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Safety and Efficacy of HMB-001 as a Prophylactic Treatment of Glanzmann Thrombasthenia: Interim Analysis of Phase 1/2 Study

Suthesh Sivapalaratnam[1,2], Laurent Frenzel[3], **Frederico Xavier[4]**, Peter Verhamme[5], Catherine Rea[6], Ashley Gosnell[6], Joseph Vogel[6], Pruthvi Nagilla[6], Tara Parsons[6], Jigar Amin[6], Ulrike Lorch[7], Matej Goricar[7], Andrew Law[6]

[1]Queen Mary University of London, [2]Barts Health NHS Trust, [3]Necker Hospital, [4]University of Pittsburgh, [5]KU Leuven, [6]Hemab Therapeutics, [7]Richmond Pharmacology. Phase I was conducted at Richmond Pharmacology Ltd (RPL)

Contact details
Frederico Xavier, MD, MS
frederico.xavier@chp.edu

Disclosures for Dr. Xavier

Conflict	Disclosure - if conflict of interest exists
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Advisory Committee	No relevant conflicts of interest to declare
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#wfhCCS

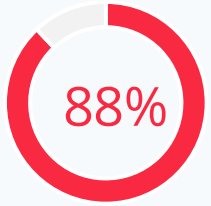
What is Glanzmann thrombasthenia (GT)?

- Rare genetic **bleeding disorder** that disrupts platelet aggregation and clot formation
- Variants in the ITGA2B and ITGB3 genes render the GPIIb/IIIa (fibrinogen) receptor absent or non-functional on platelets, **hindering formation of the platelet-fibrin mesh**
- **Frequent bleeding events** ranging from low volume epistaxis to life-threatening hemorrhages[1]
- The current standard of care for GT is reactive (tranexamic acid, platelet transfusions or recombinant FVIIa) and on-demand
- **No approved therapies for primary prophylaxis**

80

Annualized Treated Bleed Rate[2]
(median per patient)

GLANZMANN'S 360[1]
The Lived Experience of People with Glanzmann's Thrombasthenia



Reported ≥1 bleed in the past week

Experienced fatigue

Experienced pain, immobility, and anxiety/depression

Lost time from work and/or school

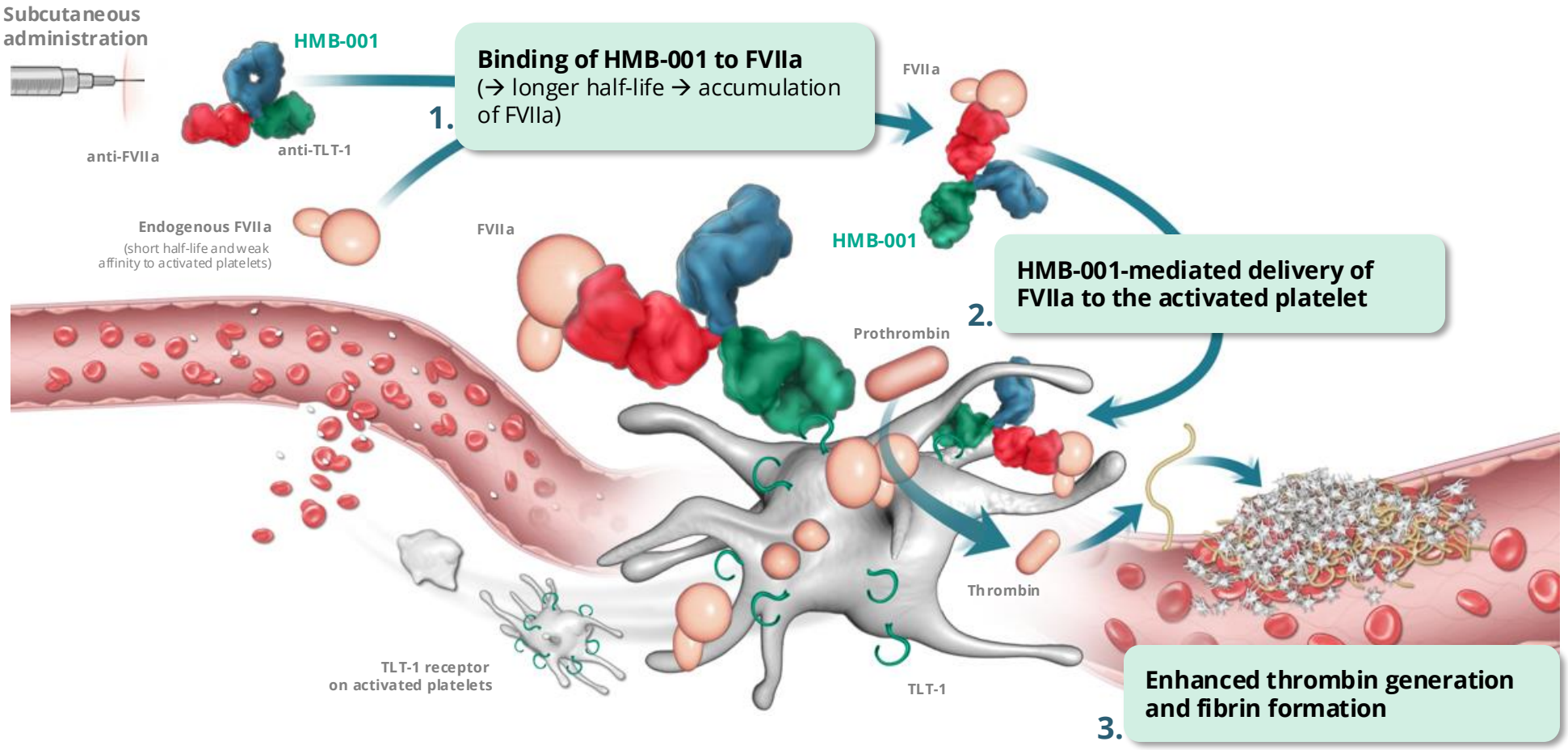
Abbreviations: GP, glycoprotein; GPIIb/IIIa, glycoprotein IIb/IIIa receptor; GT, Glanzmann thrombasthenia; rFVIIa, recombinant activated factor VII.
References: [1]Khair K, et al. Glanzmann's 360 study: bleeding & QoL in GT. Res Pract Thromb Haemost. 2024;8(7):102586.; [2]Rhea C. UK Bleed Diary [Poster]. ISTH (2024).

