

ENGINEERED CAR-T THERAPIES

A NEW PARADIGM IN ONCOLOGY

FORWARD-LOOKING STATEMENTS



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- NASDAQ: CLLS
- ALTERNEXT: ALCLS
- 35.5M SHARES OUTSTANDING
- \$272M IN CASH AS OF JUNE 30, 2017

- IMMUNO-ONCOLOGY / CAR T
- THERAPEUTIC GENE EDITING
- GENE THERAPY

80% ownership



- NASDAQ: CLXT
- IPO JULY 2017
- \$64M GROSS PROCEEDS
- 27.65M SHARES OUTSTANDING

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

Gene editing is the link

CAR T 2.0

The Next Step in CAR T-Cell Treatment

- **Allogeneic CAR T-cells**
 - ✓ Off-the-shelf pharmaceutical product
 - ✓ Not relying on patient's own T cells
 - ✓ Immediately ready to inject
 - ✓ Expanding patient access
 - ✓ Significantly lower cost
- **TALEN® Gene-Edited CAR T-cells**
 - ✓ Non-alloreactive
 - ✓ Compatibility with standard-of-care chemotherapies
 - ✓ Resistance to tumour inhibition (PD1, CTLA-4 knockout and more)
 - ✓ Reaching more targets/indications for CAR T-cells
- **Controllable CAR Activity / Persistence**
 - ✓ Mitigate risks of CAR T-cell-related toxicities
 - ✓ Possibility for a multiple dosing approach

UCART Pipeline

Addressing a large spectrum

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

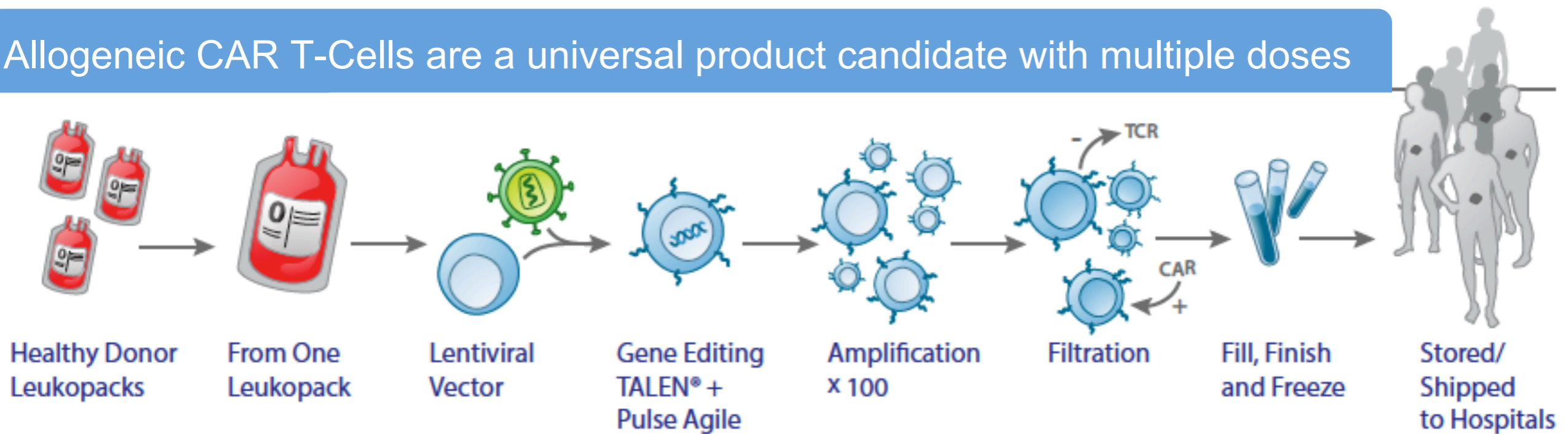
* or European equivalent

** UCART19 is exclusively licensed to Servier and under a joint clinical development program between Servier and Pfizer

cGMP Manufacturing

Patient-Oriented Therapeutic Proposal

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



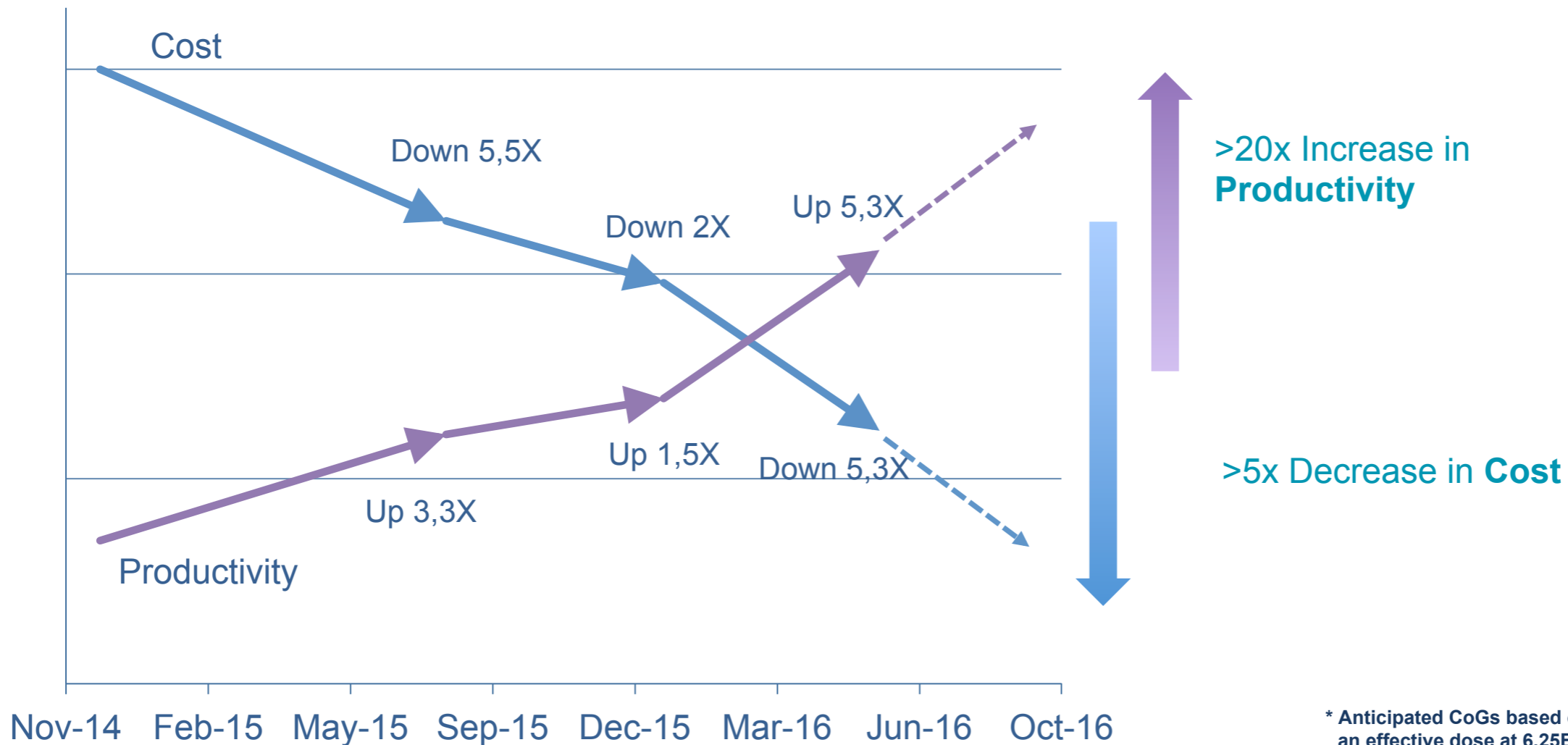
One Leukopack can yield 100s of doses at a cost of goods of less than \$4,000 per dose*

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

Entering Clinical Development

Increasing Yields, Decreasing CoGs

- Worldwide, immediate access to patients
- Since 2015, CoGs already decreased by 5x
- Productivity per manufacturing run increased by 20x



Unmet Medical Need in Clinical Oncology

US Estimate	Estimated New Cases in 2017	Estimated Deaths in 2017	Incidence	5 Year Survival (2007-2013)
AML*	21,380	10,590	4,2 per 100,000	26,9%
BPDCN	Estimated < 1% of all hematologic malignancies**		0,45 per 1,000,000***	38%***
ALL*	5,970	1,440	1,7 per 100,000	68,2%
CLL*	20,110	4,660	4,7 per 100,000	83,2%
MYELOMA*	30,280	12,590	6,6 per 100,000	49,6%
NON HODGKIN LYMPHOMA*	72,240	20,140	19,5 per 100,000	71%

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














** Riaz et al, 2014

*** Alsidawi et al, 2016

AML Landscape

Area of high unmet need

➤ Despite several late stage products in clinic, patients have minimal options

	Phase 3	Filed	Approved / Mkt.
Hypomethylating agents	 <ul style="list-style-type: none"> • SGI-110 (DNA methyl inhibitor)  <ul style="list-style-type: none"> • CC-486 (Oral Vidaza) 		 <ul style="list-style-type: none"> • Vyxeos (Liposomal formulation)
Kinase inhibitors	 <ul style="list-style-type: none"> • Quizartinib (FLT3 inhibitor)  <ul style="list-style-type: none"> • Gilteritinib (Kinase inhibitor)  <ul style="list-style-type: none"> • Venclexta (Bcl-2 inhibitor)  <ul style="list-style-type: none"> • Volasertib (Plk1 inhibitor) 		 <ul style="list-style-type: none"> • Rydapt (Kinase inhibitors)
Isocitrate dehydrogenase inhibitors		 <ul style="list-style-type: none"> • Ivosidenib (IDH1 inhibitor) 	 <ul style="list-style-type: none"> • Idhifa (IDH2 inhibitor) 
Antagonists	 <ul style="list-style-type: none"> • Idasanutlin (MDM2 antagon.) 		
ADCs		 <ul style="list-style-type: none"> • Mylotarg (Antibody drug conjugate, PDFUA Sept. 17) 	

Leadership in Cell Therapy

CAR T will be a cornerstone in AML



In vitro or Preclinical

Phase 1 or Phase 1/2

AUTOLOGOUS CAR T CELLS

Anti-CD33	Penn Universitätsklinikum Carl Gustav Carus Centre Léon Bérard	Anti-CD33 & Anti-CD123	Universitätsklinikum Carl Gustav Carus gemoab
Anti-CD123	Kite Pharma City of Hope BCM UNIVERSITY OF PENNSYLVANIA Abramson Cancer Center FONDAZIONE TETTAMANTI INTREXON ZIOPHARM Oncology, Inc. Shandong University	Anti-CD33 or Anti-CD123	BICOCCA CANCER RESEARCH UK HIROSHIMA UNIVERSITY
Anti-CD123		Anti-CD38	MOLMED OSPEDALE SAN RAFFAELE
Anti-CD123		Anti-CD44v6	
Anti-CD123		Anti-FRB	Penn
Anti-CD123		Anti-HLA-A2	THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Anti-CLL1	BCM		

Anti-CD33	Chinese PLA General Hospital INTREXON ZIOPHARM Oncology, Inc.
Anti-CD123	Affiliated Hospital to Academy of Military Medical Sciences City of Hope Penn
Anti-CD123	
Anti-CD123	Celyad
Anti-CD123	Peter Mac Peter MacCallum Cancer Centre

