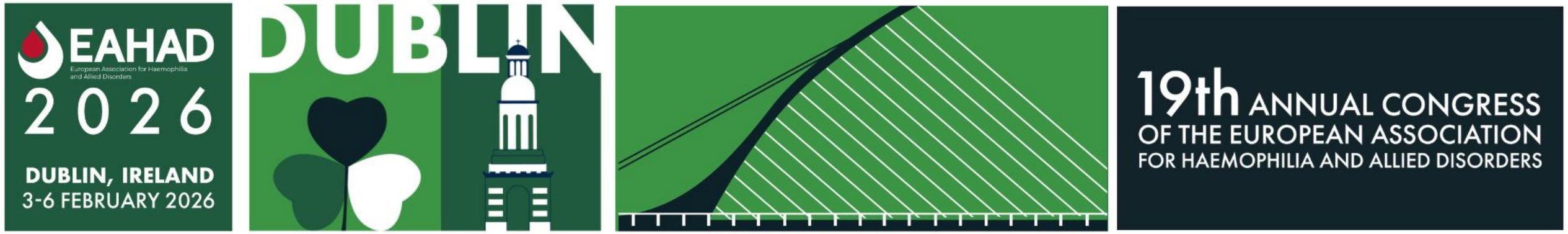

Subcutaneous, every-four-week maintenance dosing of a novel protein S antibody is well-tolerated and substantially reduces bleeding rates: Results from a phase 1/2 multi-dose study of VGA039 in patients with von Willebrand disease

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Disclosure for Gabriela Yamaguti-Hayakawa

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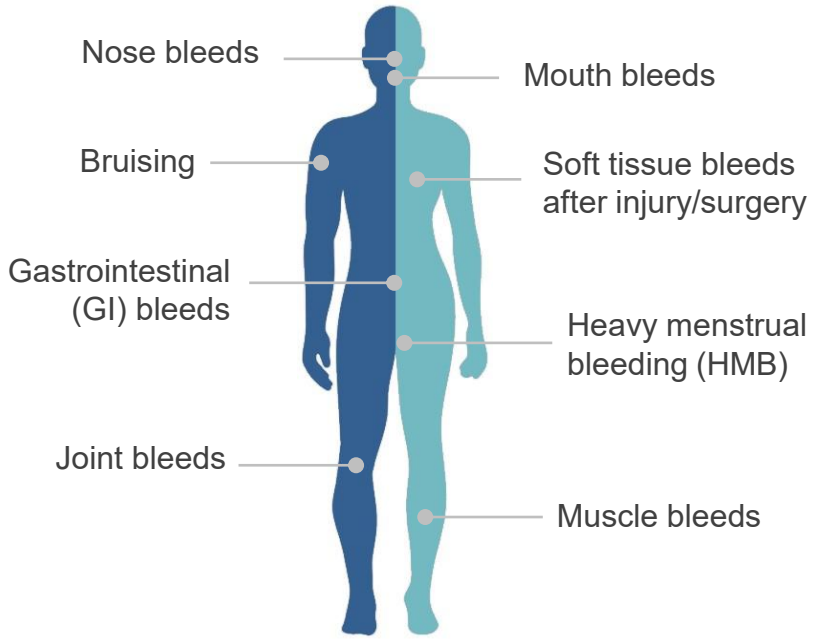
Shareholder	No relevant conflicts of interest to declare.
Grant / Research Support	BioMarin
Consultant	Pfizer, Sanofi, STAR Therapeutics
Employee	No relevant conflicts of interest to declare.
Paid Instructor	No relevant conflicts of interest to declare.
Speaker Bureau	NovoNordisk, Sanofi, Roche
Other	STAR Therapeutics

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 subcutaneous every-4-week therapy for VWD being investigated in the VIVID clinical trial program[3]**

