

GENE EDITED CAR-T THERAPIES

THE PARADIGM IN ONCOLOGY



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- NASDAQ: CLLS
- EURONEXT GROWTH: ALCLS
- 36M SHARES OUTSTANDING
- \$297M IN CASH END Q4 2017
- IMMUNO-ONCOLOGY / CAR T
- THERAPEUTIC GENE EDITING
- GENE THERAPY

~80% ownership



- NASDAQ: CLXT
- IPO JULY 2017
- \$56M IN CASH END Q4 2017
- 7.7M SHARES OUTSTANDING (27M TOTAL)
- BASED IN MINNESOTA
- CONSUMER FOCUS
- HIGH VALUE ASSET

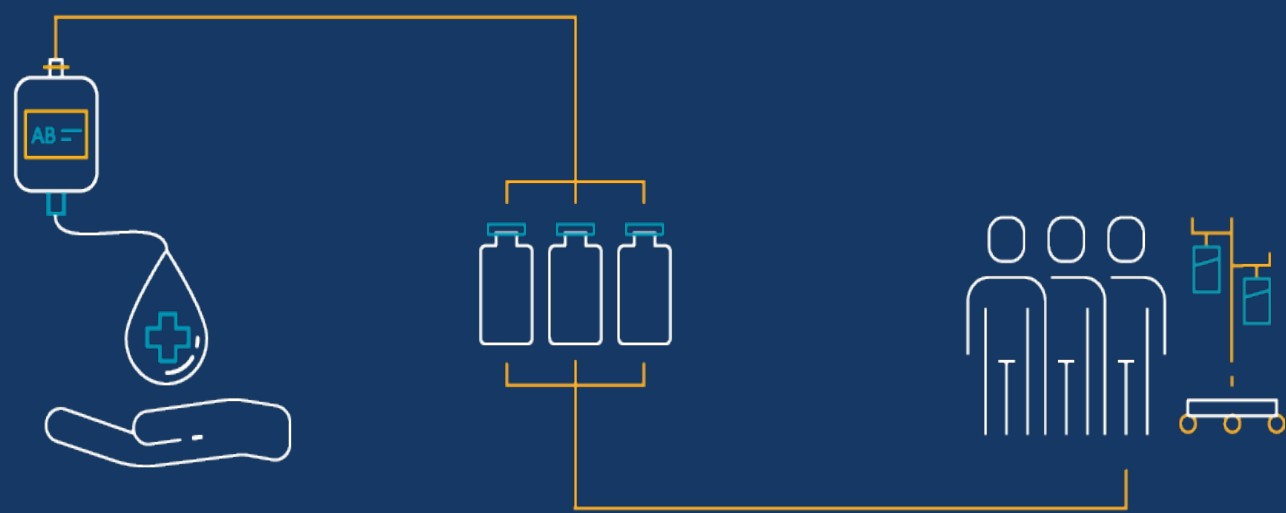
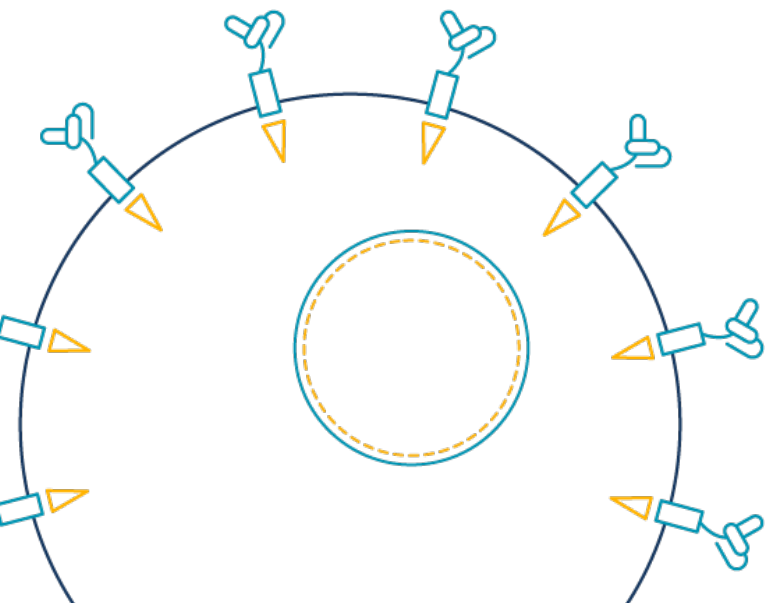
• *Gene editing is the link* •

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-Ts 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**

Rich Allogeneic CAR T Pipeline

Addressing unmet medical need with proven targets



Program	Indication	Product development	Preclinical	Manufacturing	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

Life threatening diseases with unmet needs

Allowing for potential fast track development plans



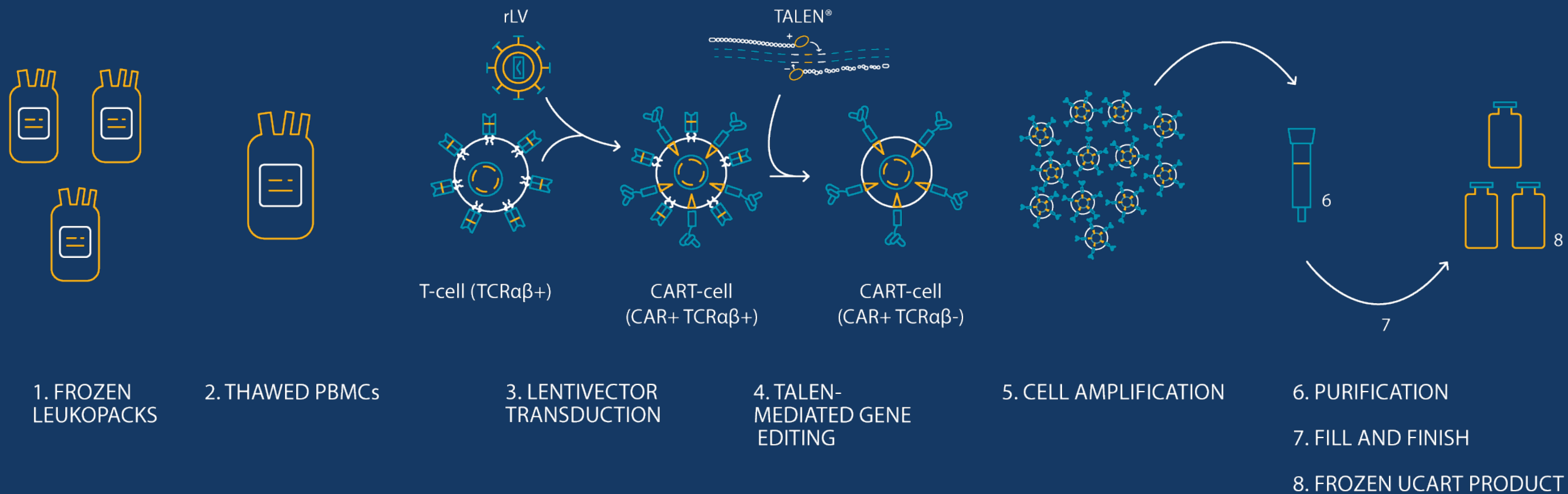
US Estimate	Estimated New Cases in 2017	Estimated Deaths in 2017	5 Year Survival (2007-2013)
AML*	21,000	10,000	26,9%
BPDCN	Estimated < 1% of all hematologic malignancies**		38%***
ALL*	6,000	1,500	68,2%
CLL*	20,000	4,500	83,2%
MYELOMA*	30,000	13,000	49,6%
NON HODGKIN LYMPHOMA*	72,000	20,000	71%

