

Subcutaneous Every-Four-Week Dosing of the Novel Protein S Antibody VGA039 (Latacibart) Demonstrates Safety and Clinically Meaningful Bleed Reductions in Patients With von Willebrand Disease: Phase 1/2 Multi-Dose Study Results

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Disclosures for Allison Wheeler

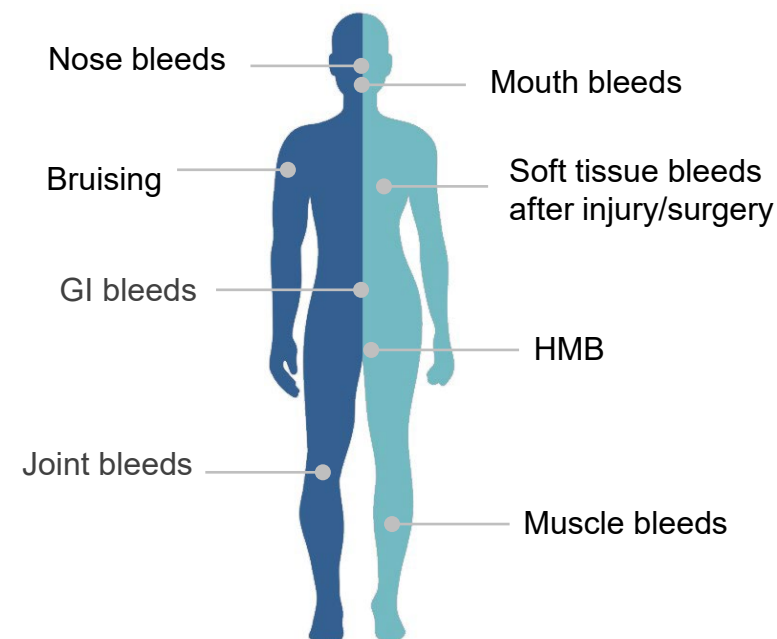
- **Grants/research support:** Octapharma
- **Advisory board memberships:** Baxalta, Bayer HealthCare Pharmaceuticals, BioMarin, Bioverative, CSL Behring, Genentech, Genzyme Corporation, Grifols, HEMA Biologics, Novo Nordisk, Octapharma USA, Pfizer Inc, Sanofi-Aventis USA, Shire North America, Spark Therapeutics, Takeda Pharmaceuticals, and UniQure

von Willebrand Disease

Unmet Therapeutic Need

- **VWD is the most common inherited bleeding disorder** characterized by recurrent, prolonged bleeding, with mucocutaneous manifestations¹
- Impaired **platelet adhesion and unstable clot formation** result in ineffective hemostasis²
- Current treatment requires frequent IV infusions and offers suboptimal bleed control, underscoring the need for effective bleed prevention to reduce the cumulative impact of frequent bleeds on quality of life and long-term health outcomes^{1,2}
- There remains a need for innovation in less frequent SC treatment options that provide hemostatic protection
- **Latacibart (VGA039) is a potential subcutaneous every-4-week therapy for VWD being investigated in the VIVID clinical trial program³**

VWD Presentation²

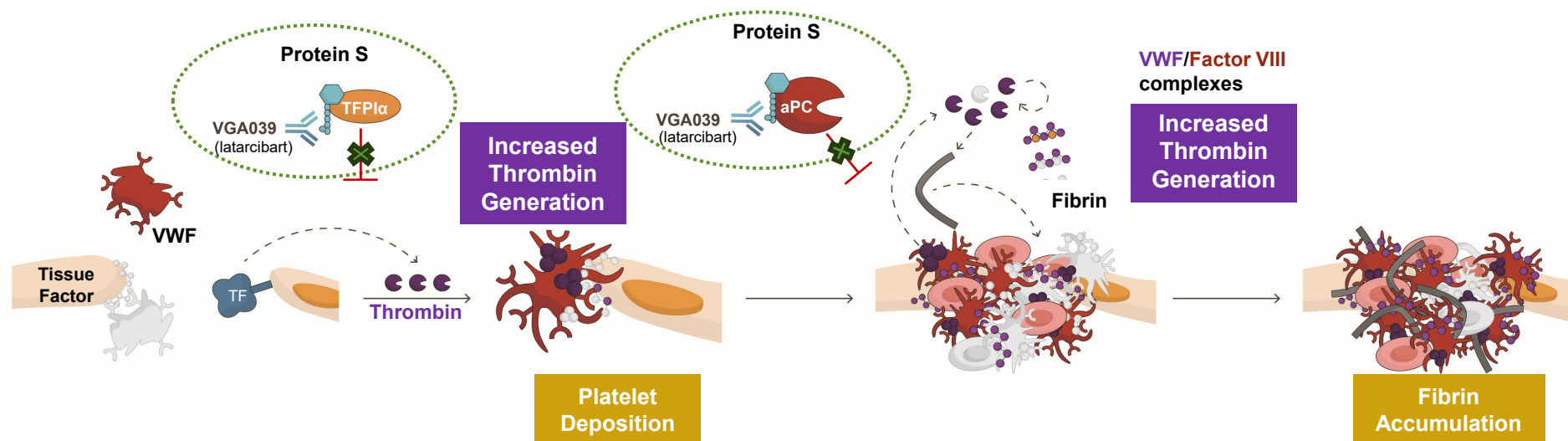


GI, gastrointestinal; HMB, heavy menstrual bleeding; IV, intravenous; SC, subcutaneous; VWD, von Willebrand disease.

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 CM, et al. *Blood*. 2024;144(Suppl 1):3981.

