GENE EDITED CAR-T THERAPIES

THE PARADIGM IN ONCOLOGY

Cellectis, January 2018

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.

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The Cellectis Group

- NASDAQ: CLLS
- EURONEXT GROWTH: ALCLS
- 36M SHARES OUTSTANDING
- $304M IN CASH END Q3 2017

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

80% ownership

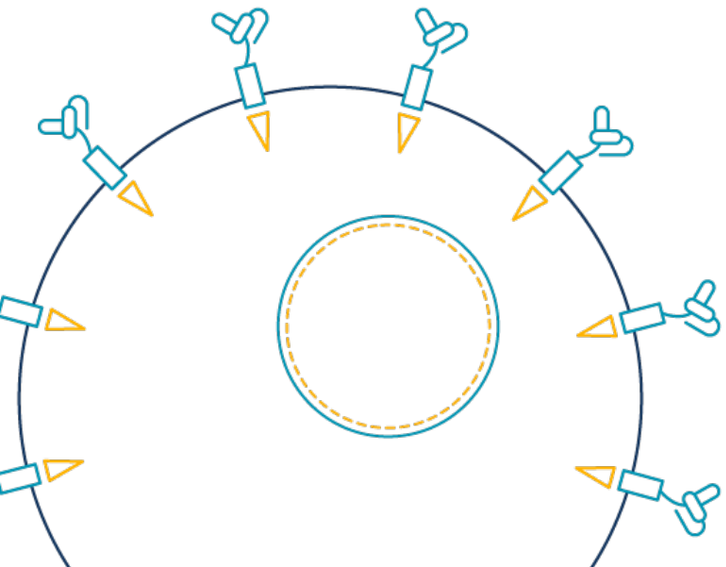
- NASDAQ: CLXT
- IPO JULY 2017
- $64M GROSS PROCEEDS
- 7.7M SHARES OUTSTANDING (27M TOTAL)

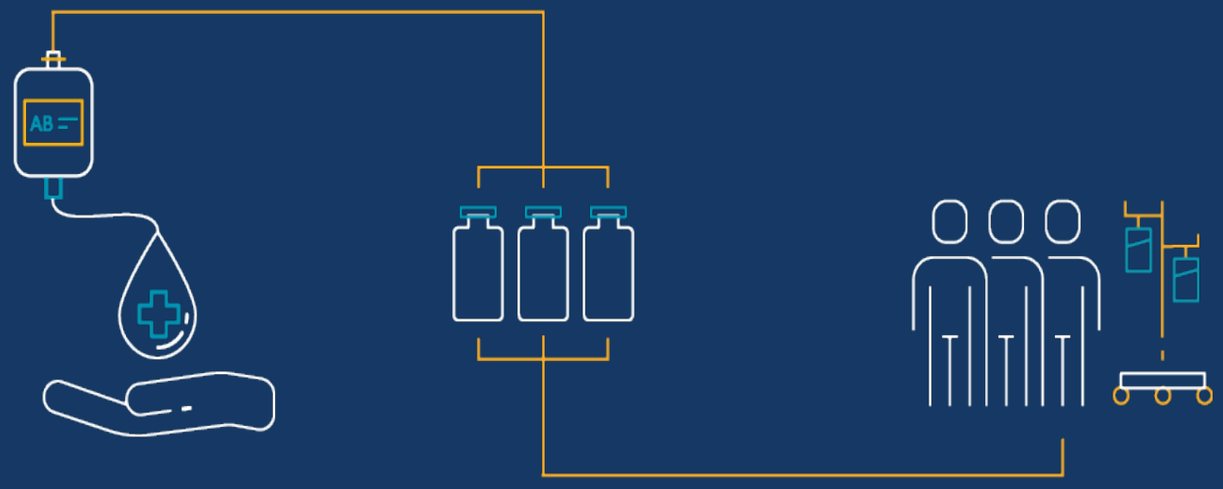
- BASED IN MINNESOTA
- CONSUMER FOCUS
- HIGH VALUE ASSET

Gene editing is the link

Leader in Allogeneic CAR-T

- **2017 market: CAR-T in the spotlight**
  - CAR-Ts are here to stay
  - First FDA approved autologous CAR-Ts on the market
  - Allogeneic CAR-T concept validated
  - First market challenges for autologous CAR-Ts





- **Allogeneic CAR-Ts: major uncertainties relativized**
  - ✓ **Industrialized manufacturing process**
  - ✓ High-precision TALEN® gene editing used in clinical trial in US and EU
  - ✓ **No significant GvHD**
  - ✓ Allogeneic CAR-T **engraft and expand**
  - ✓ **Efficacy** on par with autologous CAR-T

Rich Allogeneic CAR T Pipeline

Addressing unmet medical need with proven targets

Program	Indication	Product development	Preclinical	Manufactu-ring	IND Filing*	Phase I	Ph II	Ph III
UCART19**	ALL (PALL)							
	ALL (CALM)							
UCART123	AML							
	BPDCN							
UCART22	B-ALL							
	B-NHL							
UCARTCS1	MULTIPLE MYELOMA							

- **2 UCART in clinic: UCART19 & UCART123**
- **Rich pipeline, with proven targets**
- **Potential quick wins in next 3 years with several IND filings**

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

Severe diseases with unmet needs

Allowing for potential fast track development plans

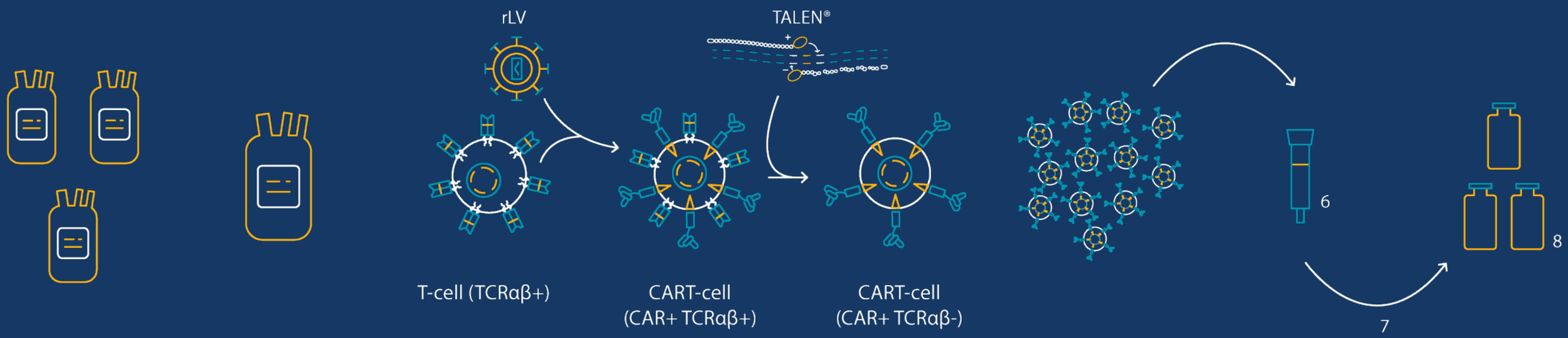
US Estimate	Estimated New Cases in 2017	Estimated Deaths in 2017	5 Year Survival (2007-2013)
AML*	21,000	10,000	26,9%
BPDCN	Estimated < 1% of all hematologic malignancies**		38%***
ALL*	6,000	1,500	68,2%
CLL*	20,000	4,500	83,2%
MYELOMA*	30,000	13,000	49,6%
NON HODGKIN LYMPHOMA*	72,000	20,000	71%

