cellectis
EDITING LIFE
COMMITMENT TO A CURE
cellectis.com

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 that our clinical trials will not be successful. The risk of not obtaining regulatory approval to commence clinical trials on additional 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 risk factors that may affect company business and financial performance, is included in our annual report on form 20-F and other filings Cellectis makes with the securities and 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.

Cellectis proprietary information.
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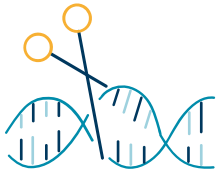
OUR MISSION

Leverage our leadership in gene editing and CAR-T therapy to bring new **hope** to cancer patients through broadly available, off-the-shelf therapies

CELLECTIS - COMMITMENT TO A CURE



INNOVATION

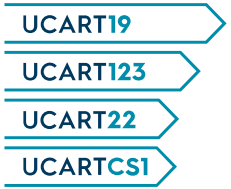
Protein engineering for best-in-class gene editing & CAR technologies, cell engineering and culture technologies

Innovative and robust gene editing (TALEN®) platform

LEADERSHIP

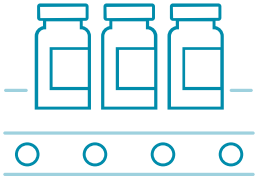
First clinical proof-of-concept for allogeneic CAR-T therapies, first pediatric ALL patient in 2015

Making cancer therapy cost-effective and available faster to patients globally



PIPELINE

Pioneering robust first-in-class allogeneic CAR T-cell programs for different hematological malignancies, as well as solid tumors (pre-clinical)



MANUFACTURING

Scalable, efficient process to generate consistent and highly potent CAR-T therapies

Two facilities being built to ensure manufacturing autonomy

Reinforced by industry leading partnerships and a strong cash position

ADVANTAGES OF ALLOGENEIC VS. AUTOLOGOUS CAR-T

Autologous process:

1. CANCER TREATMENT DECISION

2. CANCER PATIENT APHERESIS

3. MANUFACTURING OF A SINGLE PATIENT PRODUCT

4. INDIVIDUAL CAR-T THERAPY

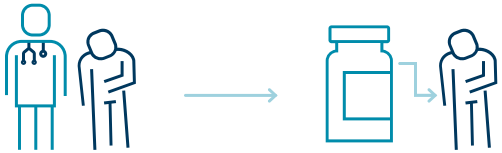
4-6 weeks before treatment

Allogeneic process:

HEALTHY DONOR APHERESIS

SCALABLE MANUFACTURING OF 100+ DOSES/BATCH

MASS PRODUCED OFF-THE-SHELF CAR-T THERAPIES

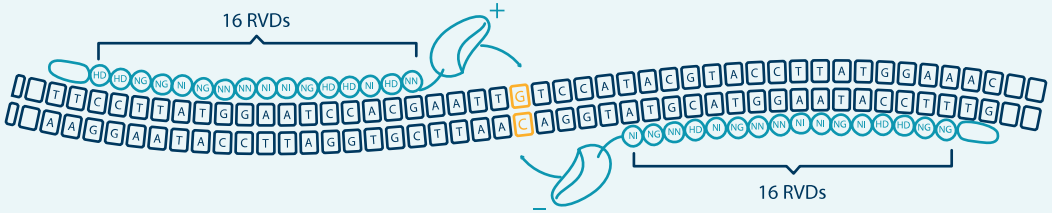


1. CANCER TREATMENT DECISION

2. OFF-THE-SHELF CAR-T THERAPY

immediate treatment

TALEN®: BEST-IN-CLASS GENE EDITING



PRECISION
targeting within 6 base pairs of any target in the genome (effective changes)

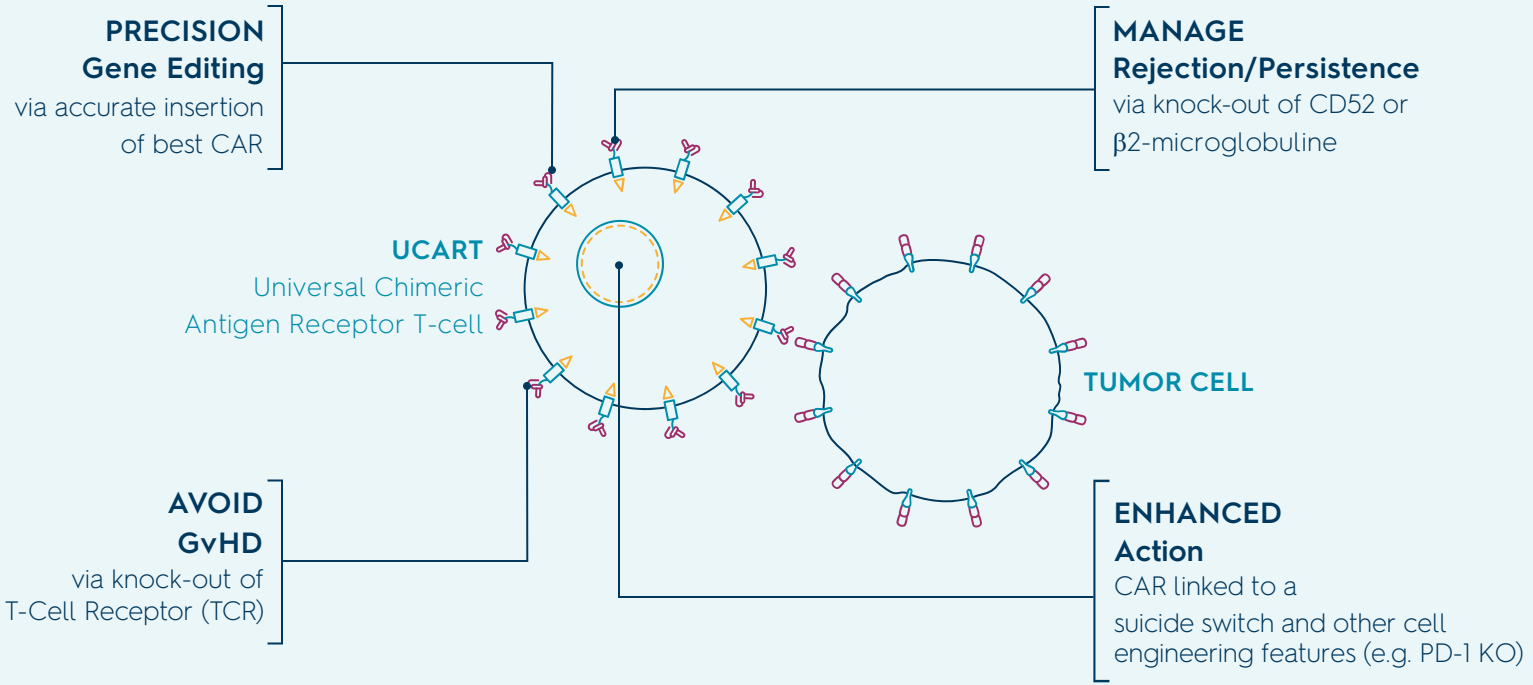
SPECIFICITY
recognition site is 32 base pairs long (avoids errors)

