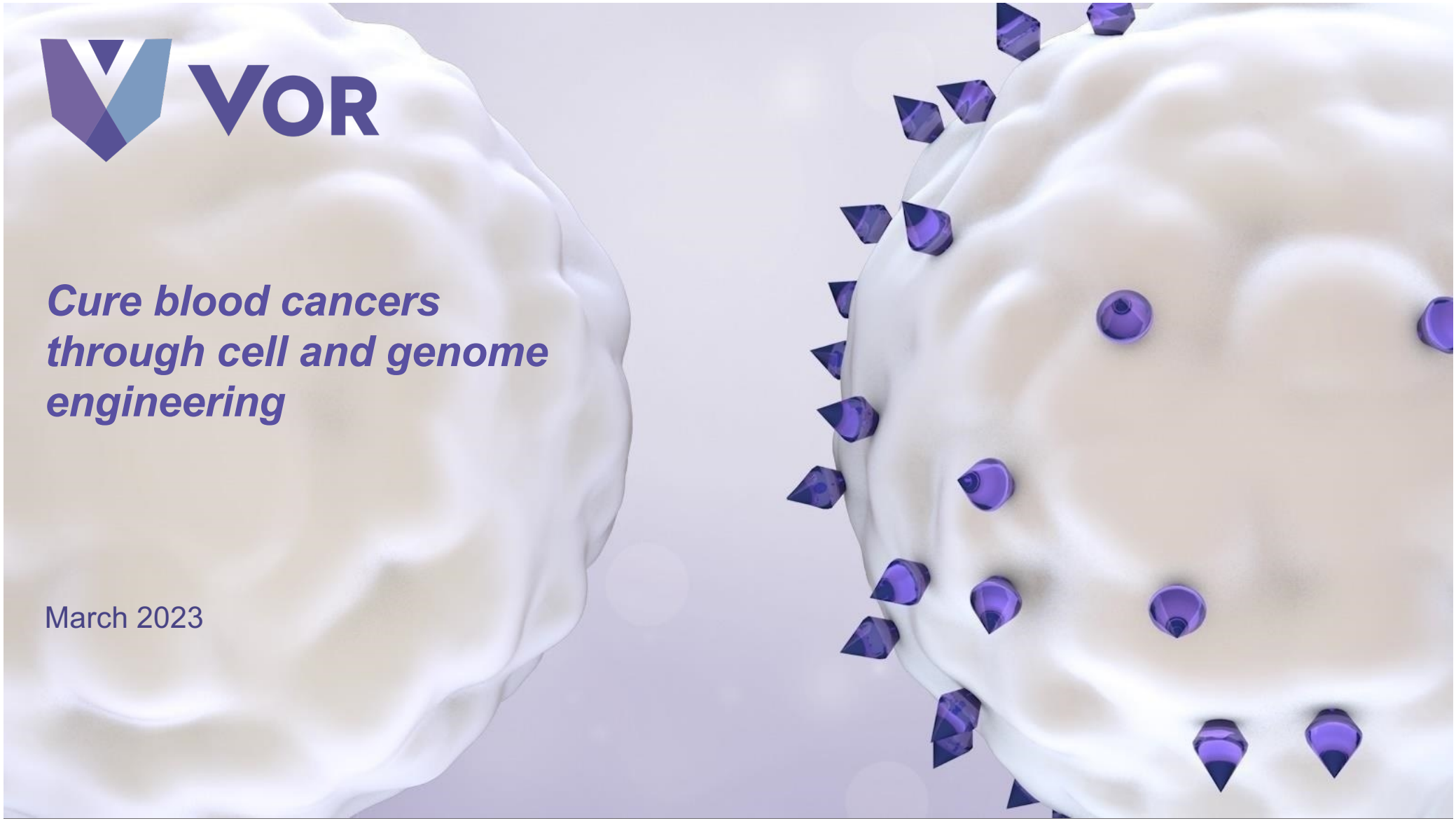
VOR

# *Cure blood cancers through cell and genome engineering*

March 2023



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# Vor's Vision: Cure Blood Cancers Through Cell & Genome Engineering

**Unique approach**
of protected eHSC transplants enabling post-transplant targeted therapy

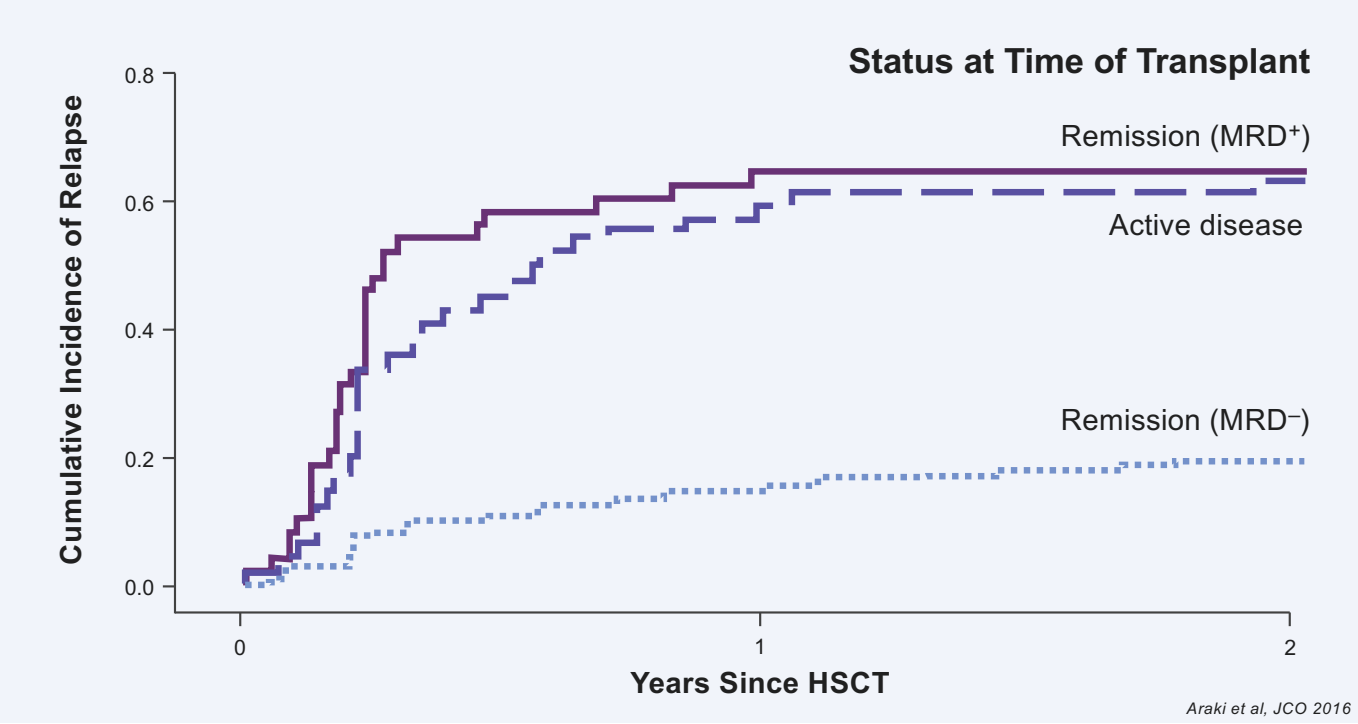
**Clinical proof of concept**
demonstrated of trem-cel eHSC in first two patients with AML