HMB-001 binds and accumulates FVIIa to enhance thrombin generation

Bispecific antibody

Low-volume (<1 ml) SQ dose

TLT-1 potentiated FVIIa-mediated thrombin generation



HMB-001 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: [1]Gandhi PS, et al. Nat Cardiovasc Res. 2024.

Phase 1/2 study of HMB-001 in Glanzmann thrombasthenia

Objectives

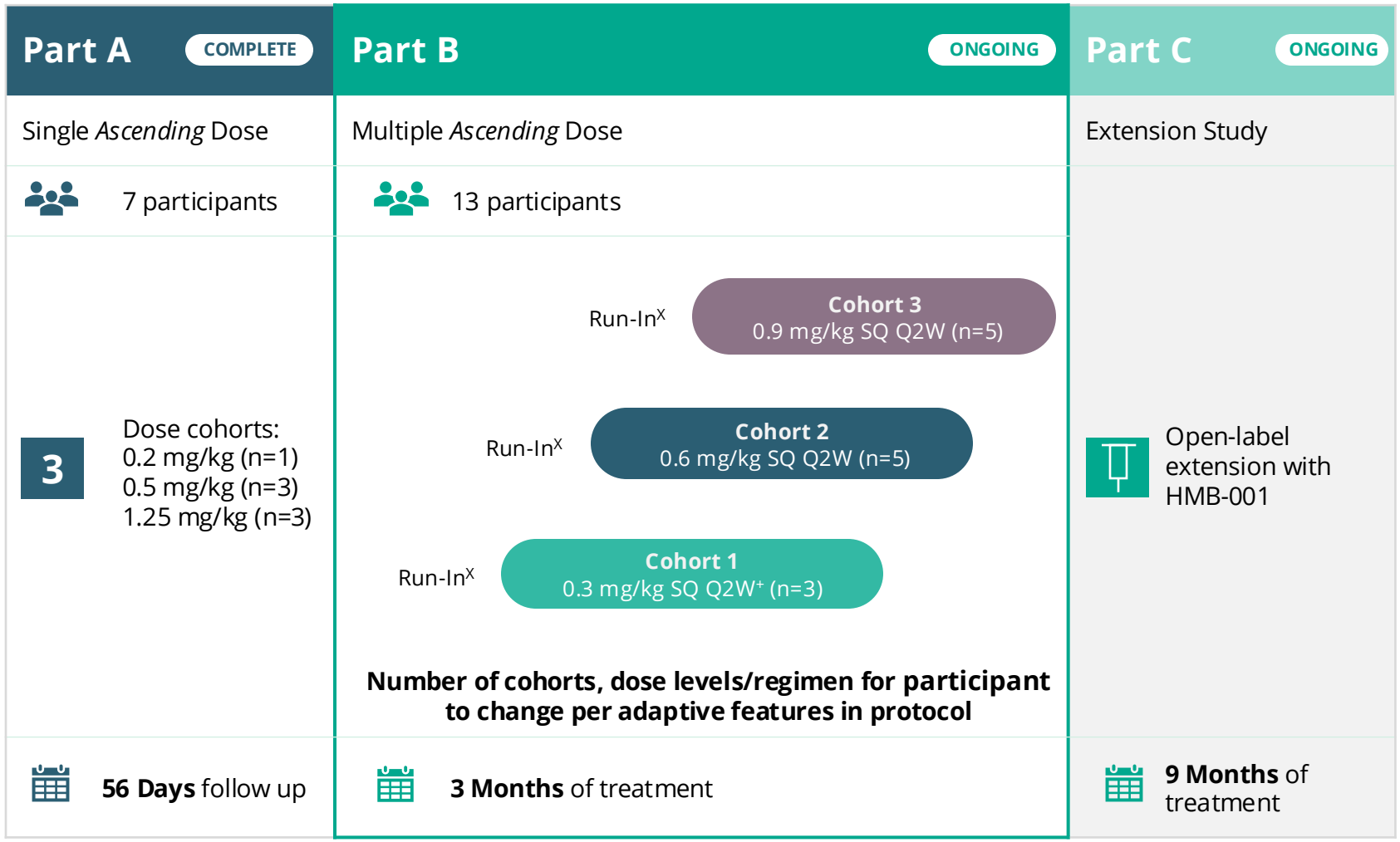
- Examine safety and tolerability of HMB-001
- Estimate prophylactic effect on frequency and severity of bleeds

