

Subcutaneous, every-four-week maintenance dosing of a novel protein S antibody is well-tolerated and substantially reduces bleeding rates: Results from A phase 1/2 multi-dose study of VGA039 in patients with von Willebrand disease

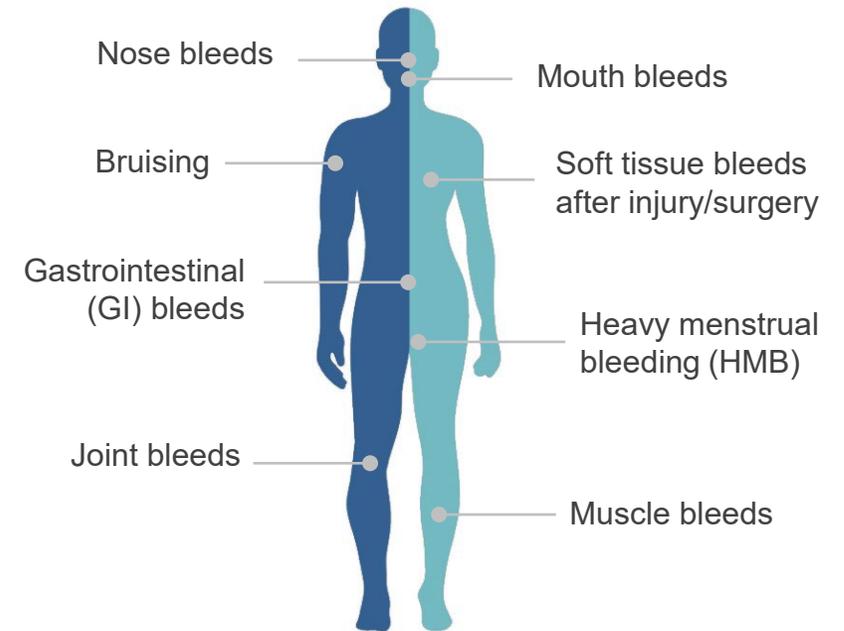
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Von Willebrand Disease - Unmet Therapeutic Need

- **VWD is the most common inherited bleeding disorder** characterized by recurrent, prolonged bleeding¹
- Impaired **platelet adhesion and unstable clot formation** result in ineffective hemostasis²
- Current treatment requires frequent IV infusions creating high burden of care and suboptimal bleed control^{1,2}
- There remains a need for innovation in less frequent SC treatment options that provide hemostatic protection
- **VGA039 is a SC, Q4-week therapy for VWD being investigated in the VIIVID clinical trial program³**

VWD Presentation²

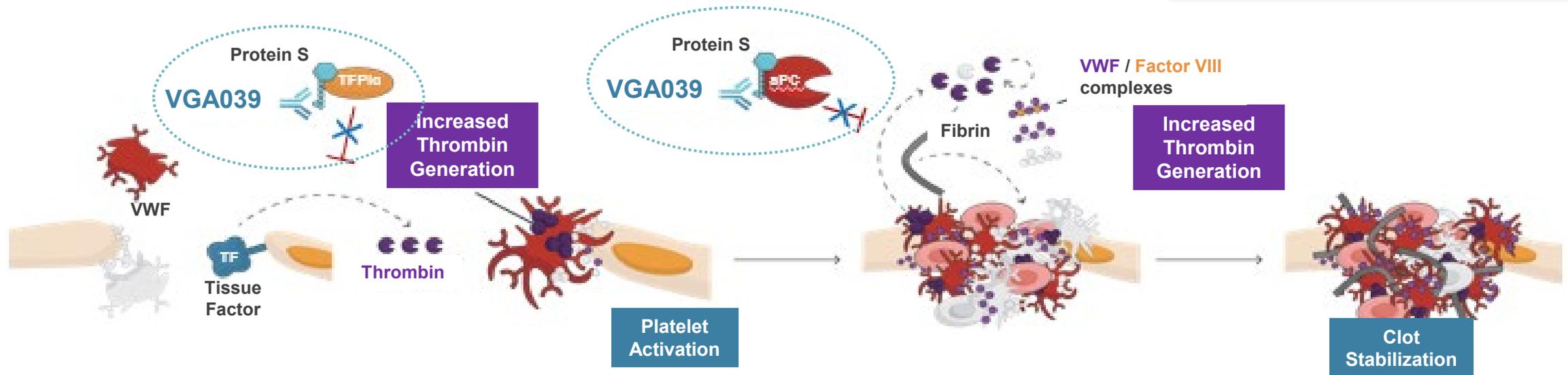


1. Sidonio RF et al. *J Blood Med.* 2020;11:1-11, 2. The diagnosis, evaluation, and management of von Willebrand disease. NIH Publication No 08-5832. 2007, 3. Millar et al. *Blood.* 2024;144(Suppl 1):3981. doi:10.1182/blood-2024-208020.; VWD, Von Willebrand Disease; IV, intravenous; SC, subcutaneous