**VCAR33$^{ALLO}$**
IND filing expected
**1H 2023**

Fully integrated in-house
**GMP manufacturing capability**

**$230M**
in cash and cash equivalents as of
**Dec 31, 2022**

# Relapse is the #1 Issue With Transplant



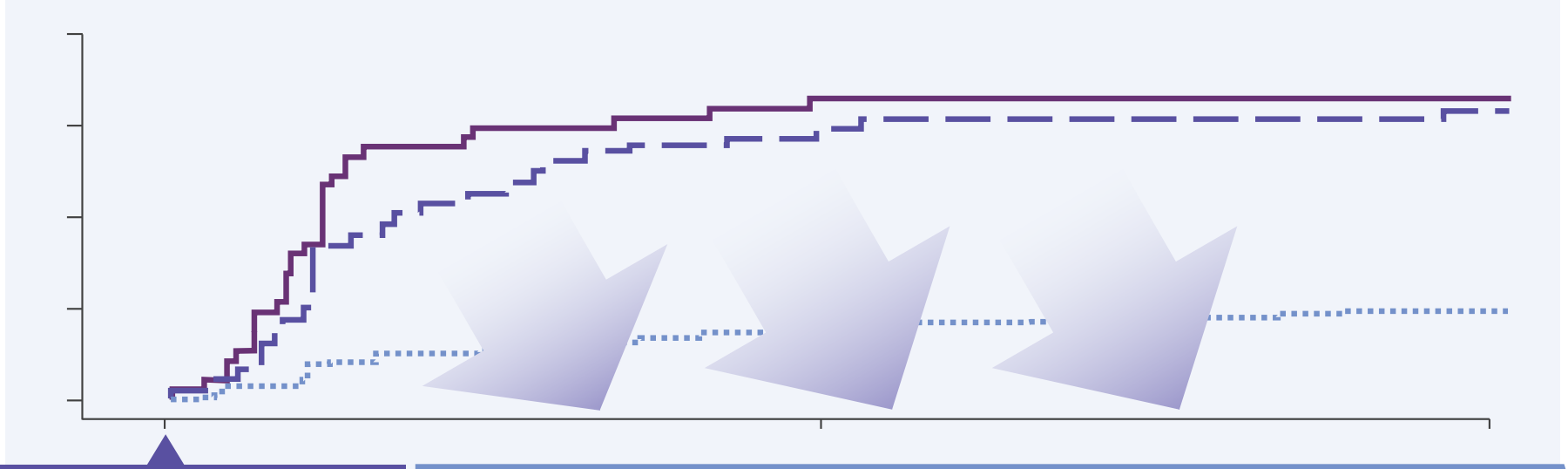

*Araki et al, JCO 2016*

**For relapsed patients, 2-year survival is <20%**

*Schmid et al, Blood 2012*

**Standard of care is watchful waiting since treatment will damage the transplant**

# Protected Transplants Could Change Relapse Outcomes



**Opportunity:**

**Protected transplants resistant to therapy**

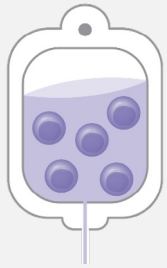
**Post-transplant targeted therapy**

**Prevent relapse (prophylaxis)**

**Treat relapse (therapeutic)**

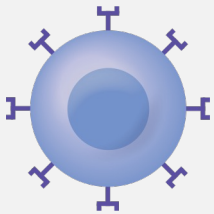
# Vor Bio's Platform Establishing Next-Generation Treatments

| Platform Elements | Purpose |
| --- | --- |
| **Target Discovery** | Identify antigens to transform into cancer-specific therapeutic targets |
| **Genome Engineering** | Permanently build in treatment resistance |
| **Cell Biology** | Develop state-of-art HSC and CAR-T processes, analysis and GMP production |



**Protected eHSC Transplants**

Designed to replace standard of care allogeneic transplants



**Healthy Donor-Derived CAR-T**

Potent and persistent post-transplant targeted therapy

# The Vision: eHSC + CAR-T Treatment Systems

**Trem-cel**

Treatment-resistant HSC transplant

+

**Mylotarg**

1st generation antibody-drug conjugate

**Clinical proof of concept**

- Engraftment
- Heme protection

**Trem-cel**

Treatment-resistant HSC transplant

+

**VCAR33**

CD33-directed CAR-T programs

**VCAR33ALLO**

- Healthy donor source, stemlike phenotype
- Tolerized to new marrow

**VCAR33AUTO**

- In Phase 1/2 NMDP-sponsored trial

**Multiplex-edited HSCs**

Multi-treatment-resistant HSC transplant

+

**Multi-specific CAR-Ts**

Abound Bio collaboration

**Addresses tumor heterogeneity and potential escape mechanisms**



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# Expanding Pipeline Driven by Innovative Platform

| Description | | | Preclinical | | Clinical | | Anticipated Milestones |
|---|---|---|---|---|---|---|---|
| **Program** | **Modality** | **Indication** | **Discovery/ Validation** | **IND-Enabling** | **Phase 1/2** | **Phase 2/3** | |
| **Trem-cel + Mylotarg** | **eHSC + ADC** | AML | | | | | Additional data updates by year-end 2023 |
| | | MDS, MPN | | | | | |
| **VCAR33$^{ALLO}$ (Allogeneic)** | **CAR-T** | AML Post-transplant | | | | | 1H 2023 IND submission |
| **VCAR33$^{AUTO}$ (Autologous)** | **CAR-T** | Bridge-to-transplant AML | NMDP-sponsored trial* | | | | |
| **Trem-cel + VCAR33 Treatment System** | **eHSC + CAR-T** | AML | | | | | IND filing following initial trem-cel and VCAR33$^{ALLO}$ data |
| **CD33-CLL1 Treatment System** | **Multiplex-edited eHSC + Multi-specific CAR-T** | AML | | | | | |

**Discovery Platform**

- Leveraging our proprietary Vor platform, we are exploring additional surface targets such as CD123, EMR2, and CD5 including multiplex genome engineering approaches where multiple surface targets are removed.
- We are conducting ongoing discovery efforts in commonly transplanted hematologic malignancies.

