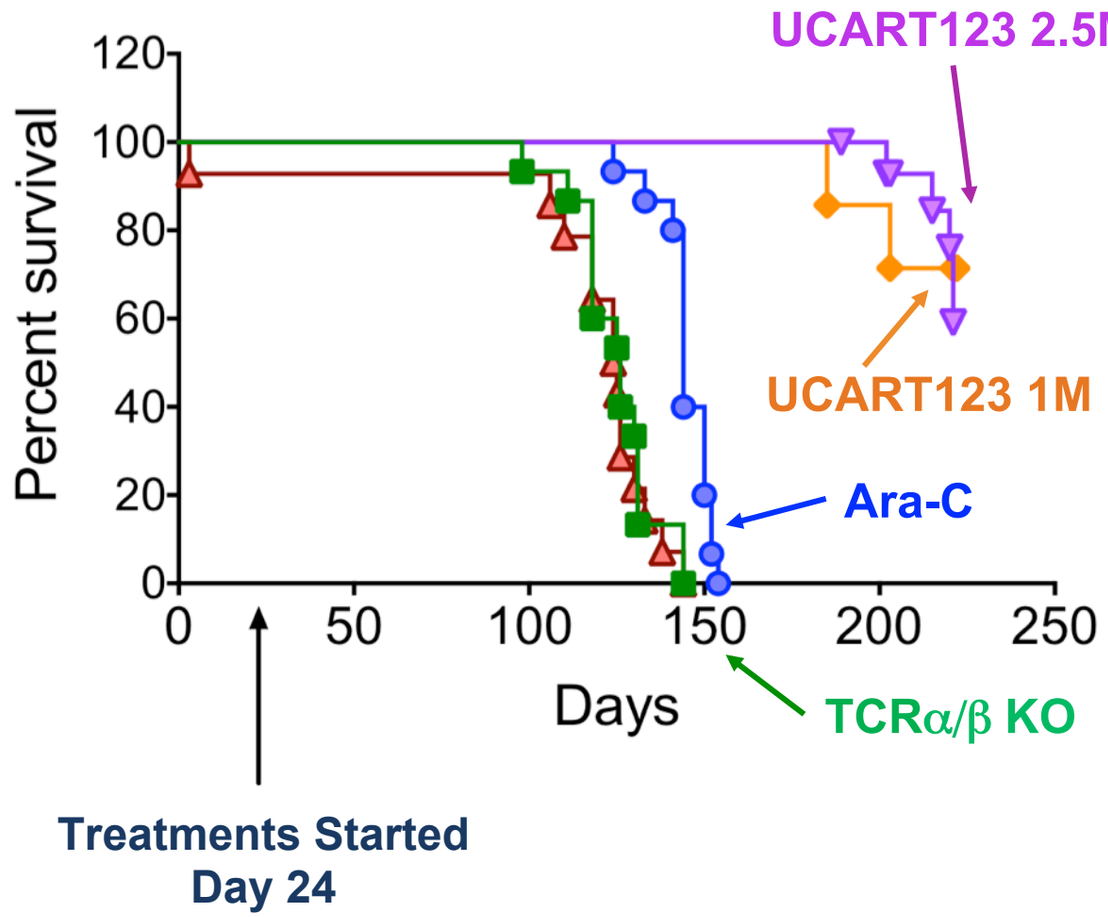
➢ UCART123 significantly decreases tumor burden and improves survival

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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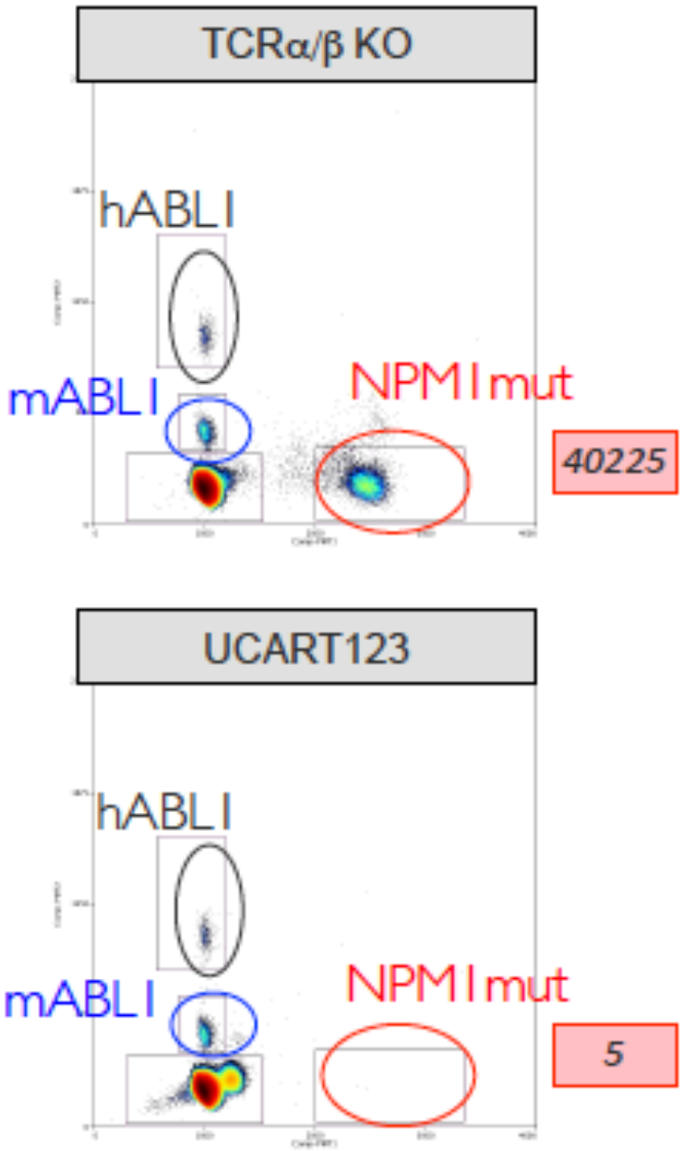
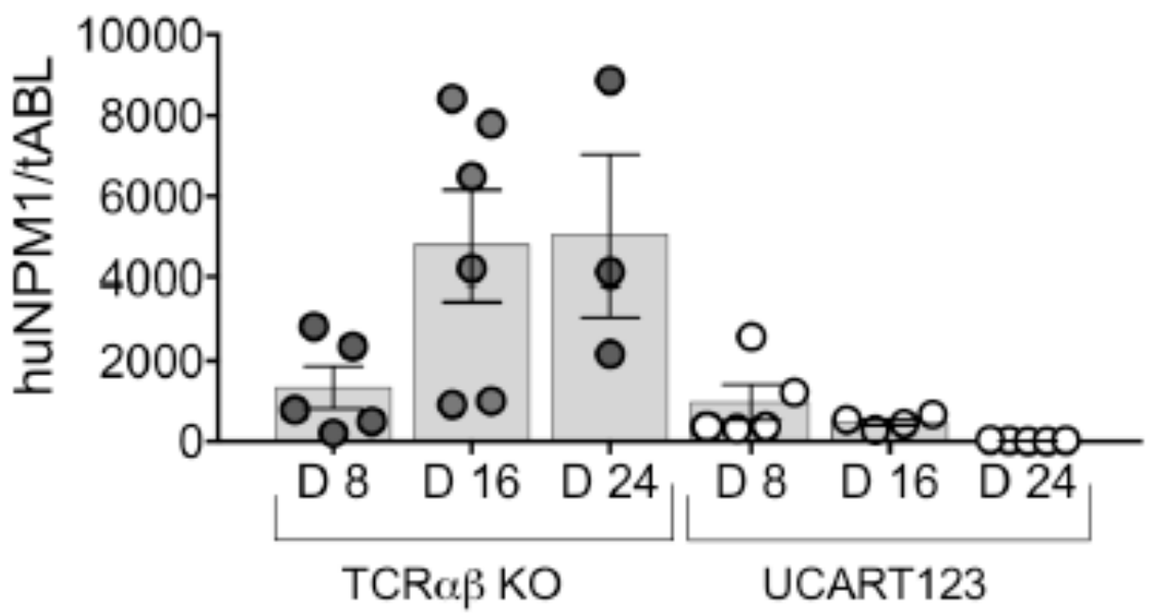
- Animals treated with UCART123 achieve molecular remission