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

** Riaz et al, 2014

*** Alsidawi et al, 2016

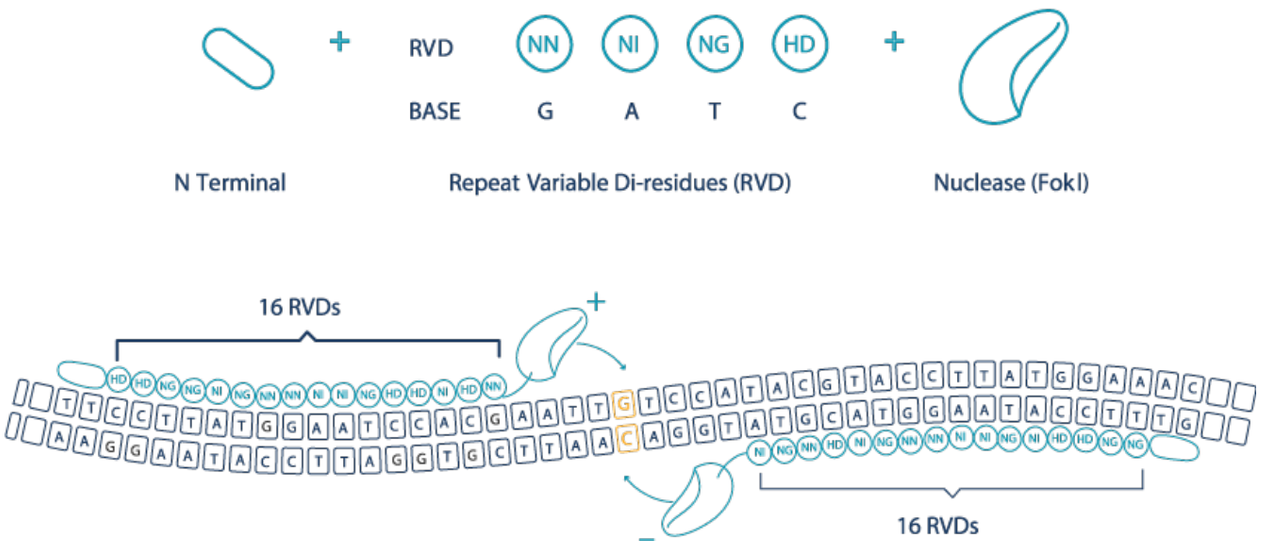
Allogeneic CAR T – GMP Manufacturing



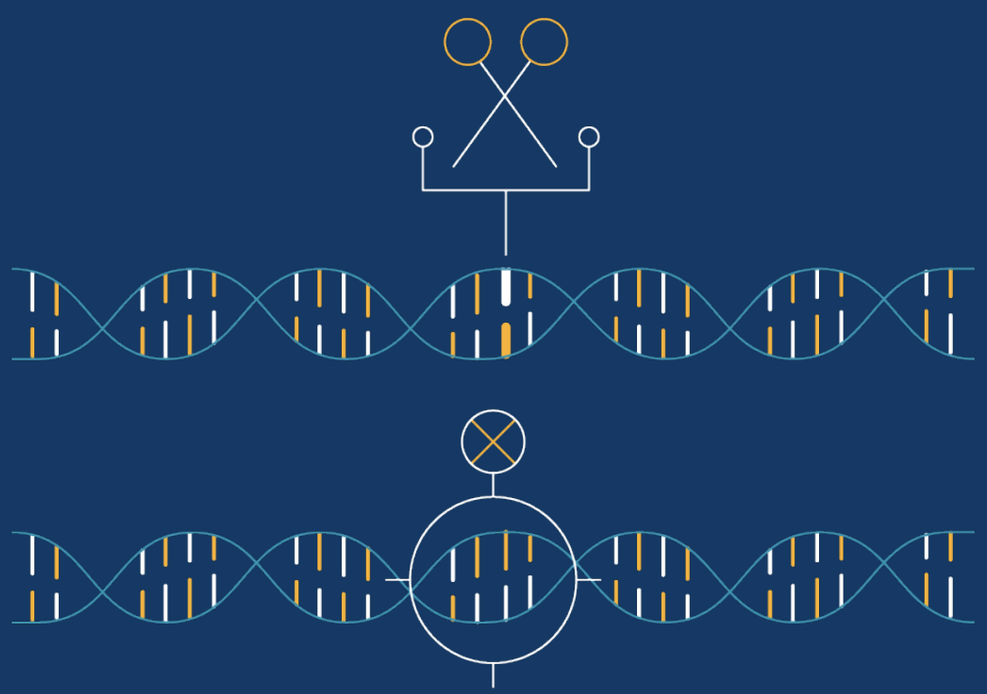
- **GMP manufacturing in place for UCART19, UCART123, UCART22**
- **Full QC system, cleared for clinical trials**

A cornerstone: TALEN® gene editing

Highest yield and precision



- ≥80% knockout efficiency
- Precision targeting to 6 base pairs
- Low off-target cleavage
- 18 years of experience in gene editing
- Strong intellectual property



