# 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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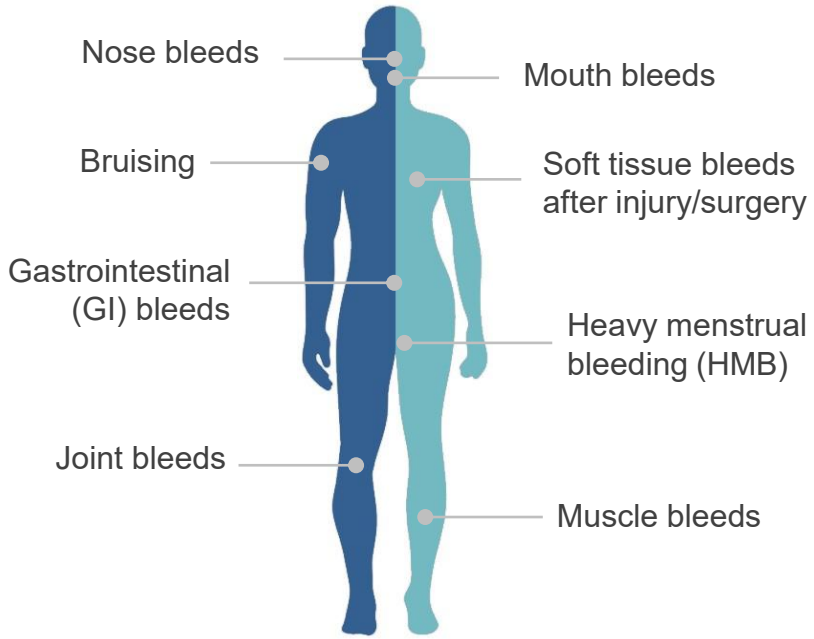
# Von Willebrand Disease - Unmet Therapeutic Need

- **VWD is the most common inherited bleeding disorder** characterized by recurrent, prolonged bleeding[1]
- Impaired **platelet adhesion and unstable clot formation** result in ineffective hemostasis[2]
- 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 VIVID clinical trial program[3]**

## VWD Presentation[2]

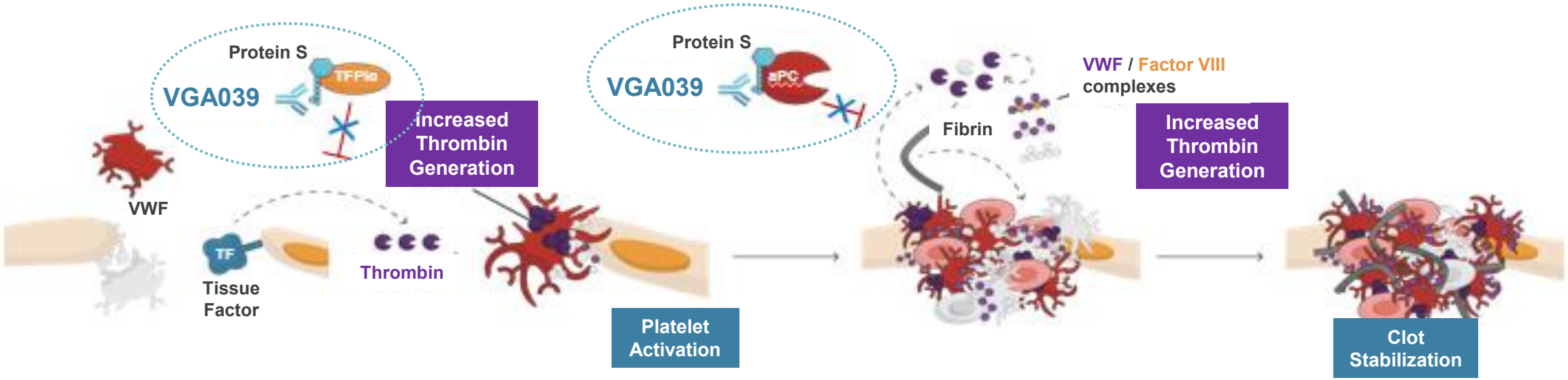



1.Sidonio RF et al. *J Blood Med*. 2020;11:1-11, 2. The diagnosis, evaluation, and management of von Willebrand disease. NIH Publication No 08-5832. 2007, 3. Millar et al. Blood. 2024;144(Suppl 1):3981. doi:10.1182/blood-2024-208020.;
VWD, Von Willebrand Disease; IV, intravenous; SC, subcutaneous

