# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**WASHINGTON, D.C. 20549**

# FORM 8-K

**CURRENT REPORT**
**Pursuant to Section 13 or 15(d)**
**of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): September 5, 2024**

# Vor Biopharma Inc.
**(Exact name of registrant as specified in its Charter)**

| **Delaware** | **001-39979** | **81-1591163** |
|---|---|---|
| **(State or Other Jurisdiction of Incorporation)** | **(Commission File Number)** | **(IRS Employer Identification No.)** |

| | |
|---|---|
| **100 Cambridgepark Drive** | |
| **Suite 101** | |
| **Cambridge, Massachusetts** | **02140** |
| **(Address of Principal Executive Offices)** | **(Zip Code)** |

**Registrant's telephone number, including area code: (617) 655-6580**

**(Former Name or Former Address, if Changed Since Last Report)**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instructions A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| Common Stock, $0.0001 par value per share | VOR | Nasdaq Global Select Market |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 7.01 Regulation FD Disclosure**

On September 5, 2024, Vor Biopharma Inc. (the "Company" or "Vor Bio") issued a press release entitled "New Clinical Data Validates Vor Bio's Approach of Using Shielded Transplants to Deliver Targeted Therapies," a copy of which is attached hereto as Exhibit 99.1 to this report and incorporated herein by reference.

The Company from time to time presents and/or distributes to the investment community presentations related to its business. A copy of its most recent presentation is attached hereto as Exhibit 99.2 and incorporated herein by reference.

The information furnished under this Item 7.01, including Exhibits 99.1 and 99.2, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or subject to the liability of that section, nor shall it be deemed incorporated by reference in any of the Company's filings under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such a filing, except as expressly set forth by specific reference in such a filing.

**Item 8.01 Other Events**

On September 5, 2024, the Company announced updated clinical data from its ongoing Phase 1/2 VBP101 study of patients with relapsed/refractory AML receiving trem-cel followed by Mylotarg™. The data included 18 patients treated with trem-cel of which ten had received Mylotarg as of the data cut-off date of July 19, 2024. The data demonstrated:

- Reliable engraftment, with 100% of patients achieving primary neutrophil engraftment (median 9 days) and robust platelet recovery (median 16.5 days). High CD33 editing efficiency (median 89%, range 71-94%) and full myeloid chimerism at Day 28.
- Shielding of the blood system, with maintained neutrophil and platelet counts across multiple Mylotarg doses of 0.5, 1, and 2 $mg/m^2$.
- Broadened therapeutic index for Mylotarg with drug exposure represented by AUC which is related to efficacy, consistent with labeled Mylotarg doses, and with maximal concentrations, measured by $C_{max}$ and related to veno-occlusive disease, well below known toxic range.
- Early evidence suggesting patient benefit as measured by relapse-free survival when compared to published high-risk AML comparators, with only four patients relapsing, two of which occurred before Mylotarg treatment, and two occurring following Mylotarg, both with TP53 mutations.

With this data, the Company plans to explore a registrational trial while it continues to pursue other synergistic opportunities for Vor Bio's platform such as $VCAR33^{ALLO}$ and VADC45.

With respect to the $VCAR33^{ALLO}$ program, the Company announced that the VBP301 study continues enrolling patients with initial focus on relapsed/refractory AML post-transplant, and that the Company is encouraged by in vivo CAR-T expansion data from three patients treated to date, all at the lowest dose of $1 \times 10^6$ CAR+ cells/kg.

The Company also announced a new preclinical asset, VADC45, which has a number of potential opportunities in oncology, gene therapy, and autoimmune disorders.

- VADC45 is an ADC that targets the CD45 protein. CD45 is a well-validated target for a wide variety of blood cancers with clinical proof of concept. The linker-payload used in VADC45 is also clinically validated.
- VADC45 has the potential to treat a number of diseases, including treatment of hematologic malignancies, as a targeted conditioning agent for gene therapies such as for sickle cell disease, holistic immune reset for autoimmune disorders, and for Vor Bio's approach of combining this asset with epitope modification of CD45 to shield healthy stem cells.

- Vor Bio already has robust preclinical data for VADC45 and is progressing IND-enabling studies to enable future Phase 1 studies.

**Forward-Looking Statements**

This Current Report on Form 8-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. The words "aim," "anticipate," "can," "continue," "could," "design," "enable," "expect," "initiate," "intend," "may," "on-track," "ongoing," "plan," "potential," "should," "target," "update," "will," "would," 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 Current Report on Form 8-K include Vor Bio's statements regarding the potential of its product candidates to positively impact quality of life and alter the course of disease in the patients it seeks to treat, the timing of regulatory filings and initiation of clinical trials, the timing and pace of patient enrollment and dosing in clinical trials and the availability of data therefrom, the expected safety profile of its product candidates, its intentions to use 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, and the ability of VADC45 to treat hematologic malignancies and to be used as a targeted conditioning agent for gene therapies, as a holistic immune reset for autoimmune disorders, and in combination with opitope modification of CD45 to shield healthy stem cells. 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 and completion of preclinical studies and clinical trials and clinical development of Vor Bio's product candidates; availability and timing of results from preclinical studies and clinical trials; whether interim results from a clinical trial will be predictive of the final results of the trial or the results of future trials; uncertainties regarding 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 and Vor Bio's ability to continue as a going concern. 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 Current Report on Form 8-K speak only as of the date hereof, 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.

**Item 9.01 Financial Statements and Exhibits**

| Exhibit No. | Description |
|---|---|
| 99.1 | Press Release, dated September 5, 2024 |
| 99.2 | Corporate Presentation, dated September 2024 |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**Vor Biopharma Inc.**

Date: September 5, 2024

By: /s/ Robert Ang
Robert Ang
Chief Executive Officer

**New Clinical Data Validates Vor Bio's Approach of Using Shielded Transplants to Deliver Targeted Therapies**

- *Trem-cel + Mylotarg demonstrated engraftment, shielding, broadened therapeutic window, and patient benefit*
- *VCAR33$^{ALLO}$ demonstrates encouraging biomarker data at lowest dose*
- *New asset VADC45 with significant potential opportunities across oncology, gene therapy, and autoimmune disorders*

CAMBRIDGE, Mass., September 5, 2024 (GLOBE NEWSWIRE) — Vor Bio (Nasdaq: VOR), a clinical-stage cell and genome engineering company, today announced new clinical data from its ongoing Phase 1/2 VBP101 study of patients with relapsed/refractory AML receiving trem-cel followed by Mylotarg™. The data demonstrated reliable engraftment, shielding from Mylotarg on-target toxicity, a broadened Mylotarg therapeutic window, and early evidence of patient benefit.

