Sutacimig - A Novel Bispecific Antibody for Prophylactic Treatment of Glanzmann Thrombasthenia: Analysis of a Phase 2 Study

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Glanzmann Thrombasthenia

Platelet Aggregation Defect Causing Frequent Bleeding Events

Severe platelet function disorder

Characterized by deficient or dysfunctional GPIIb/IIIa expression on platelets impairing platelet-fibrinogen binding and platelet aggregation during primary hemostasis

Frequent bleeding events from low-volume epistaxis to life-threatening hemorrhages[1]

88% of patients bleed weekly

> 50% bleed 3 x per week

80% miss school or work

No approved therapies for primary prophylaxis

30% develop alloimmunization to platelets

Current treatment options are limited by short half-lives, high costs, and complications with IV administration

Frequent bleeding events accumulate to create a significant clinical impact, including iron deficiency and impaired quality of life.

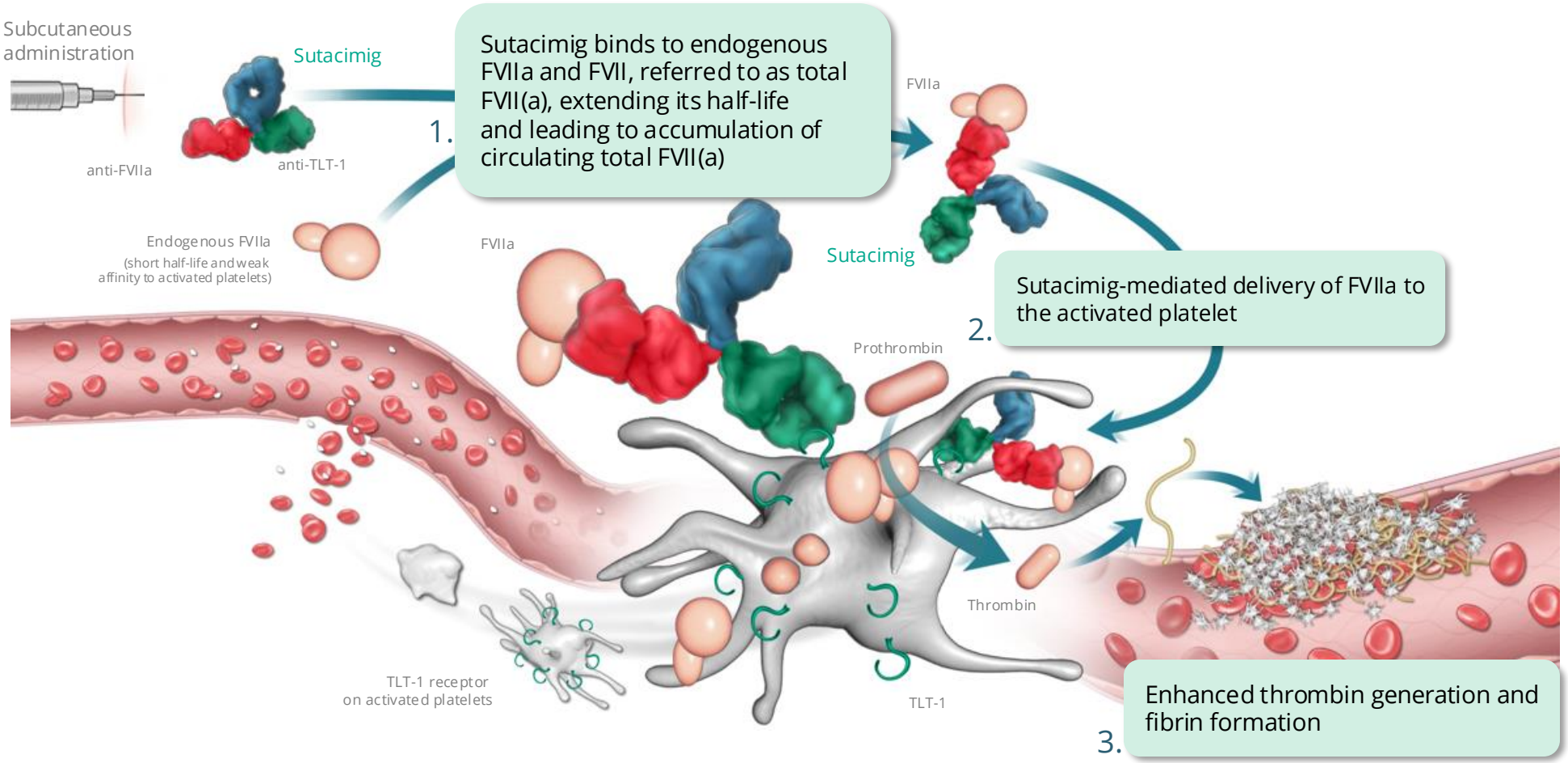
Abbreviations: GP, glycoprotein; GPIIb/IIIa, glycoprotein IIb/IIIa receptor; IV, intravenous; References: 1. Khair K, et al. Res Pract Thromb Haemost. 2024