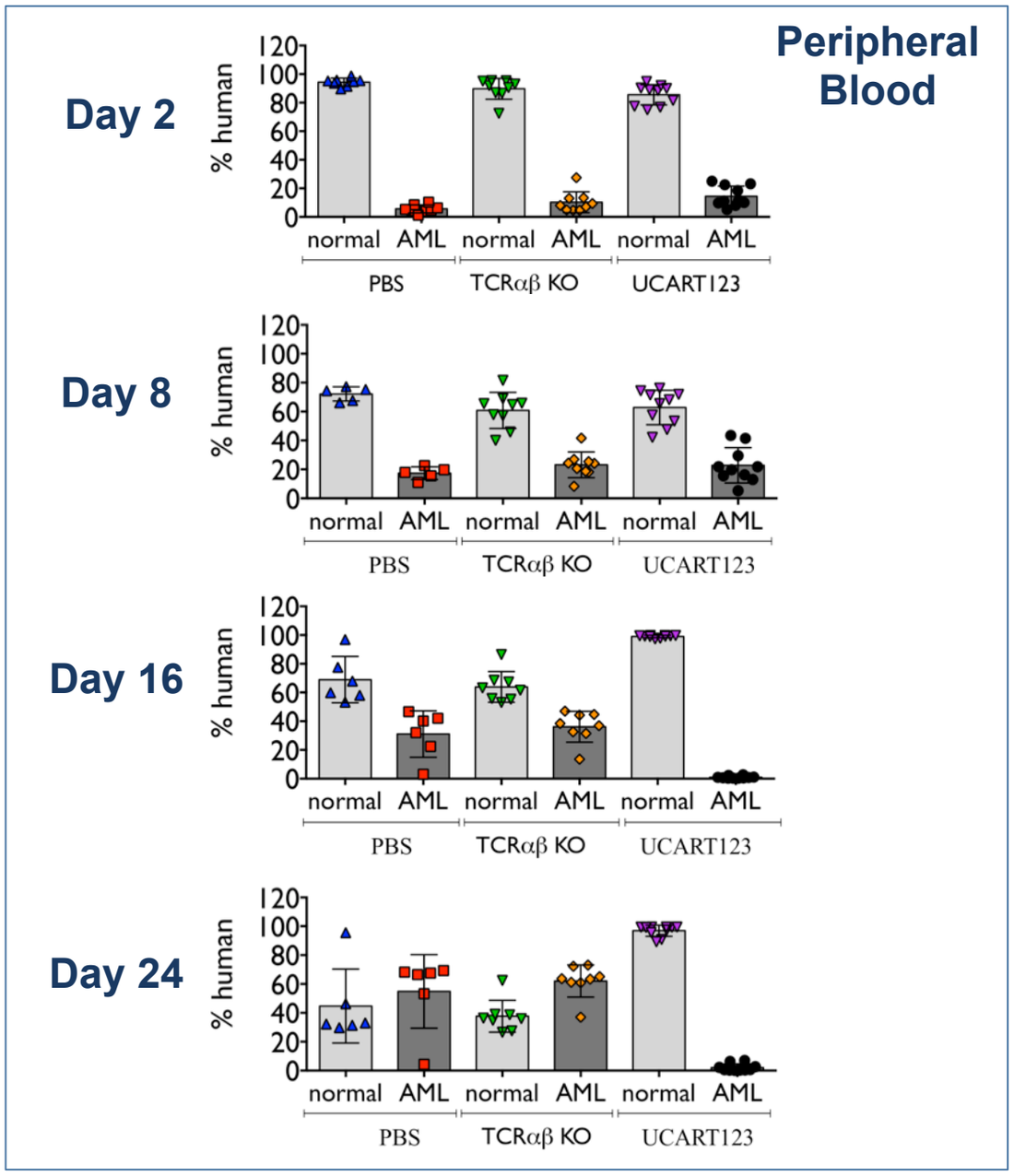


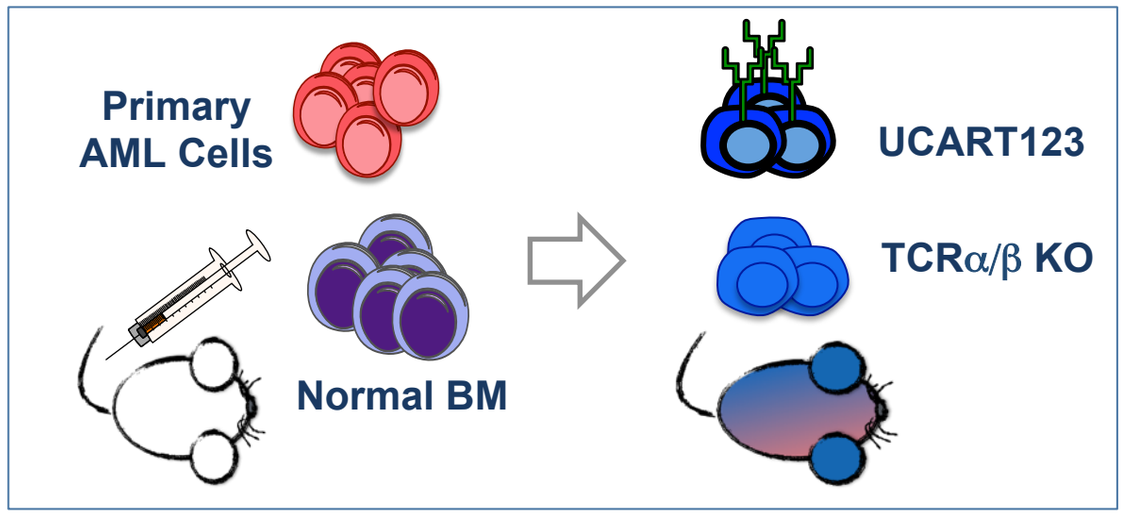


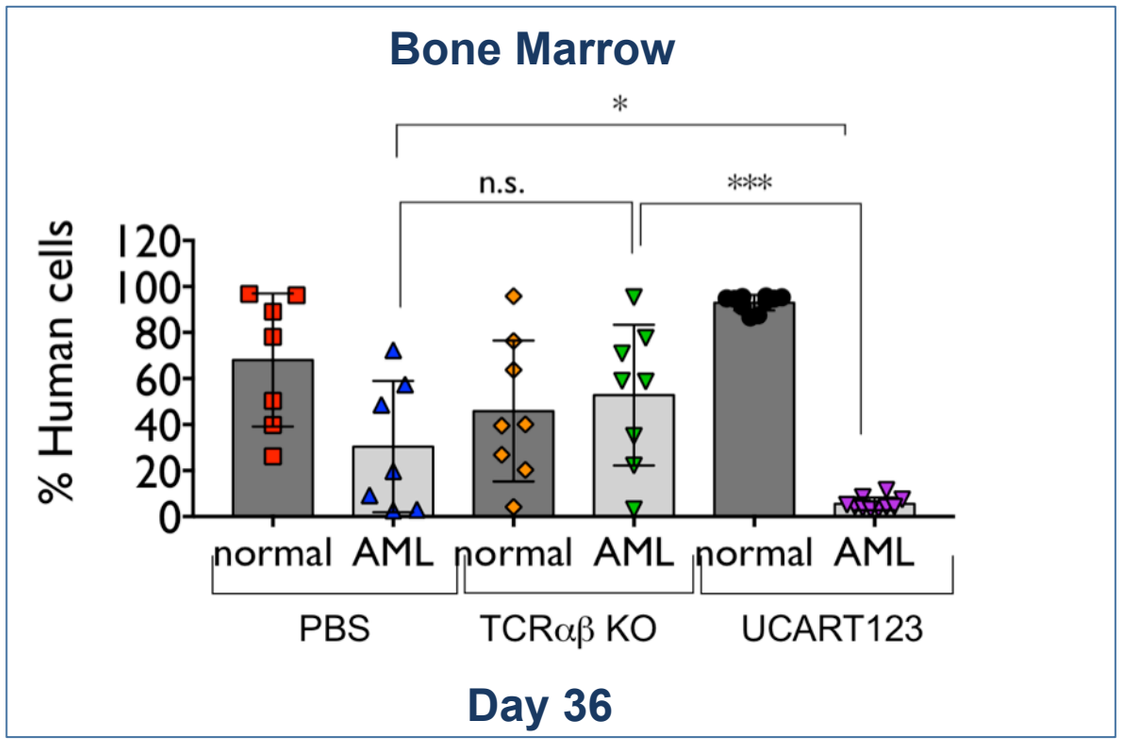
In collaboration with Dr. Monica Guzman, Cornell-Weill

UCART123
Safety

- UCART123 preferentially eliminates AML cells over normal hematopoietic cells







In collaboration with Dr. Monica Guzman, Cornell-Weill

UCART123

Study Design for AML

Weill Cornell Medicine

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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

Cleared in 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

UCARTCS1

Targeting Multiple Myeloma

Disease Description

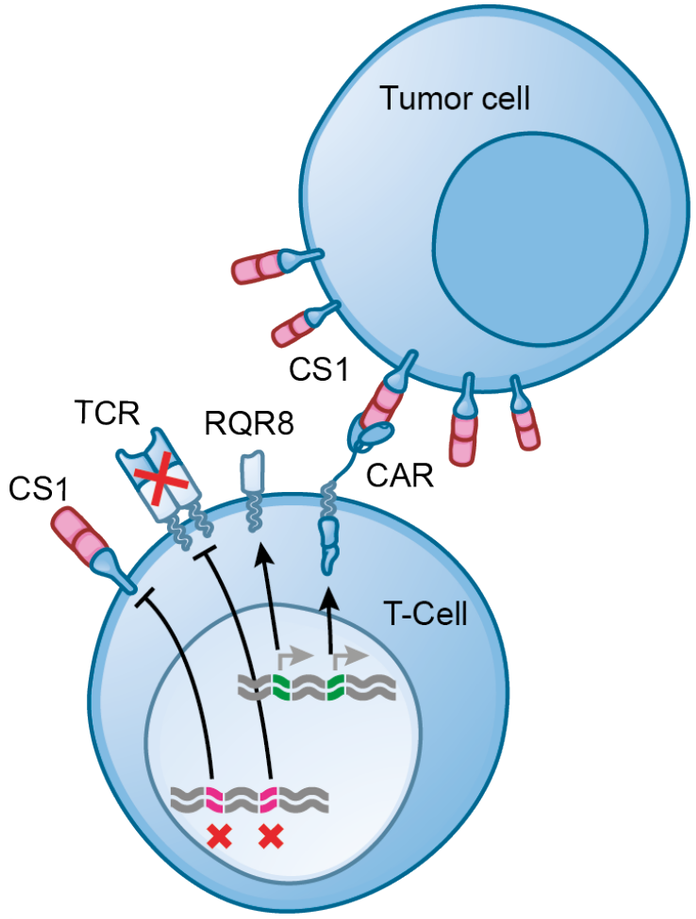
- Multiple myeloma (MM) is a hematologic malignancy characterized by proliferation of plasma cells.
- In patients relapsing after prior therapy with IMiDs and bortezomib, the median OS rate is 9 months.

Target Antigen