# VGA039 is Dual-Acting on Both TFPIα 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 TFPIα and aPC
- Inhibition of Protein S activity by **VGA039** reduces aPC and TFPIα mediated anticoagulant activity, resulting in enhanced **thrombin generation** to restore hemostasis
  - **VGA039** does not deplete Protein S
  - Preserves TFPIβ activity to limit clot expansion at site of vascular injury

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




Schweighofer, C et al. OC 73.3, ISTH 2024 2. Millar et al. Blood. 2024;144(Suppl 1):3981. doi:10.1182/blood-2024-208020; TFPIα, tissue factor pathway inhibitor alpha; TFPIβ, tissue factor pathway inhibitor beta; aPC, activated protein C; VWD, von Willebrand disease

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

VIWID 1 — 25 normal healthy volunteers[1]

VIWID 2 — 10 VWD patients (all types represented)[2]

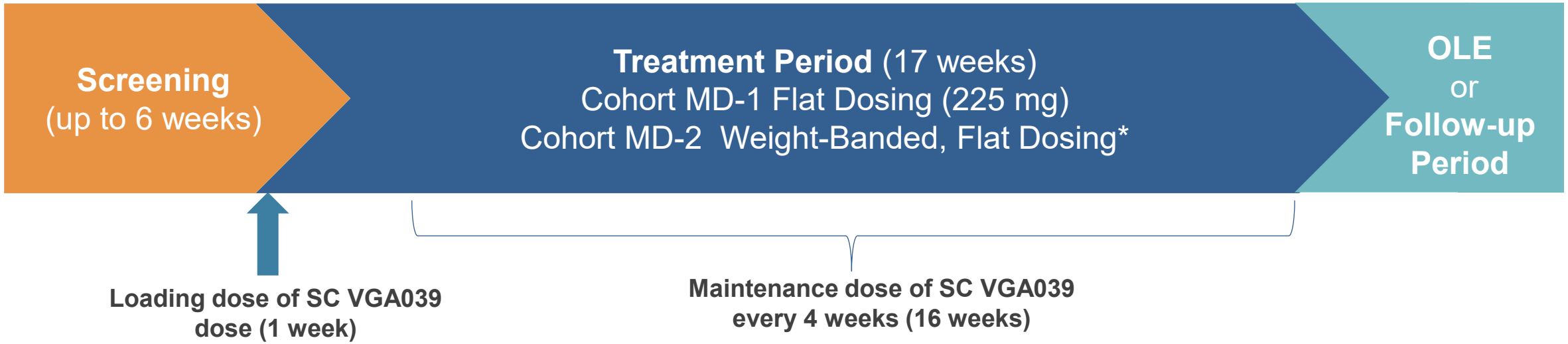
} received single dose of **VGA039**

- 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 µg/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; µg/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 ≥LLN
- History of thromboembolism or pro-thrombotic disorders
- Use of estrogen-containing hormonal therapies within 56 days of study drug