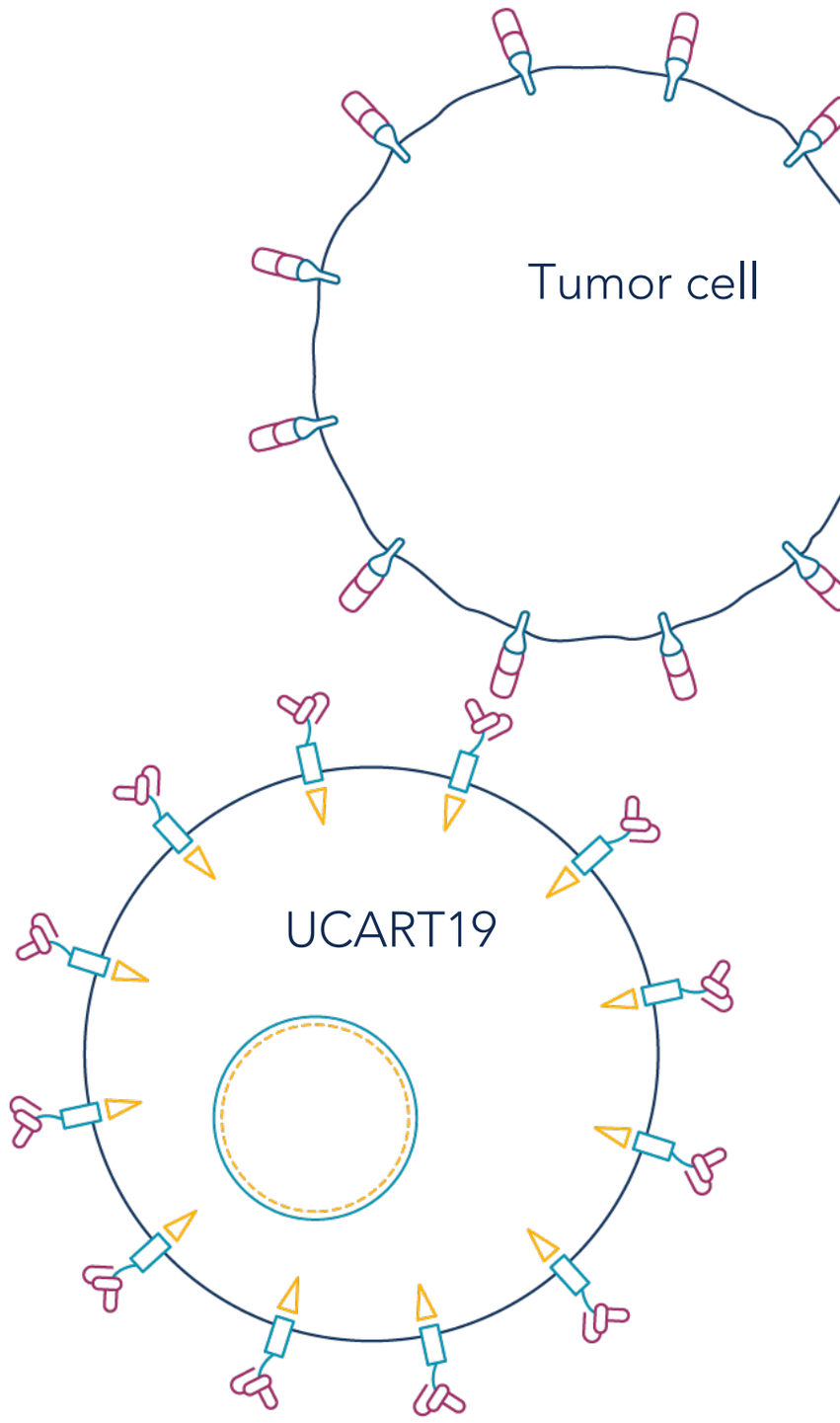
A **powerful** gene editing technology

In clinic since 2015 in US and EU

*UCART19**

Initial Proof Of Concept in ALL

- 1st patient dosed in June 2015 (compassionate)
- Phase I trials (US/EU) started in June 2016
- 4 recruiting centers (EU and US)
- 14 patients treated disclosed (7 adults and 7 pediatric)**
- Results in line with early autologous CAR-T Phase I results published in past years
- Patients failed >5 lines of treatment, including autologous CAR-T
- Ph1b expansion at U Penn and MD Anderson



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

Early Clinical Data

UCART19 in Pediatric ALL patients (ASH 2017)*

	Lymphodepletion & patient age	Disease status before treatment	Dose level (CAR-T Cells/kg)	MRD- CR/CRi	Adverse event > Grade 3	Relapse follow up
SERVIER & KCL (PALL) ASH 2017	CFA 6 m to 17 y	All patients were ineligible for or had failed autologous CAR T treatment	1.1 to 2.3x10^6	**100% (7/7)* CR or CRi**	CRS 14% (1/7) NT 0% (0/7)	29% (2/7) - 6 m 1 CD19- and 1 CD19+
KITE & NCI ASCO 2013	CF 1 to 30 y	Relapse or refractory	1x10^6	100% (2/2) CR	CRS 50% (1/2)	
JUNO & SCH (PLAT-02) ASH 2014	C or CF 4 m to 3 y	4 pts MRD_+, 2 pts MRD Relapse after allo-SCT	5x10^5	83% (5/6) CR	CRS 33% (2/6) NT 50% (3/6)	
JUNO & FHCRC AACR 2015	C or CF or CE 18 to 60y	Relapse or refractory	1x10^6	91% (20/22) CR	CRS 36% (8/22)	18% (4/22) 3 $CD19_-$ and 1 $CD19_+$
NOVARTIS (ELIANA) ASH 2016	CF or other 3 to 21 y	All patients with morphologic disease: primary refractory, chemorefractory after first relapse, relapsed after second line therapy or ineligible for allo-SCT	0.2 to 4x10^6	83% (24/29) CR or CRi	CRS 52% (15/29) NT 21% (6/29)	
NOVARTIS & UPENN (PEDI CART19) N Engl J Med 2013	+/– CE 7 & 10 y	All 2 pts MRD+ Chemorefractory after second relapse or second relapse after allo-SCT	1.4×10^6 or 1.2×10^7	100% (2/2) CR	CRS 50% (1/2) NT 0% (0/2)	50% (1/2) - 2 m
MSKCC & DFCI ASH 2014	- 13 to 22 y	3/4 pts with morphologic disease Relapse	0.3 to 1x10^6	50% (2/4) CR or CRi	CRS 50% (2/4)	

* Including 2 patients in compassionate use

C: cyclophosphamide; CF: cyclophosphamide and fludarabine; CFA: cyclophosphamide, fludarabine and Alemtuzumab; CE: cyclophosphamide and etoposide; CEVD: cyclophosphamide, etoposide, vincristine, dexamethasone; CDVP: cyclophosphamide, daunorubicin, vincristine, prednisone