- Elotuzumab (BMS/Abbvie) a monoclonal antibody targeting CS1 as proof of concept for target selection
- CS1 (CD319, SLAMF7) highly expressed on MM cells.
- CS1 antigen not expressed on normal tissues or stem cells
- Low levels of expression on natural killer (NK) cells and a subset of T lymphocytes compared with malignant plasma cells.
- CS1 is expressed on CD8+ T-cells, to facilitate CAR T-cell production CS1 can be efficiently inactivated in human T-Cells, using TALEN® mRNA electroporation

UCARTCS1 Attributes

- Anti-CS1 CAR expression to redirect T-cells to tumor antigens
- Suicide gene for safety
- TCR disruption[1] to avoid GvHD
- CS1 disruption[1] to prevent CAR T-cell cross reactivity



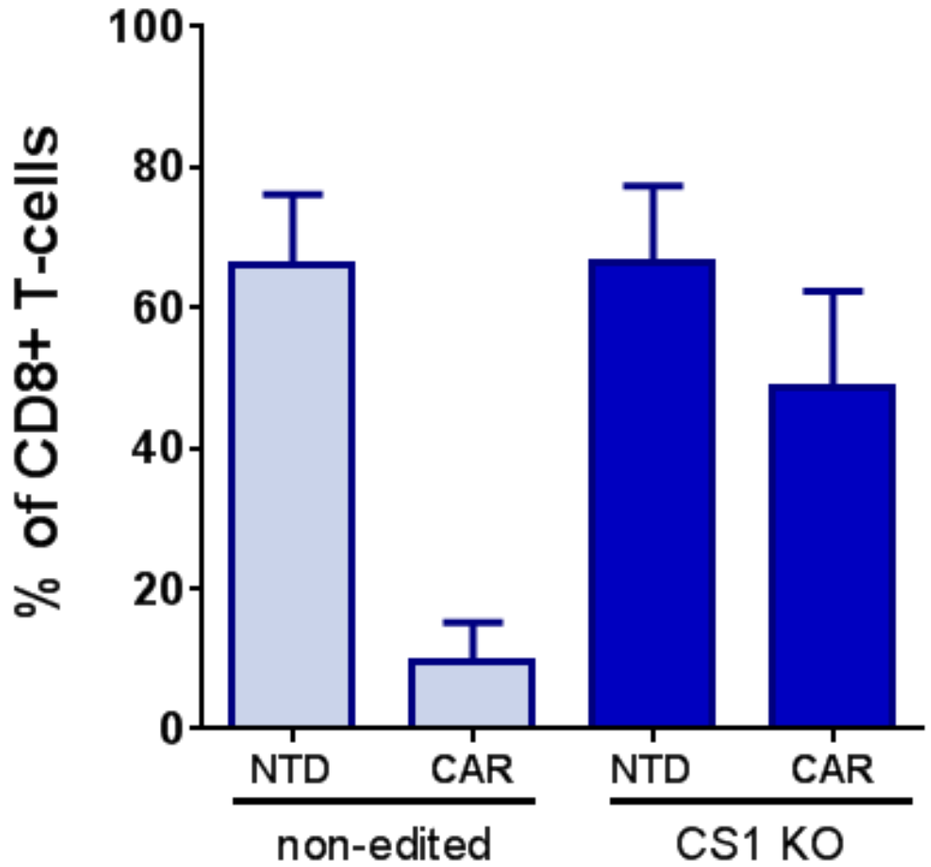
(1) *Knock-out by using TALEN®*
(2) *American Cancer Society, http://www.cancer.org/acs/groups/content/@editorial/documents/document/acspc-044552.pdf*

