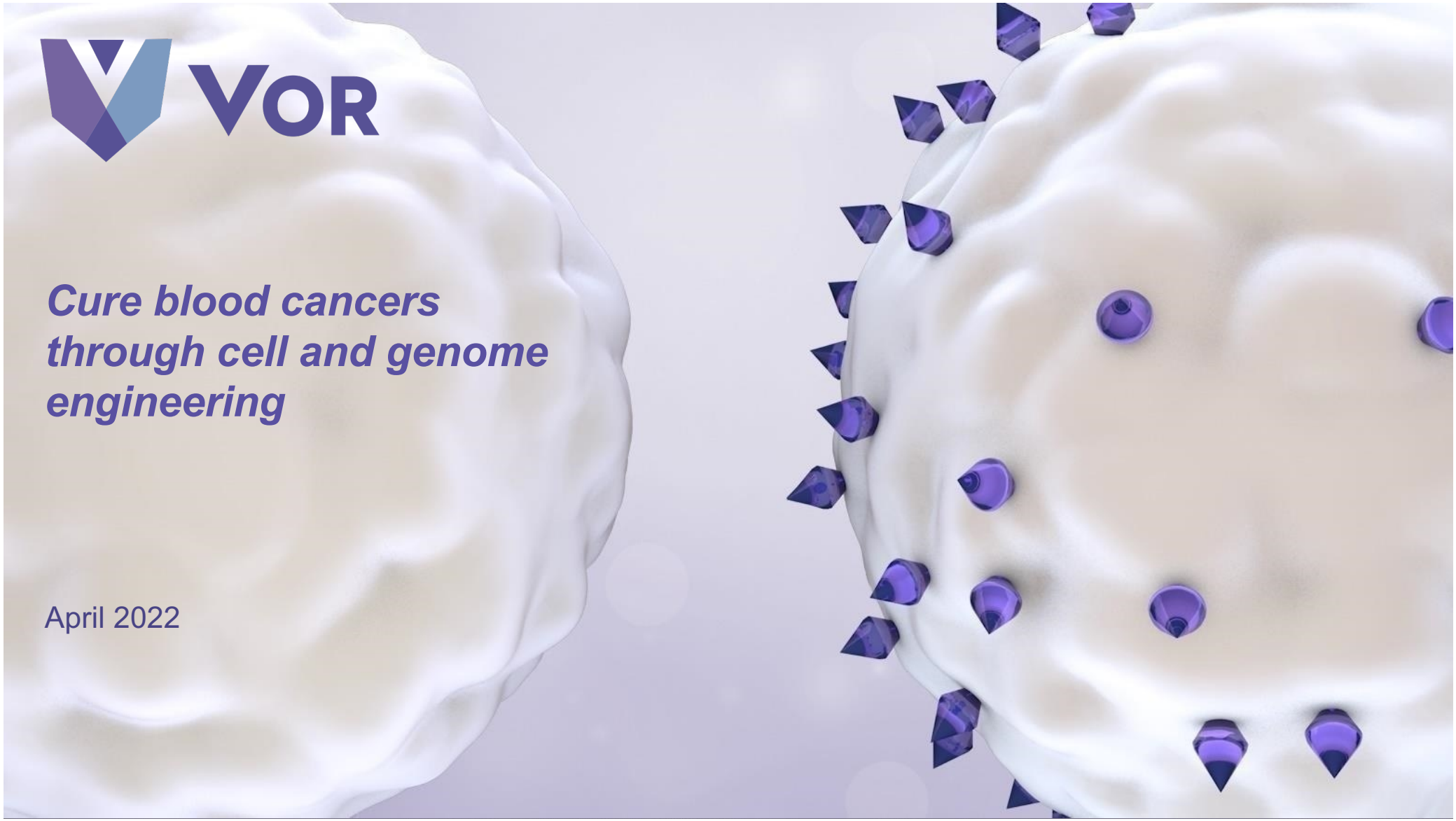
VOR

Cure blood cancers through cell and genome engineering

April 2022



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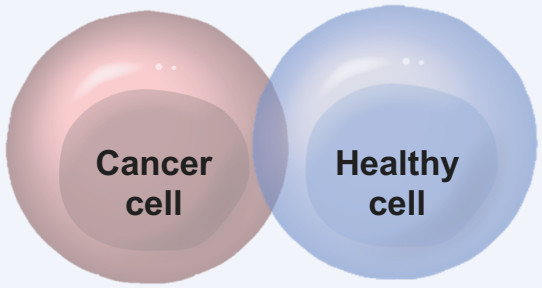
VCAR33^{AUTO} and NMDP-Sponsored Trial. A T cell therapy using the same chimeric antigen receptor construct as VCAR33^{ALLO} is being studied in a Phase 1/2 clinical trial sponsored by the National Marrow Donor Program ("NMDP"), and timing of data release is dependent on the investigators conducting the trial. Although we are not the sponsor of this trial, the NMDP has permitted us to cross-reference its IND for this trial in future IND applications that we may submit with the FDA. While we do not believe that we need to demonstrate comparability of our VCAR33^{ALLO} candidate since we intend to rely on initial clinical data from our VCAR33^{ALLO} program, if the U.S. Food and Drug Administration (the "FDA") disagrees, we may have to demonstrate comparability. The FDA may also reject the sufficiency of the data to support it or disagree with our ability to reference the data generated by NMDP in any IND we may file for VCAR33^{ALLO} or the VOR33 + VCAR33 Treatment System. For more information regarding the NMDP trial, see "Risk Factors - We have not successfully tested our product candidates in clinical trials and any favorable preclinical results are not predictive of results that may be observed in clinical trials" in our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC and such other filings that we may make with the SEC from time to time.