**Endpoints**

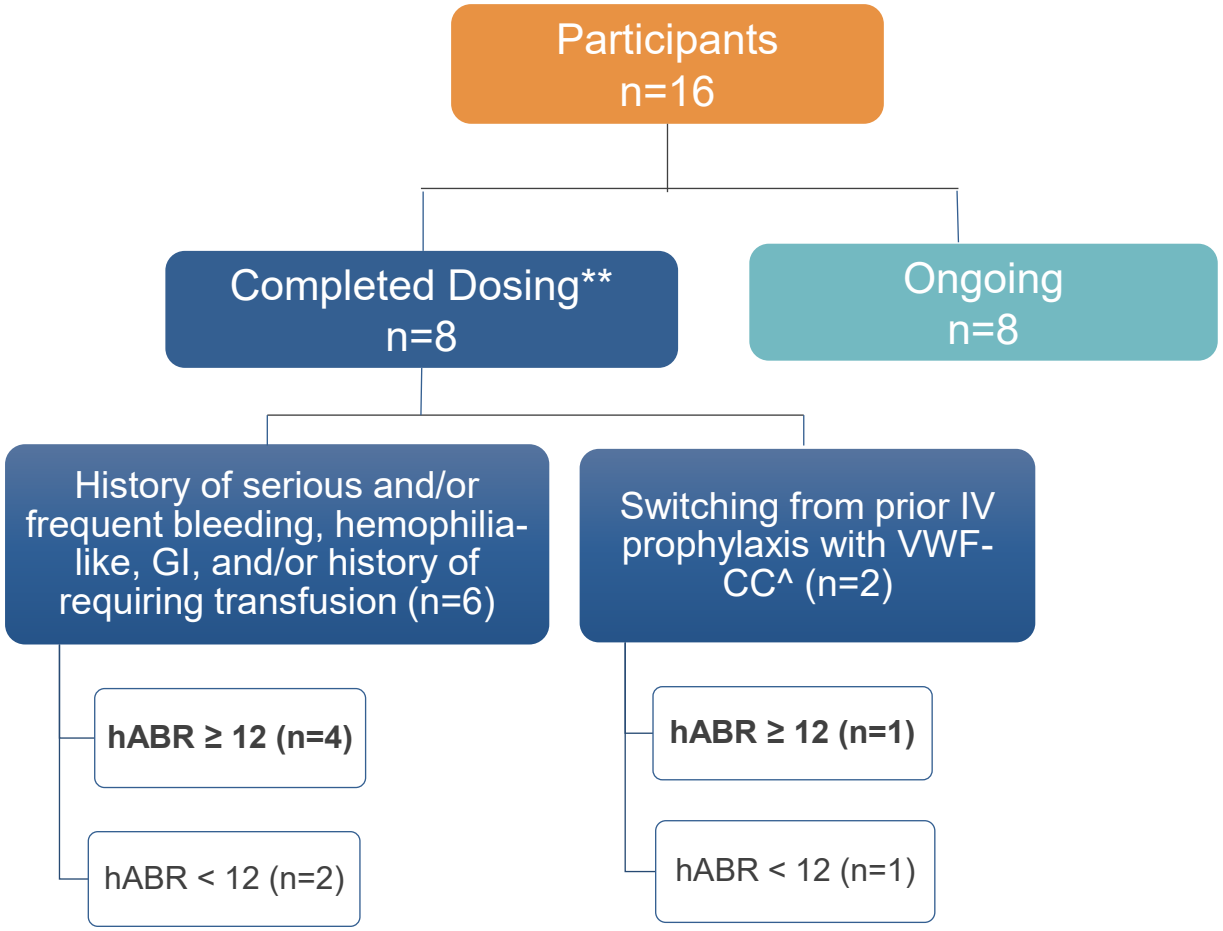
- Safety, including AEs and DLTs
- PK/PD profile
- Clinical effects on bleeding

* 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

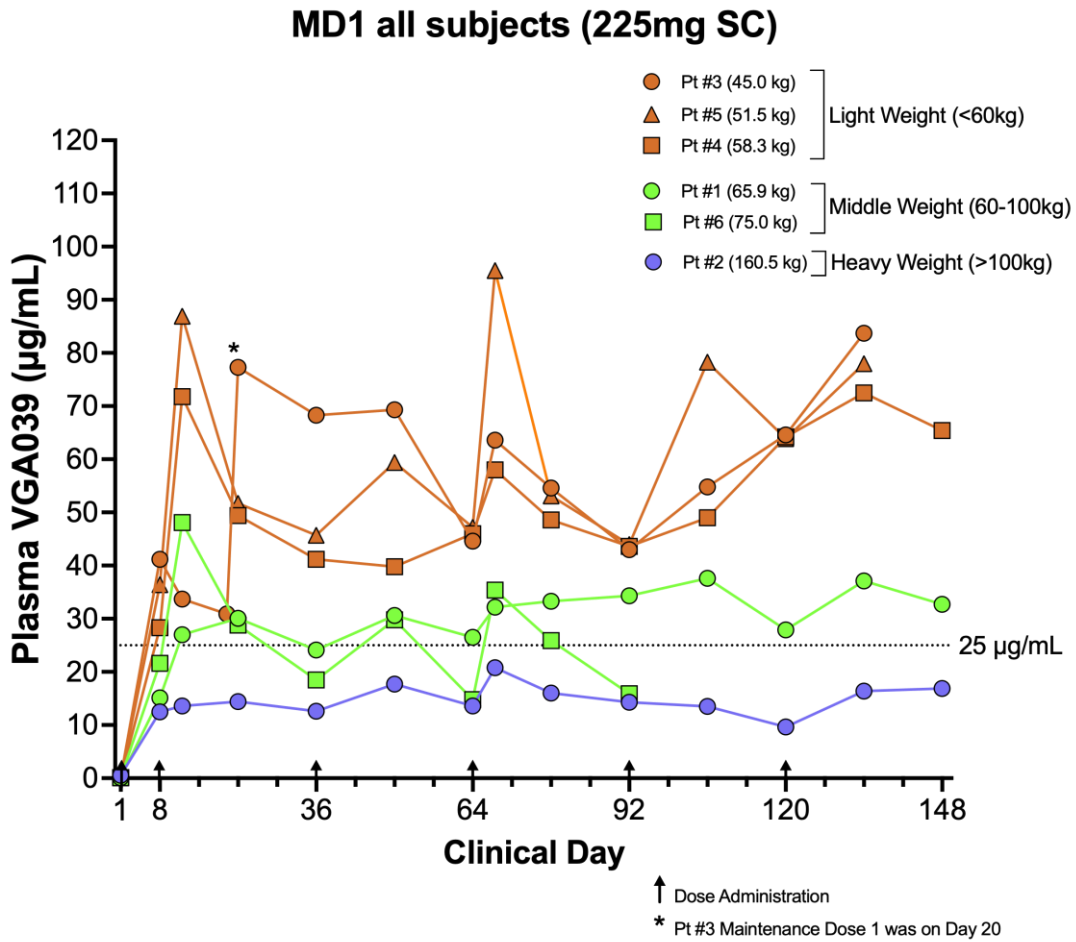
| Study Cohort | MD-1 (N=6) | MD-2 (N=10) |
|---|---|---|
| Sex (N) | M (2)<br>F (4) | M (6)<br>F (4) |
| Age Mean (range) | 24.7 yrs<br>(15-53) | 36.9 yrs<br>(22-53) |
| Race | Asian (1)<br>Black (1)<br>White (4)<br>Other (0) | Asian (1)<br>Black (0)<br>White (8)<br>Other (1) |
| Weight Mean (range)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