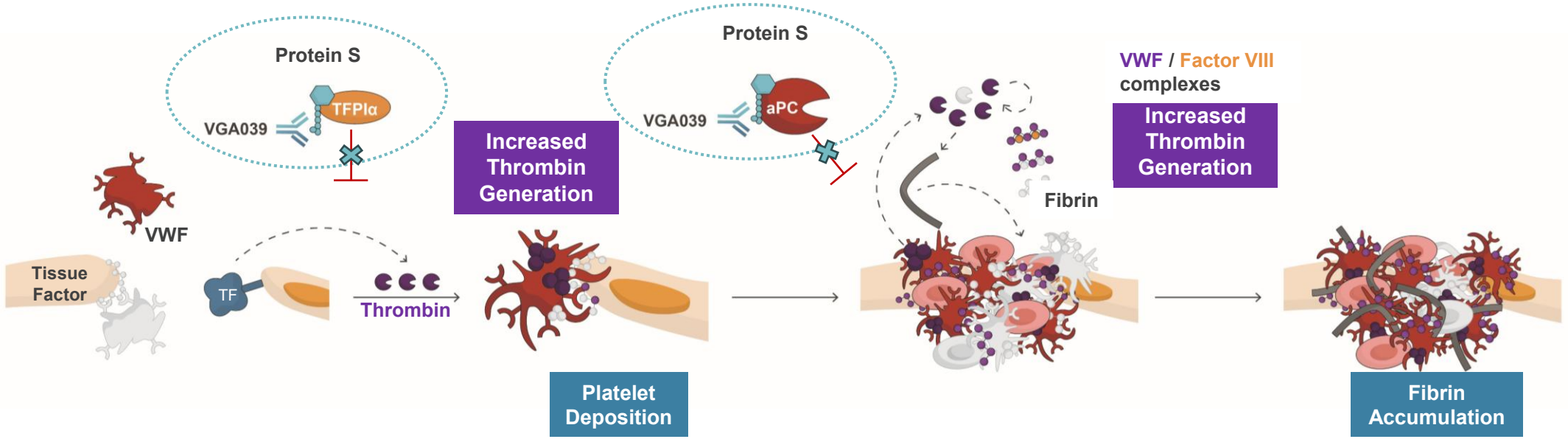
VWD Presentation[2]



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]

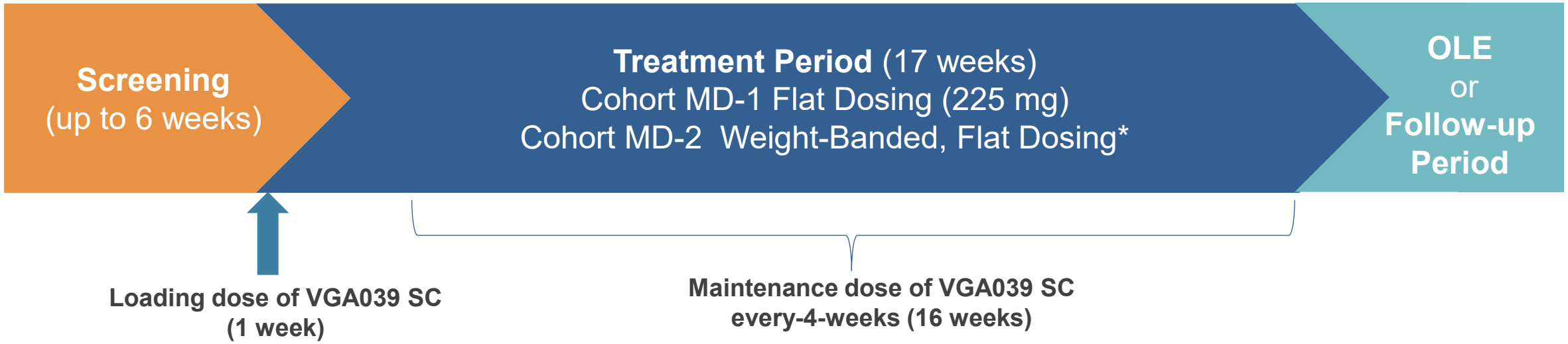
- **VGA039** is a fully human, IgG4 monoclonal antibody that targets the activity of Protein S, a cofactor for TFPIα and aPC
- The dual action of **VGA039** on the TFPIα and aPC pathways promotes both platelet deposition and fibrin accumulation at sites of endothelial cell injury to restore hemostasis[3]
  - **VGA039** does not deplete Protein S
  - Preserves TFPIβ activity to limit clot expansion at site of vascular injury