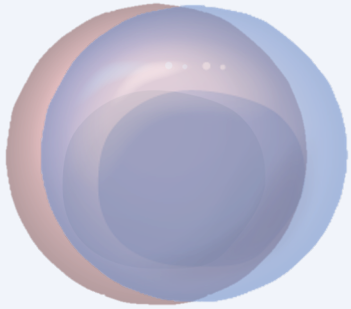
Changing the Thinking on Tumor Targeting

Traditional Paradigm for Drug Development



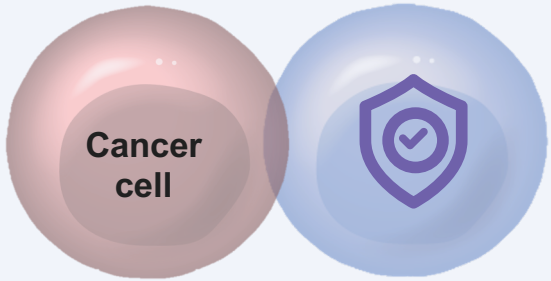
Target cancer antigens to kill cancer cells

Problem



Few unique cancer antigens, so drugs kill both cancer and healthy cells through **on-target toxicity**

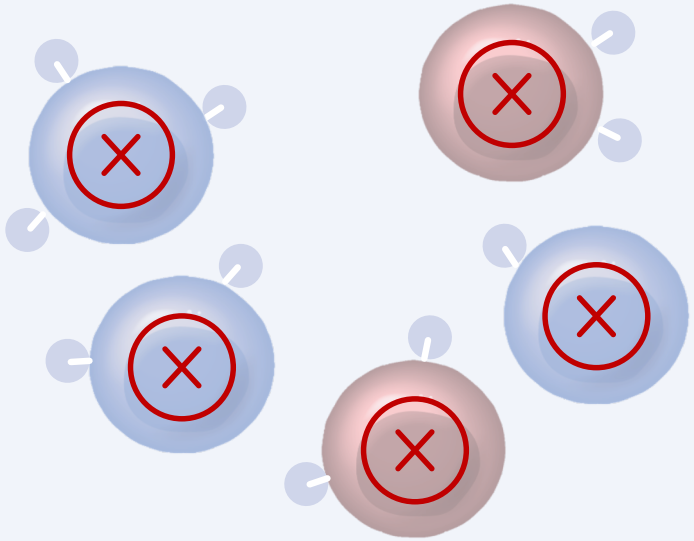
Vor Bio Paradigm: Engineered HSCs (eHSCs)



Remove target expression on healthy cells so that killing is **cancer-specific**

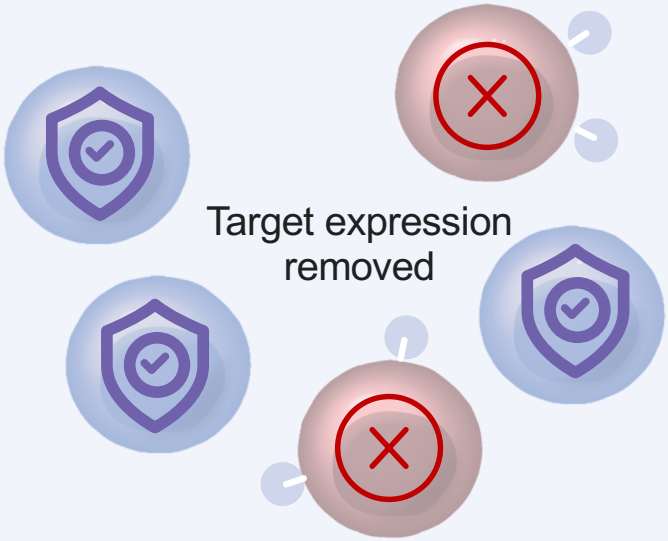
Protected eHSCs 'Invisible' to Targeted Therapies

Current Targeted Therapies



On-target toxicity

Protected eHSCs



Cancer-specific killing

The Vision: eHSC + CAR-T Treatment Systems

VOR33

Treatment-resistant HSC transplant

+

Mylotarg

1st generation antibody-drug conjugate

Clinical proof of concept in 2022

- Engraftment
- Heme protection

VOR33

Treatment-resistant HSC transplant

+

VCAR33

CD33-directed CAR-T programs

VCAR33^{AUTO}

- In Phase 1/2 NMDP-sponsored trial

VCAR33^{ALLO}

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

Multiplex-edited HSCs

Multi-treatment-resistant HSC transplant

+

Multi-specific CAR-Ts

Abound Bio collaboration

Addresses tumor heterogeneity and potential escape mechanisms

Expanding Pipeline Driven by Innovative Platform

Description			Preclinical		Clinical		Anticipated Milestones
Program	**Modality**	**Indication**	**Discovery/ Validation**	**IND-Enabling**	**Phase 1/2**	**Phase 2/3**	
VOR33 + Mylotarg	**eHSC + ADC**	AML					2H 2022: Initial clinical data
		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*				2022: Initial monotherapy clinical proof-of-concept data*
VOR33 + VCAR33 Treatment System	**eHSC + CAR-T**	AML					IND filing following initial VOR33 and VCAR33^{ALLO} data
VOR33-CLL1 + 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. See "Disclaimer" slide for more information.*

