

# **Commitment to a Cure**

**Corporate Presentation** 

September 2022

NASDAQ: CLLS

**EURONEXT GROWTH: ALCLS.PA** 



## **Forward-Looking Statements**

This presentation contains "forward-looking" statements within the meaning of applicable securities laws, including the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by words such as "designed to", "anticipate," "expected," "on track," "plan," "scheduled," and "will," or the negative of these and similar expressions.

These forward-looking statements, which are based on our management's current expectations and assumptions and on information currently available to management, including information provided or otherwise publicly reported by our licensed partners. Forward-looking statements about advancement, timing and progress of clinical trials (including with respect to patient enrollment and follow-up), the timing of our presentation of data and submission of regulatory filings, the adequacy of our supply of clinical vials, the operational capabilities at our manufacturing facilities, and the sufficiency of cash to fund operations.

These forward-looking statements are made in light of information currently available to us and are subject to numerous risks and uncertainties, including with respect to the numerous risks associated with biopharmaceutical product candidate development as well as the duration and severity of the COVID-19 pandemic and governmental and regulatory measures implemented in response to the evolving situation.

With respect to our cash runway, our operating plans, including product development plans, may change as a result of various factors, including factors currently unknown to us. Furthermore, many other important factors, including those described in our Annual Report on Form 20-F and the financial report (including the management report) for the year ended December 31, 2021 and subsequent filings Cellectis makes with the Securities Exchange Commission from time to time, as well as other known and unknown risks and uncertainties may adversely affect such forward-looking statements and cause our actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.



## Cellectis at a Glance



**Ongoing Clinical Trials** 

40+ patients dosed in Cellectis-sponsored trials



#### **Global GMP Facilities**

- Operational since mid-2021
- End-to-end manufacturing autonomy



## **Near-Term Clinical** Catalysts

UCART clinical data updates



## **Diversified Partnerships with Industry Leaders**



~200+ patients dosed to date

- Revenues > \$4B in milestones + royalties
- trials sponsored by Cellectis' licensed partners











## **UCARTs** are "Off-The-Shelf"

# Scalable Manufacturing



Reduced cost
Scalable manufacturing:
1 batch = 100s doses

## **Robustness**



The goal is to provide potency and consistency to each patient

## **Market Access**



Immediately available to all eligible patients

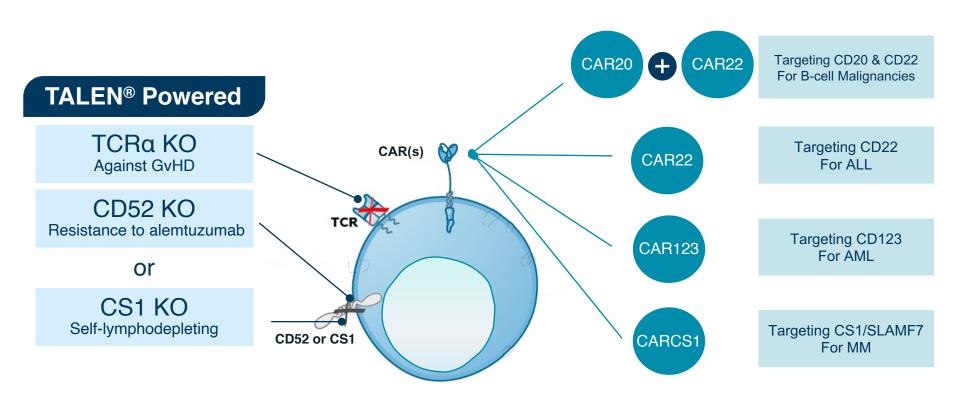
Control Production & Costs for Patients Safety and Profitability