Sutacimig targets endogenous FVIIa to activated platelet surface, leading to accumulation and potentiation of FVIIa activity

Bispecific antibody

Low-volume (<1 ml) SQ dose

TLT-1 potentiated FVIIa-mediated thrombin generation

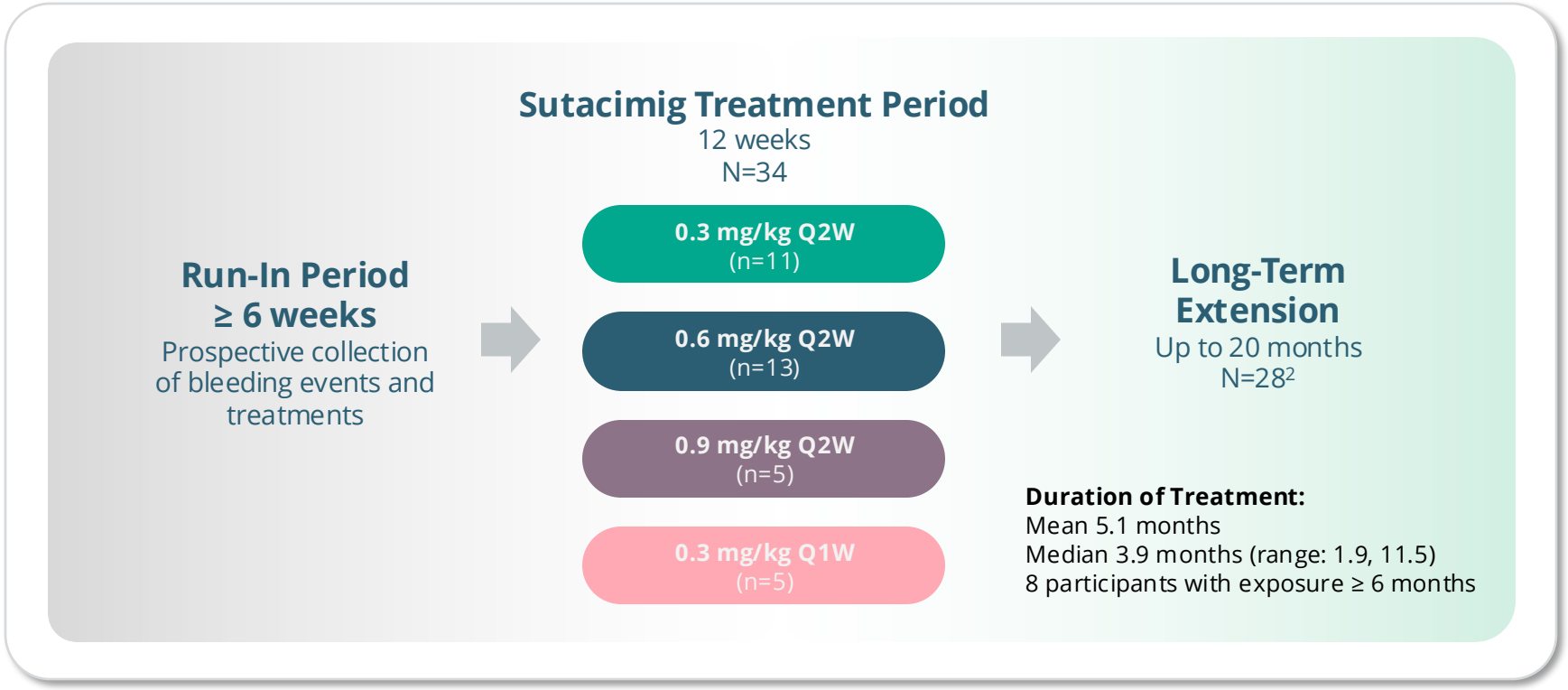


Sutacimig binds and accumulates endogenous FVIIa and, following vessel lesion, localizes FVIIa to the surface of activated platelets via TLT-1 potentiation[1]

Abbreviations: FVIIa, activated factor VII; SQ, subcutaneous; TLT-1, TREM-like transcript-1.
References: Gandhi PS, et al. Nat Cardiovasc Res. 2024.