Eligibility criteria

- Age 18–67 years
- Confirmed GT diagnosis
- ~2 bleeding events/week (any severity)
- ≥1 bleed in last 12 months requiring treatment or intervention
- Absence of concurrent thrombophilic disorder and history of clinically significant CVD

Breakthrough bleed management

- Individualized breakthrough bleed treatment plan includes anti-fibrinolytics, reduced dose (5-10 mcg/kg) rFVIIa and platelets



Abbreviations: CVD, cardiovascular disease; GT, Glanzmann thrombasthenia; rFVIIa, recombinant activated factor VII; Q2W, every two weeks; SQ, subcutaneous.
Study inclusion criteria: Genetic diagnosis of GT required for Phase 2 only. Full eligibility criteria available at ClinicalTrials.gov (NCT06211634). Interim data cutoff as of December 4, 2024.
[X]Comprehensive recording of bleeding incidents throughout the Run-In period (minimum 6 weeks) along with a 12-Month retrospective data compilation on bleeding events.

Phase 1/2 study of HMB-001 in GT: Demographics

Part A — COMPLETE	Part B — ONGOING
Single *Ascending* Dose	Multiple *Ascending* Doses
7 participants	**13** participants*
3 Dose cohorts (0.2, 0.5, & 1.25 mg/kg)	**3** Dose cohorts (0.3, 0.6, & 0.9 mg/kg Q2W)
56 Days follow up	**3 Month** treatment

Demographics		Part A (n=7)	Part B (n=13*)
Age	mean years (range)	38.9 (27-49)	41.9 (19-66)
Sex	Female	6 (86%)	7 (54%)
	Male	1 (14%)	6 (46%)
Race	Asian	6 (86%)	4 (31%)
	Black or African American	-	1 (8%)
	White	1 (14%)	4 (31%)
	Other	-	1 (8%)
	Not Reported	-	3 (22%)

Abbreviations: GT, Glanzmann thrombasthenia, Q2W, every two weeks.
*5 participants from Part A joining Part B. Interim data cutoff as of December 4, 2024; PK/PD results are based on the analysis of participants without detectable antidrug antibodies.

Phase 1/2 study of HMB-001 in GT: Safety

Summary

- Median cumulative exposure in Parts B and C is 3 months (range: 0.5-7; n=20)*. Participants in Part A received a single dose and followed 56 days
- **Overall TEAEs:** reported by 75% of participants; majority were mild or moderate and unrelated to study drug*
- **TEAEs (≥2 participants):** respiratory tract infection (10%), rhinitis (10%), headache (25%), back pain (10%), pain in extremity (10%)
- **Adverse Events of Special Interest (AESI):** Gum bleed managed by IV rFVIIa (5 mcg/kg) x1 for routine dental procedure
- **Severe AEs**: thrombocytopenia (130 × 10^9/L) and back pain. Unrelated to study drug
- **Related TEAEs**: D-dimer increase (1), injection site reaction (1), fatigue (1), headache (1), pruritic (1), rash pruritic (1), intestinal transit time increase (1), flatulence (1). All mild or moderate
- **SAE:**
  - Part A: Moderate iron deficiency anaemia, resolved (1). Unrelated to study drug.
  - Part B: None at 0.3 or 0.6 mg/kg Q2W
  - Part B: 0.9 mg/kg related DVT in participant with multiple potential risk factors, outpatient managed, recovering (1)[1]
- **No discontinuations due to AEs^ at 0.3 and 0.6mg/kg Q2W**

