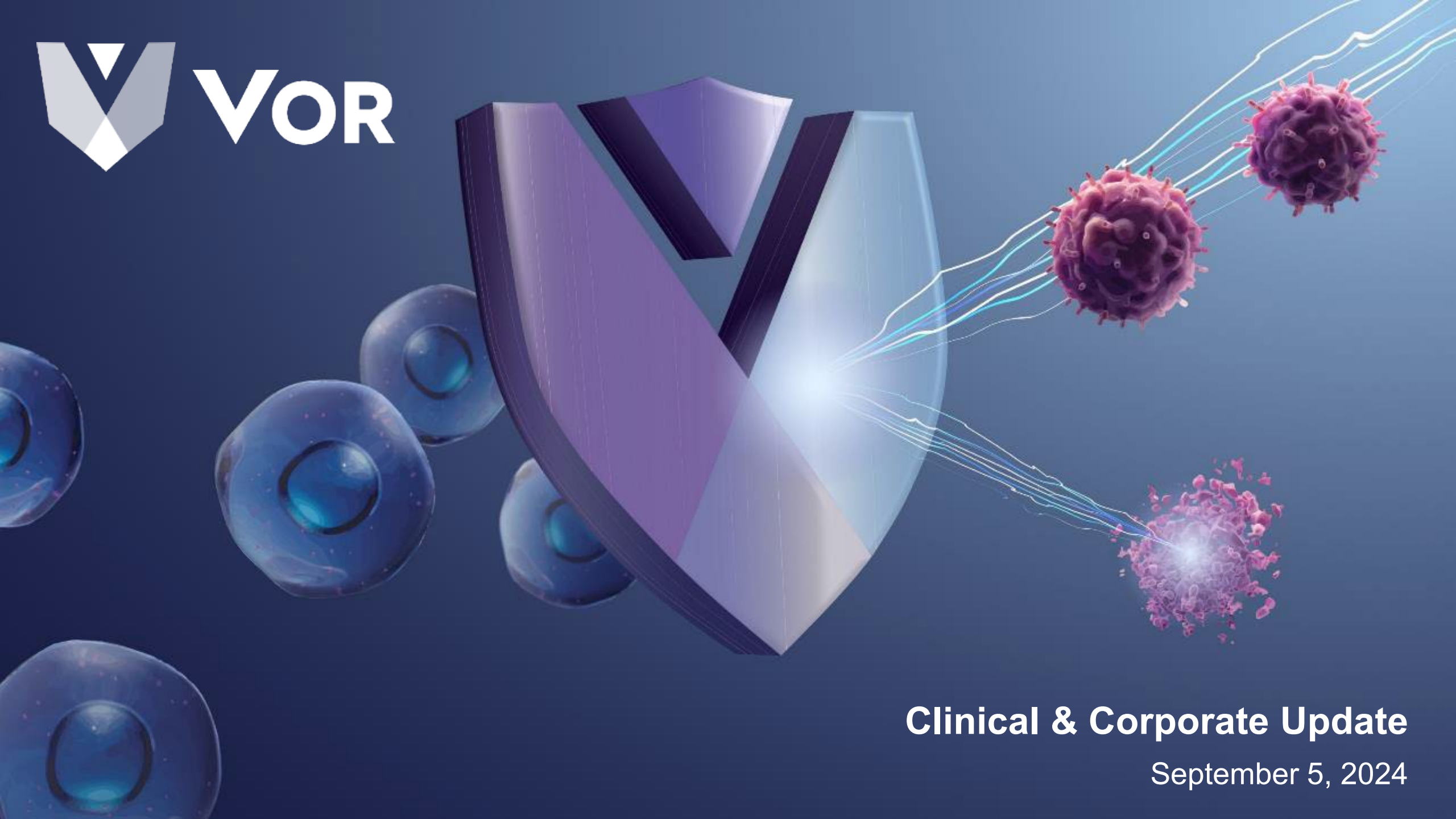

Clinical & Corporate Update

September 5, 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 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, 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, 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, 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, Vor Bio's expectations regarding commercial opportunity, 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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Today's Agenda

Agenda	Speaker
Introductory Remarks	Robert Ang, MBBS, MBA, President & CEO
VBP101 & VBP301 Clinical Update	Eyal Attar, MD, Chief Medical Officer
VADC45 and Closing Remarks	Robert Ang, MBBS, MBA, President & CEO
Summary & Perspective on VBP101	Guenther Koehne, MD, PhD, Deputy Director and Chief of Blood & Marrow Transplant and Hematologic Oncology at Miami Cancer Institute of Baptist Health South Florida
Q&A	Robert Ang, MBBS, President & CEO Eyal Attar, MD, Chief Medical Officer Guenther Koehne, MD, PhD

Introductory Remarks

Robert Ang, MBBS, MBA, President & CEO

Vor Bio Clinical Strategy

Thesis: Trem-cel as a Therapeutic Platform

Enabling multiple targeted therapy modalities

 ADCs

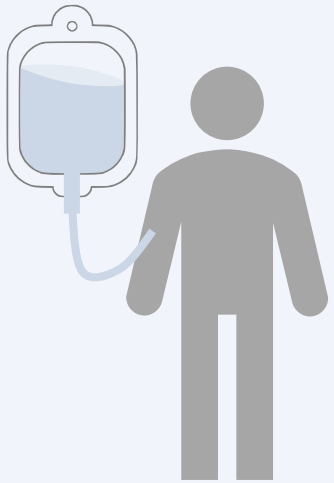
 CAR-Ts

	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

*18 patients treated with trem-cel, of which ten had received Mylotarg as of the data cut-off date of July 19, 2024 . RFS=Relapse Free Survival