1.Schweighofer, C et al. OC 73.3, ISTH 2024 2. Millar et al. Blood. 2024, 144:398, 3.Sakurai, et al., Blood 2025,146:3051; TFPIα, tissue factor pathway inhibitor alpha; TFPIβ, tissue factor pathway inhibitor beta; aPC, activated protein C; VWD, von Willebrand disease

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

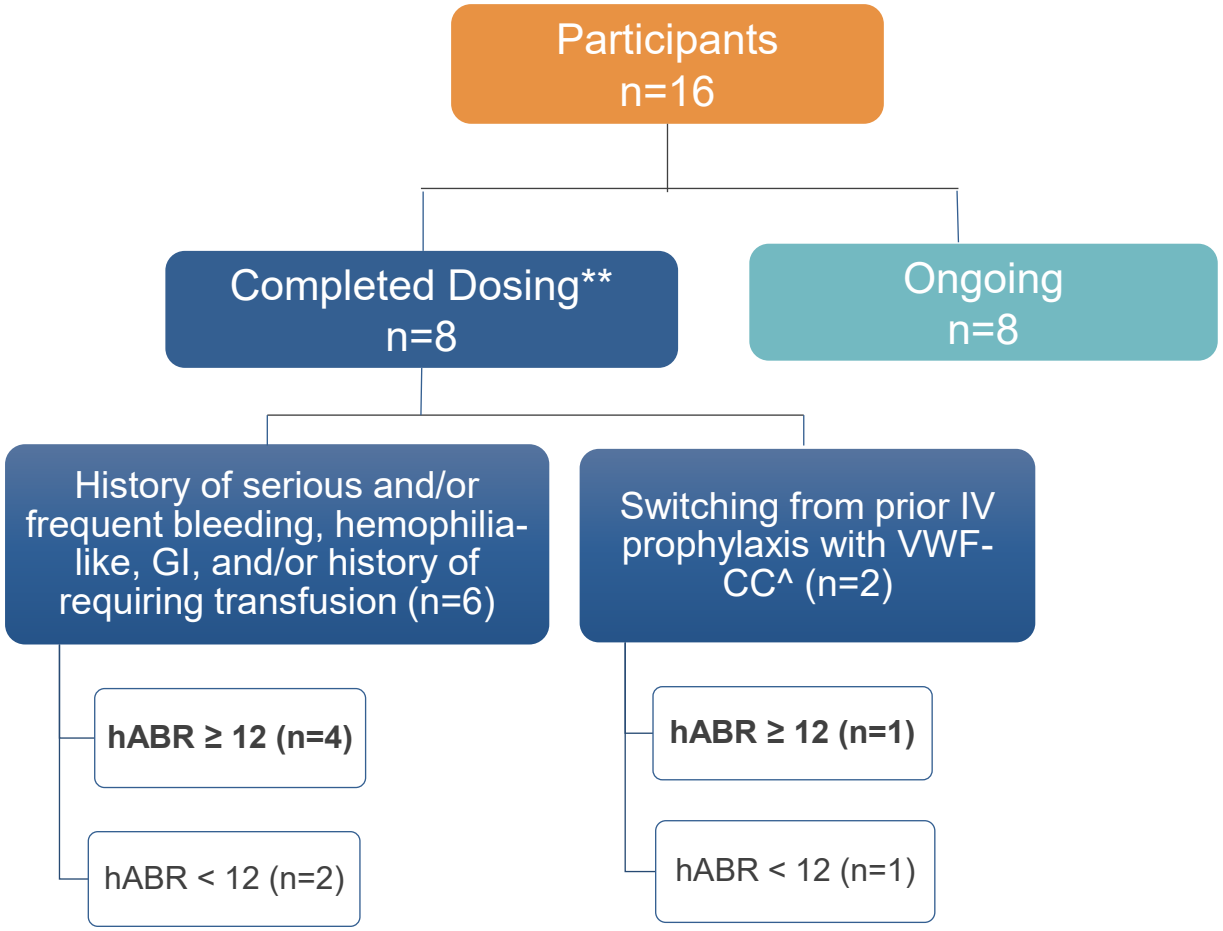
- Safety, including AEs and DLTs
- PK/PD profile
- Clinical effects on bleeding

