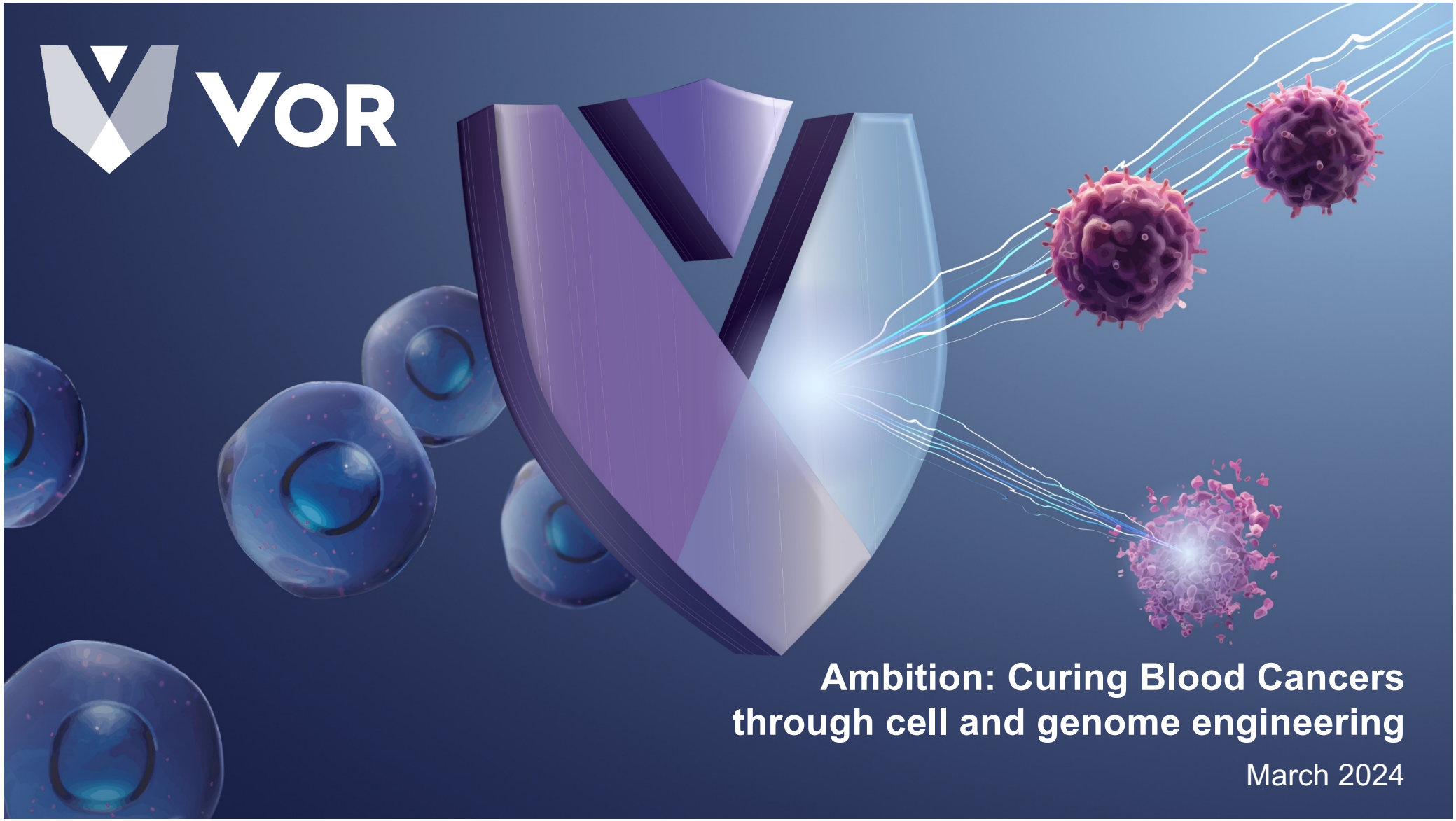
VOR
Ambition: Curing Blood Cancers
through cell and genome engineering
March 2024

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," "anticipate," "believe," "can," "could," "design," "enable" "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 (formerly VOR33) 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 VCAR33^{ALLO} in combination with trem-cel as a Treatment System, the potential of trem-cel to enable targeted therapies in the post-transplant setting including Mylotarg and CD33-targeted CAR-Ts, the potential of Vor Bio's platform, Vor Bio's plans, strategies, expectations and anticipated milestones for its preclinical and clinical programs, including the availability and timing of results from preclinical studies and clinical trials, the timing of regulatory filings, and the timing of dosing patients, Vor Bio's expectations regarding expedited regulatory review of its product candidates as a result of Fast Tracks designation or otherwise, the expected safety profile of Vor Bio's product candidates, cash runway and expected capital requirements, Vor Bio's expectations regarding addressable patient population and reimbursement rates for its product candidates, if approved, 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 preclinical data or interim results from a clinical trial will be predictive of the final results of the trial or the results of future trials; the uncertainty of 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 eight patients and future results for these patients 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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Our Vision: Cure Blood Cancers Through Cell and Genome Engineering

Unique Approach

Shielded stem cell transplants enabling targeted therapy

VCAR33^{ALLO}

CD33-directed novel transplant donor CAR-T in clinic with initial data in 2H 2024

Trem-cel

Positive POC demonstrated in AML with shielded CD33-deleted transplant

Additional data in 2H 2024

In-house GMP Clinical Manufacturing

Reliable process with rapid release time

$137M as of Dec. 31, 2023
Cash runway into 2H 2025

AML is a Common Leukemia with High Unmet Need

20,000 new cases/year (US)[2]
(10% of new blood cancer cases)[2]

10,000 deaths/year (US)[2]
(20% of blood cancer deaths)[2]

Standard of Care is Transplantation

Replace Diseased Bone Marrow with Healthy Donor Cells

1 Conditioning
Toxic therapies to kill existing bone marrow

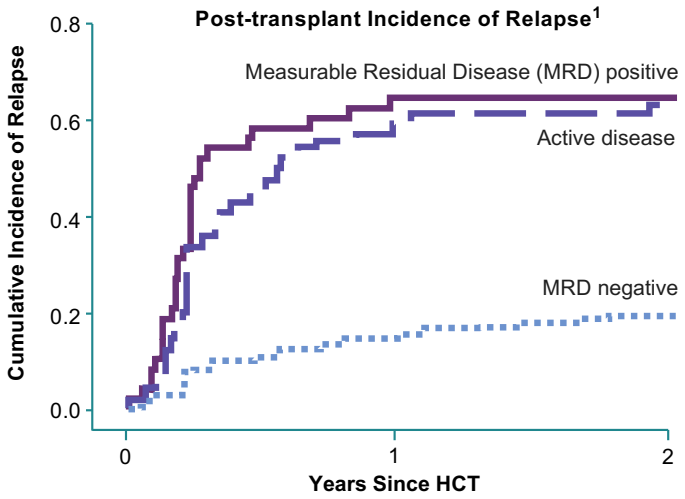
2 Harvest
Mobilize and collect stem cells from matched healthy donor

