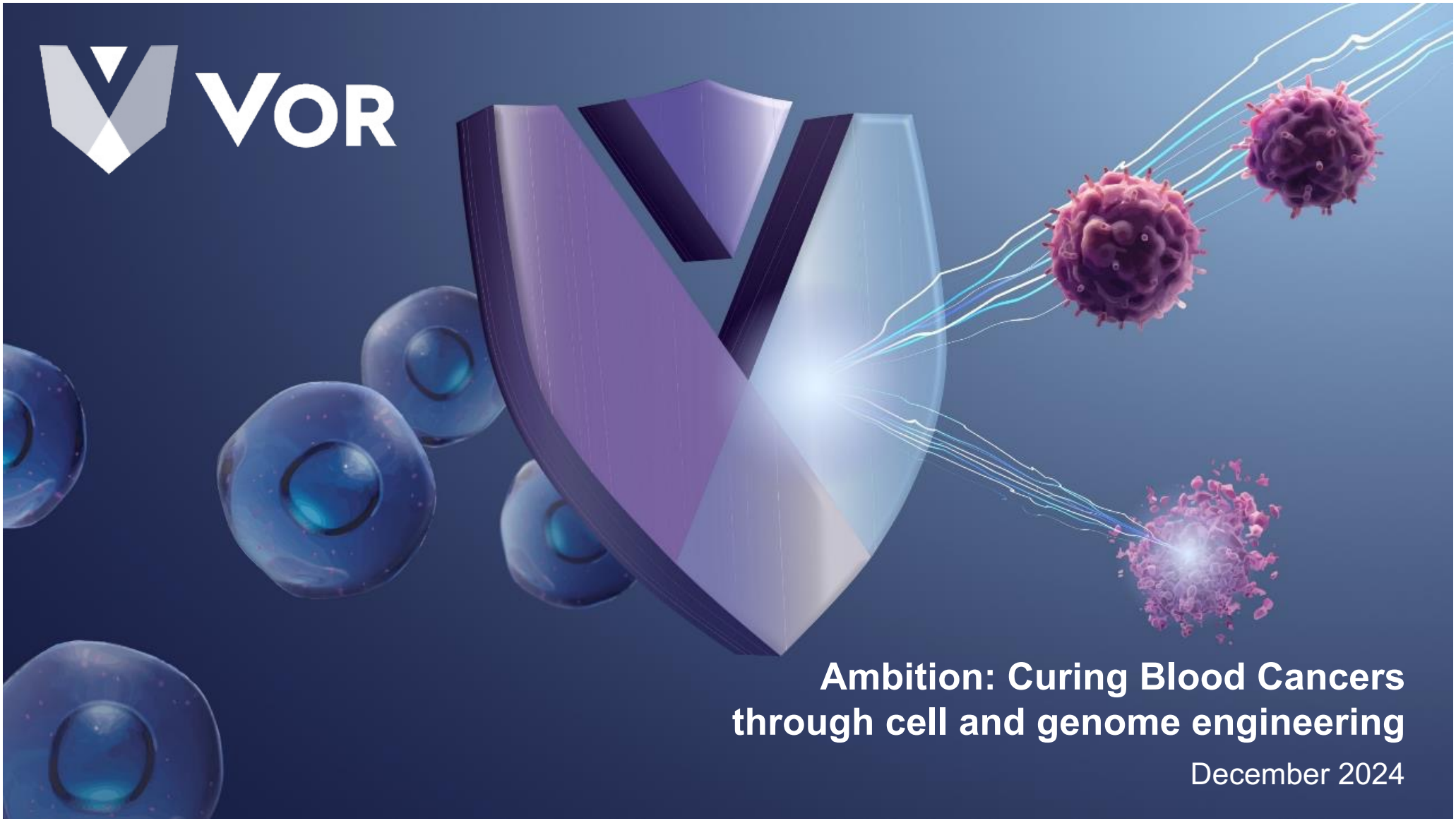

Ambition: Curing Blood Cancers through cell and genome engineering

December 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 potential of trem-cel, alone or as part of a treatment system, to replace standard of care, the potential of VCAR33^{ALLO} and ADCs 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 approach and potential opportunities for VADC45, potential opportunities for next-generation approaches including multi-targeted CAR-Ts and multiplex-edited grafts, the potential of Vor Bio's platform to enable potentially curative therapies and change the standard of care in blood cancers, the intended benefits of Vor Bio's product candidates and approach, including the potential of trem-cel + Mylotarg to improve relapse-free survival, 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 potential design of future clinical trials, the timing of regulatory filings, and the timing of dosing patients, the potential design, endpoints and timing of a Phase 3 registrational trial for trem-cel, and Vor Bio's expectations regarding expedited regulatory review of its product candidates as a result of Fast Track designation or otherwise, the expected safety profile of Vor Bio's product candidates, cash runway and expected capital requirements, and Vor Bio's expectations regarding commercial opportunity, addressable patient population and reimbursement rates for its product candidates, if approved. 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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Vor Bio Clinical Strategy

Thesis: Trem-cel as a Therapeutic Platform

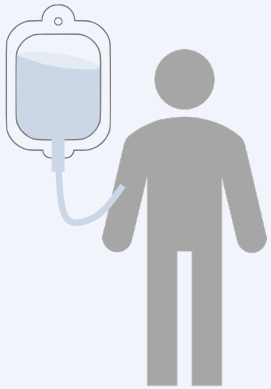
Enabling multiple targeted therapy modalities

ADCs **CAR-Ts**

	Early Clinical Strategy	Current Clinical Findings
Trem-cel + Mylotarg	• Demonstrate clinical proof-of-principle with Mylotarg as approved agent -Engraftment of gene engineered graft -Shielding the blood system • Most rapid path to Treatment System	Encouraging data with commercial promise • 100% engraftment • Robust shielding of the blood system • Broadened therapeutic index for Mylotarg • Early evidence of patient benefit (RFS)
VCAR33^{ALLO}	• Testing as monotherapy in post-transplant relapse	• Encouraging biomarker data at lowest dose

Even After Transplant, High-Risk AML Has Poor Outcomes

Transplant

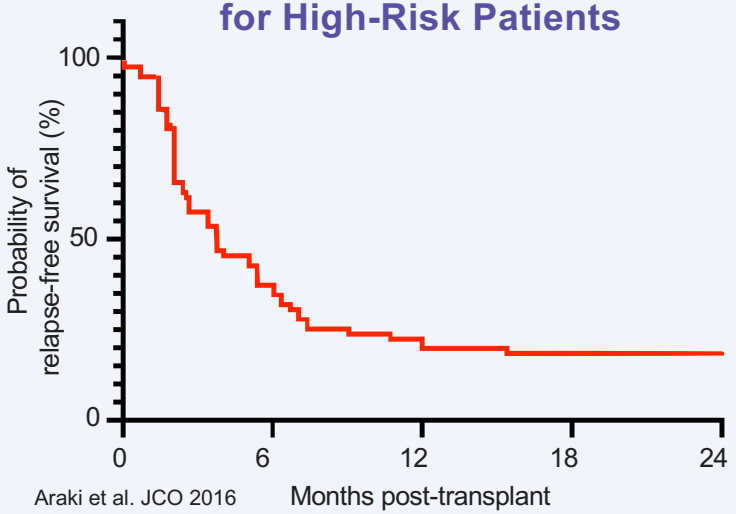


A mainstay treatment

After Transplant

Maintenance therapy unfeasible due to drug toxicity

Watchful Waiting Outcomes for High-Risk Patients



Araki et al. JCO 2016

Frequent leukemia relapses and death, poor outcomes

What If Shielding Could Lead to Improved Outcomes?

A shielded graft…

… can shield a blood system…

…enabling use of otherwise toxic maintenance therapies…

ADC

CAR-T

…potentially leading to improved outcomes

Required Shielded Graft Attributes

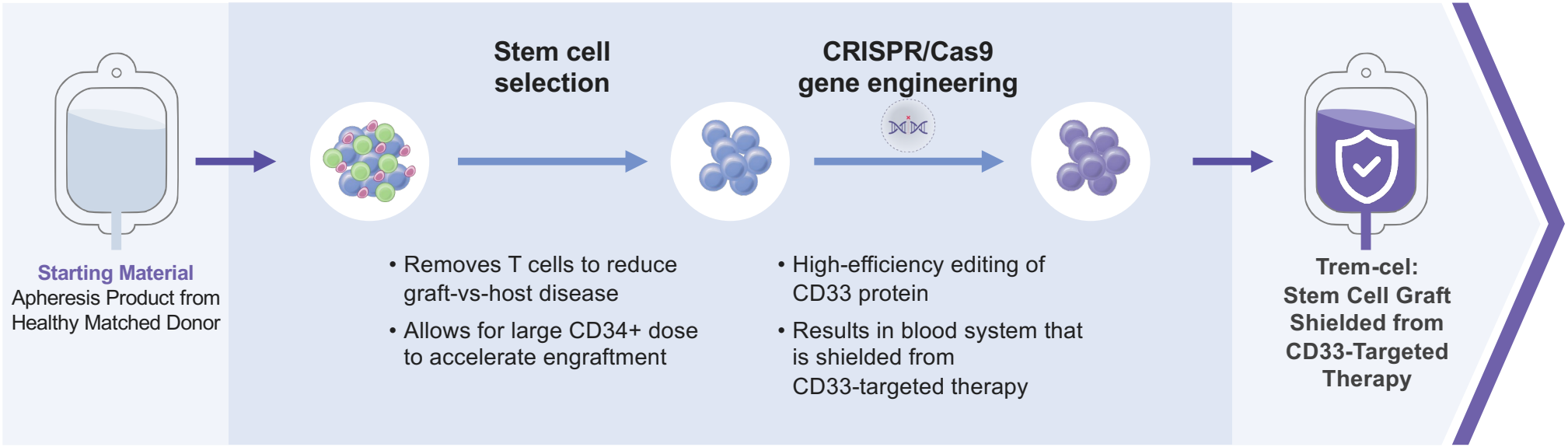
Engraftment
Reliably reconstitute the blood system

Therapeutic Index
Optimize efficacy and safety of maintenance therapies

Shielding
Protect against otherwise toxic therapies

Patient Benefit
Prolong relapse-free survival

What is Trem-Cel?