Multiple Ascending Dose (MAD) Evaluation with Long-Term Extension

- **Primary Objective:**
  - Safety and tolerability
- **Other Objectives:**
  - PK/PD
  - Efficacy based on ATBR[1] reduction
- **Key Entry Criteria:**
  - Confirmed GT diagnosis
  - History of bleeding requiring treatment
  - Adults 18-67 years



Data available as of interim data cut-off of July 1, 2025. Additional study details available at ClinicalTrials.gov NCT06211634.
[1]ATBR: annualized treated bleed rate
[2]Two participants terminated treatment, 1 each due to adverse event and physician decision due to participant noncompliance. Four participants did not consent to the long-term extension, 3 for logistical reasons (travel to site, scheduling) and 1 had ongoing medical issues that interfered with trial participation.

Demographics and Baseline Characteristics

Characteristic		N=34
Age (years)	Median (range)	40.5 (19-66)
Sex, n (%)	Female	16 (47)
	Male	18 (53)
Race, n (%)	Asian	6 (18)
	Black or African American	2 (6)
	White	16 (47)
	Other	2 (6)
	Not Reported	8 (23)
Weight (kg)	Median (range)	75 (52-134)
Total FVII(a) (%)	Median (range)	99.5 (51.1, 164.5)
Baseline ATBR during run-in[1]	Mean (SEM); range Median (Q1, Q3)	40.2 (11.8); range: 0-324.7 17.7 (4.0, 47.6)
Cause of treated bleeding events during run-in (%)[1]	Spontaneous Traumatic Iatrogenic Not categorized	75.0 19.3 4.7 1.0

[1]Per protocol efficacy set excludes 3 participants: 2 due to run-in period <6 weeks and 1 due to noncompliance with bleed diary guidelines.

Interim Safety Profile

Median Exposure: 3.9 months (range: 1.9, 11.5)

Majority of TEAEs mild to moderate in severity

- No related AE > grade 2
- 1 related SAE of DVT at highest dose level (0.9 mg/kg Q2W)
- AEs of bleeding were either before drug initiation or following procedure
  - Grade 3 melena occurred on day -1
  - Grade 3 post procedural hemorrhage following dental procedure, resolved with 5 mcg/kg rFVIIa

D-dimer elevation in 7 participants, all low grade, not associated with hypofibrinogenemia or thrombocytopenia

5/34 participants developed ADA titers impacting PK/PD

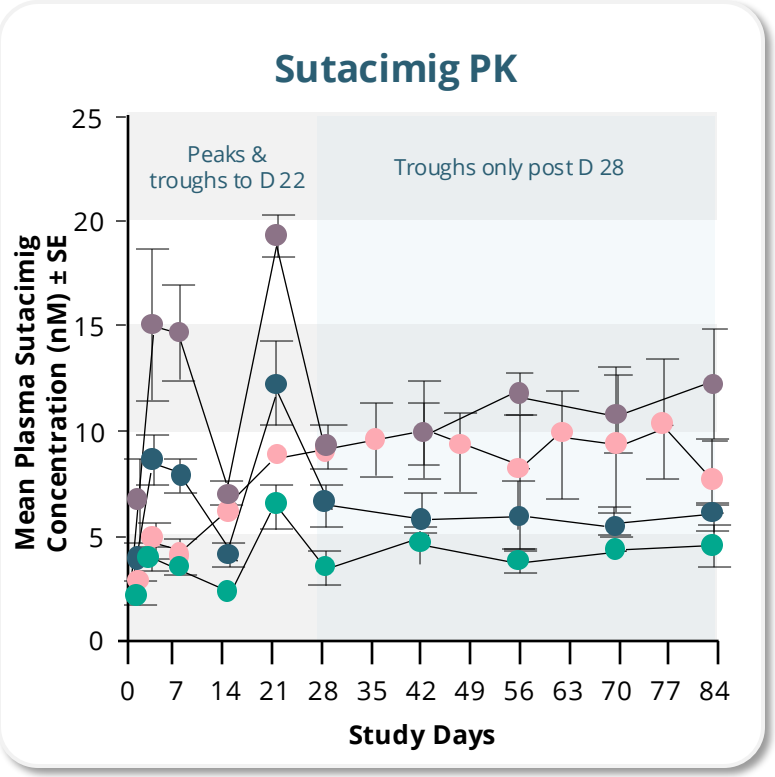
- 1/5 resolved with continued dosing
- No associated safety events