*AML: acute myeloid leukemia; MDS: myelodysplastic syndrome; MPN: myeloproliferative neoplasm*

** The VCAR33 construct is being studied in a Phase 1/2 clinical trial sponsored by the National Marrow Donor Program ("NMDP"), and the timing of data release is dependent on the investigators conducting the trial.*



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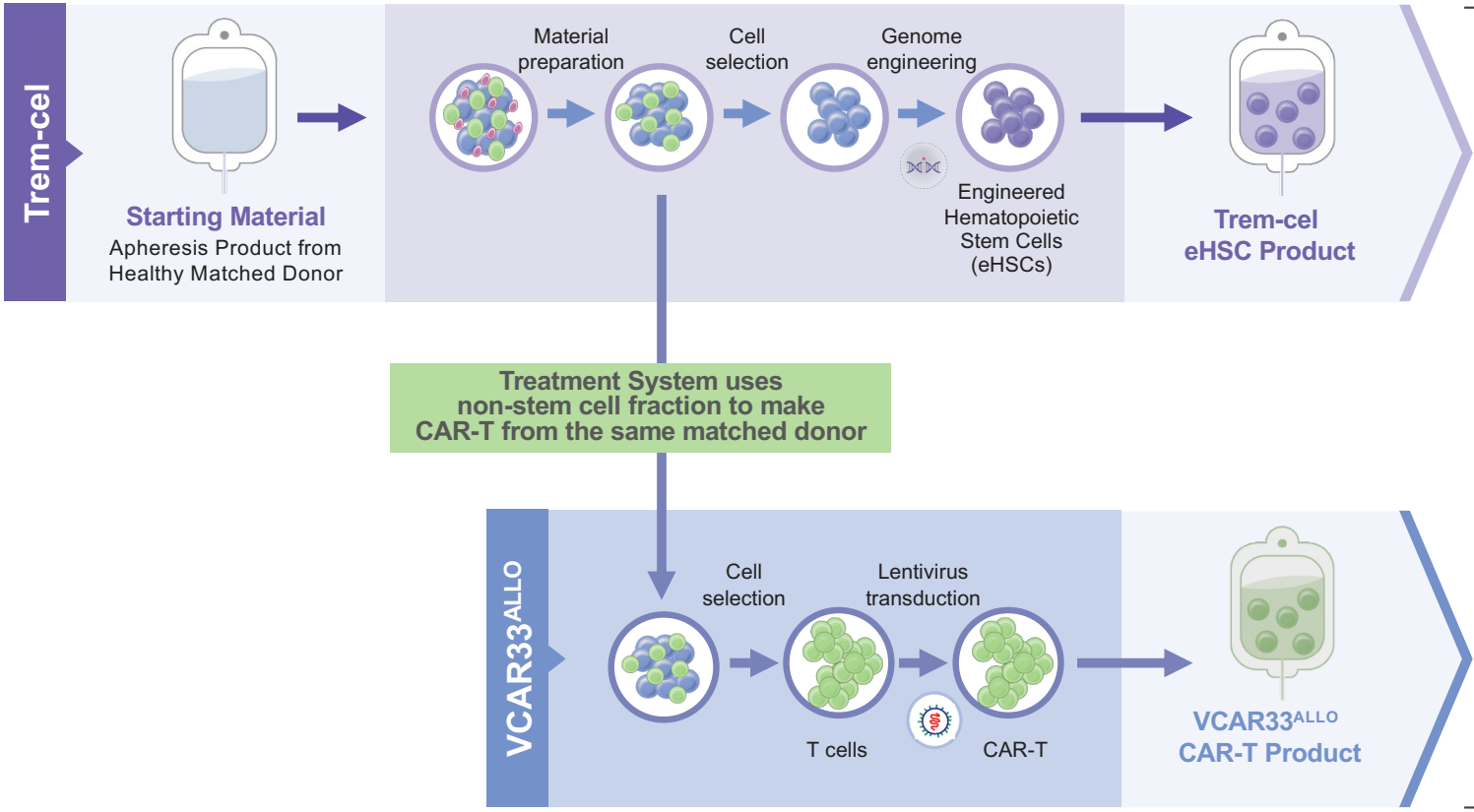
# Streamlined Cell Manufacturing Process




**State-of-the-art, multi-product GMP facility in Cambridge, MA**

**Four independent clean rooms and on-site QA/QC**

# Trem-cel (VOR33): CD33-Deleted eHSC

**Trem-cel**

Treatment-resistant
HSC transplant

+

**Mylotarg**

1st generation
antibody-drug conjugate

**Trem-cel**

Treatment-resistant
HSC transplant

+

**VCAR33**

CD33-directed
CAR-T programs

**Multiplex-edited HSCs**

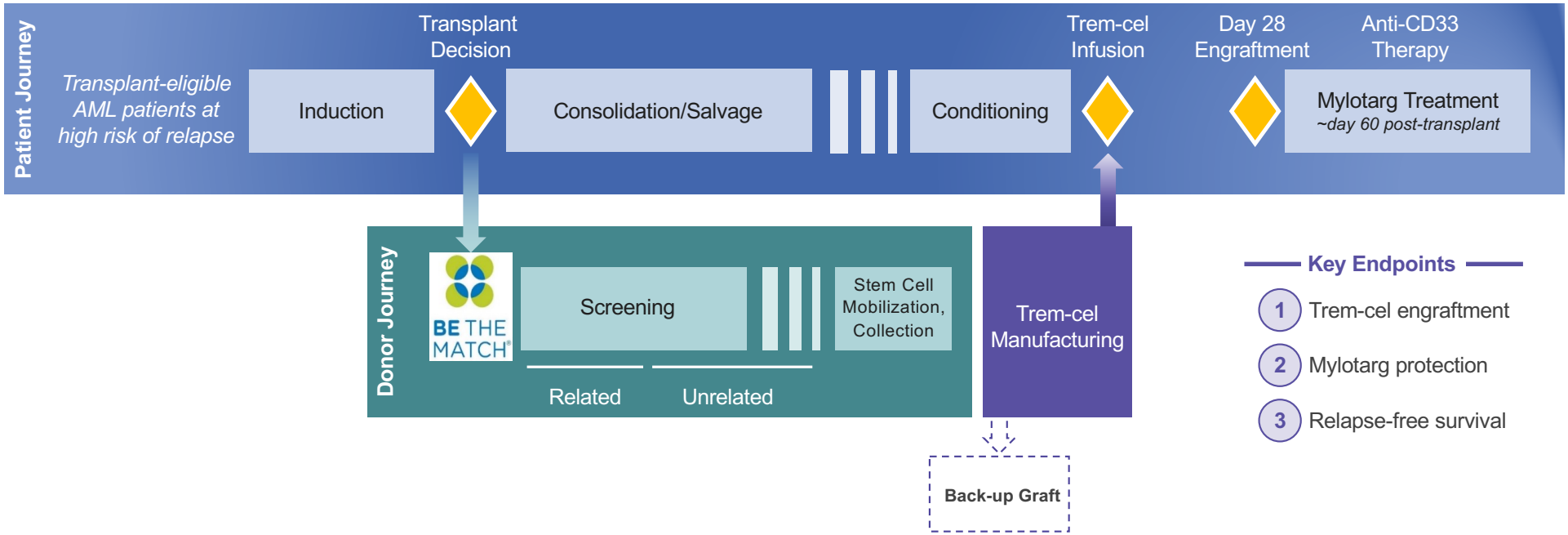
Multi-treatment-resistant
HSC transplant

+

**Multi-specific CAR-Ts**

Abound Bio collaboration

# VBP101: Trem-cel + Mylotarg Phase 1/2a Clinical Trial




**Key Endpoints**

1. Trem-cel engraftment
2. Mylotarg protection
3. Relapse-free survival

**Clinical Trial Sites**

- MSKCC (NY)
- Hackensack/Theurer Cancer Ctr. (NJ)
- Miami Cancer Inst. (FL)
- UC San Diego Cancer Ctr. (CA)
- CWRU/Seidman Cancer Ctr. (OH)
- Hôpital Maisonneuve-Rosemont (Montreal)
- The National Cancer Institute (MD)
- WashU Siteman Cancer Ctr. (MO)
- Fred Hutchinson Cancer Ctr. (WA)