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

** Riaz et al, 2014

*** Alsidawi et al, 2016

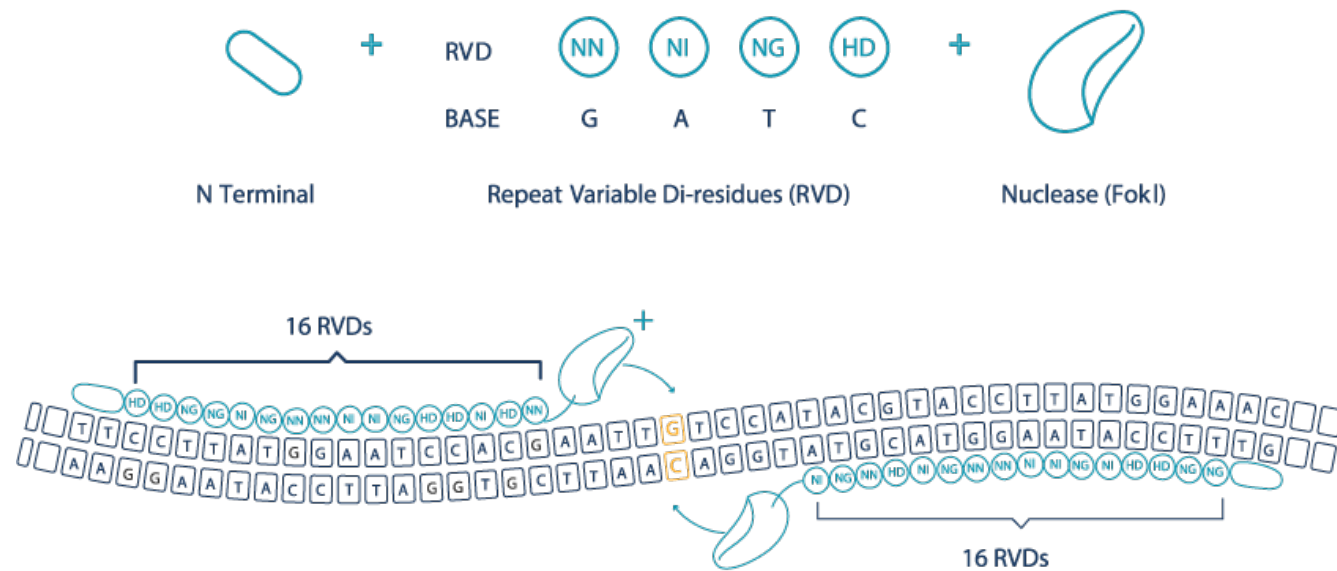
Allogeneic CAR T – GMP Manufacturing



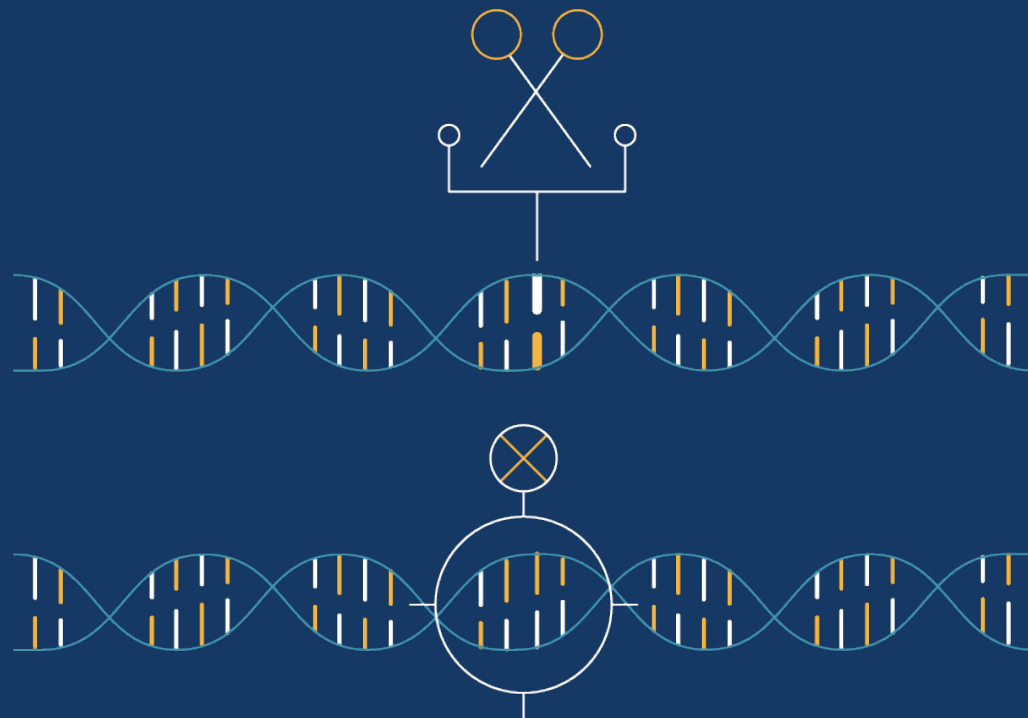
- GMP manufacturing in place for UCART19, UCART123, UCART22
- Full QC system, cleared for clinical trials

Proprietary TALEN[®] Gene Editing

Highest yield and precision



- Industry-leading knockout and knock-in efficiency
- Precision targeting to 6 base pairs at the cleavage site
- Low off-target cleavage
- 18 years of experience in gene editing
- Strong intellectual property