Minimal disease < 5% blasts, morphologic disease ≥ 5% blasts

CRi: complete remission with incomplete hematopoietic recovery

Early Clinical Data

UCART19 in Adult ALL patients (ASH 2017)*

	Lymphodepletion & patient age	Disease status before treatment	Dose level (CAR-T Cells/kg)	MRD- CR/CRi	Adverse event > Grade 3	Relapse follow up
SERVIER & KCL (CALM) - ASH 2017	CFA >16y	1-5 lines of treatment, 4/6 patients in relapse after allo-SCT	Total $6x10^6$	**71% (5/7)* CR or CRi**	CRS 14% (1/7) NT 0% (0/7)	25% (1/4) - 6 m CD19+
KITE (ZUMA-3) ESMO 2017	CF >18y	56% to 100% BM blasts before conditioning, 7 pts in relapse and 4 pts in primary refractory disease	$1x10^6$ or $2x10^6$	80% (8/10) CR, CRi or CRp	CRS 27% (3/11) NT 55% (6/11)	37% (3/8) - 3.8 m 2 CD19- and 1 CD19+
JUNO (ROCKET) ASCO 2016	C or CF >18y	30 pts with morphologic disease and 20 pts with minimal disease		82% (41/50) CR	CRS 27% (14/51) NT 29% (15/51)	
JUNO & MSKCC Sci Transl Med 2014	C Median 50y	Very high risk, refractory or relapse	$3x10^6$	88% (14/16) CR or CRi	CRS 44% (7/16) NT 25% (4/16)	
JUNO & FHCRC J Clin Invest 2016	C or CF 20 to 73y	Refractory or relapse 3 prior lines of chemotherapy (range 1-11), 11 pts in relapse after allo-SCT	$2x10^5$, $2x10^6$ or $2x10^7$	93% (27/29) CR	CRS 23% (7/30) NT 50% (15/30)	
INNOVATIVE CELLULAR THERAPEUTICS ASCO 2017	- <60y		0.4 to $10.5x10^6$	73% (8/11) CR	CRS 18% (2/11)	

* Including 2 patients in compassionate use

C: cyclophosphamide; CF: cyclophosphamide and fludarabine; CFA: cyclophosphamide, fludarabine and Alemtuzumab

Minimal disease < 5% blasts, morphologic disease ≥ 5% blasts

CRi: complete remission with incomplete hematopoietic recovery; CRp: complete remission with partial hematopoietic recovery

UCART vs autologous CART in ALL

	Expectations for UCART products	**Autologous CD19 CAR-T**
Bridge To Transplant	For eligible patients	For eligible patients
CART Persistence = Durable Response	Inconclusive	Inconclusive
Toxicities	Minimal GvHD, Minimal Neurotox, Mild CRS	Strong CRS, Medium- to Strong Neurotox
Ability to re-dose	Yes	Limited, if feasible
Cost of treatment	$	$$$$$
Market access	++++	+/-
GvHD Risk	Minimal, reversible	N/A (maximal if vials mistaken)
Current Patient Profile	RR; >5th line patients	2nd line patients