# **Experts in Gene-Editing Use TALEN®**

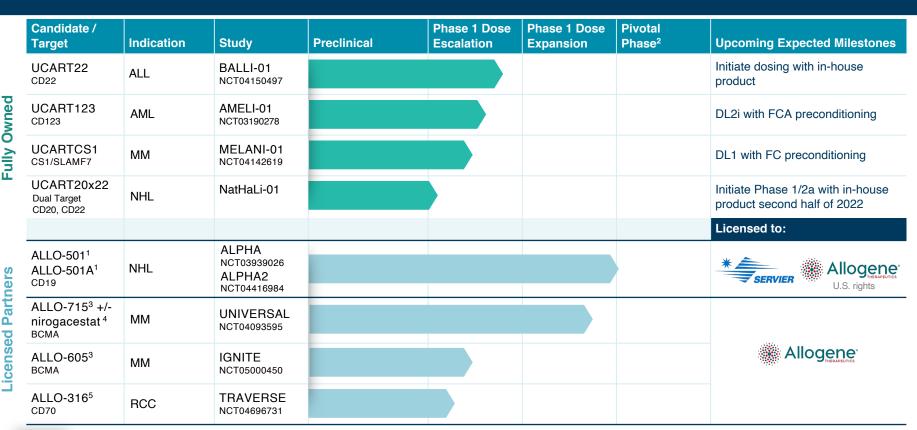


## **Cellectis' UCART Candidate Platform**





## **Differentiated Targets & Near-Term Catalysts**



ALL, Acute Lymphoblastic Leukemia; AML, Acute Myeloid Leukemia; MM, Multiple Myeloma; NHL, Non-Hodgkin's Lymphoma; RCC, Renal Cell Carcinoma.

1 ALLO-501 and ALLO-501A are exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene. The ALPHA and ALPHA2 studies targets Diffuse Large B-Cell Lymphoma (DLBCL) and Follicular Lymphoma (FL) indications, which are subtypes of NHL. 2 Phase 3 may not be required if Phase 2 is registrational.

<sup>3</sup> ALLO-715 and ALLO-605 target BCMA which is a licensed target from Cellectis, ALLO-715 and ALLO-605 utilize TALEN® gene-editing technology pioneered and owned by Cellectis, Allogene has an exclusive license to the Cellectis technology for allogeneic products directed at the BCMA target. Allogene holds global development and commercial rights for this investigational candidate.

<sup>4</sup> Allogene sponsored trial in combination with Spring/Norks Therapeutics 5 ALLO-316 targets CD70 which is a licensed target from Cellectis. ALLO-316 targets CD70 which is a licensed target from Cellectis. ALLO-316 targets CD70 which is a licensed target from Cellectis. ALLO-316 targets CD70 which is a licensed target from Cellectis. ALLO-316 targets. Allogene holds global development and commercial rights for this investigational candidate.

# Cellectis' UCART Platform



# UCART22 – BALLI-01 Trial Design

Phase I/IIa, Open Label Dose-escalation and Dose-expansion Study to Evaluate the Safety, Expansion, Persistence and Clinical Activity of UCART22 in Patients with Relapsed or Refractory CD22+ B-cell Acute Lymphoblastic Leukemia

#### **Dose Escalation**

Determine MTD and/or RP2D

Dose Expansion LD regimen: FC or FCA

Up to 30 pts; mTPI design; 2-4 pts/cohort

Up to 53 pts; binomial exact study design; LD regimen: FC or FCA

#### **Objectives**

#### **Primary/Secondary:**

- Safety and tolerability
- MTD/RP2D
- Response (NCCN criteria; investigator assessed)

#### **Exploratory**

- UCART22 expansion and persistence,
   VCN and chimerism in WB and BM
- Immune reconstitution

### Key Eligibility Criteria

- Patients aged 15 years to 70 years
- Adequate organ function
- ECOG PS ≤1
- B-ALL blast CD22 expression ≥70%
- Received ≥1 standard chemotherapy regimen and ≥1 salvage regimen

#### Dose Levels

DL-1 1 ×10<sup>4</sup> cells/kg

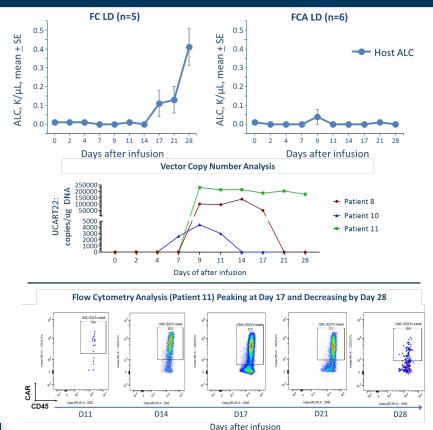
- DL1 1 ×10<sup>5</sup> cells/kg
- DL2 1 x10<sup>6</sup> cells/kg
- DL3 5 x10<sup>6</sup> cells/kg