# Patient 1 and 2 Characteristics and Trem-cel Drug Product

## Patient Characteristics

| CHARACTERISTIC | PATIENT 1 | PATIENT 2 |
|---|---|---|
| **Age** | **64** | **32** |
| **Prior Treatments/Relapse** | 2 cycles 7+3 chemo, achieved CR MRD+<br>3 cycles HiDAC<br>Relapsed<br>Salvaged w/ 2 cycles venetoclax and decitabine<br>1.8% MRD prior to transplant | 1 cycle 7+3 chemo, achieved CR MRD+ 1.8%<br>Achieved CR with persistent extramedullary abdominal disease by PET<br>3 cycles HiDAC |
| **Cytogenetics & Molecular** | Highly complex (adverse) cytogenetics<br><br>Mutant TP53, DNMT3A, KDM6A | Inv 16, +22. Subsequent additional t(3;3) (adverse)<br><br>Mutant CHEK2, MYH9, RAF1-TMEM40 fusion mRNA (t(3;3)) |

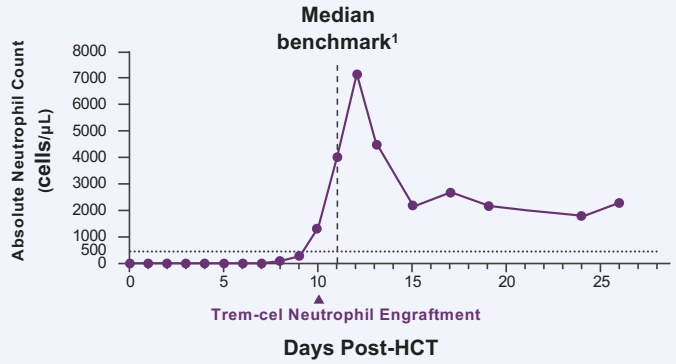
## Trem-cel Drug Product

| CHARACTERISTIC | RELEASE CRITERIA | PATIENT 1 | | PATIENT 2 | |
|---|---|---|---|---|---|
| **Product Dose** | ≥3 x $10^6$ cells/kg | 7.6 x $10^6$ cells/kg | ✓ | 3.2 x $10^6$ cells/kg | ✓ |
| **Gene Editing Efficiency** | ≥50% | 88% | ✓ | 87% | ✓ |

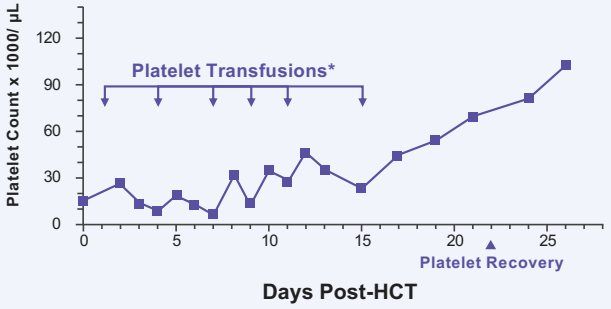
# Timely Neutrophil Engraftment and Platelet Recovery

## Patient 1

**Neutrophil engraftment**

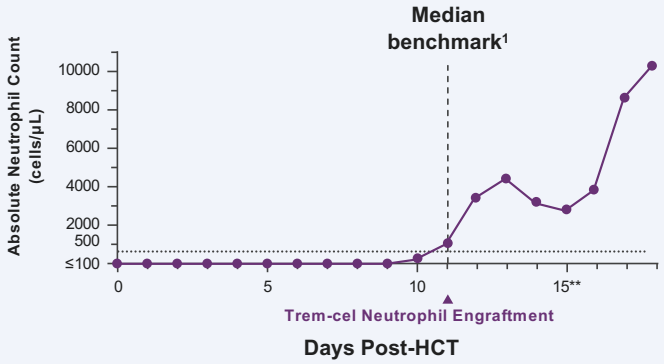



**Platelet recovery**

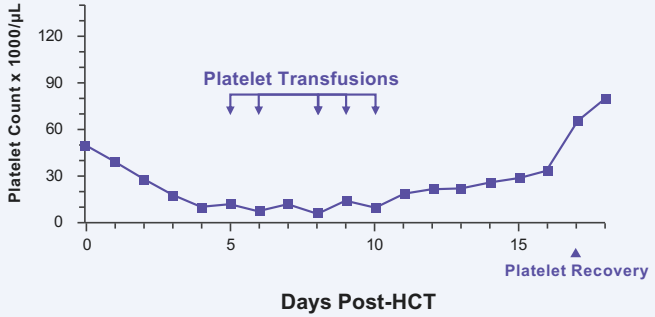



## Patient 2

**Neutrophil engraftment**




**Platelet recovery**




**Patient 1**

**Neutrophil engraftment:**
Day 10
**Platelet recovery:**
Day 22

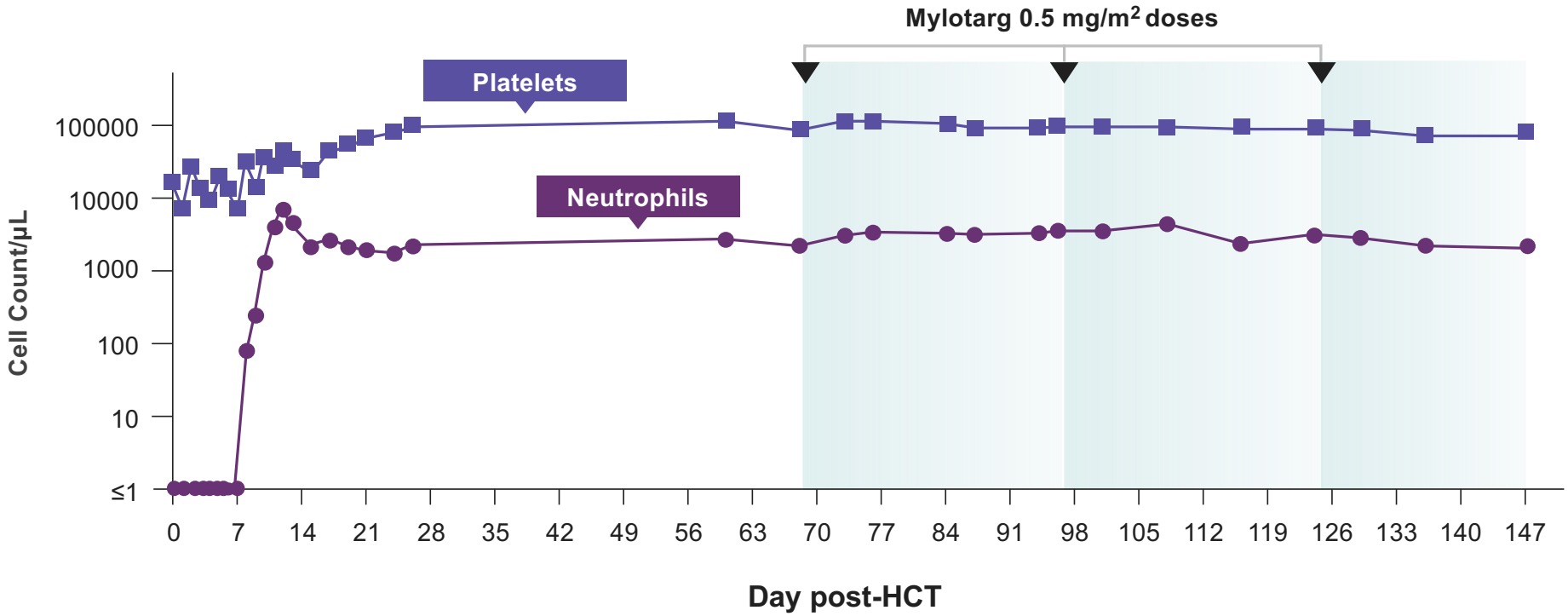
**Patient 2**

**Neutrophil engraftment:**
Day 11
**Platelet recovery:**
Day 17

*Elevated platelet transfusion threshold of 30K/µL used due to pre-existing hemorrhage risk in Patient 1; **Patient 2 received steroids on Days 15-18