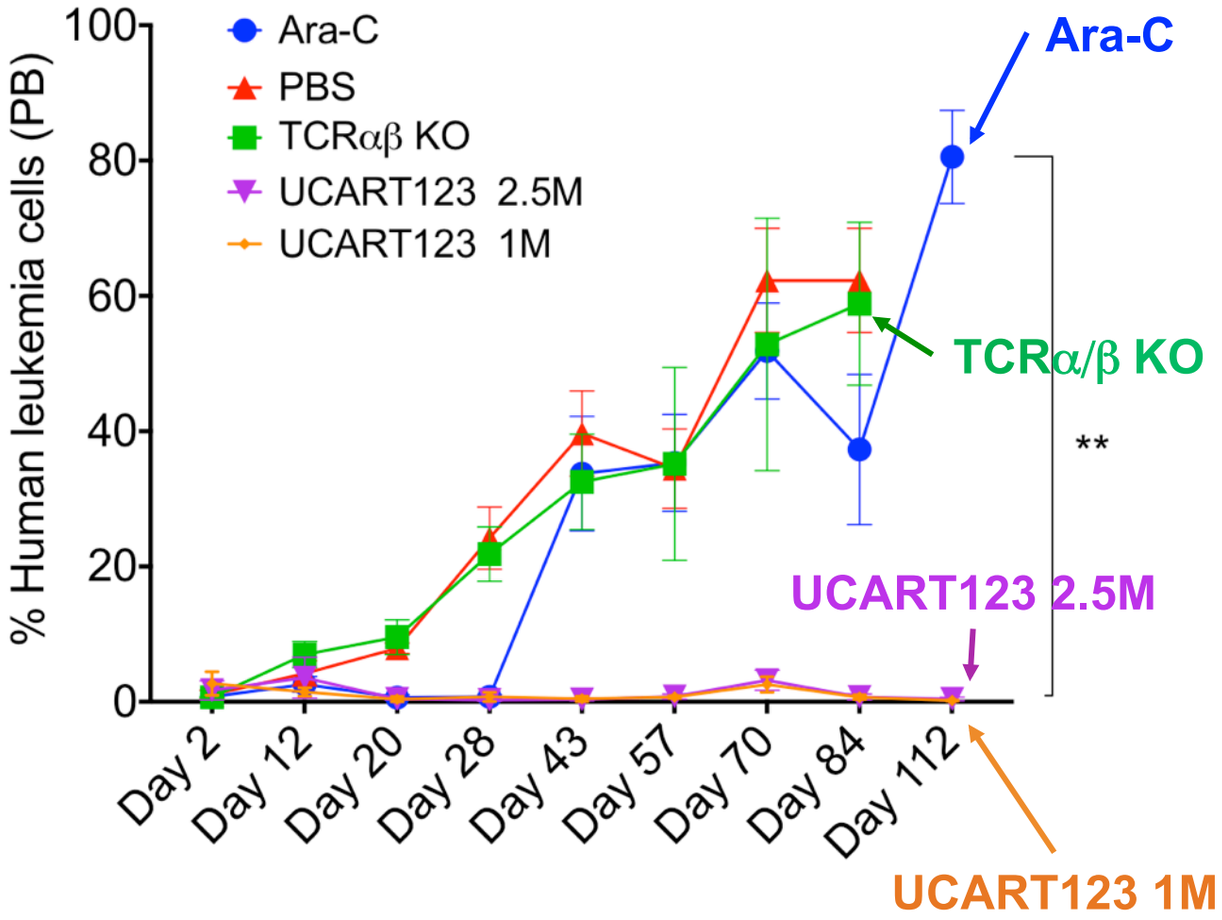
UCART123 in AML and BPDCN

Encouraging Efficacy Data

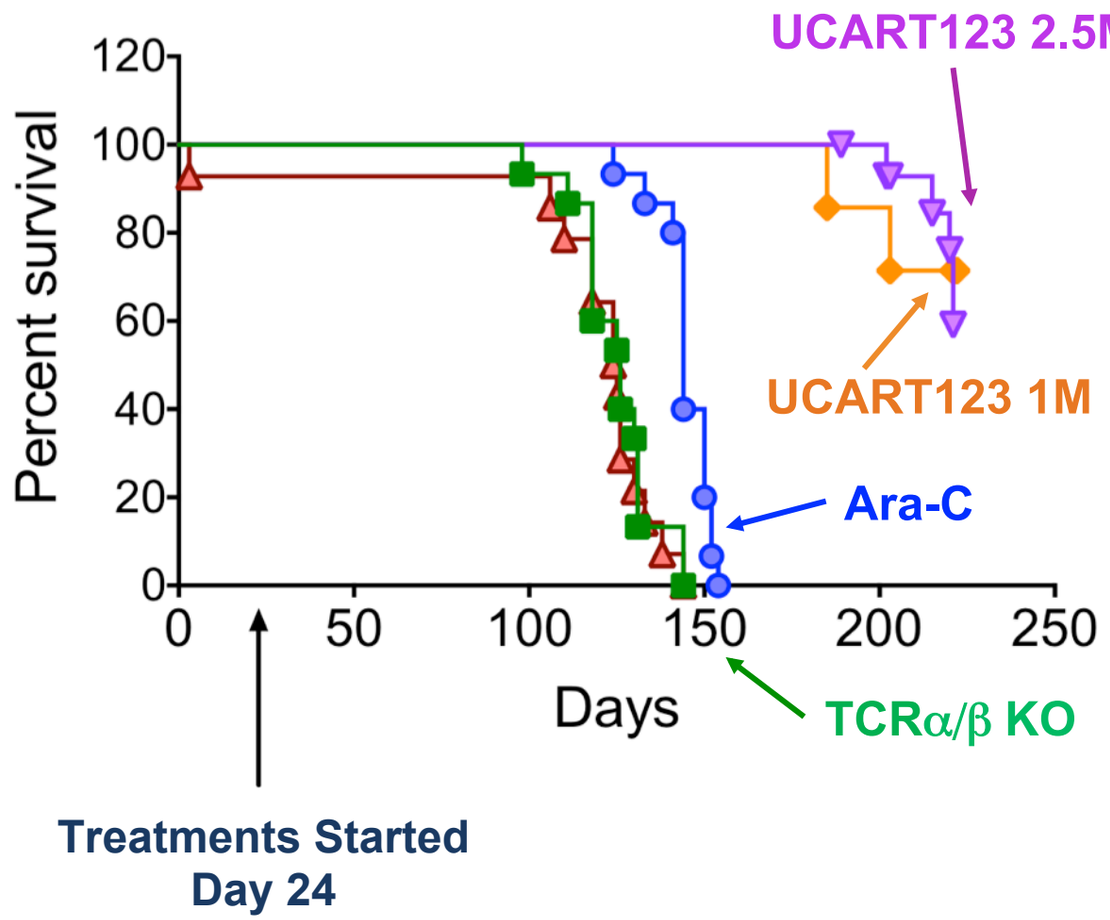
Weill Cornell Medicine

- Significant improvement compared to Cytarabine standard-of-care (Ara-C)

Peripheral Blood Evaluation



Overall Survival



- Encouraging results with CD123 target in autologous CAR-T approaches

In collaboration with Dr. Monica Guzman, Cornell-Weill

UCART123 in AML and BPDCN

First Wholly-Owned CAR-T In The Clinic

- *AML Ph 1 dose escalation trial at Weill Cornell*
- *First patient dosed in June 2017*
- *Expansion to others centers in 2018*

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

Weill Cornell Medicine

Dose Escalation Phase (R/R AML)

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

Development plan

Preclinical Proof of Concept UCART123 — Q4 2016 ✓
- *In vitro* and *in vivo* development finalized

Manufacturing UCART123 — Q4 2016 ✓
- High yield, high potency cGMP batches

IND for both indications — Q1 2017 ✓
- AML Cornell-Weill
- BPDCN MD Anderson

Phase 1 — Q2-Q3 2017 ✓
- First patient enrollment, clinical hold lifted after 2 months
- Study resumed November 2017 with protocol changes

Interim Data — Expected in 2018 ☐
- Update on first AML patients

Expansion Phase — Expected in 2019 ☐
- Phase 1b in RR and 1st line AML and BPDCN patients

UCART22

Targeting ALL, NHL and other B-Cell Malignancies

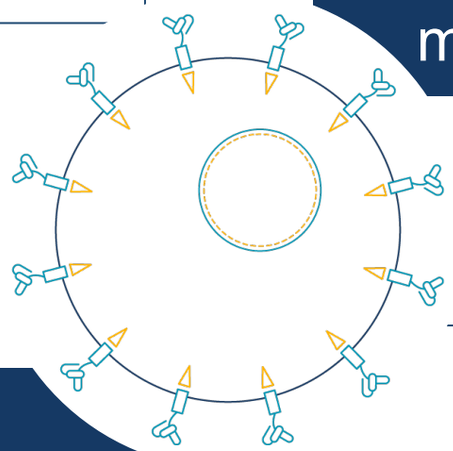
cellectis
EDITING LIFE

Unmet Medical Need

- Relapse after CD19 CAR-T treatment
- Numerous ALL relapsing patients are CD19- but CD22+

Rationale

- Both CD22 and CD19 are expressed on various B-cells
- CD22 expression frequently maintained in CD19-negative blasts[1]



Target Antigen

- CD22, is expressed on the B-cell surface, persists on mature B-cells, and is lost on plasma cells