F: 30 mg/m2/d x4d; C: 1 g/m2/d x3 d; F: 30 mg/m2/d x3 d; C: 500 mg/m2/d x3

d A: 20 mg x3d



# **Promising Anti-Leukemic Activity with UCART22**



- Host lymphocytes on average remained suppressed
- 2/6 patients achieved blast reductions to < 5% by day 28</li>
  - 1 pt in DL2: 0.4% BM blast
  - 1 pt in DL2i: 0% BM blast
- FCA demonstrates improved lymphodepletion and UCART22 expansion with encouraging anti-leukemic activity



FC: Fludarabine + Cyclophosphamide; FCA: Fludarabine + Cyclophosphamide + Alemtuzumab;

LD: Lymphodepletion; DL2: Dose Level 2; DL2i: Intermediate Dose Level 2

# **UCART22 Administration Shows Promising Tolerable Safety Profile**

## Patient Characteristics (N=12)

**Median age:** 30 (20-61)

#### WHO classification:

 B-ALL with recurrent genetic abnormalities: 7 (58%);

• CRFL2 rearrangement: 4 (33%)

## **Median prior lines of therapy:** 3 (2-6)

• Prior blinatumomab: 8 (73%)

• Prior inotuzumab: 5 (45%)

Prior CD19 CART: 3 (27%)

## Safety: FCA Cohorts (N=6)

- 0 dose limiting toxicity
- **0** ICANS (immune effector cell associated neurotoxicity)
- severe UCART22-related TEAEs (treatment emergent adverse events)
- 3 patients with mild to moderate CRS (cytokine release syndrome)
- 1 patient with GII GvHD; skin only\*

\*not confirmed by biopsy; in context of re-activation of prior allogeneic bone marrow donor



## UCART123 – AMELI-01 Trial Design

Phase I, Open Label Dose-escalation and Dose-expansion Study to Evaluate the Safety, Expansion, Persistence and Clinical Activity of UCART123 in Patients with Relapsed or Refractory Acute Myeloid Leukemia

#### **Dose Escalation**

Determine MTD and/or RP2D

### Dose Expansion

Up to 28 pts; mTPI design; 2-4 pts/cohort

18-37 pts; Simon's two-stage design

#### Objectives

#### **Primary/Secondary:**

- Safety and tolerability
- Establish MTD and identify RP2D
- Efficacy

#### **Exploratory**

- UCART123 expansion, trafficking, and persistence
- Profile cytokine, chemokine, growth factor, and C-reactive protein levels post-infusion

### Key Eligibility Criteria

- Patients with relapsed or primary refractory AML (>5% bone marrow blasts)
- Patients with CD123+ blast cells
- PS of ≤1 and adequate organ function
- Identified donor and transplant strategy prior to LD (dose-escalation)

#### Dose Levels

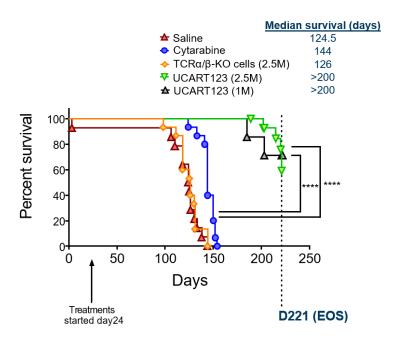
- DL-1 1.25×10<sup>5</sup> cells/kg
- DL1 2.5×10<sup>5</sup> cells/kg
- DL2 6.25×10<sup>5</sup> cells/kg
- DL3 3.30×10<sup>6</sup> cells/kg
- DL4  $5.05\times10^6$  cells/kg

F: 30 mg/m2/d x 4d; C: 750 g/m2/d x 3d;

F: 30 mg/m2/d x 4d; C: 750 g/m2/d x 3d; A: 12 mg/d x4d

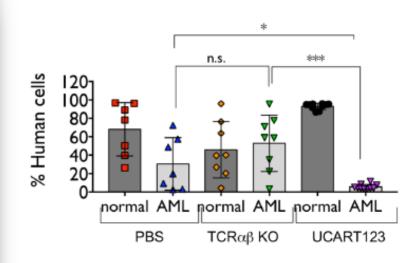


# UCART123 Effectively Eliminates AML with no Major Impact on Normal Hematopoietic Progenitor Cells in AML PDX Model



UCART123 led to increased survival compared to standard AML treatment and controls