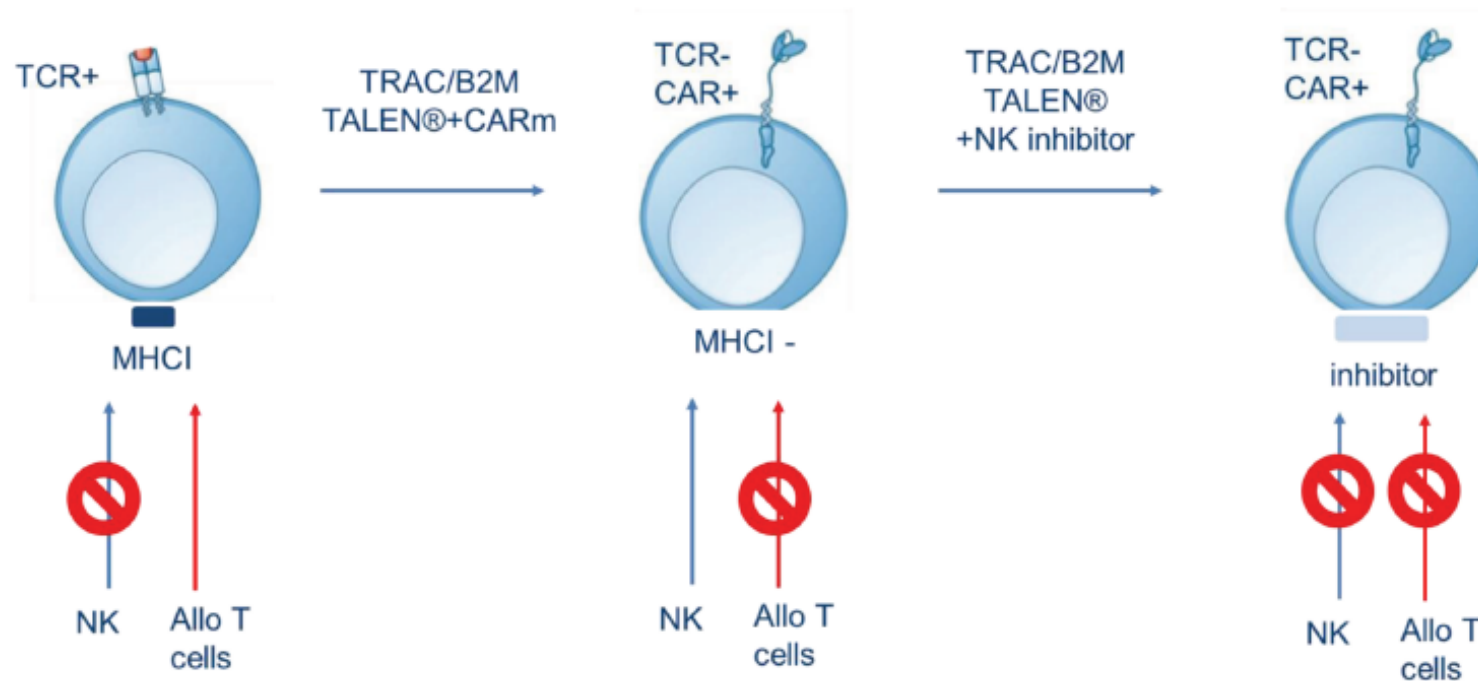


A **powerful** gene editing technology

In clinic **since 2015** in
US and EU

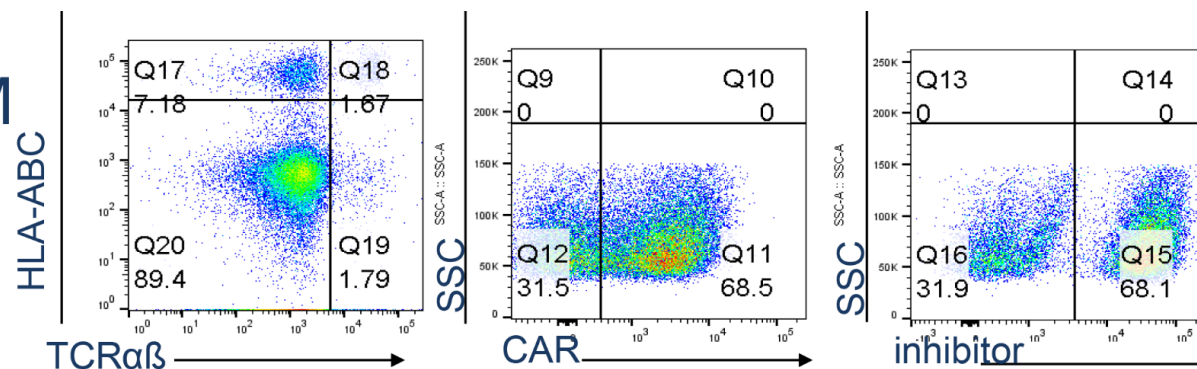
A cornerstone: TALEN[®] gene editing

Highest yield and precision



TRAC TALEN[®]+CAR

TRAC/B2M
TALEN[®]
+inhibitor



- **90% double knockout** of TCR and B2M in T Cells
- **68% efficiency targeted insertion (CAR)** with **double knockout (TCR, B2M)**
- **42% double targeted insertion (CAR, NK inhibitor)** at TRAC and B2M locus with **double knockout (TCR, B2M)**

The benefits of UCARTs



Market access

- Ability to manufacture large amounts of product in advance
- Easily available in large number of hospitals

Cost of treatment

- Possibility to lower the price range of CART therapies to other IO standard (~150k\$)
- No additional cost linked to “segment of one” supply chain