3 Transplant
Infuse stem cells into patient to restore the blood system

4 Watchful Waiting
Monitor for relapse; any follow-up treatment will damage the transplant

Relapse Despite Transplantation

is still common in AML patients

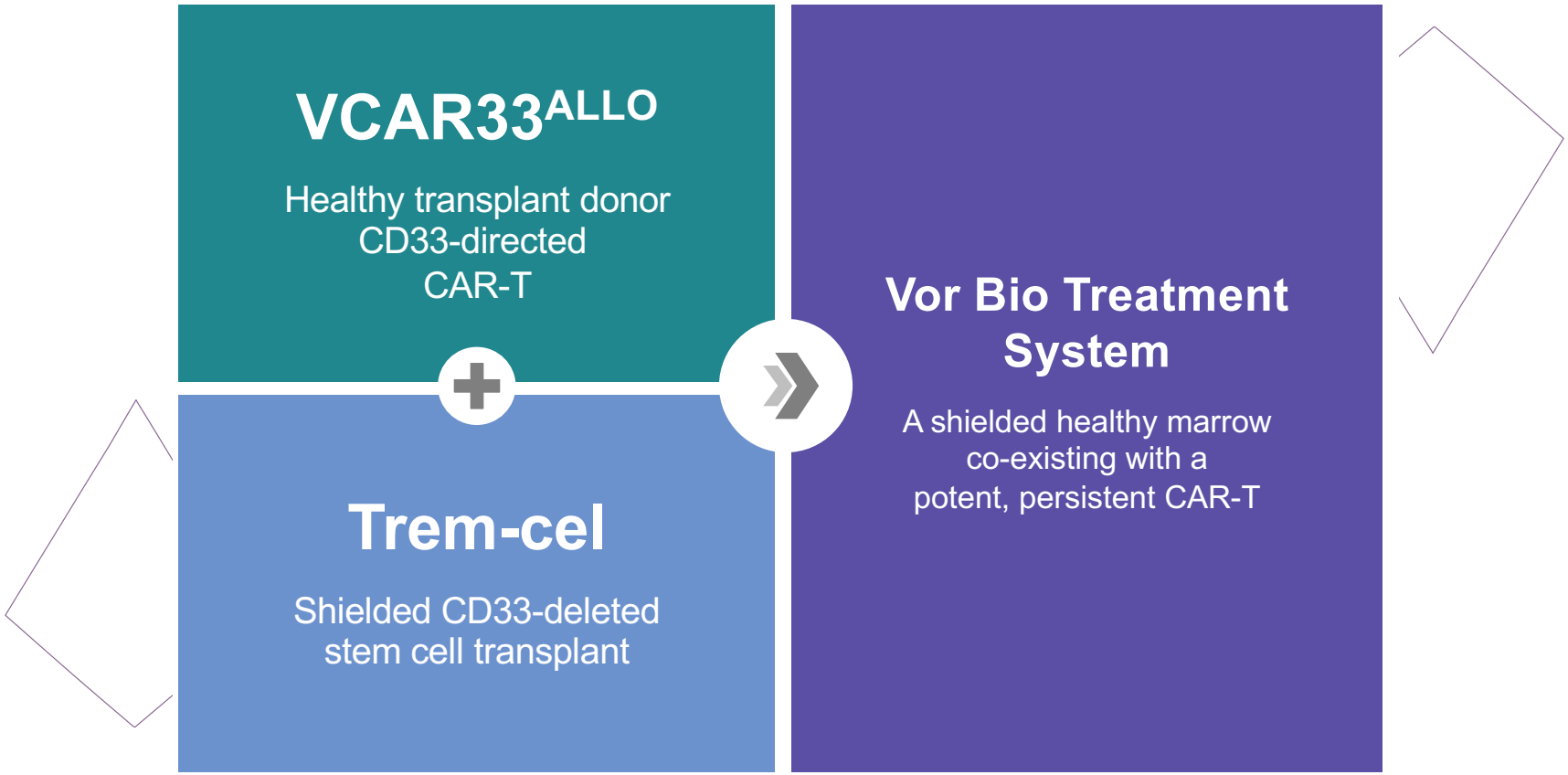


HCT, Hematopoietic Cell Transplant
1 Araki et al, JCO 2016. 2 LLS 2023

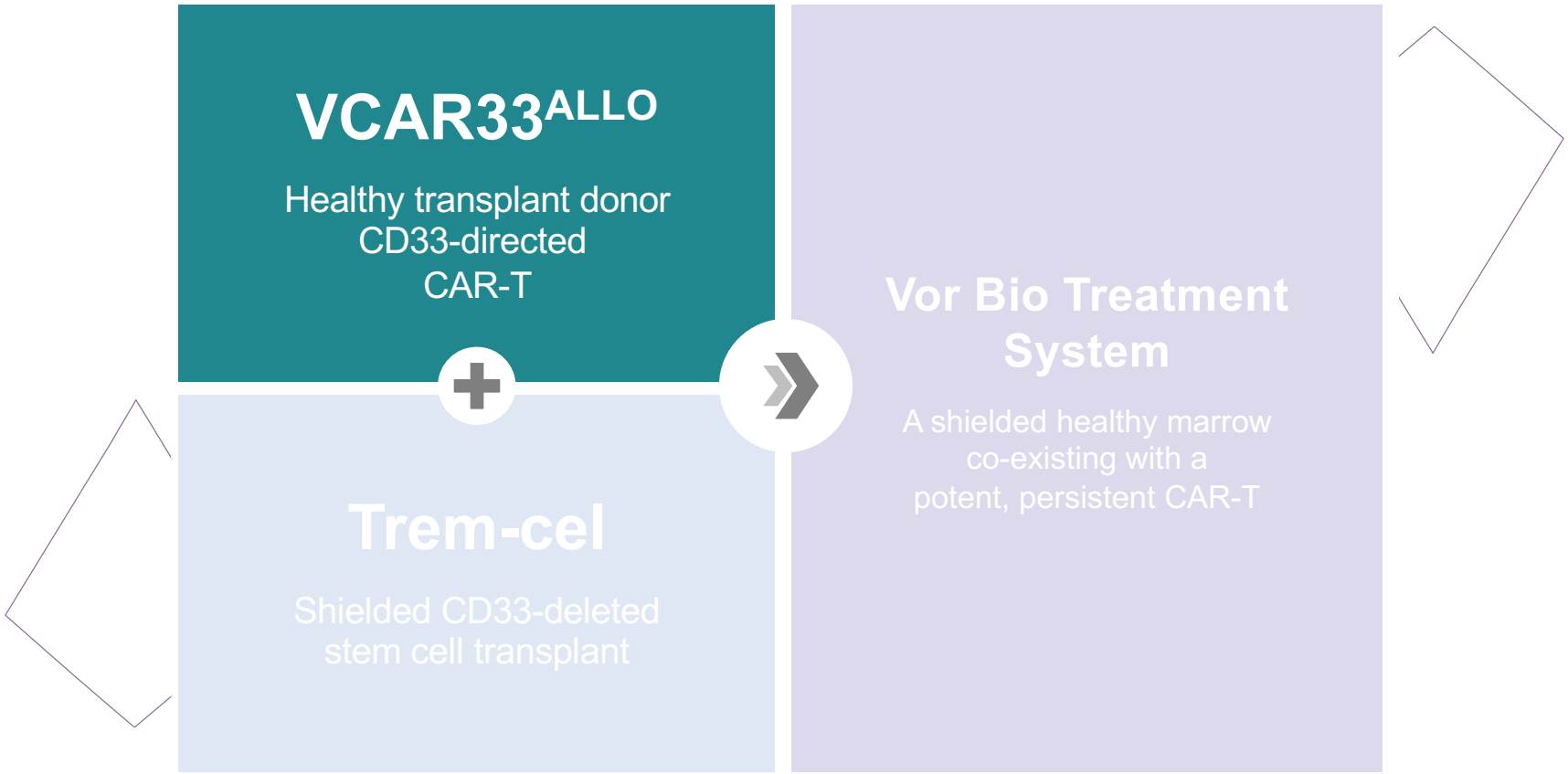
Pipeline Generating Multiple Clinical Readouts over Next 12 Months

Description			Preclinical		Clinical		Anticipated Milestones
Program / Trial	Modality	Indication	Discovery/ Validation	IND-Enabling	Phase 1/2	Phase 2/3	
VCAR33^{ALLO} (healthy transplant donor CAR-T) / VBP301	CD33-directed transplant donor CAR-T	AML Post-transplant					Initial data expected in the second half of 2024
Trem-cel + Mylotarg / VBP101	Shielded CD33-deleted transplant + CD33-directed ADC	AML					Clinical update in second half of 2024
		MDS					
Trem-cel + VCAR33 Treatment System	Shielded CD33-deleted transplant + CD33-directed transplant donor CAR-T	AML					IND filing following initial trem-cel and VCAR33^{ALLO} data
CD33-CLL1 Treatment System	Multi-specific CAR-T	AML					
	Multiplex-edited shielded transplant	AML					

Cell Therapies Designed to Synergize to Potentially Cure AML



VCAR33^{ALLO}: Healthy Transplant Donor CAR-T



A New Way of Generating CAR-T Therapy

Traditional Approaches

Autologous cells
(derived from patient)

Exhausted, depleted T cells

High manufacturing failure

Allogeneic cells
(off-the-shelf)

Poor expansion and persistence

Poorer clinical durability

Vor Bio Approach

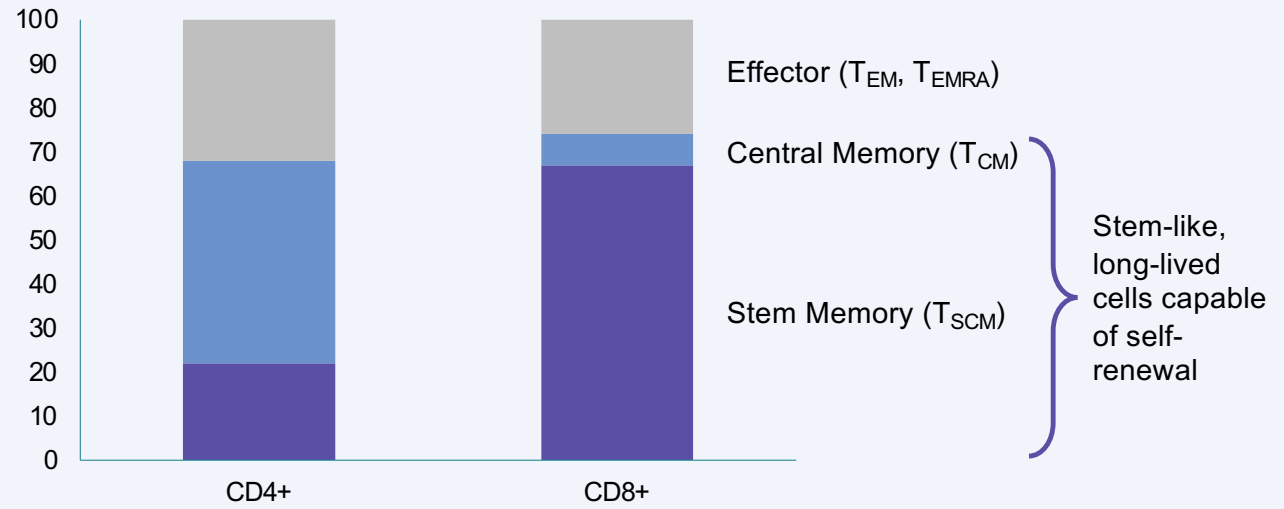
Transplant Donor Cells

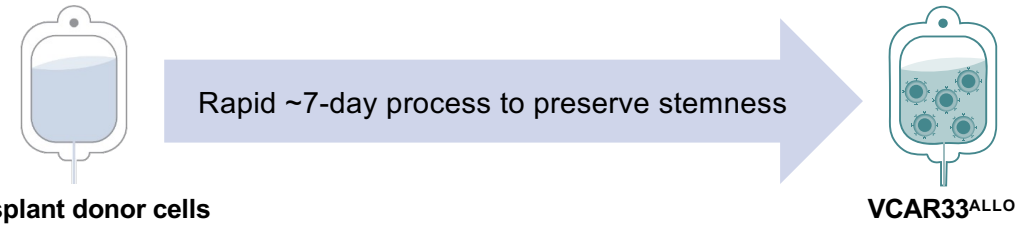
T cells exactly matched to patient's new immune system, more likely to persist