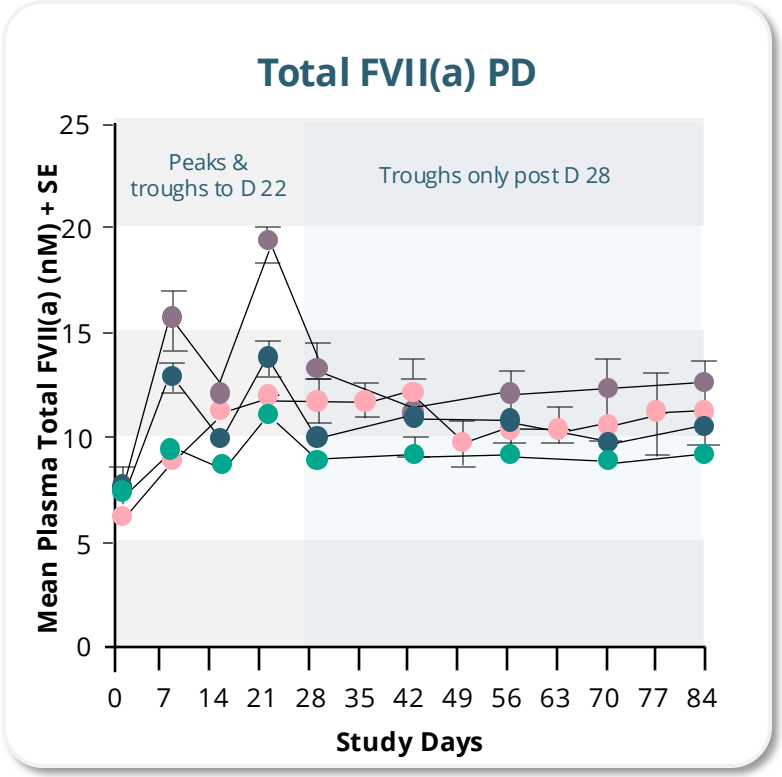
	N (%)
Safety population	34 (100)
Any grade TEAE (all causality)	32 (94)
TEAE leading to discontinuation	1 (3)
TEAE in ≥ 15%	
Headache	8 (24)
Fibrin D dimer increased	7 (21)
Nasopharyngitis	7 (21)
Iron deficiency anemia	5 (15)
≥ Grade 3 TEAE (non serious)	4 (12)
Back pain	1 (3)
Dental caries	1 (3)
Melena[1]	1 (3)
Neutropenia[1]	1 (3)
Post procedural hemorrhage	1 (3)
SAE	3 (9)
DVT (Gr 2)	1 (3)
Gastrointestinal hemorrhage (Gr 3)	1 (3)
Invasive ductal breast carcinoma (Gr 3)	1 (3)

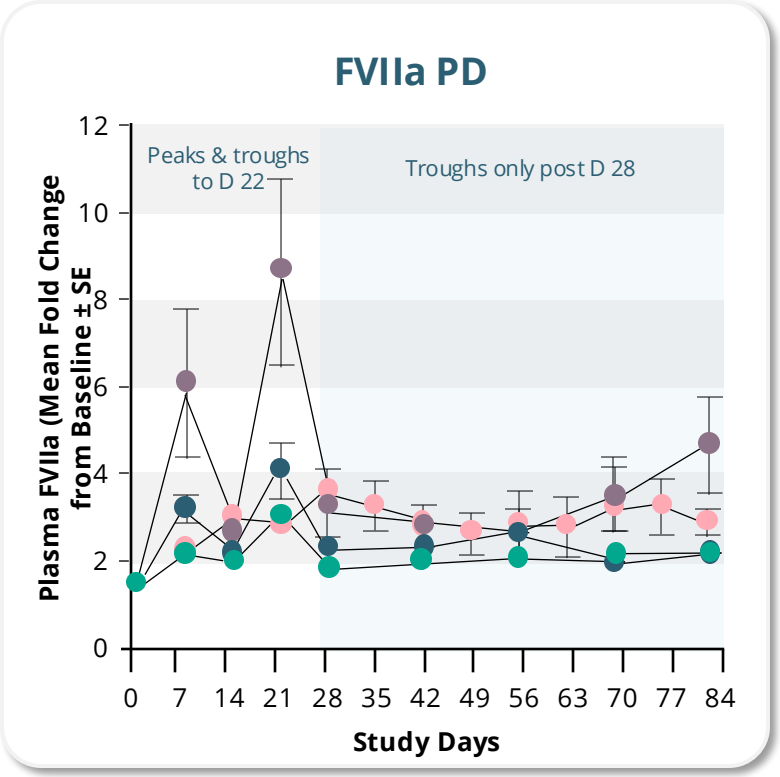
[1]Events of melena and neutropenia occurred in a single participant. Abbreviations: TEAE, treatment-emergent adverse event; ADA, anti-drug antibody; DVT, deep vein thrombosis; rFVIIa, recombinant FVIIa; SAE, serious adverse event. Safety analyses based on cumulative exposure through 12-week treatment period plus long-term extension. All AEs summarized are treatment emergent, excluding bleed events.