Proof of concept

- Anti-CD22 monoclonal antibodies
- Autologous CAR-T in development

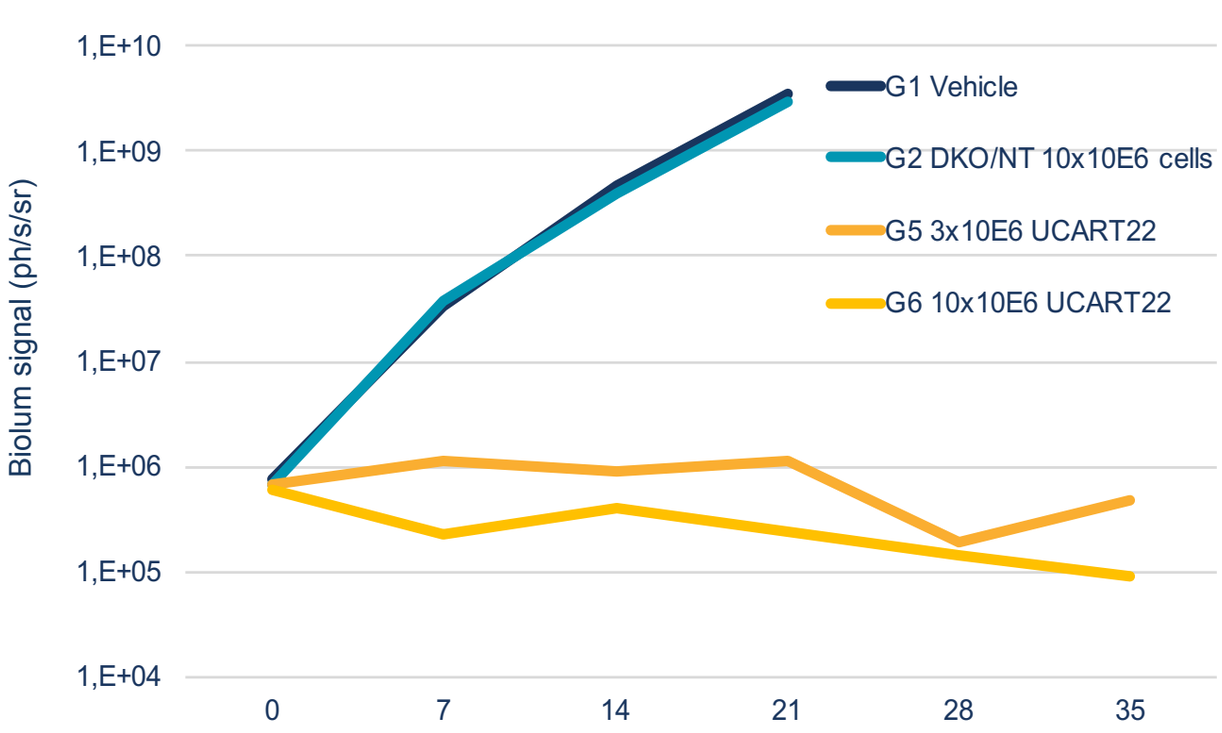
1: Maude et al, Blood 2015 125:4017-4023.

UCART22

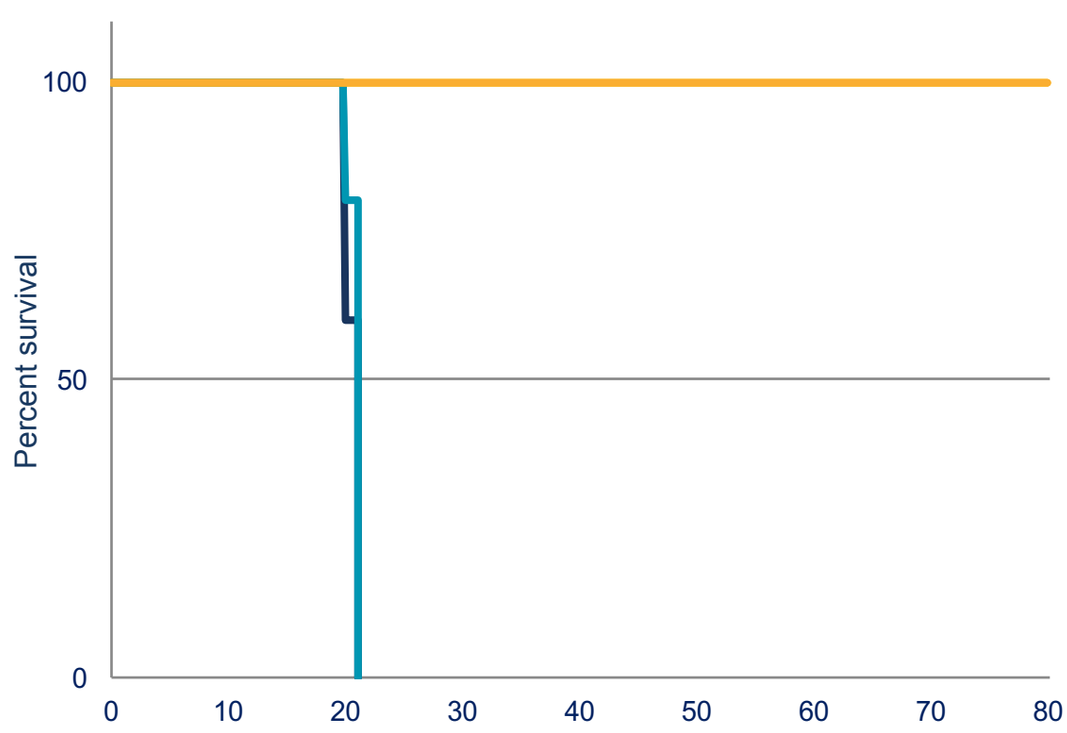
Strong anti-tumoral activity

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

CD22+ cell line show no tumor progression



Survival curves



UCART22
Development Plan

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

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

Manufacturing Q4 2017 - Q1 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 regimen after CD19 ALL / CLL treatment relapse

UCARTCS1

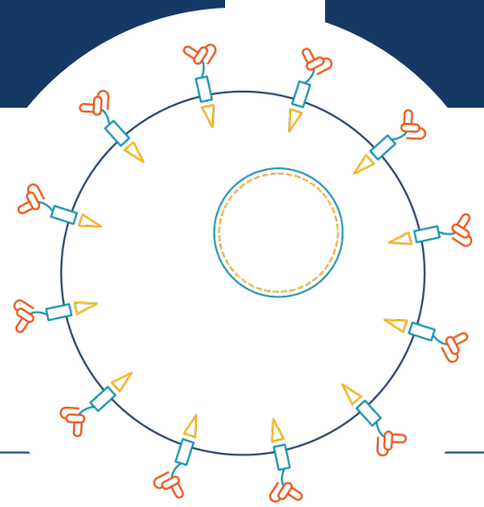
Targeting Multiple Myeloma

Unmet Medical Need

- > 30,000 patients / year in the US
- High relapse rate, median OS of 9 months

Target Antigen

- Well proven target with Elotuzumab (BMS/Abbvie) as PoC
- CS1 (SLAMF7) is highly expressed on MM cancer cells