ALLOGENEIC CAR T CELLS

Anti-CD123	cellectis
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Anti-CD123	cellectis
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AUTOLOGOUS CAR NK CELLS

Anti-CD123	MHH Hannover Medical School
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Anti-CD7	PersonGen BioTherapeutics
Anti-CD33	PersonGen BioTherapeutics

UCART123 in AML and BPDCN

Entering Clinical Development



Acute Myeloid Leukemia (AML)

- 21,380 new cases of AML were diagnosed in the US in 2017 with 10,590 deaths
- Five-year survival 27%; relapse rate 33-78%, depending on age and subtype
- Collectis trial in the setting of relapsed/refractory AML and 1st line high risk AML
- Orphan Drug Designation potential

➤ ***AML Ph 1 dose escalation at Weill Cornell; First patient dosed in June 2017***

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

- 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

➤ ***BPDCN Ph 1 dose escalation at MD Anderson; First patient dosed in August 2017***

UCART123 in AML

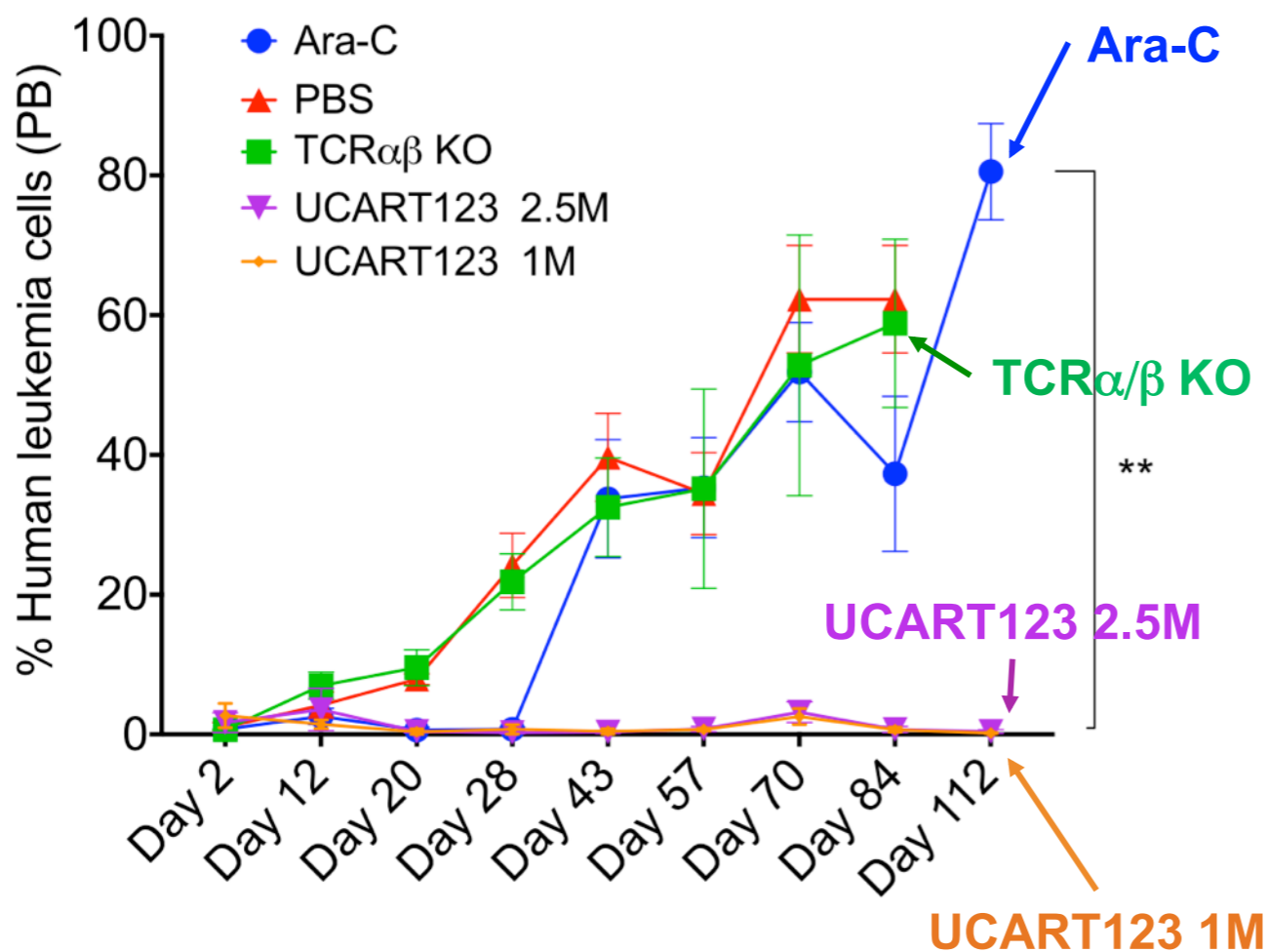
Encouraging Preclinical Efficacy Data at ASH 2016



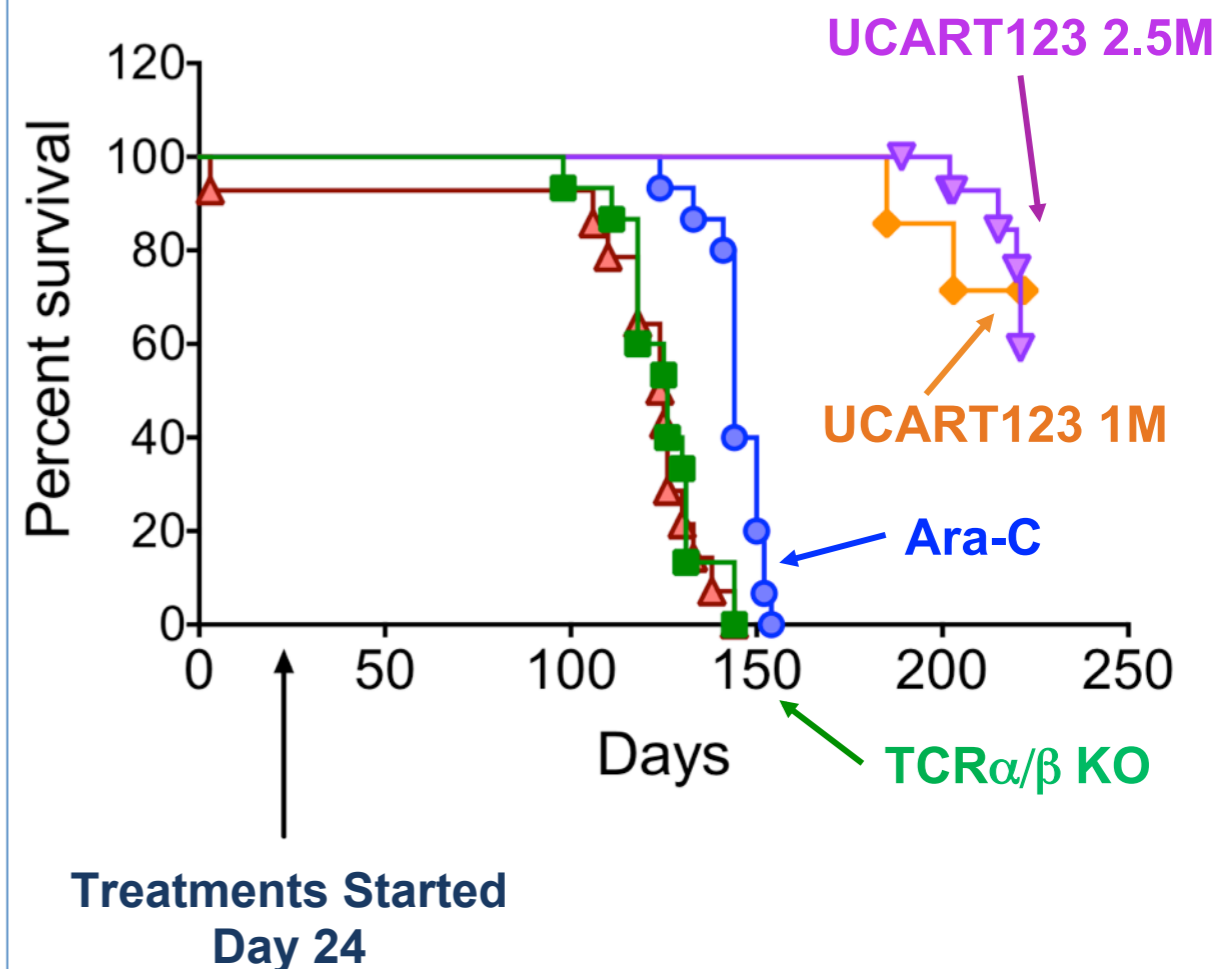
**Weill Cornell
Medicine**

- UCART123 shows significant improvement compared to Cytarabine standard-of-care (Ara-C)

