METHODS

- Adult males with severe or moderately-severe hemophilia B
  - We examined the presence of vector DNA in participants from a Phase 1/2 study of an AAV5-hFIX wildtype construct (AMT-060; NCT02396342) and a Phase 2b study utilizing the enhanced version, AAV5-hFIX Padua (etrnanacogene dezaparvovec; AMT-061; NCT03489291). 1,2
  - Assessments in both trials included efficacy and safety measurements. In the AMT-060 trial, vector clearance was also measured in whole blood and semen, nasal secretions, feces, urine, and saliva.
  - Theoretical limits of detection (LOD) were <400 copies per mL (blood, semen, saliva), <571 copies/mL or copies per swab (whole blood, urine, nasal swab) and circa 1 copy per mg (feces).
  - Vector clearance was confirmed by finding of vector DNA either zero or below the LOD for three consecutive measurements.

RESULTS

- AMT-060 resulted in sustained improvement in FIX activity for up to 3.5 years (mean FIX activity was 5.1% [low dose group at 3.5 years] and 7.5% [high dose group at 3 years]) and treatment with etranacogene dezaparvovec resulted in mean FIX activity of 45% over 36 weeks (see poster 2059).
  - Both AAV5-hFIX and AAV5-hFIX Padua were safe and well tolerated; no unexpected treatment-related adverse events (TRAEE) have been observed with longer-term follow up.
  - Table 1 describes the time in weeks to the first and last of three consecutive measures of vector DNA of either zero or <LOD for all bodily fluids for AMT-060 and etranacogene dezaparvovec.
  - AMT-060 at the higher dose was cleared from semen, feces, urine, nasal secretions and saliva in all participants by week 78 (range 7–78 weeks).
    - In blood, the lower dose of AMT-060 was cleared in all participants by 3 years (range 1.0-3.0 years).
    - The higher AMT-060 dose was cleared from the blood in all participants by 3.7 years (range 1.8–3.7 years).
    - With etranacogene dezaparvovec, vector DNA was <LOD in blood in 2 participants by weeks 31–48 and in semen by week 26 in 2 of 3 (Table 1).
    - Three consecutive <LOD values achieved by week 40 by participant 2 (blood) and by week 52 in participant 1 (semen).
    - Participants 1 and 3 achieved <lower limit of quantification (LOQ) values in blood by weeks 31-36, however, <LOQ measurements were not considered to be negative.
    - Participant 3 only had semen samples up to week 12.
  - The presence of vector DNA in bodily fluids assessed was not associated with any adverse safety or efficacy findings.

CONCLUSION

- Post-AMT-060 treatment, vector DNA in the high dose group was cleared by 18 months in all bodily fluids except blood.
- AMT-060 was cleared from the blood in 100% of participants in the low dose group at 3 years and in all participants in the high dose group by 3.7 years.
- Etranacogene dezaparvovec vector DNA was cleared from the blood in 1 participant by week 40, and was low but detectable (<LOD) in the other 2.
- Etranacogene dezaparvovec vector DNA was cleared in the semen of 1 participant by week 52 and tested <LOD on 2 consecutive tests in a second participant.
- The presence of vector DNA in bodily fluids assessed was not associated with any adverse safety or efficacy findings.

REFERENCES