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

- **Latacibart** is a fully human, IgG4 monoclonal antibody that targets the activity of Protein S, a cofactor for TFPI α and aPC, negative regulators of thrombin generation
- The dual action of **latacibart** on the TFPI α and aPC pathways promotes both platelet deposition and fibrin accumulation at sites of endothelial cell injury to restore hemostasis³
 - **Latacibart** does not deplete Protein S
 - Preserves TFPI β activity to limit clot expansion at site of vascular injury

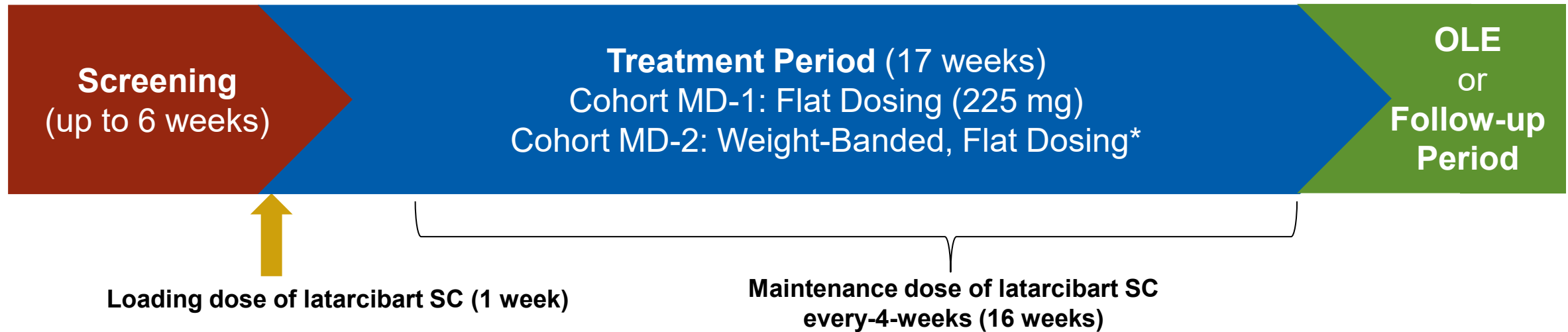


aPC, activated protein C; IgG, immunoglobulin; TF, tissue factor; TFPI α , tissue factor pathway inhibitor alpha; TFPI β , tissue factor pathway inhibitor beta.

1. Schweighofer C, et al. OC 73.3, ISTH 2024. 2. Millar CM, et al. *Blood*. 2024;144:398. 3. Sakurai, et al. *Blood*. 2025;146(Suppl):3051.

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

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

AE, adverse event; DLT, dose-limiting toxicity; LLN, lower limit of normal; PD, pharmacodynamic; PK, pharmacokinetic; MD, multiple doses; OLE, open-label extension.

* 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).

Broad Demographic Representation in Multi-Dose Study Including All VWD Types

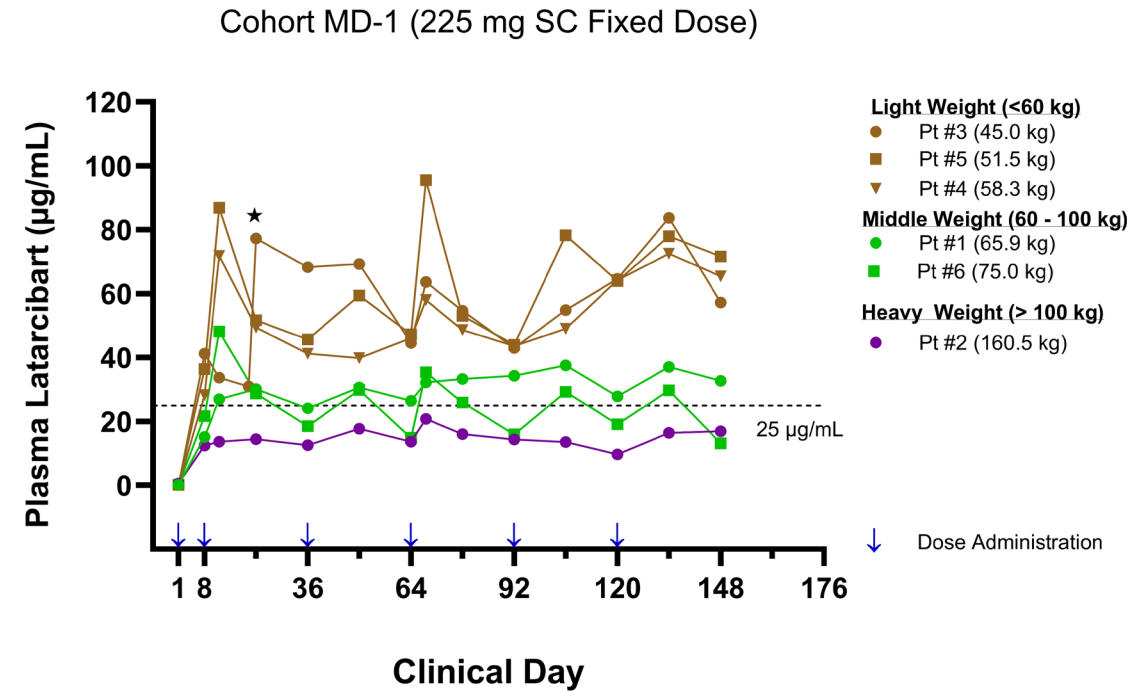
Baseline Characteristics

Characteristic	Cohort MD-1 (N=6)	Cohort MD-2 (N=10)
Sex, n		
Male	2	6
Female	4	4
Age, mean (range), y	24.7 (15–53)	36.9 (22–53)
Race, n		
Asian	1	1
Black	1	0
White	4	8
Other	0	1
Weight, mean (range), kg	76.0 (45.0–160.5)	85.6 (61.7–124.5)
Disease type/sub-types, n		
1	2	0
1C	0	1
2A	1	3
2M	1	0
2N	0	2
3	2	4
Pre-MD ABR, range	8.0–431.1	0–321.2