#### Bone Marrow evaluation at sacrifice



Leukemic cells are selectively eliminated by UCART123, while most of the normal BM human cells (expressing lower levels of CD123) are spared



# UCARTCS1 - MELANI-01 Study Schema

Phase I, Open Label Dose-Escalation Study to Evaluate the Safety, Expansion, Persistence and Clinical Activity of UCARTCS1, Administered in Patients with Relapsed or Refractory Multiple Myeloma



#### Objectives

#### **Primary/Secondary:**

- Safety and tolerability
- MTD and Efficacy

#### **Exploratory**

- CS1 expression on MM cells
- UCARTCS1 expansion and persistence
- Changes in serum biomarkers; immune cell reconstitution

### Key Eligibility Criteria

- Patients with confirmed MM (IMWG criteria) relapsed after prior MM therapy
- ECOG PS <2</li>
- No prior investigational drug or CAR therapy targeting CS1
- Adequate organ function

Dose	Levels

•	DL-1	3 ×10 <sup>5</sup> cells/kg
•	DL-I	3 × 10° CEIIS/KG

DL1 1 ×10<sup>6</sup> cells/kg

DL2 3 ×10<sup>6</sup> cells/kg

DL3  $9 \times 10^6$  cells/kg

F: 30 mg/m2/d x 4d; C: 1 g/m2/d x3 d

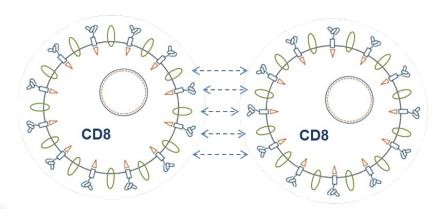


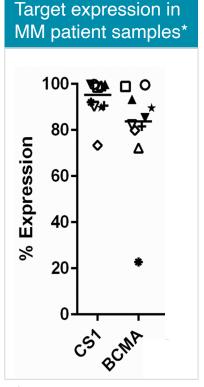
NCT04142619

\*Lymphodepletion: Fludarabine 30mg/m2/day, Day -5 to -2; Cyclophosphamide 1g/m²/day, Day -4 to -2; F: Fludarabine; C: Cyclophosphamide;

# CS1 Is a Relevant Therapeutic Target in Multiple Myeloma

- CS1 (CD319, SLAMF7)
  - Highly and consistently expressed in MM cells
  - Not expressed in normal tissues or stem cells
- CS1 is expressed on CD8+ T-cells
  - TALEN®-mediated CS1 inactivation prevents cross
     T-cell reactivity and facilitates CAR T-cell production

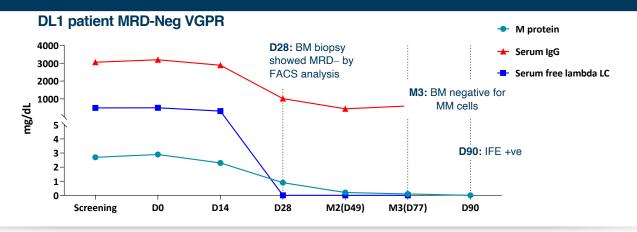


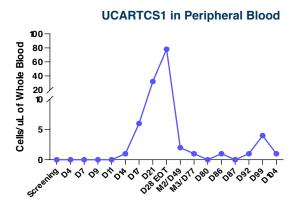


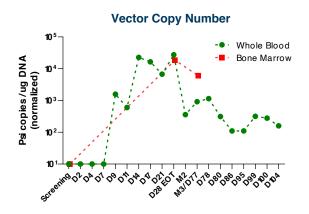
\***ASH 2017** Rohit Mathur, Sattva Neelapu