UCARTCS1

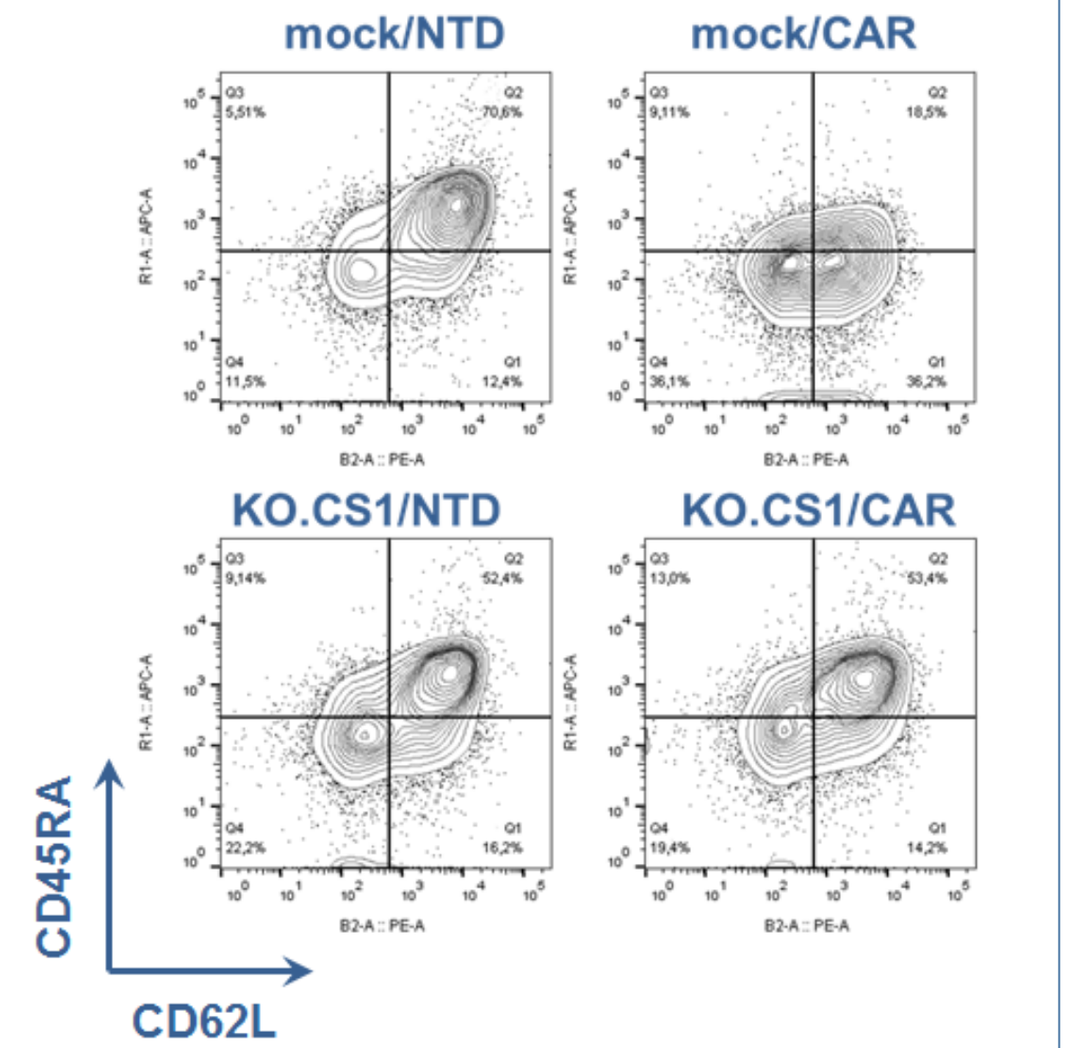
Phenotyping analysis

The inactivation of CS1 expression in T-cells leads to

- Increased yields of $CD8^+$ cells



- Prevention of the differentiation of CAR+ T-cells into memory cells

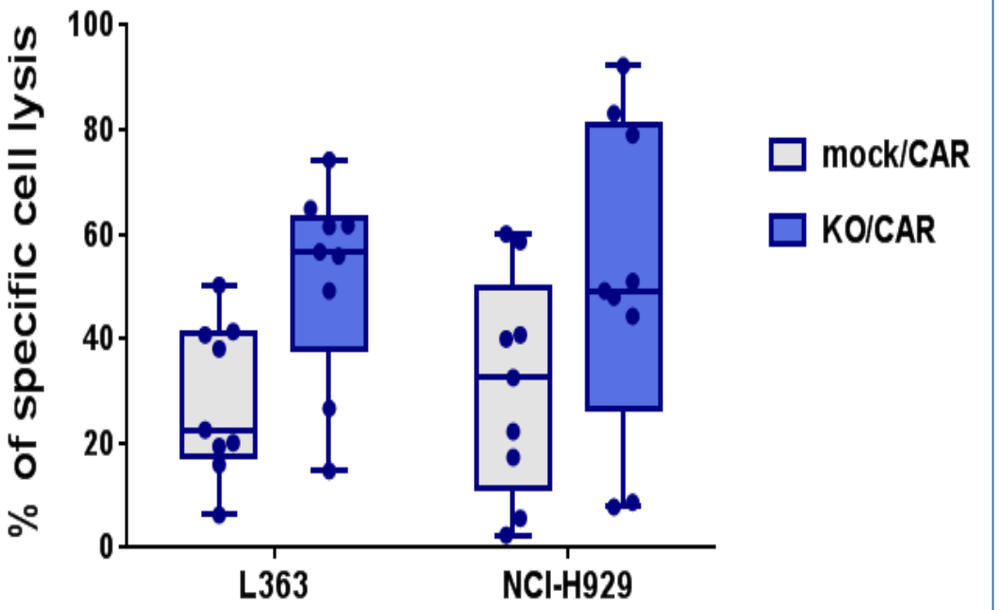


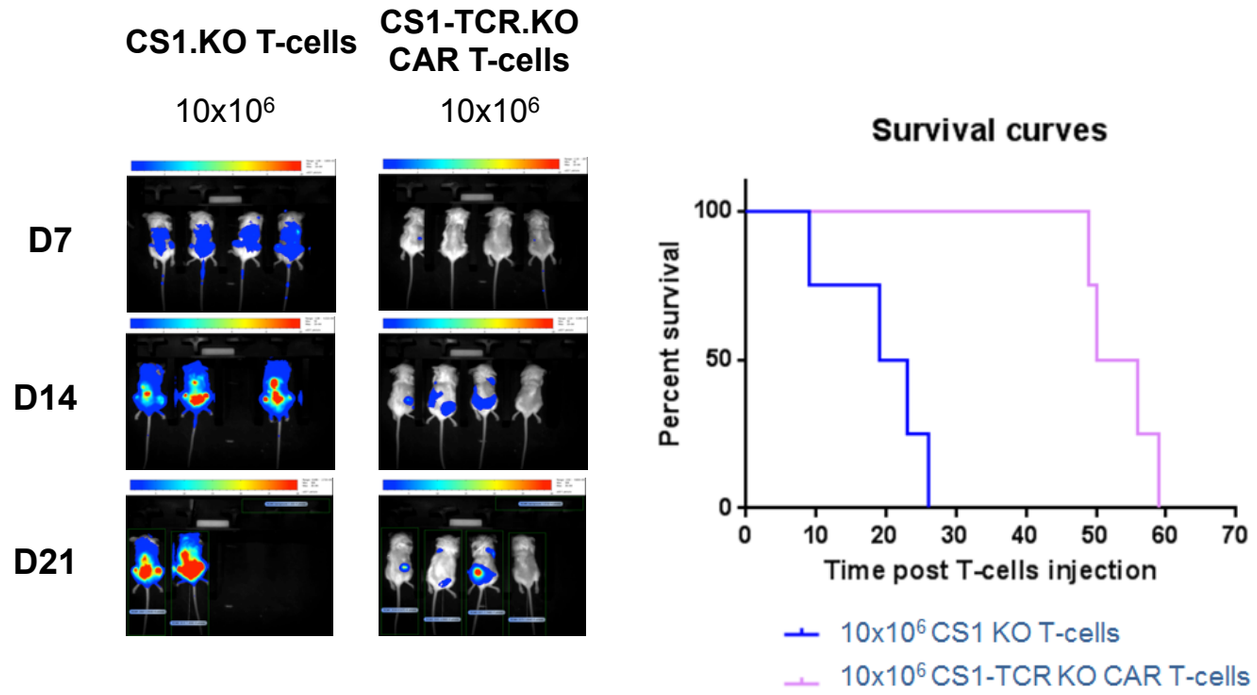
UCARTCS1

Anti-tumoral activity

The inactivation of CS1 expression in T-cells also shows

- Higher in vitro anti-tumor activity when compared to mock transfected cells
- Significant in vivo anti-tumor activity





In vitro

In vivo

UCARTCS1
Development Plan

Proof of Concept – completed in Q4 2016
- Increased cytotoxic activity compared to non-edited T-cells

***In-vivo* studies** – expected in Q2 2017
- Preclinical studies ongoing in collaboration with MD Anderson Cancer Center (Dr. Jing Yang and Dr. Sattva Neelapu)

Manufacturing – expected to start Q2-2017
- Development of a modified GMP compatible manufacturing process (inversion of transduction/electroporation steps)