VGA039 is Dual-Acting on Both TFPI α and aPC Pathways to Restore Hemostasis in VWD^{1,2}

- **VGA039** is a fully human, IgG4 monoclonal antibody that modulates the activity of Protein S, a cofactor for TFPI α and aPC
- Inhibition of Protein S activity by **VGA039** reduces aPC and TFPI α mediated anticoagulant activity, resulting in enhanced **thrombin generation** to restore hemostasis
 - **VGA039** does not deplete Protein S
 - Preserves TFPI β activity to limit clot expansion at site of vascular injury

See: VGA039 Mechanistic Data
Abstract #3051
Sunday, December 7th



VIVID-1 and VIVID-2 Phase 1/2 Single-Ascending Dose Studies: Foundational Evidence for VIVID-3

VIVID 1 25 normal healthy volunteers¹

VIVID 2 10 VWD patients (all types represented)²

received single dose of **VGA039**

- Well-tolerated without any safety signals
- Dose escalation completed (up to 7 mg/kg) SC without clinically significant D-dimer elevations
- TGA analyses established target pharmacodynamic threshold to be ≥ 25 $\mu\text{g/mL}$
- Half-life of ~ 27 days (3 mg/kg), enabling every-4-week, SC dosing for prophylaxis
- Substantial ABR reductions observed (75-88%)*²

1. Schoergenhofer C et al. OC 73.3, ISTH 2024; 2. Millar et al. Blood. 2024;144(Suppl 1):3981; *Population defined as hABR ≥ 50 ; mg/kg, milligrams per kilogram; TGA, thrombin generation assay; $\mu\text{g/mL}$, microgram per milliliter; SC, subcutaneous; ABR, annualized bleeding rate

VIVID 3: Open-label, Phase 1/2 Study of Multiple Doses of SC VGA039

Study Design



- Key inclusion criteria**
- Patients 12 to 60 years of age
 - Symptomatic **VWD of any type**

- Key exclusion criteria**
- Baseline factor VIII activity \geq LLN
 - History of thromboembolism or pro-thrombotic disorders
 - Use of estrogen-containing hormonal therapies within 56 days of study drug

Endpoints

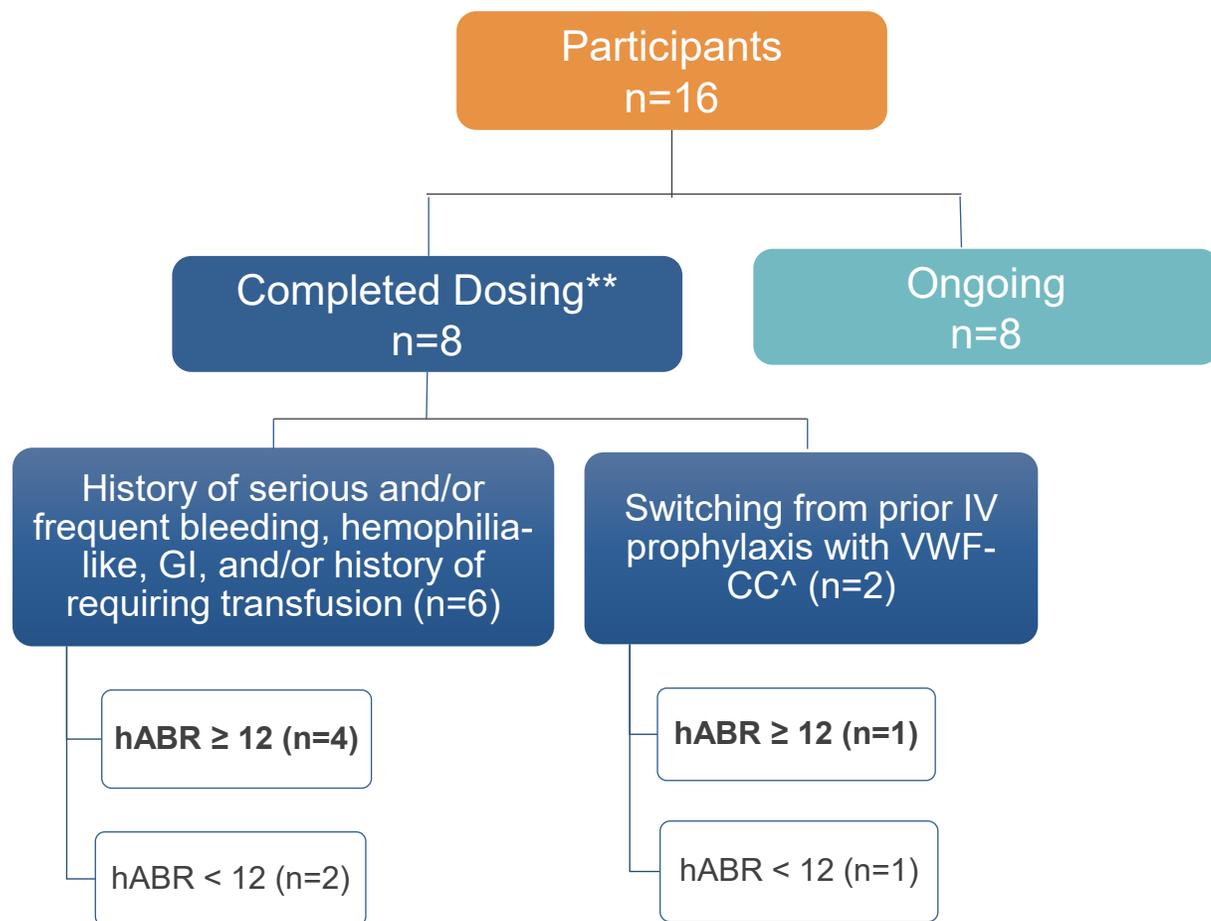
- Safety, including AEs and DLTs
- PK/PD profile
- Clinical effects on bleeding