* 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

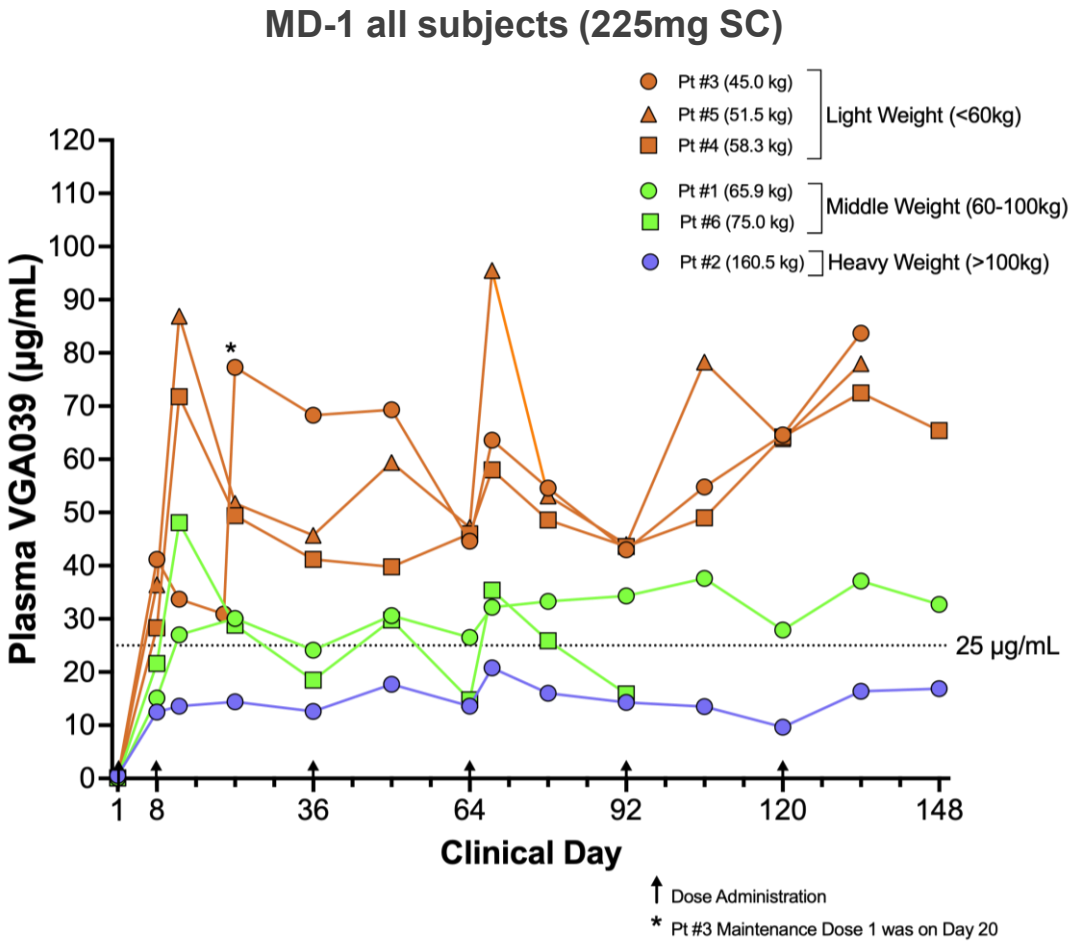
Study Cohort	MD-1 (N=6)	MD-2 (N=10)
Sex (N)	M (2) F (4)	M (6) F (4)
Age Mean (range)	24.7 yrs (15-53)	36.9 yrs (22-53)
Race	Asian (1) Black (1) White (4) Other (0)	Asian (1) Black (0) White (8) Other (1)
Weight Mean (range)	76.0 kg (45.0-160.5)	85.6 kg (61.7-124.5)
Type/ Sub-Types (N)	1 (2) 2A (1) 2M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