VOR33: CD33-Deleted eHSC

VOR33

Treatment-resistant
HSC transplant

+

Mylotarg

1st generation
antibody-drug conjugate

VOR33

Treatment-resistant
HSC transplant

+

VCAR33

CD33-directed
CAR-T programs

Multiplex-edited HSCs

Multi-treatment-resistant
HSC transplant

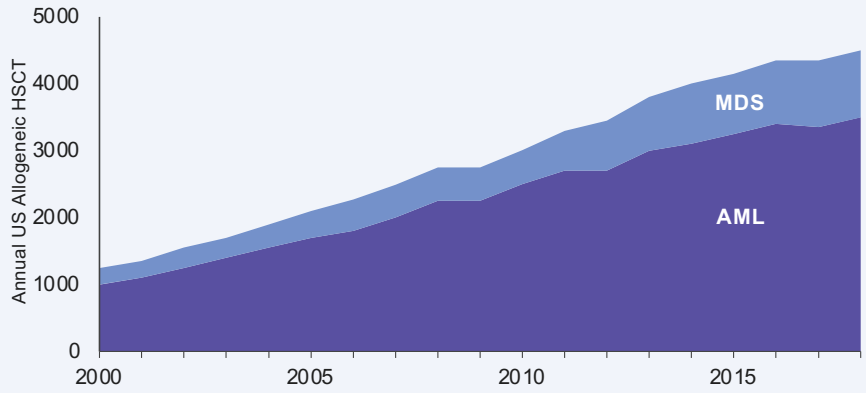
+

Multi-specific CAR-Ts

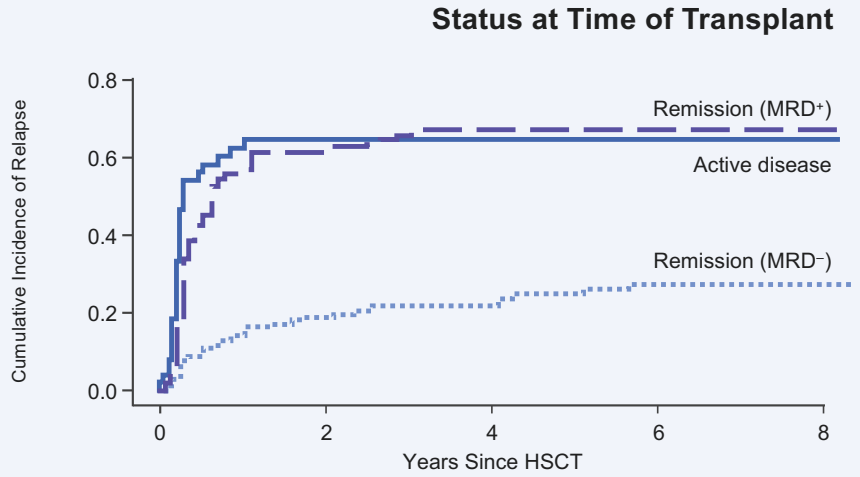
Abound Bio collaboration

AML Unmet Need Is Large and Increasing

Use of Transplant is Increasing…

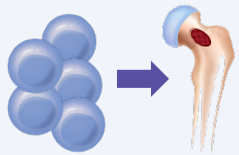


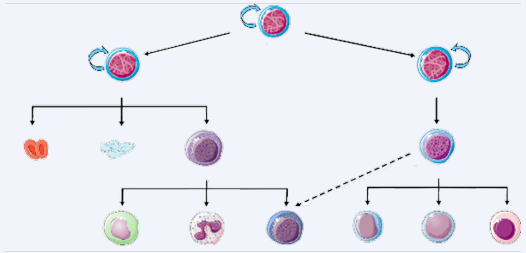
…Though Still Frequent Relapse Post-Transplant

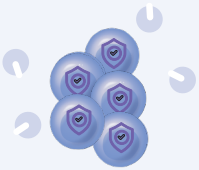


For patients who relapse post-transplant, 2-year survival is <20%

Preclinical Validation of CD33 Deletion in HSCs



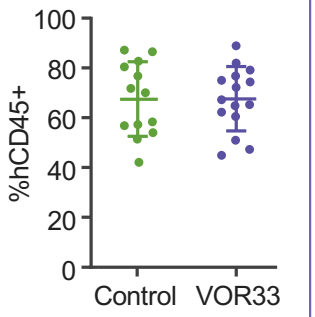




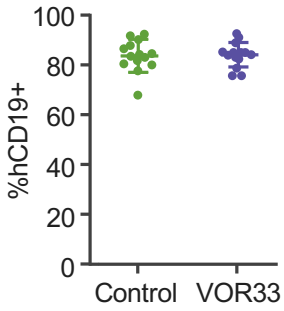
	1. Homing	2. Engraftment		3. Survival
	Migrate to bone marrow	Repopulate the blood system	Fully functional blood cells	Resistance to toxic therapy
VOR	✓	✓	✓	✓
Columbia University	✓	✓	✓	✓
Fred Hutch	✓	✓	✓	✓
Penn Medicine	✓	✓	✓	✓