EFFICIENCY
TCR-α can be knocked-out with over 95% efficacy for engineered CAR T-cells (ensures yield)

Editing genes allows disabling a functional gene, correcting a gene, or replacing or inserting a DNA sequence at a chosen location in a genome.

TALEN® has been successfully used in the clinic to solve key challenges with allogeneic CAR-T including protection from GvHD, mitigation of rejection, chimerism and enhanced safety via a suicide switch.

UCARTs – FIRST & BEST-IN-CLASS ALLOGENEIC CAR T-CELLS



PARTNERSHIPS WITH INDUSTRY LEADERS

Development & commercialization partners

SERVIER

UCART19 (with Allogene) + other targets

Up to $1.1B in development milestones

Royalties on sales

Allogene THERAPEUTICS

15 LICENSED TARGETS

Up to $2.8B in development & sales milestones

Royalties on sales

Equity investor

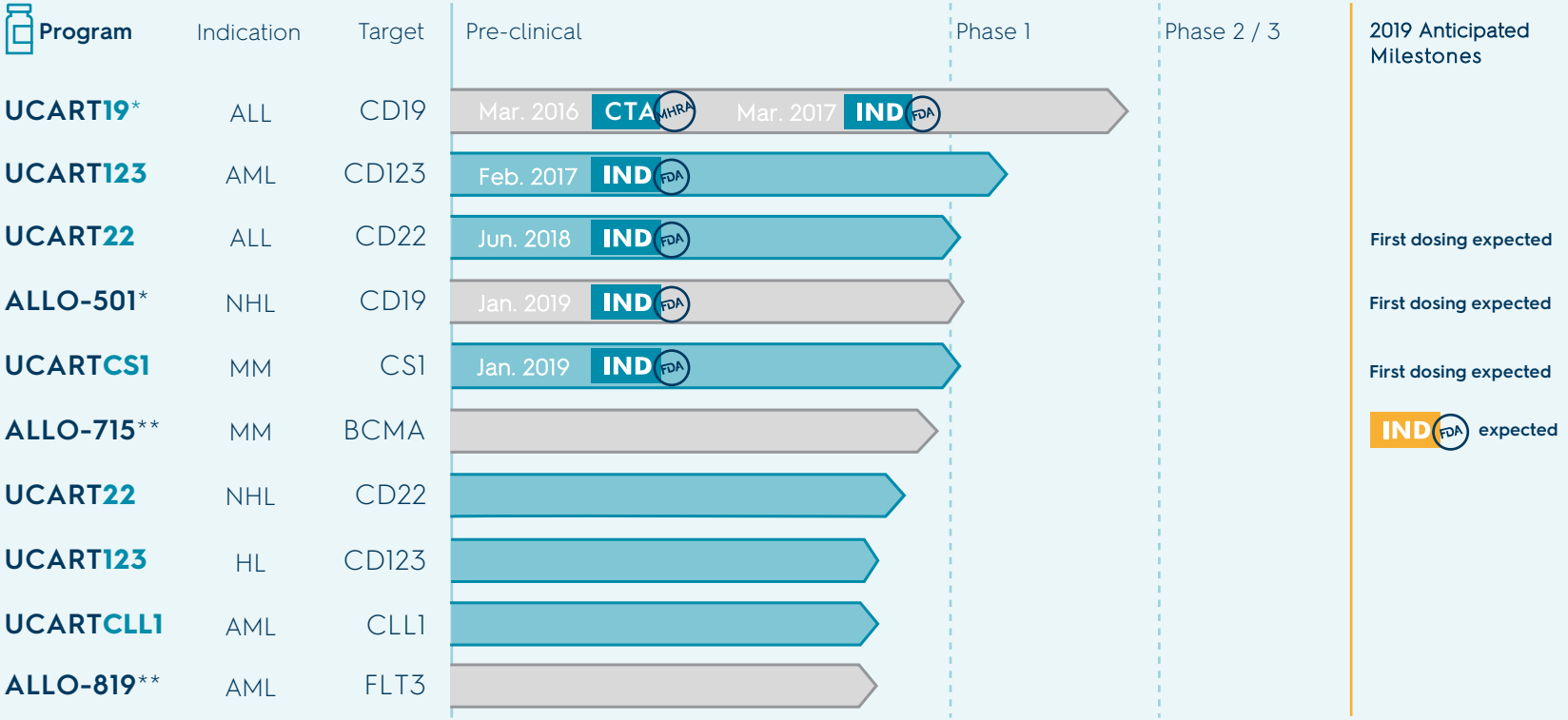
Pfizer

6.57% of outstanding shares

As of December 31, 2018

Up to $3.9B in potential milestone payments plus royalties

PIPELINE: INNOVATIVE CANCER THERAPIES FOR UNMET NEEDS



* UCART19/ALLO-501 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene.
** Product candidates exclusively licensed to Allogene