Even After Transplant, High-Risk AML Has Poor Outcomes

Transplant

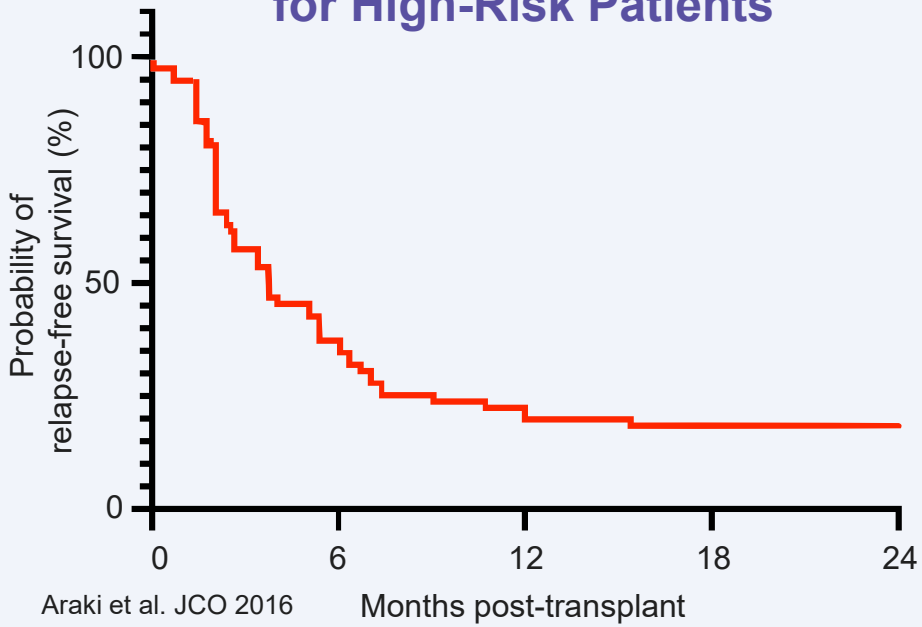


A mainstay treatment

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…

… could 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

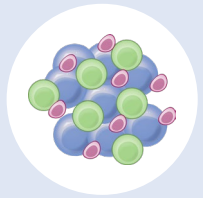
Shielding
Protect against otherwise toxic therapies

Therapeutic Index
Optimize efficacy and safety of maintenance therapies

Patient Benefit
Prolong relapse-free survival

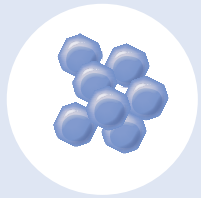
What is Trem-Cel?

Starting Material
Apheresis Product from Healthy Matched Donor



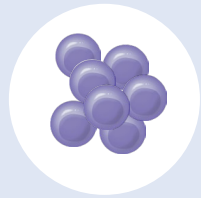
Stem cell selection

- Removes T cells to reduce graft-vs-host disease
- Allows for large CD34+ dose to accelerate engraftment



CRISPR/Cas9 gene engineering

- High-efficiency editing of CD33 protein
- Results in blood system that is shielded from CD33-targeted therapy



Trem-cel: Stem Cell Graft Shielded from CD33-Targeted Therapy

~7 day manufacturing process

VBP101 & VBP301 Clinical Update

Eyal Attar, MD, Chief Medical Officer

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/m^2

No delay in typical patient transplant process

Engraftment

Shielding

Therapeutic Index

Patient Benefit

Donor Journey

Screening

Stem Cell Mobilization, Collection

Related

Unrelated

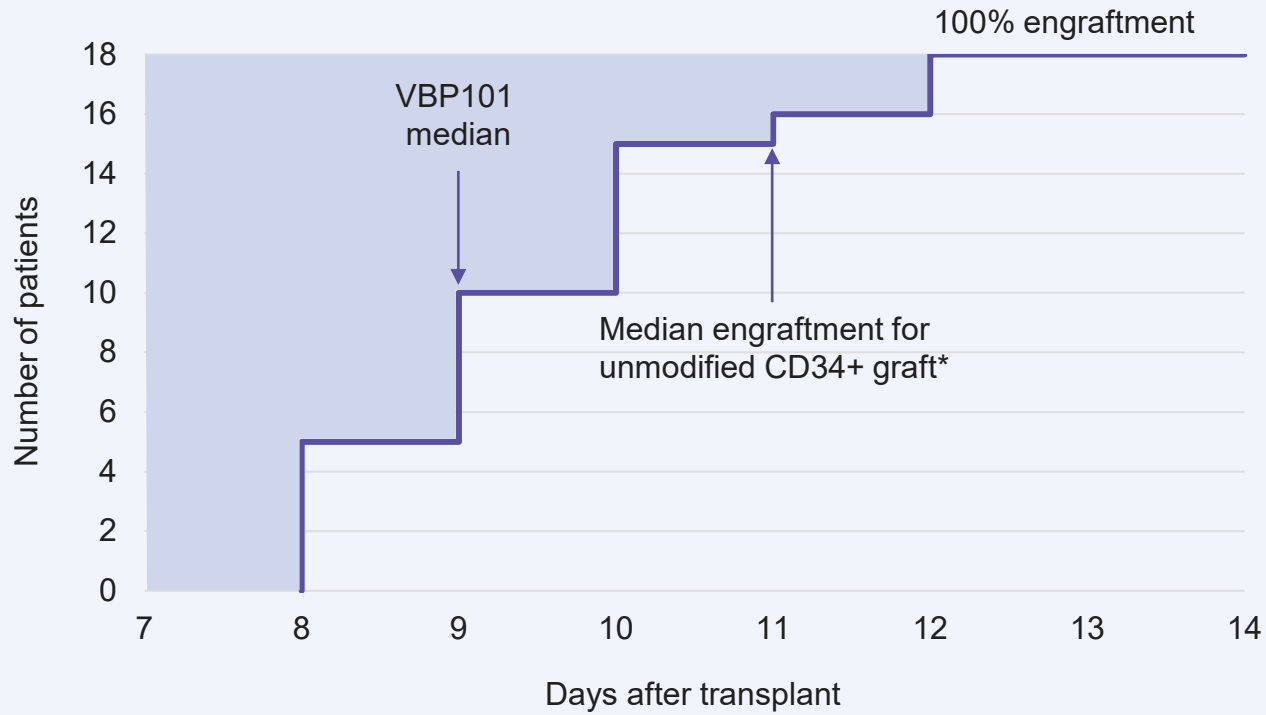
Trem-cel Manufacturing
~7-day process

Unedited back-up graft

Trem-cel Achieved Timely Engraftment

- High CD33 editing efficiency (median 89%, range 71-94%)
- 100% neutrophil engraftment
- Robust platelet recovery (median 16.5 days)
- Full myeloid chimerism at Day 28