IND Filing – expected in Q4 2017

UCART38 – Another Target for Multiple Myeloma
- Pre-clinical development ongoing

UCART22

Targeting ALL and other B-Cell Malignancies

Disease description

- Acute lymphoblastic leukemia (ALL) is a cancer of the white blood cells, characterized by the overproduction and accumulation of immature white blood cells (known as lymphoblasts).

Rationale

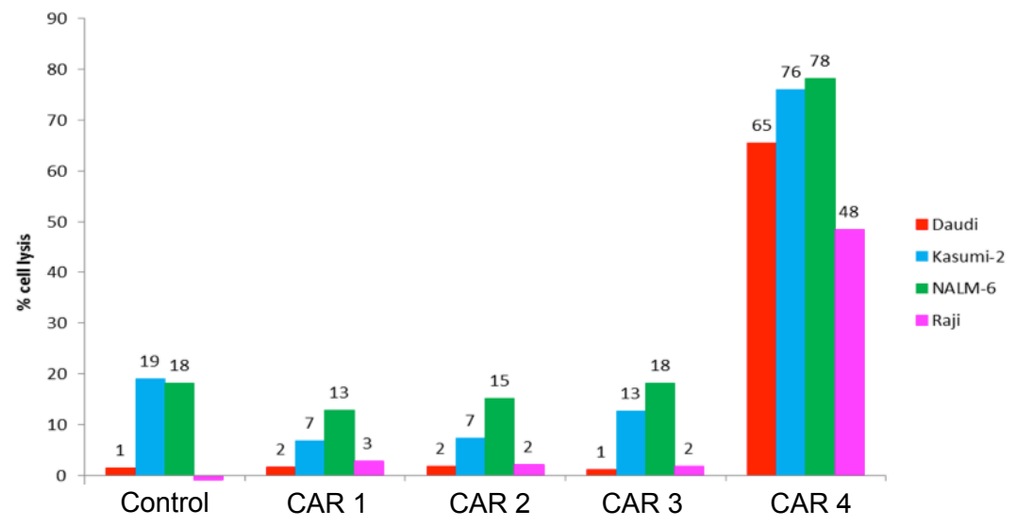
- CD22 and CD19: same expression profile on various B-Cell stages of development
- CD22 expression frequently maintained in CD19-negative blast cells in ALL [ref1]

Target Antigen

- CD22, a single-family lectin, consists of 7 extracellular IgG-like domains and is expressed on the B-cell surface starting at the pre-B-Cell stage, persists on mature B-Cells, and is lost on plasma cells.

Proof of concept

- Anti-CD22 monoclonal antibodies / immunotoxins (e.g. Inotuzumab ozogamicin).
- Autologous CAR-T in development (JCAR018)