~7 day manufacturing process

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

Patient Journey

Transplant-eligible AML and MDS patients at high risk of relapse

Transplant Decision

Consolidation/Salvage

Conditioning

Trem-cel Infusion

Engraftment

Maintenance Mylotarg

Starting ~day 60 up to 8 cycles
Dose escalation 0.5-2 mg/m²

No delay in typical patient transplant process

Engraftment

Shielding

Therapeutic Index

Patient Benefit

Donor Journey

Screening

Stem Cell Mobilization, Collection

Related

Unrelated

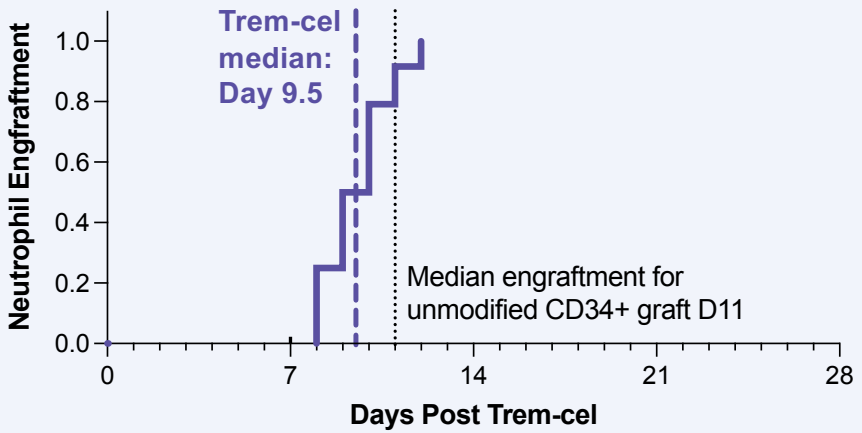
Trem-cel Manufacturing
~7-day process

Unedited back-up graft

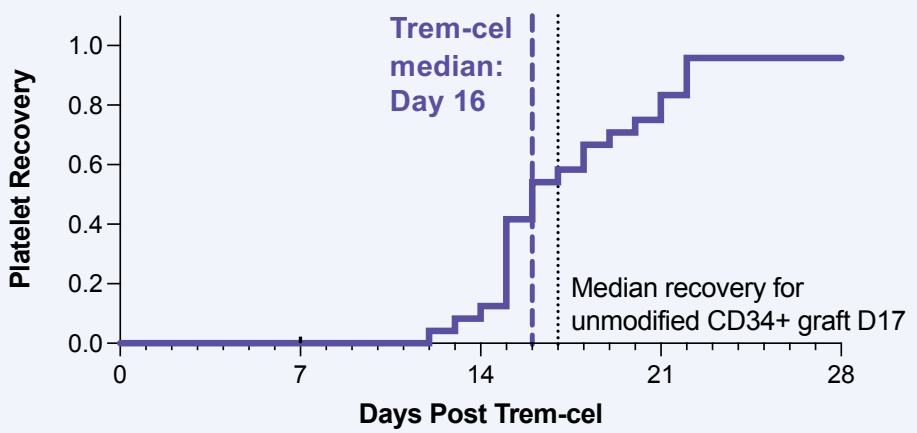
VOR

Trem-cel Achieved Timely Engraftment

Neutrophil Engraftment (n=25)



Platelet Engraftment (n=25)



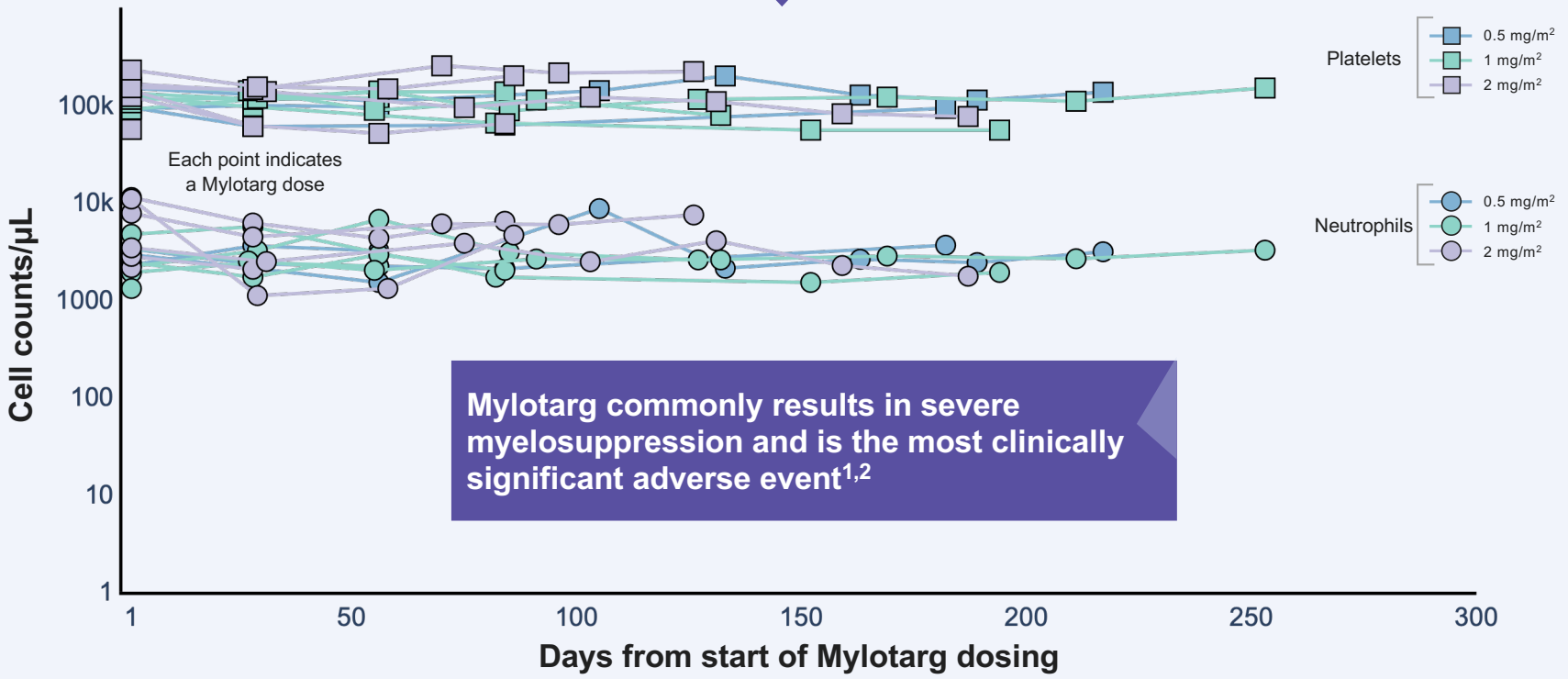
- High CD33 editing efficiency (median 90%, range 71-94%)
- 100% neutrophil engraftment
- 100% achieved full myeloid chimerism at D28

Data cut-off: 1-NOV-2024

VOR

Trem-cel Demonstrated Shielding Across Mylotarg Doses

Neutrophil and Platelet Peripheral Blood Counts with Mylotarg Doses

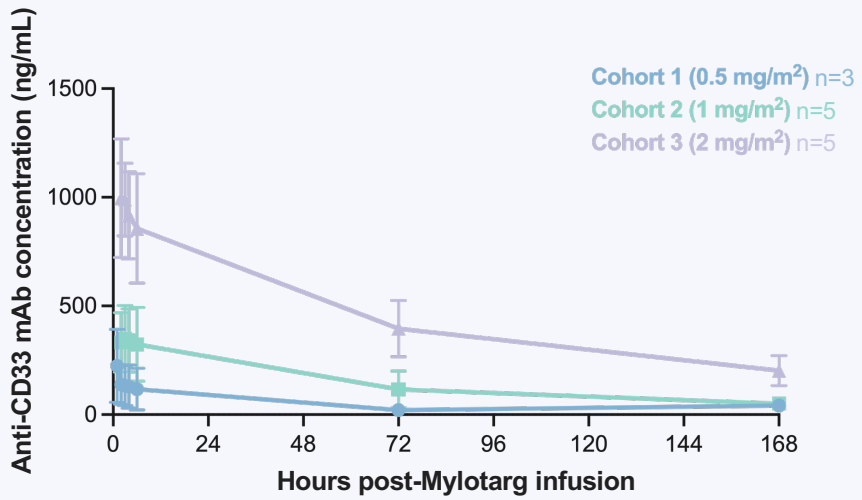


Mylotarg commonly results in severe myelosuppression and is the most clinically significant adverse event[1,2]