Proprietary development program
Licensed development program

PIPELINE TARGETS MULTIPLE UNMET NEEDS IN CANCER

ALL

UCART22

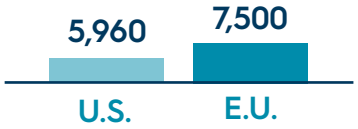
AML

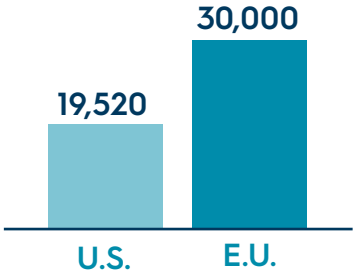
UCART123 UCARTCLL1

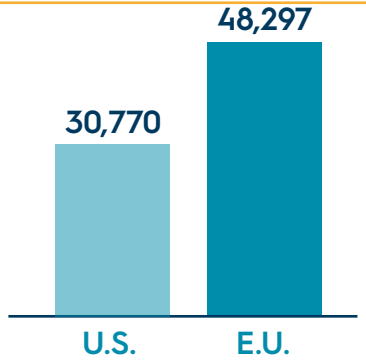
MM

UCARTCS1

Incidence rates per year







Survival data

20%

5 years OS* in adults

<6 months median disease-free survival in pediatric patients

27%

5 years OS in adults

6% 5 years OS in adults >55 years old

50%

5 years OS in adults

43-83 months median OS for stages 2-3

* Overall Survival

UCART19*: DESIGN OF PHASE 1 STUDIES IN R/R** ALL***

CD19 is a validated target expressed in B-cell malignancies

Adult ALL (CALM study)

PRIMARY OBJECTIVE
Evaluate safety, tolerability, maximum tolerated dose (MTD) and regimen

SECONDARY OBJECTIVES
Objective remission rate at Day 28. Duration of response, time to remission, progression-free survival

ONGOING

Pediatric ALL (PALL study)

PRIMARY OBJECTIVE
Evaluate safety at a fixed dose in patients aged between 6 months and 18 years old

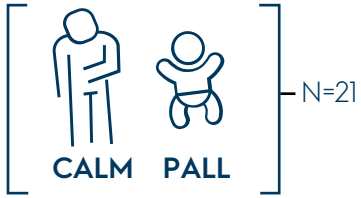
SECONDARY OBJECTIVES
Determine the ability to achieve molecular remission at Day 28

ONGOING

* UCART19 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene
** Relapsed/Refractory
*** Acute Lymphoblastic Leukemia
**** Dose Level

UCART19*: PHASE 1 R/R ALL – DATA** PRESENTED AT ASH 2018

Safety:



- **14%** Grade 3-4 Cytokine Release Syndrome
- **0%** Grade 3-4 neurotoxicity
- **0%** Grade 3-4 skin Graft vs Host Disease

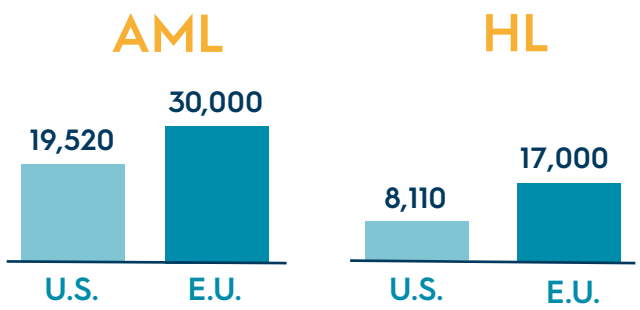
Efficacy:

- → 82% CR/CRi rate in FCA***-treated patients
- → 67% overall CR/CRi rate
- → 71% of these patients were MRD-
- → Redosing with UCART19 resulted in cell expansion and MRD- status in 2/3 patients
- → Peak expansion observed mostly at Day 14

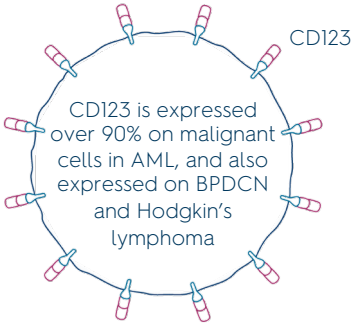
* UCART19 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene
** Pooled data
*** Lymphodepletion regimen consisting of fludarabine, cyclophosphamide and an anti-CD52 mAb

CD123 TARGET: RATIONALE FOR THERAPY

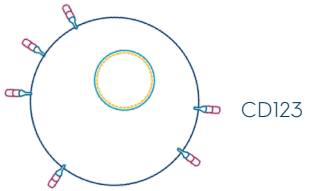
Incidence rates per year



High expression on malignant cells



Limited expression on healthy cells



Myeloid progenitor cells, pDCs

UCART123 – PHASE 1 STUDY IN AML

Patient characteristics

Age and fitness: R/R in AML
65 years and older, unfit patients

Mutation status:
genetically complex

Progression: rapid
progression following relapse

Dose escalation (mTPI*) phase (R/R AML)

R/R AML
Up to 18
patients

ONGOING at
Weill Cornell
MD Anderson
Moffitt
Dana-Farber

28 days between the first 2 patients for each dose**, then 14 days for subsequent patients

Expansion Phase

TOTAL
N=64-144

Expected
in 2020

R/R AML
PATIENTS
N=18-37

FIRST LINE AML PATIENTS
ELN*** Adverse genetic group
N=46-107

* Modified Toxicity Probability Interval Design
** 42 days if aplasia
*** European Leukemia Net

UCART123 – PRECLINICAL RATIONALE IN AML

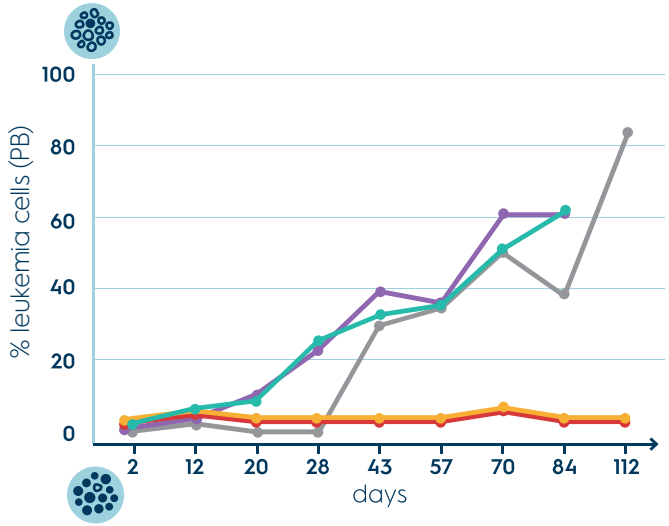
Development rationale:

High expression: blasts, independent of mutation status

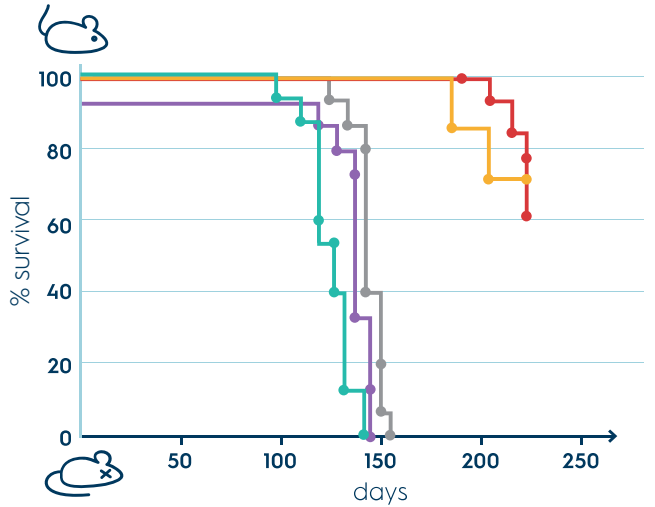
Unmet need: high relapse rate and poor survival in R/R patients

Validated target: CD123 - clinically validated in autologous CAR T-cell trials

Elimination of AML cells



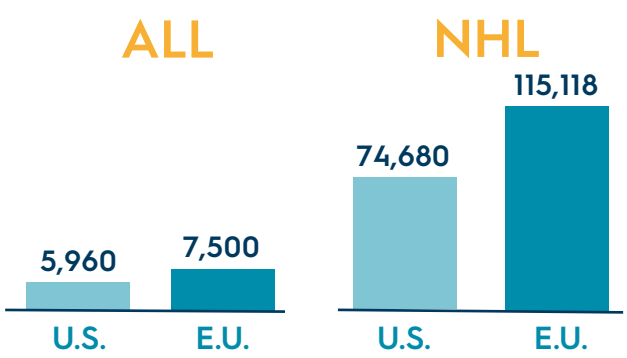
Dose-dependent enhanced survival



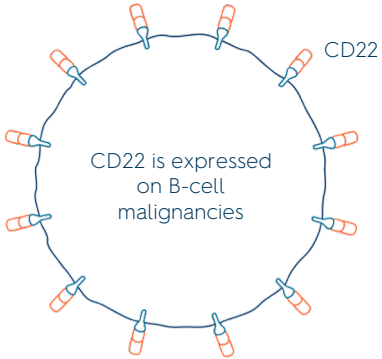
Ara-C PBS TCR αβ KO UCART123 2.5M UCART123 1M

CD22 TARGET: RATIONALE FOR THERAPY

Incidence rates per year



Expression on malignant cells



Potential in disease space

Relapses following a CAR T-cell therapy, with malignant cells expressing CD22

B-ALL patients expressing CD22

Potential combination therapy approach

UCART22 – PHASE 1 TRIAL DESIGN IN ALL

Patient characteristics

Age and fitness:
R/R B-ALL < 65 years

CD19- & CD19+ ALL
high CD22 expressing B-malignant cells

Offers a therapeutic solution to patients who cannot receive, or relapsed, after autologous CD19 CAR T-cell therapy

Dose escalation (mTPI) phase

28 days between the first 2 patients for each dose, then 14 days for subsequent patients

Expansion Phase

UCART22 – PRECLINICAL RATIONALE FOR ALL

Development rationale:

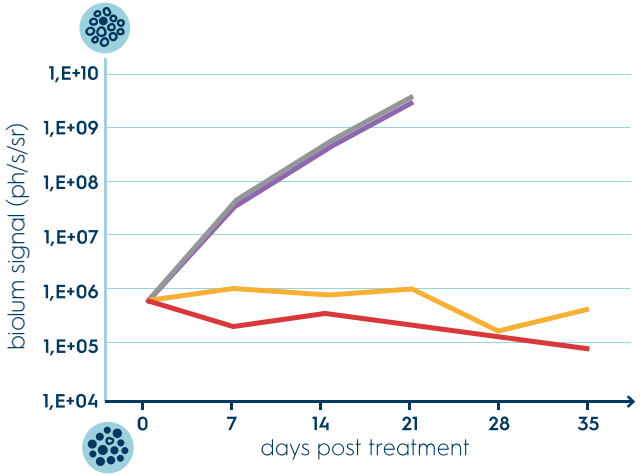
CD22 expression: in CD19 CD19 negative blasts

Unmet need: high relapse rates (CD19-) after CAR-T treatment, poor survival in R/R patients

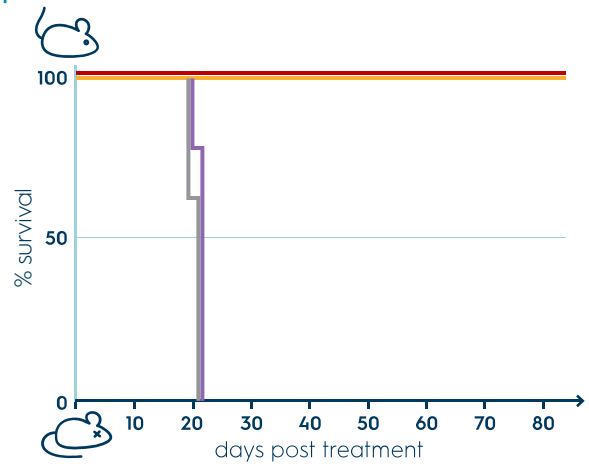
Validated target in ALL and NHL

Expandable market: potential expansion into first-line ALL

Control of tumor progression



Enhanced survival



Vehicle | DKO/NT 10x10⁶ cells | UCART22 3x10⁶ | UCART22 10x10⁶

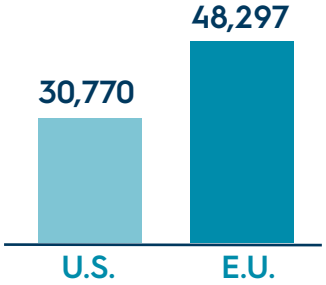
UCART22

- Is highly efficient at eradicating tumors in vivo
- Result in increased survival in mouse model