**Reference:** [1]Unmodified CD34+ graft CTN1301 study, Luznik L. et al. J Clin Oncol 2022;40(4):356–368

# Patient 1: Neutrophil and Platelet Counts Maintained Following Three Sequential Mylotarg Doses



# No Atypical Adverse Events

| | Serious adverse events (SAEs) | Infectious AEs | Hepatic / Other AEs | Trem-cel-related AEs | Mylotarg Related AEs |
|---|---|---|---|---|---|
| **Patient 1** | Renal colic (Grade 3)<br>Resolved | Skin infection (Grade 1, 2)<br>CMV reactivation (Grade 2)<br>UTI (Grade 2)<br>BK virus in urine (Grade 2)<br>All resolved or resolving | AST/ALT elevations (Grade 1, 2) attributable to anti-fungal<br>Resolved<br><br>GvHD gut (Grade 2), responding to non-systemic steroids | None reported | Nausea (Grade 1) and vomiting (Grade 2), a known side-effect of Mylotarg |
| **Patient 2** | None reported through D18 | Febrile neutropenia (Grade 3)<br>E. coli bacteremia (Grade 3)<br>reported at D8 prior to engraftment<br>Resolved | Grade 1 engraftment syndrome | None reported | Mylotarg not yet administered |

# Patient 1: Mylotarg Treatment Enriches for Edited Donor Cells

| | Post-HCT Recovery | | Mylotarg 0.5 mg/m² started D68* |
|---|---|---|---|
| **Transplant Day** | **D28** | **D60** | **D100** |
| **Monocytes (CD14+ CD15+)** | | | |
| Donor Chimerism | 100% | 100% | 100% |
| *CD33* Gene Editing (Indels) | 95.0% | 95.6% | 99.7% |
| % CD33-Negative Cells by Flow | 95.3% | 96.0% | 99.9% |
| **T cells (CD3+)** | | | |
| Donor Chimerism | - | - | 97.0% |
| CD33 Gene Editing (Indels) | - | - | 100% of donor cells |



*Mylotarg (0.5 mg/m²) was administered at D68, D96, and D124

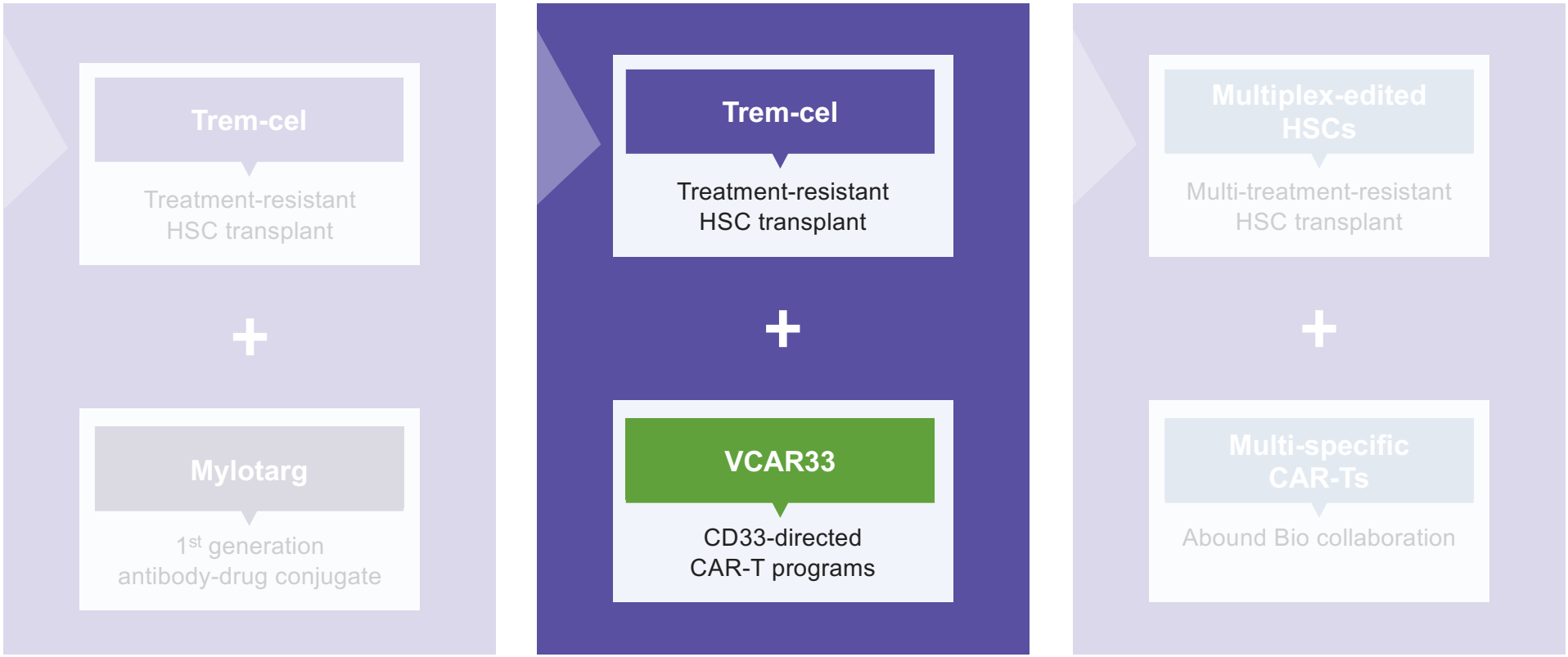
# PK of Mylotarg in Presence of Trem-cel Graft Demonstrates Higher PK than R/R AML patients with CD33

| | Patient 1 1st Dose | Relapsed/Refractory AML Population (Mylotarg Phase 1 Study 0903A1-101-US)[1] | | | | | |
|---|---|---|---|---|---|---|---|
| **Parameter** | **0.5 mg/m²** | **0.25 mg/m²** | **0.5 mg/m²** | **1 mg/m²** | **2 mg/m²** | **4 mg/m²** | **5 mg/m²** |
| **$C_{max}$** (ng/mL) | **259** | 15 | 28 | **50** | **411** | 611 | 1,325 |
| **$AUC_{inf}$** (Hr*ng/mL) | **22,923** | 82 | 468 | 943 | 11,110 | **10,970** | **29,980** |

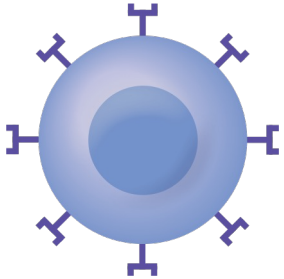


[1]Mylotarg ODAC 2017.

