AMT-060 Gene Therapy in Adults with Severe or Moderate-Severe Hemophilia B Confirm Stable FIX Expression and Durable Reductions in Bleeding and Factor IX Consumption for up to 5 Years

Frank W.G. Leebeek, MD, PhD[1], Karina Meijer, MD, PhD[2], Michiel Coppens, MD, PhD[3], Peter Kampmann, MD[4], Robert Klamroth, MD[5], Roger Schutgens, MD, PhD, MSc[6], Giancarlo Castaman, MD[7], Erhard Seifried, MD, PhD[8], Joachim Schwaeble, MD[9], Halvard Bönig, MD[1],[10], Eileen K. Sawyer, PhD[11] and Wolfgang Miesbach, MD, PhD[12]

[1]Erasmus University Medical Center, Rotterdam, Netherlands; [2]University Medical Center Groningen, Groningen, Netherlands; [3]Amsterdam University Medical Center, Amsterdam, Netherlands; [4]Rigshospitalet, Copenhagen, Denmark; [5]Vivantes Klinikum, Berlin, Germany; [6]Van Creveldkliniek, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands; [7]Azienda Ospedaliera Universitaria Careggi, Florence, Italy; [8]Institute Frankfurt, German Red Cross Blood Service Baden Wurttemberg-Hessen, Frankfurt, Germany; [9]Institute Frankfurt, German Red Cross Blood Service Baden Wurttemberg-Hessen, Frankfurt, Germany; [10]University of Washington, Seattle, WA; [11]uniQure Inc., Lexington, MA; [12]University Hospital Frankfurt, Frankfurt, Germany.

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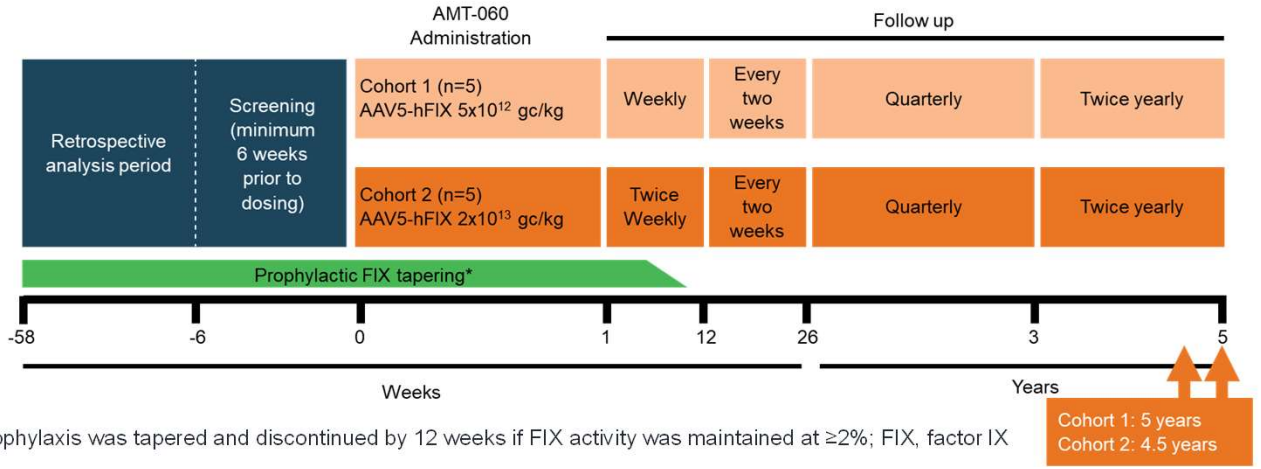
Study Design and Participants

- Multi-national, open-label, dose-escalating study (NCT02396342)
- 10 adult males with severe or moderate-severe hemophilia B were included.
  - 9 patients had severe hemophilia and 1 patient had moderate-severe hemophilia
  - Median age (range) of patients in cohort 1 and cohort 2 was 69 years (35-72) and 35 years (33-46), respectively
  - 3 patients in cohort 1 retrospectively discovered to have pre-existing anti-AAV5 NAb prior to dosing
- AMT-060 phase I/II study results up to 4 years have been previously reported.[1-3]
  - Here, an additional year of follow up is reported

Phase I/II study design



*Prophylaxis was tapered and discontinued by 12 weeks if FIX activity was maintained at ≥2%; FIX, factor IX

1. Miesbach W, Meijer K, Coppens M, et al. Blood. 2018;131(9):1022–1031. 2. Miesbach W, et al. Blood. 2019;134 (Supplement_1):2059–2059 3.Leebeek FWG, et al. Blood. 2016;128(22):2314–2314.