VOR33: No Observed Impact on Cell Populations or Function

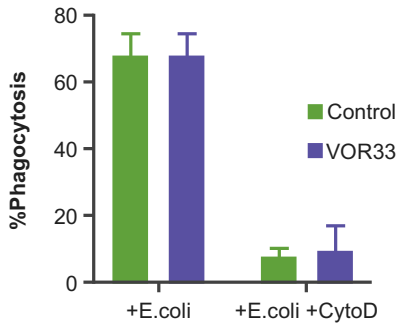
Bone Marrow Cells



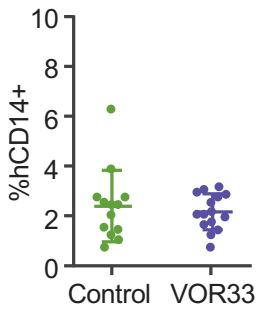
B Cells

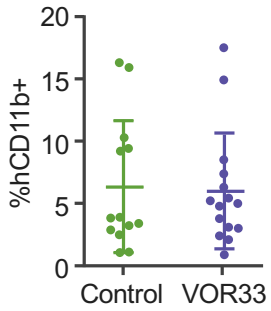


Phagocytosis

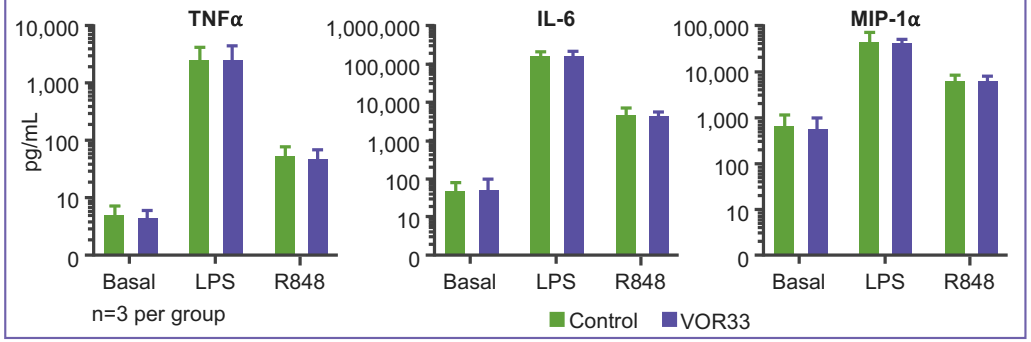


Myeloid Cells





Cytokine Production

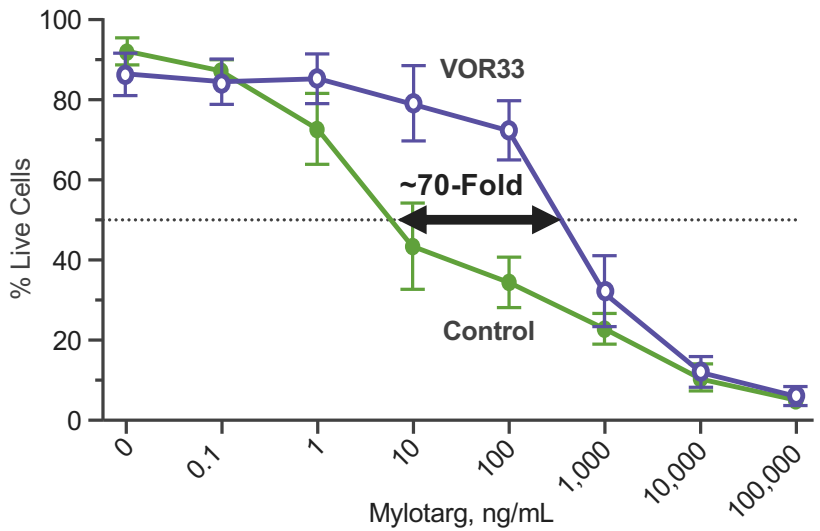


Strongest Supportive Evidence for CD33 Dispensability: Human Genetics

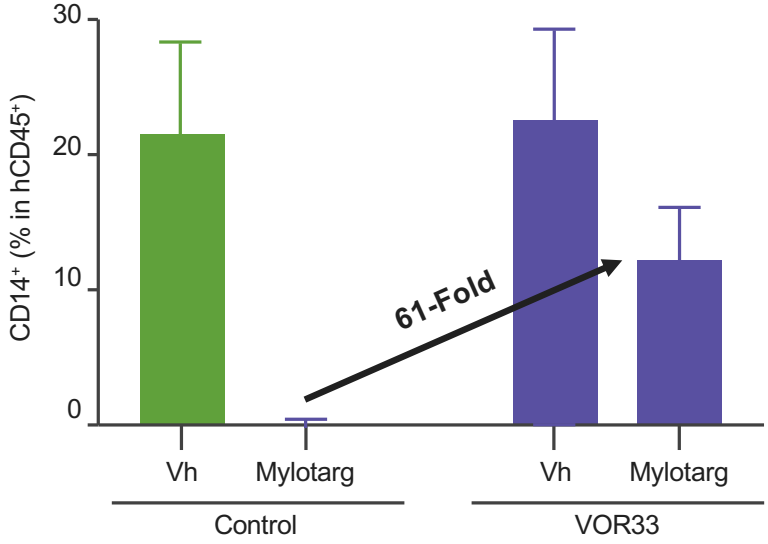
65 individuals with homozygous loss-of-function mutations in CD33	176 individuals with homozygous loss-of-function mutations in CD33
in Genome Aggregation Database	in UK Biobank

VOR33: Resistance to CD33 Therapy

In Vitro



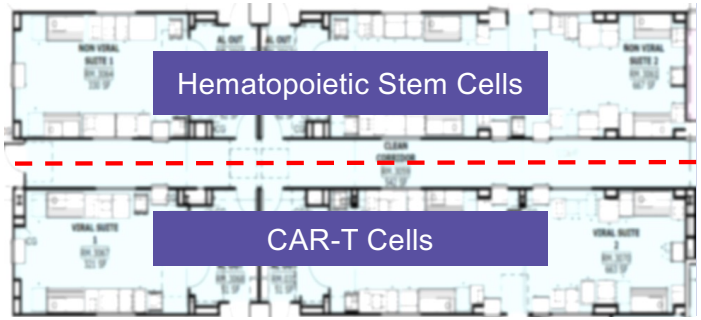
In Vivo



- Engineered cells were not enriched for CD33 deletion and some cell death was expected based on residual CD33 expression
- Free calicheamicin dissociated from Mylotarg may have led to non-specific cell death