"We are encouraged by this data and the potential benefit that trem-cel in combination with Mylotarg may offer to patients in a disease that has extremely poor outcomes even after transplant," said Dr. Eyal Attar, Vor Bio's Chief Medical Officer. "With this data, we plan to explore a registrational trial while we continue to pursue other synergistic opportunities for Vor Bio's platform such as VCAR33$^{ALLO}$ and VADC45."

***The data released today included 18 patients treated with trem-cel of which ten had received Mylotarg as of the data cut-off date of July 19, 2024. The data demonstrated:***

- Reliable engraftment, with 100% of patients achieving primary neutrophil engraftment (median 9 days) and robust platelet recovery (median 16.5 days). High CD33 editing efficiency (median 89%, range 71-94%) and full myeloid chimerism at Day 28.
- Shielding of the blood system, with maintained neutrophil and platelet counts across multiple Mylotarg doses of 0.5, 1, and 2 mg/m$^2$.
- Broadened therapeutic index for Mylotarg with drug exposure represented by AUC which is related to efficacy, consistent with labeled Mylotarg doses, and with maximal concentrations, measured by $C_{max}$ and related to veno-occlusive disease, well below known toxic range.
- Early evidence suggesting patient benefit as measured by relapse-free survival when compared to published high-risk AML comparators[1].

"All the hope I had in the safety of this approach has been supported by the data from this trial thus far," said Guenther Koehne, MD, PhD, an investigator on the VBP101 study and Deputy Director and Chief of Blood & Marrow Transplant and Hematologic Oncology at Miami Cancer Institute of Baptist Health South Florida, "I look forward to treating my next patients at high risk of relapse on this trial as their outcomes are otherwise limited with standard transplants."

Vor Bio plans to approach the U.S. Food & Drug Administration to discuss a pivotal trial design for trem-cel + Mylotarg by around year end.

[1] Araki et al. JCO 2016; Jentzsch et al. Blood Cancer Journal 2022.

***Continued progress with VCAR33$^{ALLO}$***

- VCAR33$^{ALLO}$ represents another potentially significant synergistic treatment option after trem-cel.
- The VBP301 study continues enrolling patients with initial focus on relapsed/refractory AML post-transplant.
- Vor Bio is encouraged by *in vivo* CAR-T expansion data from three patients treated to date, all at the lowest dose of 1 x $10^6$ CAR+ cells/kg.

***Vor Bio announced today, a new preclinical asset, VADC45, which has a number of potential opportunities in oncology, gene therapy, and autoimmune disorders.***

- VADC45 is an ADC that targets the CD45 protein. CD45 is a well-validated target for a wide variety of blood cancers with clinical proof of concept. The linker-payload used in VADC45 is also clinically validated.
- VADC45 has the potential to treat a number of diseases, including treatment of hematologic malignancies, as a targeted conditioning agent for gene therapies such as for sickle cell disease, holistic immune reset for autoimmune disorders, and for Vor Bio's approach of combining this asset with epitope modification of CD45 to shield healthy stem cells.
- Vor Bio already has robust preclinical data for VADC45 and is progressing IND-enabling studies to enable future Phase 1 studies.

**Conference Call & Webcast Information**

Vor Bio management, joined by Guenther Koehne, MD, PhD, will host a live webcast today at 4:30 PM ET.

Listeners can register for the webcast via this LINK

Analysts wishing to participate in the Q&A session should use this LINK

A replay of the webcast will be available via the investor section of the Company's website at www.vorbio.com approximately two hours after the call's conclusion.

**About Vor Bio**

Vor Bio is a clinical-stage cell and genome engineering company that aims to change the standard of care for patients with blood cancers by engineering hematopoietic stem cells to enable targeted therapies post-transplant. For more information, visit: www.vorbio.com.