Dose-Dependent PK and PD

Highest dose level with disproportionate PD impact







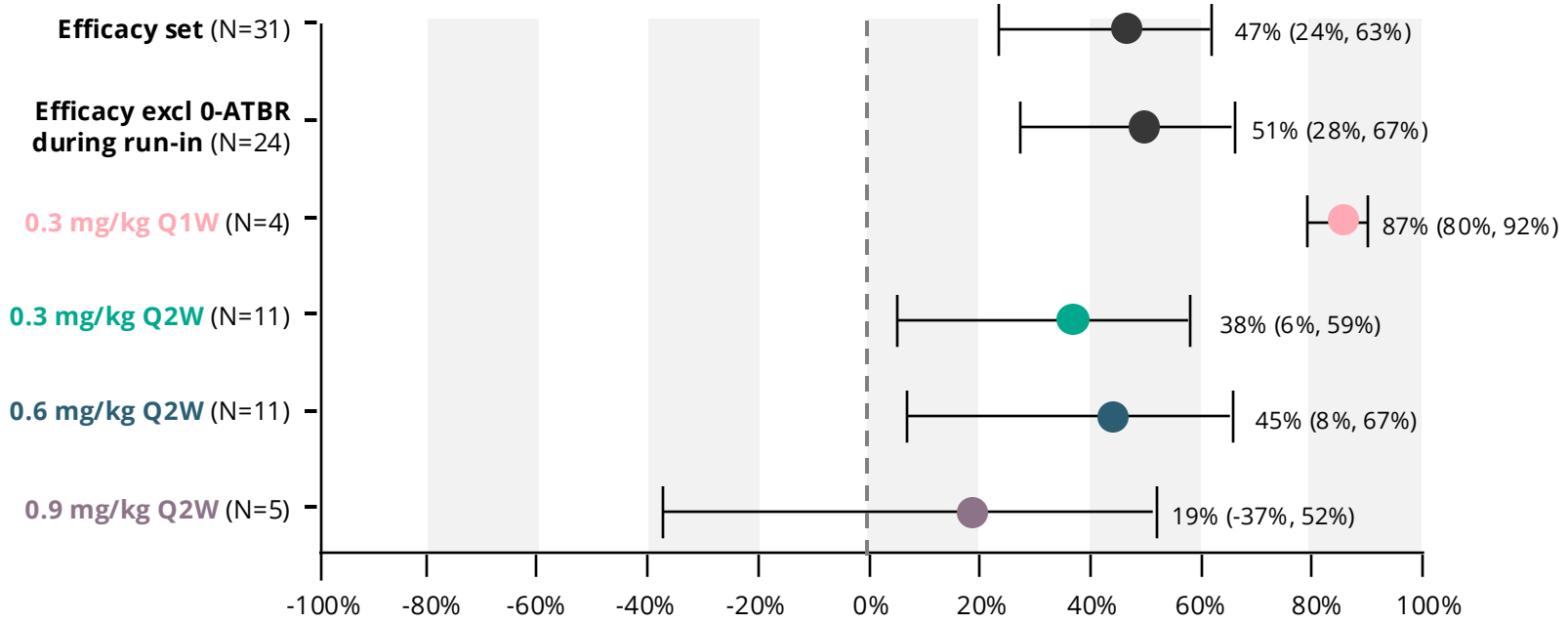
- Dose-dependent peak PK and PD elevation
- 0.9 mg/kg Q2W disproportionately high FVIIa
- Q1W regimen delivers consistent exposure and PD at peak and trough throughout dosing interval

Cohort B1: 0.3 mg/kg Q2W (n=9)
Cohort B2: 0.6 mg/kg Q2W (n=11)
Cohort B3: 0.9 mg/kg Q2W (n=5)
Cohort B4: 0.3 mg/kg Q1W (n=5)