Immunogenicity

- ADAs: 3 of 13 participants developed ADAs. No safety or tolerability issues, appear transient in nature

Coagulation

- No clinically significant changes in fibrinogen and PT/APTT
- Transient change in platelet count over first 2 weeks
- D-dimer elevation in one participant with 0.9 mg/kg (DVT) dose on day of event, and in participants on 1.25 mg/kg dose level in Phase 1 (no thrombosis)

Abbreviations: ADA, Anti-drug Antibody; AE, Adverse Event; APTT, Activated Partial Thromboplastin Time; DVT, deep vein thrombosis; GT, Glanzmann thrombasthenia; IV, intravenous; PT, Prothrombin Time; Q2W, every two weeks; rFVIIa, recombinant activated factor VII; SAE, Serious Adverse Event; TEAE, Treatment-Emergent Adverse Event. *Interim data cutoff of December 4, 2024; includes 15 unique participants, with some transitioning from Part A to Part B. ^Adverse event grouping based on MedDRA-coded terms, excluding bleed events. [1]DVT SAE occurred post data cut.

Phase 1 study: Dose-dependent PK/PD and ATBR reduction with HMB-001

Part A COMPLETE

Single *Ascending* Dose

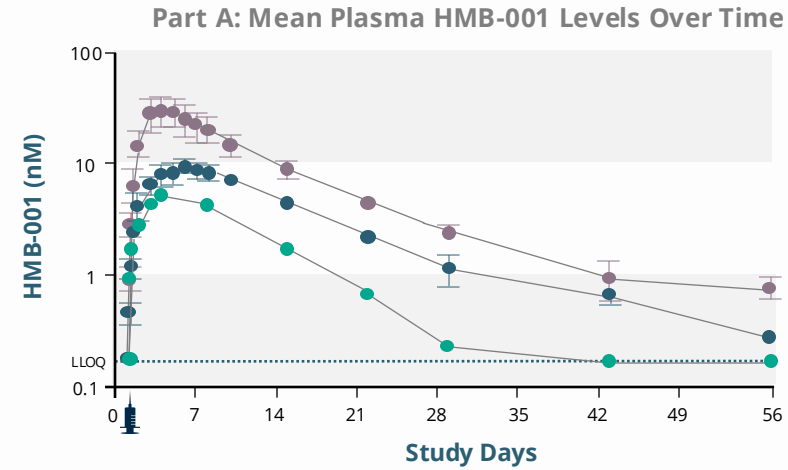
7 participants with GT

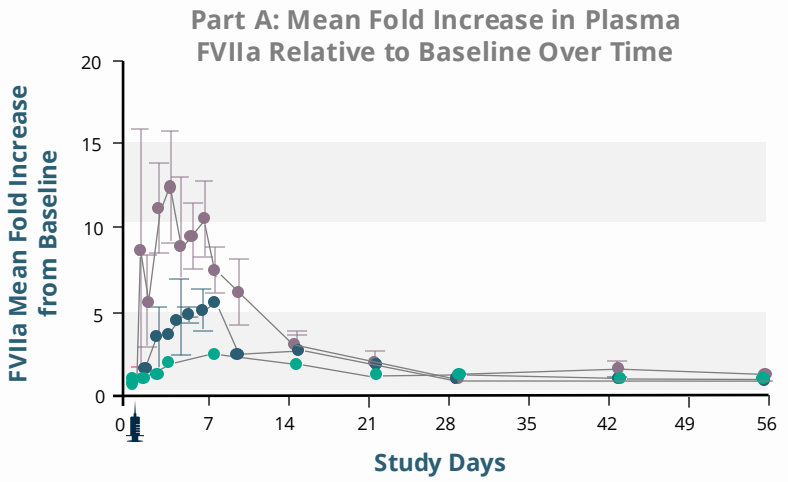
3 Dose cohorts (0.2, 0.5, & 1.25 mg/kg)