* Weight-banded doses of SC VGA039 per the following criteria: 187.5 mg (45–<60 kg), 262.5 mg (60–100 kg), or 450 mg (>100 kg).

MD, Multiple doses; OLE, open label extension; SC, subcutaneous; VWD, Von Willebrand Disease, LLN, lower limit of normal; AE, adverse event; DLT, dose limiting toxicity; PK, pharmacokinetic; PD, pharmacodynamic

Profile of Participants in VIVID-3

Participant Status

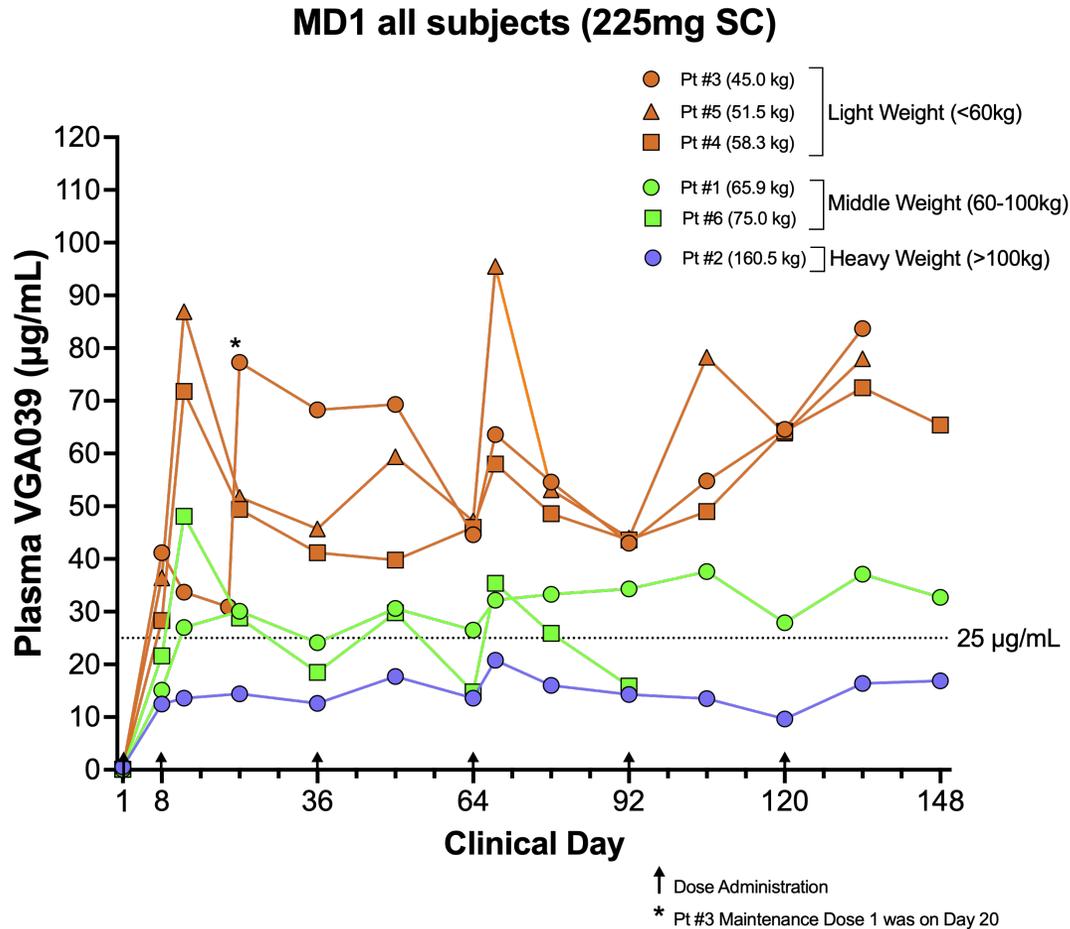