VIVID 3

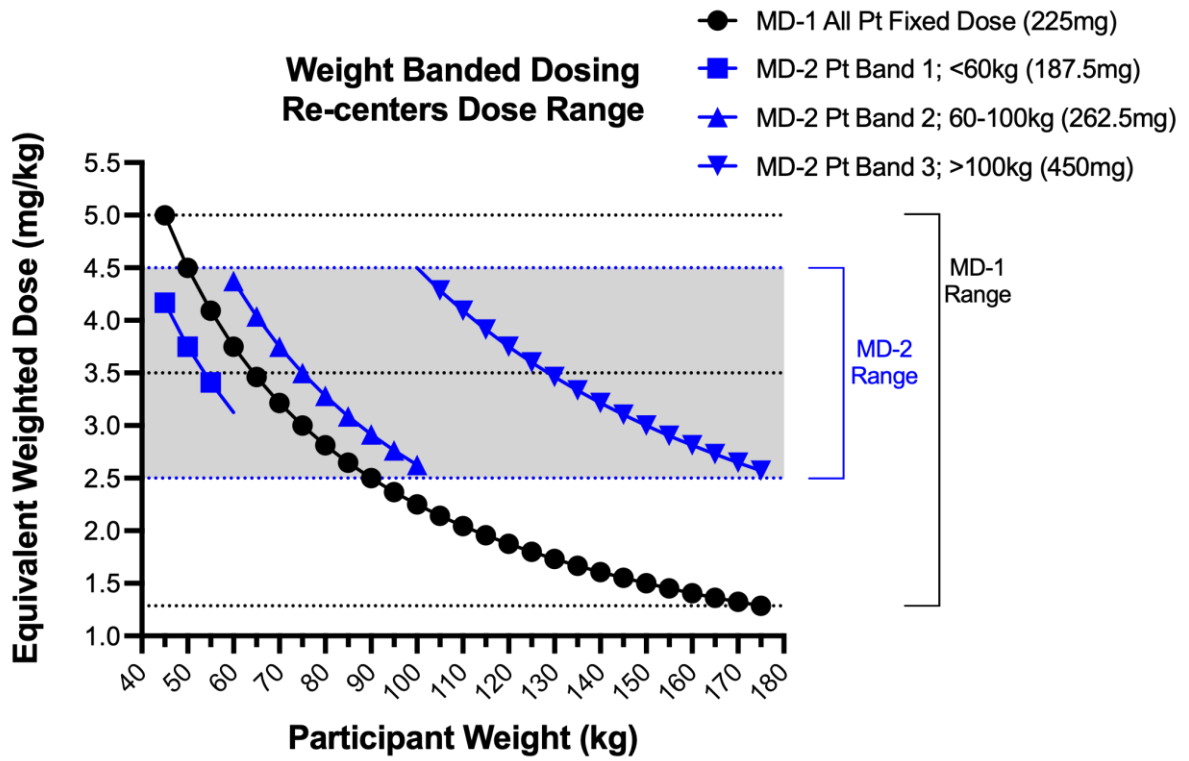
Data as of 14Nov25; *ABR calculation excludes menstrual bleeds and bruises/bleeds under the skin; ** Completed dosing (≥ Day 120 visit); ^ Defined as 1 or more infusions per week to prevent/reduce bleeding symptoms; MD, multi-dose; M, male; F, female; yrs, years; hABR, historic annualized bleeding rate; IV, intravenous; GI, gastrointestinal; VWF-CC, von Willebrand Factor containing concentrate