**Forward-Looking Statements**

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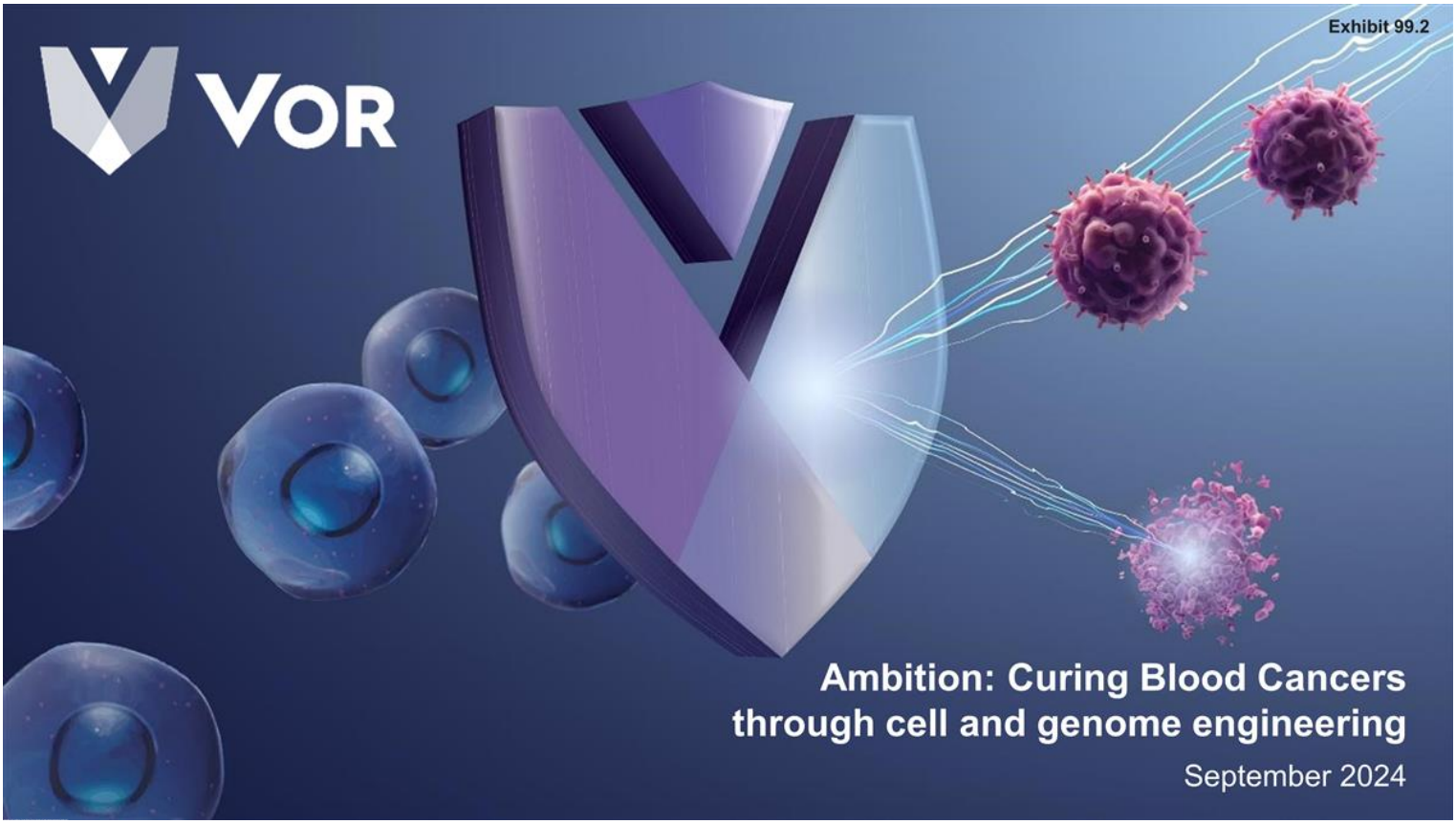
expected safety profile of its product candidates, its intentions to use VCAR33$^{ALLO}$ in combination with trem-cel as a Treatment System, the potential of trem-cel to enable targeted therapies in the post-transplant setting including Mylotarg and CD33-targeted CAR-Ts, and the ability of VADC45 to treat hematologic malignanciesand to be used as a targeted conditioning agent for gene therapies, as a holistic immune reset for autoimmune disorders, and in combination with opitope modification of CD45 to shield healthy stem cells. 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 and completion of preclinical studies and clinical trials and clinical development of Vor Bio's product candidates; availability and timing of results from preclinical studies and clinical trials; whether interim results from a clinical trial will be predictive of the final results of the trial or the results of future trials; uncertainties regarding 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 and Vor Bio's ability to continue as a going concern. 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 press release speak only as of the date hereof, 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.

**Contact:**

Investors & Media
Sarah Spencer
+1 857-242-6076
sspencer@vorbio.com

Exhibit 99.2



# Ambition: Curing Blood Cancers through cell and genome engineering

September 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.

Certain information contained in this Presentation relates to or is based on studies, publications, surveys and other data obtained from third party sources and Vor Bio's own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this Presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third party sources. In addition, there can be no guarantee as to the accuracy or reliability of any assumptions or limitations that may be included in such third-party information. While we believe our own internal research is reliable, such research has not been verified by any independent source. All brand names or trademarks appearing in this Presentation, including Mylotarg, are the property of their respective owners.

# 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<br>-Engraftment of gene engineered graft<br>-Shielding the blood system<br>• Most rapid path to Treatment System | Encouraging data with commercial promise<br>• 100% engraftment<br>• Robust shielding of the blood system<br>• Broadened therapeutic index for Mylotarg<br>• 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