Baseline Characteristics

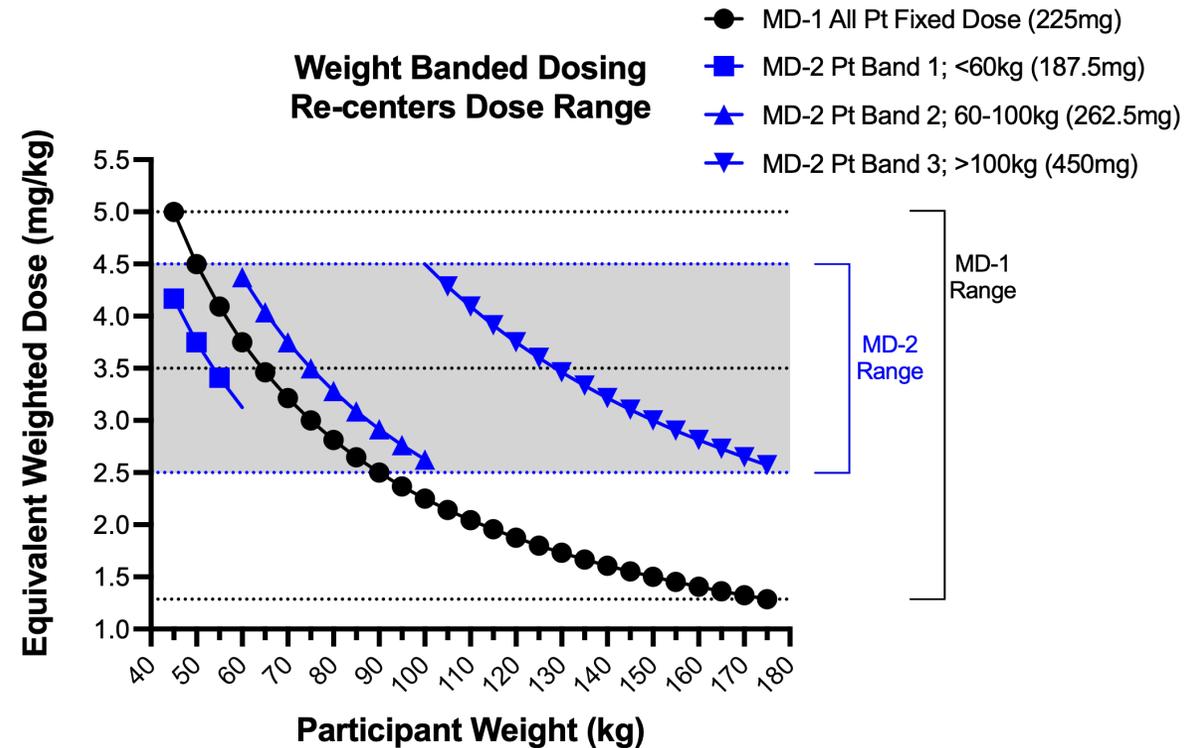
Study Cohort	MD-1 (N=6)	MD-2 (N=10)
Sex (N)	M (2) F (4)	M (6) F (4)
Age Mean (range)	24.7 yrs (15-53)	36.9 yrs (22-53)
Race	Asian (1) Black (1) White (4) Other (0)	Asian (1) Black (0) White (8) Other (1)
Weight Mean (range)	76.0 kg (45.0-160.5)	85.6 kg (61.7-124.5 kg)
Type/ Sub-Types (N)	1 (2) 2A (1) 2M (1) 3 (2)	1C (1) 2A (3) 2N (2) 3 (4)
Pre-MD ABR* (range)	(8.0-431.1)	(0.0-321.2)