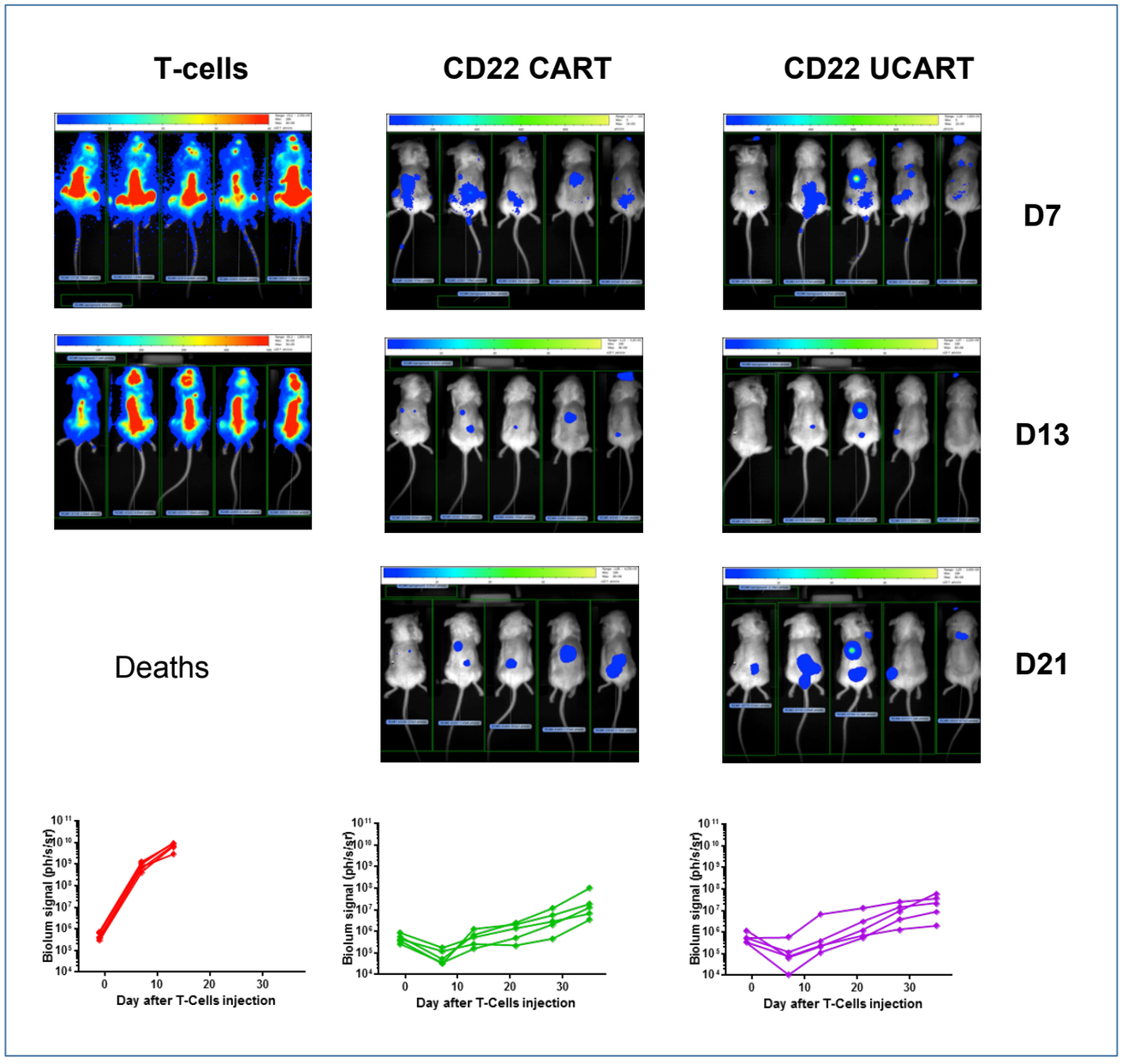


Ref 1: Maude et al, Blood 2015 125:4017-4023.

UCART22

Anti-tumoral activity

- CD22 CART cells are highly efficient at eradicating tumors in vivo
- CD22 UCART cells are as efficient as CD22 CART cells



In vivo

UCART22
Development Plan

Proof of concept – completed in Q4 2016
- In vitro cytotoxic activity demonstrated in CD22+ cell lines
- Generation of anti-CD22 proprietary monoclonal antibodies (selection on going)

***In vivo* studies** – expected in Q3 2017
- Preclinical studies ongoing in collaboration with MD Anderson Cancer Center

Manufacturing – expected to start in H2 2017
- Similar manufacturing process to UCART19

IND filing – expected 2018
- CD22 as another target for ALL/CLL relapsed patients
- Potential to use as re-dosing regiment after potential CD19 ALL / CLL treatment relapse

Entering Clinical Development

An integrated Gene Edited Cell Therapy Platform

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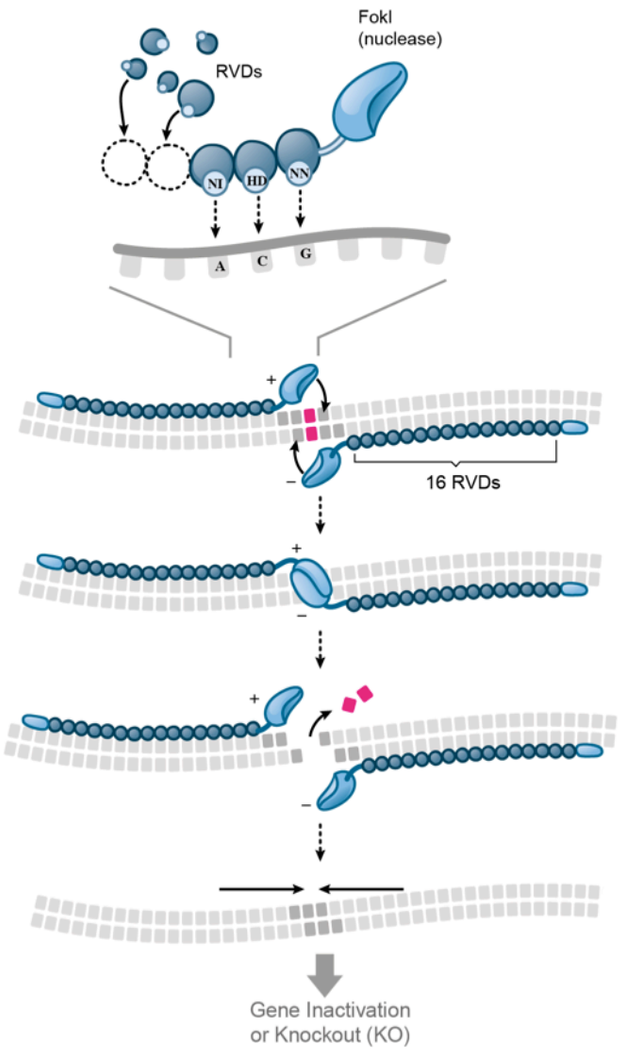
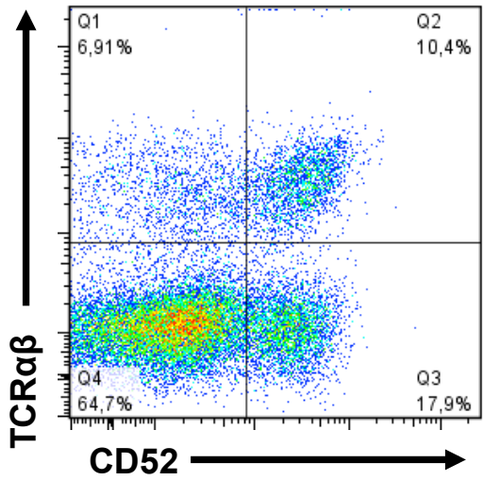
TALEN® Gene Editing



