2. SYNOPSIS

<table>
<tr><td>Name of Sponsor/Company:
Freeline Therapeutics</td><td rowspan="3">Individual Study Table Referring to Part of the Dossier
Volume:
Page:</td><td rowspan="3">(For National Authority Use Only)</td></tr>
<tr><td>Name of Finished Product:
FLT180a</td></tr>
<tr><td>Name of Active Ingredient:
FLT180a</td></tr>
<tr><td colspan="3">Protocol Title: An Open-label, Multicenter Long-term Follow-up Study to Investigate the Safety and Durability of Response Following Dosing of a Novel Adeno-associated Viral Vector (FLT180a) in Patients with Hemophilia B</td></tr>
<tr><td colspan="3">Protocol Number: FLT180a-04</td></tr>
<tr><td colspan="3">Regulatory References: EudraCT number: 2017-005080-40, ClinicalTrials.gov identification number: NCT03641703</td></tr>
<tr><td colspan="2">Development Phase: Long-term follow-up for a Phase 1/2 trial</td><td>Indication: Hemophilia B</td></tr>
<tr><td colspan="3">Coordinating Investigator: [redacted]The Katharine Dormandy Haemophilia Centre, Royal Free Hospital, Pond Street, London, NW3 2QG, UK</td></tr>
<tr><td colspan="3">Study Sites: Participants were enrolled (treated) at six sites within the UK.</td></tr>
<tr><td colspan="3">Test Product, Dose, Mode of Administration, and Batch/Lot Numbers: Not applicable; administration of FLT180a occurred in an earlier trial (15/0552), prior to enrolment in this long-term follow-up trial.</td></tr>
<tr><td colspan="3">Study Period: First participant screened: 10 July 2018. Last visit of the last participant: 15 June 2023.</td></tr>
<tr><td colspan="3">Study Rationale: This trial aimed to investigate the long-term safety and durability of the effect of FLT180a, which was administered in the previous clinical trial (15/0552).</td></tr>
<tr><td colspan="3">Study Design: This was an open-label, multicenter, long-term follow-up trial of participants with hemophilia B who received FLT180a in an earlier Phase 1/2 trial (15/0552). Participants were asked to provide consent for the long-term follow-up prior to completion of the preceding trial and, providing consent was obtained, subsequently rolled over into this extension protocol immediately upon conclusion of the preceding trial. Data on safety, durability of factor IX (FIX) response, and general health status were to be collected up to 5 years post-dose. Participants were to attend follow-up visits monthly to 24 months, then every 6 months to Year 3, and then annually at the Year 4 and Year 5 visits.
The trial was terminated by the Sponsor on 15 June 2023 due to commercial reasons. As a result, participant follow-up was terminated, and the database was locked on 05 July 2023. Participants duration of follow-up in the trial ranged between 36 and 65 months post-dose. Data included in this addendum are from the previous dosing trial (15/0552) and the long-term follow-up trial (FLT180a-04).</td></tr>
<tr><td colspan="3">Number of Participants: Planned: 10. Enrolled: 10. Analyzed: 10.</td></tr>
</table>

Participant Population: Participants with severe or moderately severe hemophilia B who were dosed in the previous dosing trial (15/0552).

Statistical Methods: For the analyses, unless otherwise stated, baseline data refers to data collected prior to FLT180a dosing from the preceding dosing trial (15/0552), and post-dose refers to data collected post-FLT180a dosing from both the preceding dosing trial (15/0552) and this long-term follow-up trial (FLT180a-04).

Summary of Results:

Disposition

- One (10.0%) participant withdrew from further trial participation and 9 (90.0%) participants were discontinued due to Sponsor termination of the trial. Participants completed between 3 and 5.4 years of follow-up.

Efficacy

- All participants continued to show FIX activity during the trial, post-FLT180a administration, with FIX activity levels remaining stable over time (model-estimated zero rate of change after 12 months across all dose groups).

Safety

- Overall, there were no deaths or adverse events (AEs) that led to trial discontinuation.
- All 10 (100.0%) participants experienced at least 1 AE post-dose, the majority of which occurred <1 year post-dose. The most commonly reported AEs in the trials were diarrhoea, arthralgia, alanine aminotransferase increased (70.0% each), and headache (60.0%).
- Eight (80.0%) participants had at least 1 adverse reaction (AR), all of which occurred <1 year post-dose. An AR of alanine aminotransferase increased occurred during FLT180a-04 in a participant who received 8.32×10^{11} vector genome (vg)/kg FLT180a, while all other ARs occurred during the preceding dosing trial.
- Seven (70.0%) participants had at least 1 serious adverse event (SAE) and at least 1 serious adverse reaction (SAR) post-dose, the majority of which occurred <1 year post-dose and during the preceding dosing trial. During FLT180a-04, there were 2 SAEs of appendicitis (Grade 3) and arteriovenous fistula thrombosis (Grade 2) in participants who received 6.4×10^{11} vg/kg and 1.28×10^{12} vg/kg FLT180a, respectively; neither event was assessed as being related to FLT180a.
- During FLT180a-04, there were no SAEs associated with laboratory abnormalities or laboratory abnormalities graded as severe in the trial and few participants had clinically significant results upon physical examination, liver function tests, and liver ultrasound.
- All participants achieved levels of vector in plasma, stool, semen, saliva, and urine samples reported as 0 (or less than the lower limit of quantification) in the 15/0552 or FLT180a-04 trials.

Conclusions:

Efficacy Conclusions

- All participants showed a FIX activity response during this trial, post-FLT180a administration.

Safety Conclusions

- FLT180a was well-tolerated. There were 2 SAEs (unrelated to FLT180a administration) reported during the trial. There were no deaths or AEs leading to trial discontinuation.

Publication References: None.

Report Addendum Version & Date: Final v1.0 15 May 2024