Long-term safety and efficacy of etranacogene dezaparvovec in haemophilia B (IX-TEND-3003 study)

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Introduction

- Etranacogene dezaparvovec (CSL222; HEMGENIX®) is an adeno-associated virus type 5 vector delivering the highly active factor IX (FIX) Padua transgene[1–3]
- In adult males with severe or moderately severe haemophilia B, a single dose of etranacogene dezaparvovec demonstrated a significant reduction in bleeding and stable FIX activity levels in the near-normal range in a phase 2b trial (NCT03489291) and the pivotal phase 3 HOPE-B trial (NCT03569891), accompanied by a favourable safety profile[1–3]
  - Long-term efficacy and tolerability data have been reported for up to 5 years post-infusion in the phase 2b trial[4] and up to 4 years post-infusion in the phase 3 pivotal HOPE-B trial[5–7]
- Longer term follow-up of gene therapy is a post-marketing requirement from regulatory agencies and is needed to substantiate the long-term safety and efficacy of gene therapy for haemophilia[8]
- The international IX-TEND-3003 extension study (NCT05962398) will assess the long-term safety and efficacy of etranacogene dezaparvovec previously administered to adult males with haemophilia B who participated in the phase 2b and phase 3 clinical trials

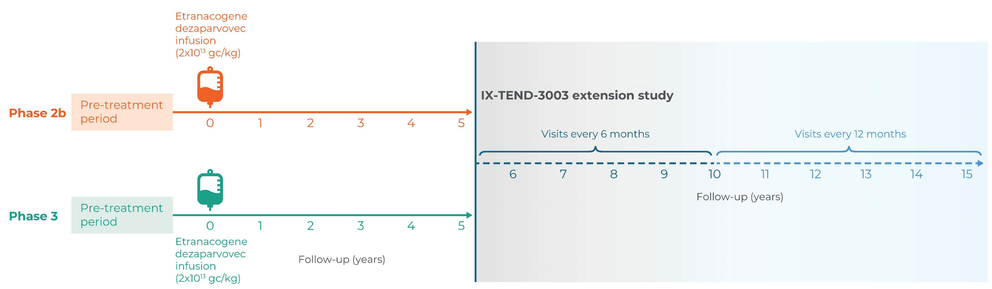
Objective

- **The primary objective of this extension study is to assess the long-term safety of etranacogene dezaparvovec in adult male participants with severe or moderately severe haemophilia B who initially entered the phase 2b and phase 3 HOPE-B studies**

Methods

- In order to be eligible to enter the extension study, participants needed to have received treatment with etranacogene dezaparvovec in the phase 2b or phase 3 trials, and have completed at least 5 years of follow up post-infusion (**Figure 1**)
- After providing consent, participants will be monitored for long-term safety and efficacy until 15 years post-infusion with etranacogene dezaparvovec in either parent trial
- Participants will visit the clinic every 6 months (Years 5 to 10 post-infusion) and then annually (Years 11 to 15 post-infusion) (**Figure 1**)
- The duration of the IX-TEND-3003 study for each participant is 10 years and currently up to 55 participants of the parent trials are eligible for enrolment
- Primary and secondary endpoints are summarised in **Table 1** and **Table 2**
- The protocol was approved by all applicable competent health authorities and institutional review boards/ethics committees
- An identified risk to the success of IX-TEND-3003 was participant interest in enrolling as well as ability to retain participants in a clinical trial for an additional 10 years; consequently, several recruitment and retention approaches will be implemented to mitigate the loss to follow-up (**Figure 2**)

Figure 1. Overview of the phase 2b and phase 3 studies and the IX-TEND-3003 extension study



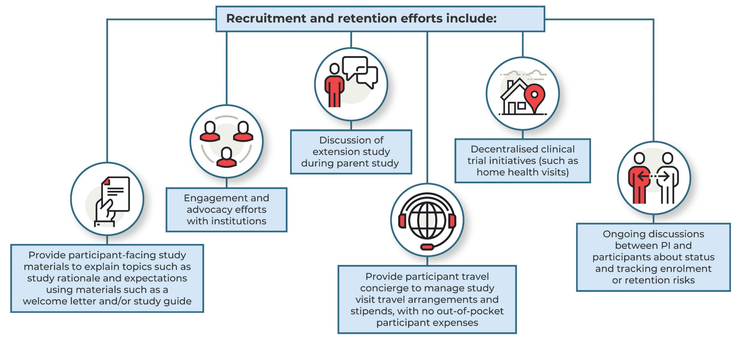
gc, genome copies.