# Preliminary Data Validate CS1 as a Target for CAR T in Multiple Myeloma







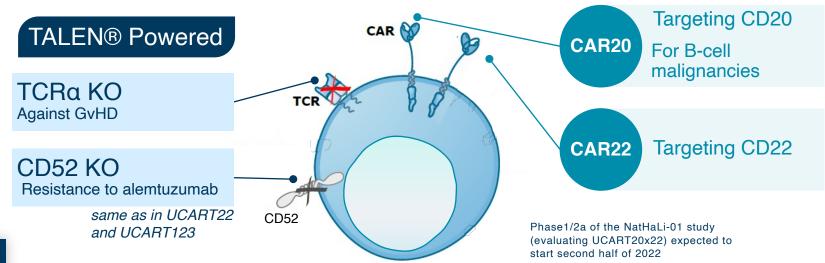


16

# UCART20x22: Overcoming CAR T Challenges with Next Generation Dual Antigen Target

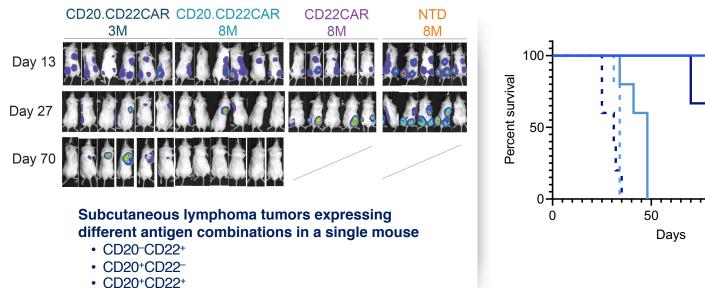
## UCART20x22

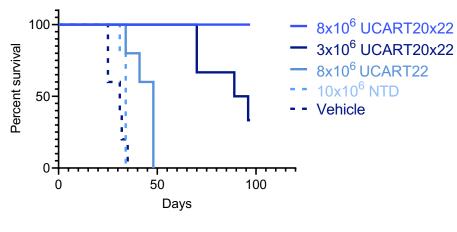
- Strong alternative to CD19 (highly competitive/crowded)
- CD22 and CD20 are validated targets in B-cell malignancies
- Dual targeting designed for better killing & prevent escape
- Strong in vitro and in vivo preclinical results & fast to develop





# UCART20x22 – Efficient Activity *in vivo* Against Multiple Target Combinations



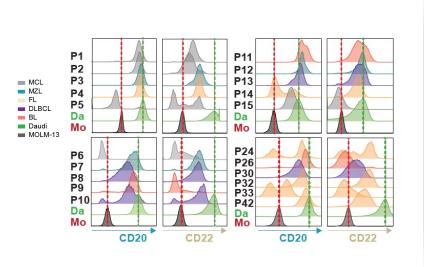


UCART20x22 efficiently eradicates *in vivo tumors expressing different CD20/CD22 antigen combinations* in a dose dependent manner

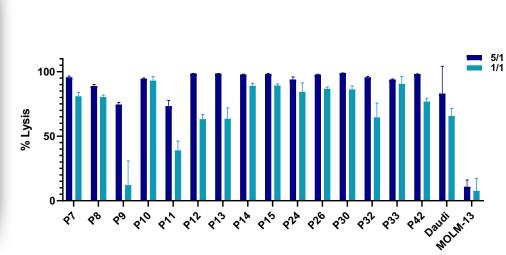


# **Efficient B-NHL Primary Sample Targeting with UCART20x22**

Primary B-NHL tumors express CD20 and CD22



#### Cytotox activity against B-NHL samples



## **UCART20x22** efficiently targets primary B-NHL cells



# **UCART Platform Takeaways from ~200 Patients\***

**GvHD** 

TCRα KO results in safe, non-alloreactive UCART

**Engraftment** 

CD52 KO + alemtuzumab provides a safe, effective & controllable therapeutic window

**Persistence** 

Redosing feasible; encouraging pre-clinical activity in NHL and ALL

Safety

Profile on par with approved autologous CAR T therapies

**Efficacy** 

Anti-tumor activity consistent with autologous products



## **Expected Milestones over the Next 12 Months**

## UCART22 r/r B-ALL

Start dosing with inhouse manufactured products

Determine RP2D and lymphodepletion

## UCART123 r/r AML

Enroll at DL2i with FCA preconditioning

Determine RP2D and lymphodepletion

## UCARTCS1 r/r MM

Enroll DL1 with FC preconditioning

Determine RP2D and lymphodepletion

## UCART20x22 r/r NHL

Initiate Phase 1/2a with in-house products second half of 2022

**Additional** 

Updates from licensed partners (Allogene, Iovance and Cytovia)



# Discover, Create, Develop, Produce and Test







New York, New York

Innovation, Clinical Development

25,000 sq ft. facility

- Gene Editing platform TALEN®
- √ I/O discovery platform
- Gene therapy discovery platform
- ✓ Clinical development