# 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)




Data as of 14Nov25; MD, Multi-dose; SC, Subcutaneous; Pt, Participant; mg, milligrams; kg, kilogram; µg/mL, microgram per milliliter

# Cumulative Safety Summary in VIVID-3

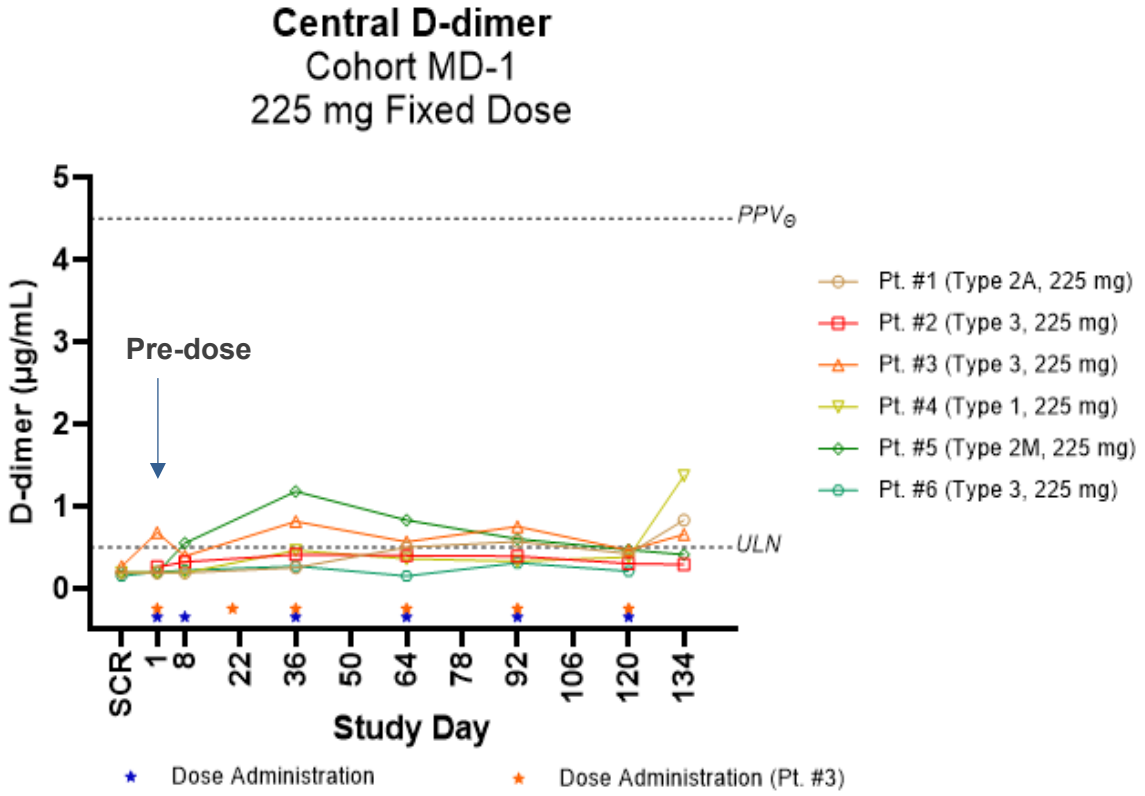
- As of 14NOV2025, 16 participants have enrolled and all have received at least 4 doses of VGA039
  - No withdrawals on therapy
  - No thromboembolic events
  - No injection site reactions
  - 39 treatment-emergent AEs reported in 10 participants
    - Two related Grade 2 events of headache reported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