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

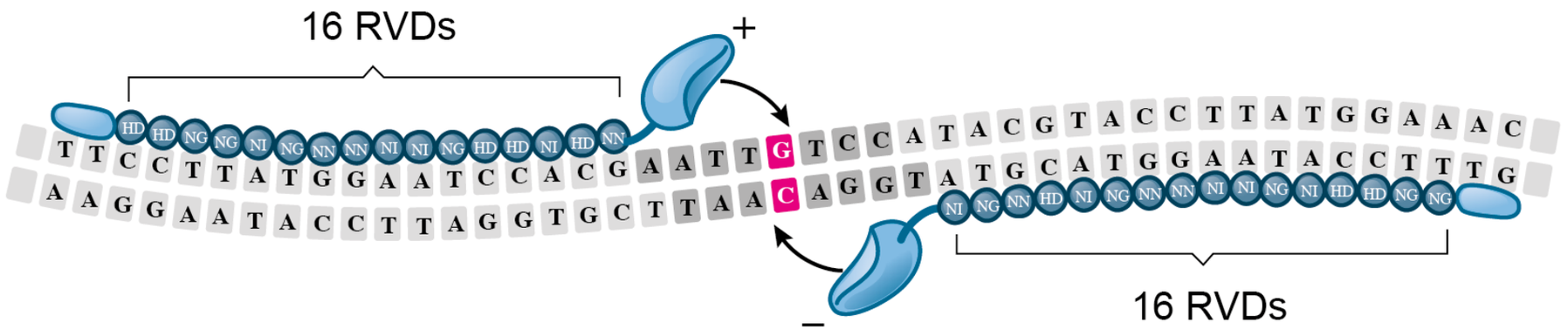
Therapeutic Cells Gene Edited

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

Disruptive innovation

Building more powerful T-Cells

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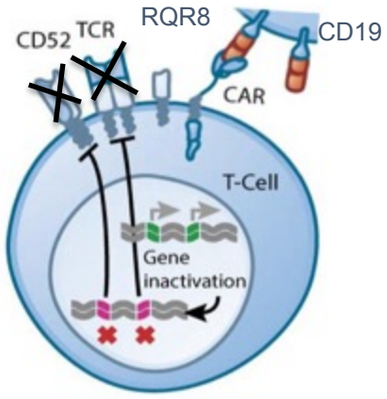
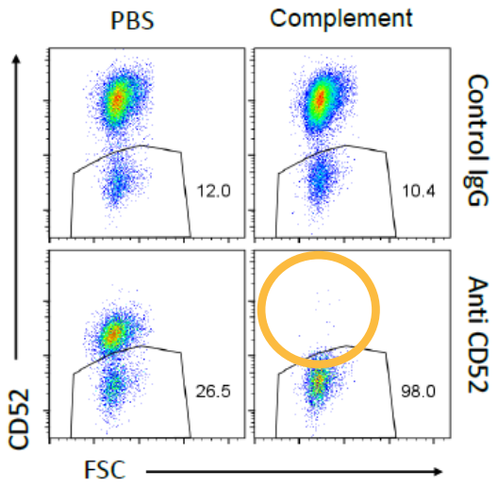
Mab-resistance

- **CD52 KO** for Alemtuzumab resistance



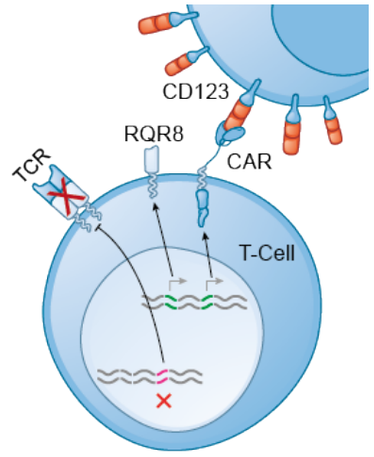


CD52-negative T-Cells are resistant to Campath

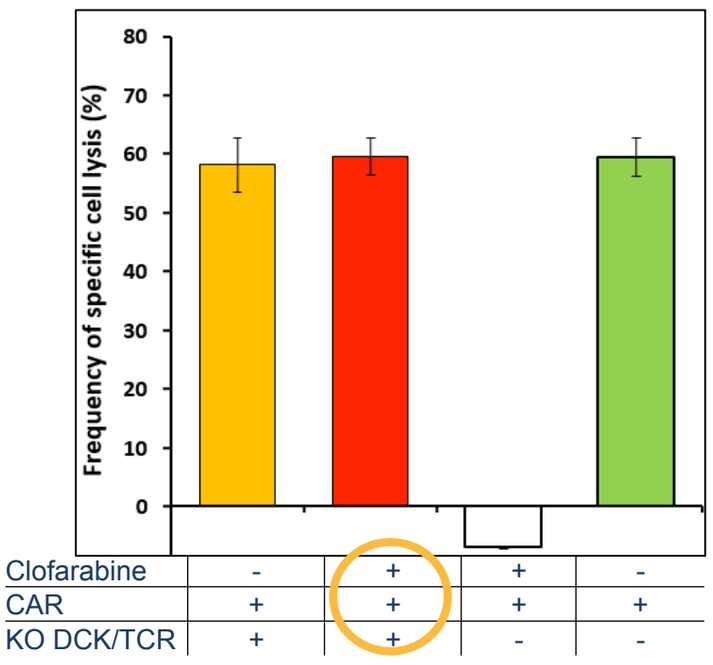
Poirot L *et al*. (2015) Cancer Res.

Chemo-resistance

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

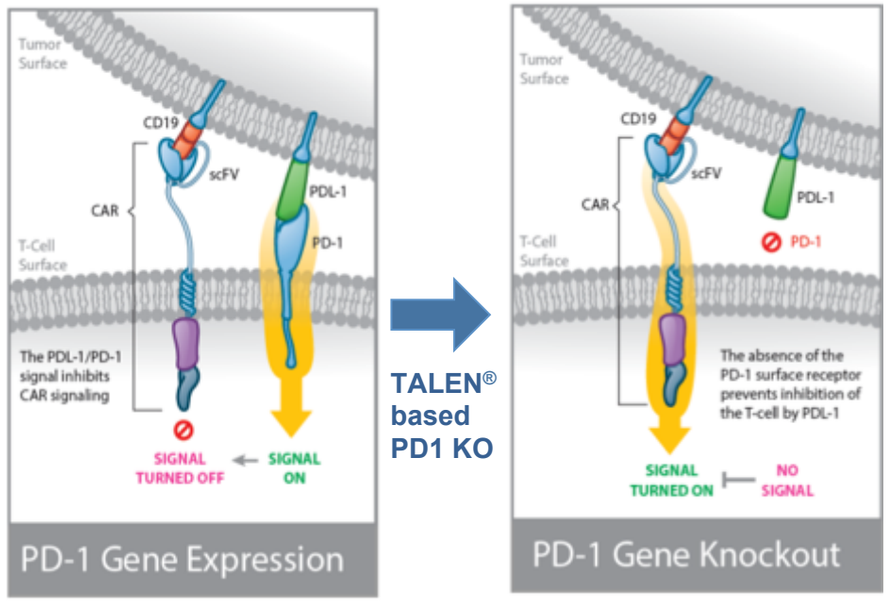


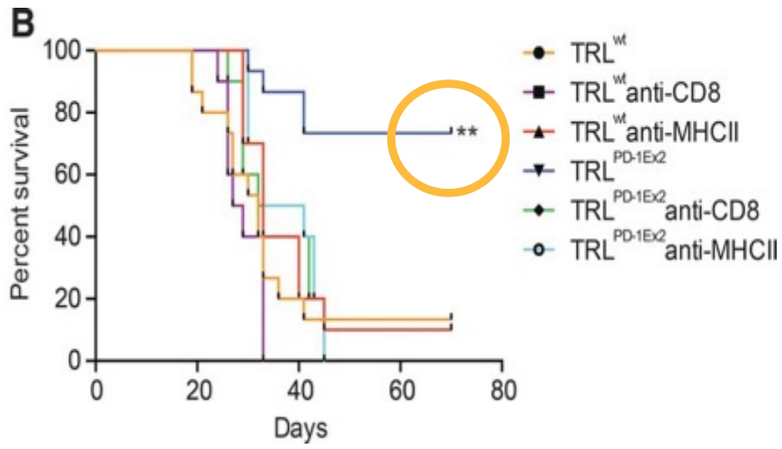
dCK-negative T-Cells are resistant to Clofarabine