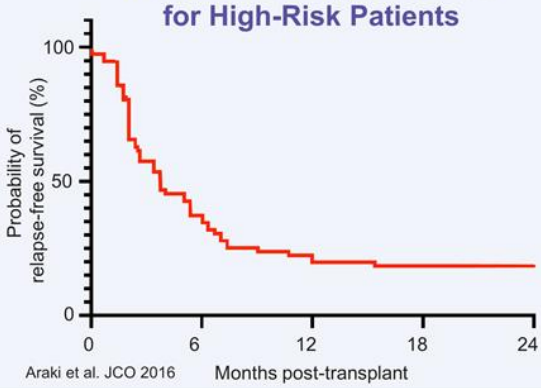
**Transplant**

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

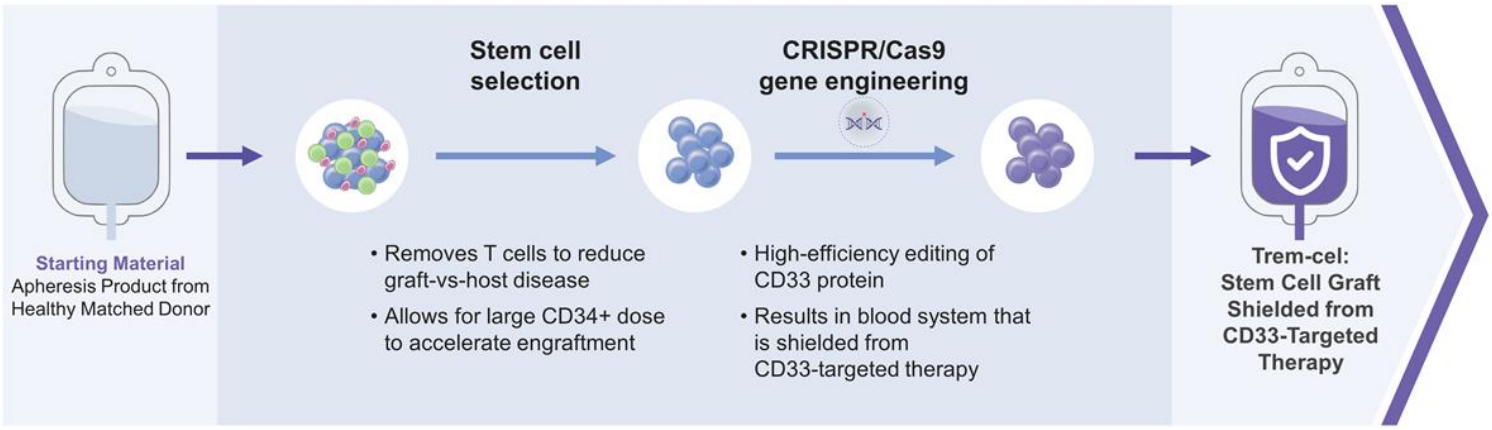
CAR-T

**…potentially leading to improved outcomes**

## Required Shielded Graft Attributes

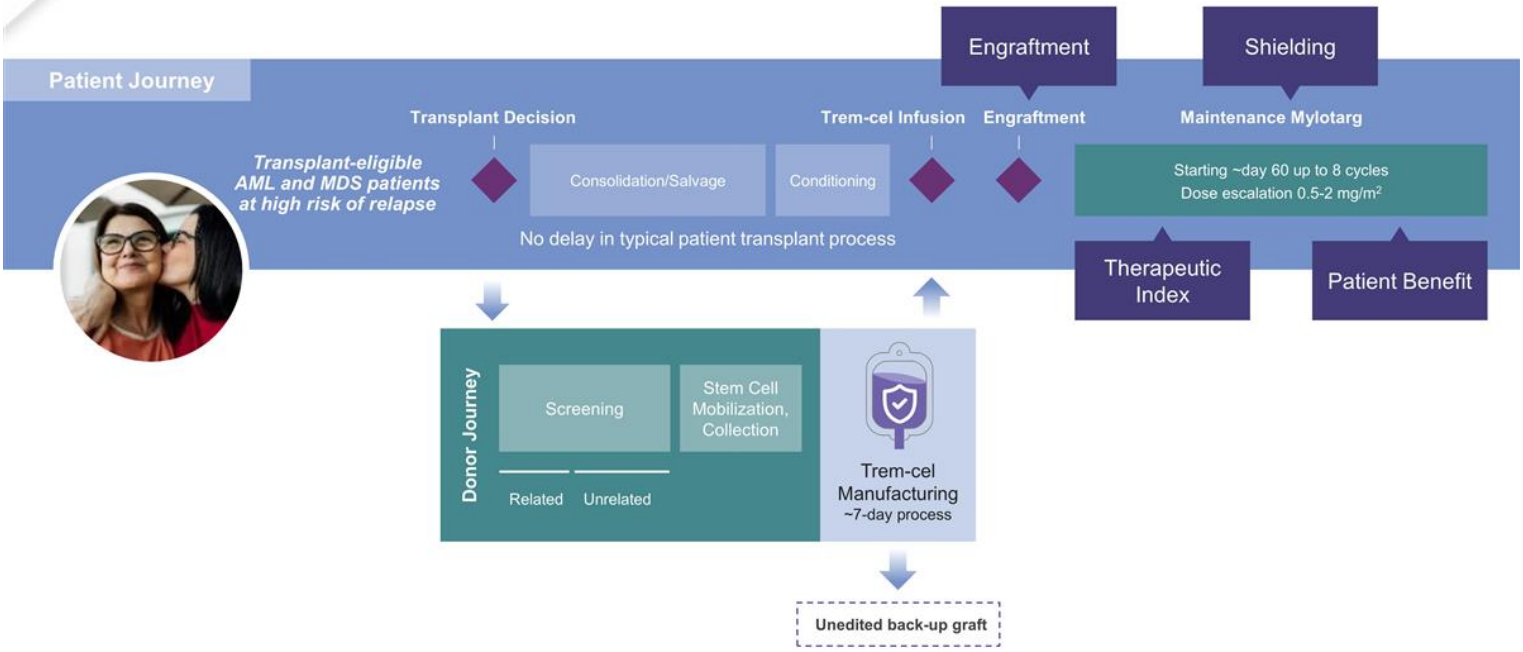
- **Engraftment**
  Reliably reconstitute the blood system
- **Shielding**
  Protect against otherwise toxic therapies
- **Therapeutic Index**
  Optimize efficacy and safety of maintenance therapies
- **Patient Benefit**
  Prolong relapse-free survival

# What is Trem-Cel?




~7 day manufacturing process

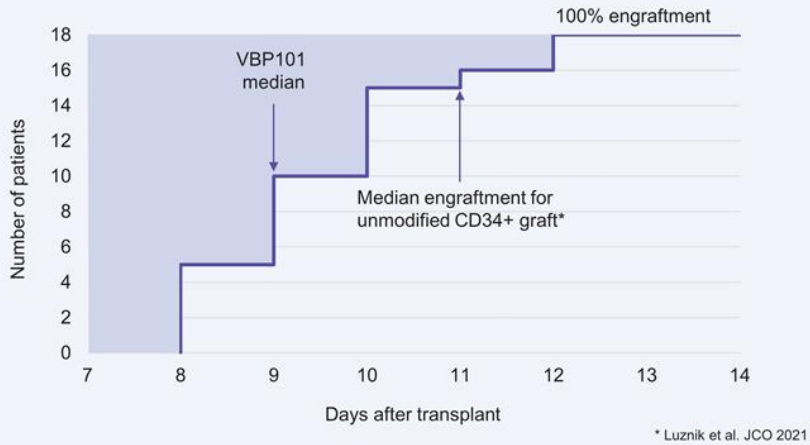
# VBP101: Trem-cel Phase 1/2a Clinical Trial