Stem-like, CAR-T cells more likely to expand and less prone to exhaustion

Vor Bio's T Cell Manufacturing Process Preserves Stemness

T Cell Phenotype from VCAR33^{ALLO} Process





Transplant donor cells

VCAR33^{ALLO}

VBP301: VCAR33^{ALLO} Phase 1/2 Clinical Trial

Patient Journey

MRD^{+} or relapsed AML following SOC transplant or trem-cel transplant

Enroll

Lymphodepletion

VCAR33^{ALLO} Infusion

Arm A: Blasts ≥ 5%

Arm B: MRD^{+}

Day 28 Follow-up

2nd transplant if required

3x3 dose escalation starting at 1 x 10^{6} CAR^{+} cells/kg

Prior Transplant Donor

Consent

Collect

VCAR33^{ALLO} Manufacturing

~7-day process

Key Endpoints

01 Safety

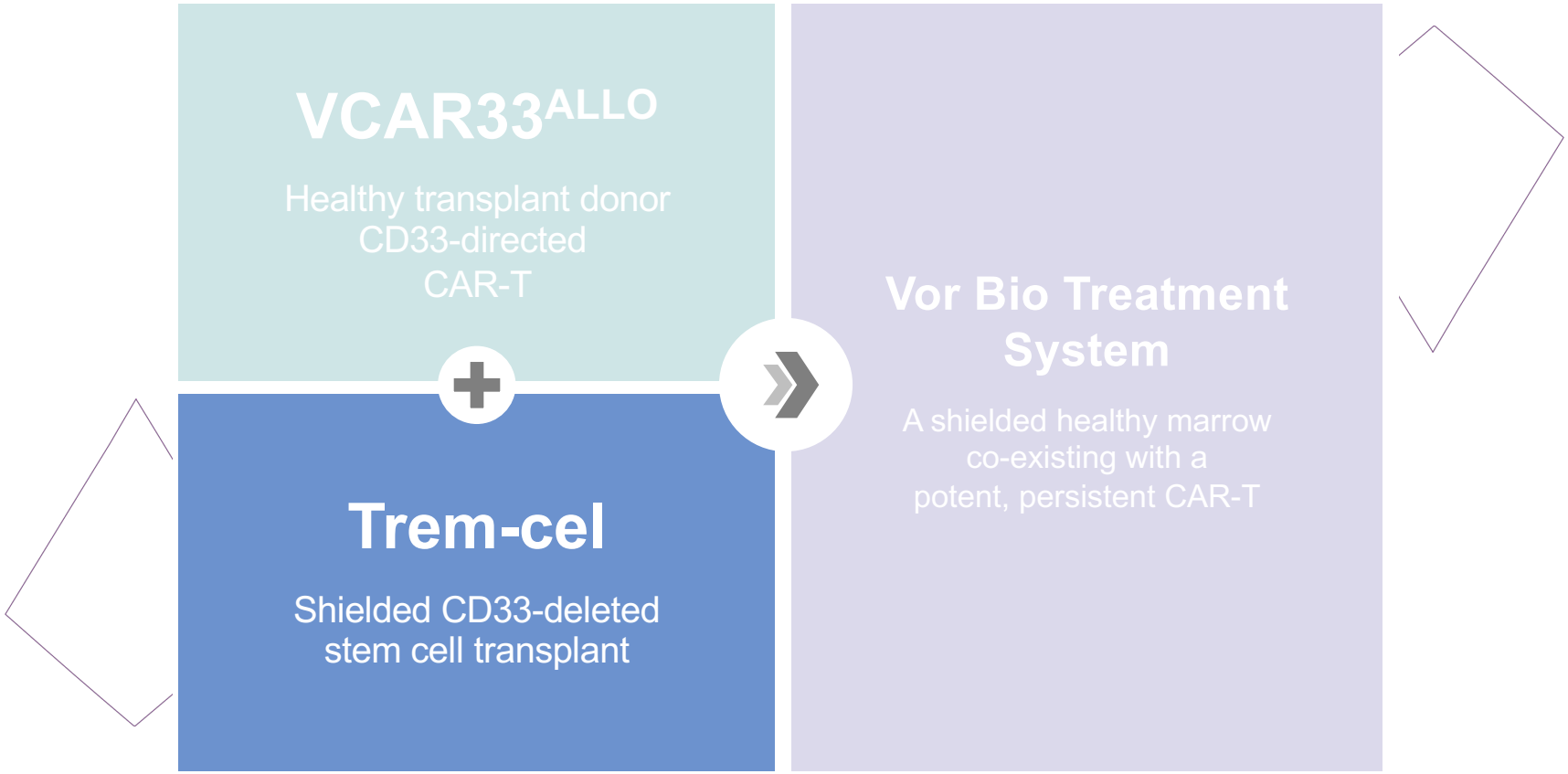
02 Expansion, persistence

03 Disease control/response

First patient treated in Jan 2024 with initial data expected in 2H 2024

Most clinical trial sites overlap with VBP101 trem-cel study

Trem-cel: Shielded Stem Cell Transplant



VBP101: Phase 1/2a to Assess Safety of Dosing Mylotarg Following Trem-Cel Transplant

Patient Journey

Transplant-eligible AML patients at high risk of relapse

Transplant Decision

Consolidation/Salvage

Conditioning

Infusion

Engraftment

No delay in typical patient transplant process

Maintenance Mylotarg

Starting ~day 60 up to 4 cycles dose escalation 0.5-2 mg/m^2

If relapse occurs:

- Induction-course Mylotarg
- VCAR33^{ALLO} (VBP301)
- Alternative treatments

Donor Journey

Screening

Stem Cell Mobilization, Collection

Related

Unrelated

Trem-cel Manufacturing ~7-day process

Unedited back-up graft

Key Endpoints

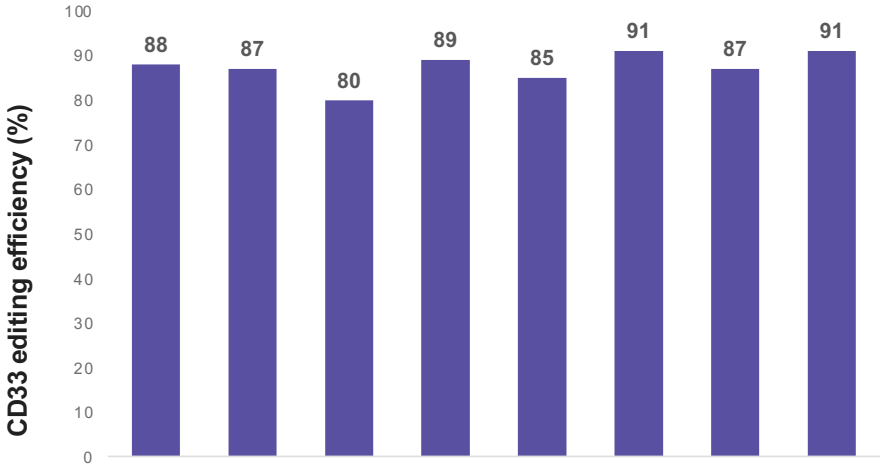
01 **Trem-cel engraftment**

02 **Heme protection from Mylotarg**

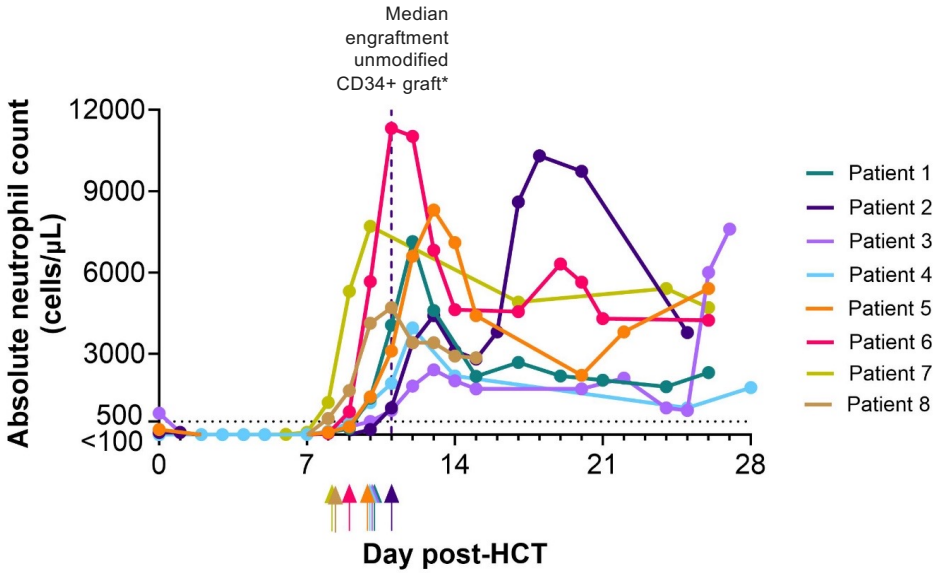
03 **Relapse-free survival**

Proof of Concept: Successful Engraftment of CD33-Deleted HSCs

Highly Efficient Removal of CD33 from Donor HSCs



Timely Post-transplant Neutrophil Engraftment



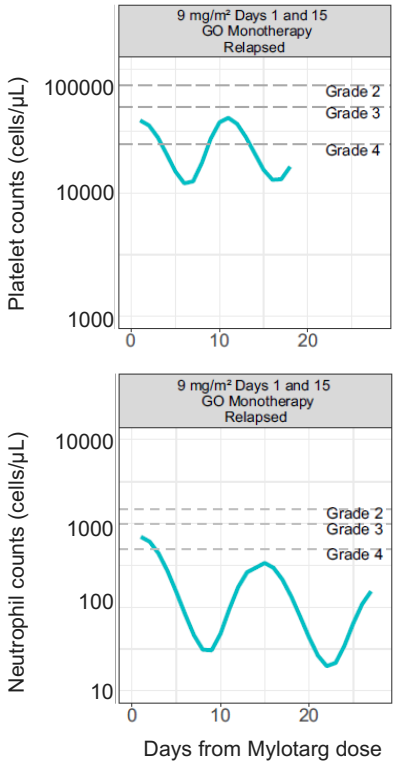
Arrows indicated day of individual patient neutrophil engraftment