Neutrophil Engraftment (n=18)

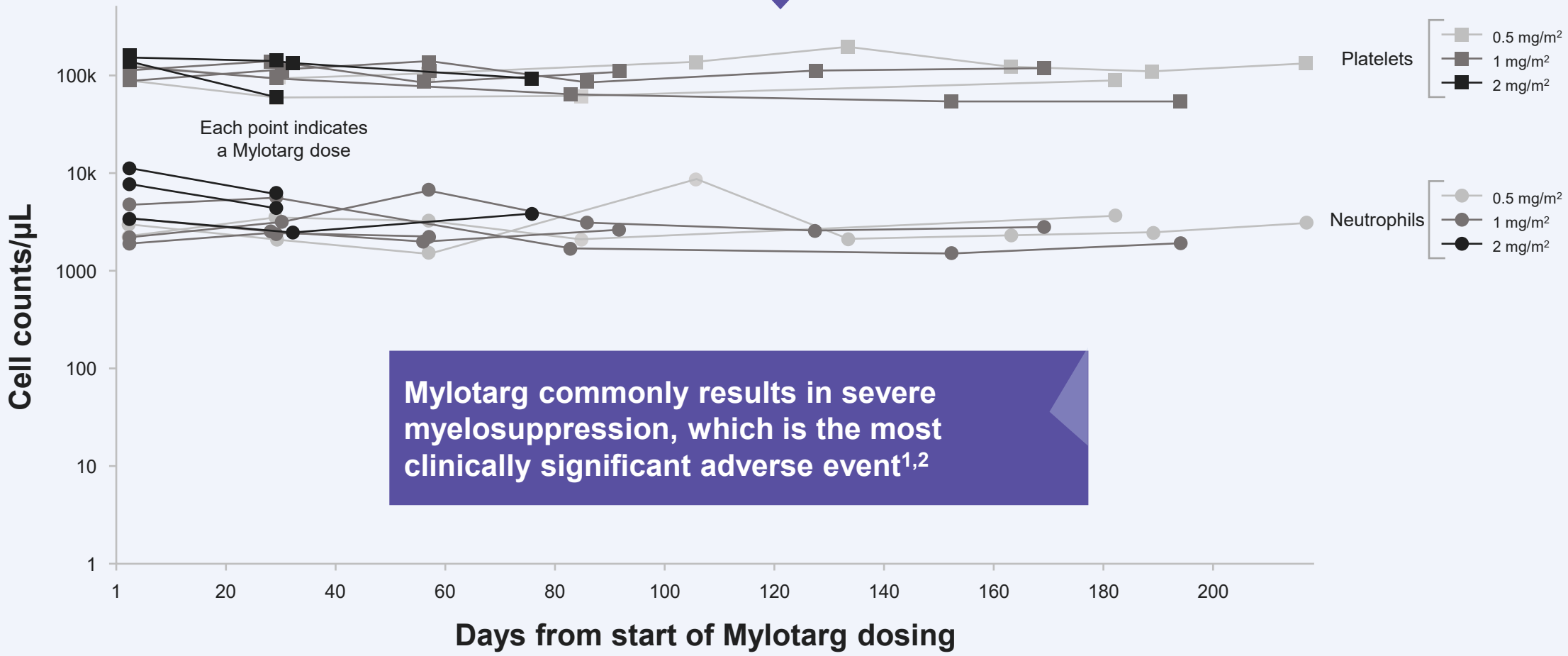


* Luznik et al. JCO 2021

Data cut-off: 19-JUL-2024

Trem-cel Demonstrated Shielding Across Mylotarg Doses

Neutrophil and Platelet Peripheral Blood Counts with Mylotarg Doses

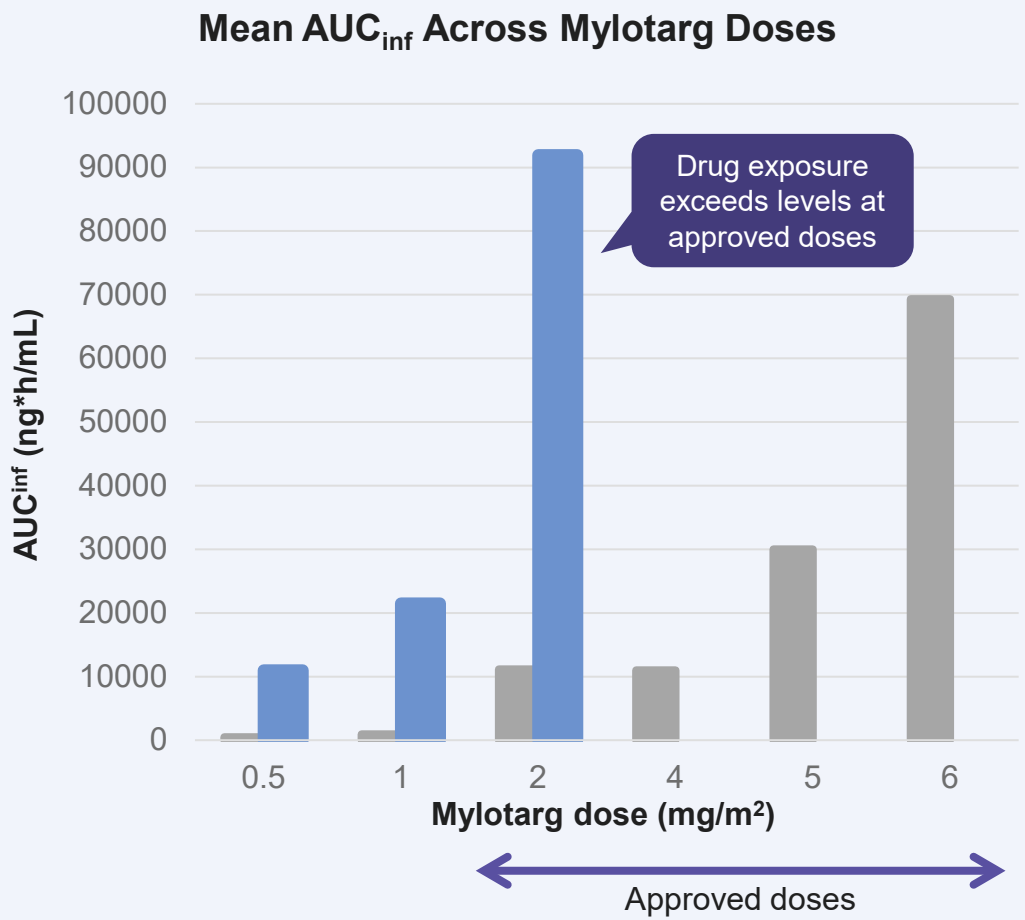


Mylotarg commonly results in severe myelosuppression, which is the most clinically significant adverse event[1,2]