Ability to re-dose

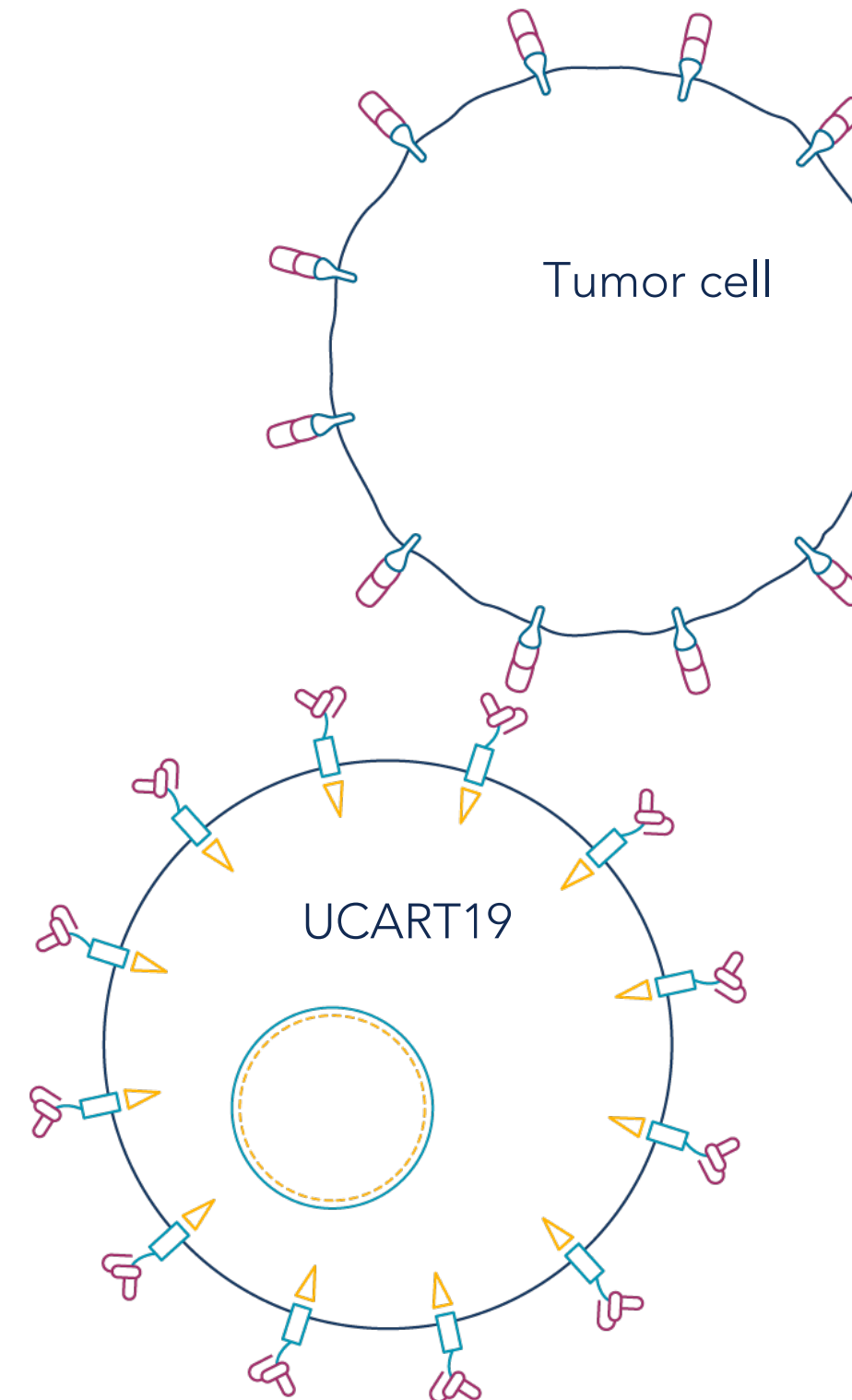
- Possibility to re-dose with same antigen
- Combine different antigen targeting CARTs
- No issue of long term persistence and related side effects

UCART19*

Initial Proof Of Concept in ALL



- 1st patient dosed in June 2015 (compassionate)
- Phase I trials (US/EU) started in June 2016
- Multiple 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



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**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	1.4x10 ⁶ or 1.2x10 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