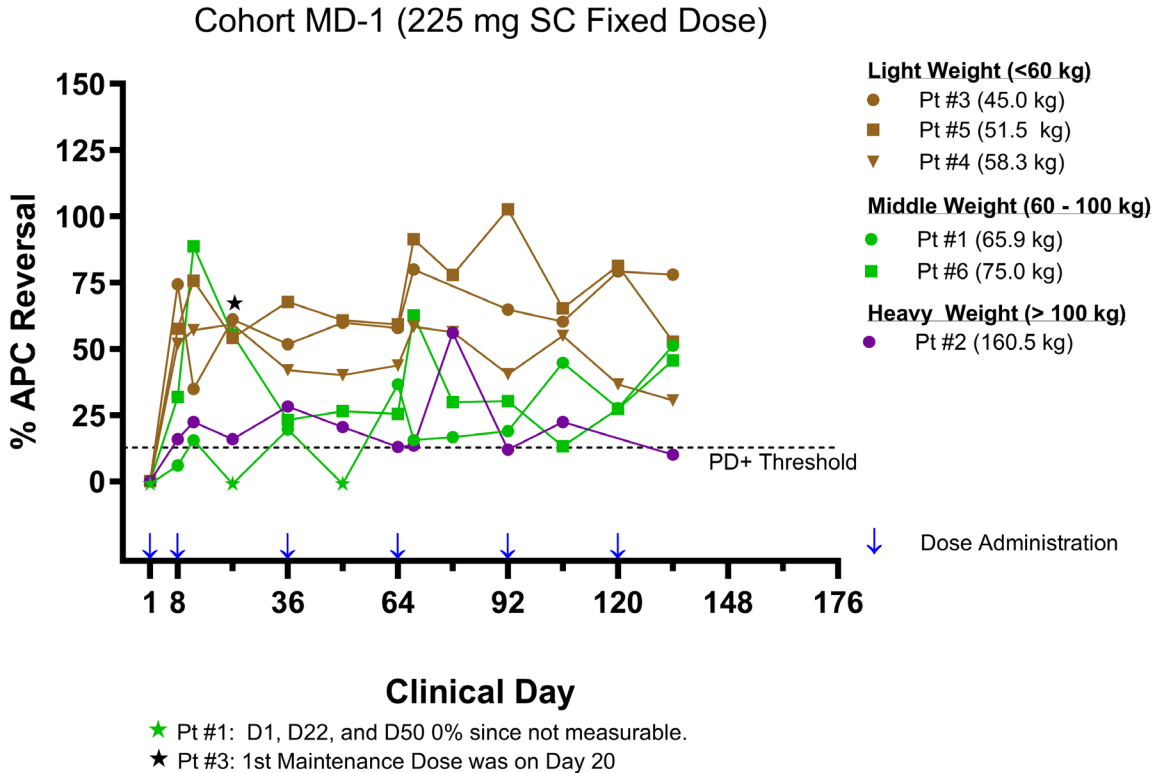
ABR, annualized bleed rate.
Data as of May 5, 2026.

Dosing & Pharmacokinetics and Pharmacodynamics in Cohort MD-1

Pharmacokinetics: Plasma Latacibart Concentrations

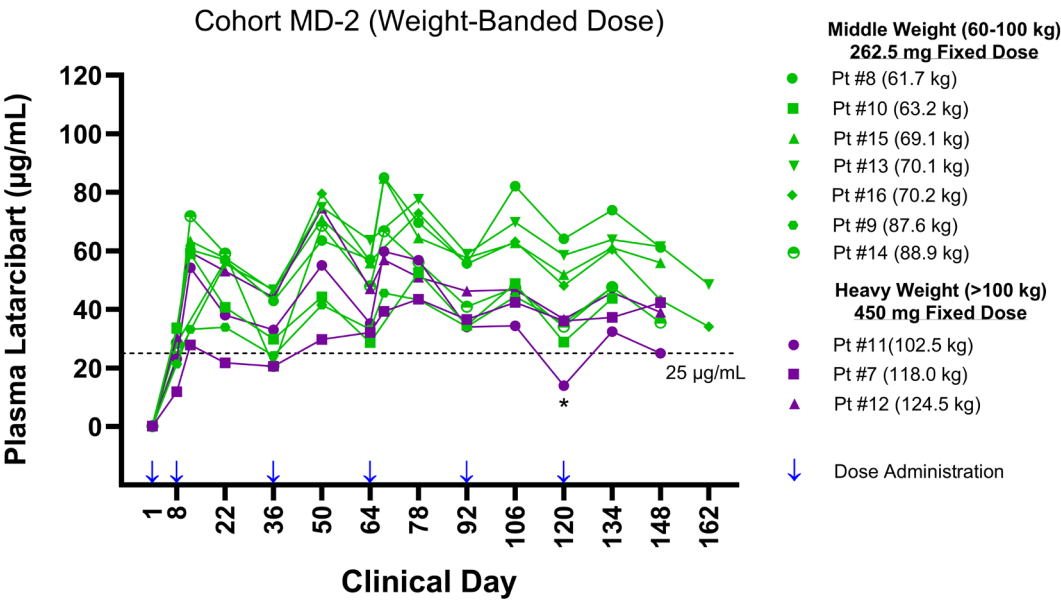


Pharmacodynamics: Thrombin Generation Assay (% APC reversal)



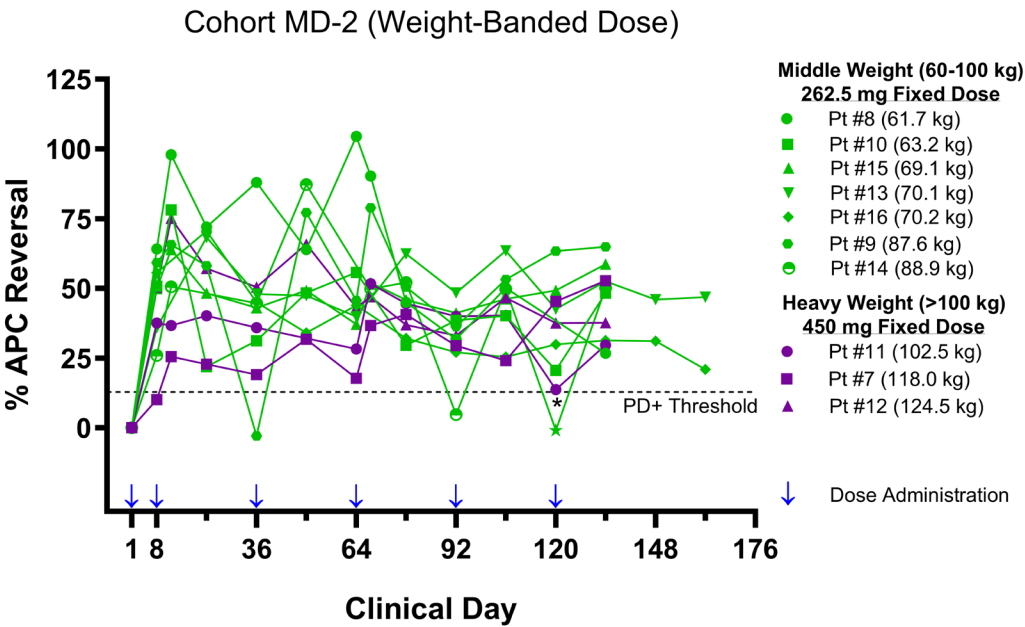
Dosing & Pharmacokinetics and Pharmacodynamics in Cohort MD-2