VIVID-3– Dosing & Pharmacokinetics in Cohort MD-1 & MD-2

Pharmacokinetics of VGA039 in Cohort MD-1



Evaluation of Fixed SC Dosing: 225 mg (MD-1) and Weight-Banded Doses (MD-2)

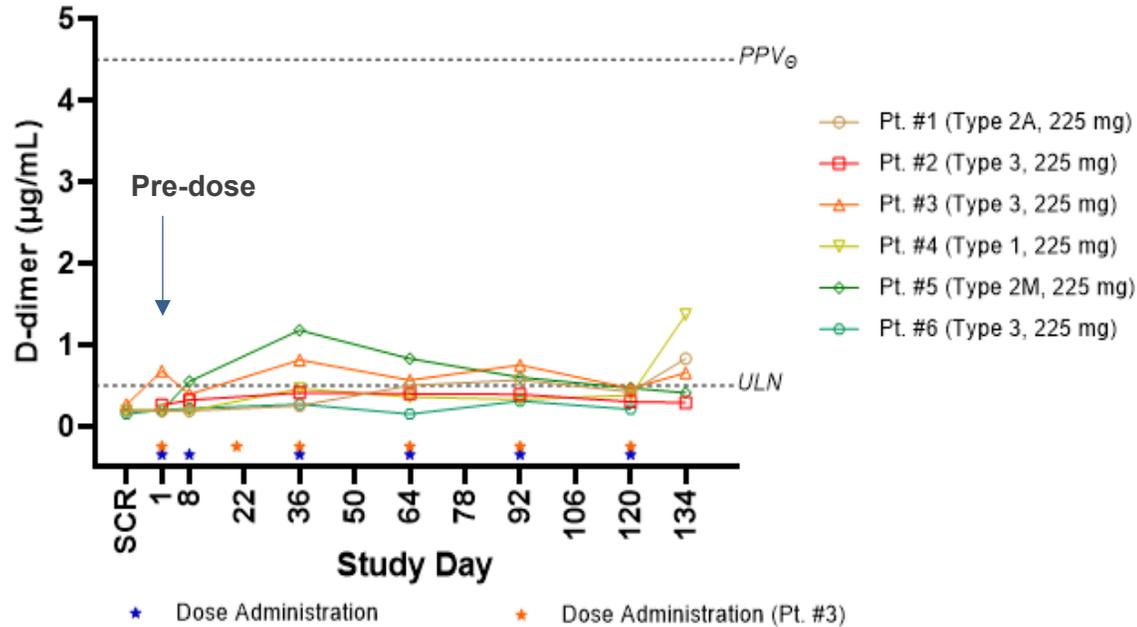


Cumulative Safety Summary in VIVID-3

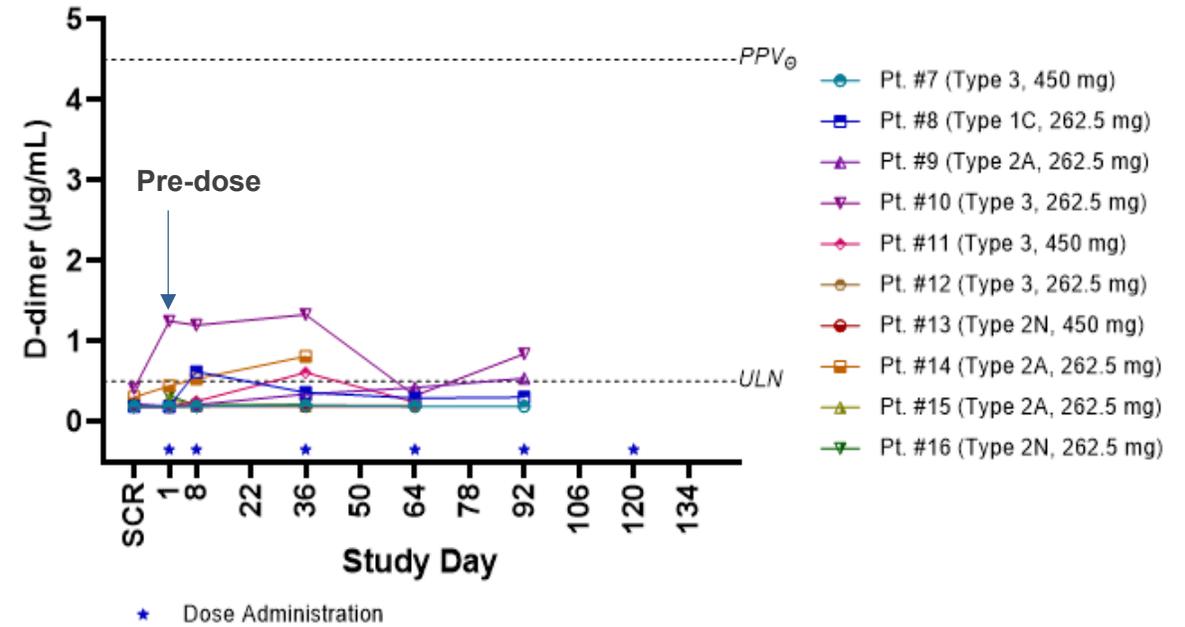
- As of 14NOV2025, 16 participants have enrolled and all have received at least 4 doses of VGA039
 - No withdrawals on therapy
 - No thromboembolic events
 - No injection site reactions
 - 39 treatment-emergent AEs reported in 10 participants
 - Two related Grade 2 events of headache reported in 1 participant
 - One unrelated, serious adverse event: severe GI bleeding (history of frequent and severe GI bleeding)
- To date, VGA039 appears safe and well-tolerated over multiple doses