Peripheral Blood Evaluation



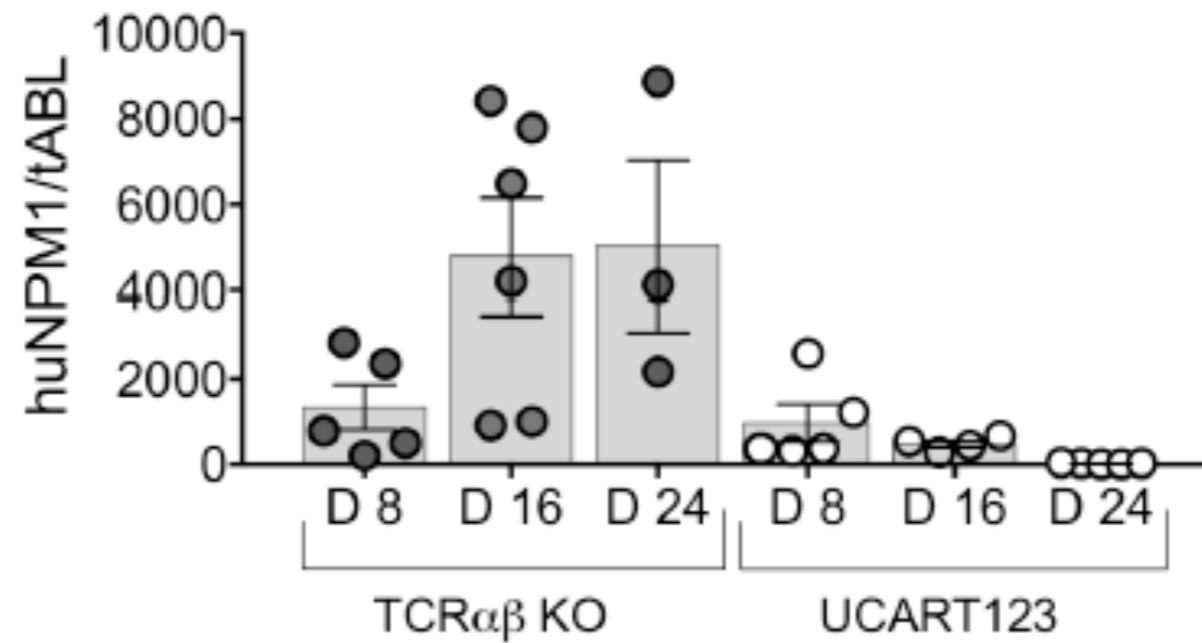
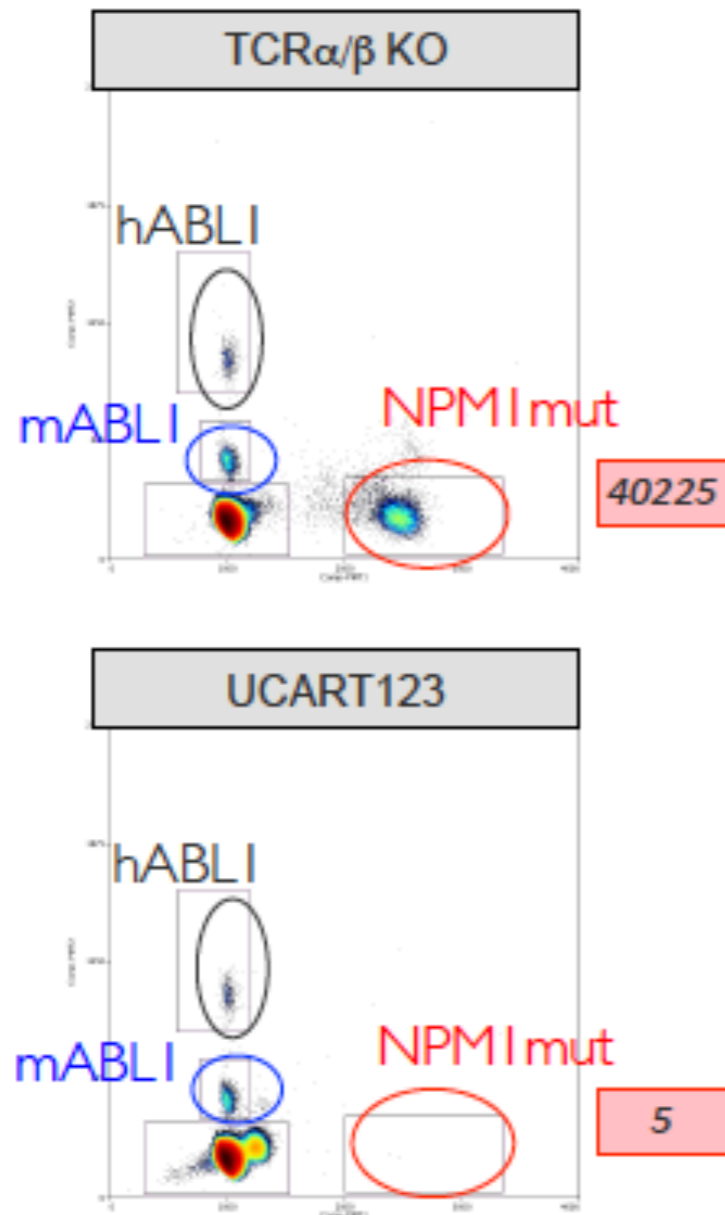
Overall Survival



UCART123 in AML

Encouraging Preclinical Efficacy Data at ASH 2016

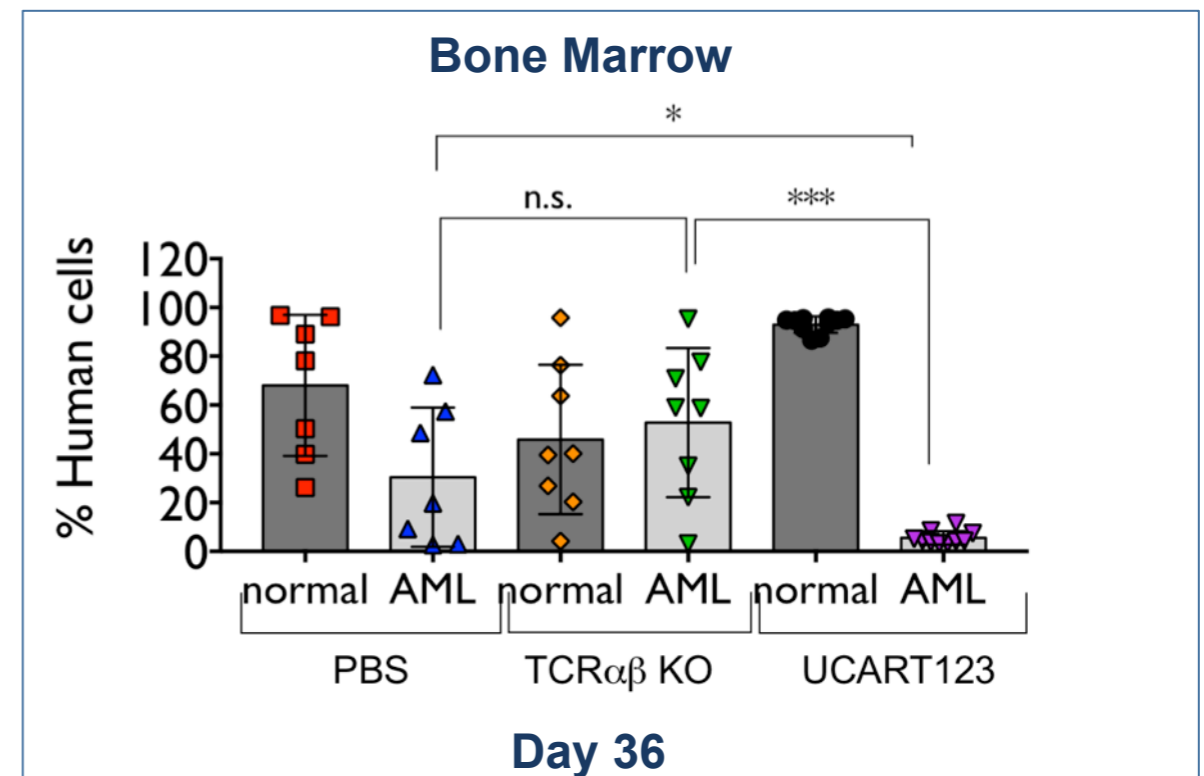
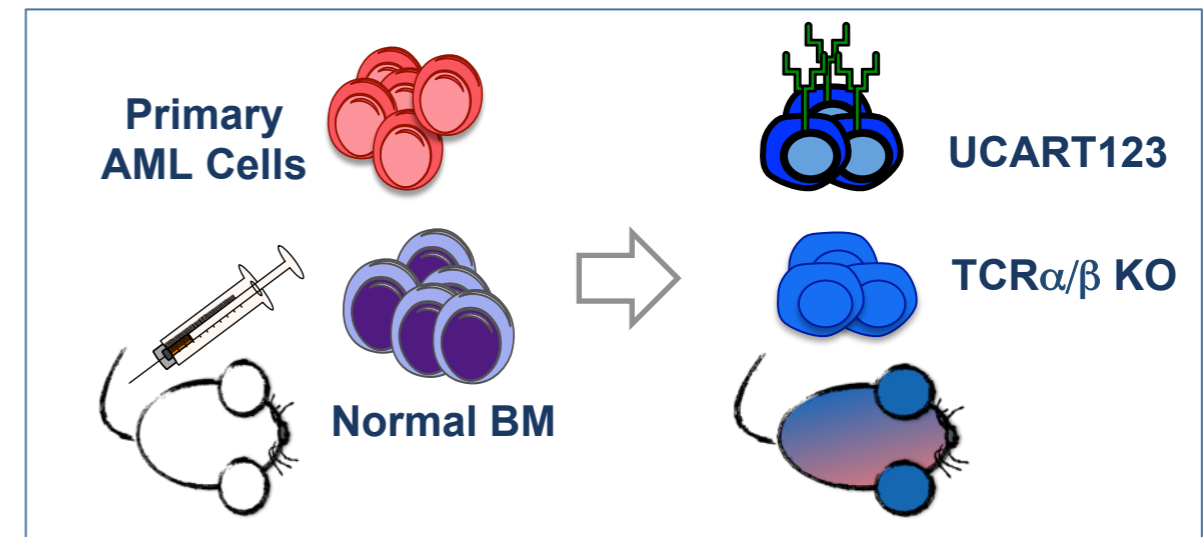
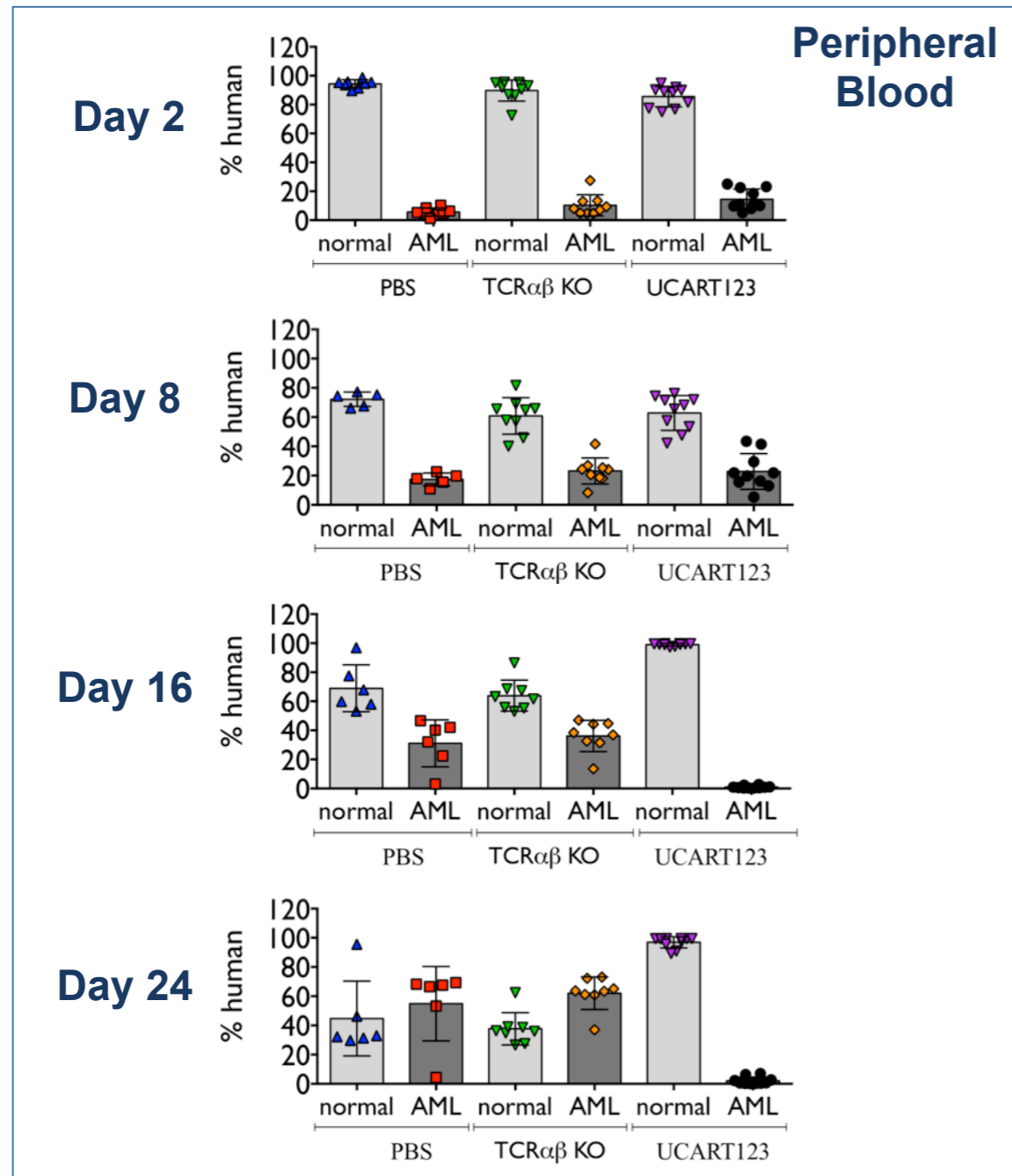
- Animals treated with UCART123 achieve lasting molecular remission