CS1-SLAMF7 TARGET: RATIONALE FOR THERAPY

Incidence rates per year

MM



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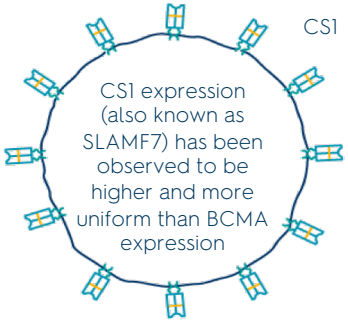
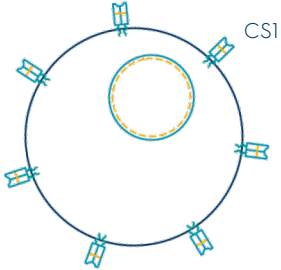


Limited expression on healthy cells



T cells, B cells, macrophages and NK cells

Monoclonal antibody validation

- **Elotuzumab** is a monoclonal antibody targeting CS1
- Elotuzumab is safe and effective in MM patients
- Elotuzumab in combination with lenalidomide and dexamethasone in R/R MM patients shows:
  5.5% CR rate and 35% partial remissions

UCARTCS1 – PHASE 1 TRIAL DESIGN IN MULTIPLE MYELOMA

Patient characteristics

Age and fitness:
R/R MM patients < 65 years

Dose escalation (mTPI*) phase

R/R MM
Up to 18 patients

To start at
MD Anderson

28 days between first 2 patients, then 14 days between each consecutive patient

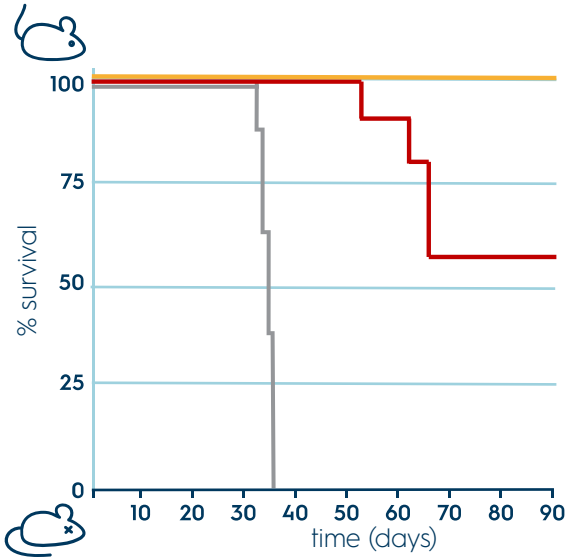
Expansion Phase

TOTAL
N=12-30

→ **Registration phase**

UCARTCS1 – PRECLINICAL RATIONALE IN MULTIPLE MYELOMA

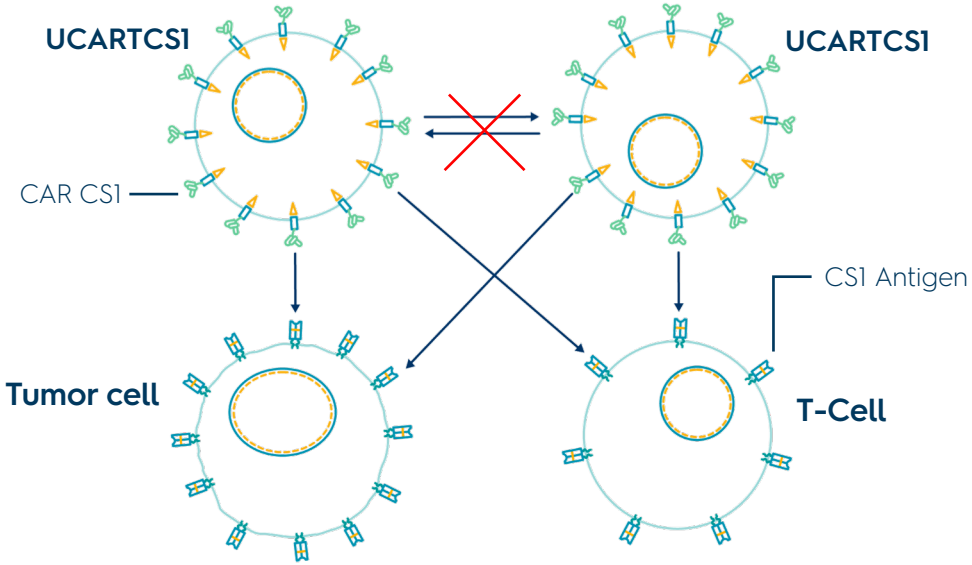
Dose-dependent enhanced survival



Day -10: **tumor cells injection** Day 0: **treatment**

Vehicle **UCARTCS1** $3x10^6$ **UCARTCS1** $10x10^6$

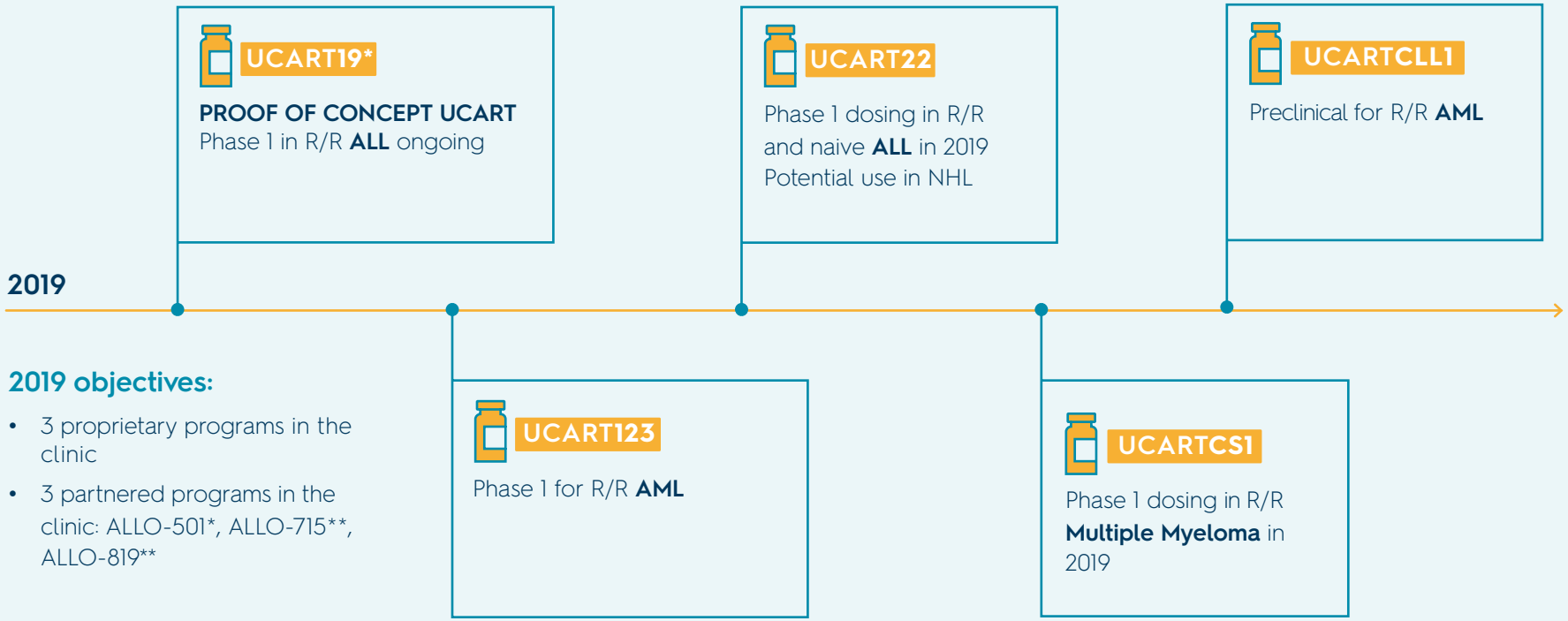
Knock-Out of CS1 on CAR T-cells to suppress cross T-cell reaction between UCARTCS1



Preclinical evidence:

- Strong anti-tumor effect in mice
- Potential engraftment enhancement

BUILDING THE FUTURE OF ALLOGENEIC CAR T-CELL THERAPY



2019 objectives:

- 3 proprietary programs in the clinic
- 3 partnered programs in the clinic: ALLO-501*, ALLO-715**, ALLO-819**

* UCART19/ALLO-501 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene.
** Product candidates exclusively licensed to Allogene

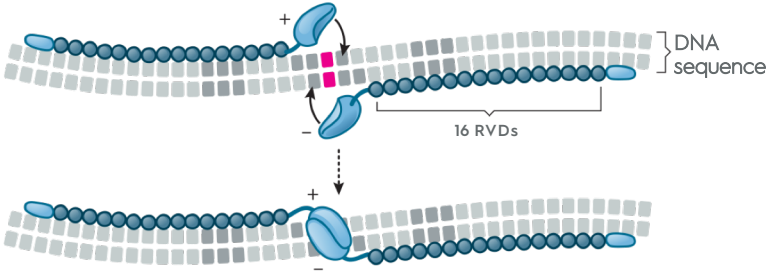
TALEN® GENE EDITING – ADVANTAGES

TALEN®:

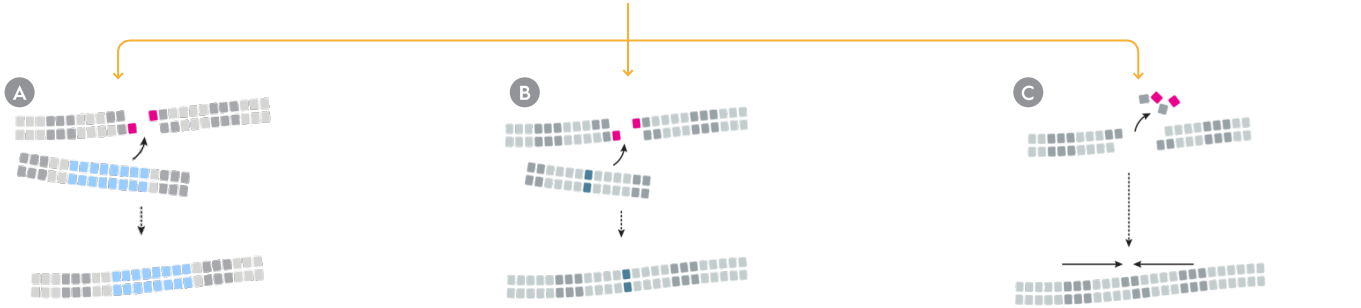
Driven by protein/DNA interactions to work on potential off-site cleavage

Releases DNA ends **accessible to homologous recombination** to perform gene insertions and corrections

Over 25 years of building a strong patent portfolio with umbrella patents on gene editing



Our nucleases act like DNA scissors to edit genes at precise target sites



Gene insertion or Knock-In (KI)

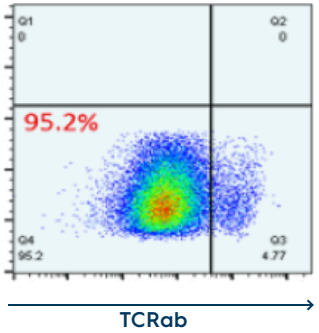
Gene correction

Gene inactivation or Knock-Out (KO)

Require homologous recombination

OPTIMIZING YIELD THROUGH HIGHEST GENE EDITING EFFICIENCY

High Knock-Out and Knock-In efficiency and specificity

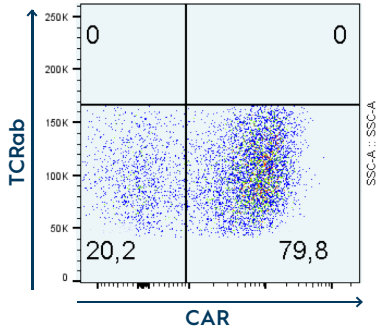


95.2% single targeted gene Knock-Out

→ TRAC Knock-Out

→ High Specificity

→ Prevents GvHD



~80% single gene integration

→ CAR Knock-In at TRAC Locus

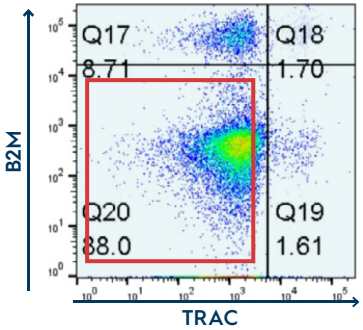
→ High specificity

→ Enables efficiency

Enables efficiency & protection from GvHD

POWER OF TALEN® GENE EDITING: MULTIPLEXING GENE REPLACEMENT

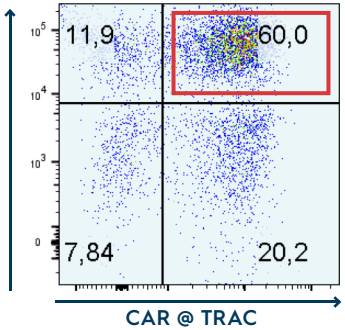
Multiple advantages from combined Knock-Out, Knock-In