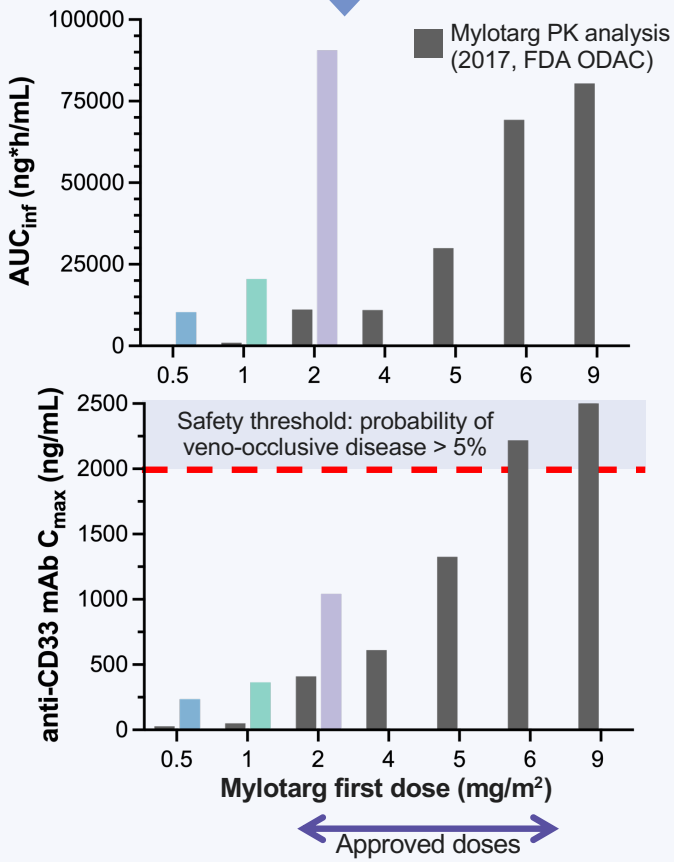
1. Sievers et al. Blood 1999 2. Mylotarg prescribing information
Data cut-off: 1-NOV-2024

Trem-cel Enabled Broadened Therapeutic Index for Mylotarg

Mylotarg Pharmacokinetic Profile



C_{max} and AUC Across Mylotarg Doses



Data cut-off: 1-NOV-2024

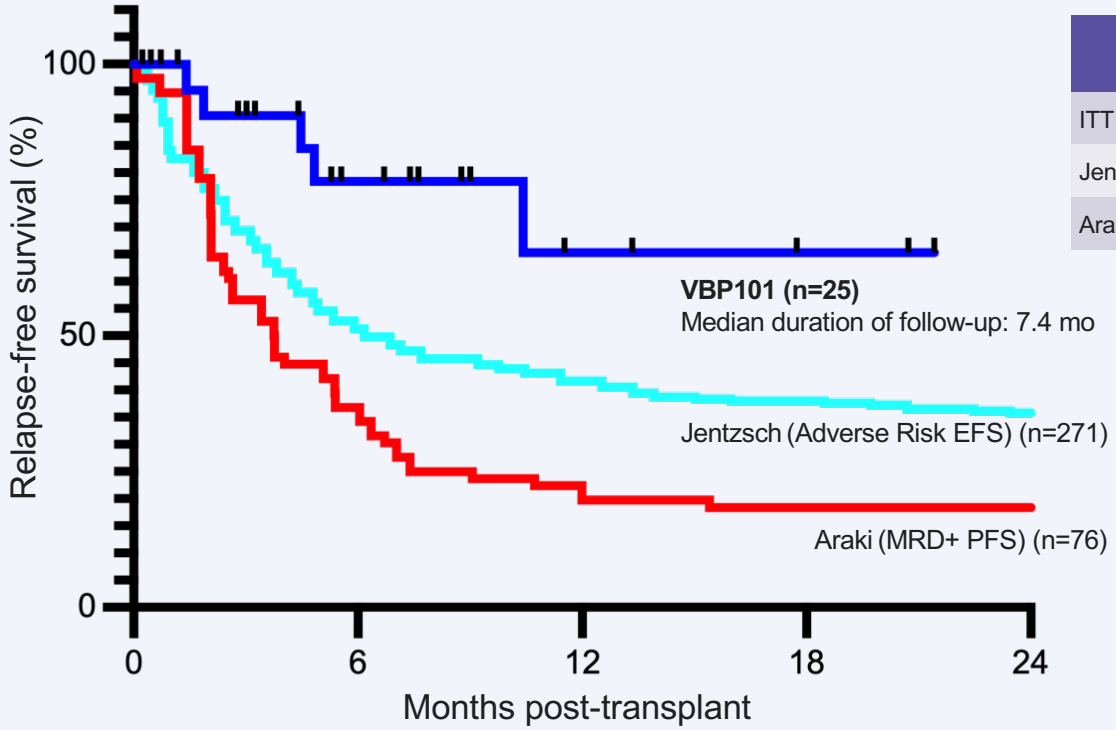
Baseline Risk Factor Demographics for AML Patients: VBP101 vs. Comparators

Disease Characteristic	VBP101 AML ITT (n=24)	VBP101 AML Treated with Mylotarg (n=15)	Araki MRD+ Cohort (2016) (n=76)	Jentzsch Adverse Risk Cohort (2022) (n=271)
Cytogenetics Risk ELN 2022				
Favorable	8%	13%	3%	N/A
Intermediate	33%	27%	58%	N/A
Adverse	58%	60%	39%**	100%*
Other AML Risk Factors				
TP53 mutation	33%	40%	NR	NR
Secondary AML[a]	42%	33%	42%	49%
Disease Burden Status				
Remission (MRDneg)	75%	73%	N/A	20%
MRD+ (>0.1-<5% blasts by flow)	13%	20%	100%*	13%
Active disease (≥5% blasts)	13%	7%	N/A	32%***
AML Disease Status				
CR1	63%	60%	67%	61%
CR2	25%	33%	33%	7%
Relapsed or refractory	13%	7%	0	32%***
Adverse Risk Features (Adverse ELN/molecular/cytogenetic, Secondary AML, MRD or active disease, CR2 or Relapsed/Refractory), n (%)				
1	11 (46%)	6 (40%)		
2 or more	13 (54%)	9 (60%)		

*Selected comparison cohort (n) from published studies. **Adverse cytogenetics. ***Includes partial remission, relapsed, refractory. Jentzsch values for disease burden status do not total 100% due to data not reported.
[a]Defined as AML with myelodysplasia-related change and therapy-related AML, NR=not reported, N/A=not applicable
Data cut-off: 01-NOV-2024

Trem-cel+Mylotarg RFS Appears Favorable vs Published High-Risk AML Comparators

Relapse-Free Survival of VBP101 (intention-to-treat) vs Araki and Jentzsch (historical controls)

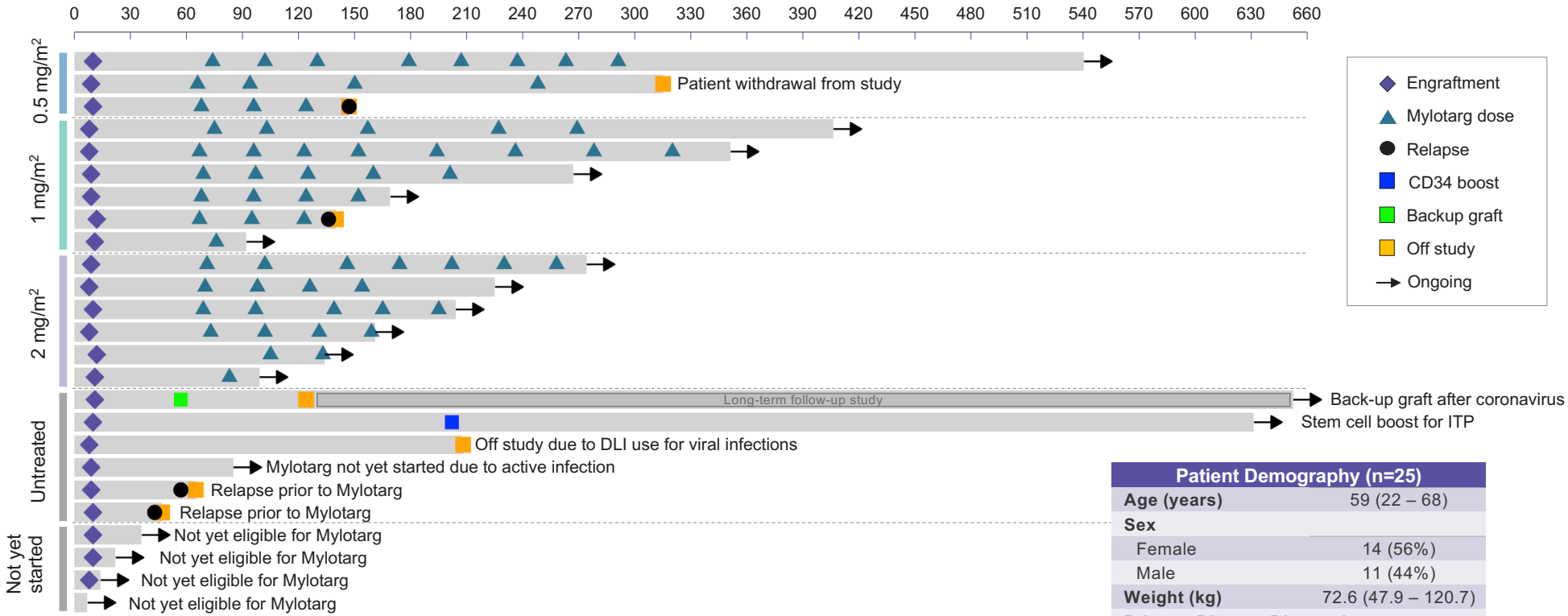


	Median RFS (mo)	P value vs VBP101*	Hazard Ratio* (HR)	HR 95% CI*
ITT	Not reached			
Jentzsch	6.2	0.02	0.36	0.21-0.64
Araki	3.8	0.0004	0.23	0.14-0.40

- Four relapses observed: (all CD33 positive at relapse)
  - 2/4 relapsed prior to Mylotarg treatment
  - 3/4 transplanted with active disease; 1/4 with MRD
  - 4/4 adverse risk cytogenetics
- One patient died off-study due to complications of viral infection

VBP101 data cut-off: 1-NOV-2024. Adapted from Fig 2B MRD+ PFS line from Araki et al. JCO 2016; Adapted from Fig 1C, ELN 2022 Adverse risk EFS line from Jentzsch et al. Blood Cancer Journal 2022. * = individual comparison to VBP101 using log-rank Mantel-Cox test. Data not from head-to-head trial.