# VCAR33: CD33-Directed CAR-T Programs



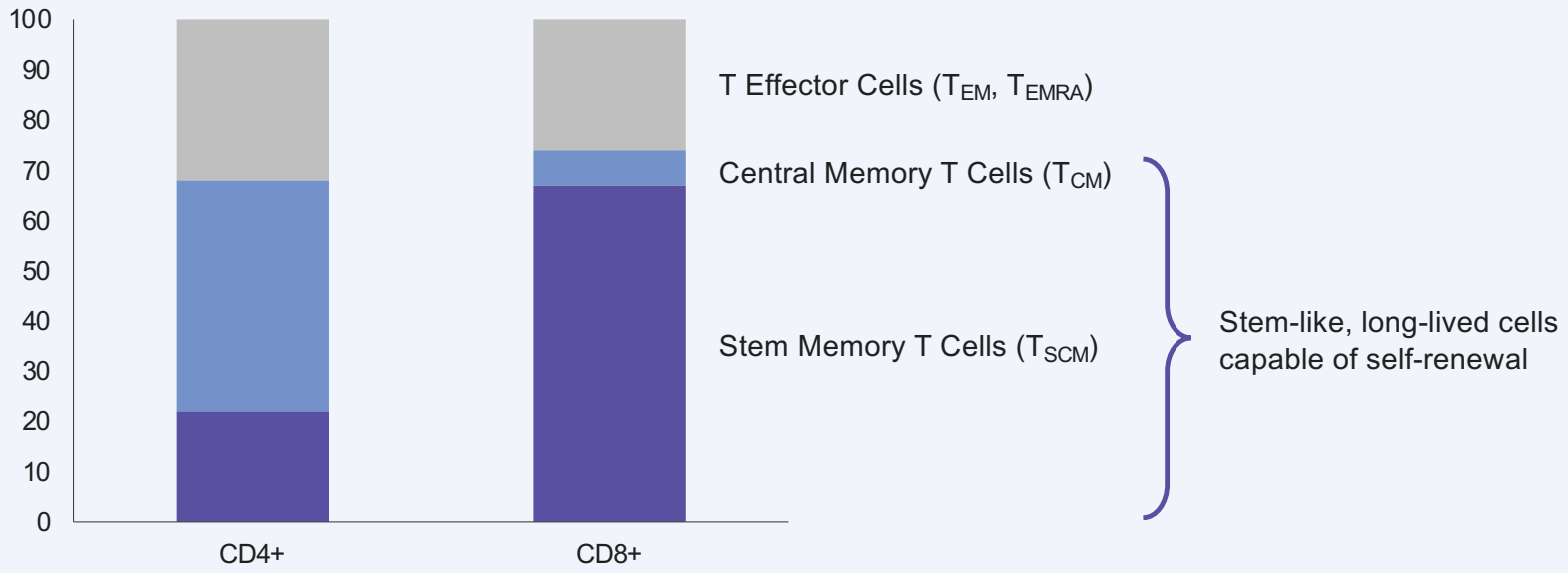
# VCAR33 CD33-Directed CAR-T Programs



| VCAR33$^{AUTO}$ | | VCAR33$^{ALLO}$ |
|---|---|---|
| Autologous | Cell Source | Allogeneic healthy donor |
| Effector subsets | Cell Phenotype | Younger, stem-like subsets |
| Relapsed/refractory AML | Treatment Setting | Relapsed/refractory AML post-transplant |
| Ongoing Phase 1/2 trial sponsored by NMDP | | IND expected 1H 2023 |

# Vor's T Cell Manufacturing Process Preserves Stemness

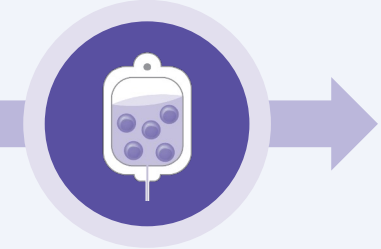
## T Cell Phenotype from VCAR Process



# Vision: Trem-cel + VCAR33 Treatment System

## Single apheresis from healthy donor

**CD34⁺ cells** → **T cells**



### Trem-cel

CD33-edited transplant

- **Normal engraftment, low GvHD**
- **Designed to enable post-transplant targeted therapies**

\+

### VCAR33

CD33-directed CAR-T

- **Healthy cells matched to new immune system**
- **Designed for long-term persistence without cytopenia**