D-Dimer Levels in Multi-Dose Cohorts MD-1 and MD-2

**Central D-dimer
Cohort MD-1
225 mg Fixed Dose**



**Central D-dimer
Cohort MD-2
Banded Fixed Dose**



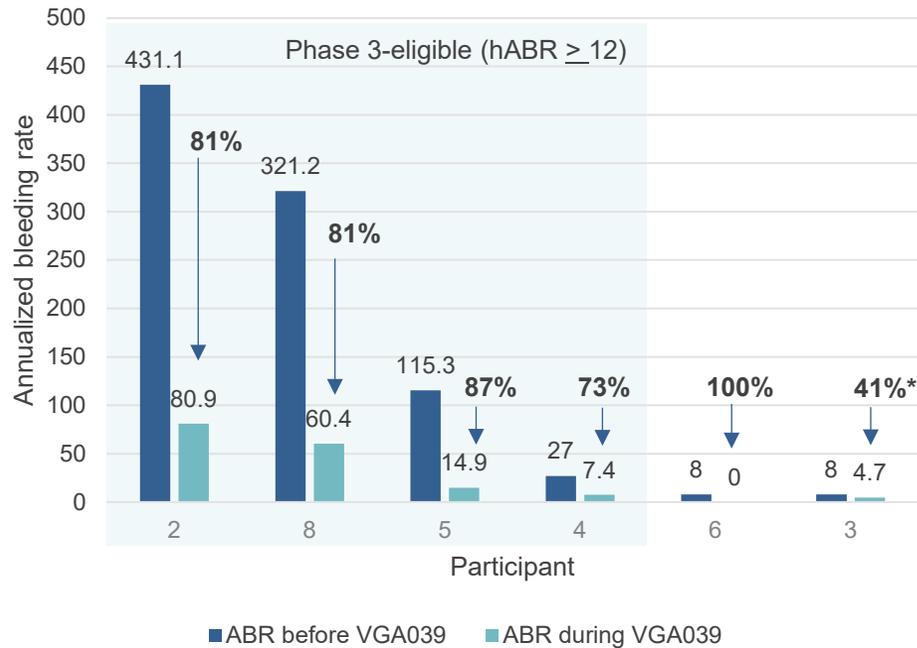
- Assumed Positive Predictive Value (PPV) = 9 X Upper Limit of Normal (ULN) (Koch V et al. *Eur Heart J Acute Cardiovasc Care*. 2021;10:559-566.)
- All samples were collected pre-dose on the days indicated

Bleeding Rates in 8 VWD Participants who Completed VGA039 Treatment Period*

Median Bleed Reduction: 81% (range 41-100%)
*Reductions of 73-87% in participants with hABR ≥ 12**

