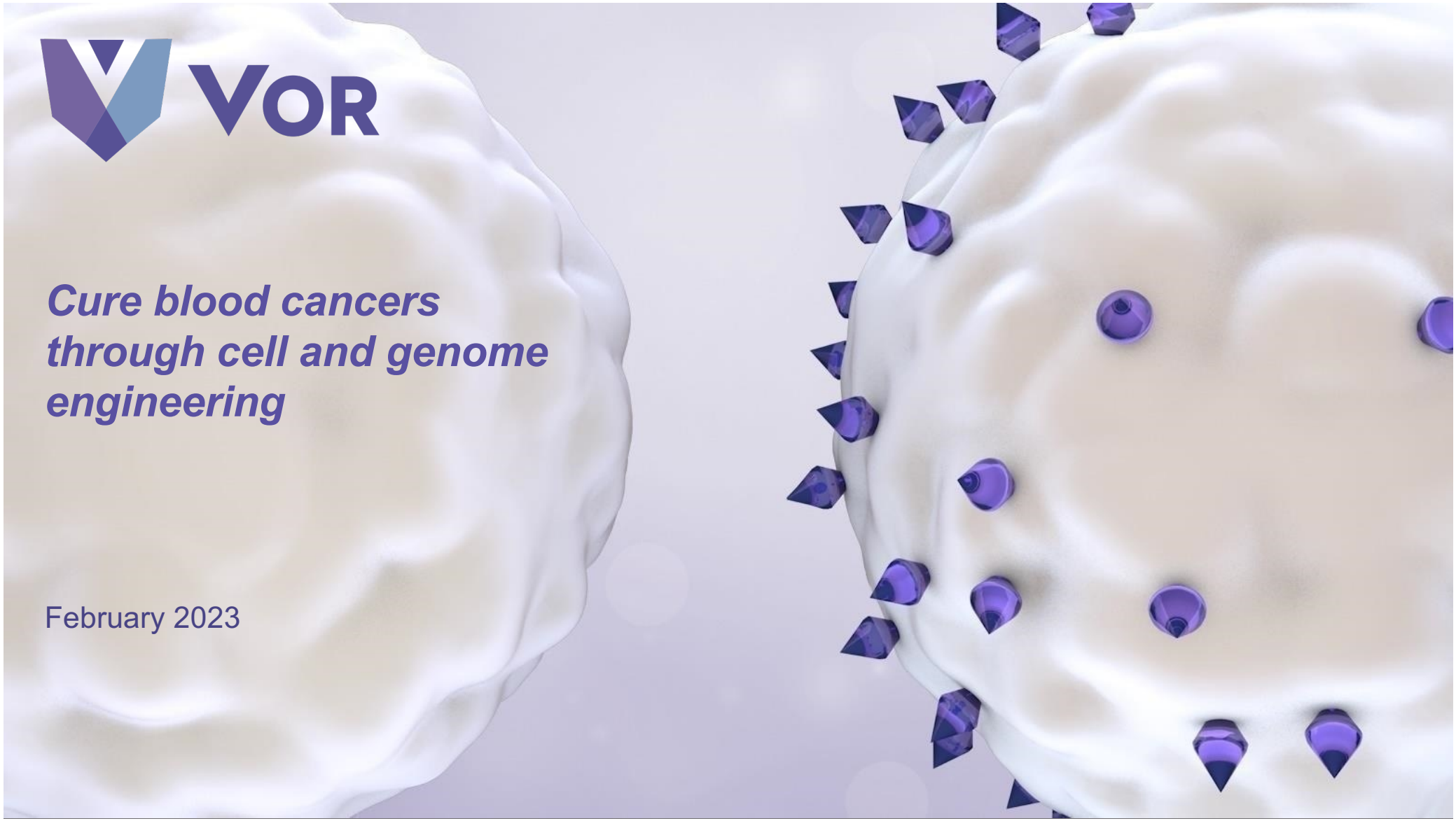
VOR

Cure blood cancers through cell and genome engineering



February 2023

Disclaimer

This presentation (the "Presentation") contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 about Vor Biopharma Inc. ("Vor," "Vor Bio" or the "Company"). The words "aim," "believe," "could," "design," "estimate," "expect," "intend," "may," "ongoing," "plan," "potential," "project," "should," "target," "towards," "will," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements in this Presentation include those regarding the feasibility of a trem-cel transplant to be successfully manufactured, to engraft normally, to maintain blood counts following treatment with Mylotarg following allogeneic hematopoietic cell transplant and to be well tolerated, the potential of Vor Bio's platform, Vor Bio's plans, strategies, expectations and anticipated milestones for its preclinical and clinical programs, its cash, cash equivalents and investments, cash runway and expected capital requirements, and its plans and expectations related to the Company's manufacturing and facilities. Vor Bio may not actually achieve the plans, intentions, or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various factors, including: uncertainties inherent in the initiation, completion of, and availability and timing of results from, preclinical studies and clinical trials and clinical development of Vor Bio's product candidates; whether interim results from a clinical trial will be predictive of the final results of the trial or the results of future trials; expectations for regulatory approvals to conduct trials or to market products; the success of Vor Bio's in-house manufacturing capabilities and efforts; and availability of funding sufficient for its foreseeable and unforeseeable operating expenses and capital expenditure requirements. The interim data for trem-cel presented in this Presentation is based on one patient and future results for this patient or additional patients may not produce the same or consistent results. These and other risks are described in greater detail under the caption "Risk Factors" included in Vor Bio's most recent annual or quarterly report and in other reports it has filed or may file with the Securities and Exchange Commission. Any forward-looking statements contained in this Presentation speak only as of the date of this Presentation, and Vor Bio expressly disclaims any obligation to update any forward-looking statements, whether because of new information, future events or otherwise, except as may be required by law.