# Future Programs

**Trem-cel**

Treatment-resistant HSC transplant

+

**Mylotarg**

1st generation antibody-drug conjugate

**Trem-cel**

Treatment-resistant HSC transplant

+

**VCAR33**

CD33-directed CAR-T programs

**Multiplex-edited HSCs**

Multi-treatment-resistant HSC transplant

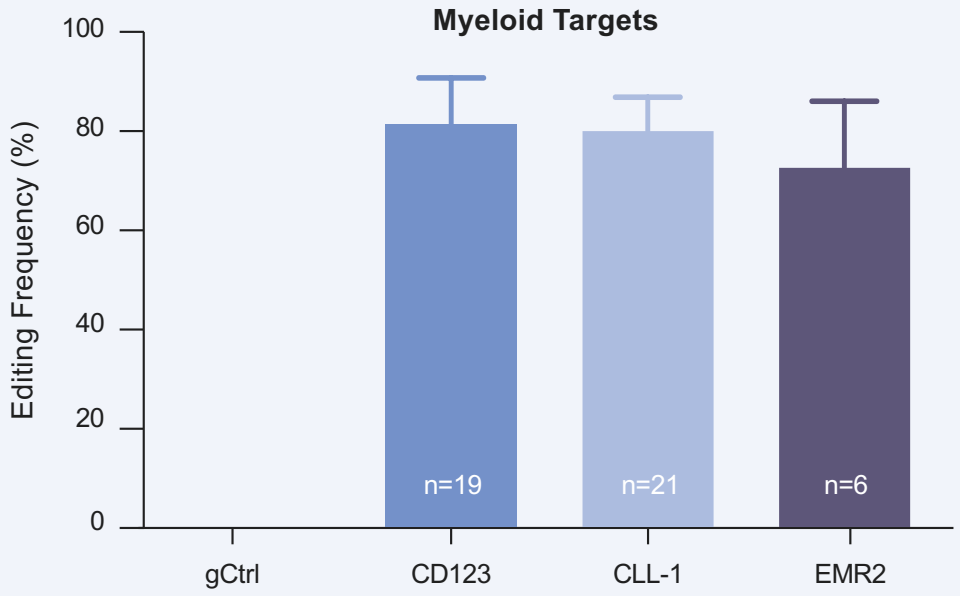
+

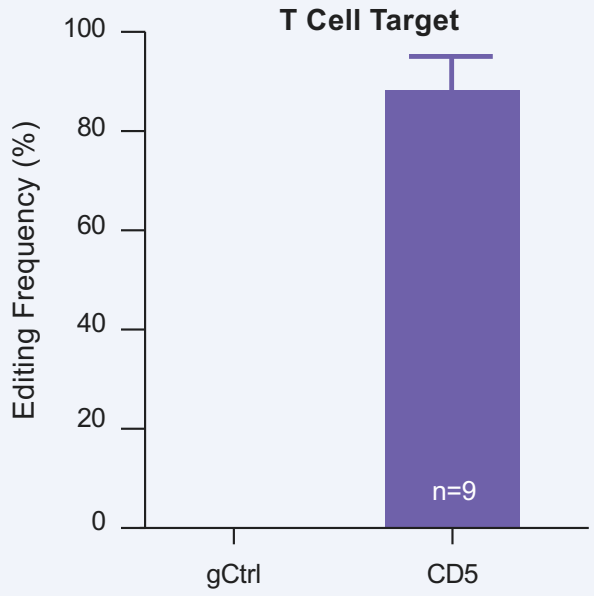
**Multi-specific CAR-Ts**

Abound Bio collaboration

# High Editing Frequency for Next-Generation Targets

## CD34+ Editing Frequency

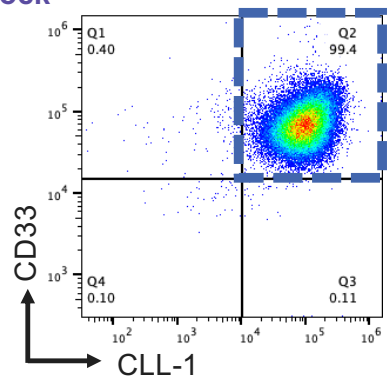


# Multiplex Editing Strategies Achieve Highly Efficient Double Knock-out

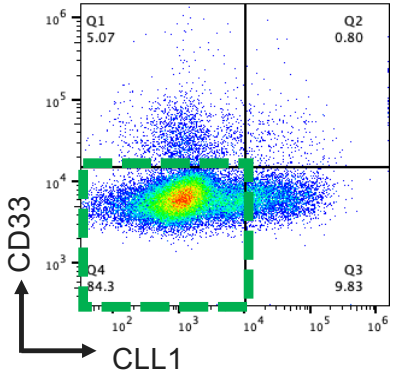
## Sequential Cas9 Editing

**Mock**




$CD33^{+}CLL\text{-}1^{+}$
Double Pos
99.4%

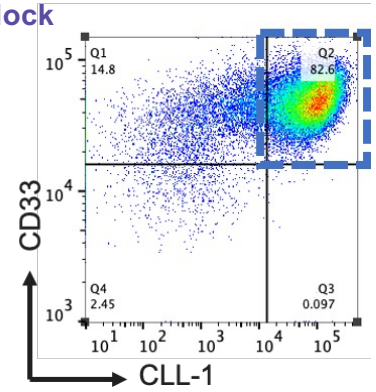
**Edited**




$CD33^{-}CLL\text{-}1^{-}$
Double KO
84.3%

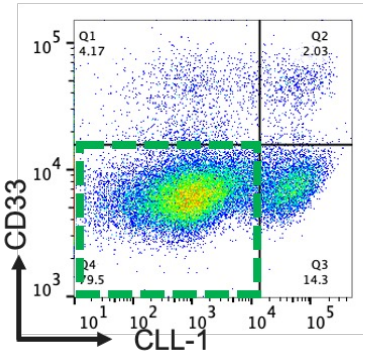
## Base Editing

**Mock**




$CD33^{+}CLL\text{-}1^{+}$
Double Pos
82.6%

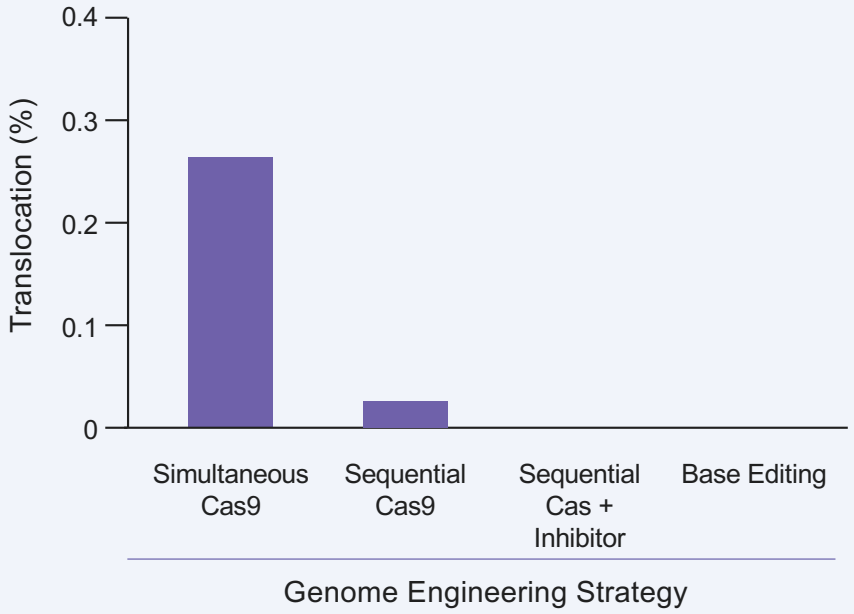
**Edited**



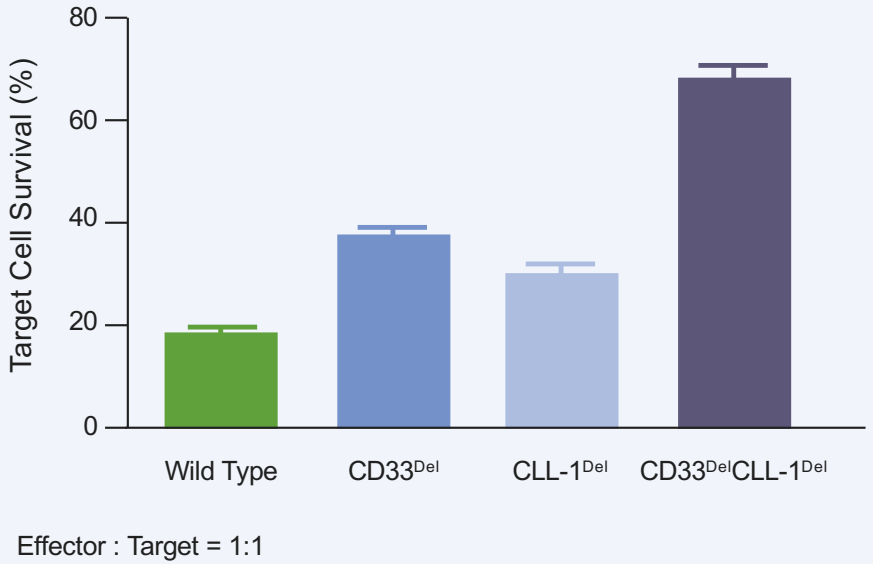

$CD33^{-}CLL\text{-}1^{-}$
Double KO
79.5%

# Multiplex Editing: Minimizing Translocations and CAR-T Protection

## Minimizing Translocation Rate



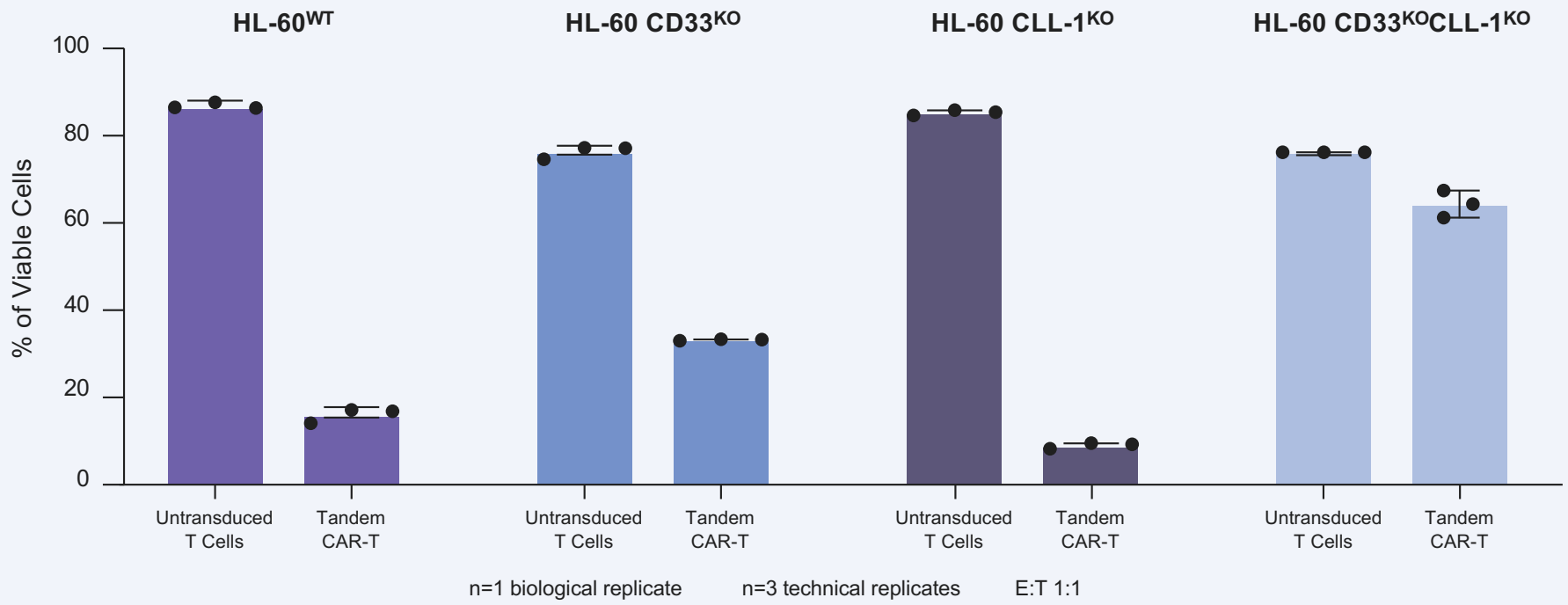

## Cell Protection from CAR-T Killing




Effector : Target = 1:1