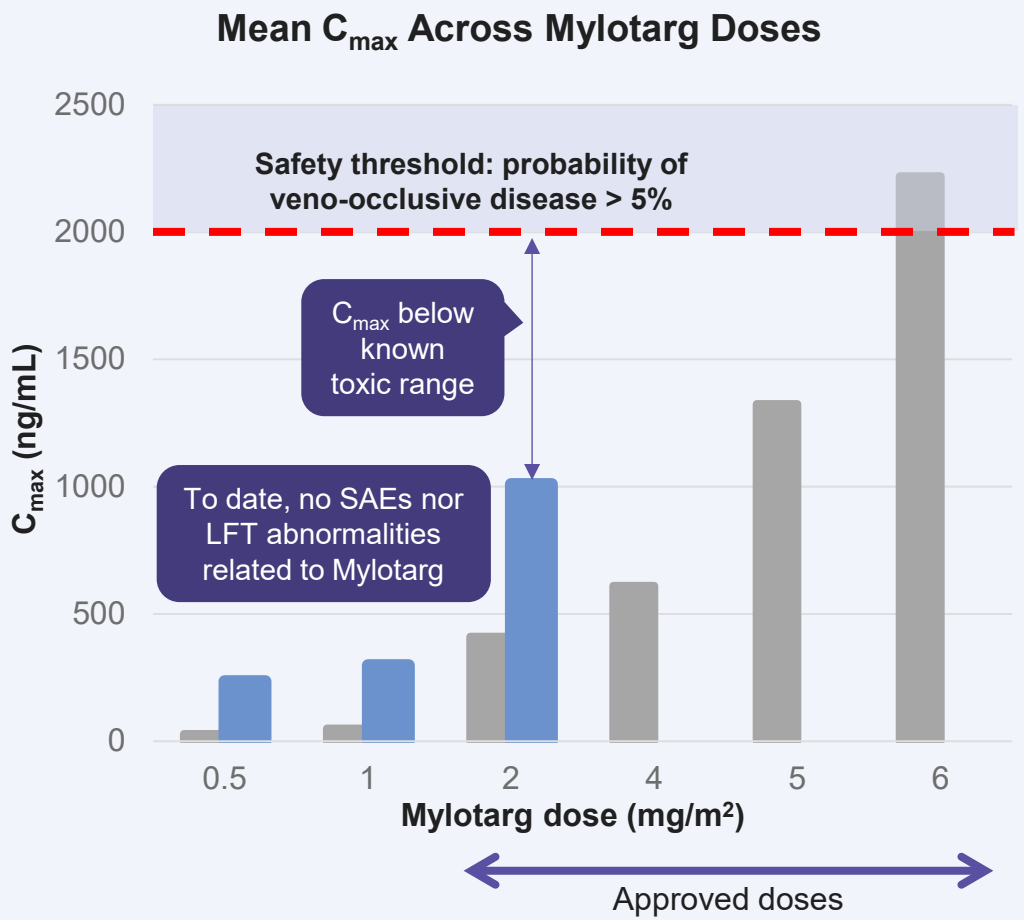
1. Sievers et al. Blood 1999 2. Mylotarg prescribing information
Data cut-off: 19-JUL-2024

Trem-cel Enabled Broadened Therapeutic Index for Mylotarg

Regarding Efficacy



Regarding Liver Toxicity



VBP101

Mylotarg PK analysis (2017, FDA ODAC)

Data cut-off: 19-JUL-2024; data not from head-to-head trial
SAE: serious adverse events; LFT: liver function test