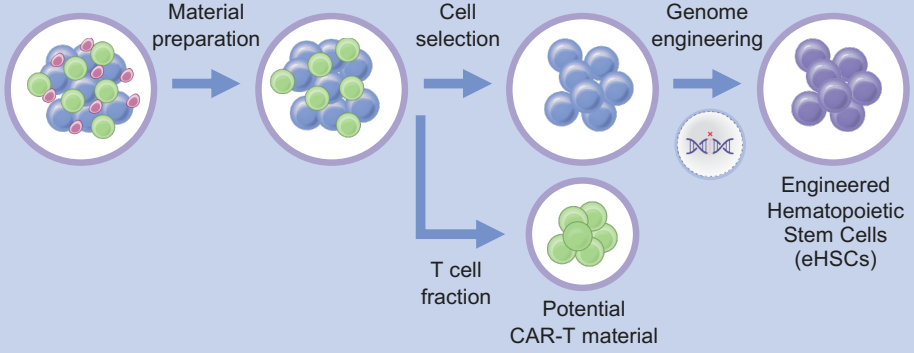
VOR33: Streamlined Cell Manufacturing Process

Vor Bio is building a fully integrated clinical manufacturing facility for eHSC and CAR-T drug products

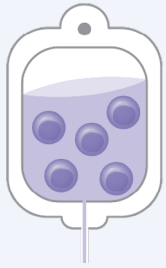


Starting Material
Apheresis Product from Healthy Matched Donor

Overnight Shipped



Overnight Shipped

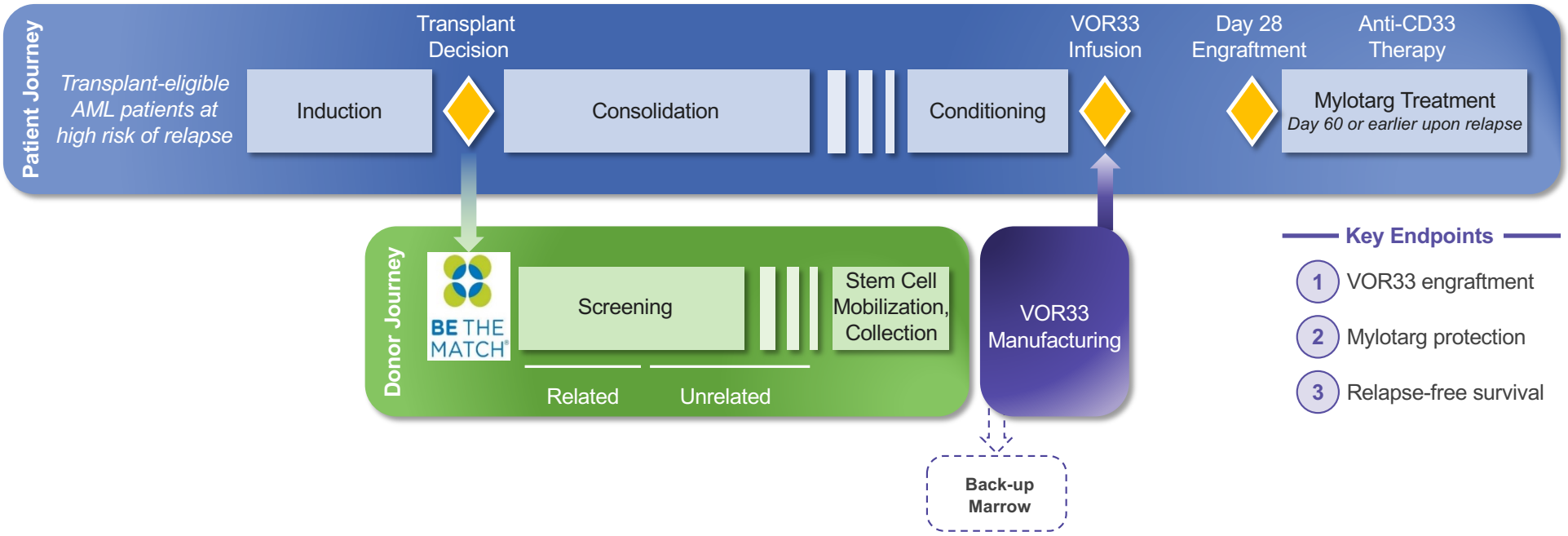


VOR33 eHSC Drug Product
Ready for Patient Dosing

VOR33: ~3-day production process; 7–10-day vein-to-vein time

- No new genetic material nor viral vectors
- No cell expansion

VBP101: VOR33 + Mylotarg Phase 1/2a Clinical Trial



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)
- • WashU Siteman Cancer Cntr. (MO)
- • Fred Hutchinson Cancer Ctr. (WA)
- • The National Cancer Institute (MD)

VBP101: Defining Success

Measure	Current Standard of Care	VBP101
Short-term Engraftment	~95% typical for modern transplants[1]	Expect equivalent for VOR33
Protection against Mylotarg-mediated heme toxicities	Hematological toxicity expected in virtually all patients dosed down to 0.25 mg/m^2 [2]	VOR33 allows improved tolerability with less severe cytopenia enabling repeat Mylotarg dosing
Clinical outcomes*	Relapse-free survival as poor as 28% (1-year) and 25% (2-year) post-HCT[3]	Trending towards improved outcomes due to post-HCT therapy

1. Olsson, et al. Leukemia. (2015) 29, 1754–1762. 2. Sievers, et al. Blood (1999) 93 (11): 3678–3684. 3. Walter, et al. Blood (2013) 122 (10): 1813–1821.
* VBP101 not designed for comparative efficacy outcomes

VCAR33: CD33-Directed CAR-T Programs

VOR33

Treatment-resistant
HSC transplant

+

Mylotarg

1st generation
antibody-drug conjugate

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Treatment-resistant
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VCAR33