UCART123 in AML and BPDCN

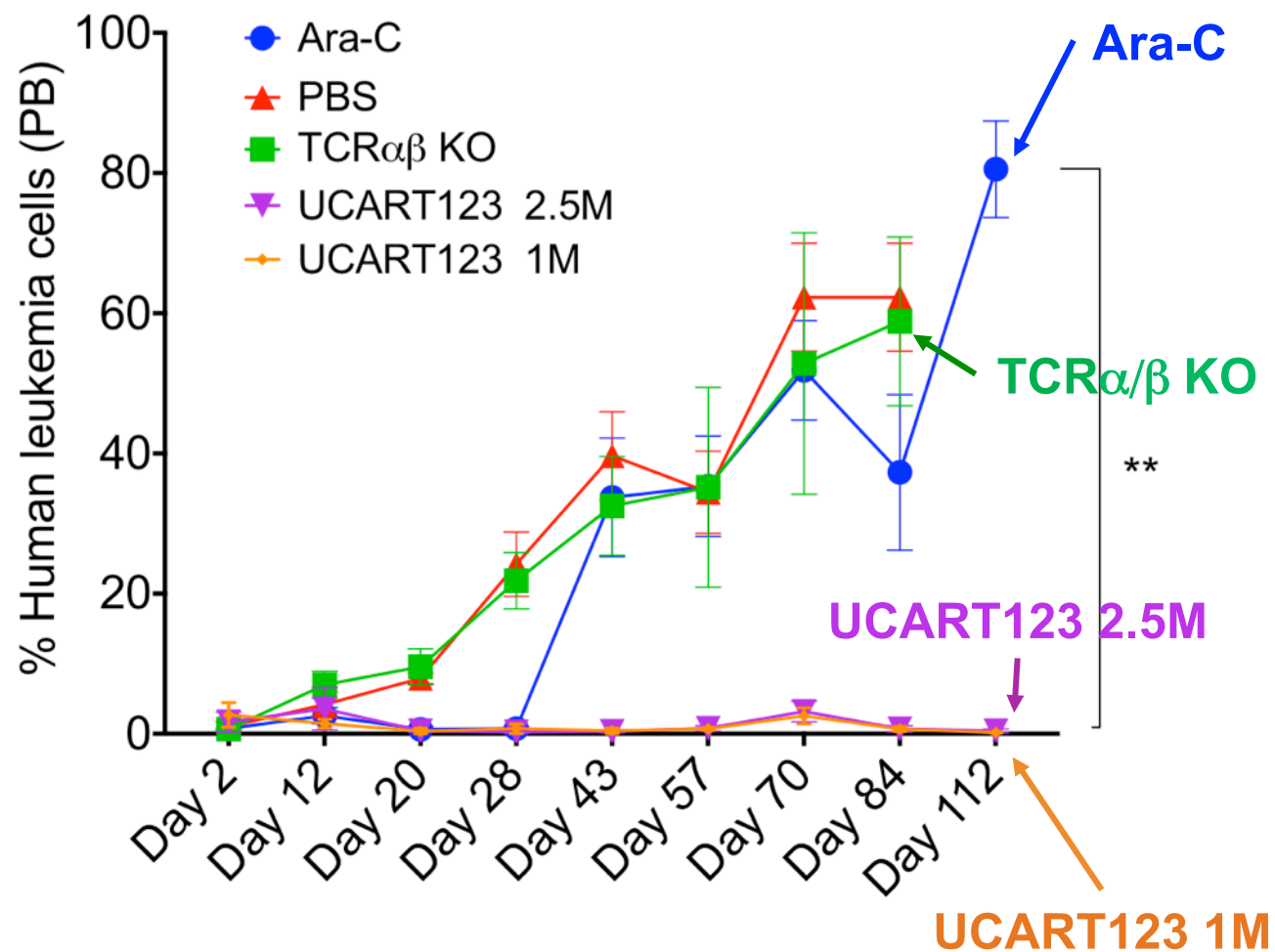
Encouraging Efficacy Data



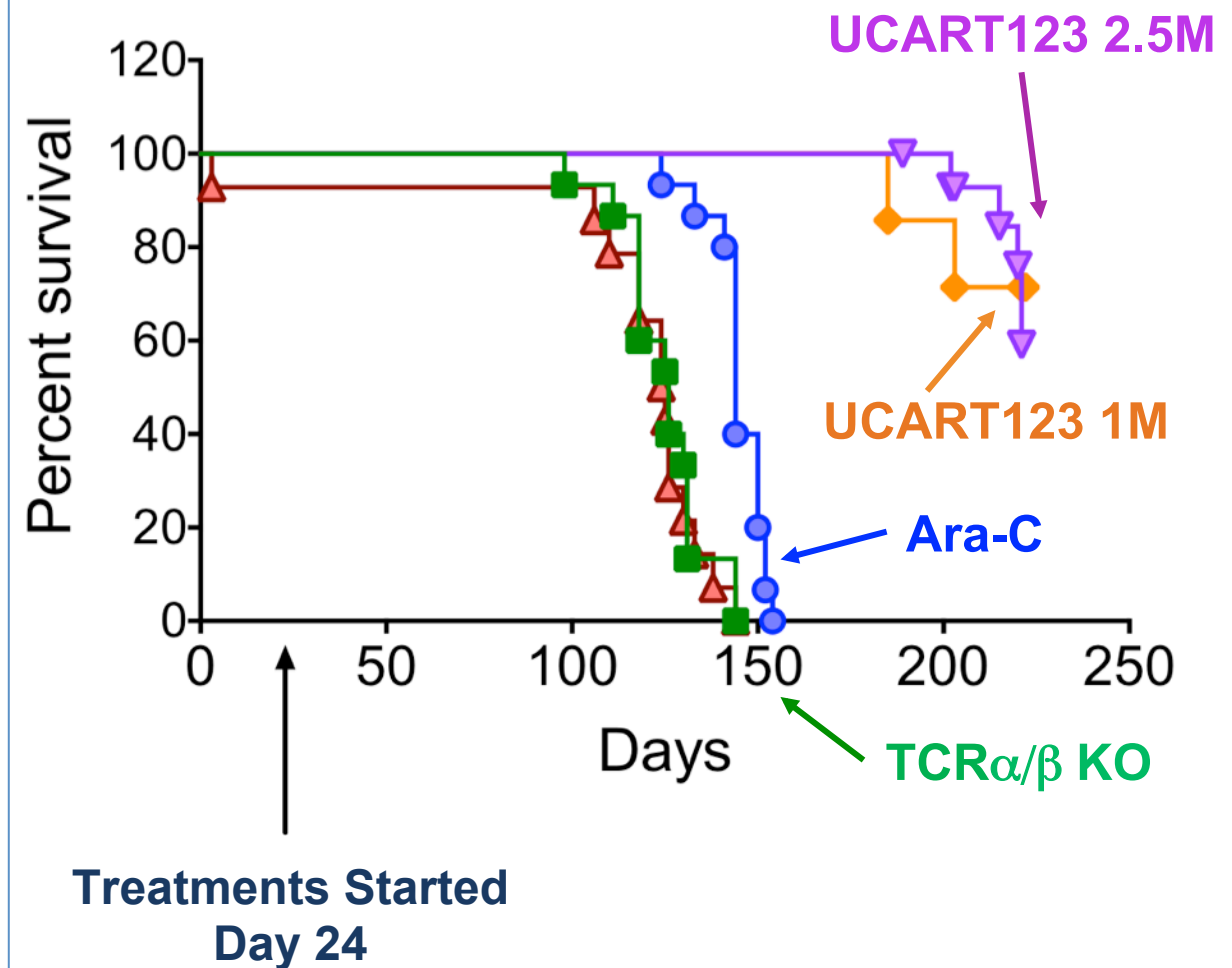
Weill Cornell
Medicine

- 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

UCART123 in AML and BPDCN

First Wholly-Controlled 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
MDAnderson
Cancer Center
Making Cancer History®



Weill Cornell
Medicine

Dose Escalation Phase (R/R AML)

DL3
N=3

$1.25 \times 10^6/\text{kg}$

DL2
N=3

$1.25 \times 10^5/\text{kg}$

DL1 new start dose
N=3

$6.25 \times 10^4/\text{kg}$

DL-1

$1.25 \times 10^4/\text{kg}$

Total Dose Escalation N= 9-12 pts

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

Expansion Phase

RR AML
N=18-37

Untreated AML
ELN Adverse Genetic Group
N=46-107

Total Phase I Expansion
N=64-144

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



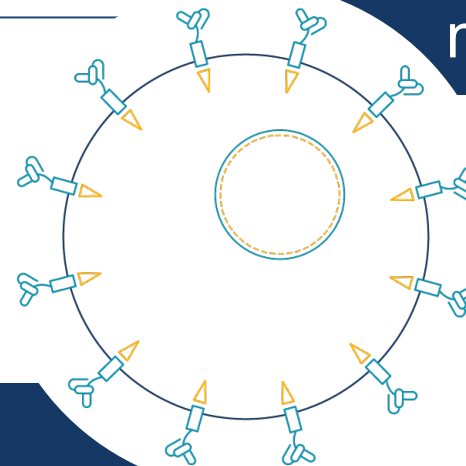
Targeting ALL, NHL and other B-Cell Malignancies