UCART123 in AML

Encouraging Safety Profile

- UCART123 preferentially eliminates AML cells over normal hematopoietic cells

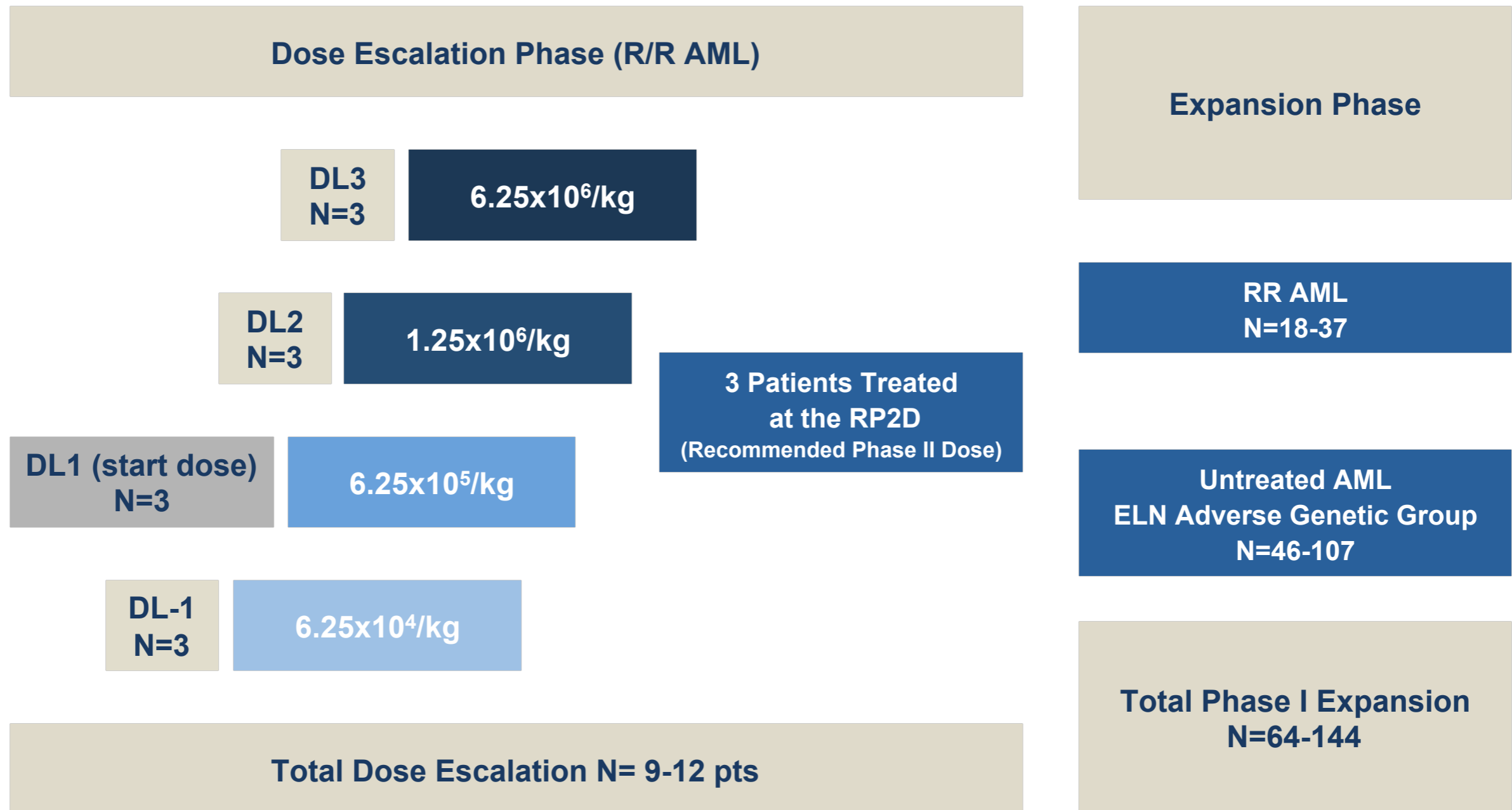


UCART123 in AML

Study Design

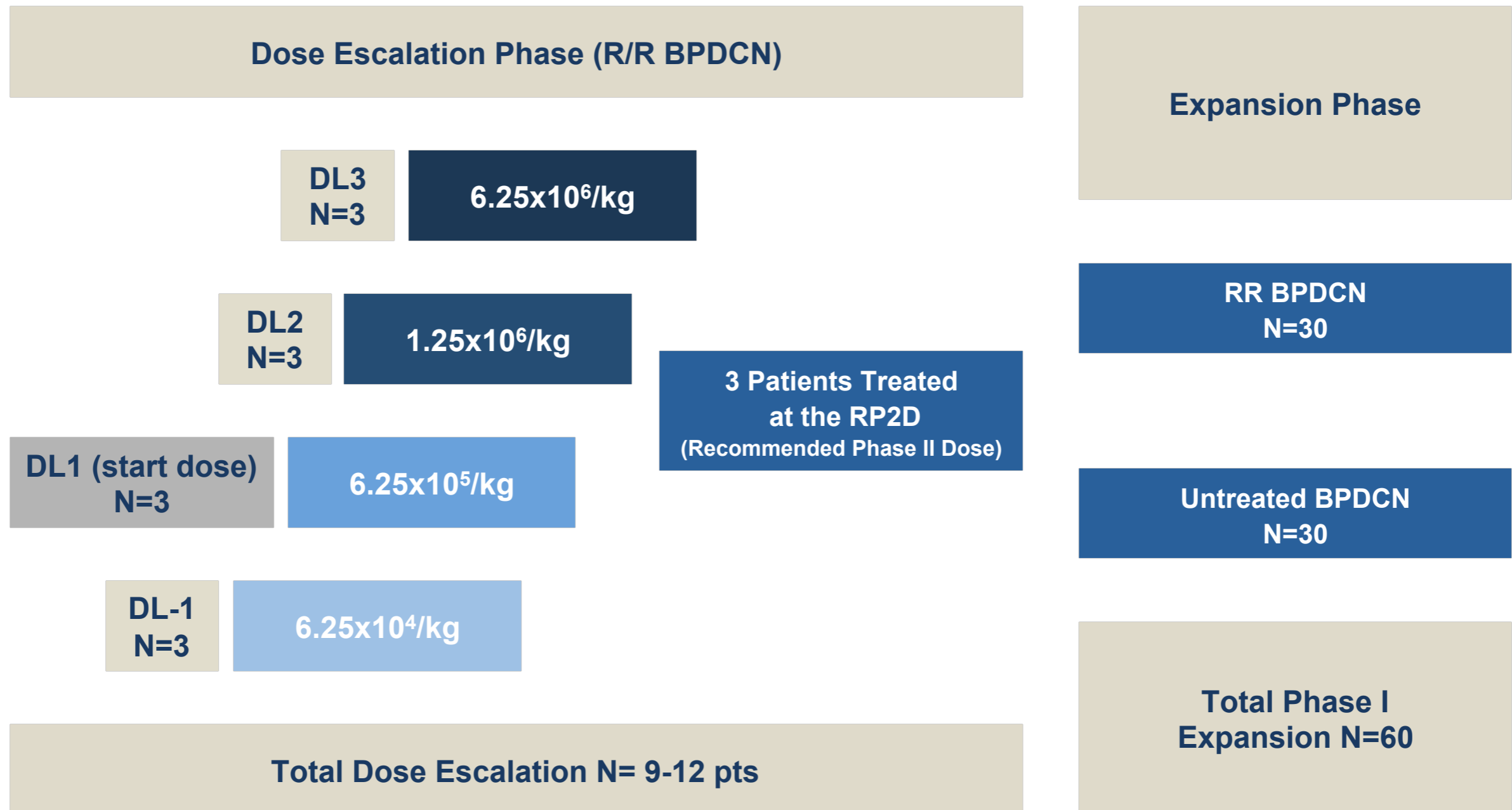


**Weill Cornell
Medicine**



UCART123 in BPDCN

Study Design



UCART123 in AML and BPDCN

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



IND for both indications

- AML Cornell-Weill
- BPDCN MD Anderson

Cleared in February 2017



Phase 1

- First patient enrollment

Dosing started in Summer 2017



Interim Data

- Update on first AML patients

Expected in Q1 2018



Expansion Phase

- Phase 1b in up to 200 first line AML and BPDCN patients

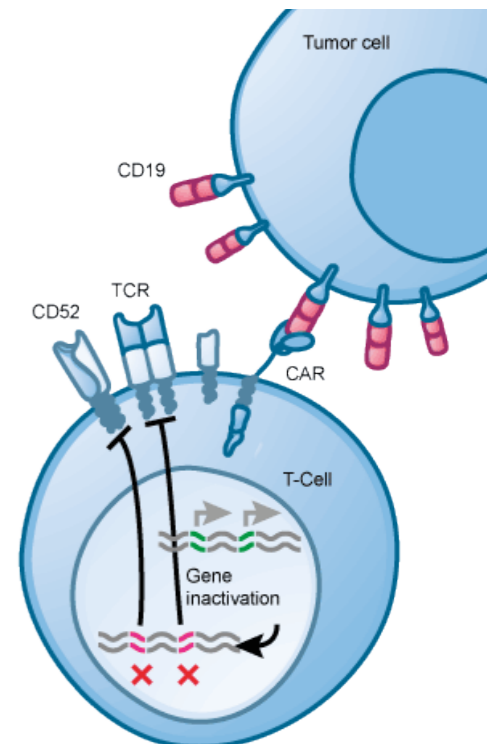
Expected in 2018



Entering Clinical Development

UCART19 as Proof of Concept

- Servier acquired exclusive rights to UCART19 from Cellectis in November 2015
- Joint clinical development program between Servier and Pfizer
- Servier has granted Pfizer exclusive rights to develop and commercialize UCART19 in the US
- 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
- Servier and Pfizer received IND clearance in March 2017 to proceed in the U.S. with the clinical development of UCART19
 - CALM study will be expanded to include several centers in the U.S., including the MD Anderson Cancer Center in Houston (Texas)



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

UCART19 in ALL

Development plan

Preclinical Proof of Concept UCART19

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

Completed 2014



Manufacturing UCART19

- High yield, high potency cGMP batches

achieved Nov 2015



Successful Compassionate Use in Pediatric ALL

- Two infants injected with UCART19
- Still in complete remission today

dosed in Jun and Dec 2015



Phase 1

- First patient enrollment

Dosing started in Jun 2016



First Interim Data

- Update on first seven patients with 100% ORR and 60% CR at 4+ months post injection