Baseline Risk Factor Demographics: VBP101 vs. Comparators

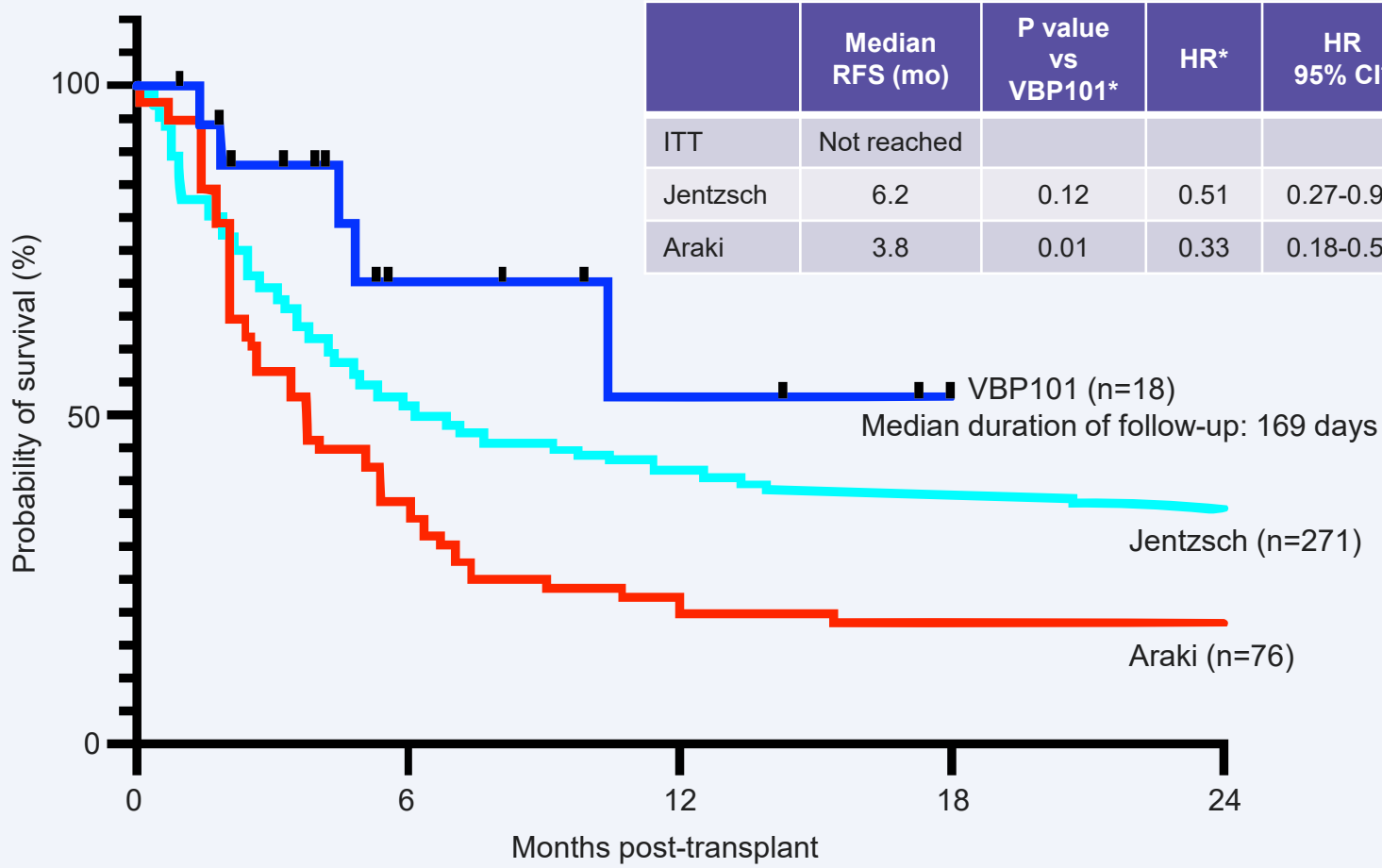
Study (Publication Year)	VBP101 Intent to Treat N=18	VBP101 As Treated with Mylotarg n=10	Araki MRD+ (2016) n=75	Jentzsch Adverse Risk (2022) n=271
CR1 (%)	61	50	67	90
CR2 (%)	22	40	33	10
Active Disease (≥5% blasts, %) (median blast %)	17 (16%)	10 (78%)	--	--
MRD+ (0.1-<5% blasts, %) (median blast %)	11 (2.7%)	10 (1.8%)	100* (0.60%)	13
Adverse Risk (%) (ELN 2022)	61	60	39**	100*
Secondary AML (%) [a]	44	50	42	49
TP53 Mutation (%)	28	50	--	--

*selected comparison cohort (n) from published studies. **Adverse cytogenetics
[a]Defined AML with myelodysplasia-related change and therapy-related AML
Data cut-off: 19-JUL-2024

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

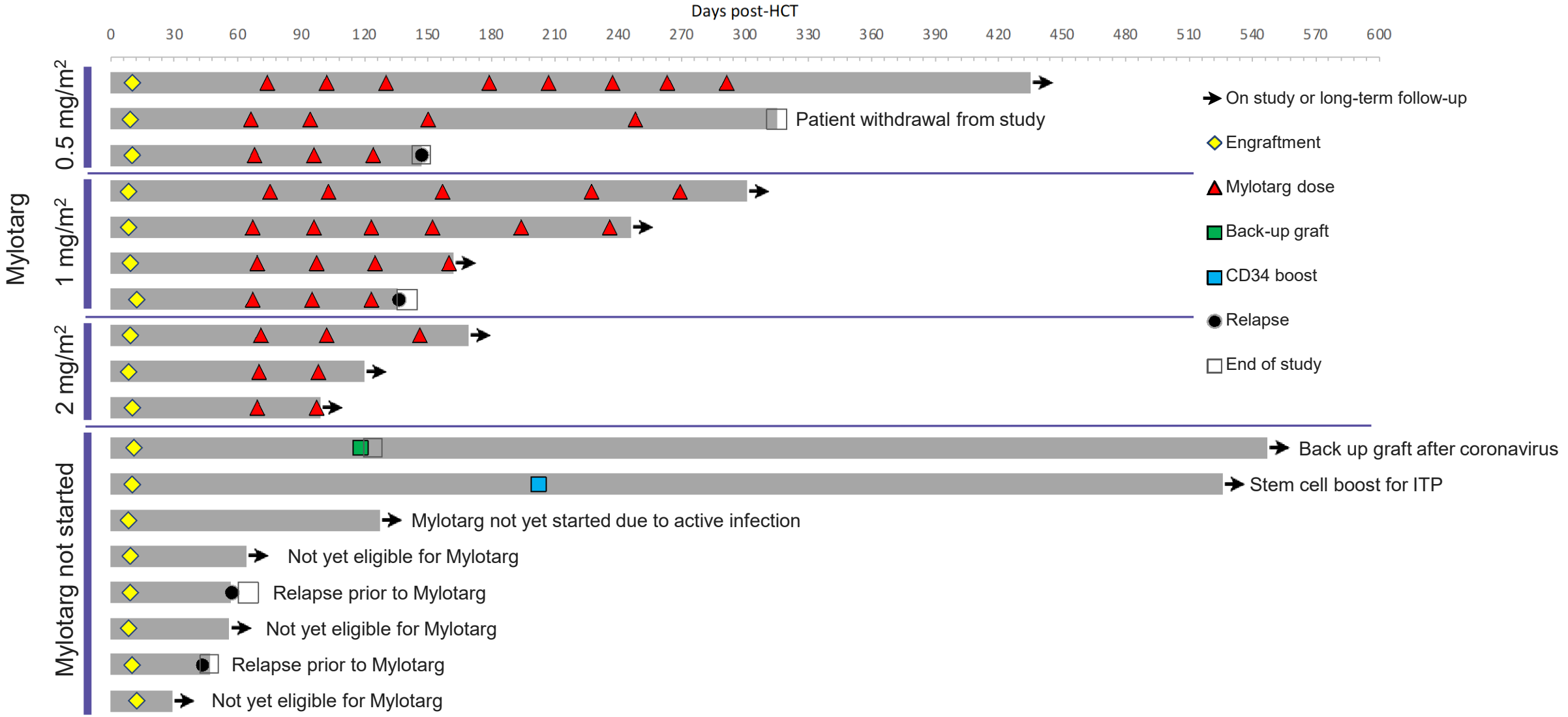
Relapse-Free Survival of VBP101 (intention-to-treat) vs Araki and Jentzch (historical controls)