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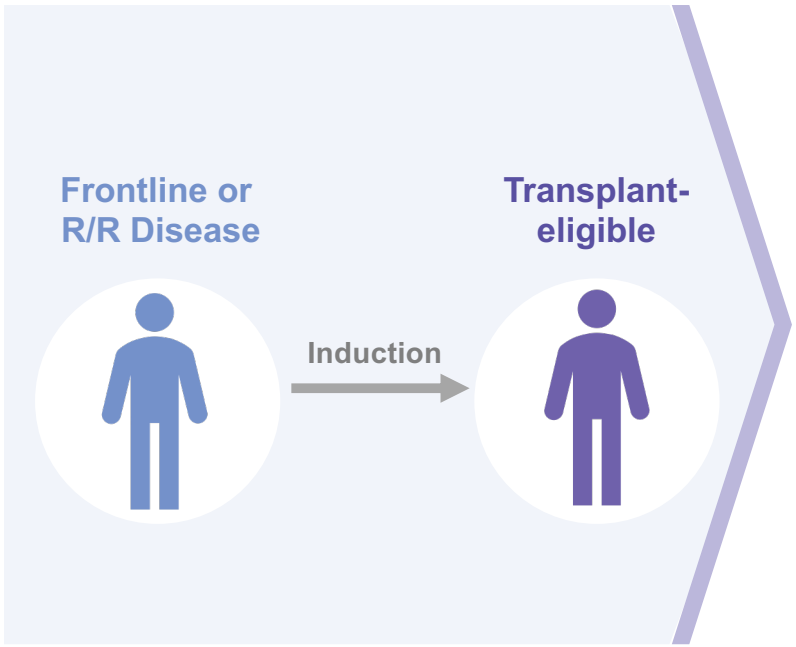
A Novel Treatment Approach for Blood Cancers



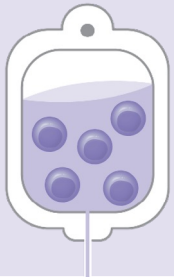
Standard HSC Transplant

Post-Transplant Relapse

Watchful waiting despite likelihood of relapse

Any therapy will compromise stem cell transplant

Protected Engineered HSC Transplant



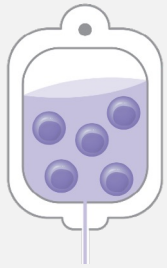
New Treatment Paradigm

Unlocked post-transplant targeted therapies

Aiming for prolonged remission or cure

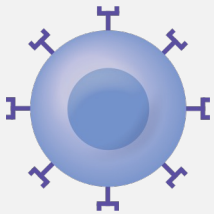
Vor Bio's Platform Establishing Next-Generation Treatments

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 in 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 eHSC + VCAR33-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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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