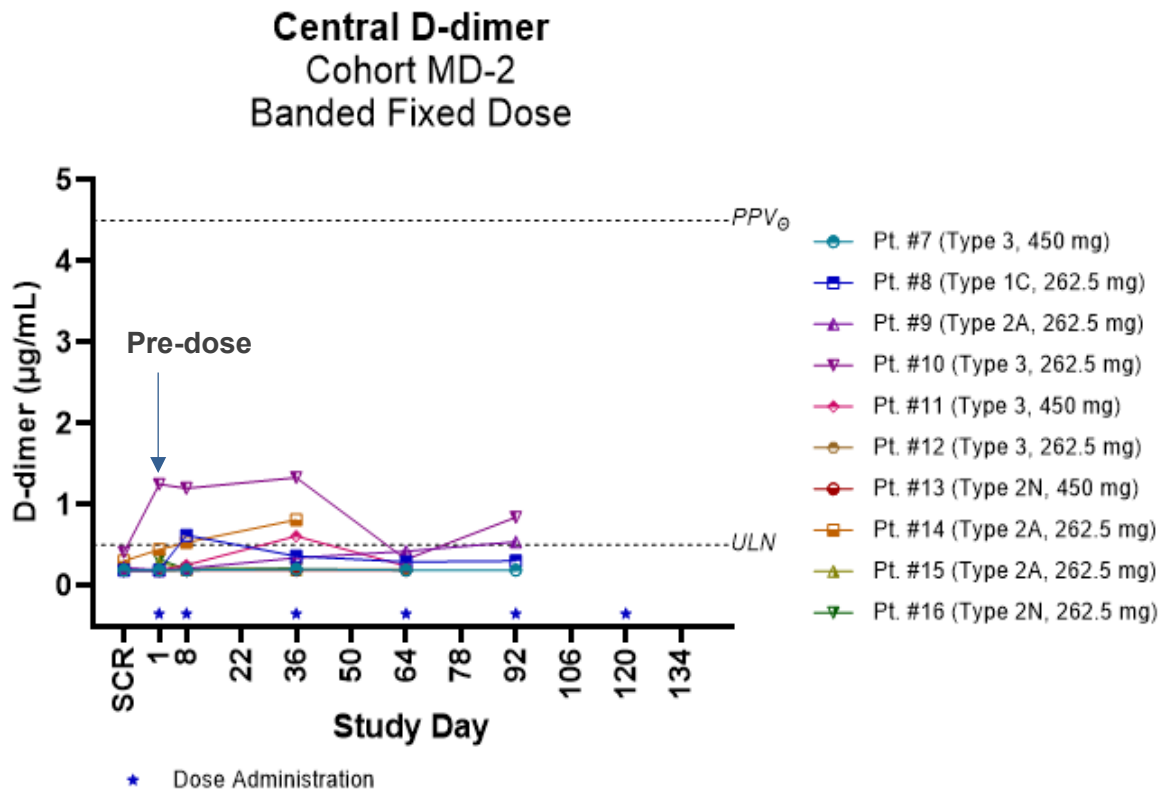
- To date, VGA039 appears safe and well-tolerated over multiple doses



Data as of 14Nov25; AE, adverse event; GI, gastrointestinal

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




- 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

VIVID 3

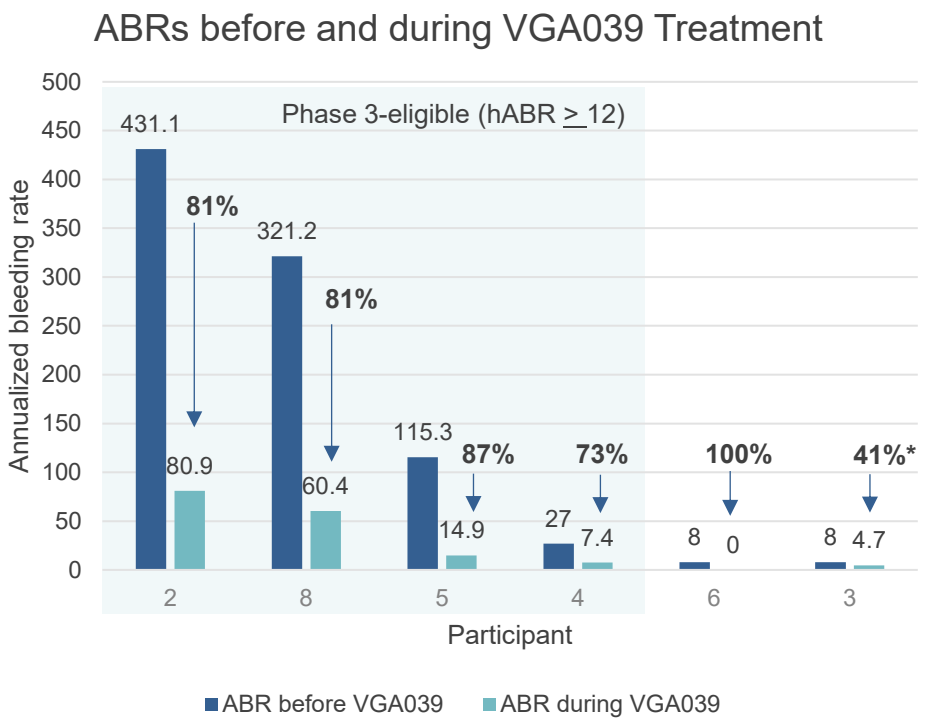
Data shown from an active database as of 14Nov25; MD, Multi-dose; Pt, Participant; mg, milligrams;