CD33-directed
CAR-T programs

Multiplex-edited HSCs

Multi-treatment-resistant
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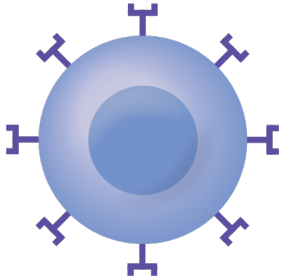
Multi-specific CAR-Ts

Abound Bio collaboration

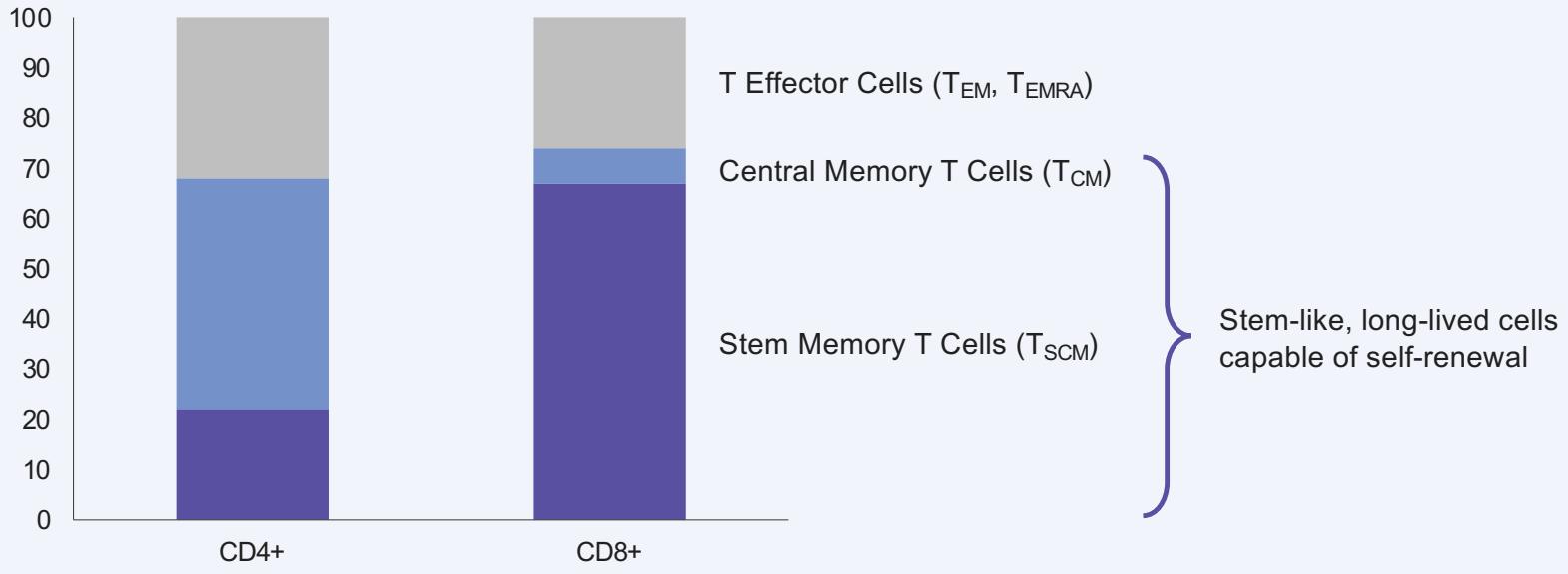
VCAR33 CD33-Directed CAR-T Programs



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 Initial data expected in 2022		IND expected 1H 2023