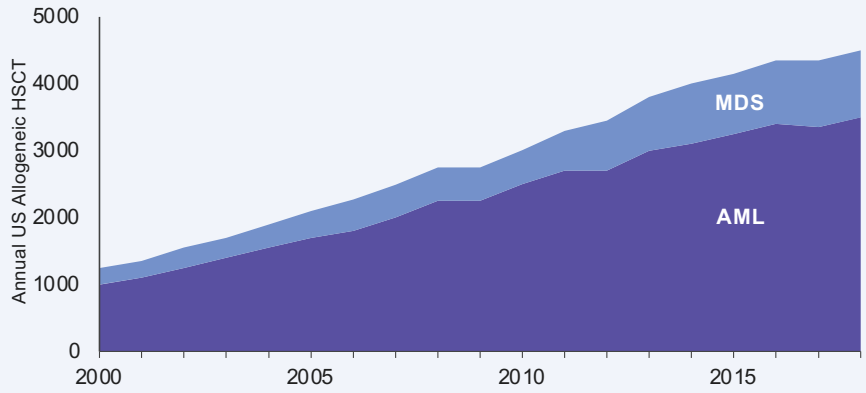
+

Multi-specific CAR-Ts

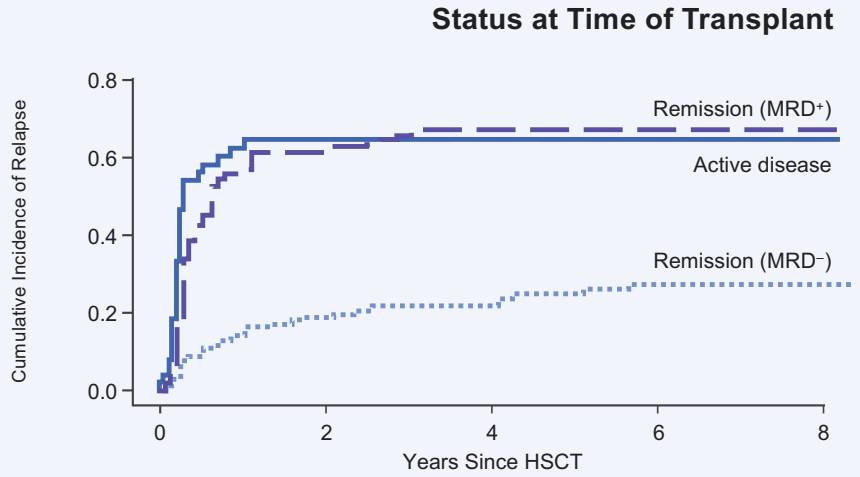
Abound Bio collaboration

AML Unmet Need Is Large and Increasing

Use of Transplant is Increasing…

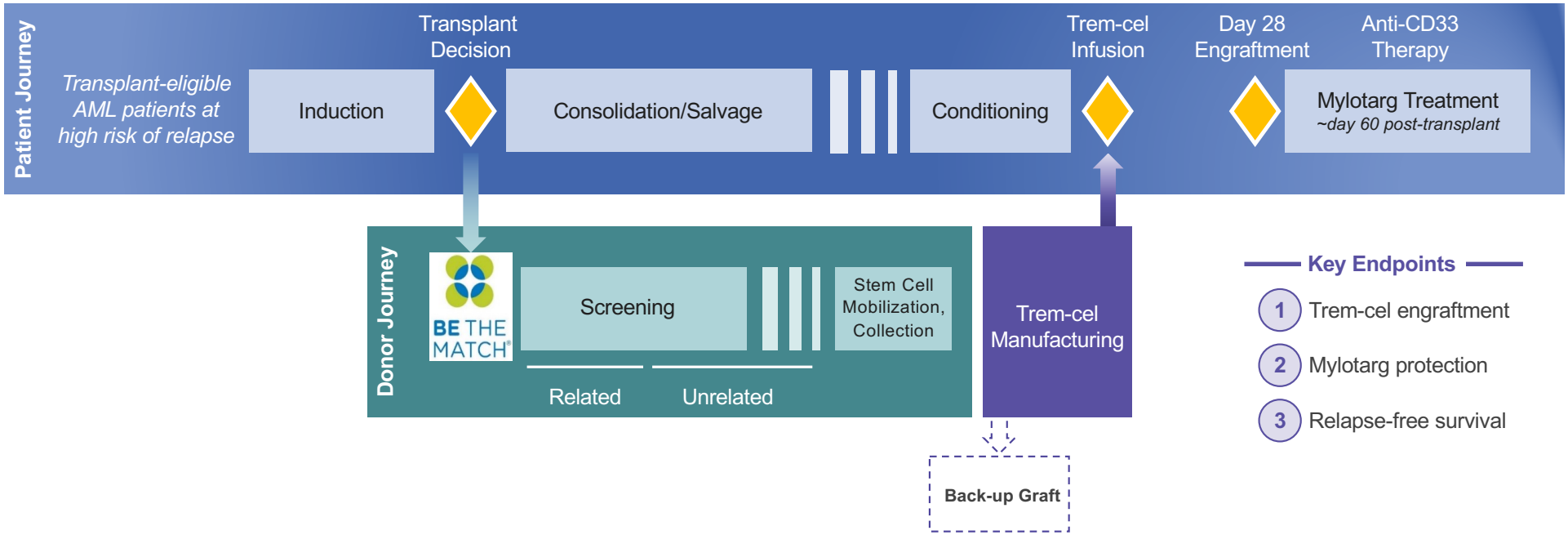


…Though Still Frequent Relapse Post-Transplant



For patients who relapse post-transplant, 2-year survival is <20%

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

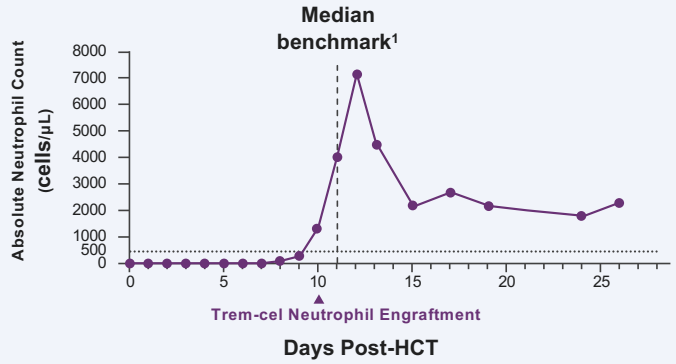
Trem-cel Drug Product

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%	✓

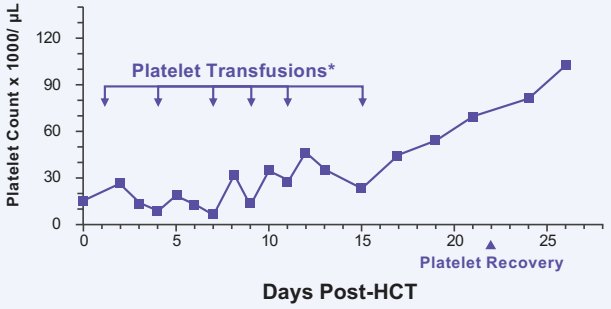
Timely Neutrophil Engraftment and Platelet Recovery