Low Rate of Relapse (2/15) Among Patients Receiving Mylotarg



Patient Demography (n=25)	
Age (years)	59 (22 – 68)
Sex	
Female	14 (56%)
Male	11 (44%)
Weight (kg)	72.6 (47.9 – 120.7)
Primary Disease Diagnosis	
AML	24 (96%)
MDS	1 (4%)

ITP: idiopathic thrombocytopenic purpura or similar immune-mediated thrombocytopenia
Data cut-off: 1-NOV-2024

Any Grade Treatment Adverse Events After Receiving Mylotarg (n=15)

Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4
Hematologic				
Anemia	-	1/15 (7%)	3/15 (20%)	-
Autoimmune hemolytic anemia	-	-	1/15 (7%)	-
Leukopenia	-	-	1/15 (7%)	-
Lymphocyte count decreased	1/15 (7%)	-	-	-
Lymphopenia	-	-	1/15 (7%)	-
Neutropenia	-	2/15 (13%)	3/15 (20%)	-
Platelet count decreased	-	-	2/15 (13%)	-
Thrombocytopenia	-	1/15 (7%)	1/15 (7%)	1/15 (7%)[a]
Hepatobiliary				
ALT increased	2/15 (13%)	1/15 (7%)[b]	-	-
AST increased	1/15 (7%)	-	1/15 (7%)[b]	-
Biliary colic	1/15 (7%)	-	-	-
Alk Phos increased	3/15 (20%)	-	-	-
Blood bilirubin increased	1/15 (7%)	-	-	-
LDH increased	2/15 (13%)	-	-	-
Cholecystitis	-	2/15 (13%)	-	-
Veno-occlusive disease	1/15 (7%)[c]	-	-	-

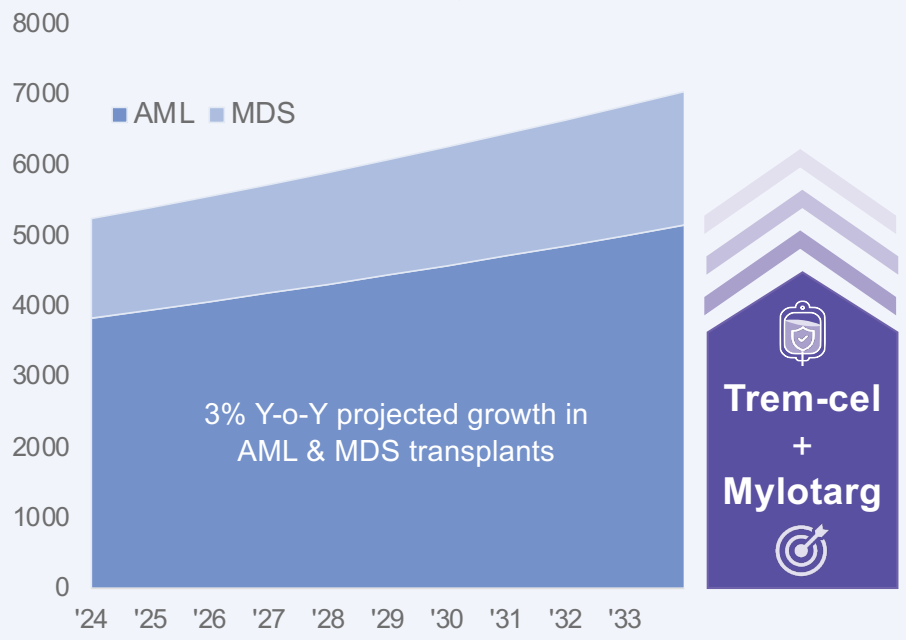
[a]Following adverse event, patient continued to receive multiple cycles of Mylotarg
[b]ALT/AST elevation attributed to fluconazole toxicity and resolved after discontinuation
[c]Mild grade late-onset veno-occlusive disease occurred 97 days after 0.5 mg/m^2 Mylotarg dose. Predisposing factors included azole toxicity, concurrent norovirus infection and gram-negative bacteremia.
ALT = Alanine aminotransferase; AST = Alanine aminotransferase; Alk Phos = blood alkaline phosphatase; LDH = blood lactate dehydrogenase
Data cut-off: 1-NOV-2024

Clinical Update Summary

- Robust neutrophil engraftment, platelet recovery and full donor myeloid chimerism
- Consistent shielding from Mylotarg-related cytopenias during repeated 0.5, 1, and 2 mg/m^2 doses
- Immune reconstitution, multilineage chimerism, and safety profile similar to unedited CD34-selected grafts
- Broadened Mylotarg therapeutic index following trem-cel
- Preliminary data suggesting improved RFS compared to published groups of AML patients at high risk of relapse post-HCT

Trem-cel Platform with Potential >$1B Commercial Opportunity

Opportunity to Replace Standard of Care Transplant



Transformative Treatment

- Shielded transplants to prevent on-target toxicity
- Targeted treatments to improve relapse free survival

Concentrated Market Opportunity

- ~80% of transplants in 65 US centers
- ~5,000 AML & MDS transplants per year

Reimbursement Pathway

- 100% cost-based reimbursement for eHSCs*
- Commercial example: Omisirge® at $338,000

*2020 - IPPS (Inpatient Prospective Payment System), MS DRG-014 – Section 108, stem cell acquisition & processing for allo-SCTs

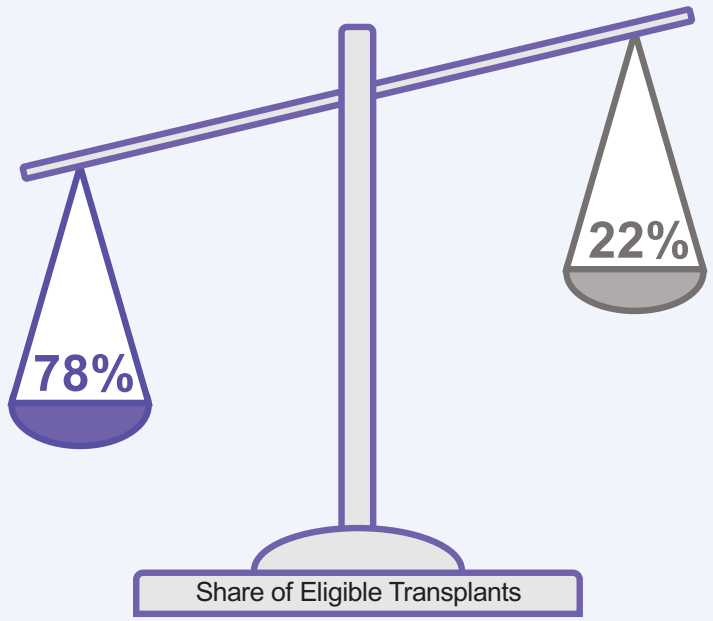
Physician Feedback on Trem-cel + Mylotarg Value Proposition

Perceptions of Trem-Cel

- Streamlined manufacturing with **consistent engraftment**
- Provides **protection of donor cells** from on-target toxicity
- Positive impact on patient outcomes and **reduced GvHD**
- **Enable maintenance therapy** to reduce relapse is compelling

Perceptions of Mylotarg

- As **monotherapy, concern for hepatoxicity** and neutropenia
- With **trem-cel, relative safety concerns are alleviated**
- Benefit of protection with **improved RFS vs. traditional HSCT**



I think using that [Trem-Cel + Mylotarg] would aid in the optimization of transplant outcomes and reduce relapse, which is one of the major causes for post transplant mortality." Hematologist-Oncologist

Trinity qual/quant demand research with 12 transplant specialists (Sept '24); shares based on low sample size and directional only

Potential Registrational Trial Design for Trem-cel/Mylotarg

Patient Journey

Key Eligibility Criteria

- 18-70 years of age
- 8/8 HLA-matched related or unrelated donor
- Suitable for myeloablative conditioning
- CD33+ AML
- High-risk features:
  - MRD+
  - Adverse genetics
  - 2°AML or AML-MRC

AML (n~80) → Myeloablative conditioning → Trem-cel → 30d or later → Mylotarg (8 cycles)

AML (n~80) → Myeloablative conditioning → Standard of care (T-cell replete) transplant

Potential registrational endpoint: Relapse-free survival (RFS)