	Median RFS (mo)	P value vs VBP101*	HR*	HR 95% CI*
ITT	Not reached			
Jentzsch	6.2	0.12	0.51	0.27-0.97
Araki	3.8	0.01	0.33	0.18-0.59



VBP101 data cut-off: 19-JUL-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 ITT using log-rank Mantel-Cox test. Data not from head-to-head trial.

Low Rate of Relapse (2/10) Among Patients Receiving Mylotarg



ITP: idiopathic thrombocytopenic purpura or similar immune-mediated thrombocytopenia
Data cut-off: 19-JUL-2024

Two Patients Relapsing Following Mylotarg, Both with TP53 Mutations

	Age/ Sex	AML Risk Factors	Outcome and post-HCT Day	Mylotarg Maintenance Dose and Cycles	CD33 Expression at Time of MRD/Relapse
Relapses Prior to Mylotarg	68/M	• AML-MRC, adverse cytogenetics (ELN) • Complex cytogenetics • High risk molecular: NRAS, ZRSR2, TET2 mutations • Active disease at time of HCT: 16% blasts	Relapse D43 in blood and CNS prior to Mylotarg	N/A	Yes
	26/M	• High risk molecular: RUNX1-RUNX1T1, KMT2A rearrangement, adverse cytogenetics (ELN) • FLT3-TKD and BCORL1 • Active disease at time of HCT: 8% blasts (local)	Relapse D57 prior to Mylotarg	N/A	Yes
Relapses Following Mylotarg	64/F	• AML-MRC, adverse cytogenetics (ELN) • Complex karyotype • CR2 • **TP53** mutation • MRD at time of HCT: 1.8% blasts	MRD ~D95 after Mylotarg 1st cycle, received two additional cycles Mylotarg	0.5 mg/m^2 x 3	Yes
	51/F	• Complex karyotype, adverse cytogenetics (ELN) • High risk molecular: ASXL1 • **TP53** mutation • Active disease at time of HCT: 78% blasts	MRD after 1st Mylotarg cycle, received 2 additional cycles before relapse	1.0 mg/m^2 x 3	Yes

Data cut-off 19-JUL-2024, Day post HCT and Disposition as of 26-JUL-2024
AML-MRC: AML with myelodysplasia-related change

Potential Registrational Trial Design for Trem-cel/Mylotarg

Patient Journey

Key Eligibility Criteria

- 18-70 years of age
- 8/8 HLA matched related/unrelated donor
- Suitable for MAC
- AML:
  - CD33+ AML
  - Morphological CR1/CR2 or CRi
  - High-risk disease (MRD+ or genetics)

AML (n=60-80) → MAC → Trem-cel → 60d → Mylotarg

Assess engraftment, GVHD, CD33 negativity

Option A: Observational control group
Option B: Randomized study with control arm

Potential registrational endpoint: relapse-free survival

- RFS (primary)
- Median time to relapse
- Hematologic protection from Mylotarg-induced cytopenias

Plan is to continue enrollment at 2.0 mg/m^2 and,
if data continues to be favorable, approach regulators around year end