56 Days follow up

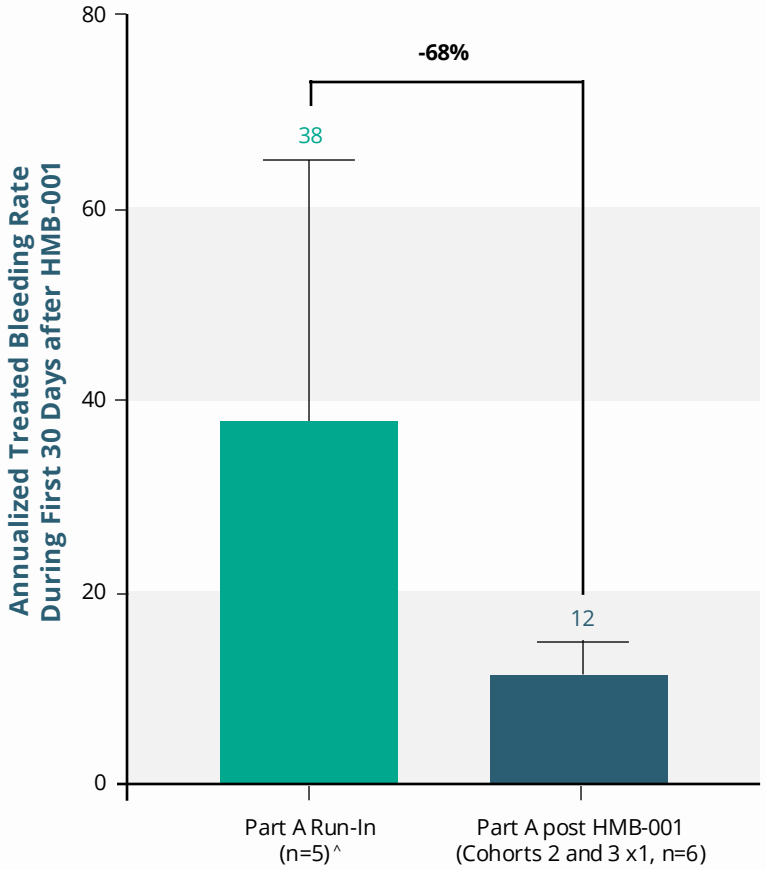
- **Cohort 1:** 0.2 mg/kg (n=1)
- **Cohort 2:** 0.5 mg/kg (n=3)
- **Cohort 3:** 1.25 mg/kg (n=3)
- **HMB-001 Dose**

Dose-dependent PK*/PD





68% Reduction in ATBR



Abbreviations: ATBR: Annualized Treated Bleed Rate; GT: Glanzmann thrombasthenia; PK: Pharmacokinetic; PD: Pharmacodynamic.
*PK data were re-analysed using a newly developed assay. ^One participant did not complete the run-in period.

Phase 2 study: Dose-dependent PK/PD after Q2W dosing with HMB-001

Part B ONGOING

Multiple *Ascending* Dose

13 participants with GT

3 Dose cohorts (0.3, 0.6, & 0.9 mg/kg)

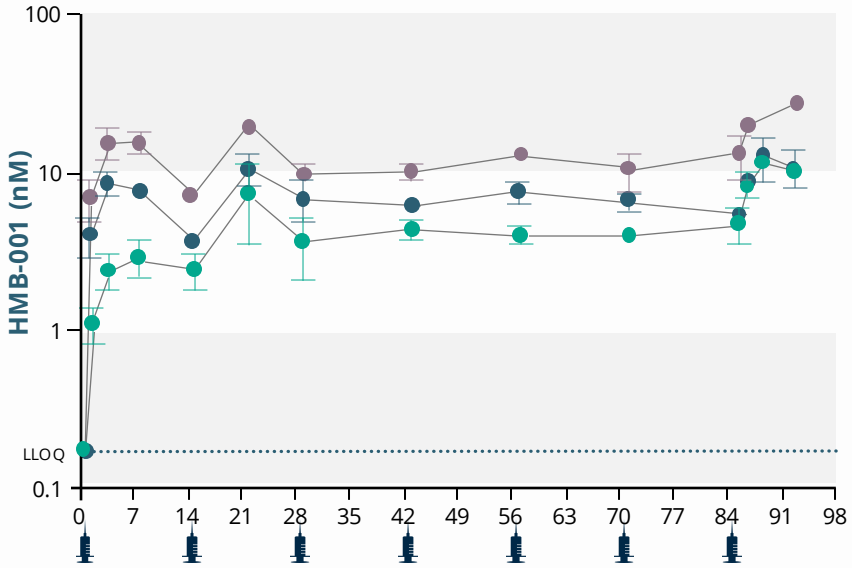
3 Month treatment

- **Cohort 1:** 0.3 mg/kg (n=2)
- **Cohort 2:** 0.6 mg/kg (n=3)
- **Cohort 3:** 0.9 mg/kg (n=5)
- **HMB-001 Dose**

HMB-001 exhibits dose-dependent PK and PD after Q2W dosing over a 3-month period.