# In Vitro Proof of Concept for Multi-Specific CAR-T

## Tandem CAR-T Active Against Wild Type and Single Knock-outs



# Potential Value Proposition and Reimbursement Pathways

HSC

## ngineered for Protection

### Seamless Integration

- Comparable engraftment
- Well-characterized, regulated

### Protected Bone Marrow

- Invisible and resistant to targeted therapy

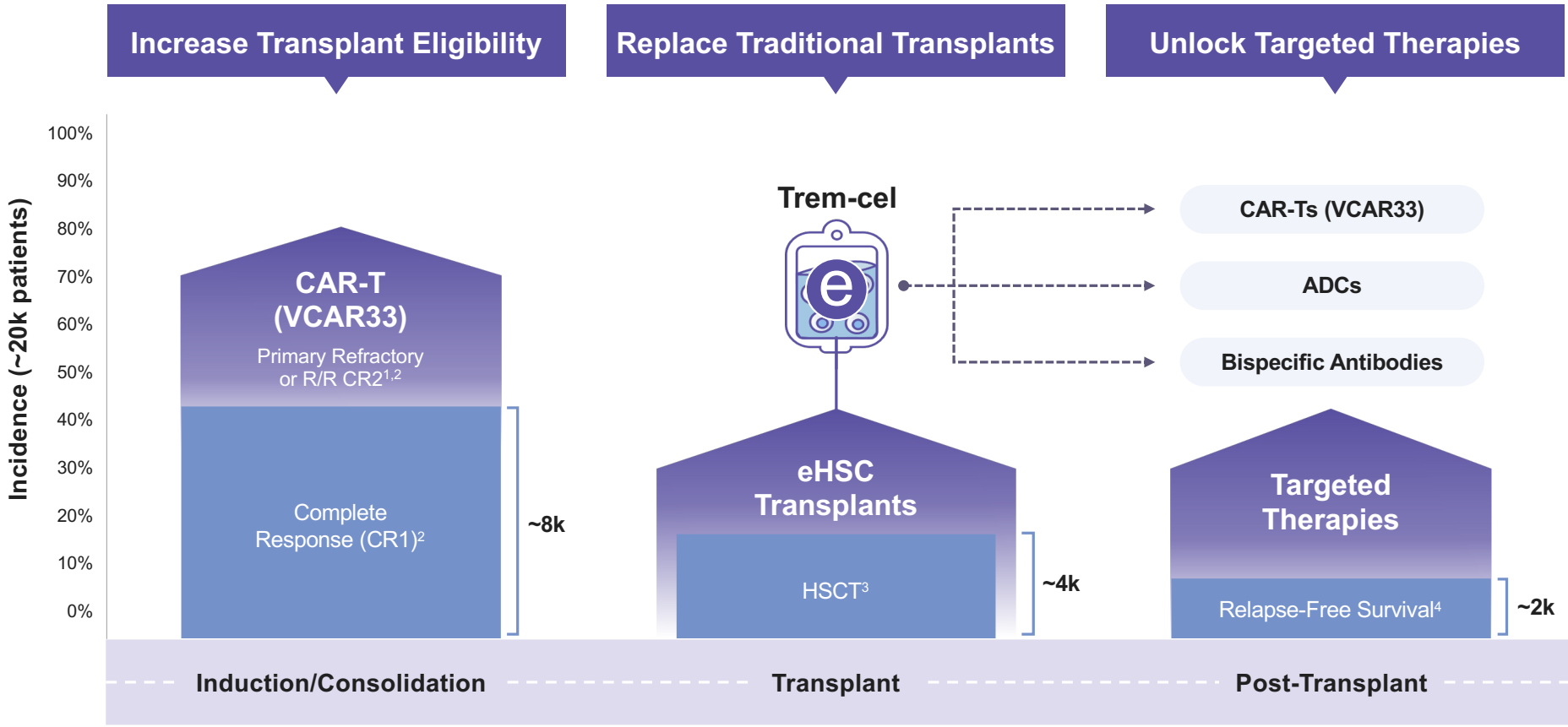
### Curative Intent

- Unlock new treatments
- Relapse-free survival

## Reimbursement Pathways

| Medicare | Commercial |
|---|---|
| Carve-out for actual cost of stem cell acquisition & processing *(new IPPS ruling)* or New technology add-on payment (NTAP) or PPS-exempt | Incremental carve-out or Outcomes-based agreement or Negotiated case rate |

# Opportunity to Transform Each Step of the Patient Journey



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**Unique approach**
of protected eHSC transplants enabling post-transplant targeted therapy

**Clinical proof of concept**
demonstrated of trem-cel eHSC in first two patients with AML

**VCAR33$^{ALLO}$**
IND filing expected
**1H 2023**

Fully integrated in-house
**GMP manufacturing capability**

**$230M**
in cash and cash equivalents as of
**Dec 31, 2022**


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