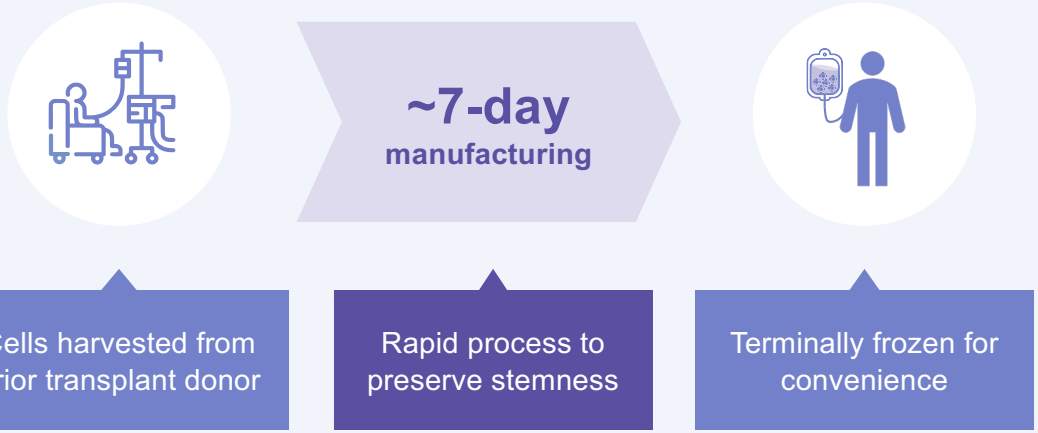
Proposed key secondaries:

- GVHD-free RFS
- Overall survival
- cGVHD free survival
- Time to neutrophil engraftment

Summary of FDA Response to Type C Meeting Request

- Agreement that trem-cel engrafts neutrophils and platelets and has a similar safety profile to unedited CD34+ grafts
- Agreement with the trem-cel-Mylotarg registrational clinical trial design with respect to study population, control arm, primary endpoint, stratification factors, and statistical design
- Agreement to provide further updates to FDA from the VBP101 trial alongside submission of the full registrational clinical trial protocol

VCAR33^{ALLO}: CD33-Directed Healthy Donor-Derived CAR-T



T cells exactly matched to patient's immune system

Healthy, stem-like cells more likely to expand and less prone to exhaustion

Clinically validated construct:
NIH study using autologous cells showed efficacy at 1 x 10^7 CAR+ cells/kg (2/5 assessable pts)[1]

1. Shah et al. ASH 2023

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

Patient Journey

MRD$^+$ or relapsed AML following standard or trem-cel transplant

Enroll

Lymphodepletion

VCAR33^{ALLO} Infusion

Arm A: Blasts ≥ 5%

Arm B: MRD$^+$

Day 28 Follow-up

2nd transplant if required

Prior Transplant Donor

Consent

Collect

VCAR33^{ALLO} Manufacturing

~7-day process

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

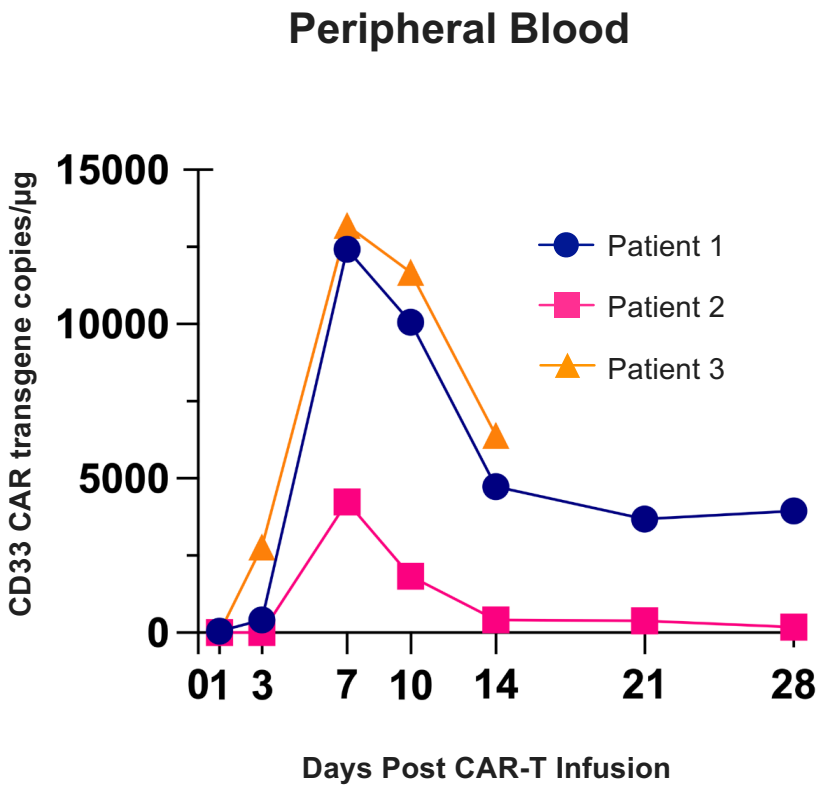
Key Endpoints

01 Safety

02 Expansion, persistence

03 Disease control/response

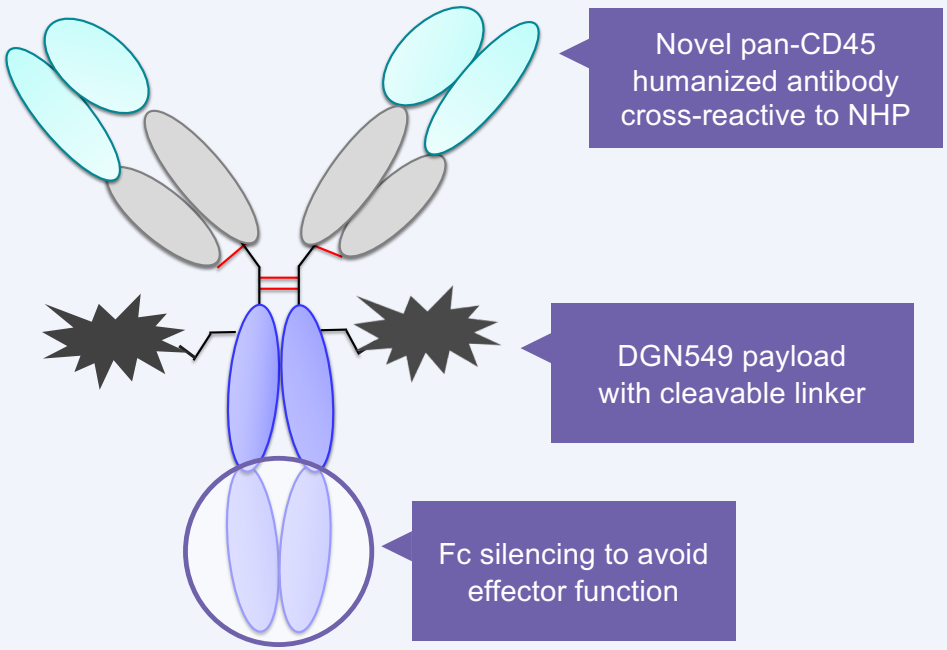
VCAR33^{ALLO}: Encouraging Signs of *In Vivo* Expansion



- Dose escalation schedule:
  - 1 x 10^6 CAR+ cells/kg
  - 3 x 10^6 CAR+ cells/kg
  - 1 x 10^7 CAR+ cells/kg
- NCI CD33CART trial (autologous) saw in vivo expansion and 2 responses out of 5 assessable patients at 1 x 10^7 CAR+ cells/kg*

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

VADC45, a Novel CD45-Targeted Antibody Drug Conjugate



CD45 is highly expressed throughout the heme compartment (minus mature RBCs)

Clinically validated linker-payload (Immunogen, alkylating agent)

Robust preclinical data package

IND-enabling studies progressing to completion

VADC45: Potential Commercial Opportunities

Treating Relapse - Heme Malignancies

- CD45 is highly expressed in AML and DLBCL
- Target may be oncogenic, driving tissue infiltration, high expression and poor prognosis
- **Opportunity:** R/R AML and MDS

Non-Chemo Conditioning - Gene Therapies

- Gene therapies such as for sickle cell urgently need non-chemo conditioning agents
- Could avoid oncogenicity and sterility concerns
- **Opportunity:** SCD, TDT alternative conditioning

Immune Reset - Autoimmune Diseases

- Immune disorders that may require more holistic reset of the entire immune system
- Holistically remove immune cell compartments
- **Opportunity:** Refractory MS, SLE, SSc

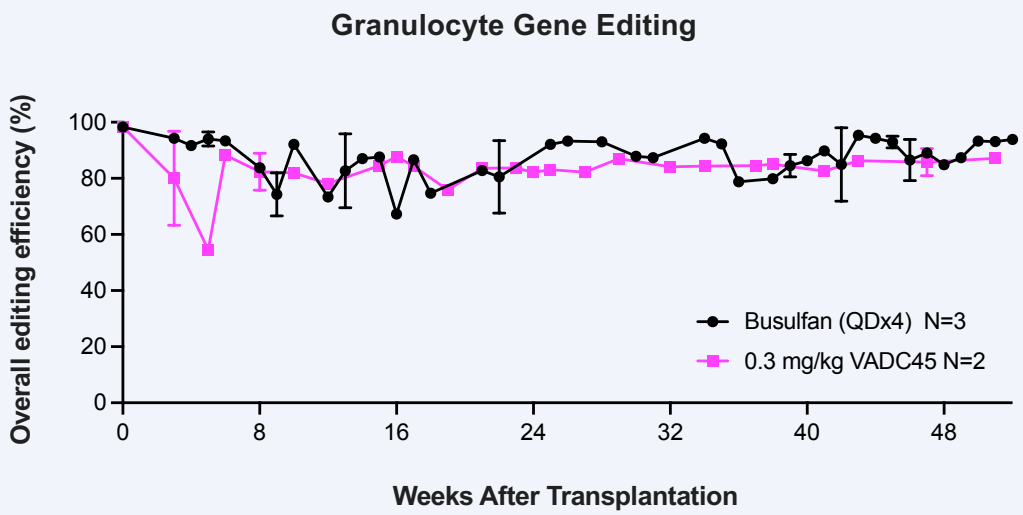
Epitope Engineering - Shielded Grafts

- Precise epitope for VADC45 has been identified
- Experiments are ongoing for epitope modification which retains protein functionality
- **Opportunity:** Heme malignancies