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

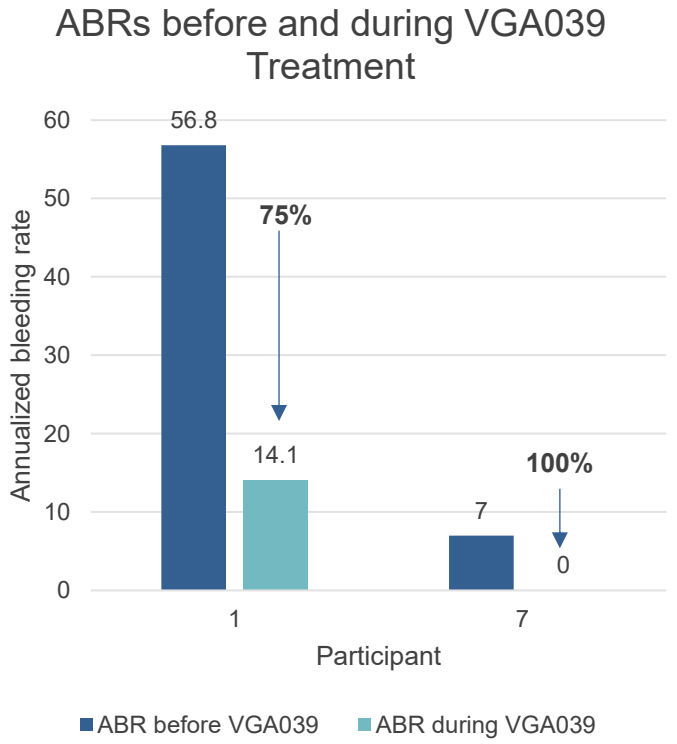
**Median Bleed Reduction: 81% (range 41-100%)**

*Reductions of 73-87% in participants with hABR ≥ 12**

***Participants with no prior IV prophylaxis***




***Participants switching from prior IV prophylaxis***

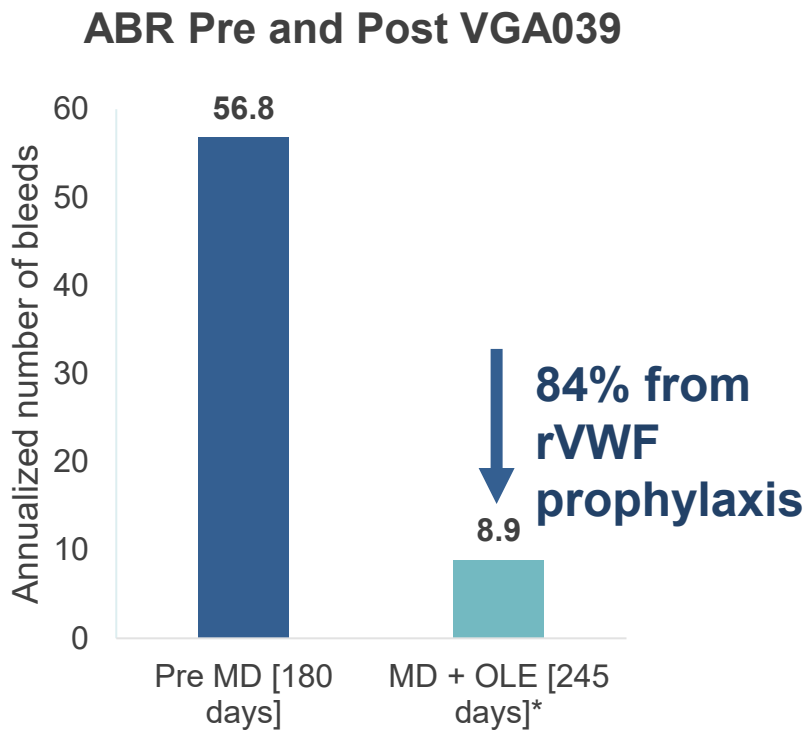



VIVID 3

Data as of 14Nov25; *ABR excludes bruising and menstrual bleeding. Blanchette VS et al. JTH. 2014;12; **hABR comprised of primarily epistaxis, no epistaxis observed during study; hABR, historic annualized bleeding rate; ABR, annualized bleed rate; IV, intravenous

# 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 11$^{th}$ dose, resolved with loratadine and ondansetron**

Pre-study history provided by PI report.