Patient 1

Neutrophil engraftment

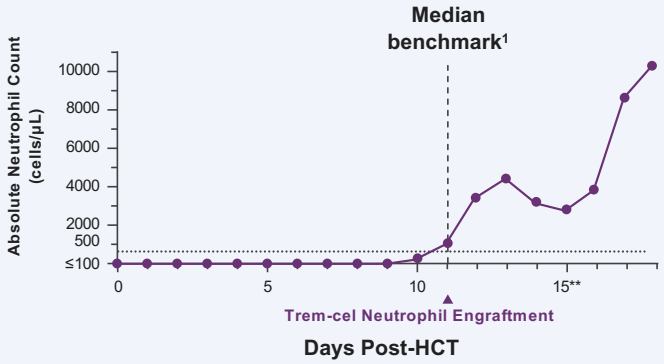


Platelet recovery

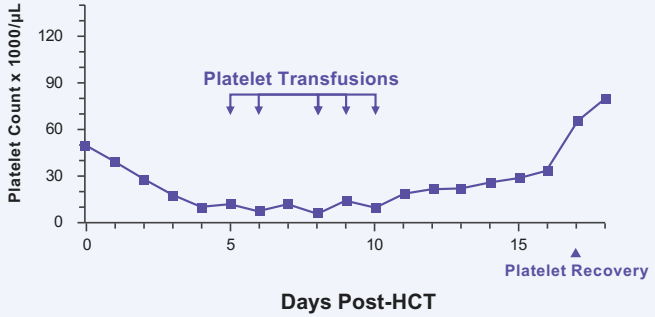


Patient 2

Neutrophil engraftment



Platelet recovery



Patient 1

Neutrophil engraftment: Day 10
Platelet recovery: Day 22

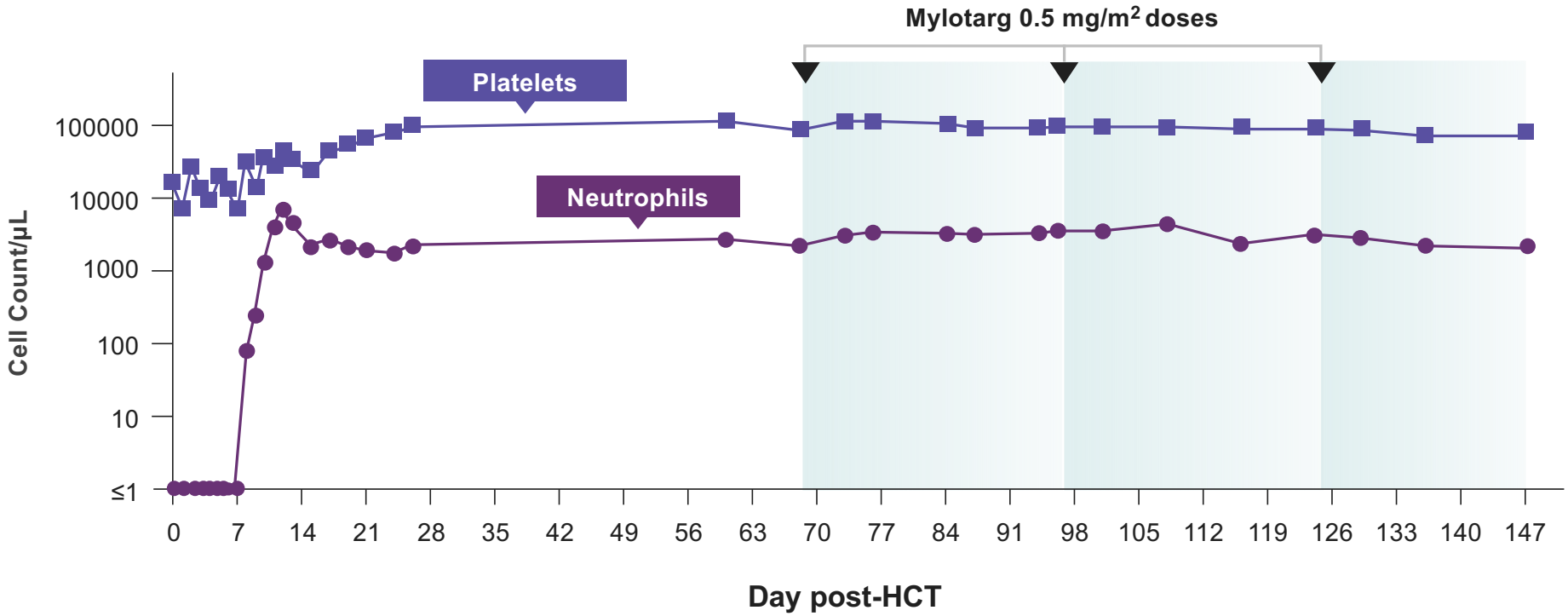
Patient 2

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) Resolved	Skin infection (Grade 1, 2) CMV reactivation (Grade 2) UTI (Grade 2) BK virus in urine (Grade 2) All resolved or resolving	AST/ALT elevations (Grade 1, 2) attributable to anti-fungal Resolved 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) E. coli bacteremia (Grade 3) reported at D8 prior to engraftment 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

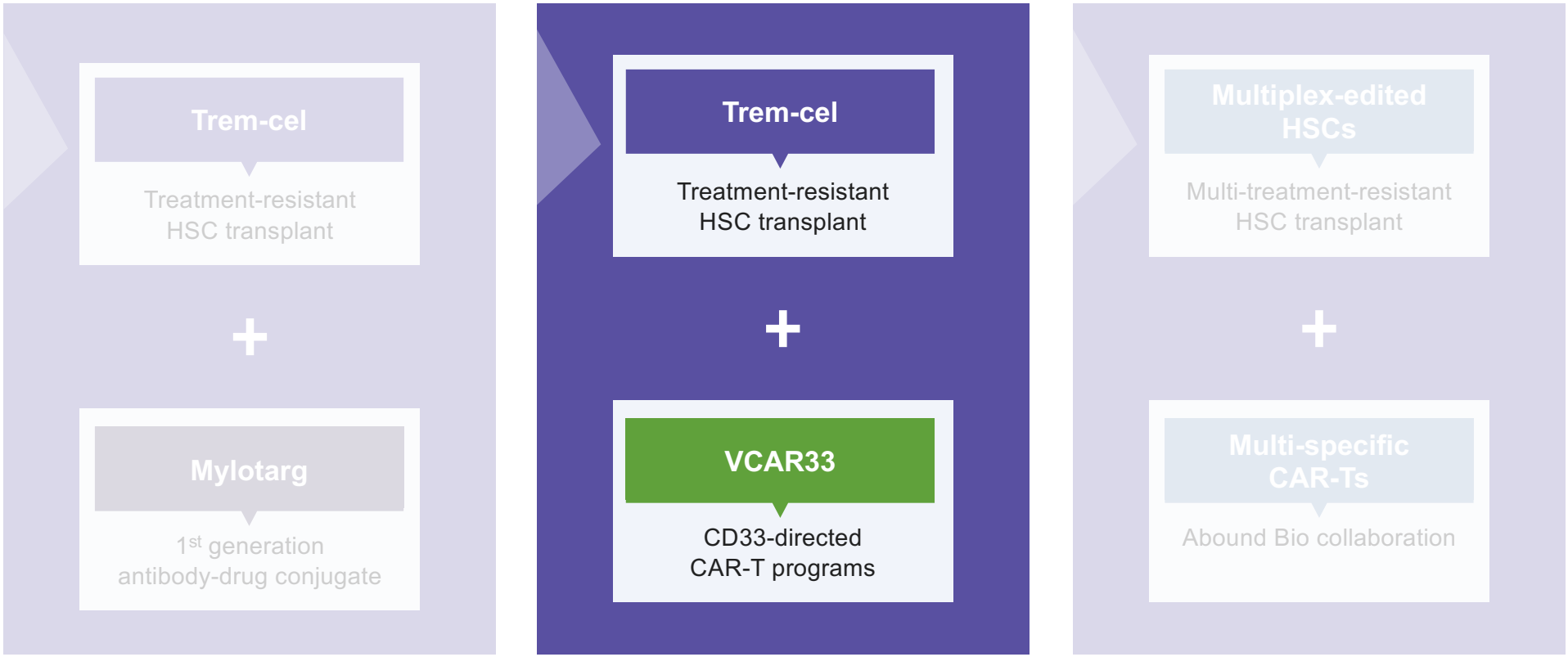
*Mylotarg (0.5 mg/m²) was administered at D68, D96, and D124.