DLBCL= Diffuse large B-cell lymphoma, TDT= Transfusion-dependent β-thalassemia, SLE= Systemic lupus erythematosus, SSc = Systemic sclerosis

Single Dose of VADC45 Enabled Gene-edited HSC Engraftment

Engraftment and Persistence of Gene-edited Stem Cells



NHPs received autologous transplantation of BCL11A-edited HSCs with conditioning via chemo (busulfan) compared to single dose of VADC45

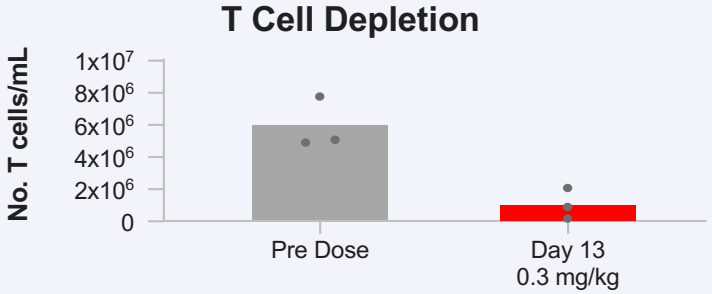
Very high myeloid chimerism achieved within days of transplant

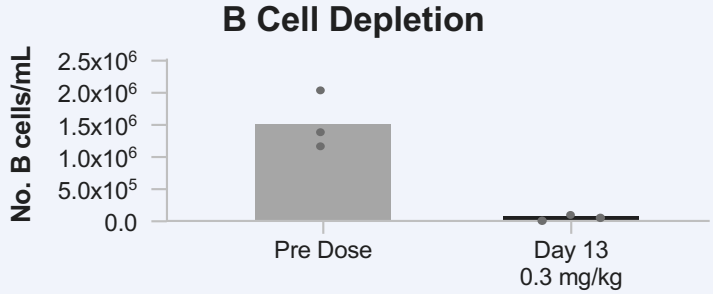
Persistently high edited populations through one year from transplant

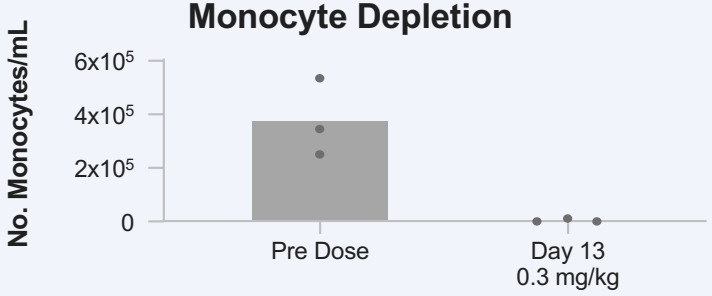
Tisdale et al. (NIH), preclinical data

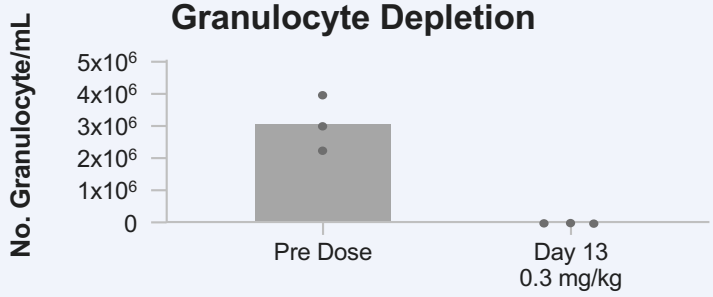
Single Dose of VADC45 Efficiently Depleted Immune Cells

Immune Cell Depletion from Peripheral Blood (NHP)







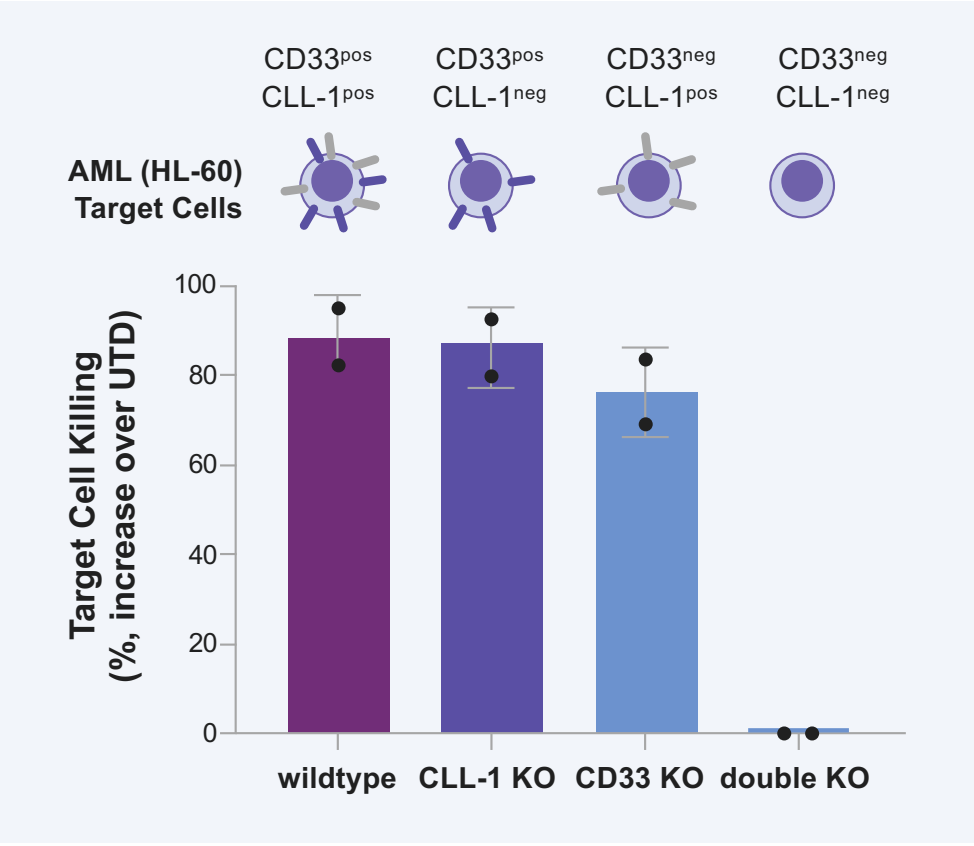


Preclinical data

Next-Generation Approaches

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

In Vitro PoC for Multi-Specific CAR-T: Cell Killing and Shielding



- 2 independent T cell donors
- 48h co-culture of CAR-T cells with HL60 (AML) target cells
- E:T ratio 1:1

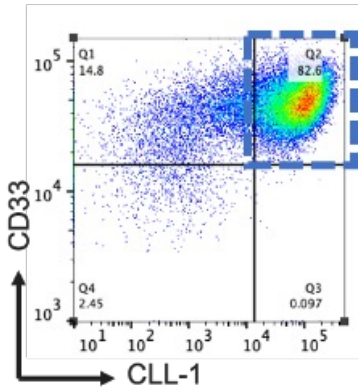
Multi-Specific CAR-T cell (CD33+CLL-1)

- Highly effective AML target cell killing
- "OR gated" CAR which eliminates target cells expressing both OR one target only
- Highly specific CAR leaving double knock-out target cells intact
- Can be paired with Multiplex (CD33+CLL-1)-edited HSPCs which provide shielding

Vor internal data. UTD: untransduced T cell control, KO: knock-out

Multiplex HSC Editing: Minimize Translocations

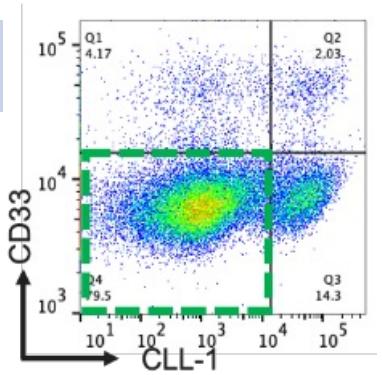
Mock



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

82.6%

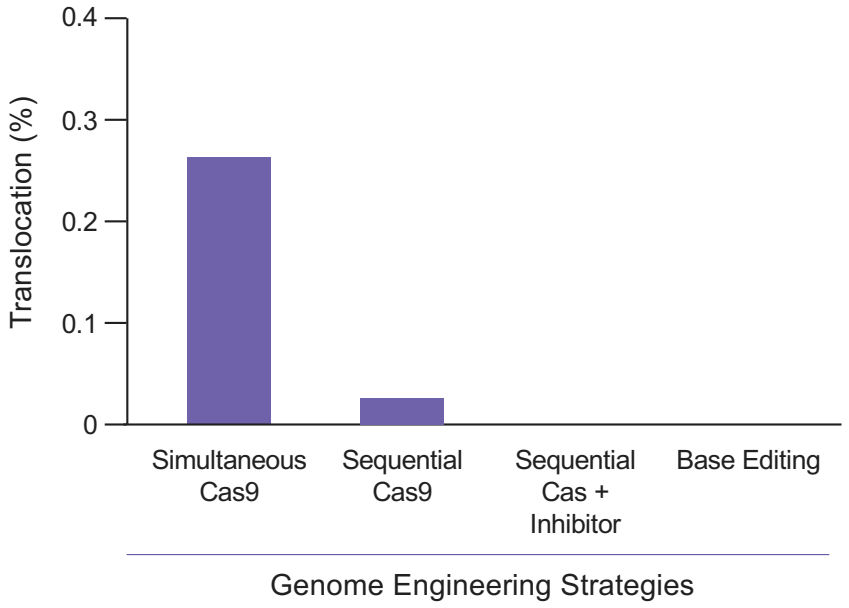
Base Edited



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

79.5%

Minimized Translocation



Adapted from Precision Genome Engineering Keystone Symposia – 2022 Poster 3002

Precision Genome Engineering Keystone Symposia – 2022 Poster 3001

Vor Bio Unique Approach to Potentially Cure Blood Cancers

Trem-cel, a first-in-class investigational* shielded stem cell transplant
- Reliable engraftment, robust shielding of the blood system
- Platform therapy addressing >$1B potential market opportunity