Pharmacokinetics: Plasma Latacibart Concentrations



* Pt #11 had gastrointestinal bleeding (D94 to D122) and IV infusions that affected the plasma Latacibart concentration

Pharmacodynamics: Thrombin Generation Assay (% APC reversal)



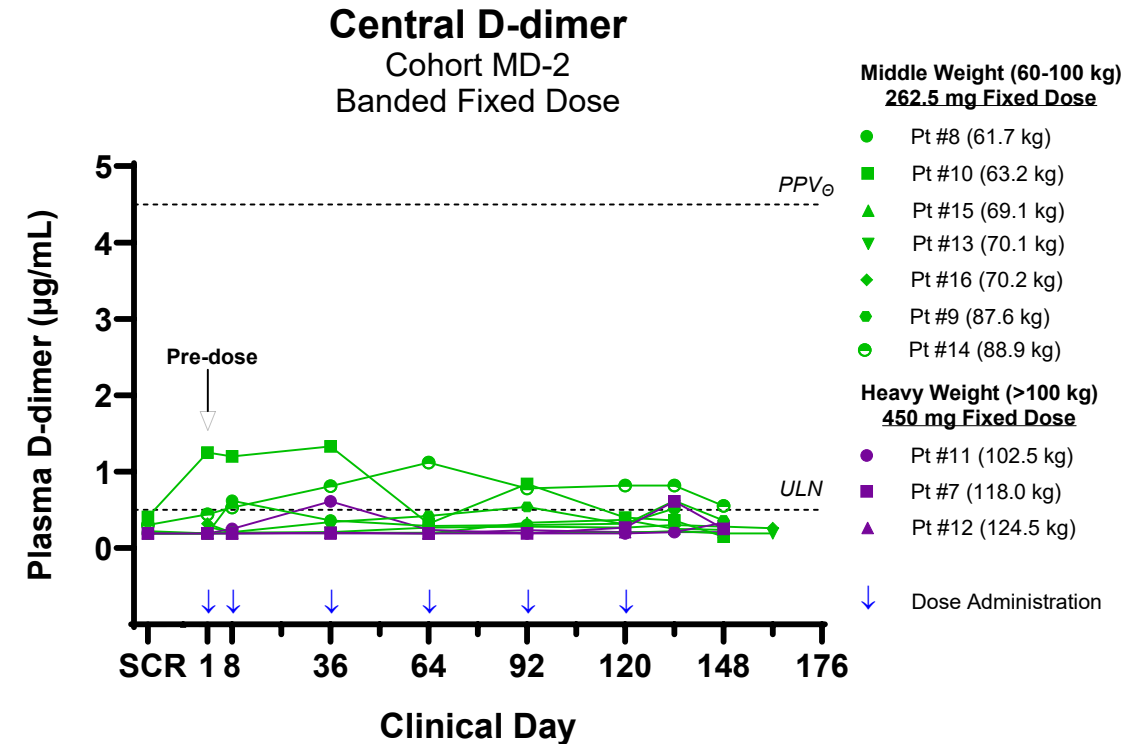
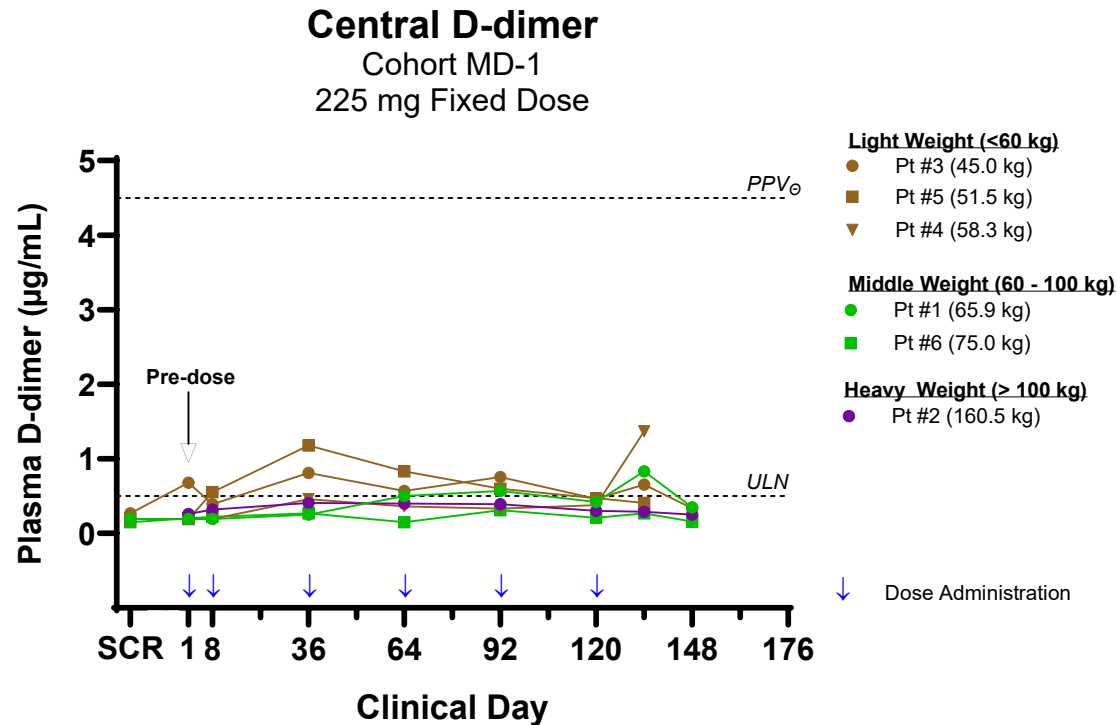
★ Pt #14: D120 is 0% APC Reversal since not measurable.
* Pt #11 had gastrointestinal bleeding (D94 to D122) and IV infusions that affected the results