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

~7-day
manufacturing

Cells harvested from prior transplant donor

Rapid process to preserve stemness

Terminally frozen for convenience

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

Prior Transplant Donor

Consent

Collect

Lymphodepletion

VCAR33^{ALLO} Infusion

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

VCAR33^{ALLO} Manufacturing

~7-day process

Arm A: Blasts ≥ 5%

Arm B: MRD$^+$

Day 28 Follow-up

2nd transplant if required

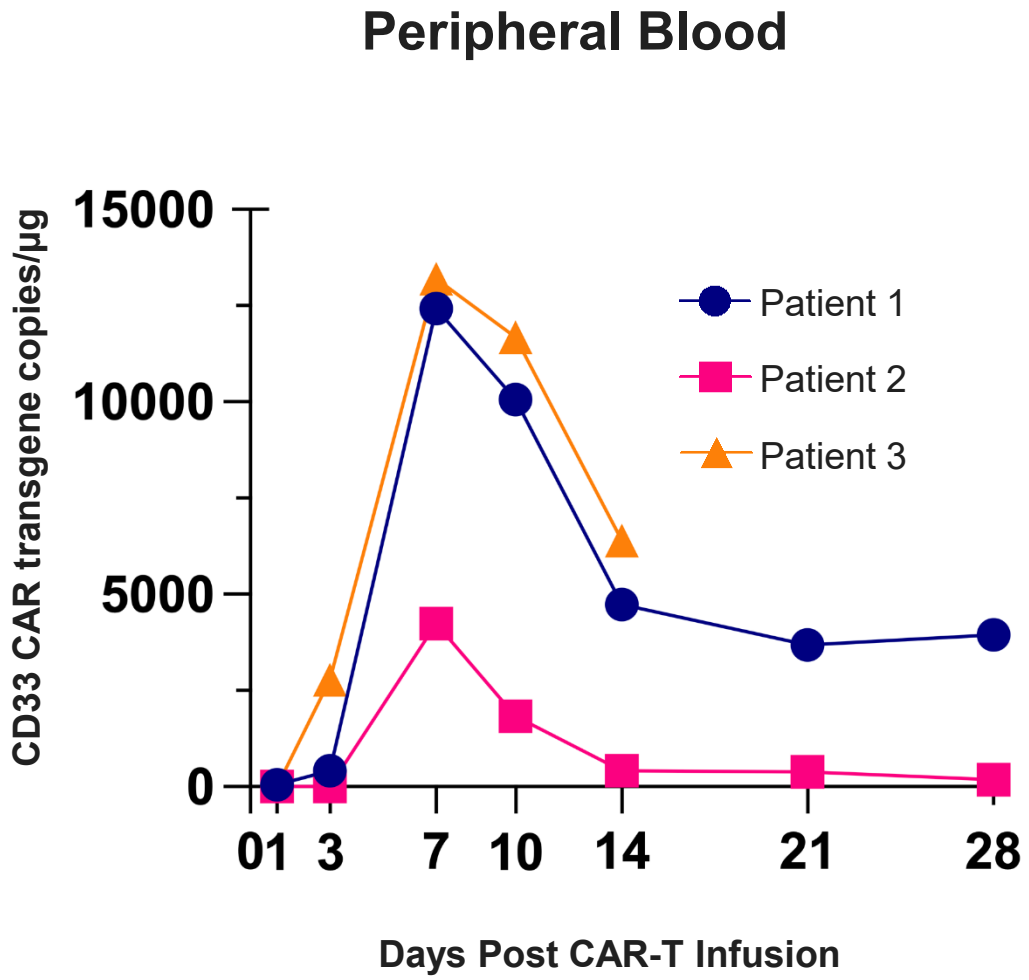
Key Endpoints

01 Safety

02 Expansion, persistence

03 Disease control/response

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



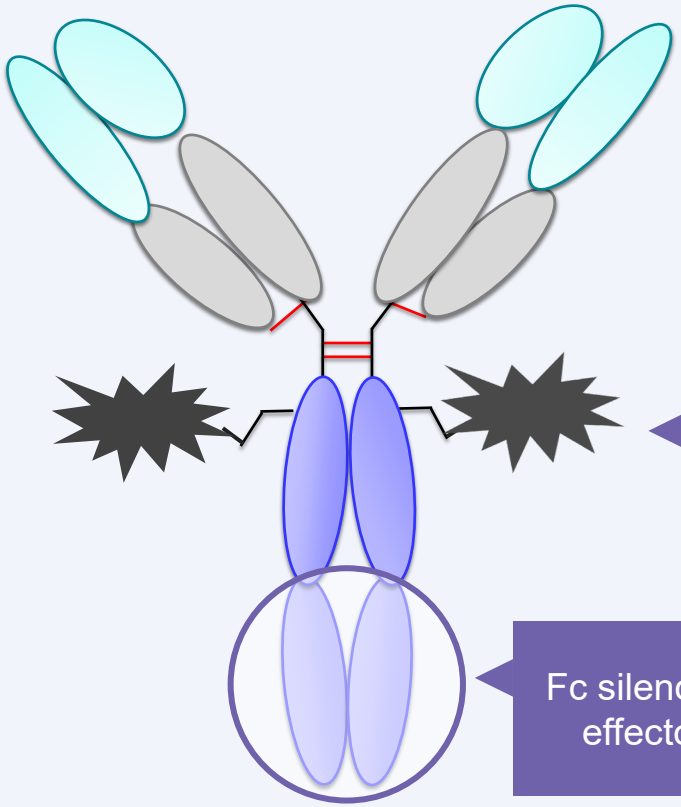
- Dose escalation schedule:
  - 1 x 10^6 CAR+ cells/kg
  - 3 x 10^6 CAR+ cells/kg
  - 1 x 10^7 CAR+ cells/kg
- NCI CD33CART trial (autologous) saw in vivo expansion and 2 responses out of 5 assessable patients at 1 x 10^7 CAR+ cells/kg*