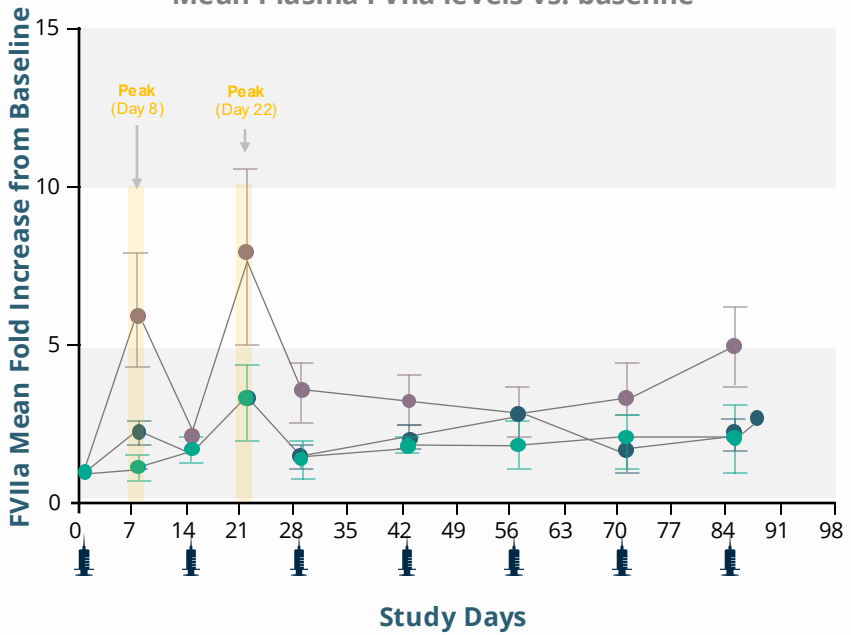
HMB-001 Exposure

Mean Plasma HMB-001



FVIIa

Mean Plasma FVIIa levels vs. baseline



Peak Factor VIIa levels (Day 8, Day 22): 0.9 mg/kg: 5–10-fold elevation & 0.3 mg/kg and 0.6 mg/kg: 2–4-fold elevation

Abbreviations: FVIIa: factor VIIa; GT: Glanzmann thrombasthenia; LLOQ: lower limit of quantification; PD: pharmacodynamic; PK: pharmacokinetic; Q2W: every two weeks; SEM: standard error of the mean. Dose Dependent PK/PD of HMB-001 in Cohorts B1, B2 and B3. Mean (with SEM) pharmacokinetic and pharmacodynamic response by cohort in ADA negative participants