Presented at RAC in Dec 2016



Second Interim Data

- Update on Ph1 ALL trial ongoing in UK

Expected in Q4 2017



Expansion Phase

- Pfizer received IND clearance for adult ALL trial
- Ph1b expansion phase planned at U Penn and MD Anderson

Expected in 2018



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

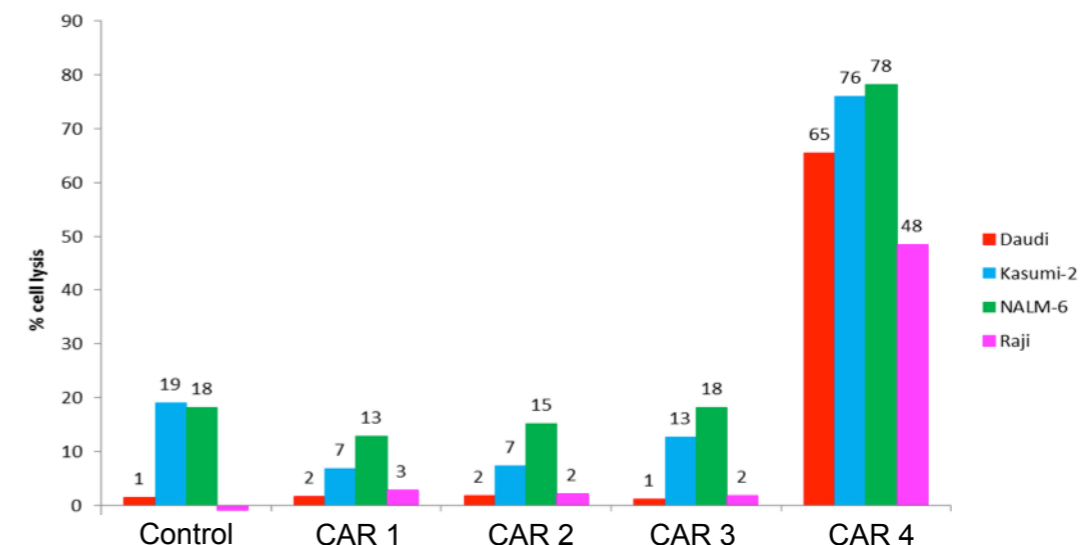
- CD22 and CD19: same expression profile on various B-cell stages of development
- CD22 expression frequently maintained in CD19-negative blast cells in ALL ^{ref1}

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)

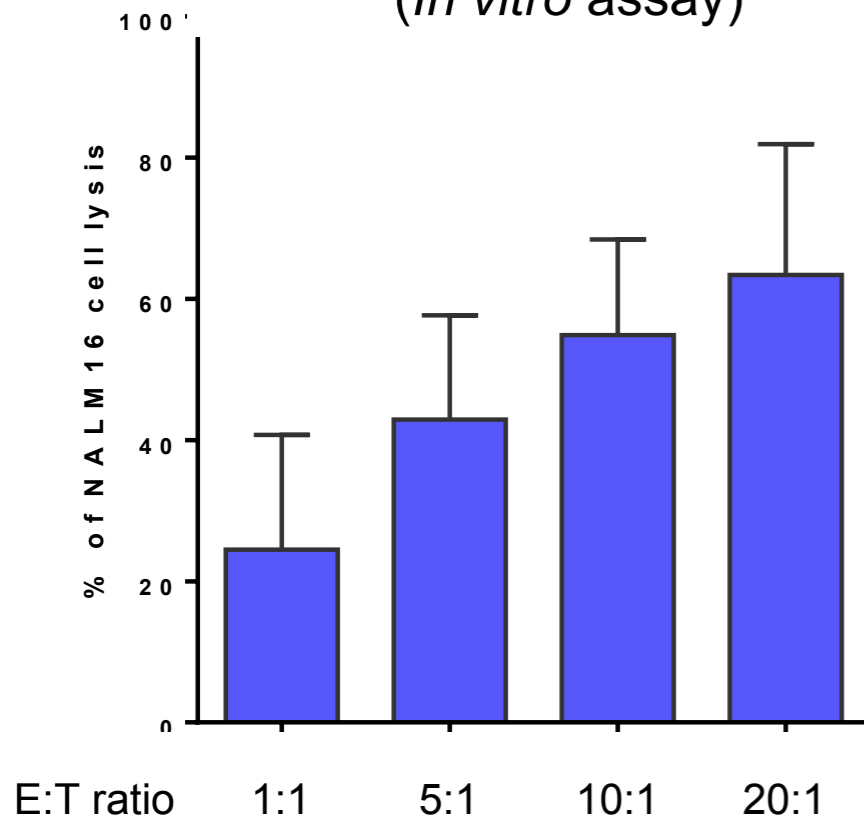


UCART22

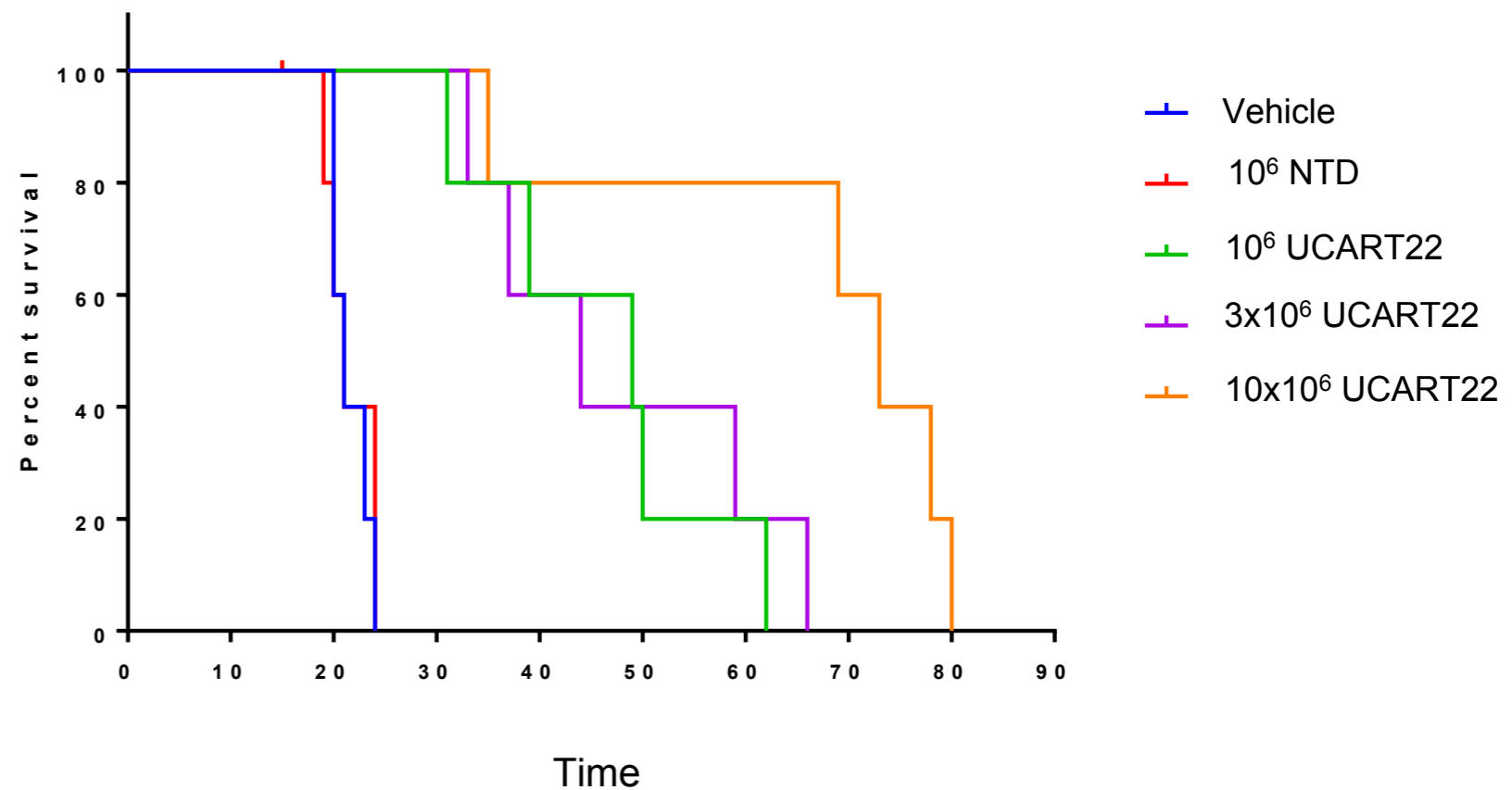
Anti-tumoral activity

- CD22 CART cells are highly efficient at eradicating tumors *in vivo*
- Large Scale batches of UCART22 cells show comparable *in vitro* activity and increased mice survival

UCART22 large scale batches
(*In vitro* assay)



UCART22 treated mice survival



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 in 2018



- Similar manufacturing process to UCART19

IND filing

Expected in 2018



- CD22 as another target for B-cell malignancies (e.g. ALL,CLL,NHL)
- Potential to use as alternative dosing regiment after CD19 ALL / CLL treatment relapse

UCARTCS1

Targeting Multiple Myeloma

Disease Description

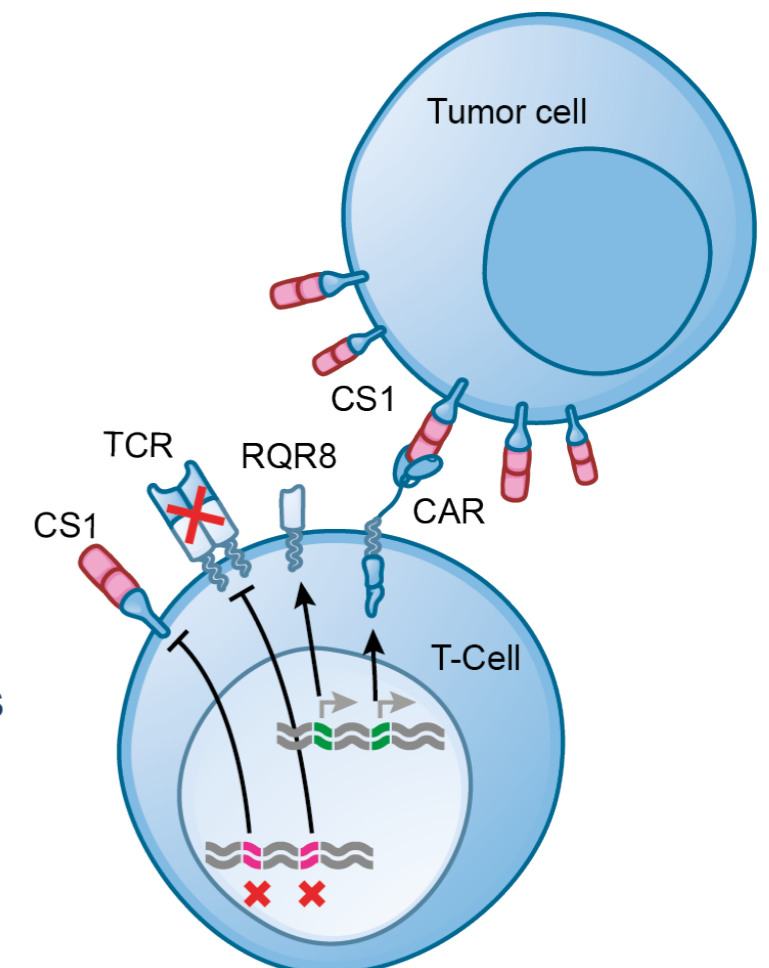
- Multiple myeloma (MM) is a hematologic malignancy characterized by proliferation of plasma cells
- In patients relapsing after prior therapy with immunomodulatory drugs (IMiDs) and bortezomib, the median overall survival rate is 9 months