Paris, France

HQ, PD/AD, Starting Materials

55,000 sq ft. facility

- ✓ Process & analytical development
- Raw materials manufacturing
- ✓ QC labs
- ✓ Warehouse
- ✓ Cryogenic Storage rooms



Raleigh, North Carolina

UCART – Clinical & potential for Commercial

82,000 sq ft. facility

- ✓ Cell therapy GMP manufacturing
- ✓ QC labs
- ✓ Warehouse
- ✓ Cryogenic Storage rooms



# **Key Takeaways – Why Cellectis?**



Innovative
Allogeneic CAR T

Breaking Paradigms with Life-Saving Therapies



End-to-end In-house Manufacturing

Owning Manufacturing is Owning the Product



Best-In-Class Gene Editing Platform

Safe, Precise & Efficient, Backed by Strong IP



**Strong Partnerships** 

Anticipated Milestones, Diversified Financial Upsides



# **Thank You**

# Reach us at: investors@cellectis.com

#### **Cellectis Paris**

8, rue de la Croix Jarry 75013 Paris – France



#### **Cellectis New York**

430 East 29th Street New York, NY, 10016 – USA



### **Cellectis Raleigh**

2500 Sumner Boulevard Raleigh, NC, 27616 – USA

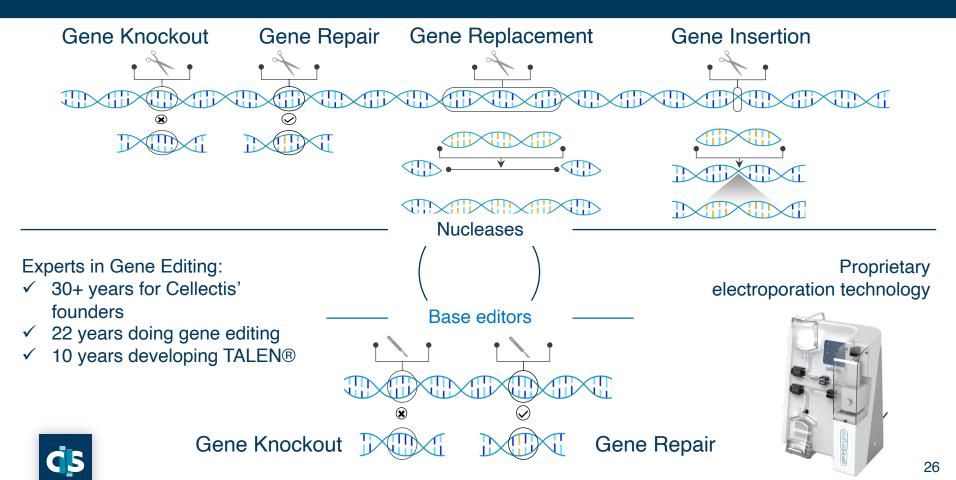




# Appendix



# **Powerful and Comprehensive Gene Editing Platform**



# Why TALEN®?

	Maturity	Genome Outreach	Recognition Site # base pairs	Chromotrypsis	Precision	Vectorization	IP •
TALEN®	In clinic since 2015	Euchromatin & heterochromatin	32	Not reported	Every 7 base pairs	mRNA	Strong for CLLS
CRISPR	In clinic since 2018	Euchromatin only	~20	Yes	Every 64 base pairs	RNP	Scatter ed



## **Diversified Partnerships with Industry Leaders**



Exclusive worldwide license to CD19directed allogeneic CAR T-cells

CAR T CD19 Up to \$410M In Development & Sales Milestones

2015<sup>1</sup> Allogene

U.S. rights sublicensed to Allogene by Servier

+ Low Double-Digit Royalties on Sales

2014<sup>1</sup>



Exclusive worldwide license to 15 allogeneic CAR T-cell targets

CAR T BCMA CD70

Up to \$2.8B In Development & Sales

Milestones

+ High Single-Digit Royalties on Sales

2020



Research collaboration and exclusive worldwide license agreement to develop gene-edited TILs

**TILs** 

**Undisclosed Financials** 

202



Worldwide research collaboration and license agreement to develop gene-edited iPSC-derived NK and CAR-NK cells

iPSCderived NK

\$20M Upfront Convertible Note Up to \$805M in Development & Sales Milestones + Single-Digit Royalties on Sales