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 blasts¹



Target Antigen

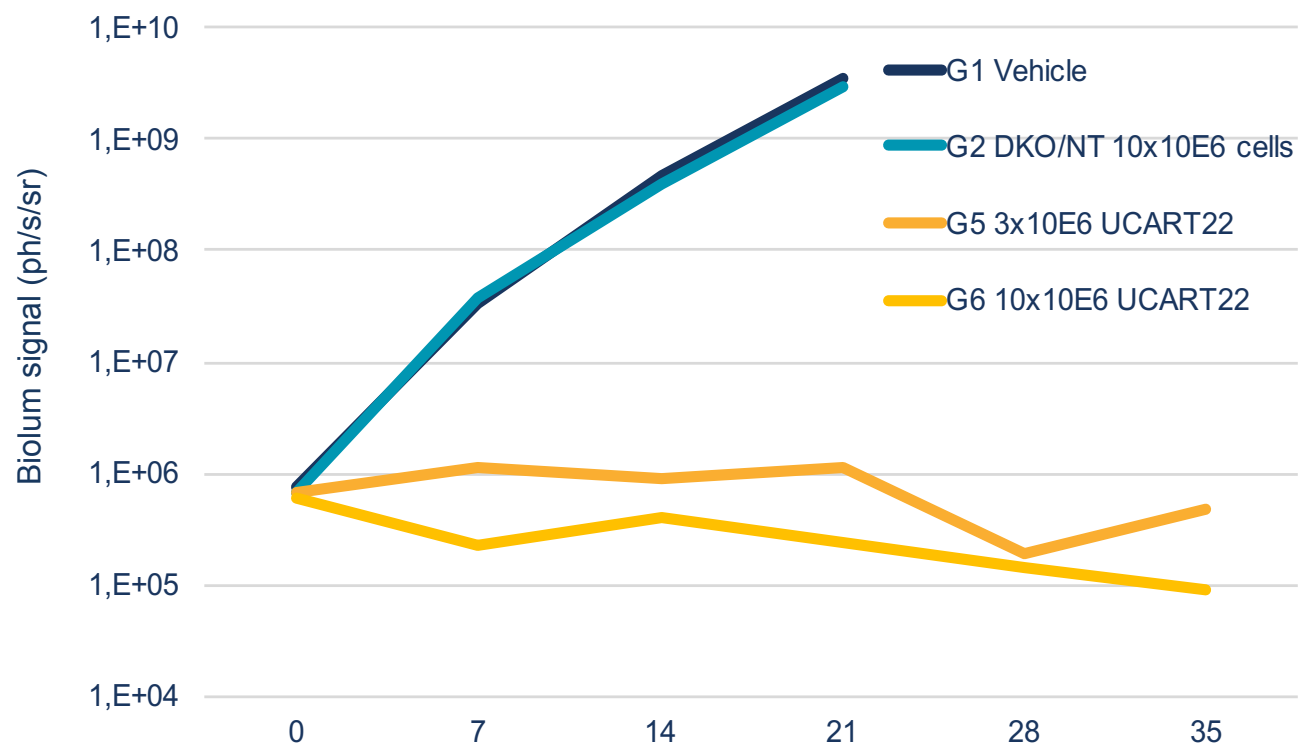
- CD22, is expressed on the B-cell surface, persists on mature B-cells, and is lost on plasma cells

Proof of concept

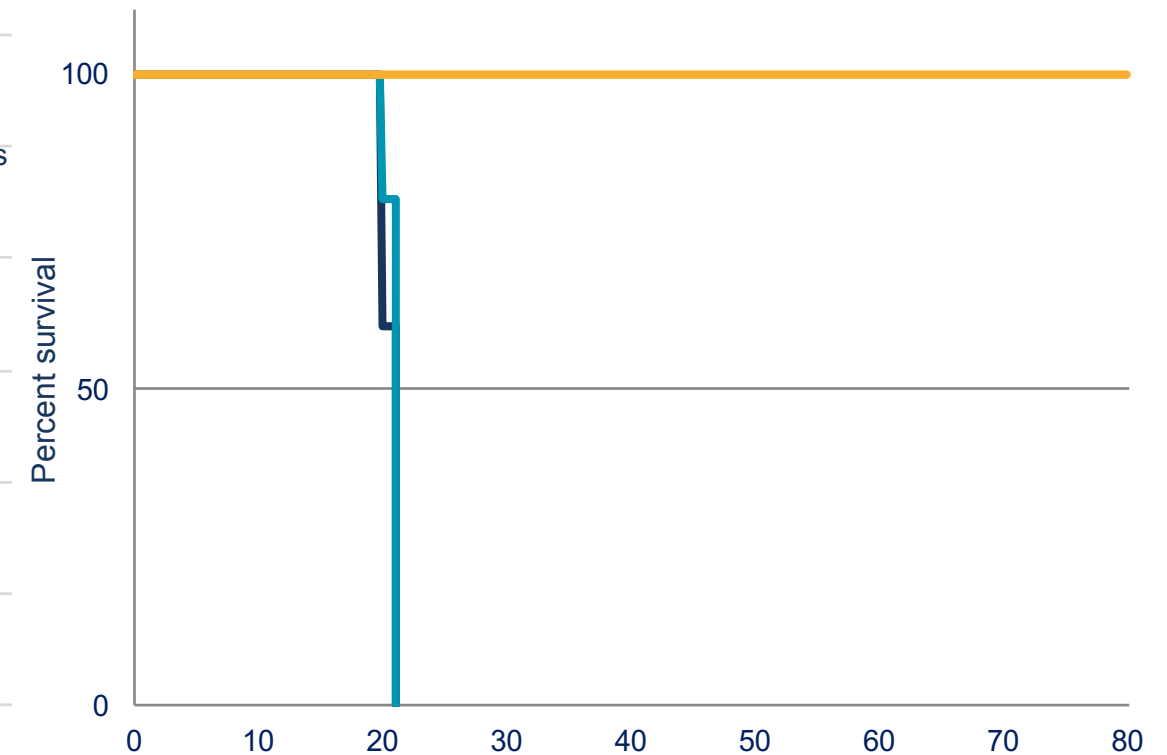
- Anti-CD22 monoclonal antibodies
- Autologous CAR-T in development

- 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 in collaboration with MD Anderson Cancer Center