Table 1. Primary endpoints

Endpoints (safety)	
SAEs and AESIs*	Adverse events considered to be of special interest in this study were hepatotoxicity, new malignancy, thromboembolic events, development of FIX inhibitors, and AEs related to mandatory concomitant medication (such as immunosuppression); additionally, pregnancies of partners will be followed

AESIs, adverse events of special interest; FIX, factor IX; SAEs, serious adverse events.
*Number and percentage of participants, and number of events.

Figure 2. Recruitment and retention approaches for IX-TEND-3003



PI, principal investigator.

Table 2. Secondary endpoints

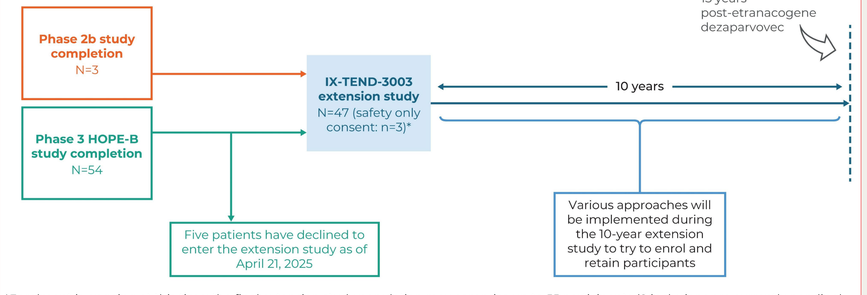
Endpoints
Key secondary efficacy endpoints
Annualised bleeding rate (all bleeds)
Endogenous FIX activity
Other secondary efficacy endpoints
Annualised spontaneous bleeding rate
Annualised joint bleeding rate
Annualised traumatic bleeding rate
Annualised consumption of FIX replacement therapy
Annualised infusion rate of FIX replacement therapy
Participants remaining free of continuous FIX prophylaxis
Occurrence of new target joints and resolution of pre-existing target joints
Patient-reported outcomes
EQ-5D-5L VAS and index scores and Haem-A-QoL total score

EQ-5D-5L VAS; 5-level EuroQol-5-Dimension visual analogue scale; FIX, factor IX; Haem-A-QoL; Haemophilia Quality of Life Questionnaire for Adults.

Results

- The first participant enrolled on August 30, 2023, and the first interim analysis is planned for 3 years past this date (August 2026); the final clinical study report is expected in 2035
- As of April 21, 2025, 3 and 44 participants from the phase 2b and phase 3 studies, respectively, have been enrolled into the IX-TEND-3003 study
  - Of the 47 participants enrolled, 44 gave consent for inclusion in all extension study analyses and 3 participants gave consent for inclusion in safety analyses only (**Figure 3**)
- An additional long-term real-world study is ongoing for post-marketing follow-up purposes (Phase 4 IX-TEND-4001; NCT06008938)[9]

Figure 3. IX-TEND-3003 study enrolment and retention



*Enrolment is ongoing at this time; the final extension study population may comprise up to 55 participants (8 inclusions are currently pending).

Summary

- **To date, IX-TEND-3003 has recruited 47 participants in total and the first interim analysis will be performed in August 2026**
- **IX-TEND-3003 is planned to be completed in 2035**
- **A proactive approach is being taken to retain participants in the IX-TEND-3003 trial, including anticipation of and addressing barriers to patient retention in this long-term follow-up study**
- **A real-world study (IX-TEND-4001) will provide additional long-term post-marketing data in participants with haemophilia B who have received HEMGENIX®**

References

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Disclosures

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