# 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)



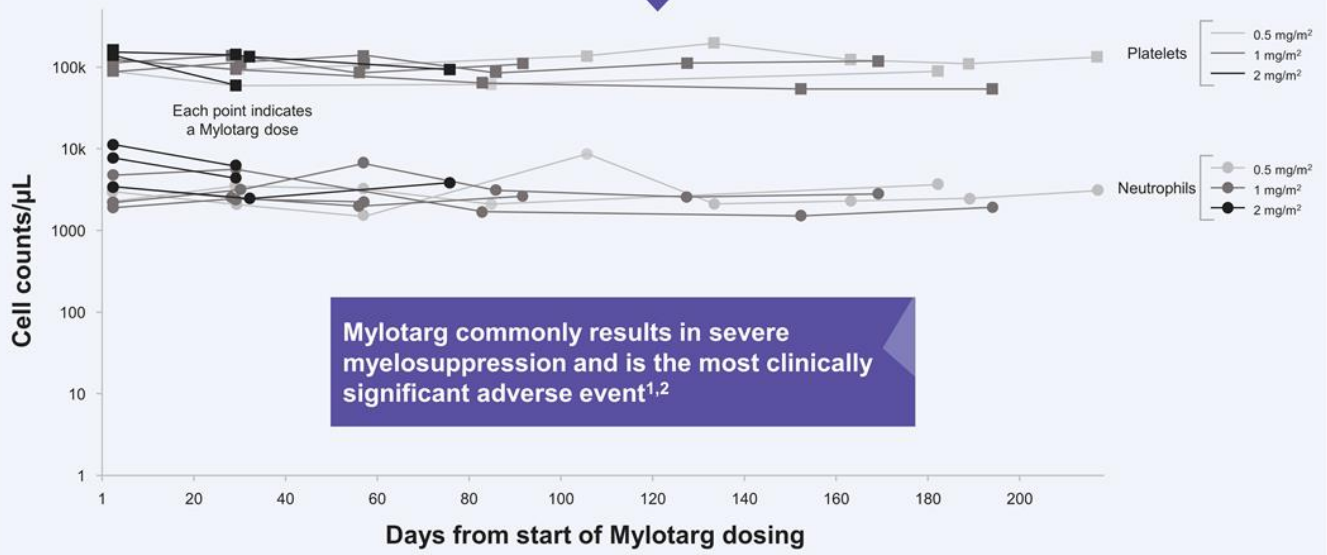

* Luznik et al. JCO 2021



Data cut-off: 19-JUL-2024

# Trem-cel Demonstrated Shielding Across Mylotarg Doses

## Neutrophil and Platelet Peripheral Blood Counts with Mylotarg Doses

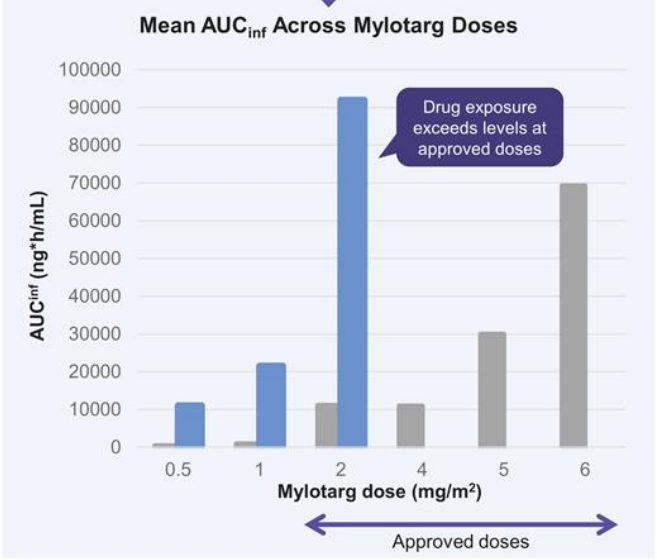



**Mylotarg commonly results in severe myelosuppression and is the most clinically significant adverse event[1,2]**

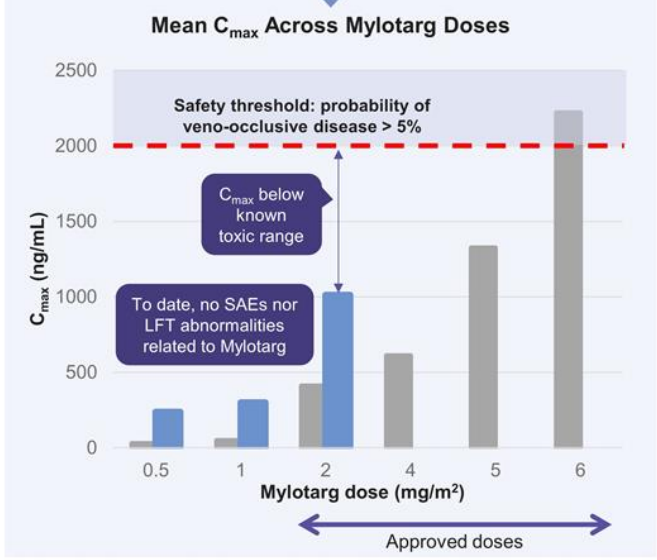
1. Sievers et al. Blood 1999 2. Mylotarg prescribing information
Data cut-off: 19-JUL-2024

# 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

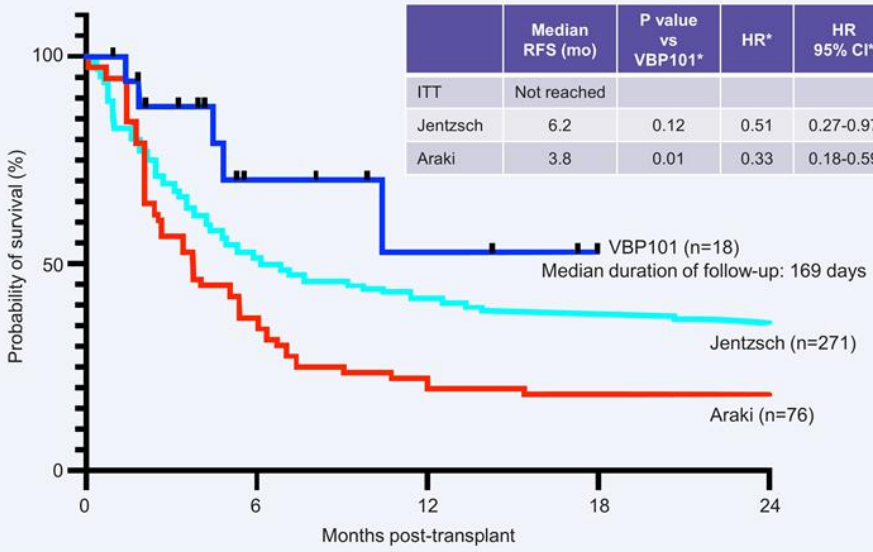
| Study (Publication Year) | VBP101 ITT N=18 | VBP101 AT n=10 | Araki MRD+ (2016) n=75 | Jentzsch Adverse Risk (2022) n=271 |
|---|---|---|---|---|
| **CR1 (%)** | 61 | 50 | 67 | 90 |
| **CR2 (%)** | 22 | 40 | 33 | 10 |
| **Active Disease(%)** (median blast %) | 17 (16%) | 10 (78%) | -- | -- |
| **MRD+(%)** (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