Neutrophil engraftment = 3 days ≥ 500 cells/µL

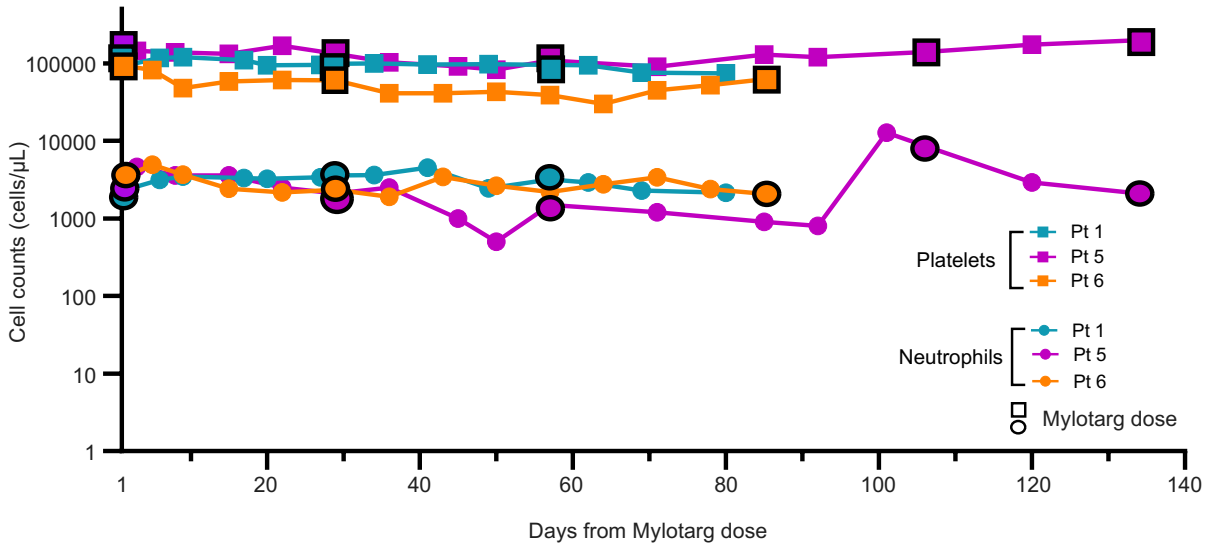
*Luznik L. et al. J Clin Oncol 2022;40(4):356–368

Evidence of Protective Effect from Mylotarg at 0.5 mg/m²

Time Course of Mylotarg-Induced Cytopenias



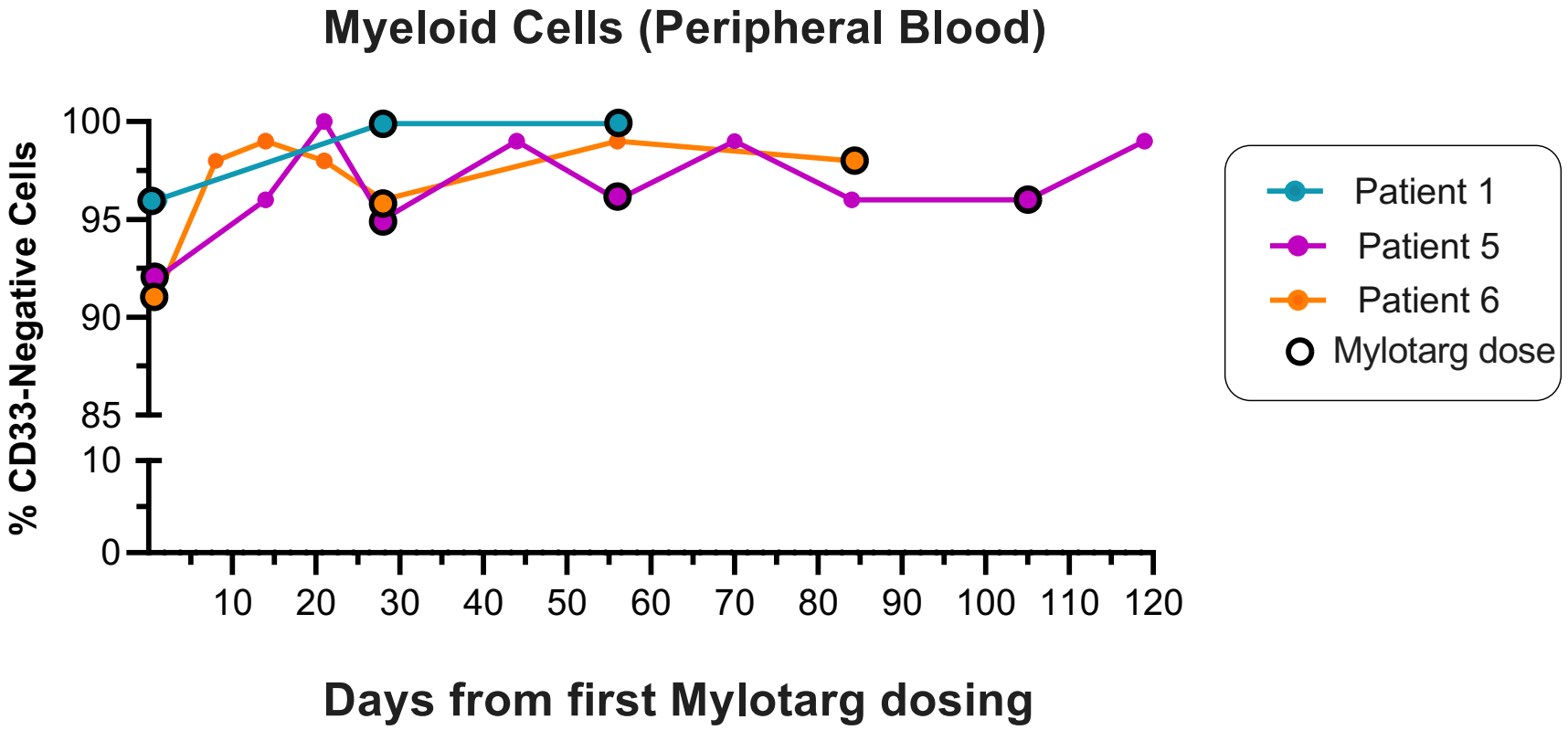
VBP101: Cell Counts Following Mylotarg Dosing at 0.5 mg/m²



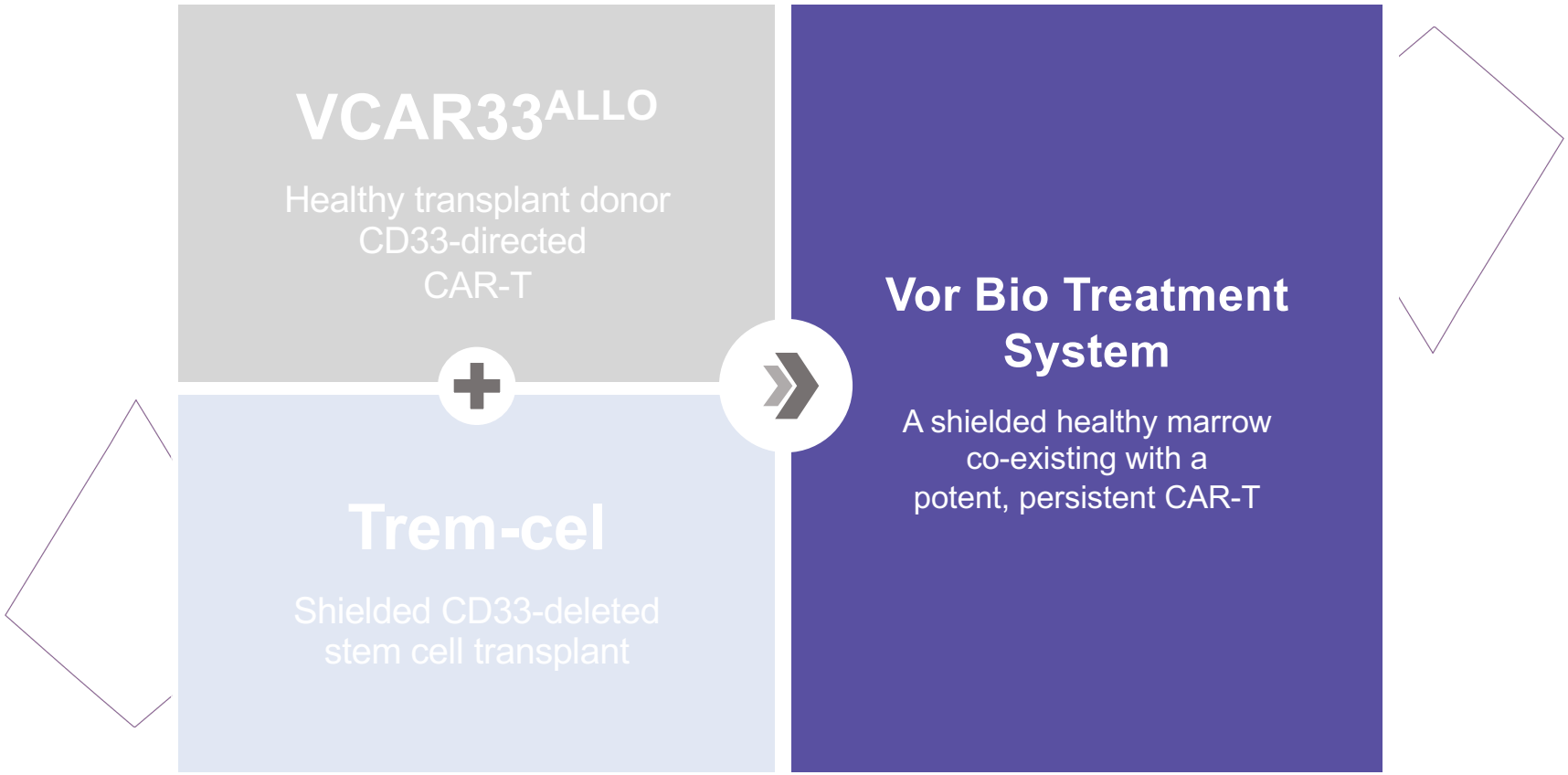
Mylotarg C1 Start: Pt 1 D+68; Pt 5 D+74; Pt 6 D+66 post-HCT