Reduction in Mean ATBR Across Multiple Dose Cohorts

- Robust and clinically meaningful efficacy in all participant efficacy set,
- Enhanced response with weekly dosing
- 95% CIs for Q1W regimen distinct from Q2W regimens with an estimated 87% (CI: 80%, 92%) ATBR reduction

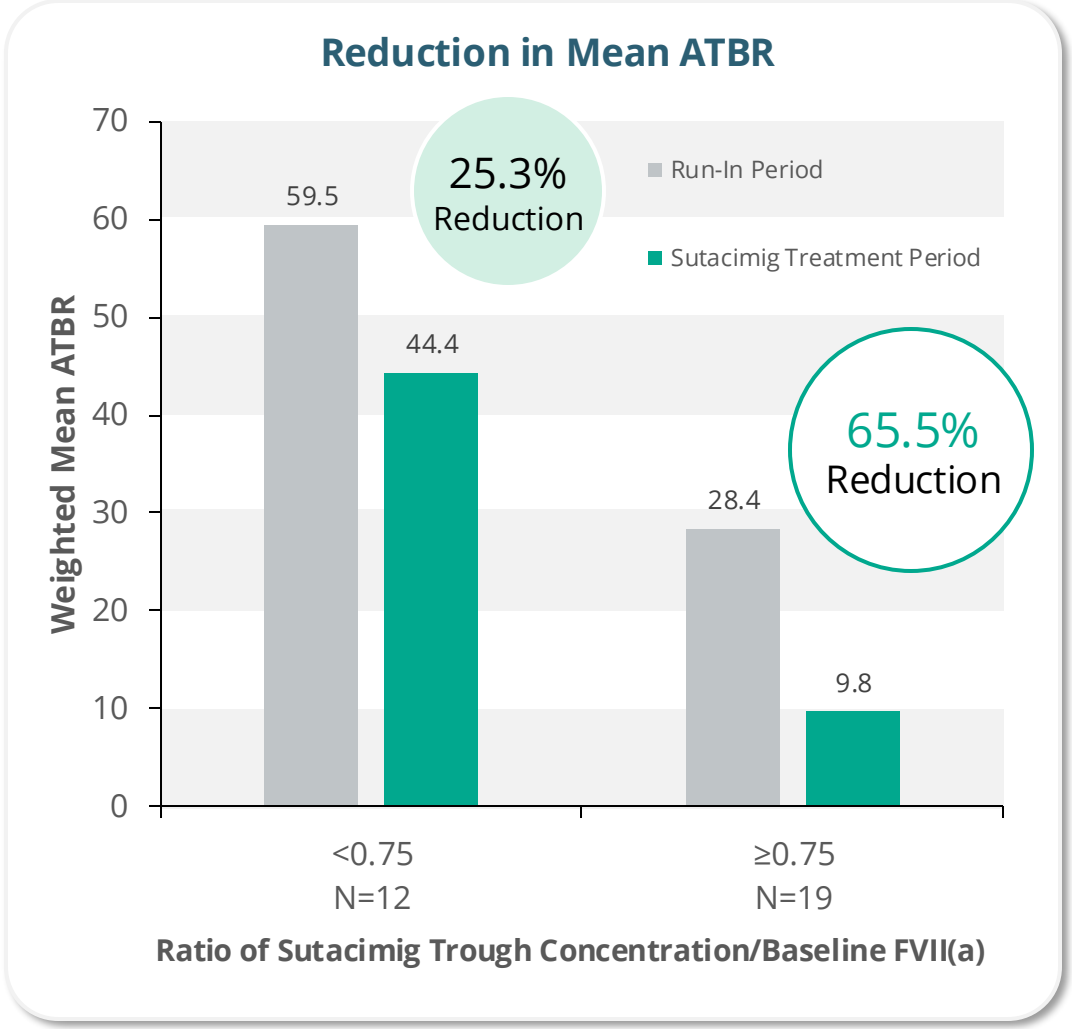
Estimated reduction in ATBR with 95% confidence interval
(Efficacy set)



A GEE negative binomial regression model with an offset for duration of study period was fitted to estimate the mean ATBR during each study period and reduction in mean ATBR along with corresponding 95% CIs.
Efficacy analyses included comparison of the run-in and 12-week treatment period (data cut-off July 1, 2025).