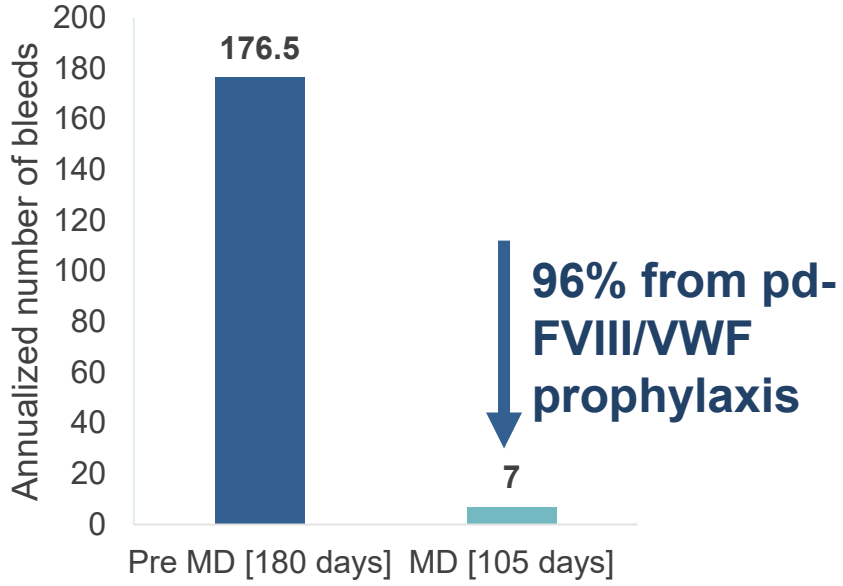
VIVID 3

Data as of 14Nov25; *At D148, patient rolled over to the Open Label Extension to continue VGA039 prophylaxis; Bleed-Free = time since onset of last new bleed excluding bruises and menstrual bleeding; **OLE data from active database as of 14Nov25

# 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**



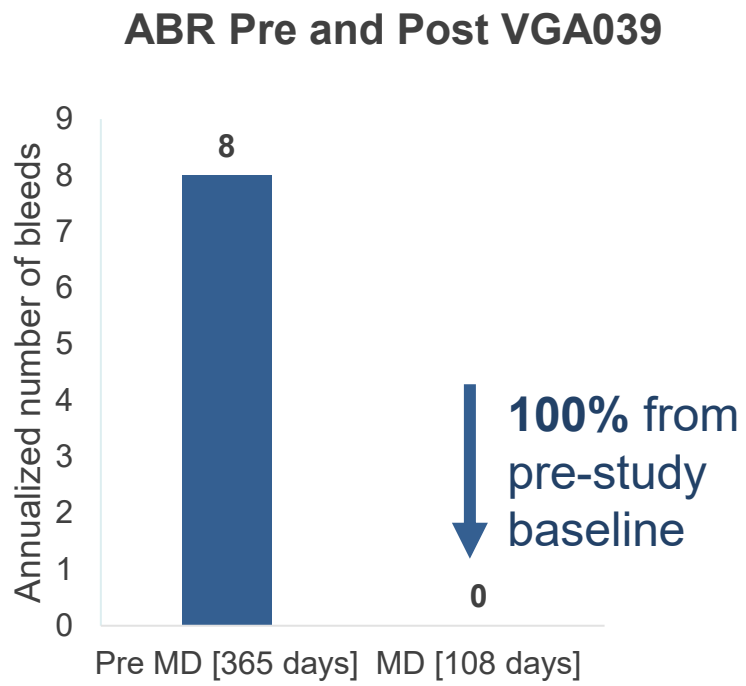

- **Prior VWD History**
  - Complex history of recurrent and refractory GI bleeding
  - Progressively ↑ intensity of prophylaxis from TXA + 20 IU/kg pdFVIII/VWF 3x/week to TXA + 40 IU/kg pdFVIII/VWF daily
  - Reported 60 cuts on skin, 27 bleeds from rectum
- **Bleed Reduction**
  - ⬇ 96%
  - Tapered 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)

VIVID 3

Data as of 14Nov25; *Regular prophylaxis with Immunate. Dose of VGA039 450 mg; Bleed-Free = time since onset of last new bleed excluding bruises and menstrual bleeding; TXA, tranexamic acid; pd, plasma derived; VWF, von Willebrand factor, SAE, serious adverse event; GI, gastrointestinal

# Participant Narrative: Prevention of Serious and Hemophilia-like Bleeds

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




- **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

VIVID 3

Data as of 14Nov25. *Bleeds occurred during the 365 days prior to study entry; pd, plasma derived; VWF, von Willebrand factor, AE, adverse event

# 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



Data as of 14Nov25; SC, subcutaneous; ABR, annualized bleeding rate;, VWD, Von Willebrand Disease; OLE, Open-label extension

# Thank You

## VIVID 6

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

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  Campinas, Brazil

**With sincere gratitude to the patients and families whose participation made this research possible, and to the clinical trial sites, coordinators, and investigators for their dedication and partnership**