Fostvedt et al. Clin Pharm Thera 2019;106(5):1006-1017

Enrichment of CD33-negative Cells following Mylotarg

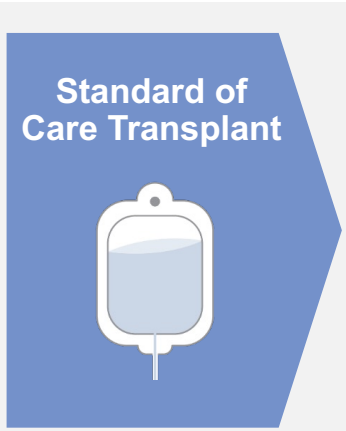


First Ever Cell Therapy Treatment System Aiming to Cure AML

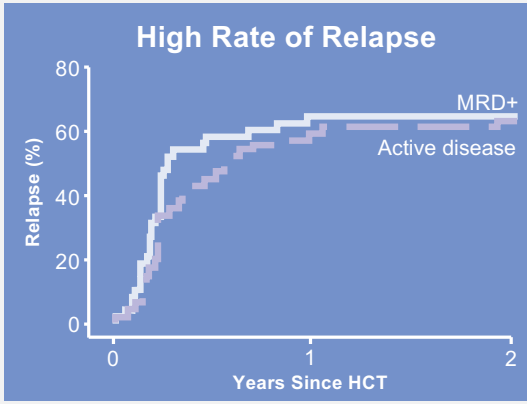


Combining Trem-cel and VCAR33, Aiming for Cures

AML, transplant eligible



Standard of Care Transplant



Any therapy causes deep cytopenias and puts transplant at risk

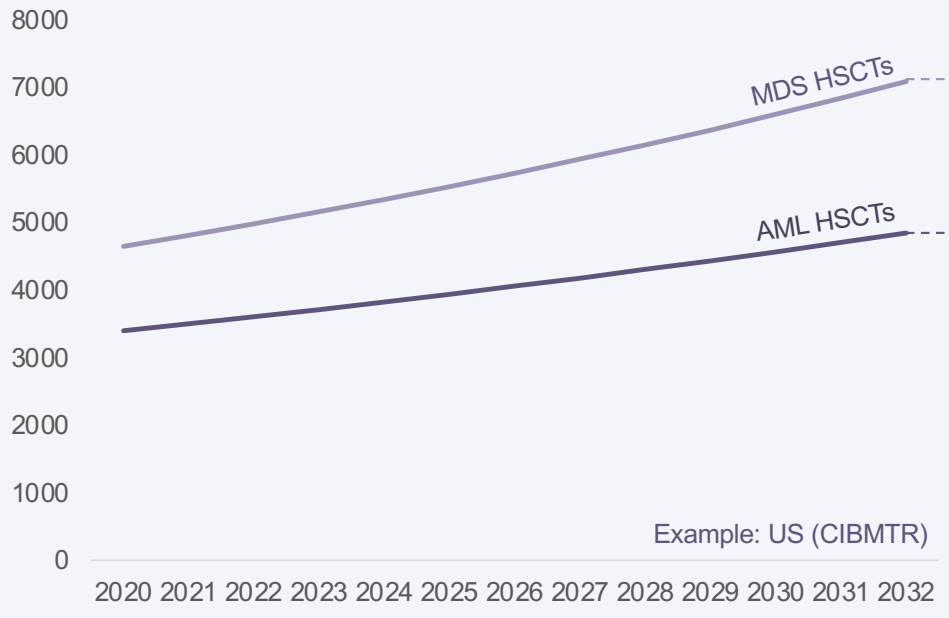
VOR Trem-cel Shielded Transplant

VOR VCAR33 CAR-T

Persistent CAR-T with shielded blood system

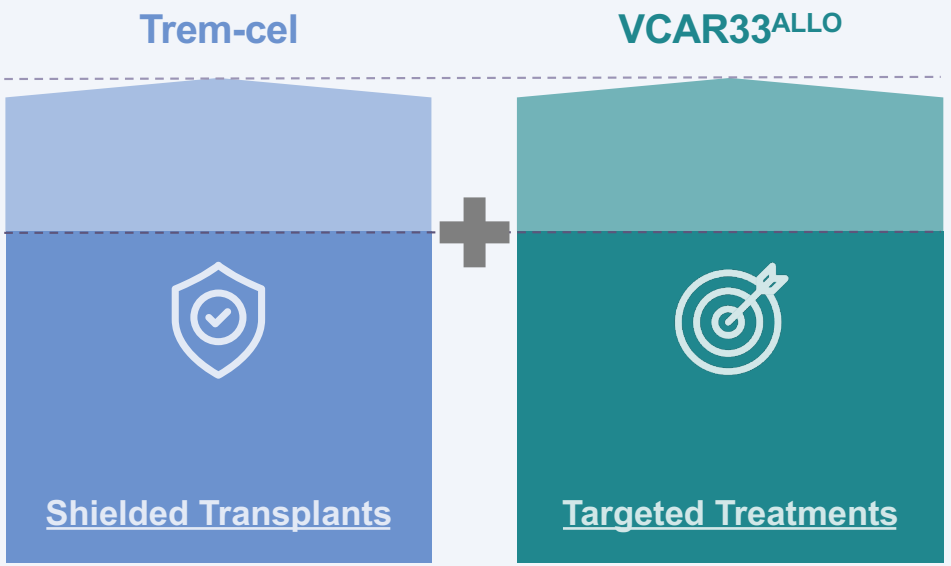
Large Addressable Patient Population for Vor Bio's Treatment System

Surge in Stem Cell Transplants for AML & MDS



Increasing patient eligibility + population growth

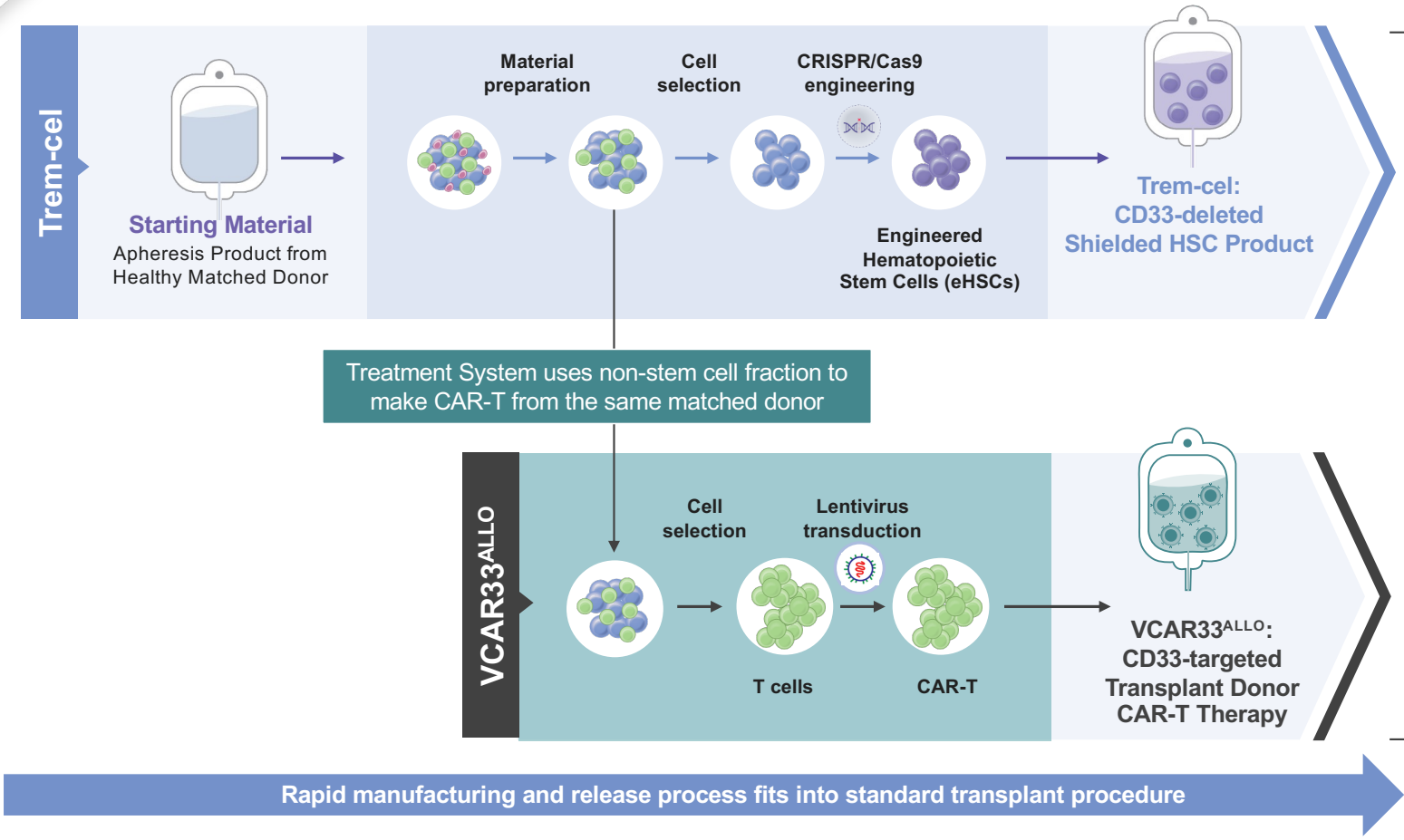
Opportunity to Transform Treatment Paradigm



MS-DRG 014 (allo-HCT) + **Section 108** *(cost-based reimbursement for 100% of stem cell acquisition, processing)*

MS-DRG 018 (CAR-T) base reimbursement rate of $247,939

Proprietary Dual Cell Product Potential



Unique In-house Manufacturing:

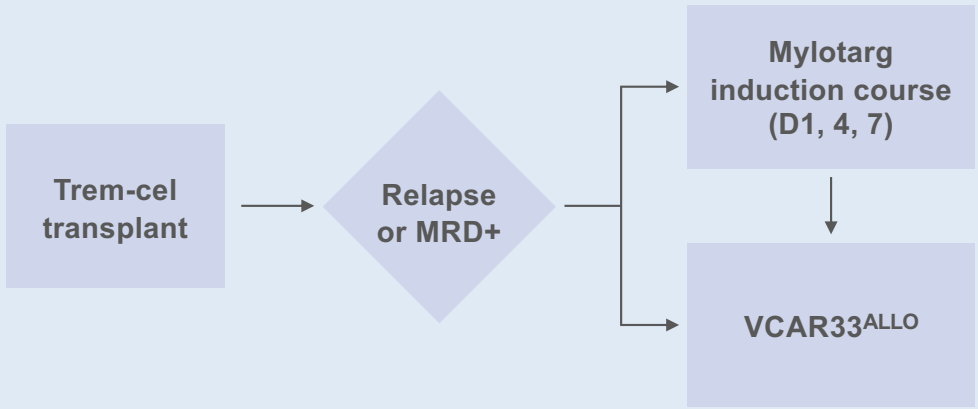
Multi-product GMP facility in Cambridge, MA

Four independent clean rooms and on-site QA/QC

In 2024: Harnessing the Power of Trem-cel and VCAR33

Prior efforts in AML have led to poor response rates (CR < 25%), safety concerns, or both

Opportunity



Activity Benchmark

- Blast count reduction
- Heme protection

Significant Clinical Progress and Upcoming Milestones

	Progress to Date	Upcoming Milestones
Trem-cel	Efficient CD33 deletion Reliable engraftment (8/8) Heme protection from Mylotarg (3/3) Multiple patients treated at 1.0 mg/m^2 dose	Multiple options for patients who relapse: • Induction-course Mylotarg • VCAR33^{ALLO} Clinical data update expected in 2H 2024
VCAR33	Potentially superior transplant donor cell source First patient dosed Jan 2024 Trem-cel patients are eligible	Expecting multiple patients dosed in 1H 2024 Preliminary data anticipated in 2H 2024

Moving Beyond Proof of Concept to Pivotal

Targeting Short Registrational Pathway

Fast Track granted on basis of trem-cel heme protection

- Exploring heme protection endpoints with agency

High unmet need in AML

- Precedence for single-arm pivotal trials
- CR and CR/CRh are approvable endpoints

R/R AML Single Arm Pivotal Trials

Agent	Indication	# pts	Endpoint
Ivosidenib *IDH1, Agios*	R/R AML	174	CR 25% CRh 8%[1]
Enasidenib *IDH2, Agios*	R/R AML	199	CR 19% CRh 4%[2]
Gilteritinib *FLT3, Astellas*	R/R AML	138	CR 12% CRh 9%[3]
Revumenib *KMT2Ar, Syndax*	R/R AML	57	CR 18% CRh 5%[4]
Mylotarg *ADC, Pfizer*	R/R AML	57	CR 26%[5]

CR: Complete Remission CRh: Complete remission with partial hematologic recovery

1. Norsworthy KJ, et. al. FDA Approval Summary: Ivosidenib for Relapsed or Refractory Acute Myeloid Leukemia with an Isocitrate Dehydrogenase-1 Mutation. Clin Cancer Res. 2019 Jun 1;25(11):3205-3209.
2. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-granted-regular-approval-enasidenib-treatment-relapsed-or-refractory-aml
3. Pulte ED, et. al. FDA Approval Summary: Gilteritinib for Relapsed or Refractory Acute Myeloid Leukemia with a *FLT3* Mutation. Clin Cancer Res. 2021 Jul 1;27(13):3515-3521.
4. https://cms.syndax.com/wp-content/uploads/2023/12/Aldoss-2023-AUGMENT-101-3.pdf. Per company, NDA initiated with FDA under RTOR program.
5. https://labeling.pfizer.com/showlabeling.aspx?id=9548

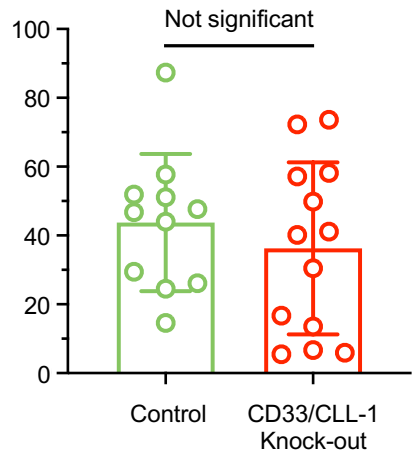
Next-Generation Approaches

Targets Beyond CD33	»	Expansion into additional indications
Multi-targeted CAR-Ts	»	Avoidance of potential tumor escape
Multiplex-edited transplants	»	Broader options for treatment

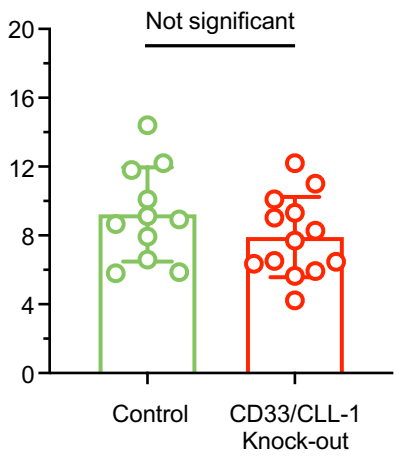
CD33/CLL-1 Double Knock-out Engrafts Normally

16-week Mouse Engraftment of Human HSCs

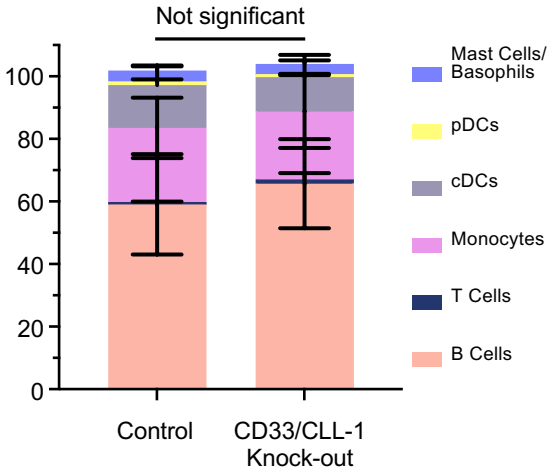
% Human Chimerism



% Human HSCs

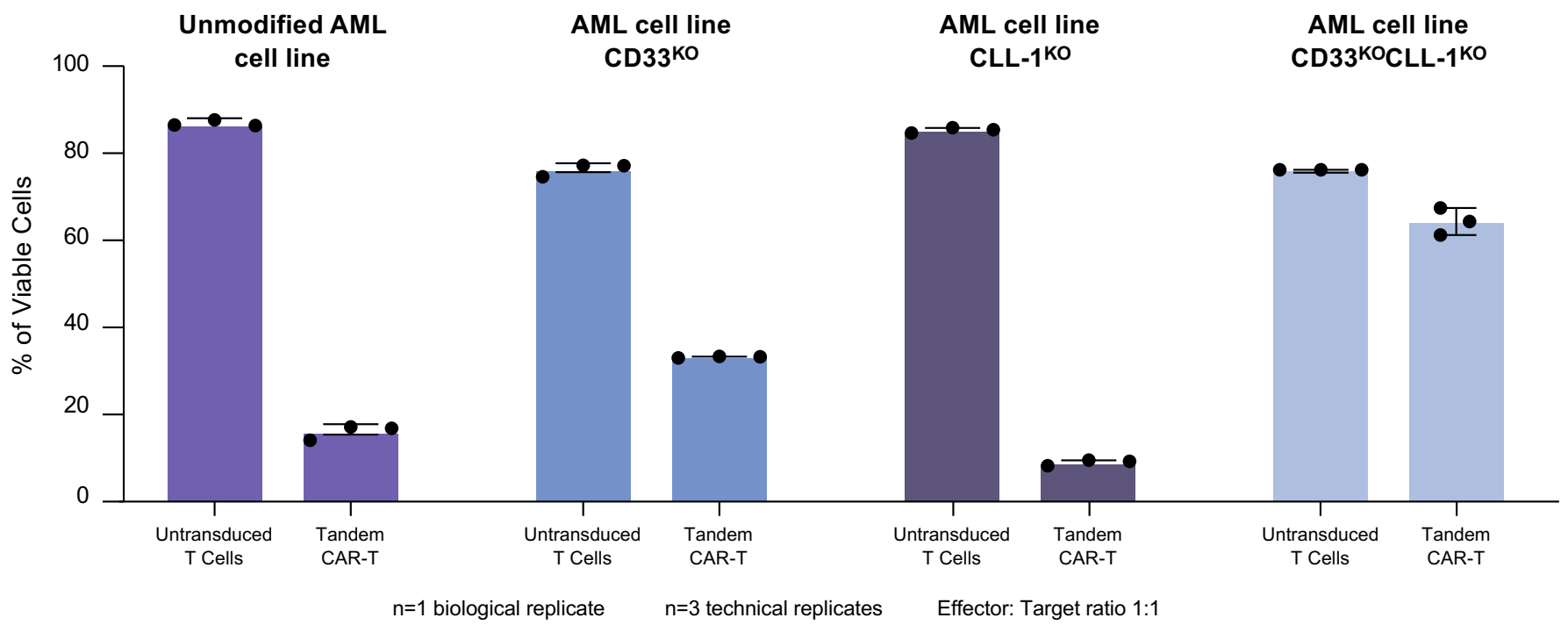


% Multilineage Distribution



In Vitro Proof of Concept for Multi KO Target Cell + Multi-Specific CAR-T

CD33 and CLL-1 Dual-CAR-T Active Against Wild Type and Single Knock-out Target Cells