Phase 2 study: Reduction in ATBR at all dose levels with HMB-001

Part B ONGOING

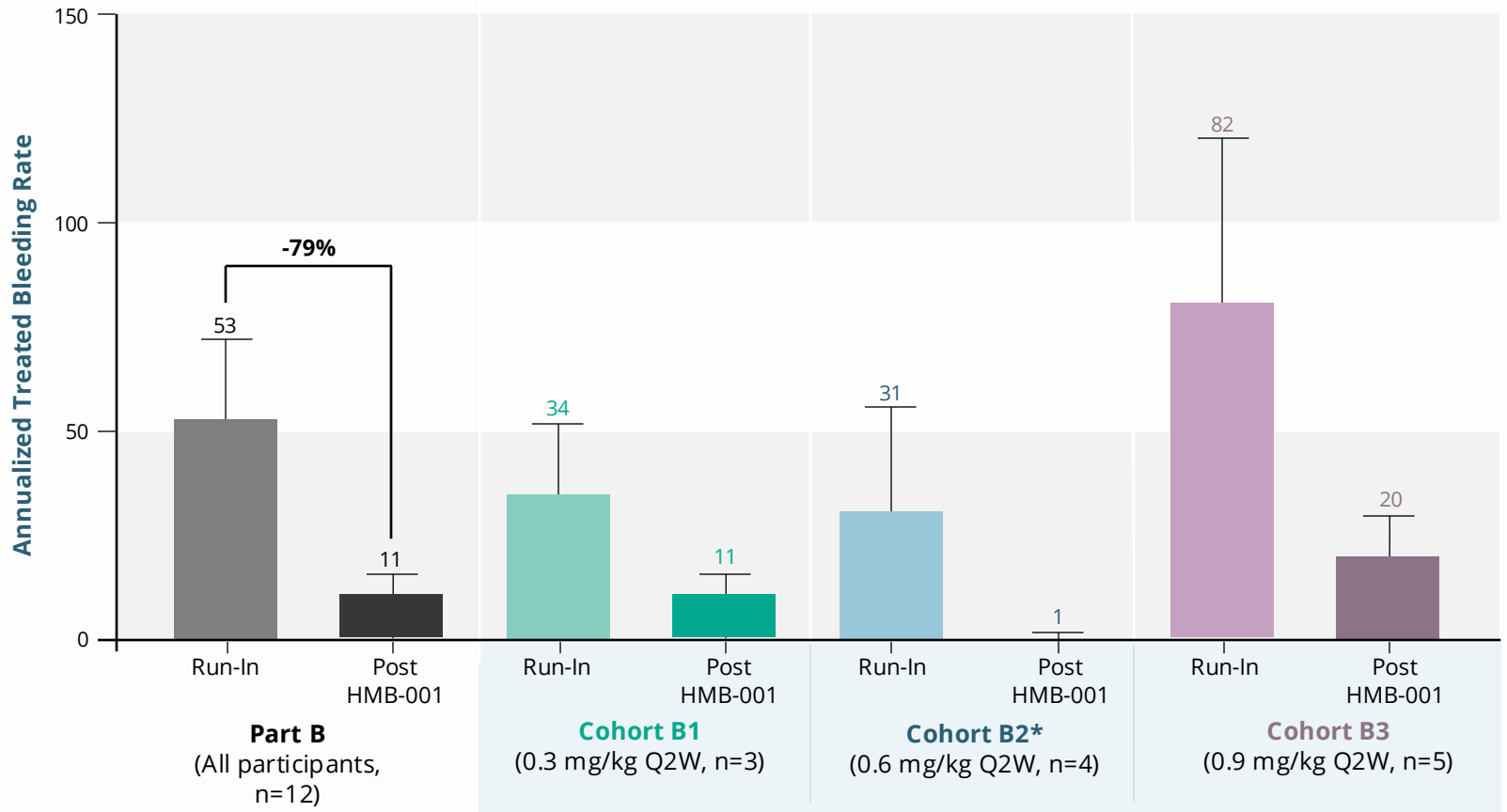
Multiple *Ascending* Dose

13 participants with GT

3 Dose cohorts (0.3, 0.6, & 0.9 mg/kg)

3 Month treatment

Group Mean Reduction of >50% in Treated Bleeds at all dose levels



Abbreviations: ATBR, annualized treated bleed rate; GT, Glanzmann thrombasthenia. Interim data cutoff as of December 1st 2024. The Efficacy Set includes all participants who received at least 1 dose of HMB-001 and passed through minimum of 28 days post-dose. ATBR reductions were calculated using an unpaired mean analysis comparing pre- and post-HMB-001 values. *1 Participant was excluded from bleed data analysis due to non-compliance with bleed diary guidelines

Transfusion independence in Glanzmann thrombasthenia from prophylaxis with HMB-001: Case presentation from Phase 2 study