88% double targeted gene Knock-Out

→ TCR and B2M

→ B2M Knock-Out exposes cells to potential killing by NK cells – which is prevented as shown



60% double targeted gene insertion

→ CAR insertion at TCR

→ NK inhibitor at B2M

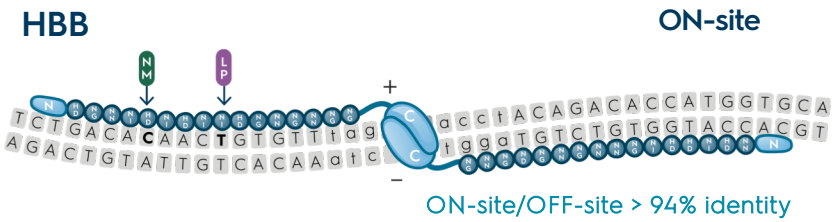
→ Provides protection from NK cell-mediated rejection

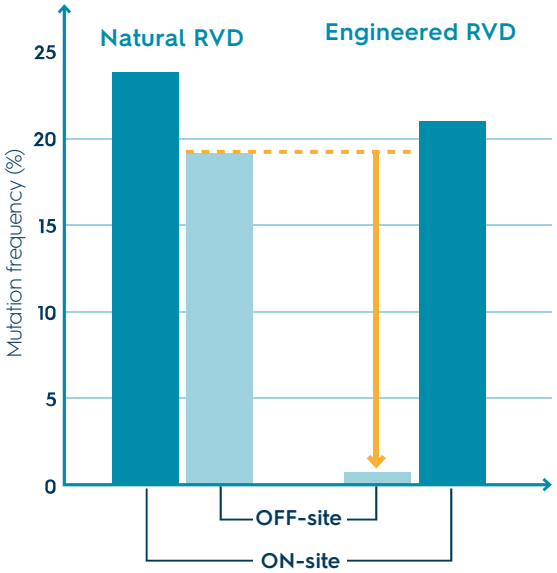
Provides protection from GvHD and avoids rejection

WITH TALEN® WE CONTROL OFF-TARGET CLEAVAGE

Discrimination between ON and OFF-site prevents OFF-site cleavage

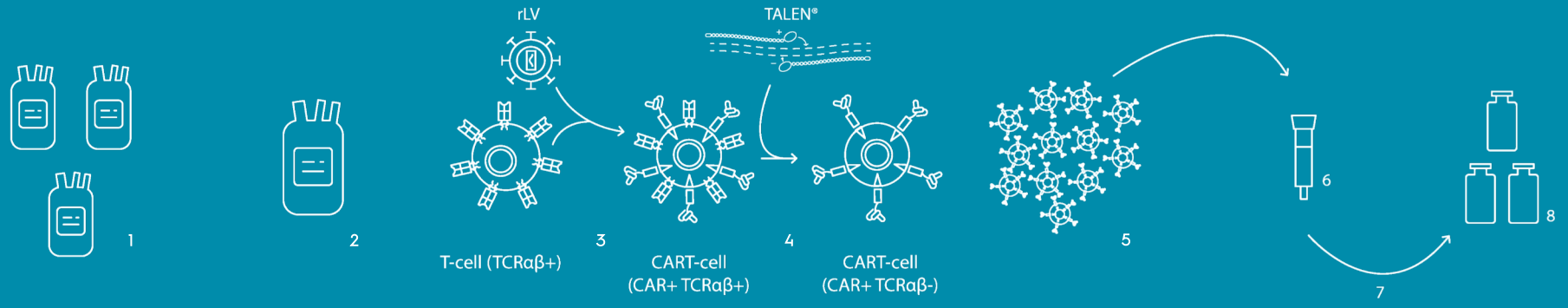
Utilization of engineered RVDs to discriminate HBB* and HBD** loci
preventing unwanted OFF-site cleavage





* HBB - Hemoglobin subunit beta
** HBD - Hemoglobin subunit delta

UCART MANUFACTURING



1. Frozen leukopaks
2. Thawed PBMCs
3. Lentivector transduction
4. TALEN®-mediated gene editing
5. Cell amplification
6. Purification
7. Fill & Finish
8. Frozen UCART products

- More than 5 years of experience in allogeneic CAR T manufacturing
- Validated gene editing technology for cell manufacturing
- 5 UCART product candidates manufactured so far
- Full QC system in place, 3 wholly-controlled product candidates cleared for 4 clinical trials by the U.S. Food and Drug Administration