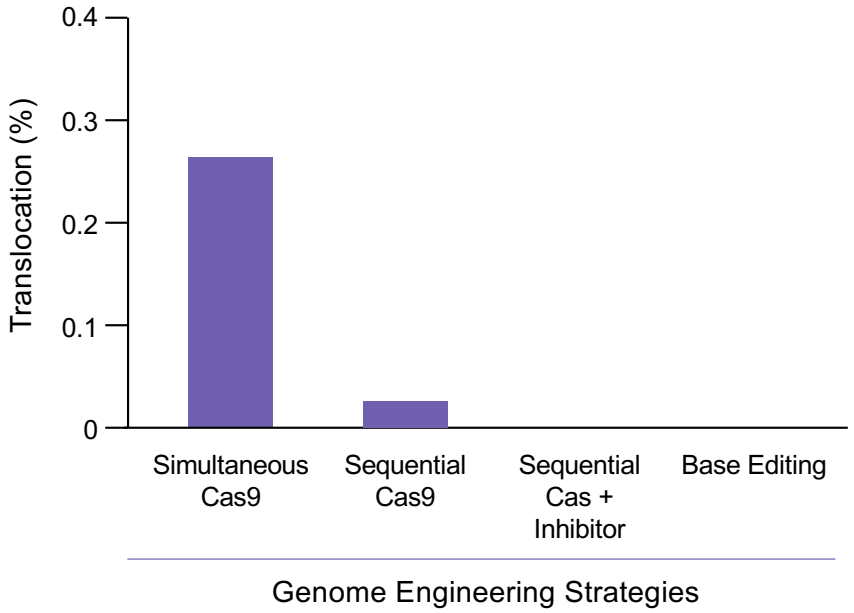


n=1 biological replicate n=3 technical replicates Effector: Target ratio 1:1

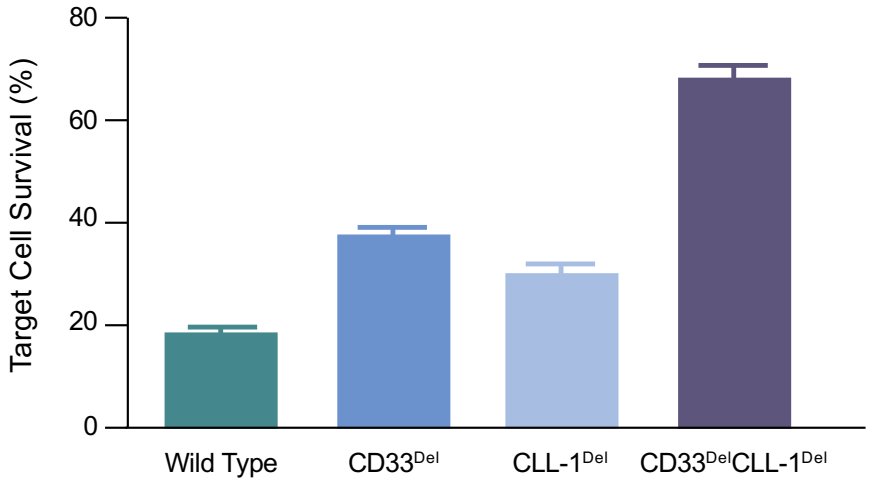
● Denotes individual experiment

Multiplex Editing: Proprietary Capabilities Minimize Translocations and Protects from CAR-T

Minimized Translocation Rate



Cell Protection from CAR-T Killing



Effector : Target = 1:1

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Experienced and Passionate Leadership Team

Robert Ang, MBBS, MBA
President and CEO

Eyal Attar, MD
Chief Medical Officer

Tirtha Chakraborty, PhD
Chief Scientific Officer

Nathan Jorgensen, PhD MBA
Chief Financial Officer

Tania Philipp
Chief People Officer

Robert Pietrusko, PharmD
Chief Regulatory & Quality Officer

John King, MBA
Chief Commercial Officer & Head of Business Development

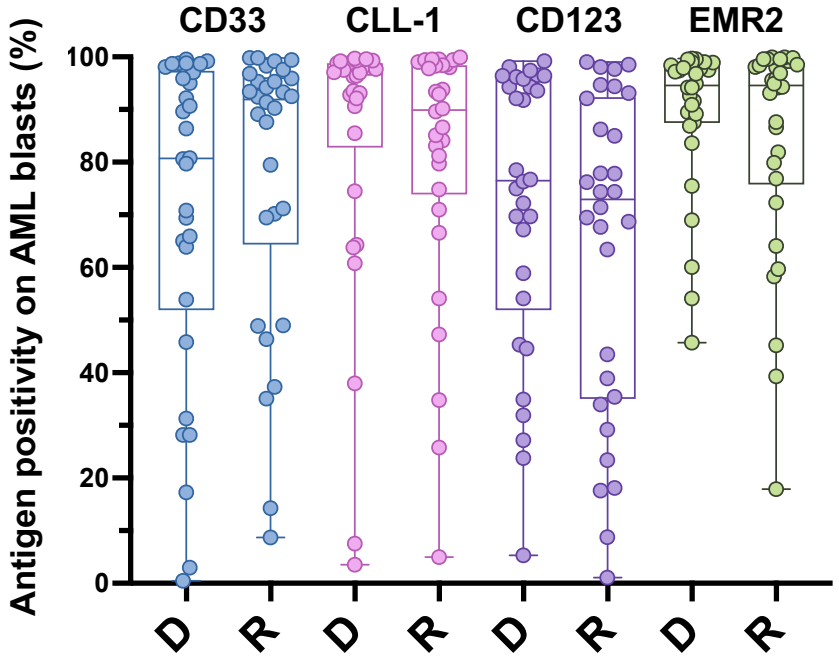
David Phillips, MBA
Senior Vice President, Head of Quality

Samir Vattompadam, MS
Senior Vice President, Portfolio Strategy and Program Management

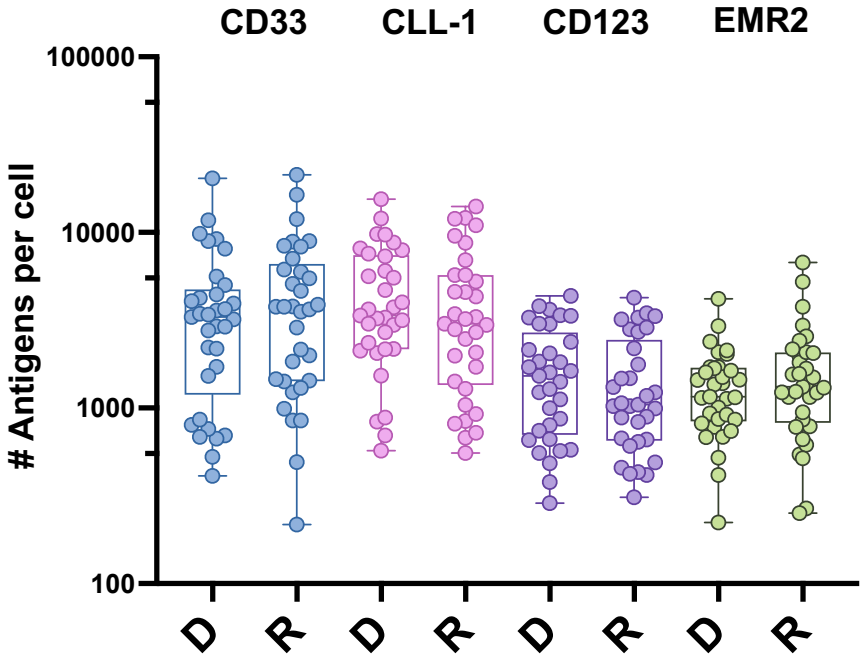
Deep Cell & Gene Therapy Expertise

CD33 is Amongst Highest Quality Targets in AML

Ubiquity of Antigen Expression (Flow Cytometry)



Density of Antigen Expression (QuantiBRITE)