Manufacturing

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

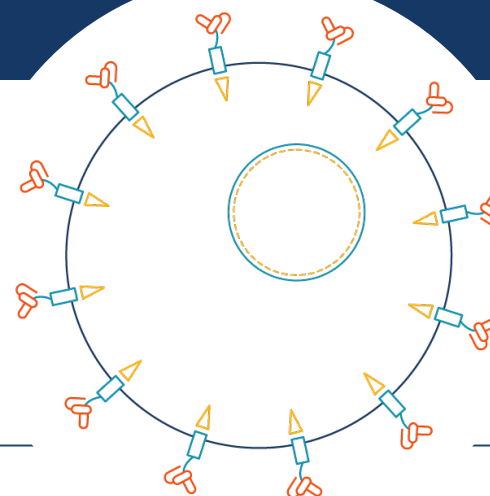


Unmet Medical Need

- > 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



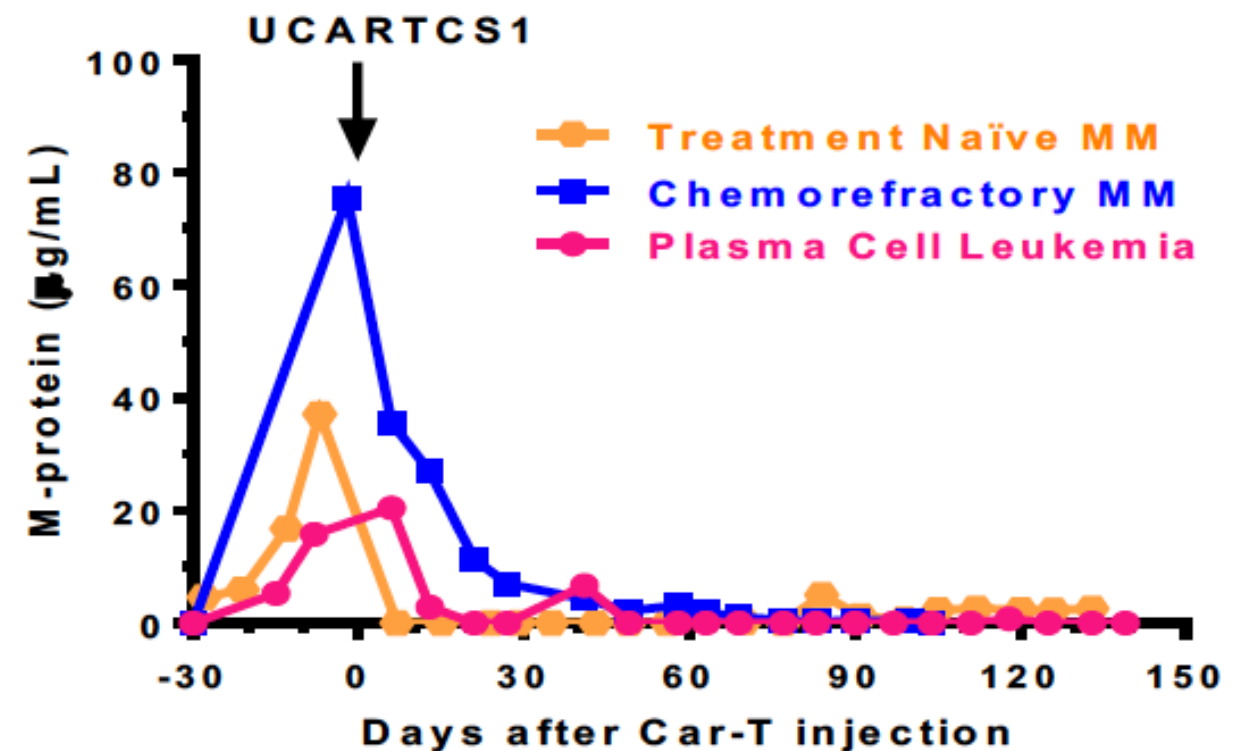
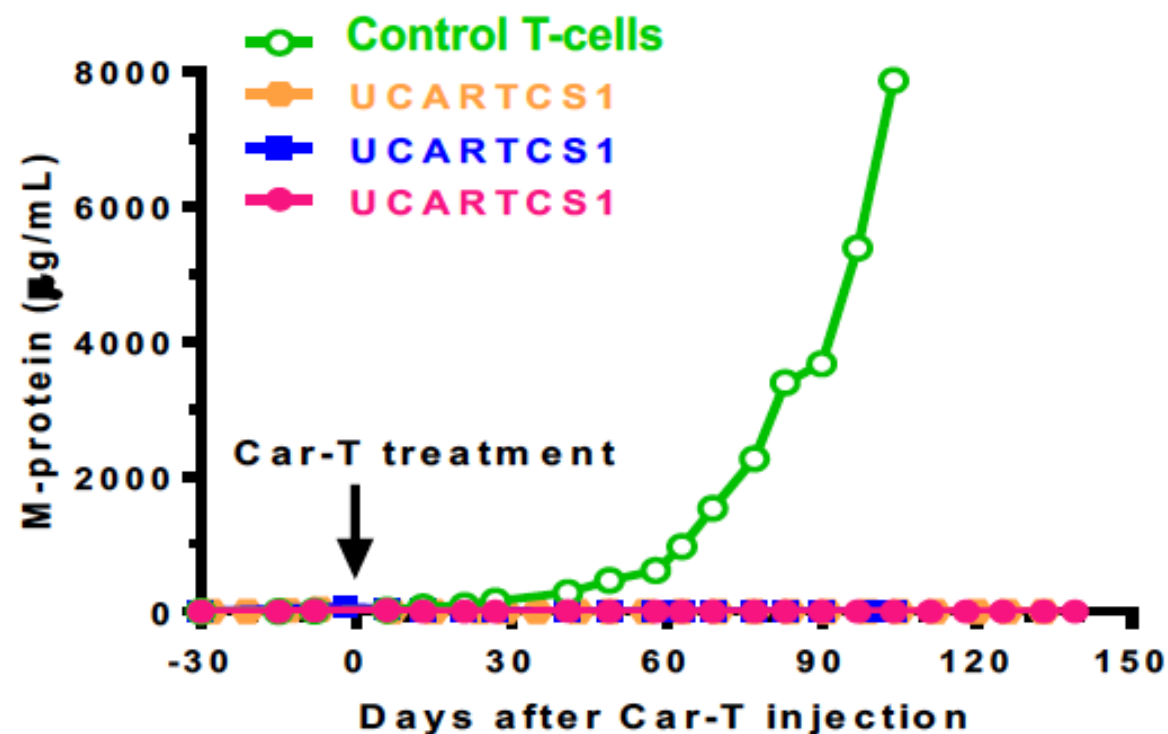
UCARTCS1 Attributes