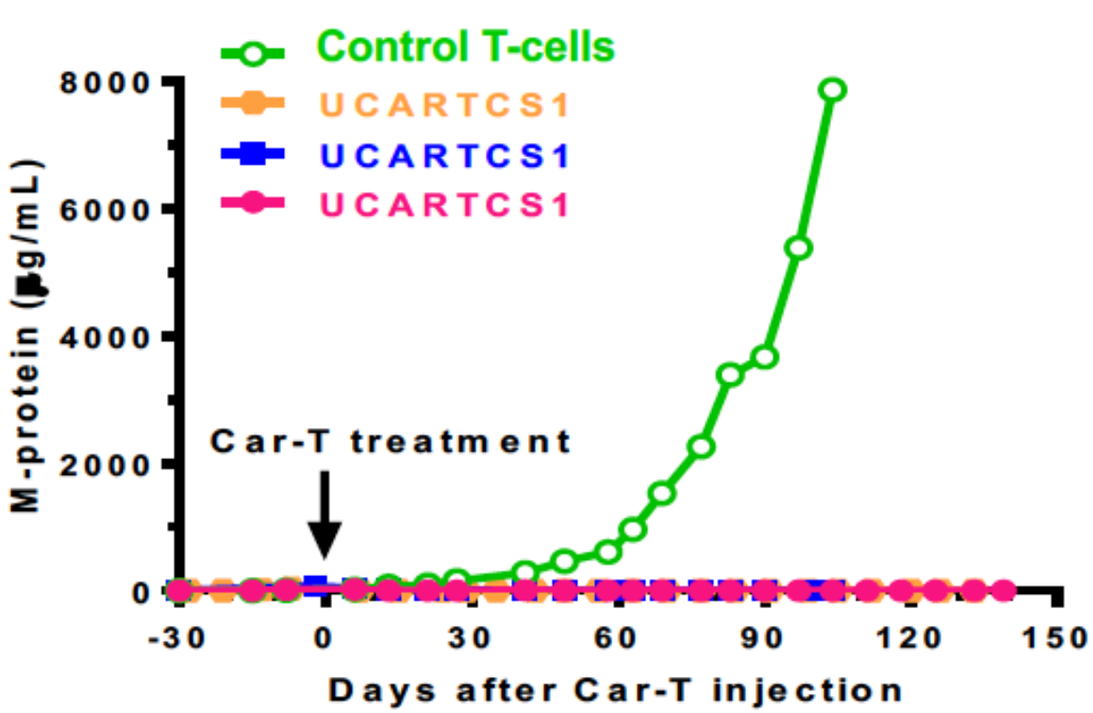
UCARTCS1 Attributes

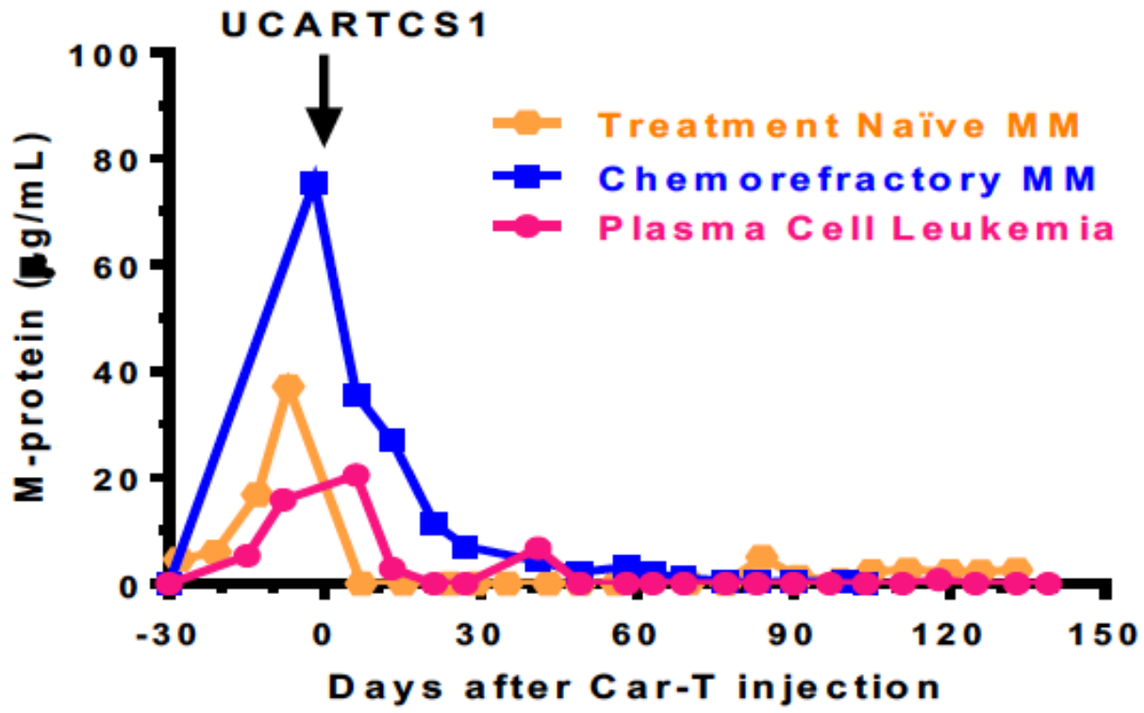
- Pre-clinical data shows high efficacy of re-dosing strategies
- Suicide gene is included for safety
- TCR gene disruption using TALEN® to avoid GvHD
- CS1 gene is disabled by TALEN® to prevent CAR-T Cell cross-reactivity (CS1 is naturally expressed on CD8+ T Cells)