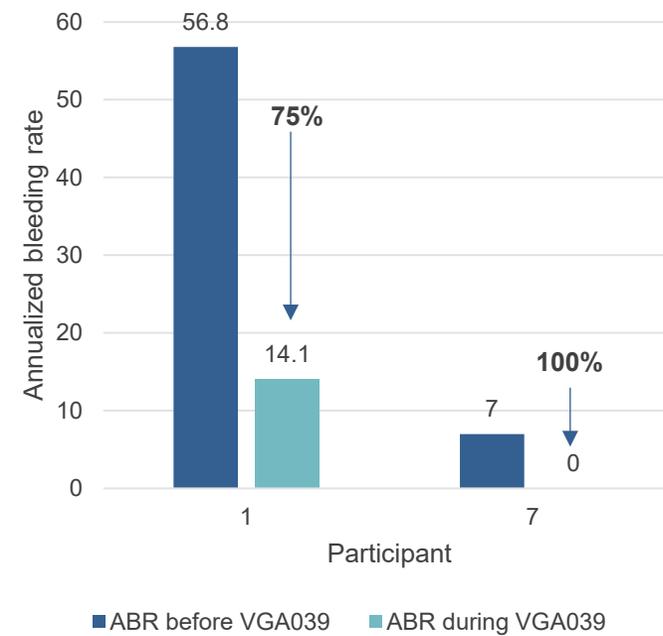
Participants with no prior IV prophylaxis

ABRs before and during VGA039 Treatment



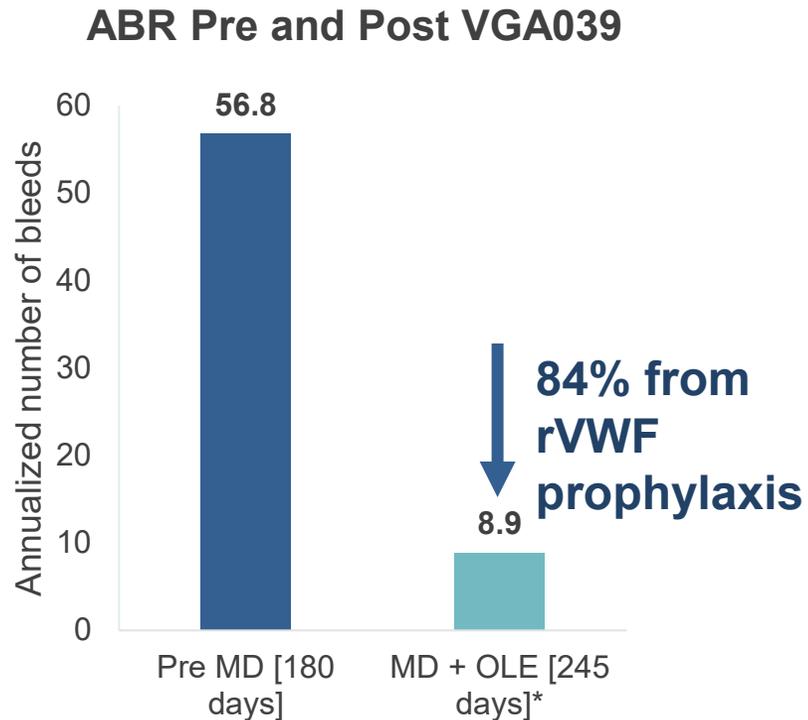
Participants switching from prior IV prophylaxis

ABRs before and during VGA039 Treatment



Participant Narrative: Substantial Bleeding Improvement After Switching From Twice Weekly IV Prophylaxis to SC Q4 Week VGA039

Cohort MD-1 Participant #1. 21-year-old female, 65.9 kg, Type 2A



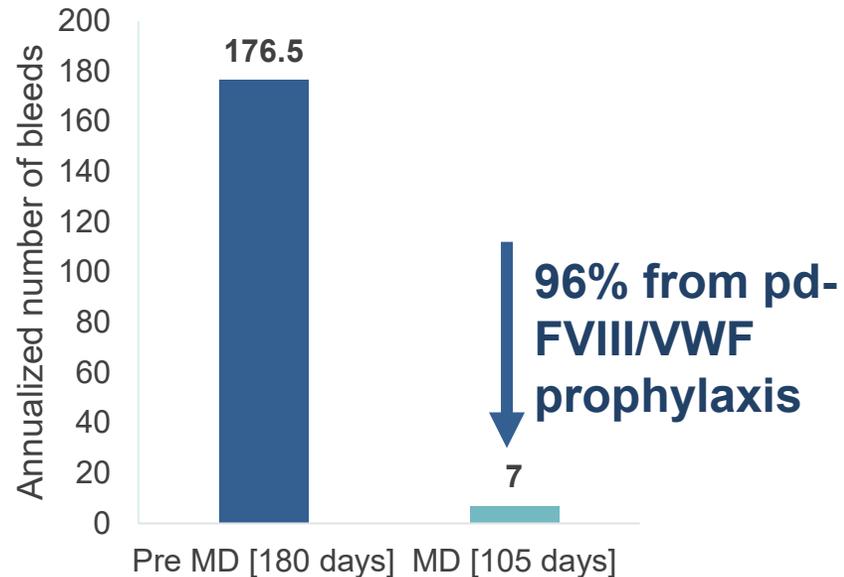
- **Prior VWD History**
 - rVWF prophylaxis 1-2x/week infusions
- **Bleed Reduction**
 - **VIVID-3: ↓ 75%**
 - **Reduction in mucosal bleeding** was observed, with epistaxis decreasing from 22 to 5 events and oral bleeds from 6 to 1
 - **OLE: ↓ 100%**
 - **Bleed-Free for 125 days** (VIVID-3 + OLE)
- **Safety**
 - **OLE:** Grade 2 injection site reaction (redness, pruritis, swelling), nausea, and dizziness after 11th dose, resolved with loratadine and ondansetron**