Cumulative Safety Summary in VIVID-3

- All 16 participants have completed the MD regimen (6 doses)
 - No thromboembolic events
 - 67 treatment-emergent AEs reported in 12 participants
 - Two related Grade 2 events of headache in 1 participant, resolved with acetaminophen
 - One Grade 1 report of injection site reaction* in 1 participant, resolved with oral antihistamine
 - One unrelated, serious AE: severe GI bleeding (history of frequent and severe GI bleeding)
- Latarcibart has demonstrated a favorable safety and tolerability profile over multiple doses in this study

* Consisting of injection site itching, injection site rash, and injection site swelling.
Data as of May 5, 2026.

No Clinically Relevant D-Dimer Levels in Cohorts MD-1 and MD-2



- Assumed PPV = 9 X ULN¹
- All samples were collected pre-dose on the days indicated

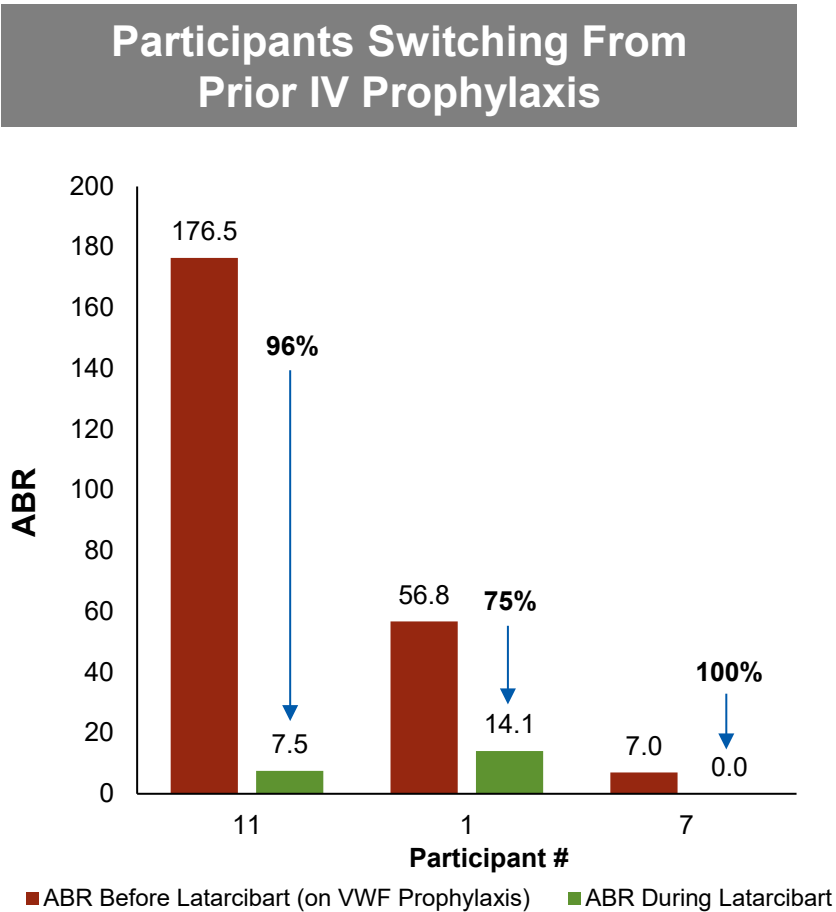
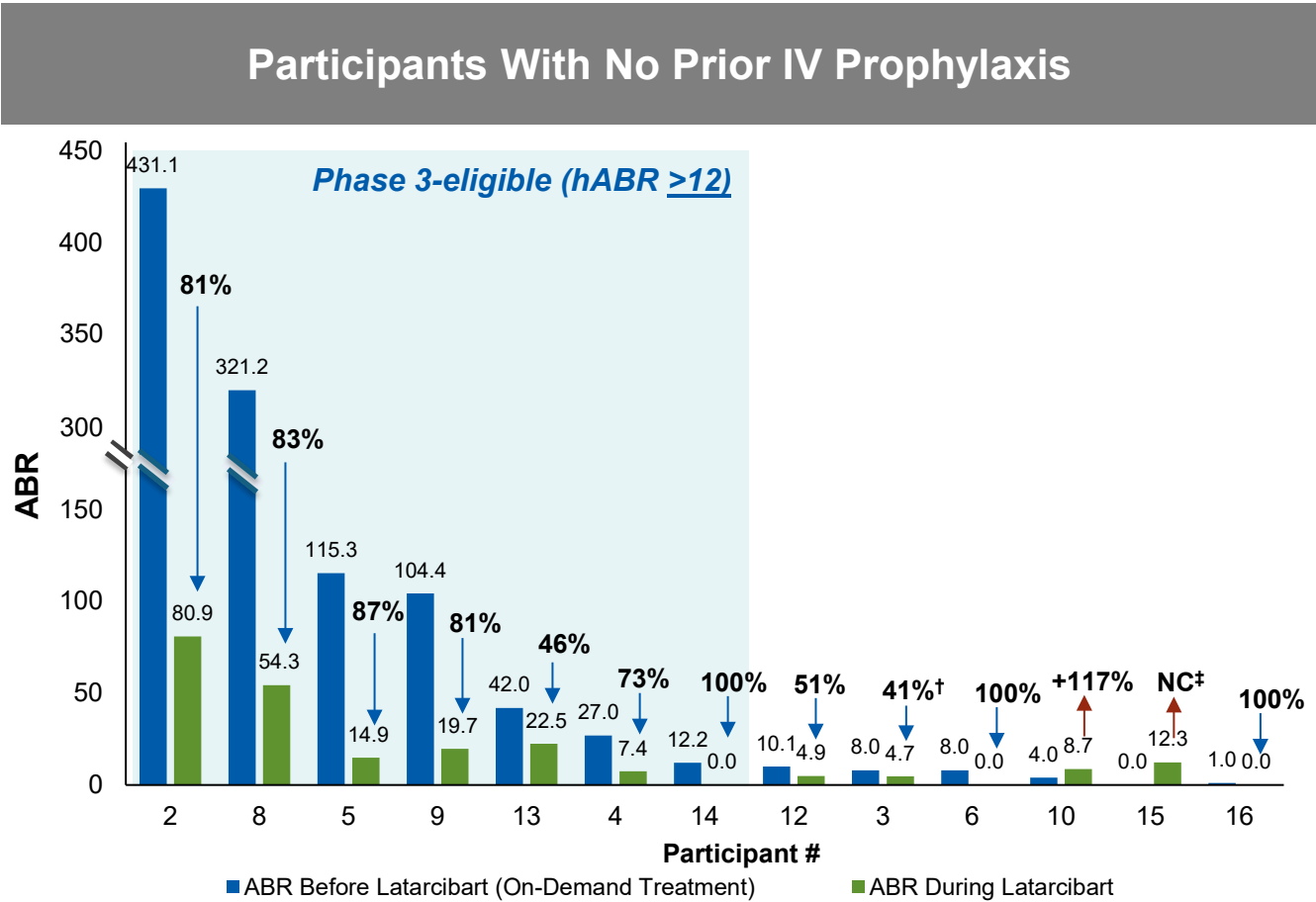
PPV, positive predictive value; ULN, upper limit of normal.