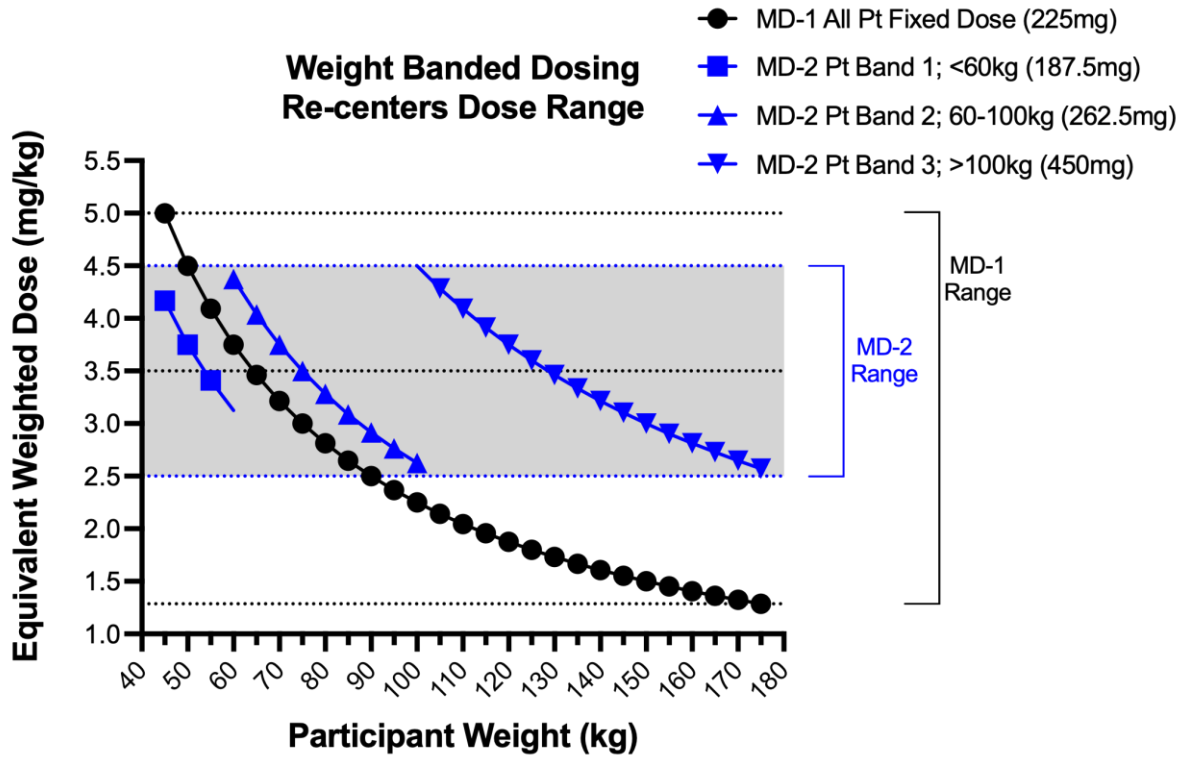
Data as of 14Nov25; *ABR calculation excludes menstrual bleeds and bruises/bleeds under the skin; ** Completed dosing (≥ Day 120 visit); ^ Defined as 1 or more infusions per week to prevent/reduce bleeding symptoms; MD, multi-dose; M, male; F, female; yrs, years; hABR, historic annualized bleeding rate; 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 VIWID-3