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

UCARTCS1 Attributes

- Anti-CS1 CAR expression to redirect T-cells to tumor antigens
- Suicide gene for safety
- TCR disruption using TALEN® to avoid GvHD
- CS1 is expressed on CD8+ T-cells; to facilitate CAR T-cell production, CS1 is disrupted using TALEN® to prevent CAR T-cell cross reactivity



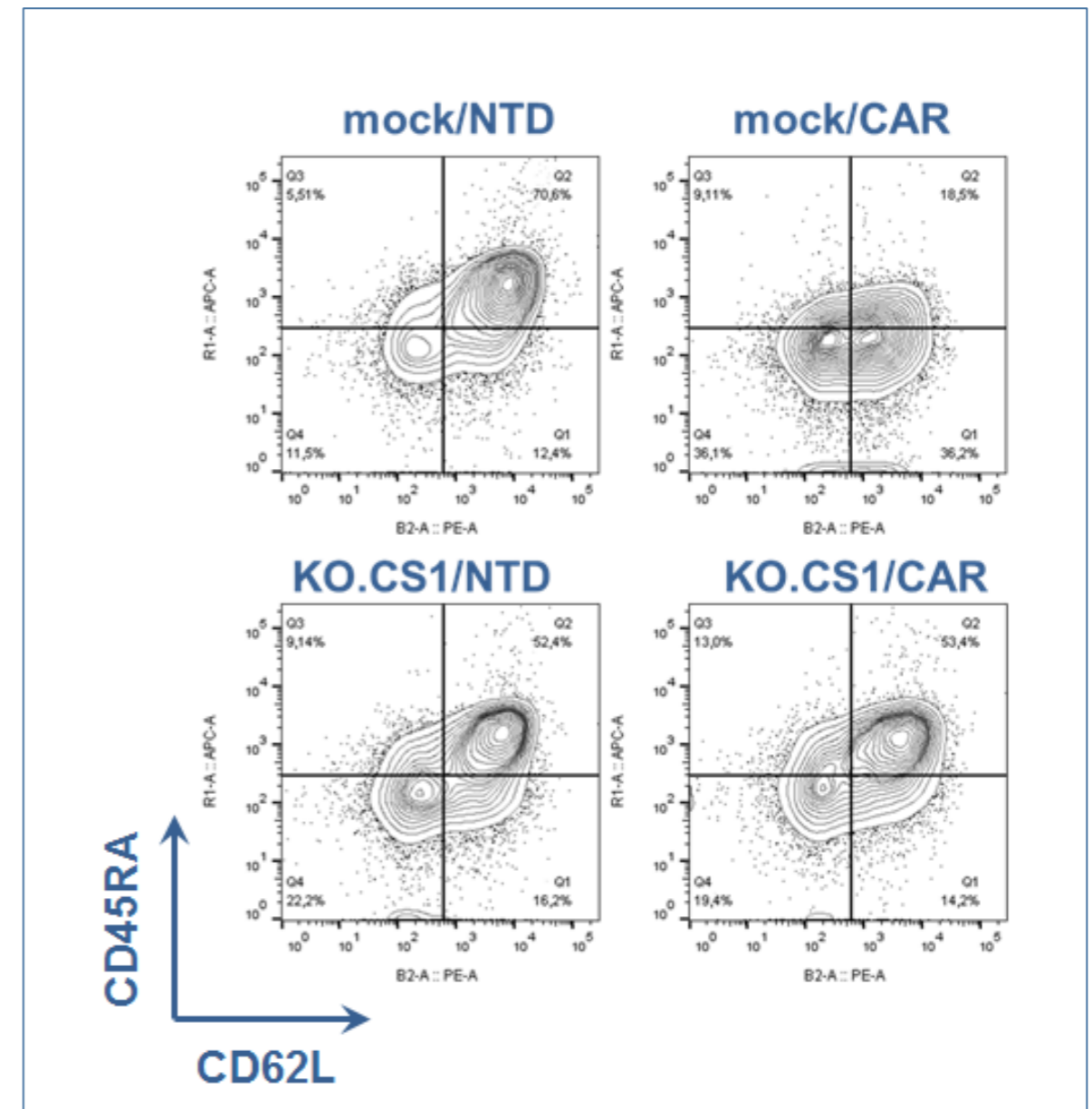
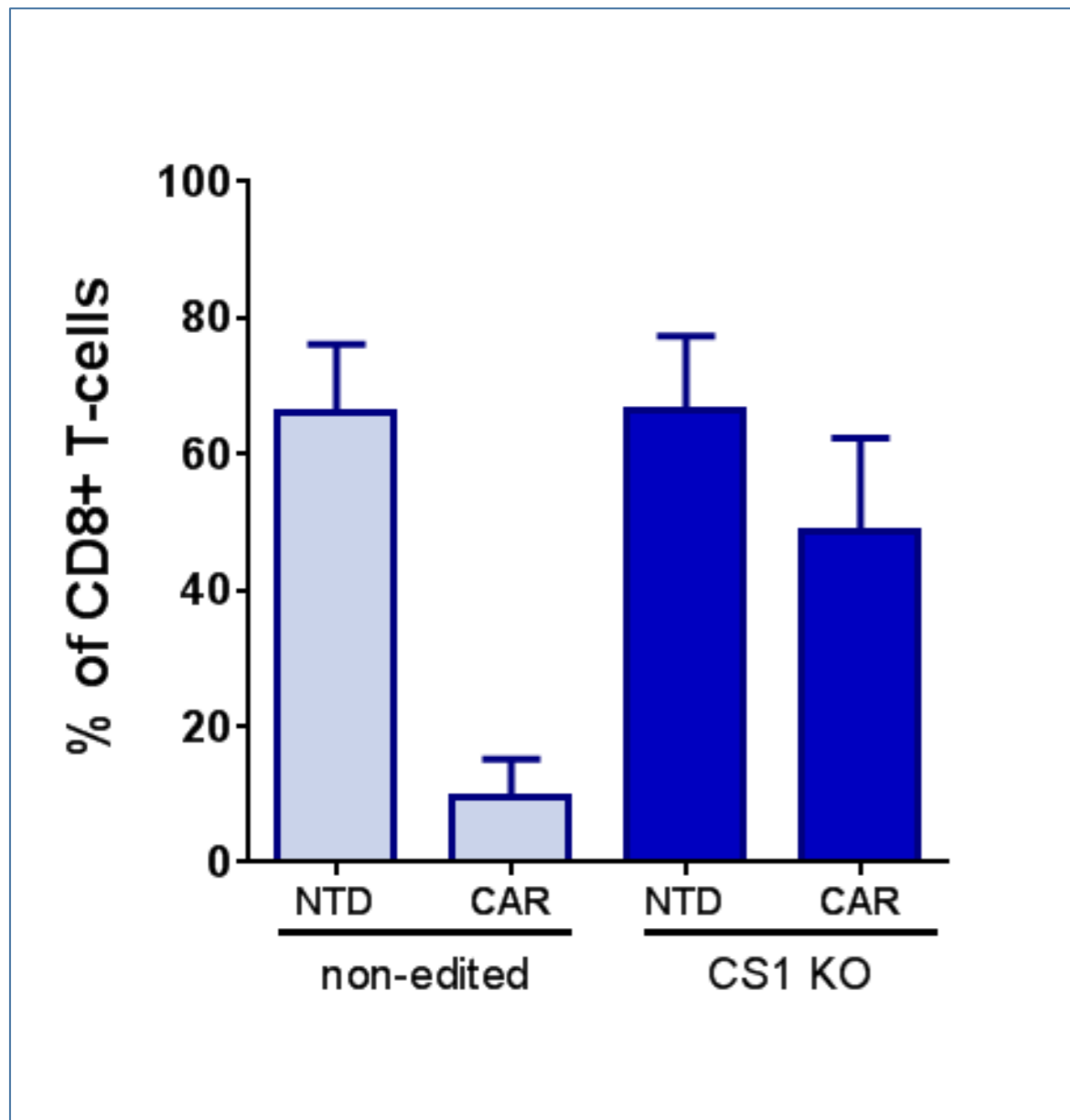
UCARTCS1

Phenotyping analysis

The inactivation of CS1 expression in T-cells leads to:

➤ Increased yields of CD8⁺ T-cells

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

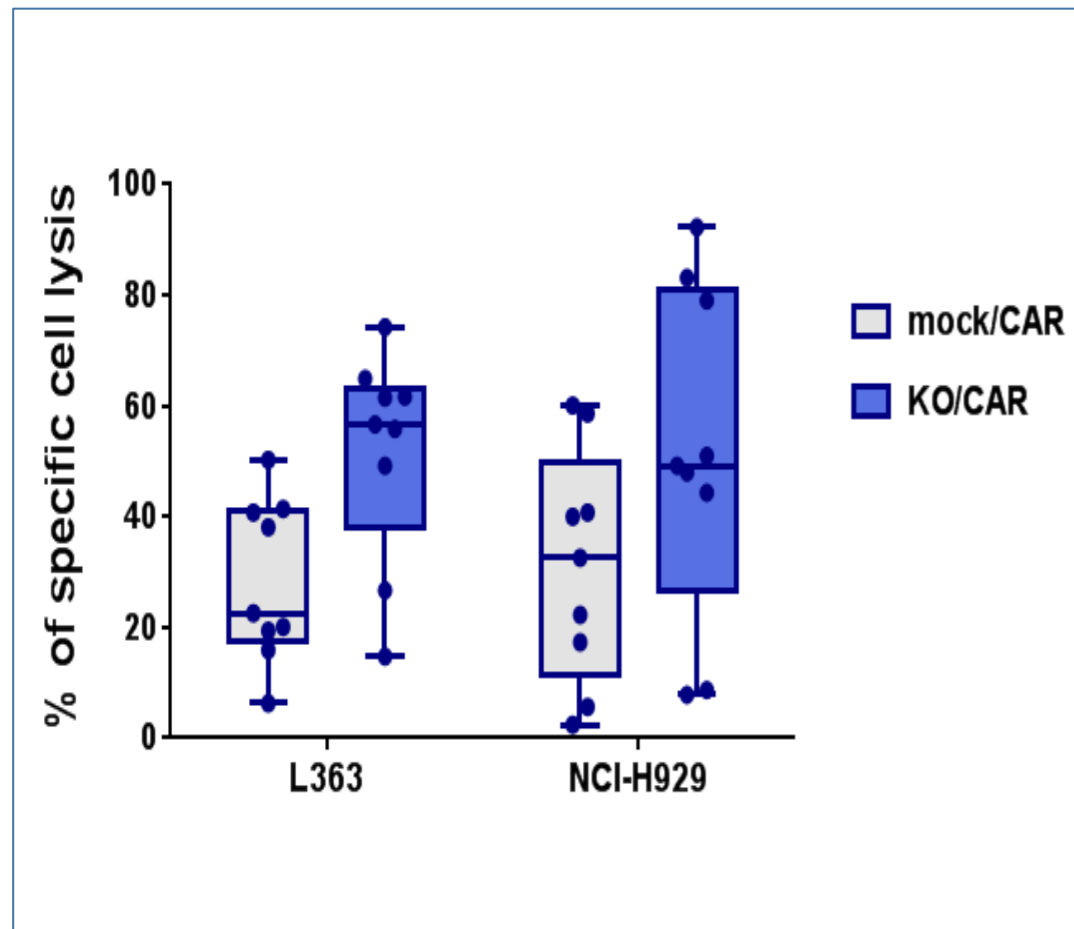


UCARTCS1

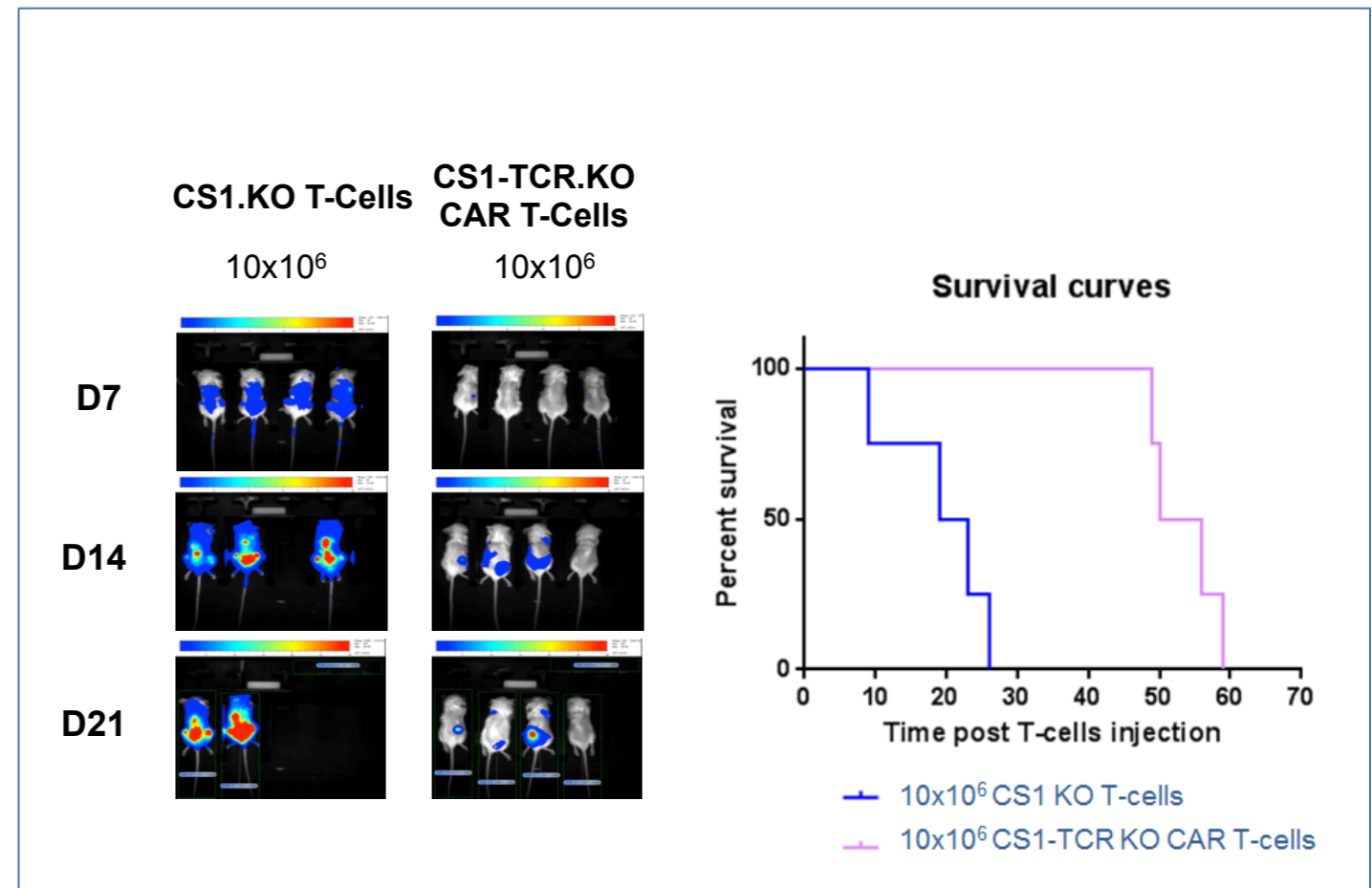
Anti-tumoral activity

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

- Increased cytotoxic activity compared to non-edited T-cells

Completed in Q4 2016



In vivo studies

- Preclinical studies ongoing in collaboration with MD Anderson Cancer Center (Dr. Jing Yang and Dr. Sattva Neelapu)

Ongoing



Manufacturing

- Development of a modified GMP compatible manufacturing process (inversion of transduction/electroporation steps)

Started in Q2 2017



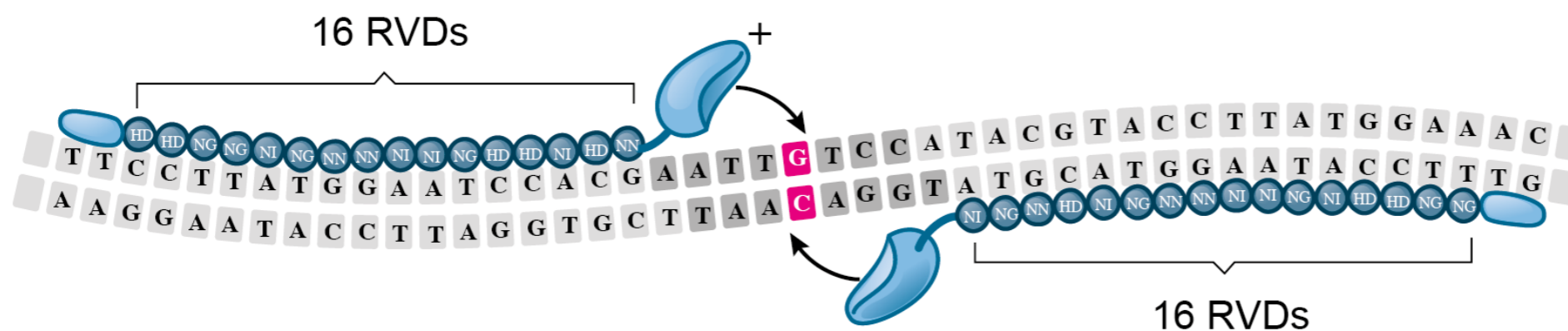
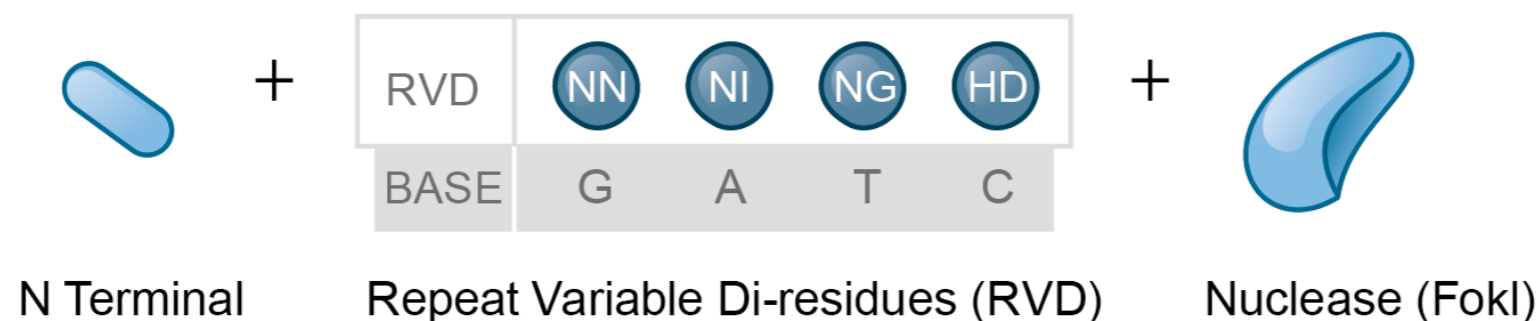
IND Filing

Expected in 2018



Controlled Gene Editing

Best-in-class technologies for therapeutic development

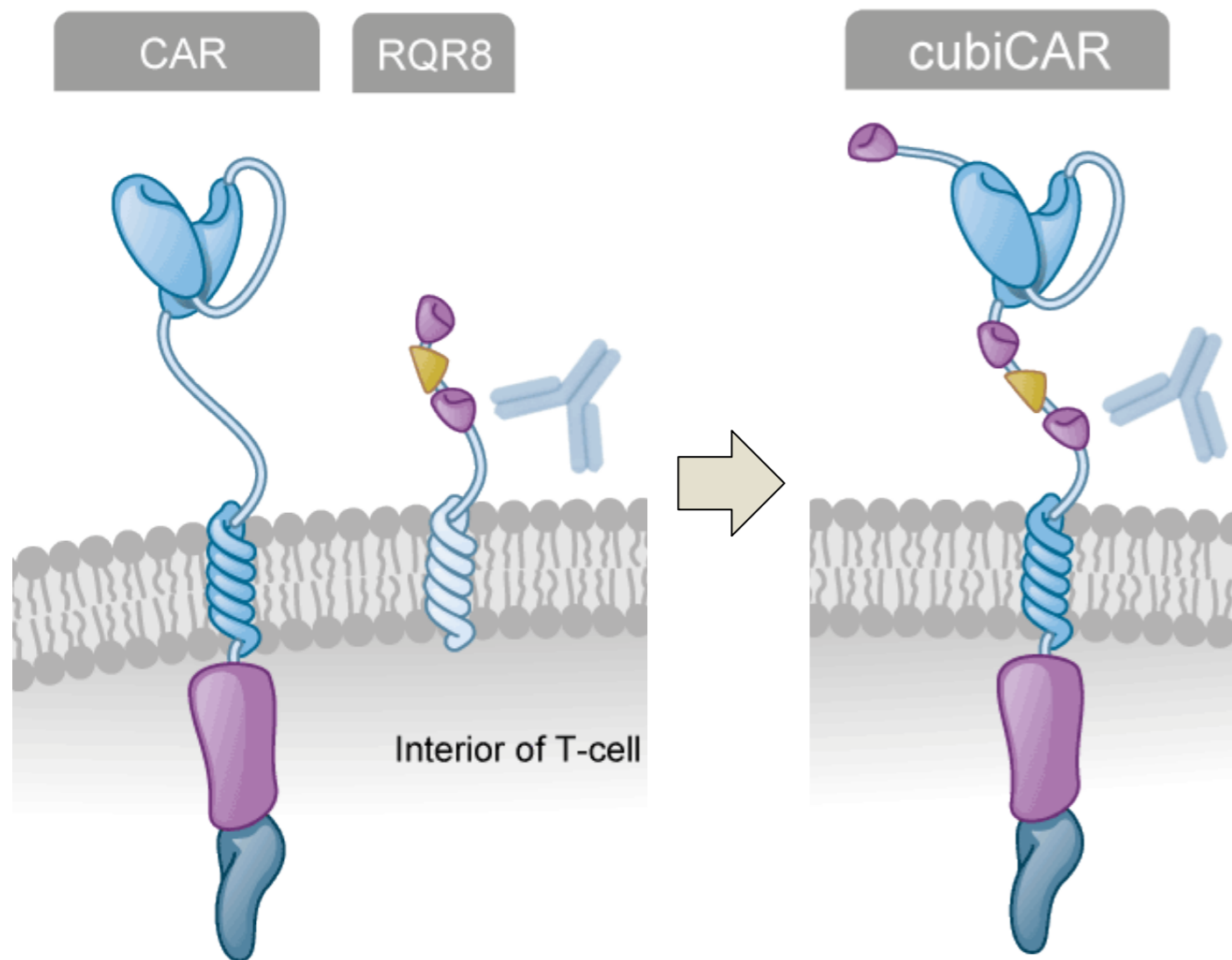


- Highly active: >80% knockout efficiency under GMP conditions
- Highly accurate: 6 base pair specific
- Low off target effect
- TALEN® discovered in 2010 but built on 17 years of experience in gene editing