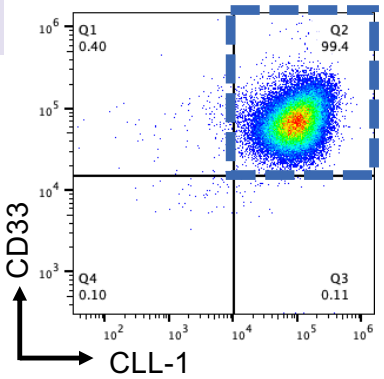


D = Diagnosis **R** = Relapse

Multiplex Editing Strategies Achieve Highly Efficient Double Knock-out

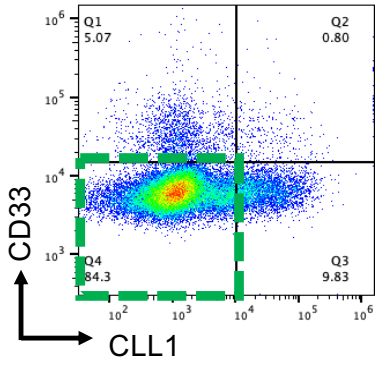
Sequential Cas9 Editing

Mock



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

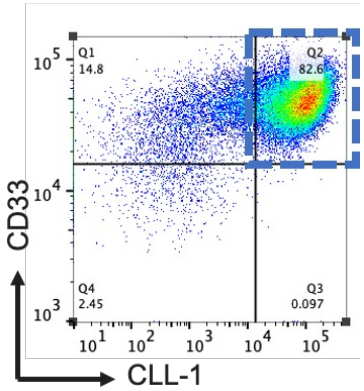
Edited



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

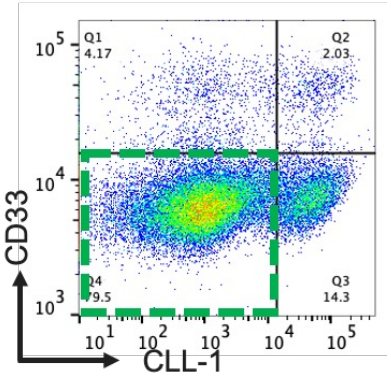
Base Editing

Mock



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

Edited



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

VBP101: Patient Characteristics

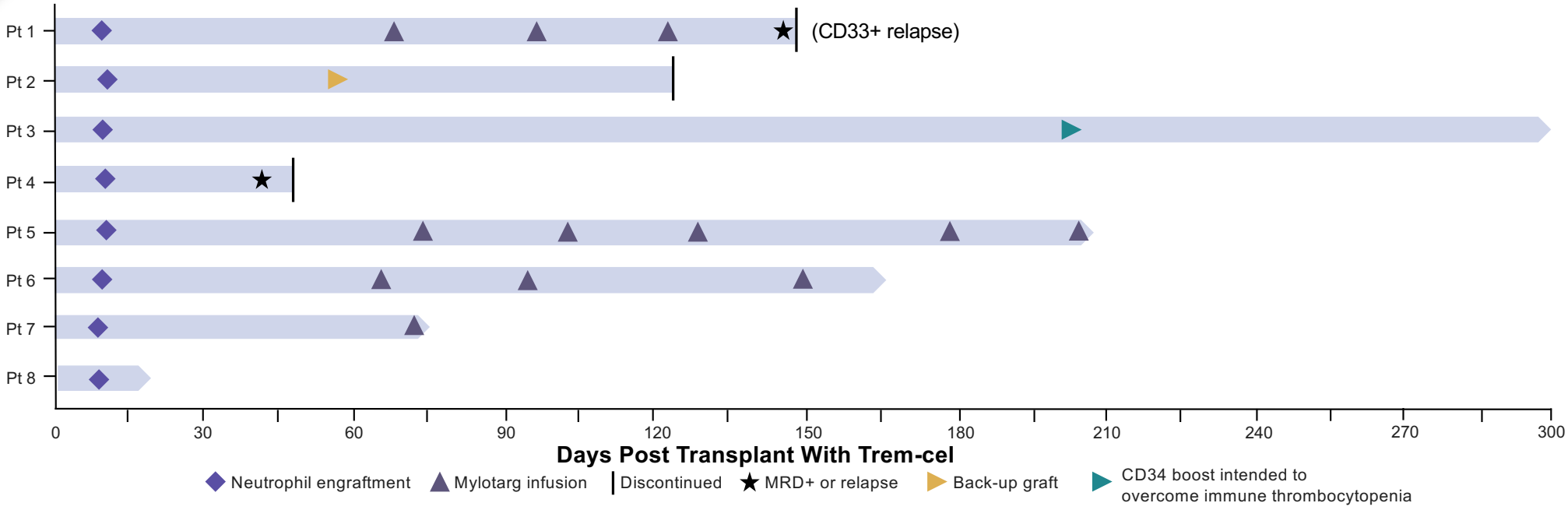
Pt	Age/ Sex	Disease and Genetics	Weight	Donor, Dose, *CD33* gene-editing efficiency
1	64/F	AML-MRC Highly complex cytogenetics; CR2; TP53 mutation MRD: 1.8%	69.9 kg	10/10 HLA MUD 7.6 × 10^6 CD34 cells/kg, 88% *CD33* gene editing
2	32/M	AML after myeloid sarcoma resected from abdomen Inv 16 and +22, t(3;3)	120.7 kg	10/10 HLA MUD 3.2 × 10^6 CD34 cells/kg, 87% *CD33* gene editing
3	55/F	AML-MRC DNMT3A, IDH2 and SMC1A mutations	114.1 kg	10/10 HLA MUD 2.6 × 10^6 CD34 cells/kg, 80% *CD33* gene editing
4	68/M	AML-MRC Complex cytogenetics; active disease; NRAS, ZRSR2, TET2 mutations 16% marrow blasts	72.4 kg	10/10 HLA MSD 5.8 × 10^6 CD34 cells/kg, 89% *CD33* gene editing
5	66/M	Secondary AML KIT D816V, CBL, SRSF2, RUNX1/2, BCORL1 mutations	102.1 kg	10/10 HLA MUD 4.6 × 10^6 CD34 cells/kg, 85% *CD33* gene editing
6	63/F	AML-MRC Highly complex cytogenetics; TP53, NRAS, WT1 mutations	66.2 kg	10/10 HLA MUD 5.7 × 10^6 CD34 cells/kg, 91% *CD33* gene editing
7	67/M	AML with recurrent abnormalities CR2; NPM1, TET2, EZH2, SETBP1, PIGA mutations	72.8 kg	10/10 HLA MUD 9.4 × 10^6 CD34 cells/kg, 87% *CD33* gene editing
8	57/M	AML (myelomonocytic) with nml karyotype CR2 (CRi/CRp)	68.9kg	10/10 HLA MUD 9.5 × 10^6 CD34 cells/kg, 91% *CD33* gene editing

MRC = myelodysplasia-related changes, MRD = Measurable Residual Disease, MUD = Matched Unrelated Donor, MSD = Matched Sibling Donor

All patients received myeloablative conditioning with busulfan/melphalan/fludarabine/rabbit anti-thymocyte globulin (ATG), with exception for patient #3, who received equine ATG.

Data Cutoff: 4 Dec 2023. Presented data from EDC and site/PI communication; pending full source verification

VBP101: Patient Clinical Timelines (Patients 1-8)



Patients Ineligible for Mylotarg:

Patient 2

Secondary graft failure in context of prior sepsis, TMP-SMZ/possible DRESS and persistent hKU1 coronavirus infection. Graft failure resolved after back-up graft given.

Patient 3

Immune thrombocytopenia. Resolving after treatment with IVIg, steroids, rituximab, CD34 boost.

Patient 4

CNS and systemic relapse prior to Mylotarg dosing.

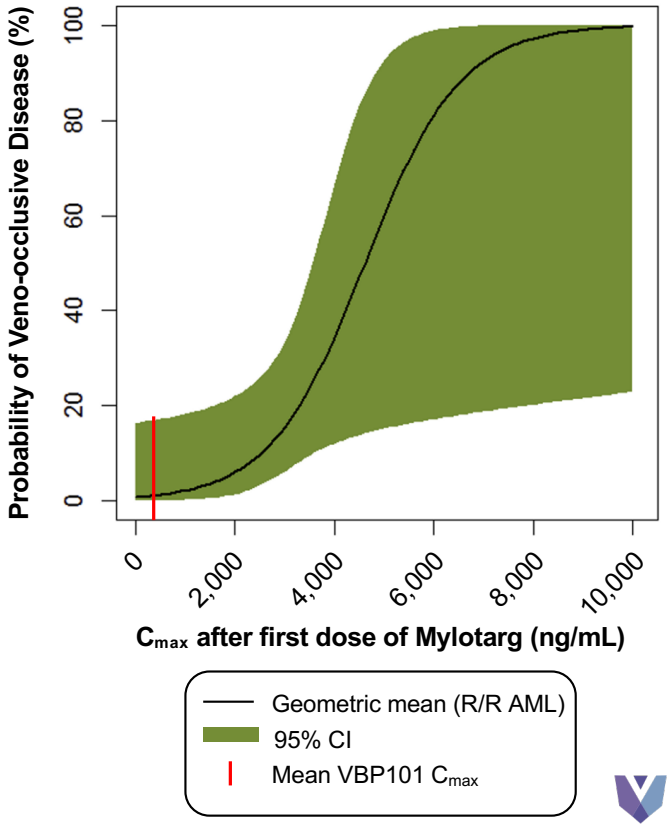
Data cutoff: 04 Dec 2023

VBP101 Patients 1, 5, 6: PK after 1st Dose of Maintenance Mylotarg

Pharmacokinetics

	VBP101	Relapsed/Refractory AML Population (Mylotarg Phase 1 Study 0903A1-101-US)[1]					
Parameter	Mean +/- SD 0.5 mg/m^2	0.25 mg/m^2	0.5 mg/m^2	1 mg/m^2	2 mg/m^2	4 mg/m^2	5 mg/m^2
C_{max} (ng/mL)	**236 (+/- 151)**	15	28	**50**	**411**	611	1,325
AUC_{inf} (Hr*ng/mL)	**10,890 (+/- 13958)**	82	468	**943**	**11,110**	**10,970**	**29,980**

Relationship Between Mylotarg C_{max} and Veno-occlusive Disease in Prior Transplant[1]



[1]Mylotarg ODAC 2017

VBP101: Safety Events Reported as Possibly Related to Either Trem-cel or Mylotarg (AE ≥ Grade 3 or any Grade SAE)

Adverse Event	Max Grade	Related to Trem-cel (# of events)	Related to Mylotarg (# of events)	SAE (# of events)
Anemia	3	1	—	—
Neutropenia	3	1	—	—
Thrombocytopenia	3	2	—	—
Graft Failure	4	1	—	1
Platelet count decreased	3	—	1	—
Platelet count decreased, worsening	3	1	1	—
Worsening maculopapular rash of whole body	2	1	—	1

For Mylotarg dosing:

- No dose-limiting toxicity criteria met
- No increase in liver function tests above upper limit of normal
- No observed sinusoidal obstruction syndrome / veno-occlusive disease

Data as of Oct. 31, 2023, presented at HSCT[2]

VCAR33^{AUTO} Shows Signs of Activity; VCAR33^{ALLO} Potentially More Active

VCAR33^{AUTO} (NCI CD33CART)

- Autologous starting material
- 6-site IST
- Young adults and children (median 16 y, range 1-35)
- Academic manufacturing process
- Accepted for oral presentation at ASH
  - N=24 enrolled, 19 infused
  - Manageable tox (n=4 with CRS ≥ Grade 3)

Dose (CAR$^+$ cells/kg)	Total	3 x 10^5	1 x 10^6	3 x 10^6	1 x 10^7
# infused	19	3	3	7	6 (resp assess in 5)
# with CR, (%)	2 (11%)	0 (0%)	0 (0%)	0 (0%)	2 (40%)*

Data from ASH 2023 Abstract: https://ash.confex.com/ash/2023/webprogram/Paper179667.html

VCAR33^{ALLO}

- Transplant donor starting material
- FPD January 2024
- Targeting ~12 sites
- Streamlined manufacturing process with objective of stem like cell phenotype
- Allows trem-cel patients to enroll
- Starting dose 1 x 10^6 CAR$^+$ cells/kg

*CR achieved alongside myeloid aplasia, which could potentially be obviated with a trem-cel transplant