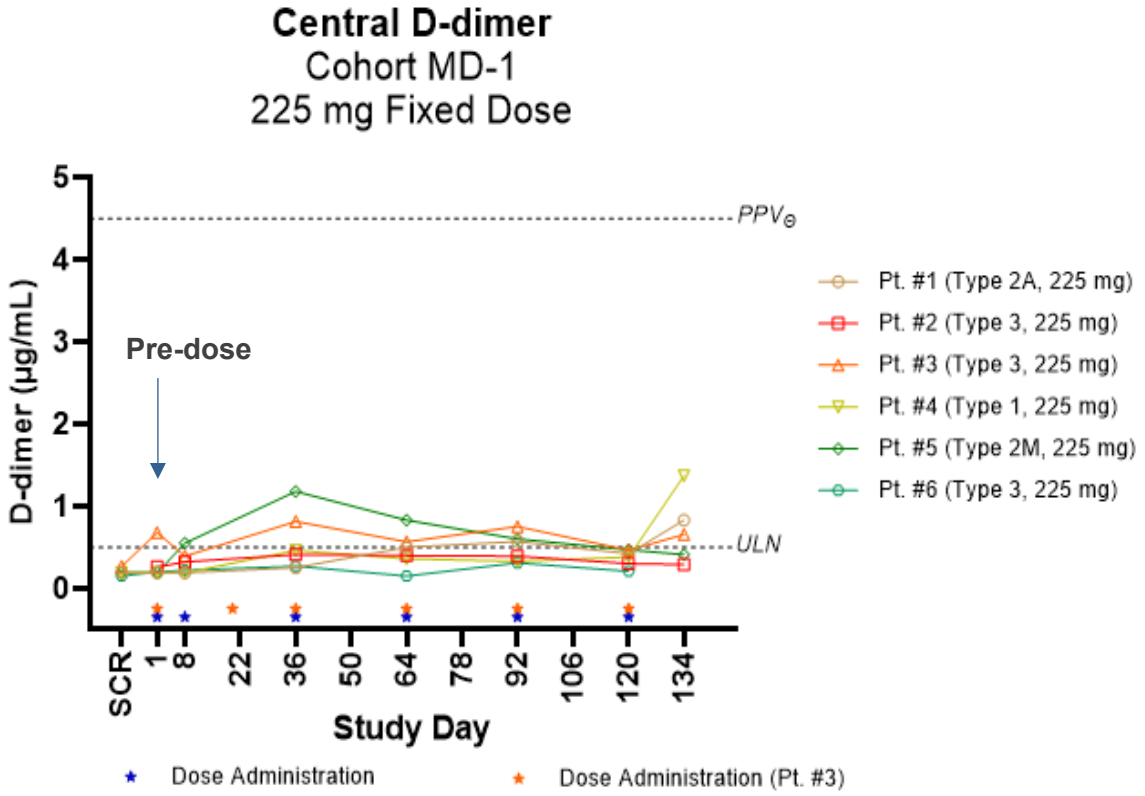
- As of 14NOV2025, 16 participants have enrolled and all have received at least 4 doses of VGA039
  - No withdrawals on therapy
  - No thromboembolic events
  - No injection site reactions
  - 39 treatment-emergent AEs reported in 10 participants
    - Two related Grade 2 events of headache reported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

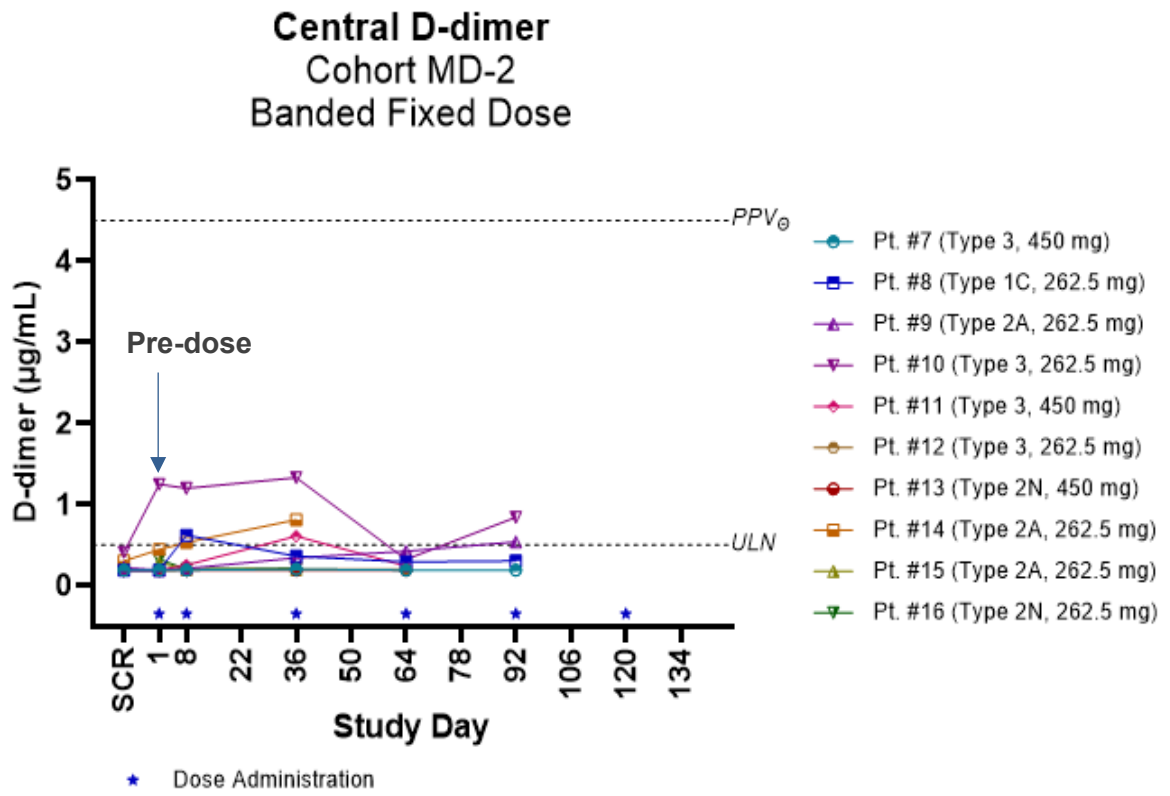
- To date, VGA039 appears safe and well-tolerated over multiple doses