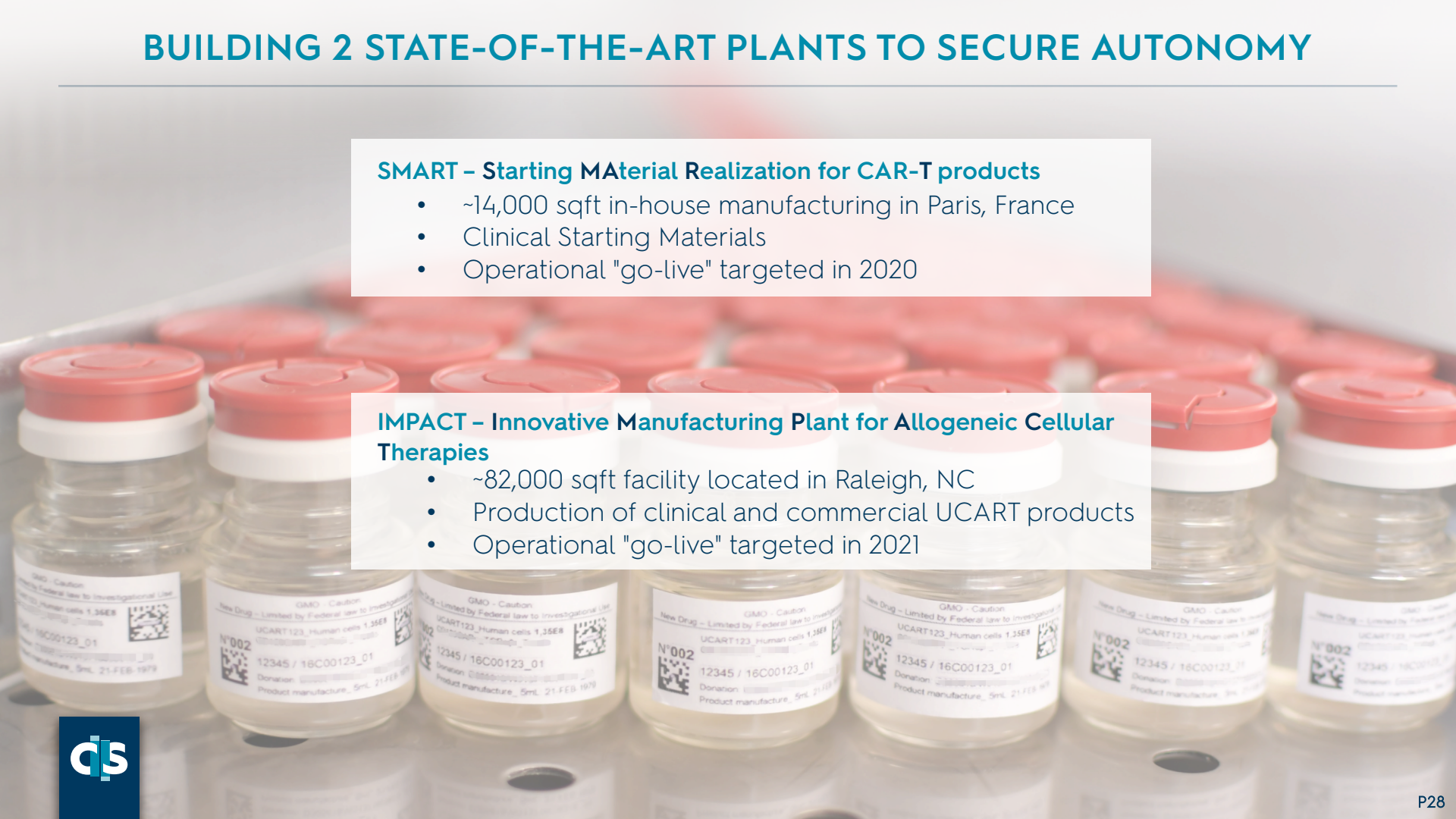
BUILDING 2 STATE-OF-THE-ART PLANTS TO SECURE AUTONOMY

SMART – Starting MAterial Realization for CAR-T products

- ~14,000 sqft in-house manufacturing in Paris, France
- Clinical Starting Materials
- Operational "go-live" targeted in 2020

IMPACT – Innovative Manufacturing Plant for Allogeneic Cellular Therapies

- ~82,000 sqft facility located in Raleigh, NC
- Production of clinical and commercial UCART products
- Operational "go-live" targeted in 2021



ANTICIPATED 12-MONTH MILESTONES

12 months

Clinical programs:

UCART19*: Phase 1 updates in R/R ALL in 2019

UCART123: Phase 1 for R/R AML
Expansion phase expected in 2020

UCART22: Expect Phase 1 first patient dosing in R/R ALL in 2019

UCARTCS1: Expect Phase 1 first patient dosing in R/R MM in 2019

ALLO**501*** : Expect Phase 1 first patient dosing in R/R NHL in 2019

ALLO715 : Expect IND in 2019**

Manufacturing:

Focusing on refinements to improve efficiency and capacity to support future commercial launch of **UCART** products

Internalizing large parts of our proprietary manufacturing chain for clinical starting material:
SMART plant in Paris, France

Building a proprietary GMP, commercial scale manufacturing facility in 2019:
IMPACT plant in Raleigh, North Carolina

Gene editing:

Explore applications into new areas: solid tumors and outside oncology space

* UCART19/ALLO-501 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene.
** Product candidates exclusively licensed to Allogene

CELLECTIS HIGHLIGHTS

INDUSTRY LEADER IN GENE EDITING & ALLOGENEIC CAR T (UCART) TECHNOLOGY

- → First clinical proof-of-concept: **UCART19** treated the first pediatric ALL patient in June 2015
- → Innovative gene editing (TALEN®) platform: to generate best-in-class allogeneic CAR T-cells
- → Bringing innovative off-the-shelf therapies to a broader market, without treatment delays

BEST-IN-CLASS MANUFACTURING

- → Scalable, efficient, greater consistency and potency
- → Two facilities being built to ensure manufacturing autonomy

PARTNERSHIPS WITH LEADERS: UP TO $3.9B IN POTENTIAL MILESTONES PLUS ROYALTIES

- → **UCART19** – Licensed to Servier (U.S. rights to Allogene) and other undisclosed targets
- → 15 licensed targets to Allogene and other licensed targets to Servier

ROBUST PROPRIETARY PIPELINE

- → **UCART123** – Phase 1 AML ongoing; dose escalation in AML in 2019; *wholly- controlled asset*
- → **UCART22** – Phase 1 first dosing in ALL in 2019; *wholly-controlled asset*
- → **UCARTCS1** – Phase 1 first dosing MM in 2019; *wholly-controlled asset*
- → **UCARTCLL1** – Preclinical development for AML; *wholly-controlled asset*

FINANCIAL POSITION:

- → Cash trough 2021
- → ~69.5% ownership of CLXT*

* As of December 31, 2018

THE CELLECTIS GROUP

cellectis
EDITING LIFE

~69.5%* ownership

calyxt™

- → NASDAQ: CLLS
- → EURONEXT GROWTH: ALCLS
- → $452M** cash as of December 31, 2018
- → Expected to fund operations through 2021
- → Based in Paris, France & New York, USA
- → Patient focused

- → NASDAQ: CLXT
- → $95M cash as of December 31, 2018
- → Based in Minnesota, USA
- → Consumer focused
- → High value asset

Gene editing is the link

* As of December 31, 2018
** Including $95M of cash, cash equivalents and current financial assets from Calyxt for plant activities

THANK YOU

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