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

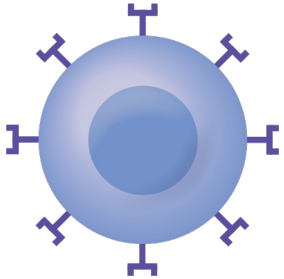
	Patient 1 1st Dose	Relapsed/Refractory AML population (GO phase 1 study 0903A1-101-US)[1]					
Parameter	**0.5 mg/m³**	**0.25 mg/m²**	**0.5 mg/m²**	**1 mg/m²**	**2 mg/m²**	**4 mg/m²**	**5 mg/m²**
C_{max} (ng/mL)	**259**	15	28	**50**	**411**	611	1,325
AUC_{inf} (Hr*ng/mL)	**22,923**	82	468	943	11,110	**10,970**	**29,980**

Reference: [1]Mylotarg ODAC 2017.

VCAR33: CD33-Directed CAR-T Programs



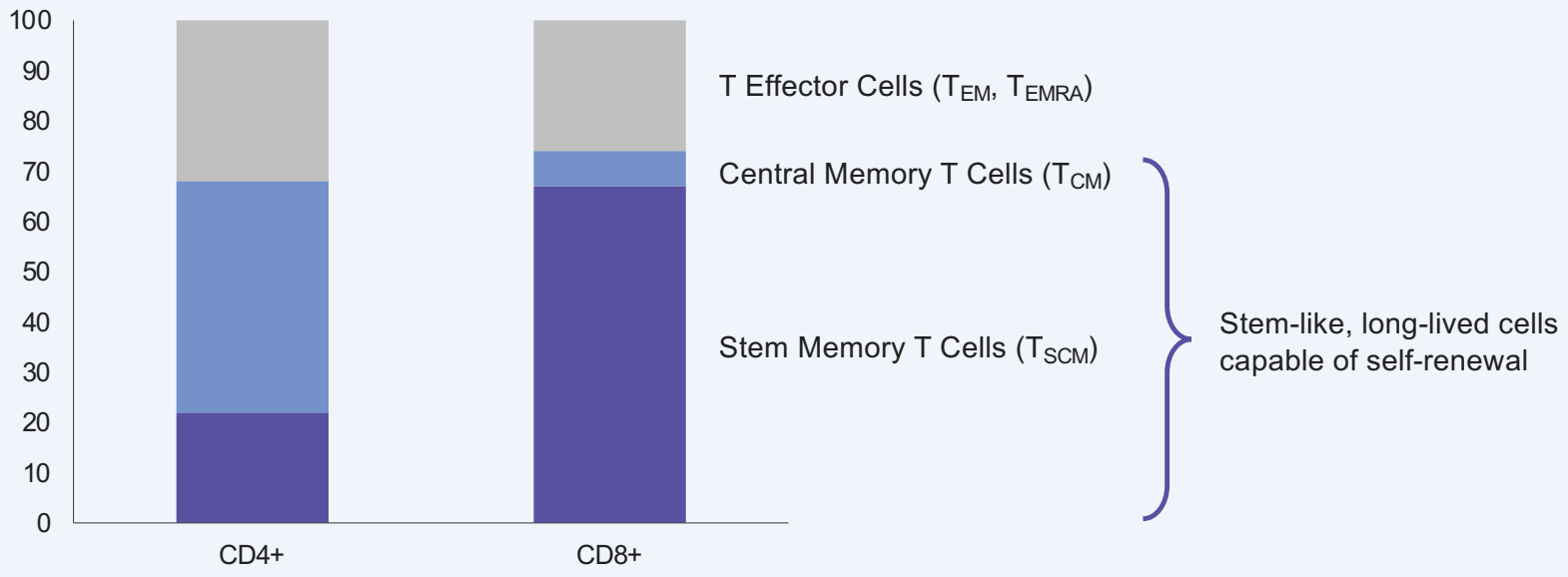
VCAR33 CD33-Directed CAR-T Programs



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

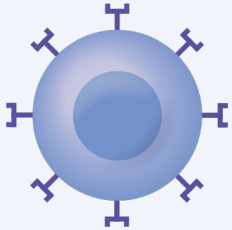
T Cell Phenotype from VCAR Process



Vision: Trem-cel + VCAR33 Treatment System

Trem-cel
CD33-deleted HSC transplant protected from CD33-targeted therapies

+



VCAR33
CD33-directed CAR-T derived from same healthy donor