VIWID 3

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

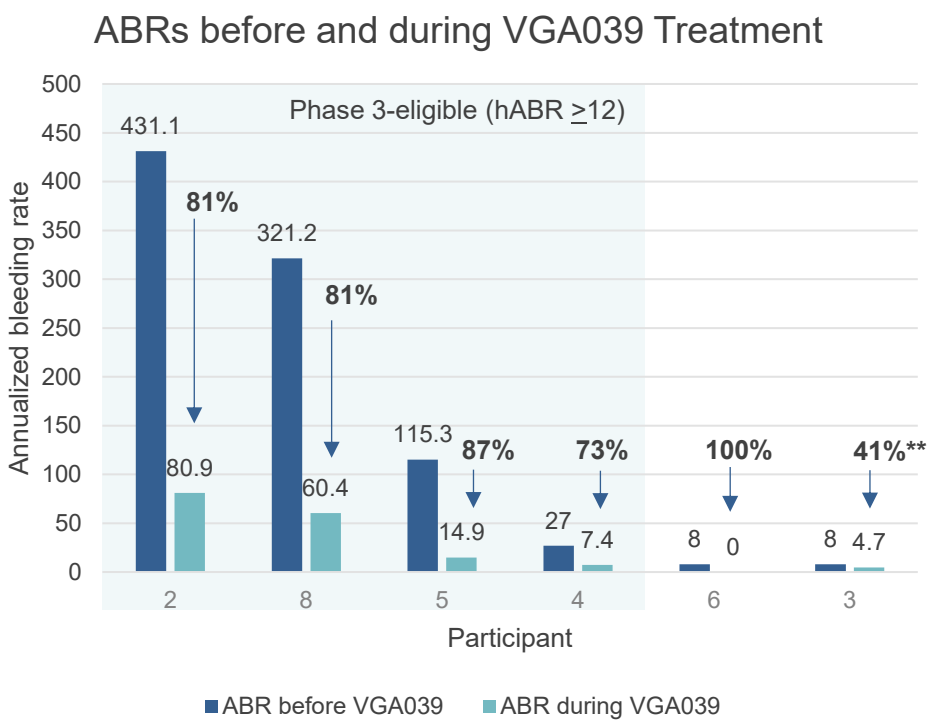
Data shown from an active database as of 14Nov25; MD, Multi-dose; Pt, Participant; mg, milligrams;

Substantial Reductions in Bleeding Rates in All Participants who Completed the VGA039 Treatment