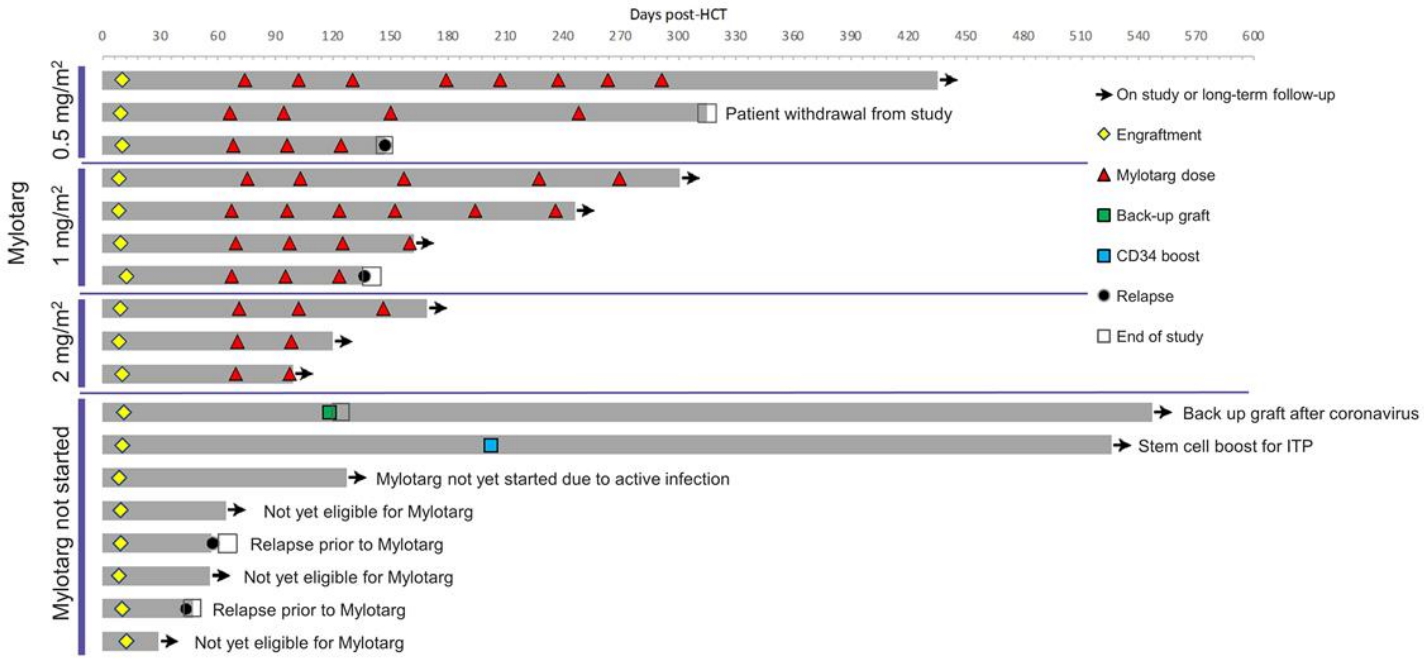
**Relapse-Free Survival of VBP101 (intention-to-treat) vs Araki and Jentzch (historical controls)**

| | 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.

# 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)<br>• Complex cytogenetics<br>• High risk molecular: NRAS, ZRSR2, TET2 mutations<br>• 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)<br>• FLT3-TKD and BCORL1<br>• 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)<br>• Complex karyotype<br>• CR2<br>• **TP53** mutation<br>• 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)<br>• High risk molecular: ASXL1<br>• **TP53** mutation<br>• Active disease at time of HCT: 78% blasts | MRD after 1$^{st}$ 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

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

## Significant Unmet Need

~35,000 AML & MDS new patients and
16,000 deaths per year[3,4,5]

## Concentrated Market Opportunity

~5,000 AML & MDS transplants per year with majority conducted at ~65 US centers[1,2]

## Reimbursement Pathway

100% cost-based reimbursement for stem cells*
(commercial example: Omisirge® at $338,000)



*2020 - IPPS (Inpatient Prospective Payment System), MS DRG-104 – Section 108, stem cell acquisition & processing for allo-SCTs
1. CIBMTR 2020 2. CIBMTR Summary Slides 3. ACS 4. LLS 5. Polednak AP, J Registry Mgmt 2011

# 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**

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

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

# 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

2$^{nd}$ 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

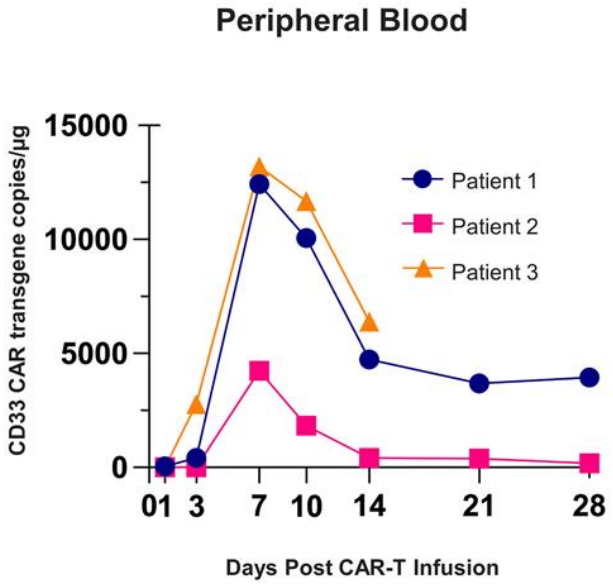
### Key Endpoints

01 Safety

02 Expansion, persistence

03 Disease control/response

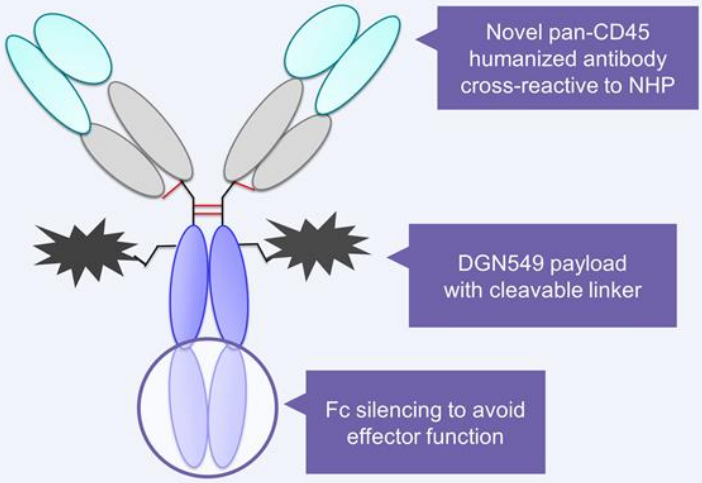
# VCAR33$^{ALLO}$: Encouraging Signs of *In Vivo* Expansion