Trem-cel + Mylotarg combination
- Broadened Mylotarg therapeutic index
- Early evidence of patient benefit prolonging relapse-free survival
- Supportive feedback from FDA on registrational trial design

VCAR33^{ALLO}, differentiated transplant donor CAR-T therapy
- Encouraging signs of in vivo expansion with strong trial enrollment

VADC45
- Four distinct potential commercial opportunities

*Potential to be first-in-class if approved

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Pipeline to Change the Standard of Care in Blood Cancers

Description			Preclinical		Clinical		Anticipated Milestones
Program / Trial	Modality	Indication	Discovery/ Validation	IND-Enabling	Phase 1/2	Phase 2/3	
Trem-cel + Mylotarg / VBP101	Shielded CD33-deleted transplant + CD33-directed ADC	AML, MDS					
VCAR33^{ALLO} (healthy transplant donor CAR-T) / VBP301	CD33-directed transplant donor CAR-T	AML post-transplant					
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
VADC45 ADC	CD45-directed ADC	AML, conditioning, immune reset					Finalizing IND preparedness
CD33-CLL1 Treatment System	Multi-specific CAR-T	AML					
	Multiplex-edited shielded transplant	AML					

Experienced Leadership Team

Robert Ang, MBBS, MBA
President and CEO

Han Choi, M.D., LL.M
Chief Financial Officer

Eyal Attar, MD
Chief Medical Officer

Tirtha Chakraborty, PhD
Chief Scientific Officer

Tania Philipp
Chief People Officer

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

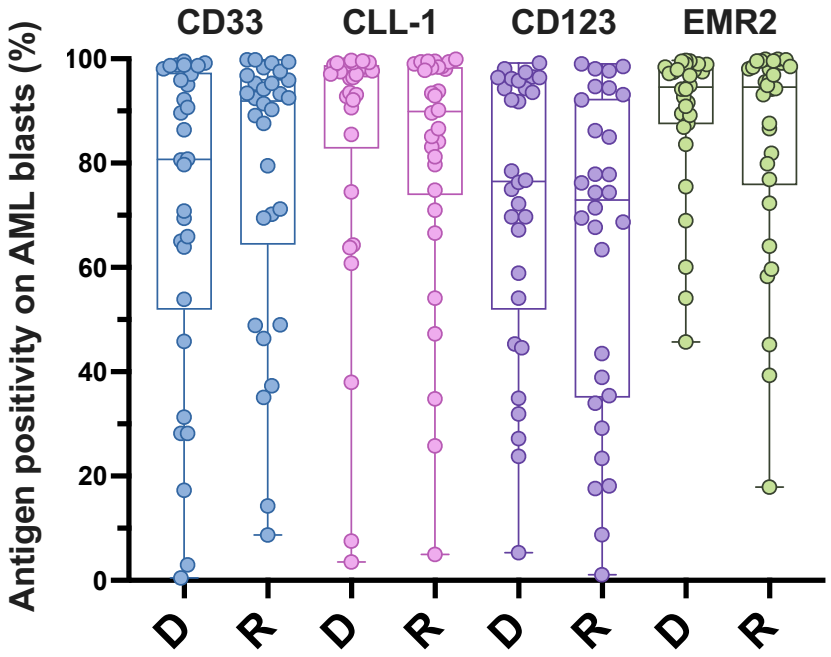
David Phillips, MBA
Senior Vice President, Head of Quality

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

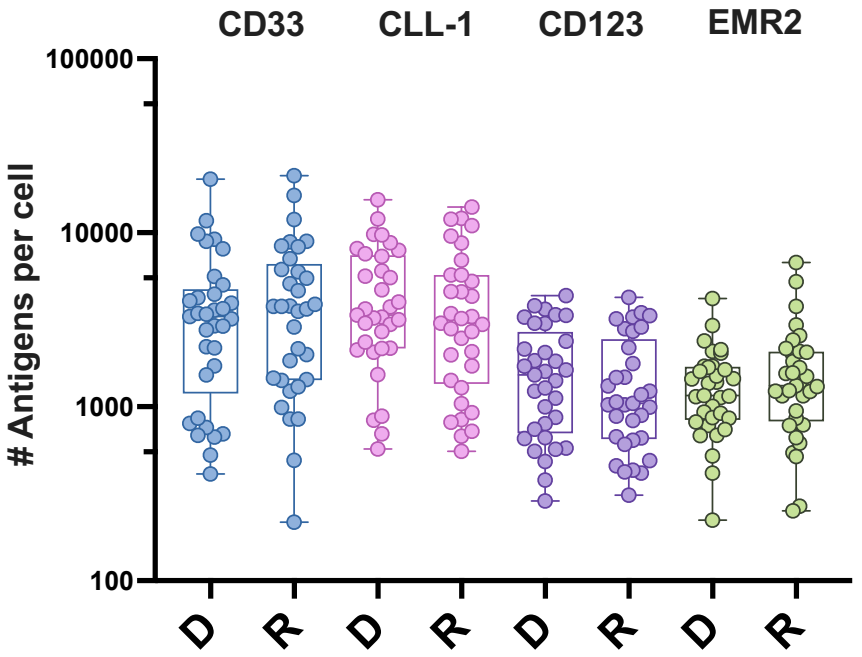
Deep Cell & Gene Therapy Expertise

CD33 is Amongst Highest Quality Targets in AML

Ubiquity of Antigen Expression (Flow Cytometry)

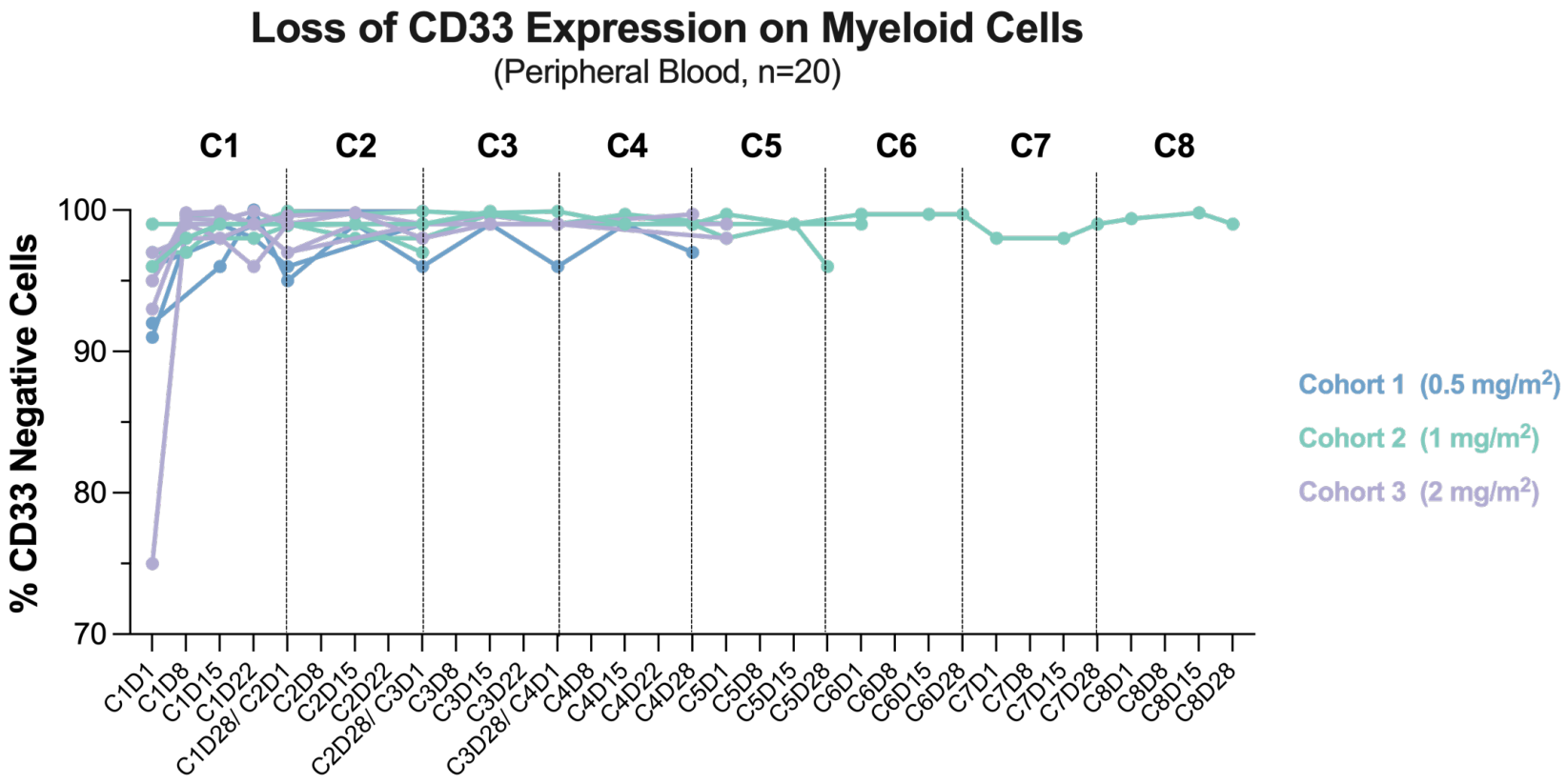


Density of Antigen Expression (QuantiBRITE)