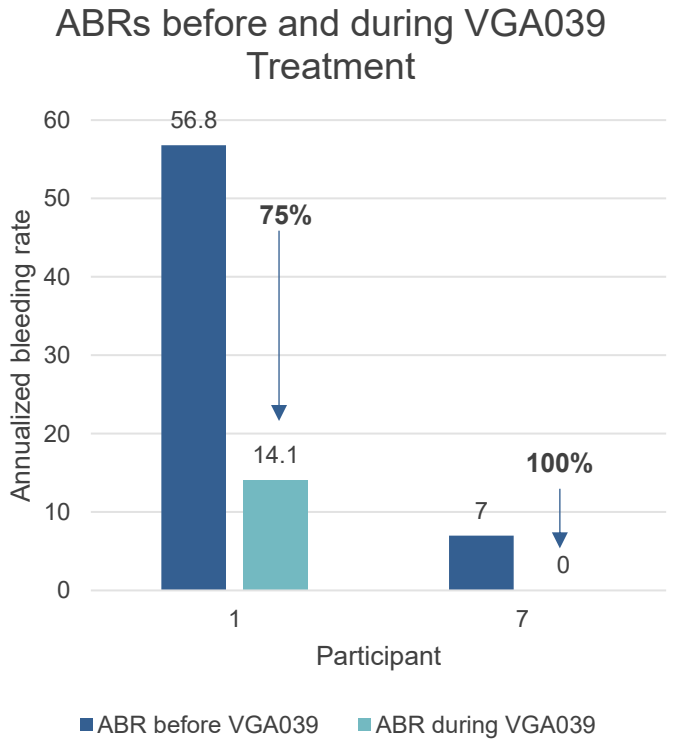
Median Bleed Reduction: 81% (range 41-100%)

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

Participants with no prior IV prophylaxis



Participants switching from prior IV prophylaxis



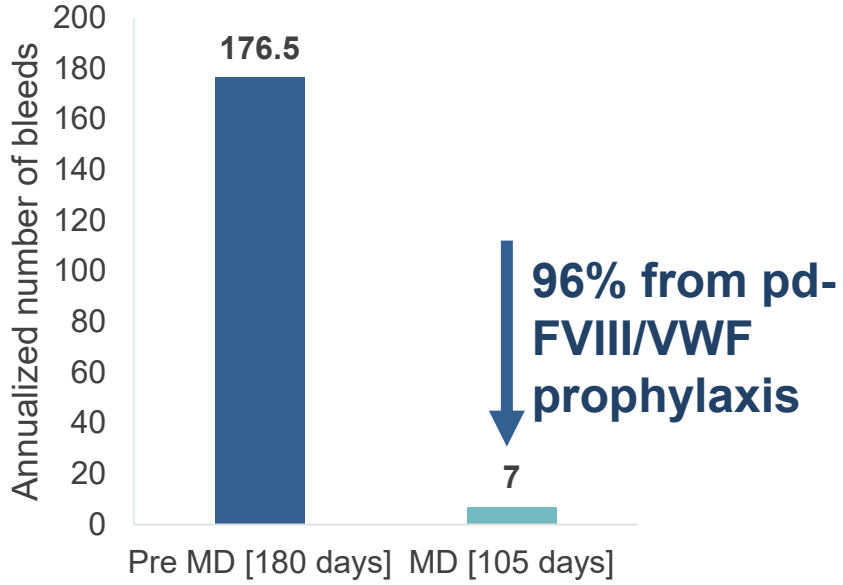
VIVID 3

Data as of 14Nov25; *ABR excludes bruising and menstrual bleeding. Blanchette VS et al. JTH. 2014;12(11), 1935-1939; **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 Daily IV Prophylaxis to VGA039 SC Q4 Week Prophylaxis

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)

VIWID 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

Conclusions: Interim Analysis of VIWID 3

- VGA039 SC every-4-week 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

VIWID 3

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

Thank You

EAHAD 2026

VIVID 6

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

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- University of California, Davis, USA
- The University of Colorado, Denver Hemophilia and Thrombosis Center, USA
- Emory University School of Medicine, USA
- Charlotte Maxeke Johannesburg Academic Hospital, South Africa
- Royal Brisbane Women's Hospital. Australia
- Hospital Das Clínicas Da Faculdade De Medicina Da Universidade De São Paulo, Brazil
- Los Angeles Orthopaedic Hemophilia Treatment Center, USA
- University of Texas, Southwestern, USA
- Medical University of Vienna, Austria
- Imperial College Healthcare NHS Trust, UK
- Royal Free London NHS Trust, UK
- Barts Health NHS Trust, UK
- Vanderbilt University Medical Center, USA

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