Case Presentation

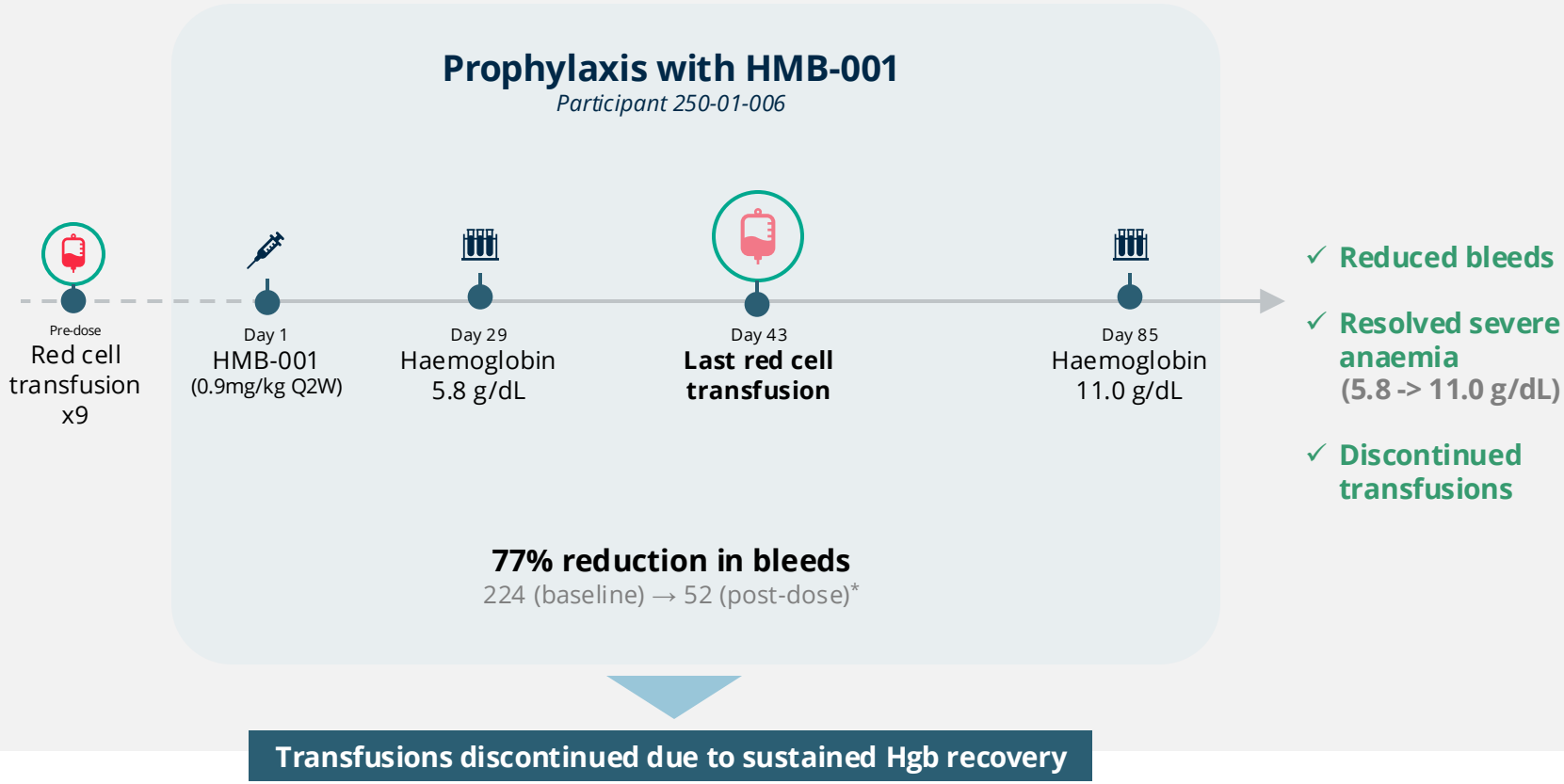
Participant

43-year-old male with GT. Persistent **GI bleeding** requiring red cell **transfusions every ~10 days.**

Past Medical History

Iron deficiency anaemia and sequalae (asthenia, pallor, dizziness, exertional dyspnoea, osteomalacia secondary to IV iron).

Antiplatelet alloimmunization.



Abbreviations: GI, Gastrointestinal; GT, Glanzmann thrombasthenia; Hgb, haemoglobin; IV, intravenous; Q2W: every two weeks
*Post-dose ATBR refers to the annualized treated bleed rate calculated from the 3 months post-dose

Conclusions

HMB-001 is a bispecific antibody targeting FVIIa and TLT-1 on activated platelets being studied in Glanzmann thrombasthenia

- Dose-proportionate PK and PD demonstrated with peak FVIIa accumulation at day 4-8 post dose in Part A and B.
- FVIIa accumulation in Q2W dosing regimen: <5X baseline at 0.3 and 0.6 mg/kg; >5x baseline at 0.9 mg/kg.
- D-dimer increase and one SAE (DVT) at 0.9 mg/kg, multiple potential risk factors, resolving with outpatient care.
- No thromboses, SAEs, discontinuations due to AE at 0.3 and 0.6 mg/kg.
- Clinically meaningful reduction in treated bleeds across all dose levels.

Next Steps

- The ongoing Phase 2 study will continue investigating 0.3 and 0.6 mg/kg to confirm safety and efficacy of HMB-001 as prophylaxis in people with GT.

Abbreviations: AE, adverse event; DVT, deep vein thrombosis; FVIIa, factor VIIa; PD, pharmacodynamic; PK, pharmacokinetic; Q2W, every two weeks; SAD, single ascending dose; SAE, serious adverse event; TLT-1, TREM-like transcript 1.

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Sponsor: Hemab Therapeutics

HMB-001:
Glanzmann thrombasthenia

Country	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
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