Data as of May 5, 2026.

1. Koch V et al. *Eur Heart J Acute Cardiovasc Care*. 2021;10:559-566.

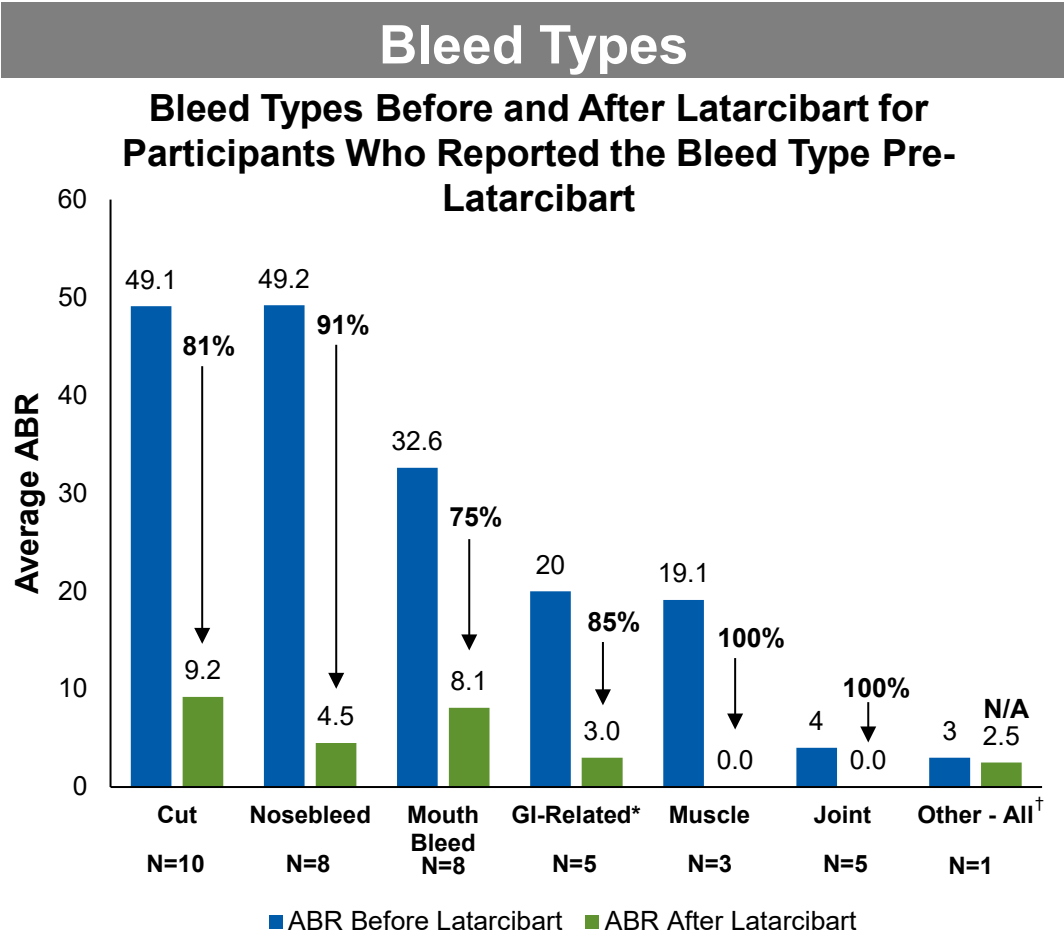
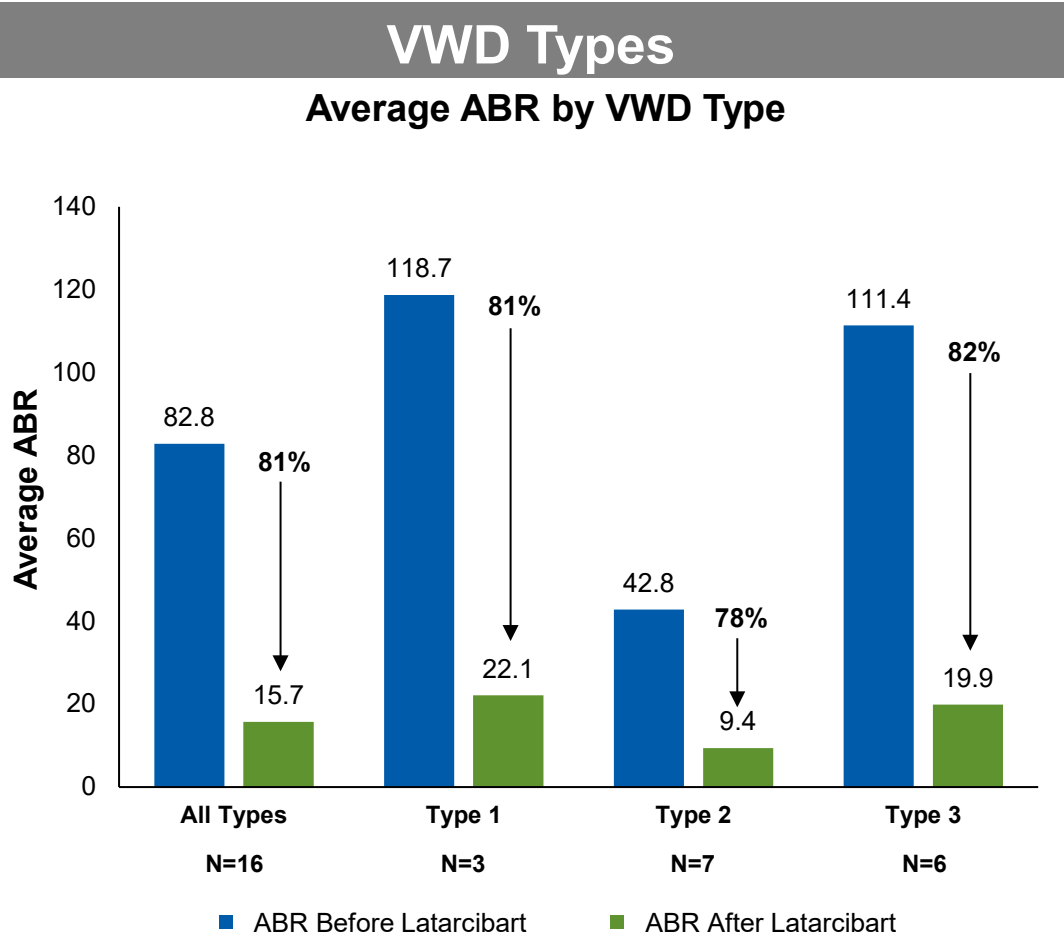
Substantial Median Bleed Reduction Observed in Multi-Dose Study