Pre-study history provided by PI report.

Participant Narrative: Substantial Bleeding Improvement After Switching From Daily IV Prophylaxis to SC Q4 Week VGA039

Cohort MD-2 Participant #11. 50-year-old male, 102.5 kg, Type 3*

ABR Pre and Post VGA039

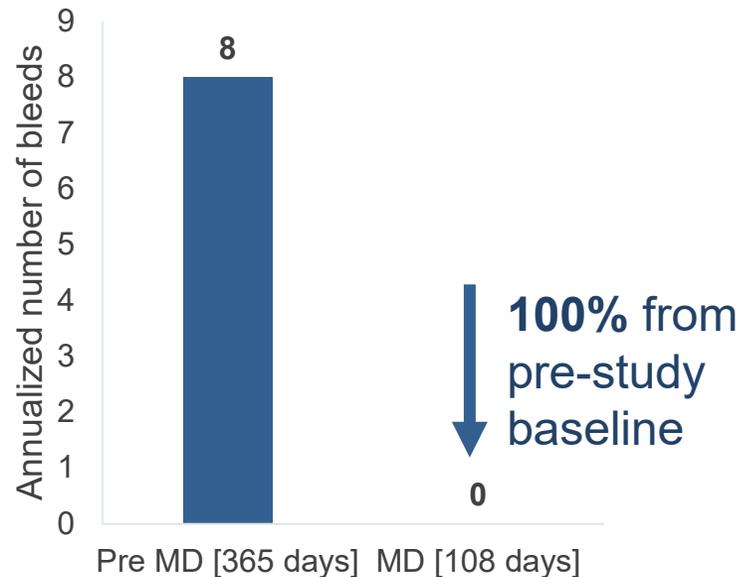


- **Prior VWD History**
 - Complex history of recurrent and refractory GI bleeding
 - Progressively ↑ intensity of prophylaxis from TXA + 20 IU/kg pdFVIII/VWF 3x/week to TXA + 40 IU/kg pdFVIII/VWF daily
 - Reported 60 cuts on skin, 27 bleeds from rectum
- **Bleed Reduction**
 - ↓ 96%
 - Tapered pdFVIII/VWF prophylaxis with one mouth bleed prior to discontinuation on day 15
 - **Bleed-Free for 85 days**
- **Safety**
 - Unrelated Grade 3 SAE of GI bleed (hospitalization)

Participant Narrative: Prevention of Serious and Hemophilia-like Bleeds

Cohort MD-1 Participant #6. 18-year-old male, 75 kg, Type 3

ABR Pre and Post VGA039



- **Prior VWD History***
 - Baseline Factor VIII: 10%
 - 3 joint and 3 muscle bleeds treated with pdVIII/VWF
 - 2 episodes of hematemesis
- **Bleed Reduction**
 - ↓100% (follow-up ongoing)
 - No on-demand treatments
- **Safety**
 - No related AEs

Conclusions: Interim Analysis of VIWID 3

- VGA039 every 4-week SC prophylaxis was safe and well tolerated
- Across all VWD types median ABR reduction was 81% (range 41-100%)
 - Switching from prior IV prophylaxis (75-100%)
 - No prior IV prophylaxis (41-100%)
- All participants completing the study to date have transitioned to the OLE
- Phase 3 VIWID 6 (NCT07115004) is currently enrolling

Thank You

VIVID 6

**Phase 3 Study to
Evaluate Subcutaneous
VGA039 in Patients With
Von Willebrand Disease
(NCT07115004)**

NOW ENROLLING

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- Vanderbilt University Medical Center
Nashville, TN USA
- Hemocentro UNICAMP, University of Campinas
Campinas, Brazil

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