- 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

# Introducing 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

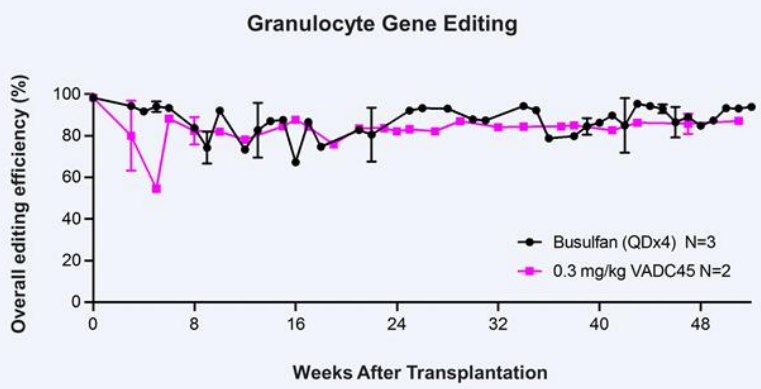
- Precise epitope for VADC45 has been identified
- Experiments are ongoing for epitope modification which retains protein functionality
- **Opportunity:** Heme malignancies



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

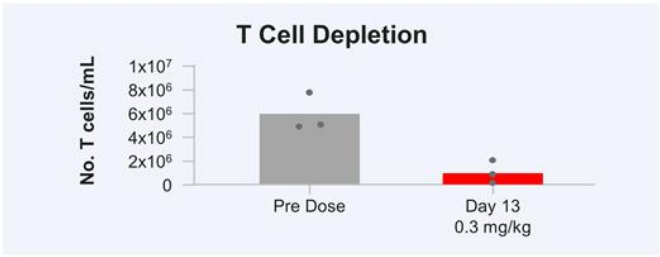
Very high myeloid chimerism achieved within days of transplant

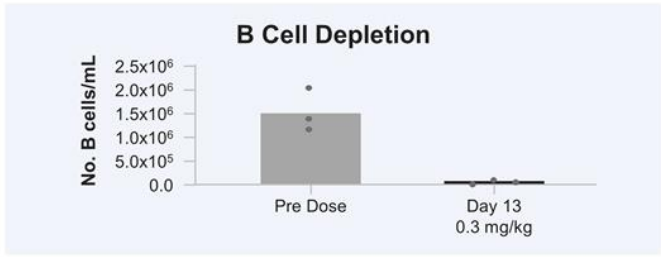
Persistently high edited populations through one year from transplant

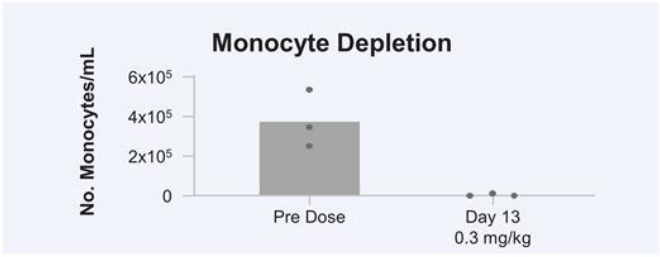
Tisdale et al. (NIH), preclinical data

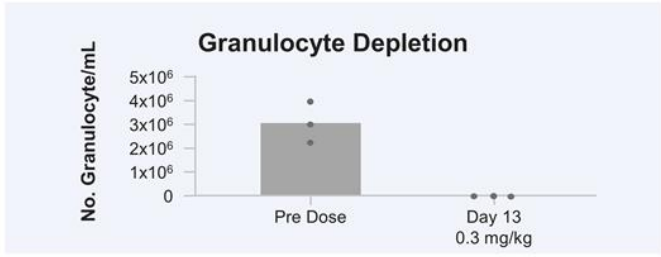
# Single Dose of VADC45 Efficiently Depleted Immune Cells

## Immune Cell Depletion from Peripheral Blood (NHP)



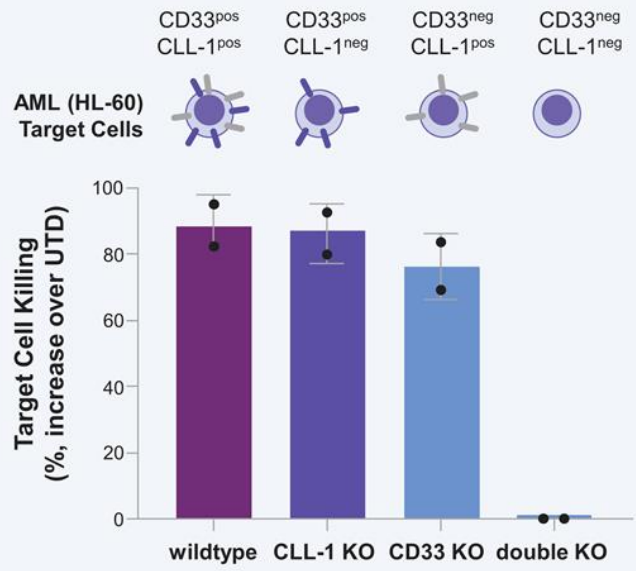



# Next-Generation Approaches

| | | |
|---|---|---|
| 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

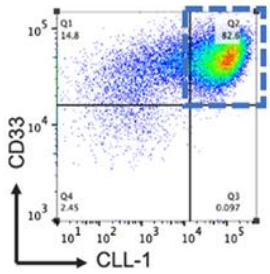
**Multi-Specific CAR-T cell (CD33+CLL-1)**

- 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

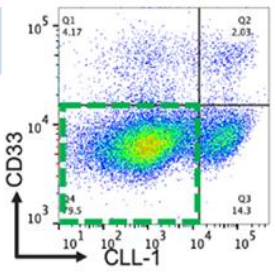
# Multiplex HSC Editing: Minimize Translocations

