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AMT-061 (AAV5-Padua hFIX variant) an Enhanced Vector for Gene Transfer in Adults with Severe or Moderate-Severe Hemophilia B: Follow-up up to 9 Months in a Phase 2b trial

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Abstract

Objective: Gene therapy for hemophilia offers the potential for sustained-disease amelioration with a single treatment. AMT-061 is an investigational gene therapy for hemophilia B comprised of an adeno-associated virus serotype 5 (AAV5) vector containing a codon-optimized Padua variant human factor IX (FIX) gene with liver-specific promoter. The aim of the study was to confirm that a single dose of AMT-061 will provide a minimum-therapeutic response of FIX activity 6-weeks post-dose in participants with severe or moderate-severe hemophilia B. Methods: Phase 2b, open-label, multi-center trial (NCT03489291) in adult males requiring FIX prophylaxis and without active hepatitis or uncontrolled HIV. Participants were not excluded based on neutralizing antibodies to AAV5. Participants received a single intravenous dose of AMT-061 (2x1013 gc/kg) and will be followed for 5-years. The primary endpoint was FIX activity at Week 6. Secondary endpoints include e-diary recordings of bleeds and FIX concentrate use, laboratory parameters, joint health, patient-reported outcomes, and adverse events (AEs). Summary: All participants had FIX <1% (severe FIX deficiency) and had neutralizing activity to AAV5 at baseline. Following AMT-061 treatment, FIX activity increased rapidly (Figure) to a mean of 31% at Week 6 and increased further to a mean of 47% at Week 26. At Week 26, FIX activity was 51%, 33%, and 57% in participants 1-3, respectively. There were no bleeds post-treatment and no requirement for FIX replacement. No clinically significant liver enzyme elevations above upper limit of normal were observed after dosing in any participant. One participant experienced 2 mild AEs possibly related to treatment (self-limiting headache and slightly elevated CRP). Updated results to 39 weeks of follow-up will be presented. Conclusions: Sustained therapeutic responses of FIX activity were observed 26-weeks after treatment with AMT-061. AMT-061 was well-tolerated with no requirement for immunosuppression. These data support the ongoing Phase 3 study.