Median ABR* Reduction For All Participants: **81%**



hABR, historic ABR; NC, non-calculable.
* ABR excludes bruising and menstrual bleeding. Blanchette VS, et al. *J Thromb Haemost.* 2014;12(11):1935-1939.
† hABR comprised of primarily epistaxis, no epistaxis observed during study.
‡ hABR 99 in VIVID2; 0 bleeds prior to VIVID3 enrollment.
Data as of May 5, 2026.

ABR Reductions Observed in All VWD Types and Bleed Types



N/A, not applicable based on varied nature of bleeds.

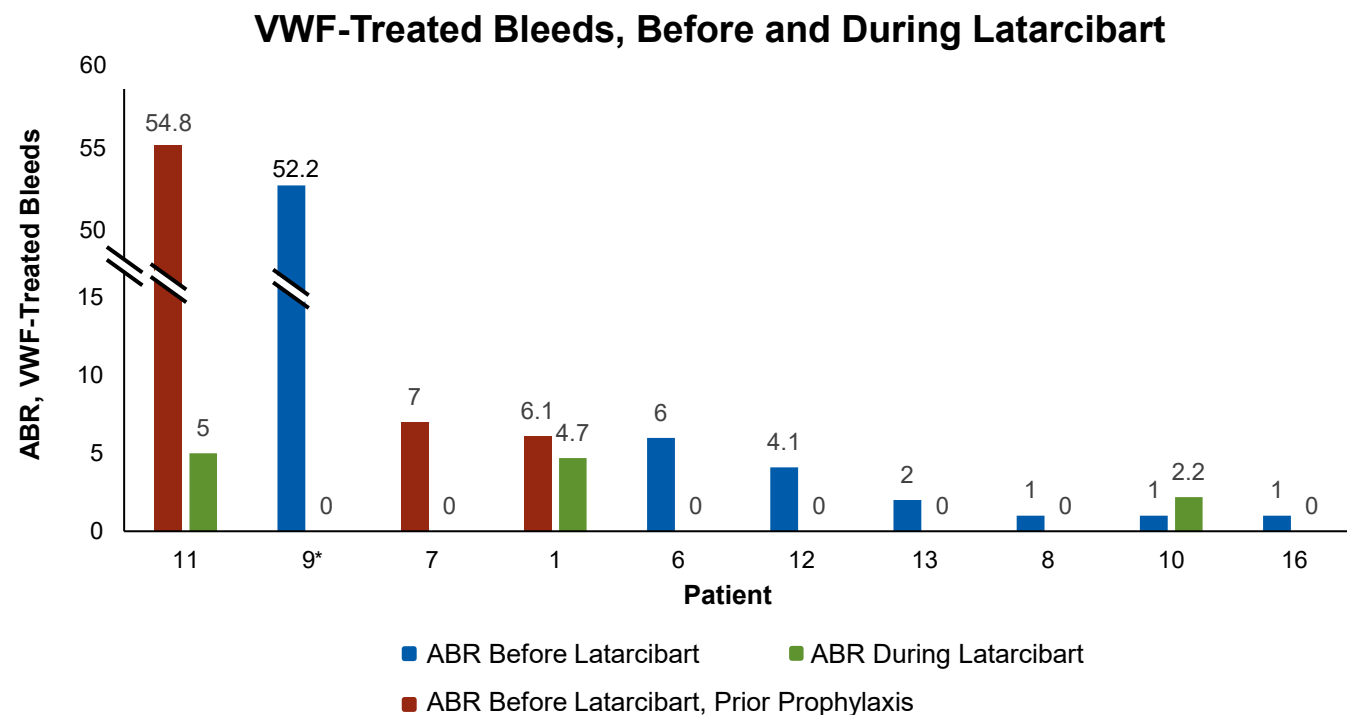
*GI-Related includes GI, vomit and rectal bleeds.