**Mock**



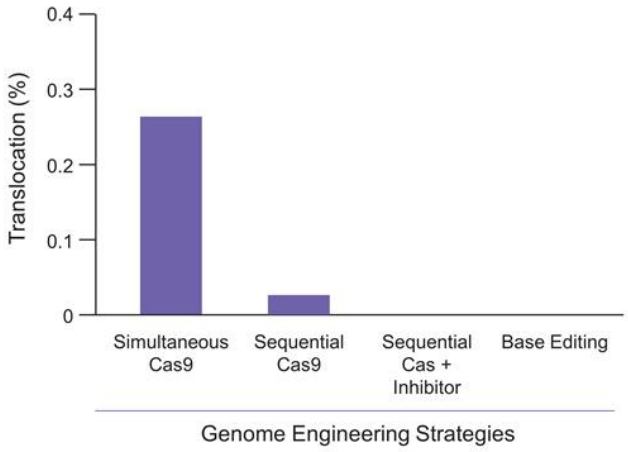

$CD33^{+}CLL\text{-}1^{+}$
Double Pos
**82.6%**

**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

**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

www.vorbio.com

Confidential

# 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

**Eyal Attar, MD**
Chief Medical Officer

**Tirtha Chakraborty, PhD**
Chief Scientific Officer

**Tania Philipp**
Chief People Officer

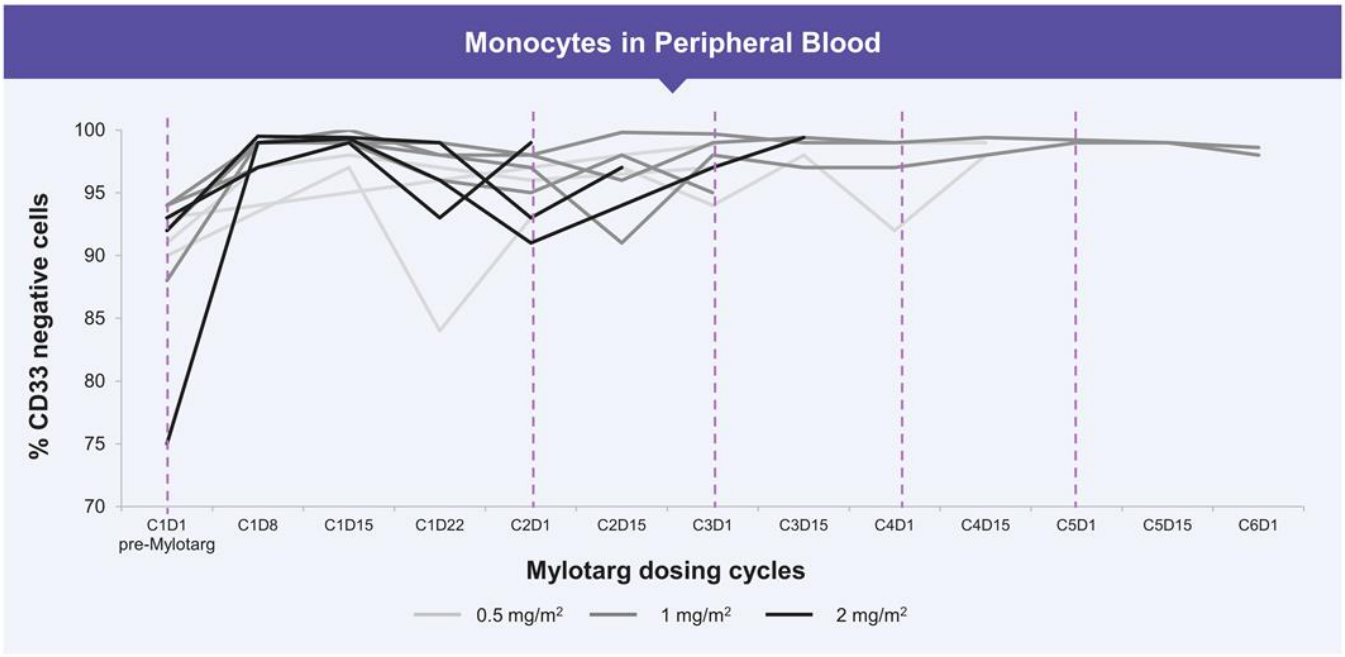
**John King, MBA**
Chief Commercial Officer & Head of Business Development

**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

# Mylotarg Enriched Blood System to ~100% CD33 Negative Cells

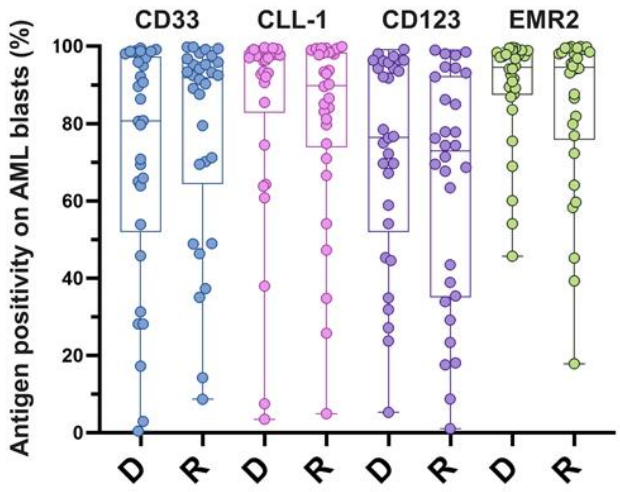




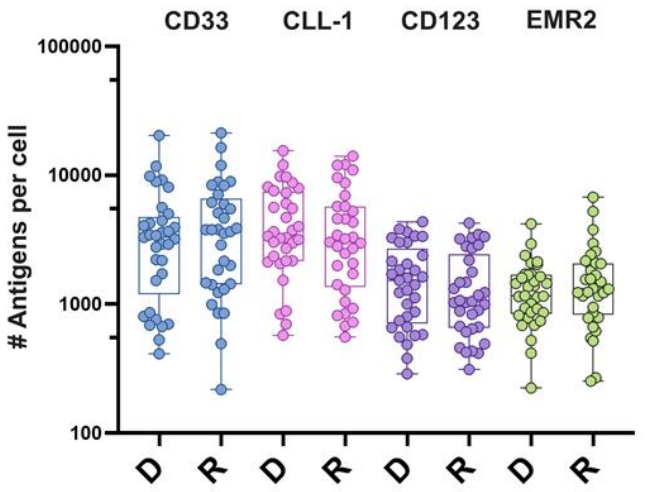
Data cut-off: 19-JUL-2024

# CD33 is Amongst Highest Quality Targets in AML

**Ubiquity of Antigen Expression (Flow Cytometry)**




**Density of Antigen Expression (QuantiBRITE)**






**D** = Diagnosis **R** = Relapse

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

**Probability of Veno-occlusive Disease in Patients with Prior Transplant**