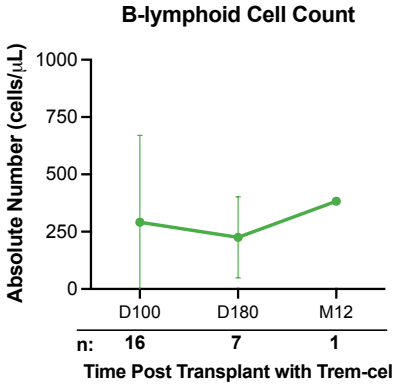
D = Diagnosis **R** = Relapse

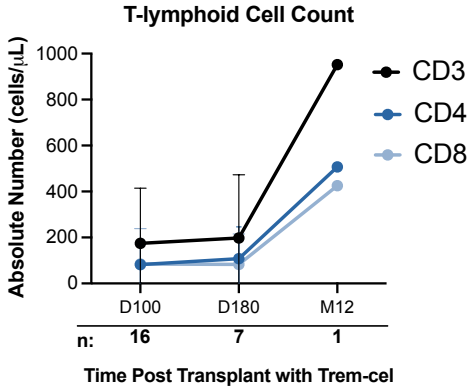
CD33 Negative Cells Enriched with Mylotarg Doses

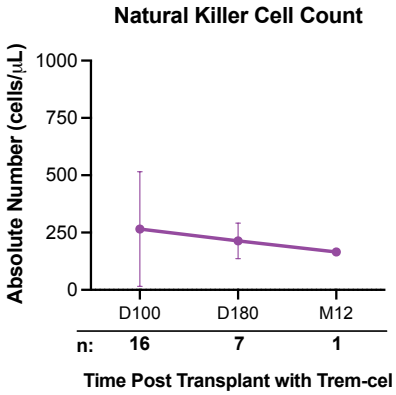


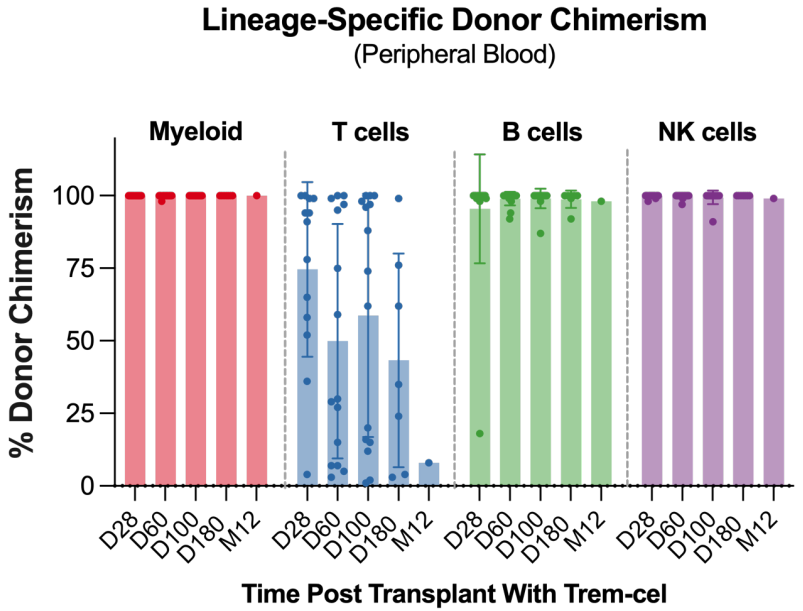
Data cut-off: 1-NOV-2024

Immune Reconstitution, Full and Sustained Myeloid Chimerism, and CD33-negative Myeloid Cells Are Observed









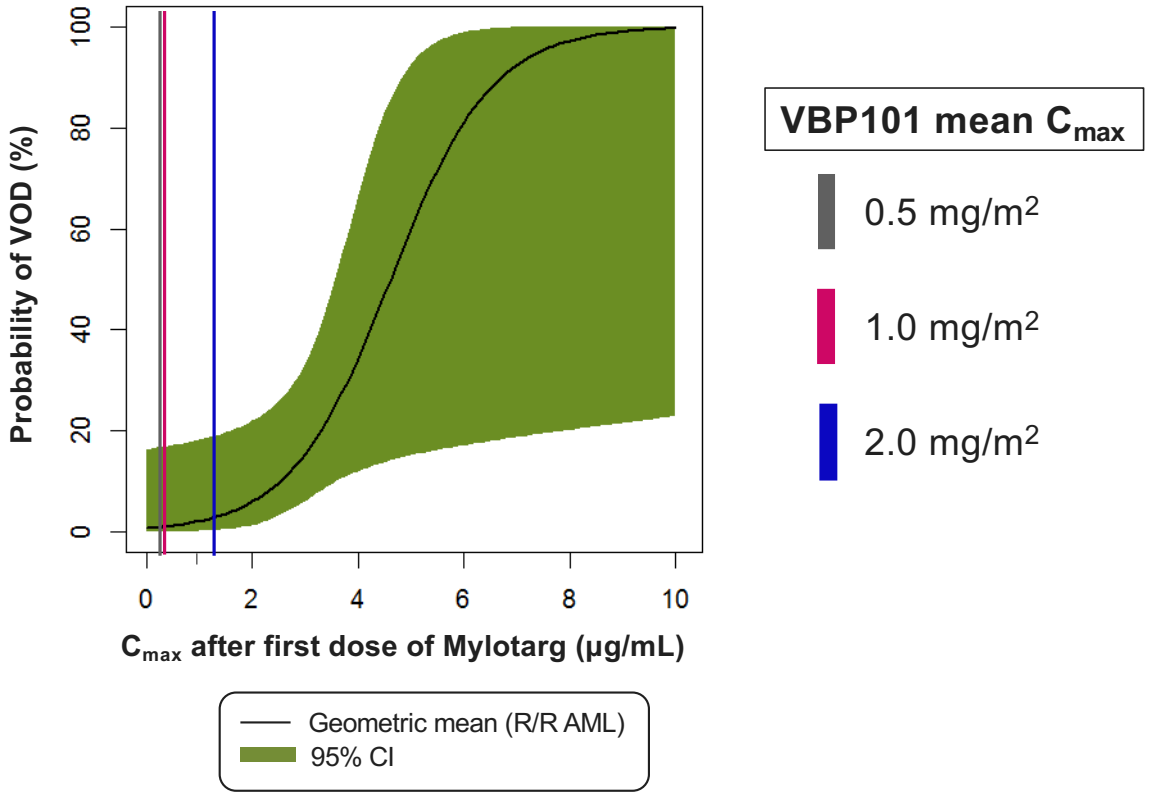
% CD33-Negative Analysis	Drug Product*	D28*	D60*
NGS Gene Editing	**90** (78-94) n=18	**94** (85-98) n=19	**94** (86-97) n=16
Flow Cytometry	N/E	**93** (74-98) n=22	**94** (78-99) n=19

*Mean % (range), Editing and flow data from peripheral blood monocytes and myeloid cells respectively
N/E: not evaluated

Data cut-off: 1-NOV-2024. Reference unedited CD34-selected reconstitution: Goldberg et al Leuk and Lymph 58 (217); Llaurador et al. Transplantation and Cellular Therapy 27 (2021)

Risk of Veno-Occlusive Disease Related to Mylotarg C_{max}

Probability of Veno-occlusive Disease in Patients with Prior Transplant



Selected Precedent Randomized Trials in AML

	AML Studies			Transplant Studies	
	MORPHO	**SIERRA**	**ALFA-0701**	**Precision-T**	**Omidubicel**
Drug and Comparisons	Gilteritinib vs placebo	^{131}I-apamistamab + Flu-TBI + alloHCT vs conventional care	Daunorubicin + cytarabine ± Mylotarg (D1, 4, 7)	Orca-T transplant vs SoC alloHCT	Omidubicel vs double cord graft
Treatment Setting	Post-HCT maintenance, FLT3-ITD AML	R/R AML	Newly-diagnosed de novo AML	Transplant-eligible AML, ALL, MDS	Transplant-eligible high-risk malignancies
1º Endpoint	RFS	Rate of dCR (CR/CRp ≥ 180 days)	EFS (induction failure, relapse, or death)	Survival free of moderate-to-severe chronic GVHD (cGFS)	Time to neutrophil engraftment
2º Endpoints	OS (key), EFS, Time to NRM, Relapse, GVHD, MRD	OS, EFS	Rate of CR/CRp, OS, RFS, Safety	Time to moderate-to-severe GVHD, GRFS, OS	Platelet engraftment by 42 days, grade 2-3 bacterial or invasive inf, NRM, OS
Sample Size	178 per arm	76 per arm	140 per arm	85 per arm	62 per arm