†Includes urine, tooth extraction-related, and other bleeds.

Data as of May 5, 2026.

Substantial Reduction in Use of VWF-Containing Concentrates to Treat Break-Through Bleeds During the MD Study

- **86% reduction in VWF-treated break-through bleeds while on latarcibart***
- **7/10 participants (70%) with a history of VWF-treated bleeds in the historical ABR period **did not have** a VWF-Treated bleed while on latarcibart**



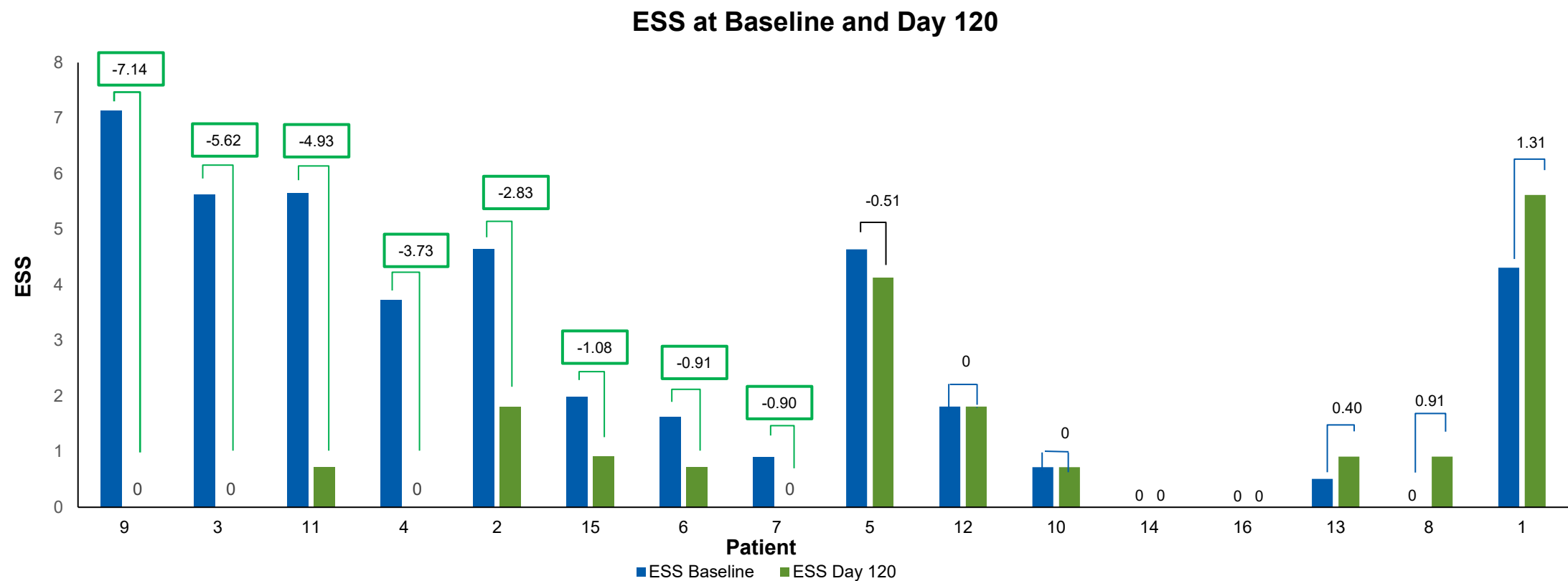
Additional Detail on VWF-Treated Bleeds On-Study:

- **Participant 11** – GI bleeding event on study with associated procedure to address angiodysplastic lesion; bleed free subsequently for the MD and continued into OLE
- **Participant 1** – 2 VWF-treated bleeds in the MD; bleed free after D121 and throughout the OLE
- **Participant 10** – Single treated oral bleed associated with severe periodontitis

* Historic ABR derived from 7-day recall period. Patient 9 was excluded from break through bleed population due to short historical ABR period.
Data as of May 5, 2026.

Clinically Meaningful Reductions in Epistaxis Severity Score

- Median change in ESS among participants with ESS > 0 at BL was −0.91 (range, −7.14 to 1.31)
 - 8/13 participants **exceeded** the minimally important difference (−0.71¹) with baseline ESS > 0 at baseline



ESS, epistaxis severity score.
1. Yin LX, et al. *Laryngoscope*. 2016;126(5):1029–1032.
Data as of May 5, 2026.

VIVID-3 Conclusions

- Latarcibart SC every-4-week dosing is well tolerated with no safety signals in this multidose study
- Across all VWD types, median ABR reduction was 81%
 - All participants switching from prior IV prophylaxis (75-100%)
 - Most participants not receiving prior IV prophylaxis, demonstrated reductions (41-100%)
- Reduction in ABR across all VWD types and reported bleed categories
- Substantial reduction in use of VWF-containing concentrates to treat breakthrough bleeding
- All participants with a substantial bleed burden entering the study have transitioned to the OLE
- Phase 3 VIVID-6 study (NCT07115004) is currently enrolling

Latarcibart Poster Presentations

**PB2083- PKPD &
Phase 3 dose
(7/13)**

**PB3420 Qualitative
Outcomes of VIVID3
(7/14)**

Thank You

VIVID-6

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

NOW ENROLLING

- University of Pittsburgh/Hemophilia Center of Western Pennsylvania, USA
- Hemocentro UNICAMP, University of Campinas
- K. J. Somaiya Medical College & Research Center, India
- Washington Institute of Coagulation
- University of Toronto, St. Michaels Hospital, Canada
- 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

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.