Vor's T Cell Manufacturing Process Preserves Stemness

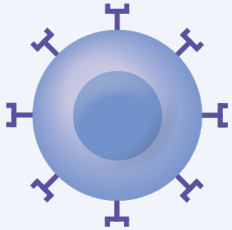
T Cell Phenotype from VCAR Process



Vision: VOR33 + VCAR33 Treatment System

VOR33
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

VOR33

Treatment-resistant HSC transplant

+

Mylotarg

1st generation antibody-drug conjugate

VOR33

Treatment-resistant HSC transplant

+

VCAR33

CD33-directed CAR-T programs

Multiplex-edited HSCs

Multi-treatment-resistant HSC transplant

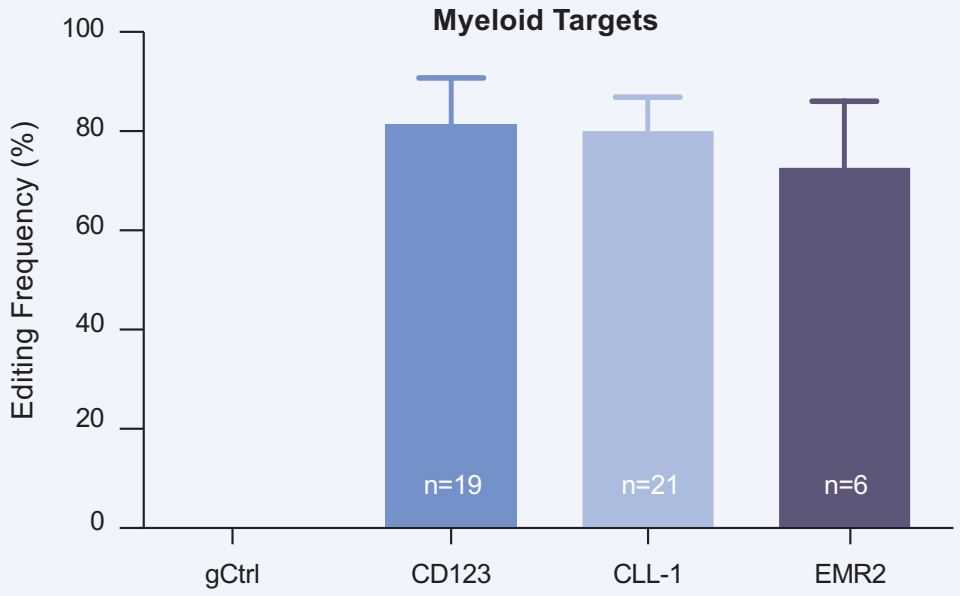
+

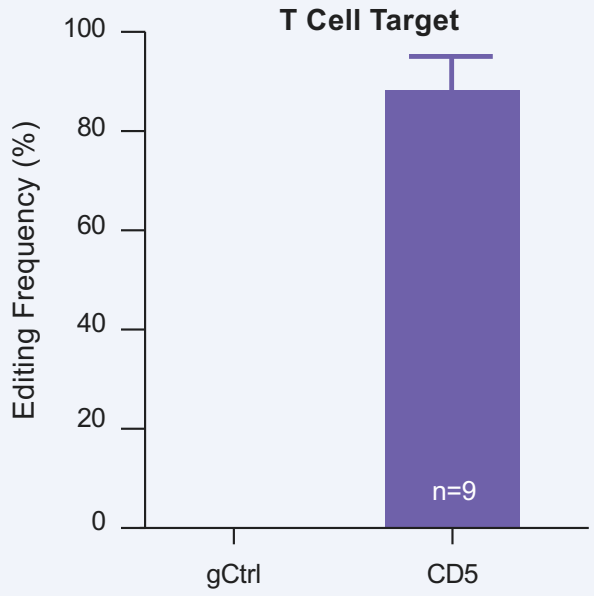
Multi-specific CAR-Ts

Abound Bio collaboration

High Editing Frequency for Next-Generation Targets

CD34+ Editing Frequency

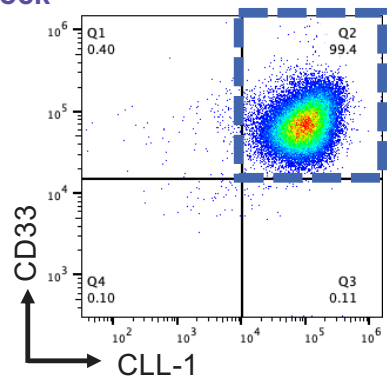




Multiplex Editing Strategies Achieve Highly Efficient Double Knock-out

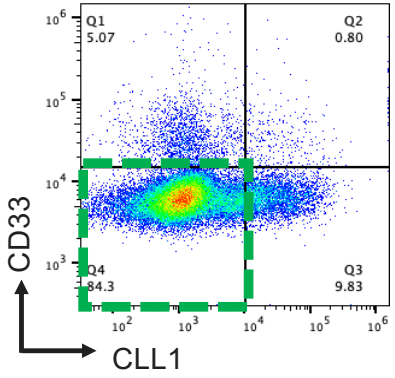
Sequential Cas9 Editing

Mock



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

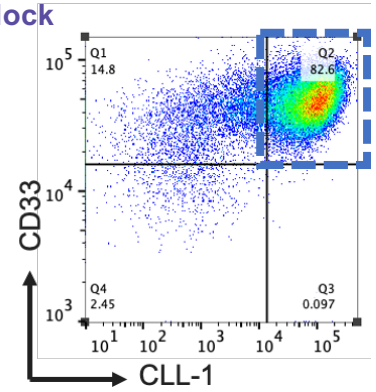
Edited



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