Aiming for durable remissions or cures for AML and beyond

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

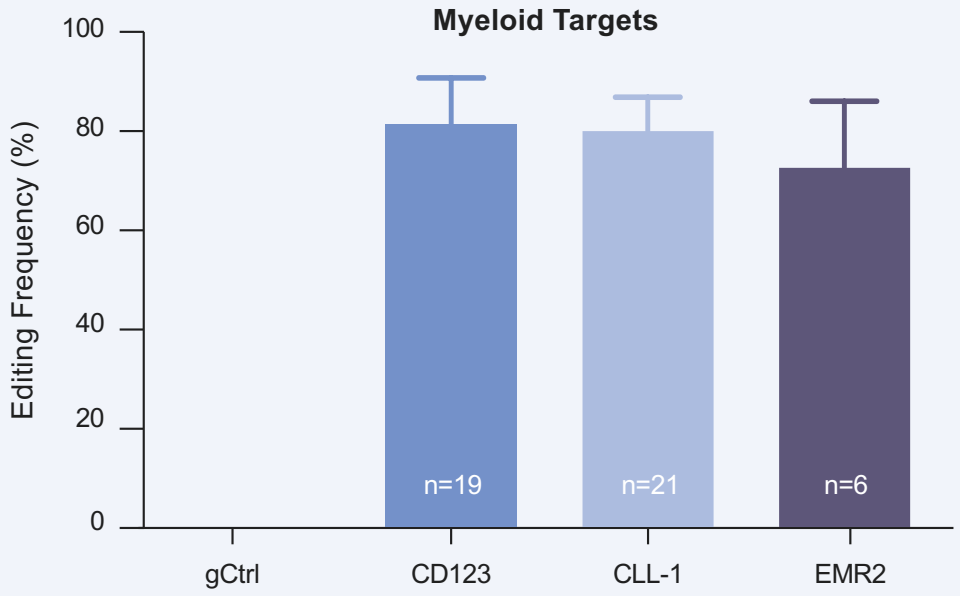
+

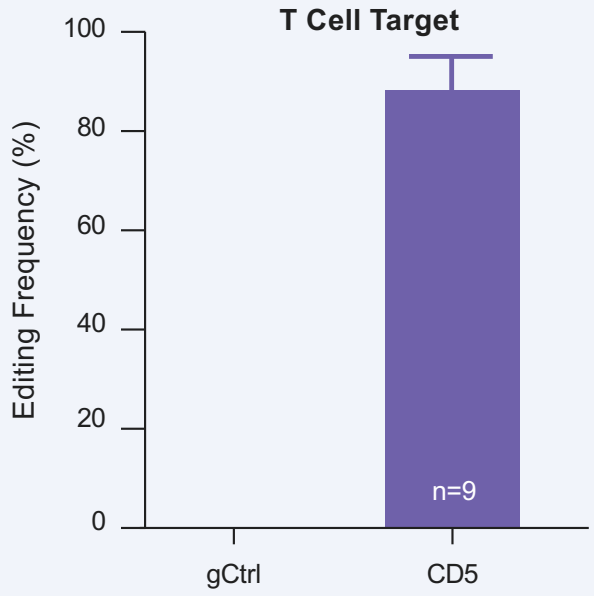
Multi-specific CAR-Ts

Abound Bio collaboration

High Editing Frequency for Next-Generation Targets

CD34+ Editing Frequency

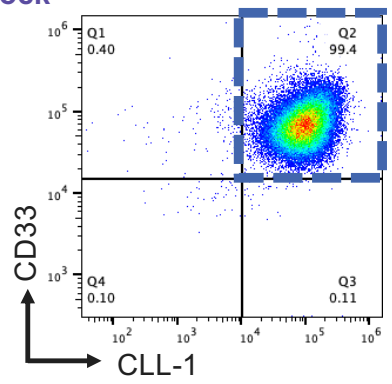




Multiplex Editing Strategies Achieve Highly Efficient Double Knock-out

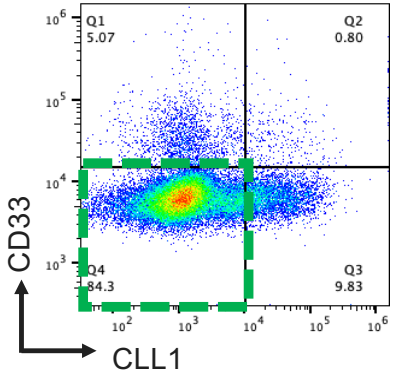
Sequential Cas9 Editing

Mock



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

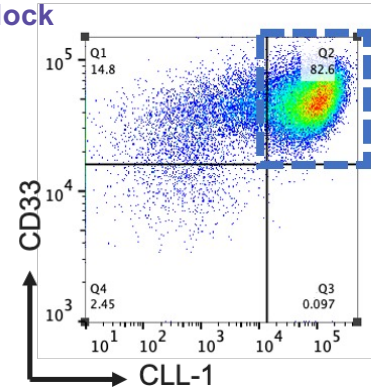
Edited



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

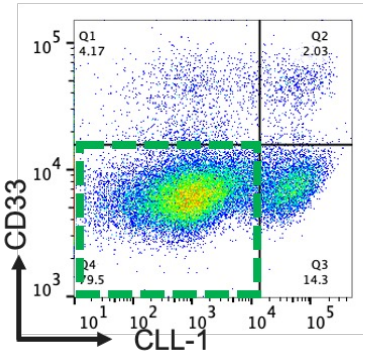
Base Editing

Mock



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

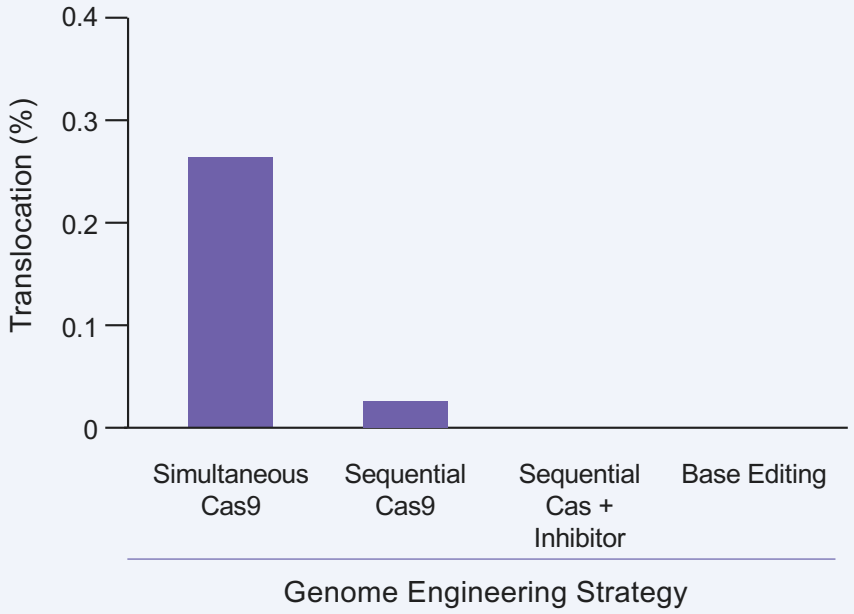
Edited



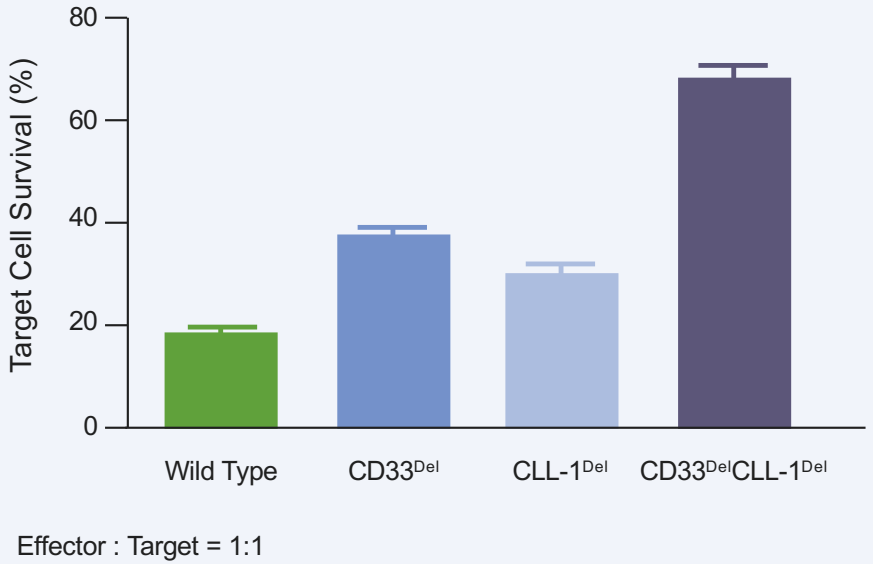
$CD33^{-}CLL\text{-}1^{-}$
Double KO
79.5%