UCARTCS1

Anti-tumor activity with durable efficacy

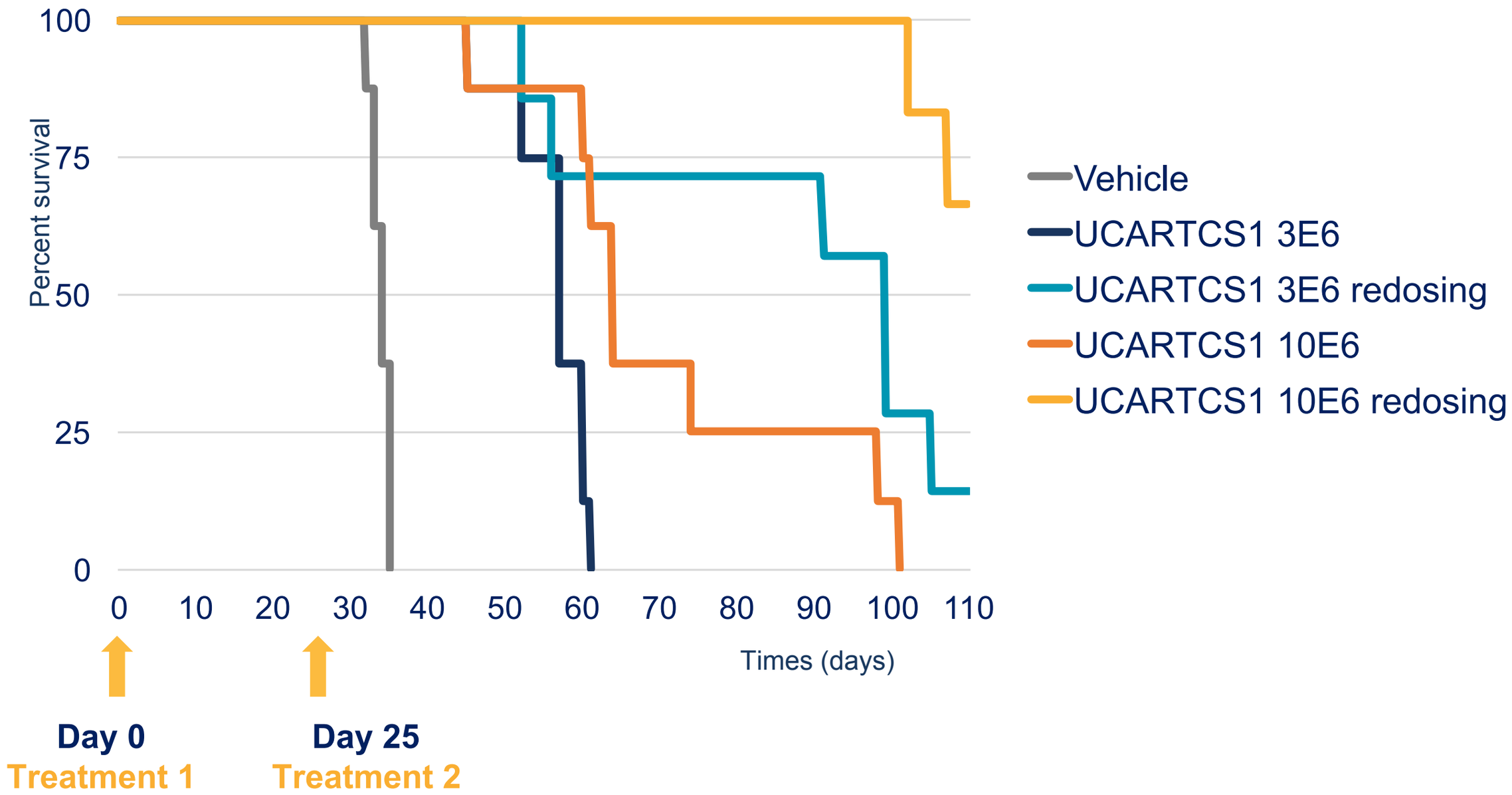
- UCART CS1 exhibits durable *in vivo* efficacy in high-risk MM in PDX-MM models





UCARTCS1

Anti-tumor activity: high performance with re-dosing



UCARTCS1
Development Plan

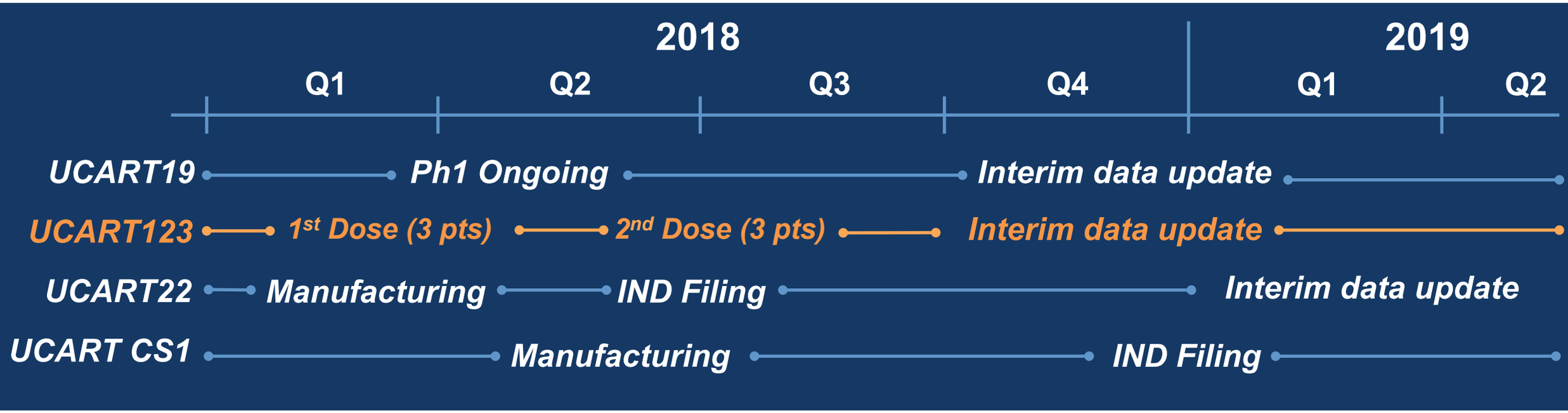
Proof of Concept — Q4 2016 ☑
- Increased cytotoxic activity compared to non-edited T Cells

***In vivo* studies** — Ongoing ☑
- Preclinical studies ongoing in collaboration with MD Anderson Cancer Center (Dr. Jing Yang and Dr. Sattva Neelapu)

Manufacturing — Expected in 2018 ☐
- Development of a modified GMP compatible manufacturing process (inversion of transduction/electroporation steps)

IND Filing — Expected in 2019 ☐

18 months expected Milestone Timeline



- **UCART19** in **ALL patients**
  – Ph1 clinical trials ongoing; interim data was presented at ASH 2017

- **UCART123** in **AML and BPDCN patients**
  – Ph1 clinical trials on-going

- **UCART22** IND in 2018, **UCARTCS1** IND will follow

- **Cash Runway into 2020** – providing funding through multiple data readouts

THANK YOU

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