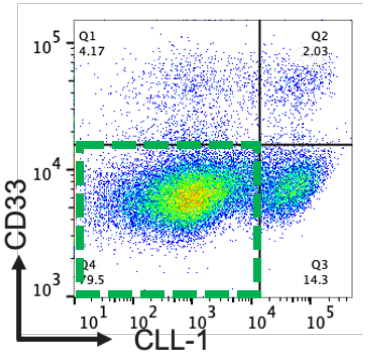
Base Editing

Mock



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

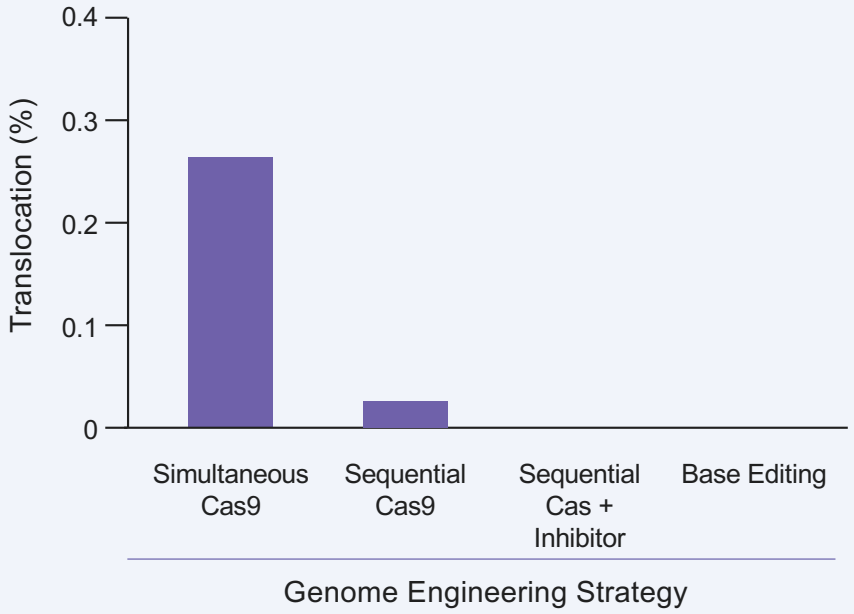
Edited



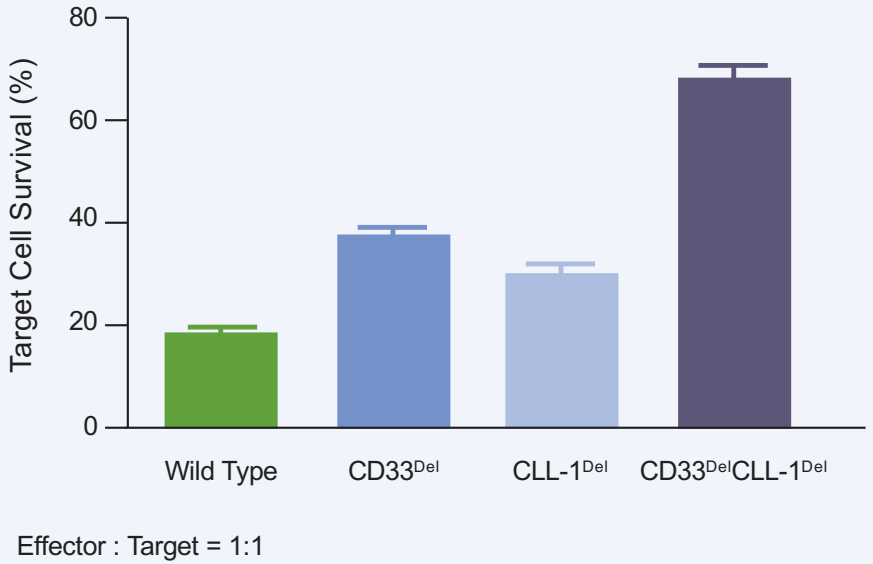
$CD33^{-}CLL\text{-}1^{-}$
Double KO
79.5%

Multiplex Editing: Minimizing Translocations and CAR-T Protection

Minimizing Translocation Rate



Cell Protection from CAR-T Killing



Effector : Target = 1:1

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

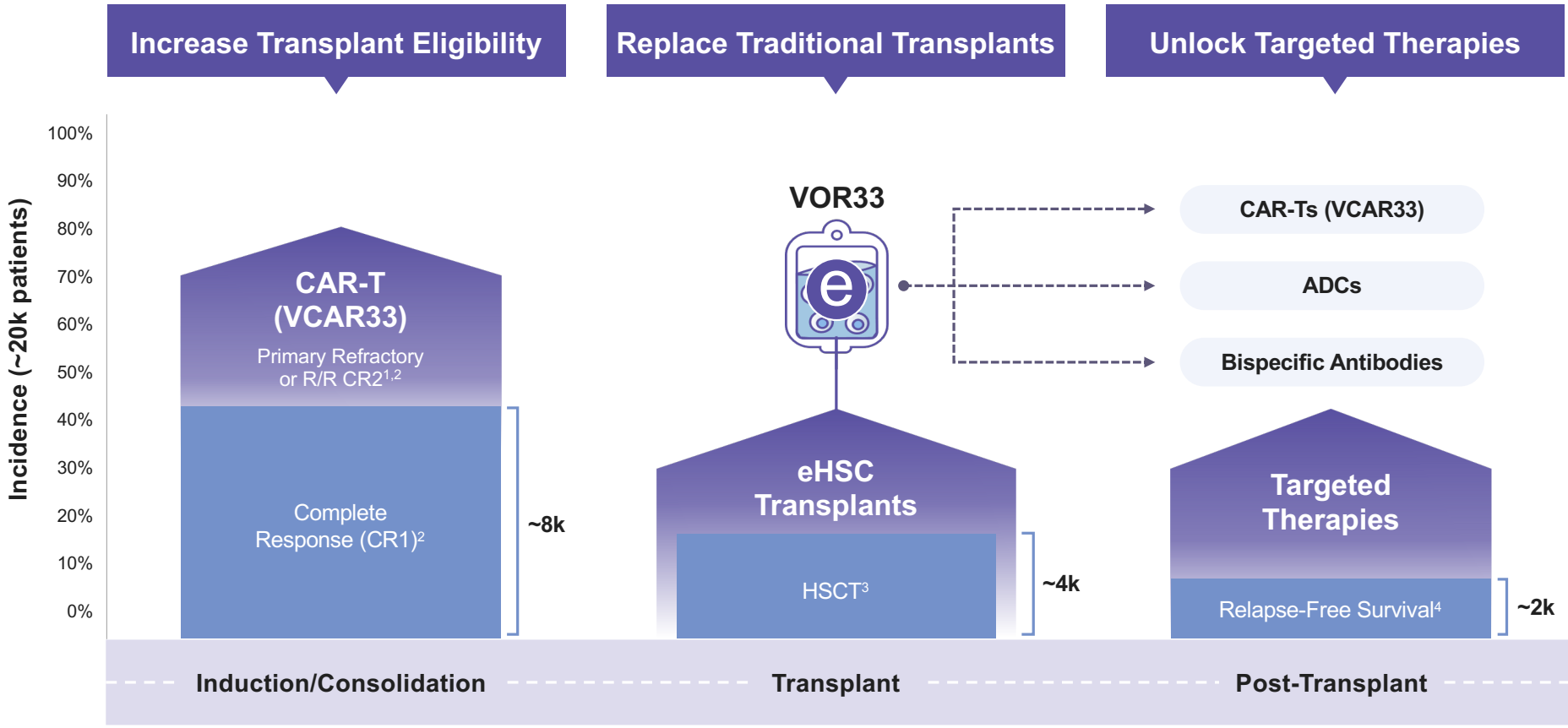
Curative Intent

- 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
  - Multiple upcoming milestones:
    - VOR33 initial clinical data in second half of 2022
    - VCAR33^{AUTO} initial clinical data in 2022
    - VCAR33^{ALLO} IND filing in the first half of 2023
- Building out in-house GMP manufacturing capability to support clinical development
- Experienced and proven management team
- Cash runway into Q4 2023

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