ATBR Reduction Enriched with Achievement of Target Drug Concentration

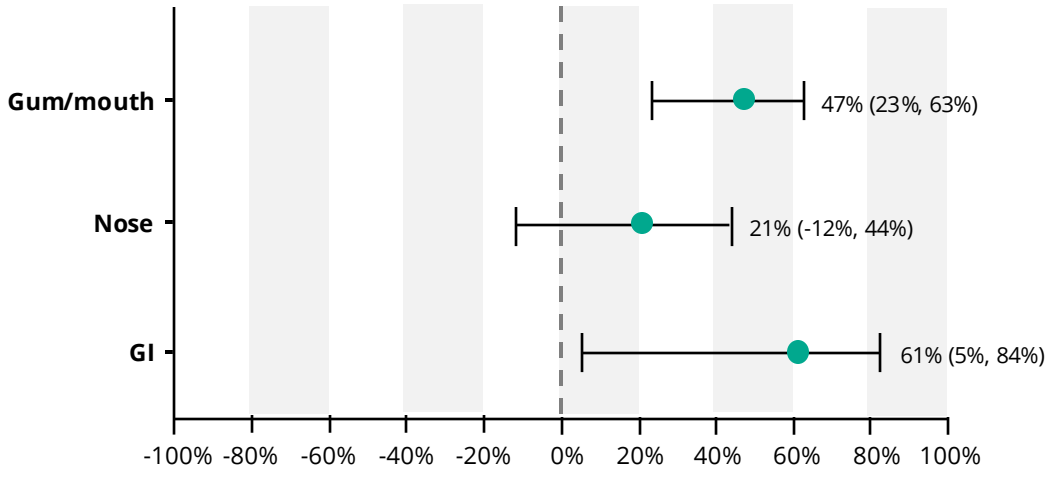
- Exploratory analysis to assess ATBR reduction in participants achieving target drug concentration
- Higher trough sutacimig concentration associated with greater ATBR reduction
- ATBR reduction enriched in those achieving higher sutacimig exposure adjusted for baseline Factor VII(a) levels
  - Allows for saturation of pool of activated FVIIa



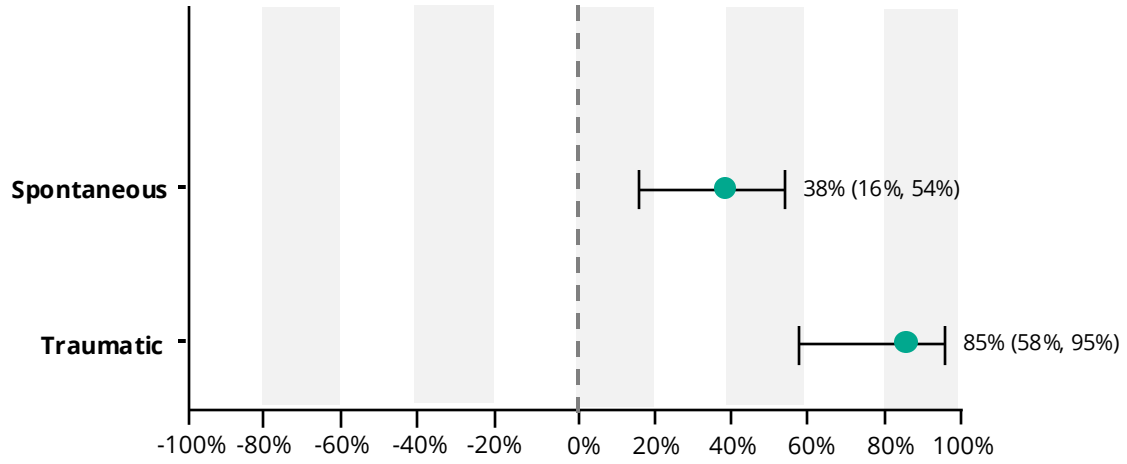
Mean ATBR during run-in and treatment period was weighted by duration of follow-up during run-in and treatment period, respectively.
Efficacy analyses included comparison of the run-in and 12-week treatment period (data cut-off July 1, 2025).

Mean ATBR Reduction Consistent across Bleeding Event Type and Cause

Estimated reduction in ATBR by type of bleeding event
(Efficacy set N=31)