Controlling CAR T-Cell Persistence

A new generation of suicide switches

- Suicide switch is imbedded in the CAR molecule
- 1:1 expression of CAR and suicide switch on cell surface



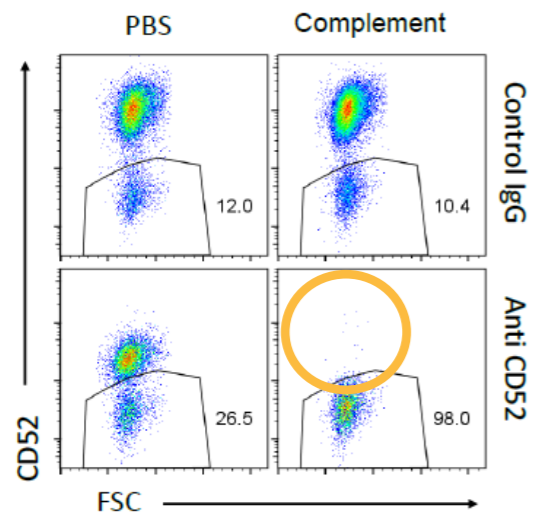
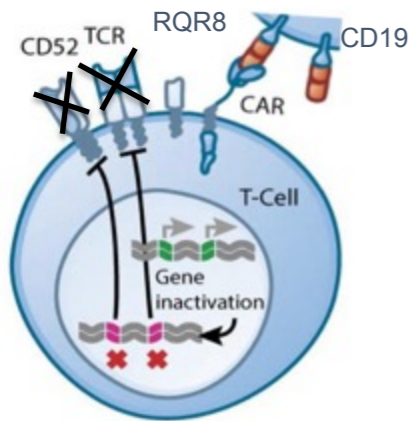
- ✓ Compact
- ✓ Specific cytotoxicity
- ✓ FDA-approved trigger molecule (Rituximab)

Disruptive innovation

Building more powerful T-Cells

Mab-resistance

- CD52 KO for Alemtuzumab resistance

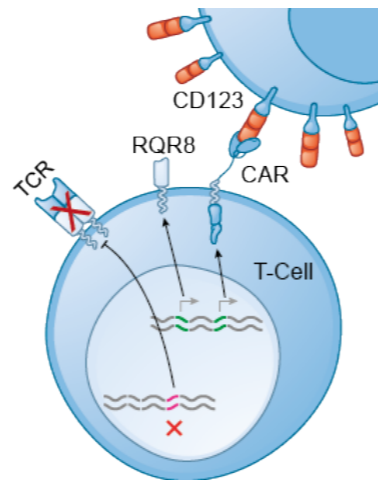


CD52-negative T-cells are resistant to Campath

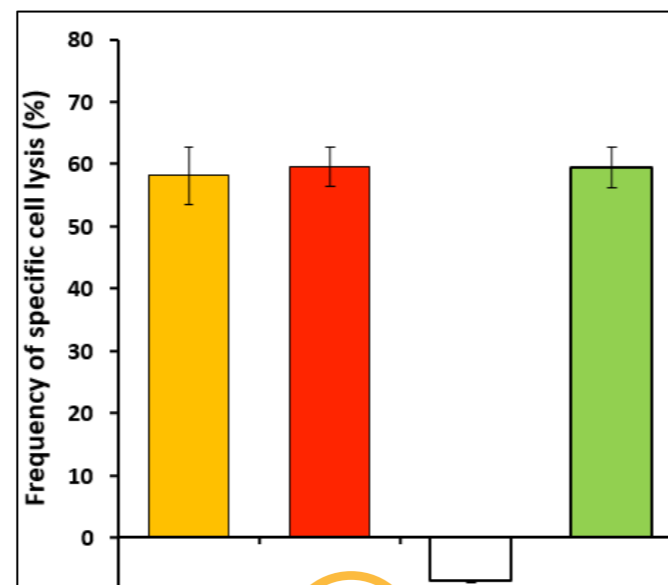
Poirot L *et al.* (2015) Cancer Res.

Chemo-resistance

- dCK KO for Fludarabine and Clofarabine resistance



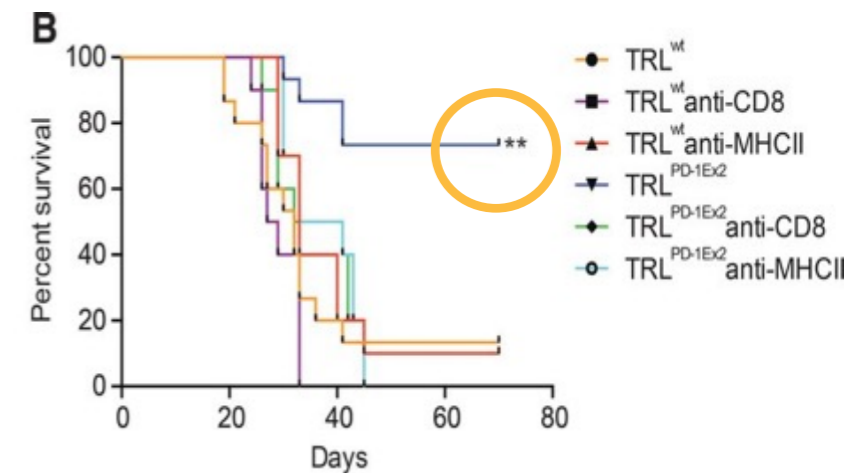
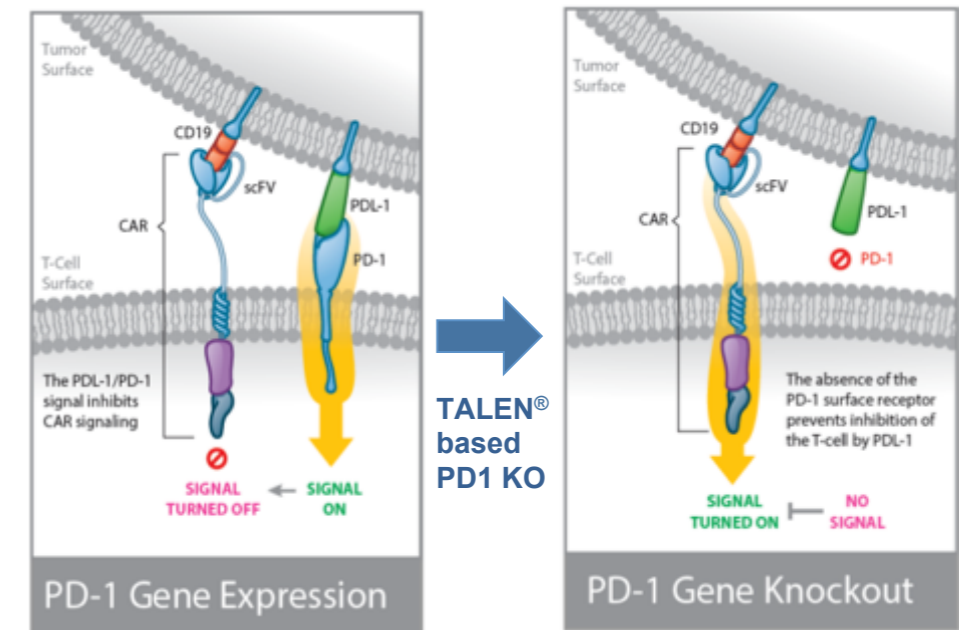
dCK-negative T-cells are resistant to Clofarabine



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

PDL1-resistance

- PD1 KO to be insensitive to PD-L1 inhibition



PD1-negative T-cells have a higher efficacy on PD-L1 tumor

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



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



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

World Class Clinical Centers



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 all of the United States.

THE UNIVERSITY OF TEXAS

MD Anderson Cancer Center

Making Cancer History®



- Development of UCARTCS1 for Multiple Myeloma, UCART22 for ALL, UCART38 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



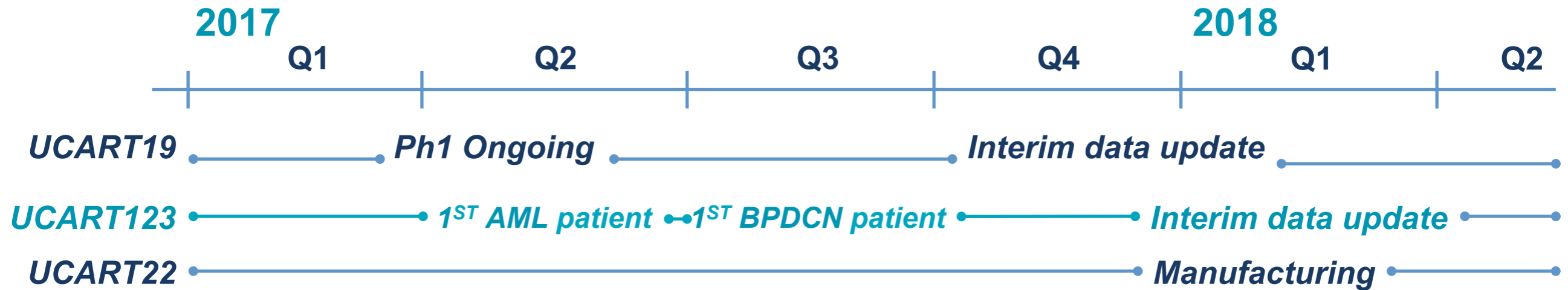
- Phase 1 clinical trial of Servier UCART19 in pediatric patients
- Great Ormond Street Hospital, London is ranked among the top best hospitals in the UK and top ranking in the world



KING'S
College
LONDON

- 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

Milestone Timeline



- **UCART19 in ALL patients**
 - Ph1 clinical trials ongoing; interim data expected in Q4 2017
- **UCART123 in AML and BPDCN patients**
 - Ph1 dose-escalation trial ongoing; interim data expected in Q1 2018
- **UCART22, UCARTCS1** INDs will follow
- Potential solid tumor targets
- Strong partnerships with Servier and Pfizer producing additional CAR T programs

THANK YOU

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