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

VADC45 and Closing Remarks

Robert Ang, MBBS, MBA, President & CEO

Introducing VADC45, a Novel CD45-Targeted Antibody Drug Conjugate



Novel pan-CD45 humanized antibody cross-reactive to NHP

DGN549 payload with cleavable linker

Fc silencing to avoid effector function

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

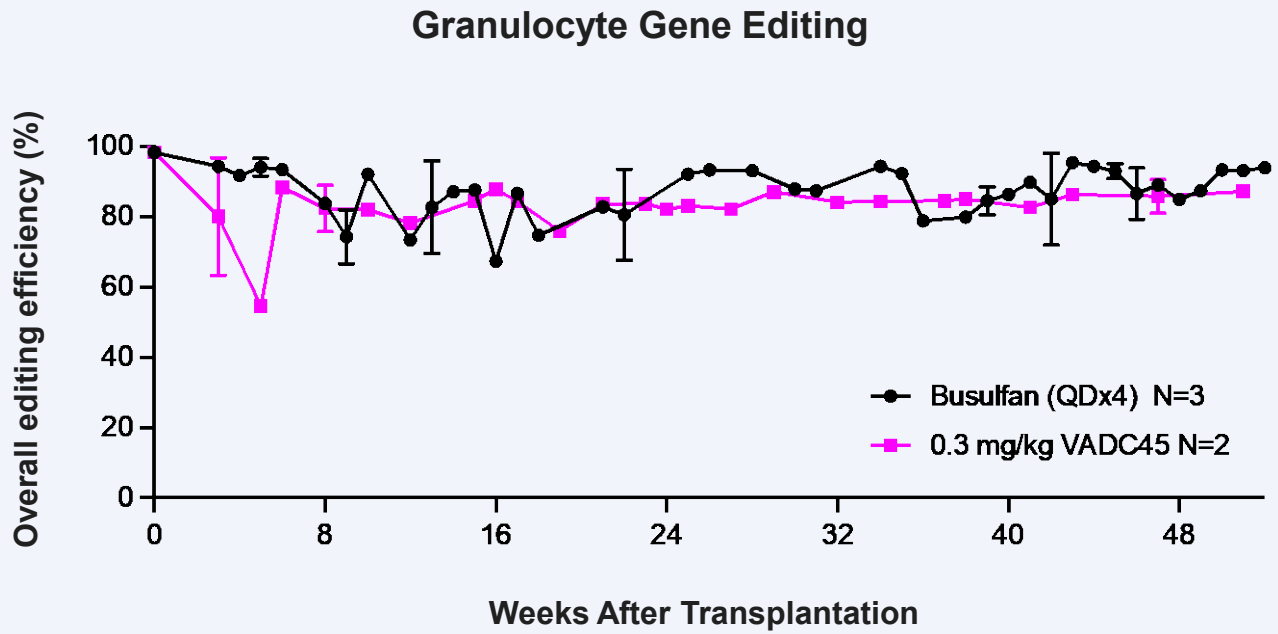
Epitope Engineering - Shielded Grafts

- 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

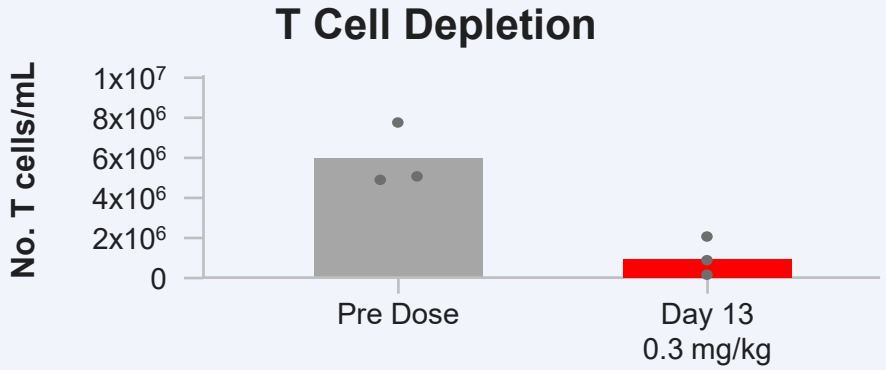
Very high myeloid chimerism achieved within days of transplant

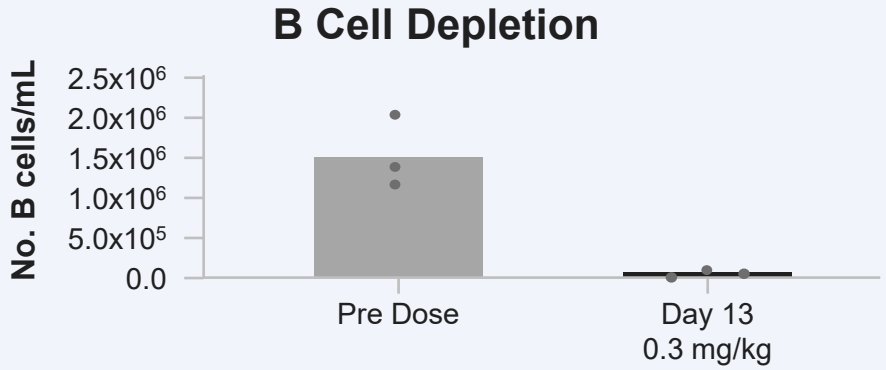
Persistently high edited populations through one year from transplant

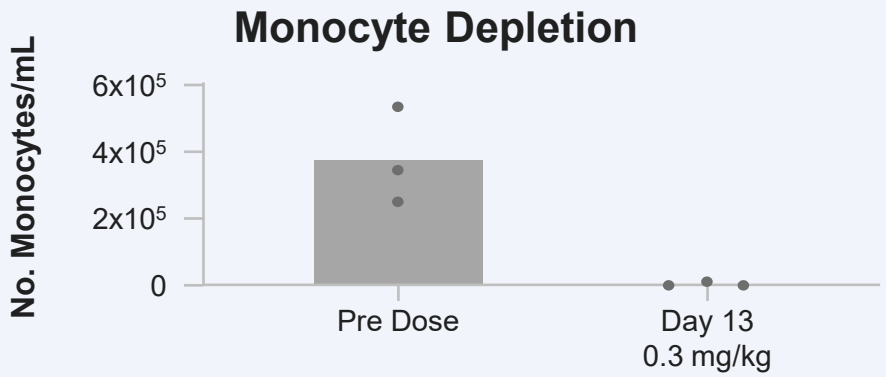
Tisdale et al. (NIH), preclinical data

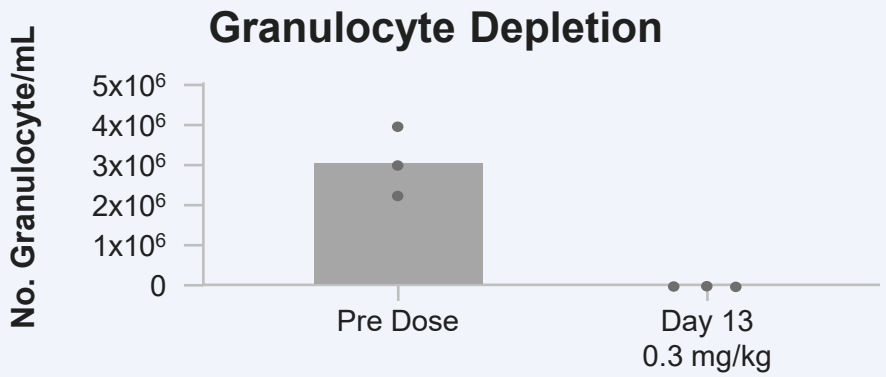
Single Dose of VADC45 Efficiently Depleted Immune Cells

Immune Cell Depletion from Peripheral Blood (NHP)









Preclinical data

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

VCAR33^{ALLO}, differentiated transplant donor CAR-T therapy

- Encouraging signs of in vivo expansion with strong trial enrollment

New asset: VADC45

- Four distinct potential commercial opportunities

*Potential to be first-in-class if approved

Summary & Perspective on VBP101

Guenther Koehne, MD, PhD

www.vorbio.com