PDL1-resistance

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





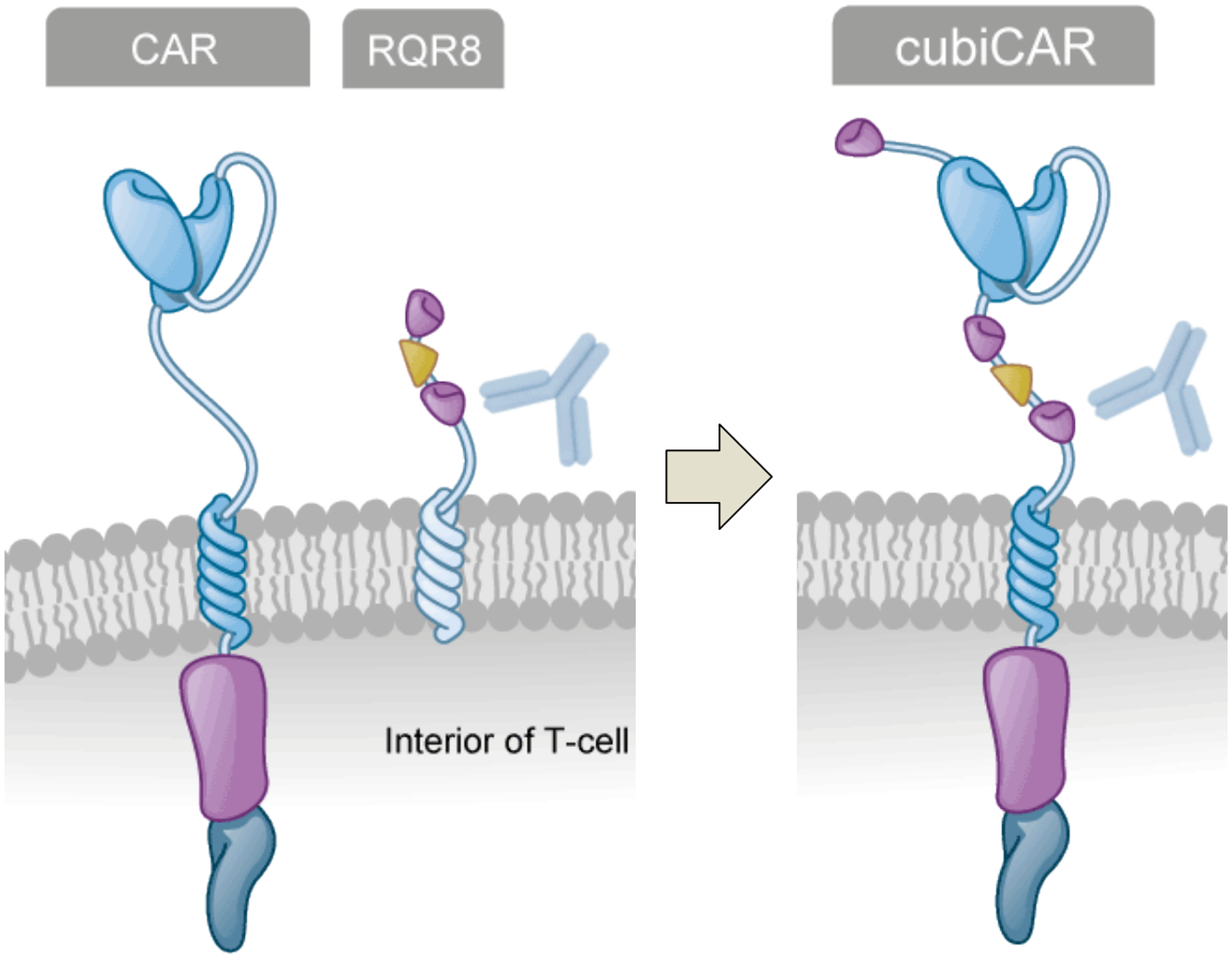
PD1-negative T-Cells have a higher efficacy on PDL1 tumor

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

Disruptive innovation

High Tech at the Service of Patients

A suicide switch imbedded in the CAR molecule



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

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 all of the United States.

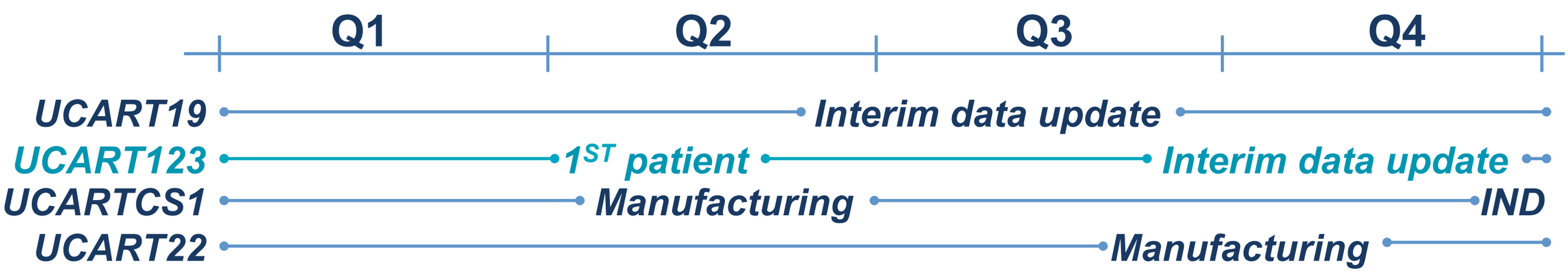
- Development of UCARTCS1 for Multiple Myeloma, UCART22 for ALL, UCART38 in for T-Cell ALL and UCART123 for BPDCN
- MD Anderson is ranked the No. 1 hospital for cancer care in the nation by U.S. News & World Report's "Best Hospitals" survey

- Phase 1 clinical trial of Servier UCART19 in pediatric patients
- Great Ormond Street Hospital, London is ranked among the to 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

Cellectis expectations in 2017

What to watch?



In 2017:

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

Beyond 2017:

- UCART22, UCART38, UCARTCLL1 INDs will follow
- Potential solid tumor targets
- Strong partnerships with Servier and Pfizer producing multiple CAR T programs
- Exclusivity with Pfizer ends June 2018

Strong Cash Position:

- $291M in cash at year end 2016; Cash runway into 2019 for the Cellectis Group, including Calyxt

The Future
of CAR T-Cell Treatment

Cellectis Innovation

- Allogeneic, non alloreactive CAR T-Cells
- Resistance to chemotherapy
- Resistance to lympho-depleting agents
- Resistance to tumor inhibition
- Suppressed cross T-Cell reaction
- Controllable CAR expression / activity
- Versatile Gene Editing

Targeted Patient Benefits

- ✓ Off-the-shelf product (TCR knockout)
- ✓ Compatible with standard of care therapies
- ✓ Enhanced engraftment (DCK knockout)
- ✓ Enhanced efficacy (PD1, CTLA4 knockout and more)
- ✓ Better suited for specific tumor types
- ✓ Mitigate risks of CAR T-Cell-related toxicities
- ✓ Reaching more targets/indications for CAR T-Cells

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EDITING LIFE

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

Calyxt, Inc.
600 County Rd D
New Brighton, MN 55112 – USA

investors@cellectis.com