No new treatment related adverse events over the last 12 months of follow up

Previously reported TRAEs

TRAE	n (E) Cohort 1 (N=5)	n (E) Cohort 2 (N=5)
Any TRAE	**4 (5)**	**3 (10)**
Liver enzyme increased	1 (1)	2 (3[a])
Pyrexia	1 (1)	2 (2)
Anxiety	1 (1)	1 (1)
Drug ineffective	1 (1)	0
Joint swelling*	1 (1)	0
Palpitations	0	1 (1)
Headache	0	1 (1)
Prostatitis	0	1 (1)
Rash	0	1 (1)

TRAE, treatment emergent adverse event reported as possibly/probably related to treatment by the investigator; FIX, factor IX; n, Number of participants with events; (E), number of events; [a]2 events reported in the same participant
*This TRAE occurred in year 4 post-AMT-060

Serious AE (all within first 3.5 months)[1]

- 1 participant: short, self-limiting fever in first 24 hours post-AMT-060
- 2 participants (1 in Cohort 1, 1 in Cohort 2): mild, asymptomatic elevations in liver enzymes

Overall

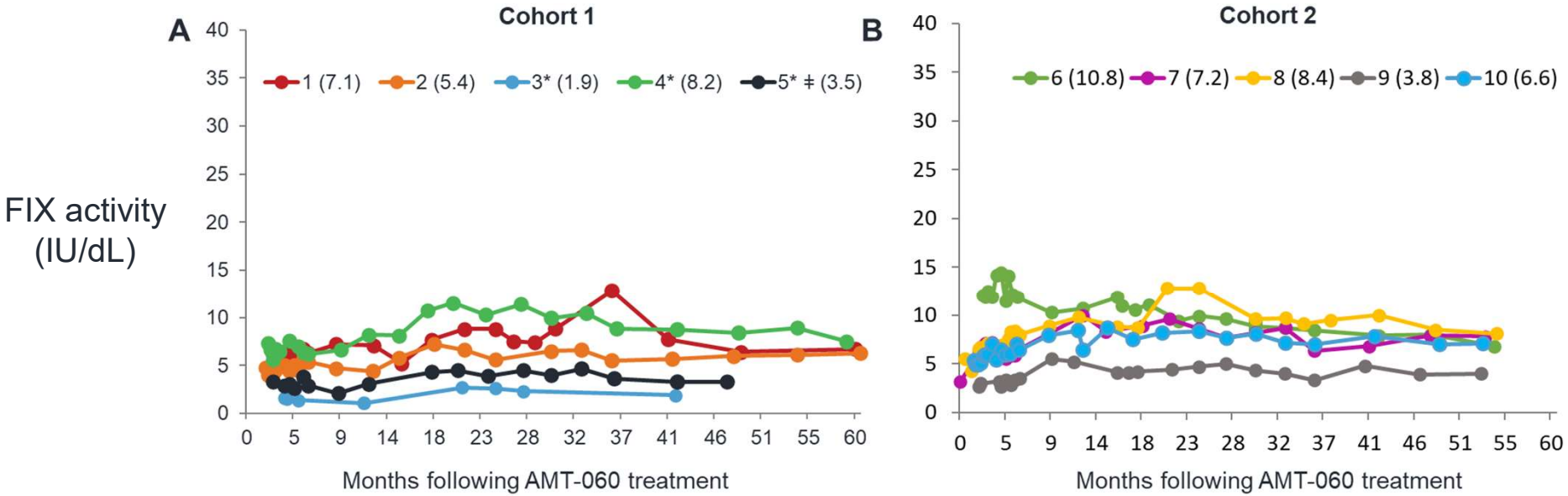
- **No new TRAE observed during the last 12 months of observation post-treatment**
- No participants developed FIX inhibitors

1. Miesbach W, Meijer K, Coppens M, et al. Blood. 2018;131(9):1022–1031.

Multi-year durable and stable increases in FIX activity

- Following AMT-060, mean endogenous FIX activity:
  - 5.2% (95% CI 2.0 - 8.4) during 5 years of follow-up in the lower-dose cohort (**Panel A**) (Cohort 1)
  - 7.4% (95% CI 4.2 - 10.6) during 4.5 years in the higher dose cohort (**Panel B**) (Cohort 2)
- **Stable FIX activity over 4.5-5 years post-dosing across both cohorts**