Multiplex Editing: Minimizing Translocations and CAR-T Protection

Minimizing Translocation Rate



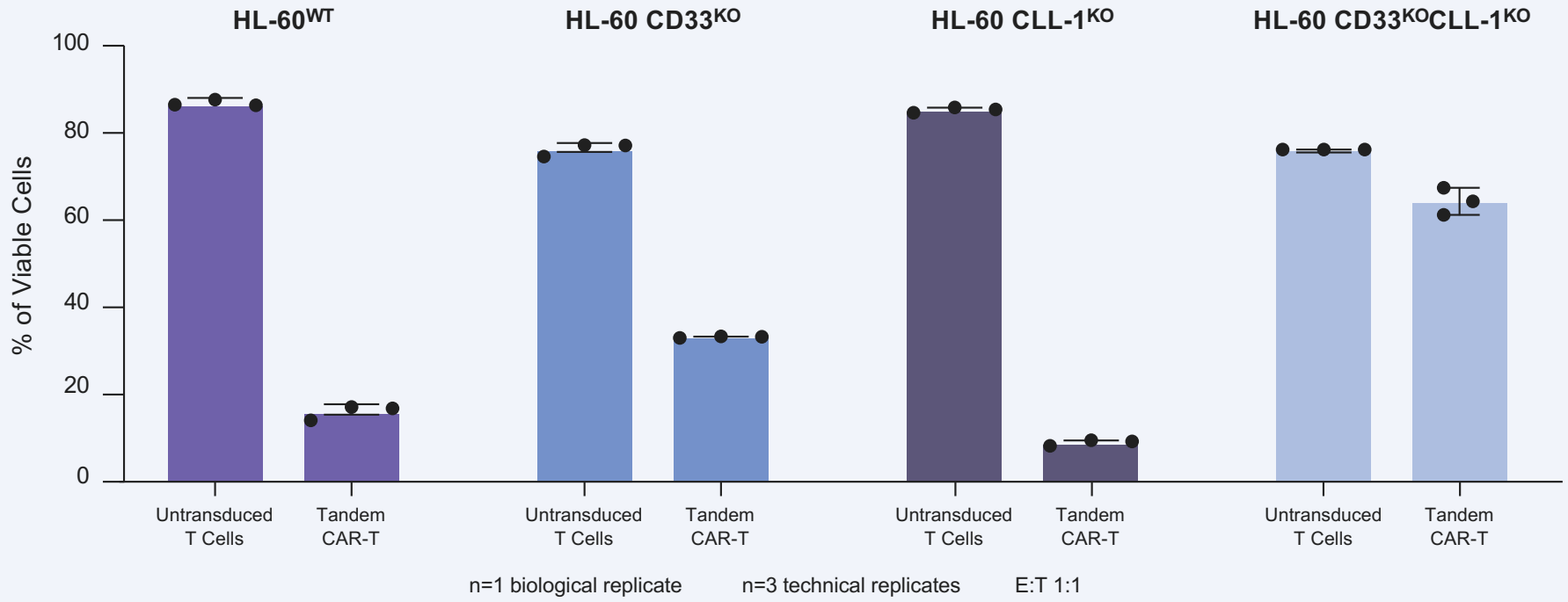
Cell Protection from CAR-T Killing



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

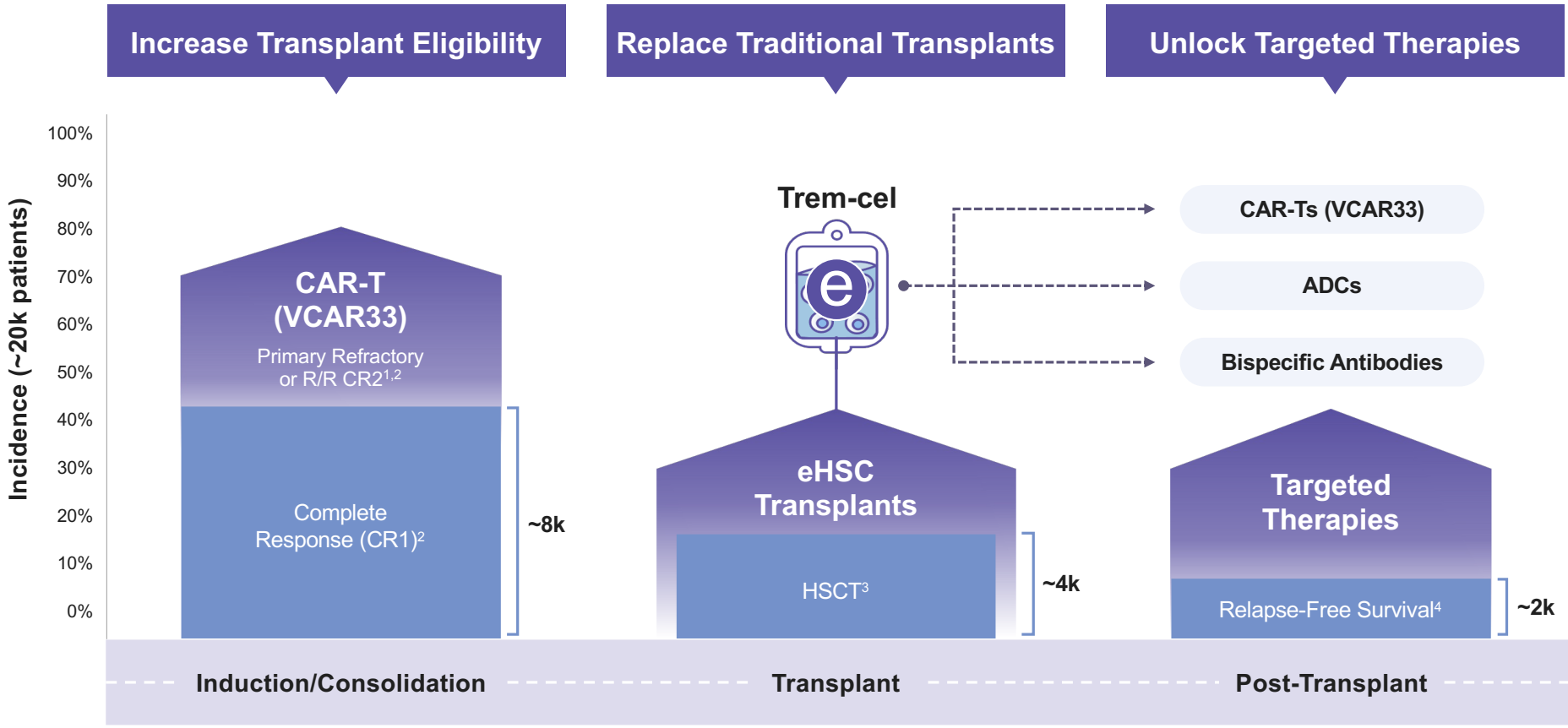
Curative Intent

- 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



Vor Bio: Cure Blood Cancers Through Cell and Genome Engineering

- Cell and gene engineering company with fundamentally different approach to target cancer
  - Proprietary engineered hematopoietic stem cell transplant (eHSC) platform unlocking the potential of targeted therapies with curative intent
  - Current pipeline covering hematologic malignancies with an initial focus on AML
  - Upcoming milestones:
    - Additional trem-cel engraftment and hematologic protection data updates expected in 2023
    - VCAR33^{ALLO} IND filing in the first half of 2023
- Fully integrated in-house GMP manufacturing capability to support clinical development
- Experienced and proven management team
- Recent financing raised $116 million

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