- 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)
- Suicide gene included

UCARTCS1

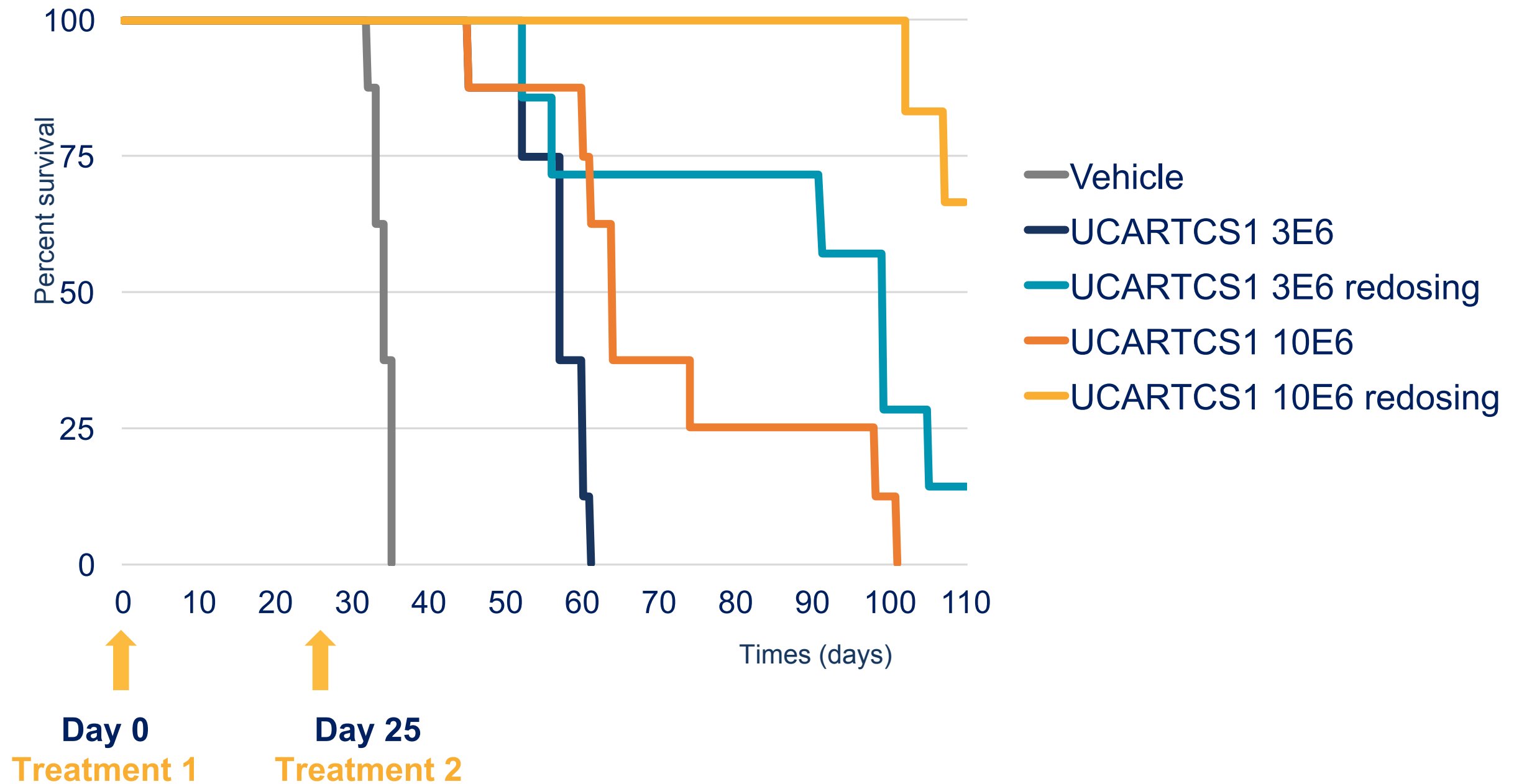
Anti-tumor activity with durable efficacy

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



UCARTCS1

Anti-tumor activity: re-dosing can increase efficacy



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)

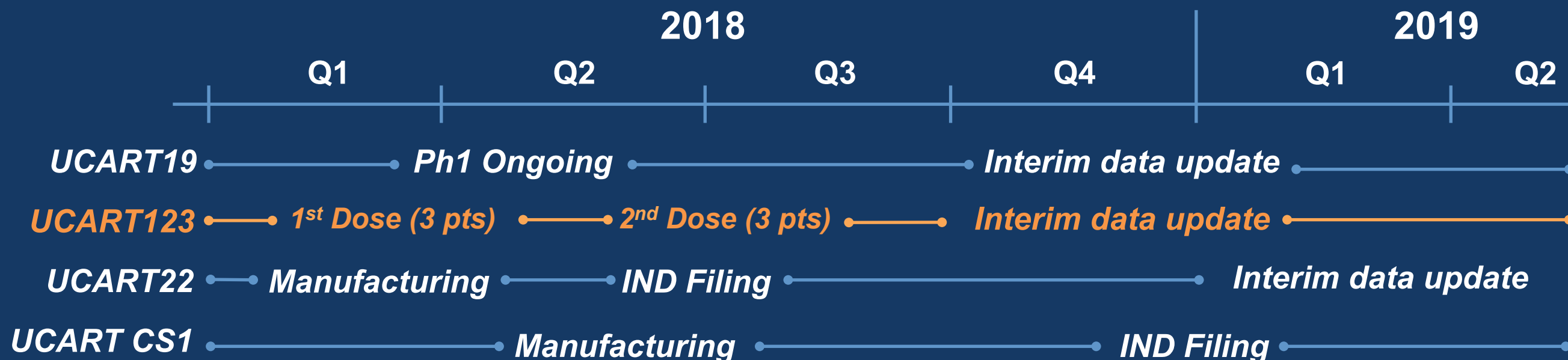


IND Filing

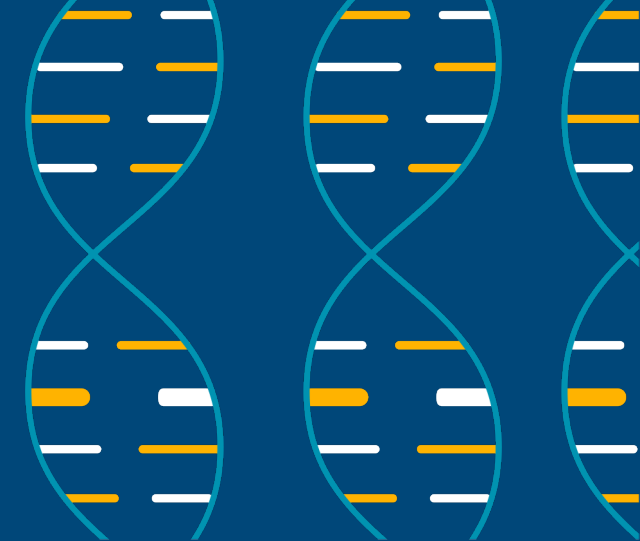
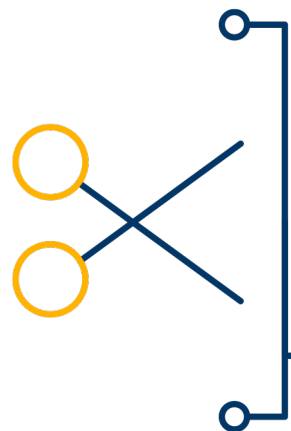
Expected in 2019



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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