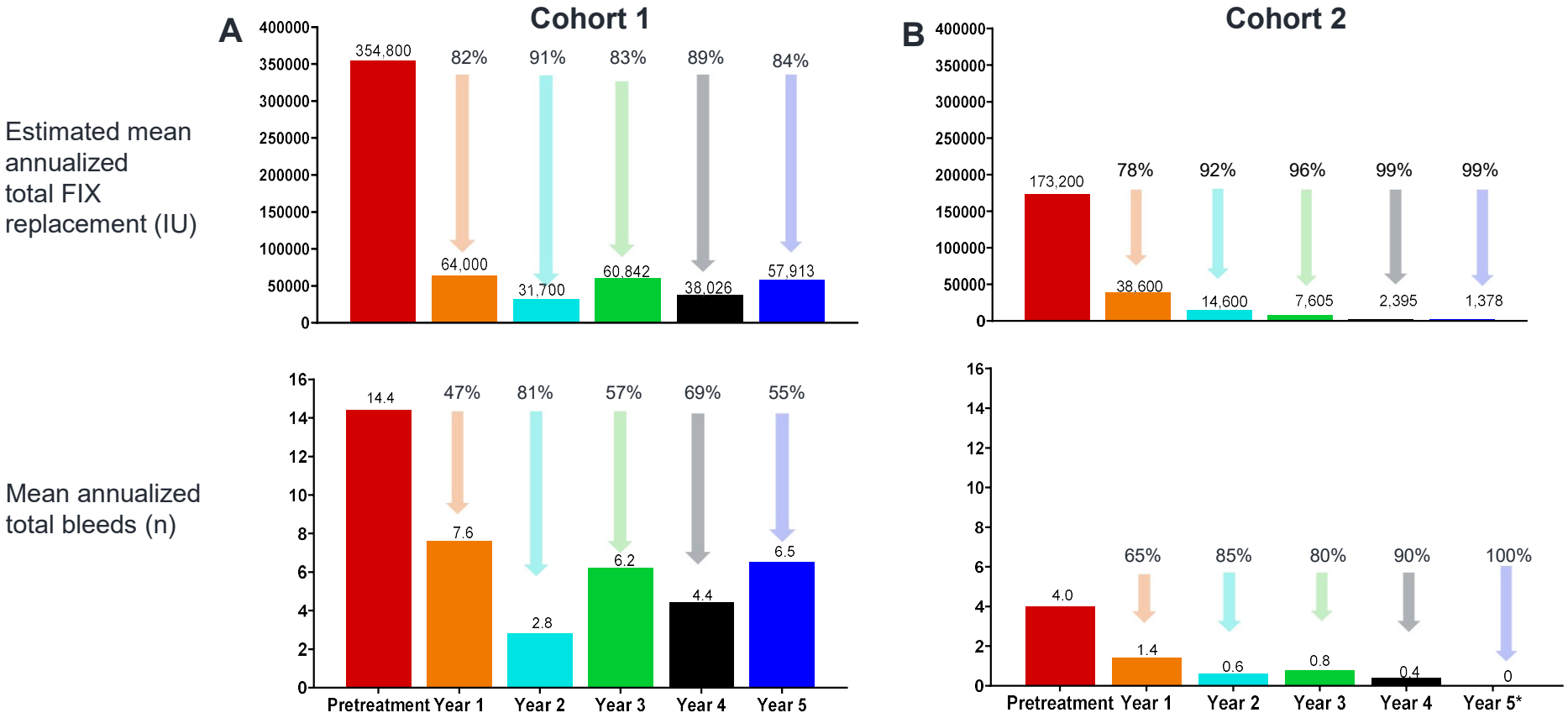
Sustained dose-dependent increases in FIX activity



Values in parentheses represent mean FIX activity over time. Only values at least 10 days after last FIX concentrate administration are included. FIX prophylaxis was continued after AMT-060 and tapered between Weeks 6 and 12. *Patients 3, 4 and 5 retrospectively tested positive for AAV5 neutralizing antibodies using the luciferase-based assay. ǂPatient 5 was unable to attend 4.5yr follow-up visit due to COVID-19 and 5yr follow-up blood sample was obtained within 10 days of exogenous FIX use for bleed and therefore excluded per protocol; FIX, factor IX; CI, confidence interval; IU, international units.

Sustained reductions in bleeds and estimated FIX use

- Cohort 1: By year 5, FIX use was reduced relative to pre-AMT-060 up to 84% and bleeds by up to 55% (**Panel A**)
- Cohort 2: By year 4.5, FIX use and bleeds were both reduced relative to pre-AMT-060 by ~100% (**Panel B**)



*Prophylaxis was tapered and discontinued by 12 weeks if FIX activity was maintained at ≥2%; * Cohort 2 data for year 5 represents 6 months. FIX, factor IX

Conclusions

- FIX increases were **sustained and durable** up to 5 years in all participants
  - Corresponding clinical benefit (freedom from prophylaxis, reduction in bleeds & FIX use) also sustained multi-year
- The **long-term safety profile of AMT-060 remains positive** with no late-emergent adverse events
- This represents the **second longest follow up** reported in a successful gene therapy trial in hemophilia B
- Data support the ongoing Phase 3 HOPE-B study (NCT03569891) of the enhanced construct etranacogene dezaparvovec (AMT-061), which encodes the highly active Padua FIX variant
  - Data to be presented on Tuesday, December 8, 2020 at 8:45 AM [4]

[4] Pipe S, et al. ASH 2020: Late Breaker Abstract