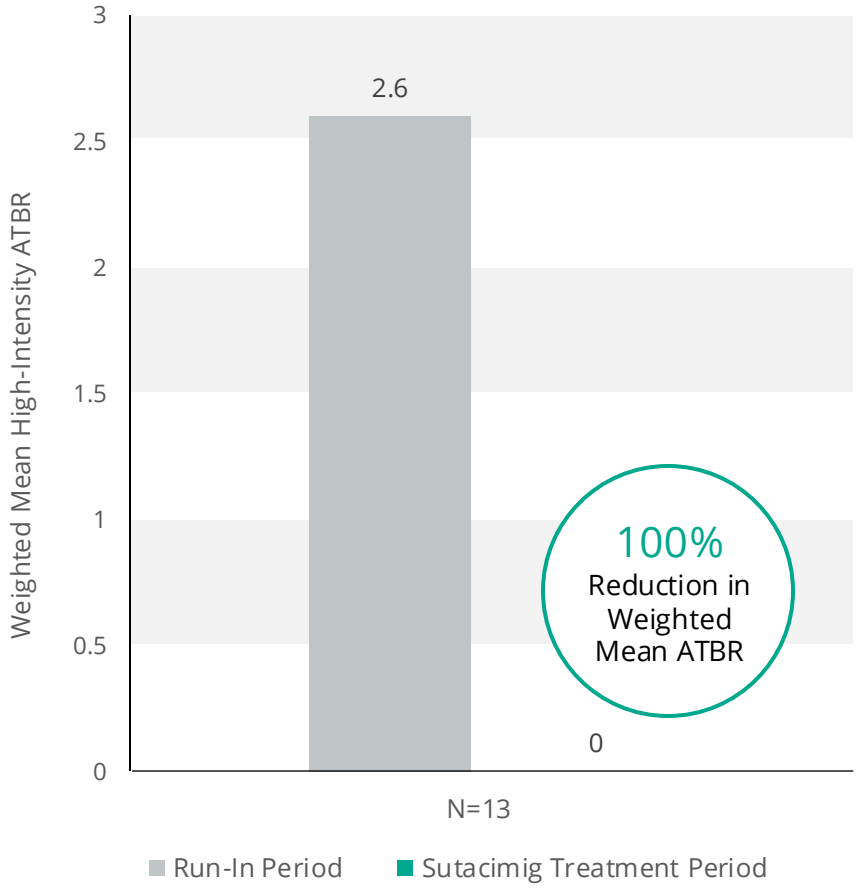
Estimated reduction in ATBR by cause of bleeding event
(Efficacy set N=31)



A GEE negative binomial regression model with an offset for duration of study period was fitted to estimate the mean ATBR during each study period and reduction in mean ATBR along with corresponding 95% CIs.
Efficacy analyses included comparison of the run-in and 12-week treatment period (data cut-off July 1, 2025).

Marked Reduction in Bleeding Events Treated with High-Intensity Treatments

- A subset of participants were identified as experiencing bleeding events treated with high-intensity treatments within 12-month period prior to first dose of sutacimig[1]
- High-intensity treatments include the following:
  - Systemic hemostatic intervention (rFVIIa, platelet transfusion, plasma, cryoprecipitate)
  - Medical, surgical, or radiologic procedures for hemostasis
- Mean reduction of high-intensity ATBR of 100% during the initial 12-week treatment period



[1]Treated bleeding event data collected as past medical history and during the run-in period was used to perform this analysis.
A GEE negative binomial regression model with an offset for duration of study period was fitted to estimate the mean ATBR during each study period and reduction in mean ATBR along with corresponding 95% CIs.
Efficacy analyses included comparison of the run-in and 12-week treatment period (data cut-off July 1, 2025).

Conclusions

- Glanzmann thrombasthenia is a severe bleeding disorder
- MAD portion complete and >80% retention for long-term extension
- Robust and clinically meaningful mean ATBR reduction demonstrated
  - Consistent clinical activity across dose levels, type, and cause of bleed
  - Enrichment of activity in those achieving target drug concentrations
  - Marked reduction in bleeding events requiring high-intensity treatment on sutacimig
- Clinical data indicate Q1 week regimen improves clinical activity over Q2 week regimen
- Safety and clinical activity support potential as prophylactic treatment in GT
- **Next steps:** Finalization of Phase 3 dose and regimen

Acknowledgements

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ENROLLMENT COMPLETE: Glanzmann thrombasthenia

Country	Phase 1/2 sites
Belgium	University Hospital Leuven
France	AP-HP Hôpital Bicêtre
	AP-HP Hôpital Necker
	AP-HM - Hôpital de la Timone
Italy	Careggi University Hospital
	IRCCS Ca' Granda Maggiore Hospital
Netherlands	University Medical Centre Utrecht
United Kingdom	Leeds Teaching Hospitals
	The Royal London Hospital
	Richmond Pharmacology
	Royal Free London
	Queen Elizabeth Hospital Birmingham
United States	University of California, San Diego
	Tulane University Medical Centre
	Mayo Clinic - Rochester
	University of Pittsburgh
	Washington Institute for Coagulation