A Single Infusion of AMT-061 (AAV5-Padua hFIX) Is Safe and Effective in Adults with Hemophilia B: Interim Results from Dose-Confirmation Phase 2b Trial

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INTRODUCTION

Gene transfer for severe hemophilia B can shift the disease phenotype to moderate (Factor IX [FIX] ≥40%) or normal (FIX >40%)1,2 and significantly reduce or abrogate bleed risk3,4.

AMT-060 (adenosine-associated virus 5 [AAV5]) wildtype [wt] human FIX has demonstrated efficacy and safety in an ongoing Phase 1/2 trial in hemophilia B (CT-AMT-060-01)-1,5

AMT-061 (AAV5-Padua hFIX) is expected to result in the naturally occurring highly active change into the transgene coding sequence of AMT-060, resulting in the FIX activity with AMT-061 (AAV5-Padua hFIX): Changes to the vector-transgene construct result in improvements in FIX activity

METHODS

Trial design: Phase 2b, open-label, single-dose, single-arm, multi-center trial (NCT03489291)-5

Single intravenous administration 2x10^11 gc/kg of AMT-061

Study participants:

Three adult hemophilia B participants with FIX activity ≤22%.

Controlled HIV, cleared hepatitis B/C, and no FIX inhibitors.

Pre-existing neutralizing antibodies (NABs) to AAV5 were evaluated but were not an exclusion criteria

Outcomes:

Primary efficacy was assessed by FIX activity at 6 weeks (central one-stage clotting assay).

Historical bleeds and FIX use were assessed from medical records.

From screening participants recorded bleeds and FIX use in their e-diary.

52 week follow-up to assess FIX activity, bleeding rates and FIX replacement, and safety will be monitored for five years.

This poster includes 26-week data from an interim analysis

RESULTS

AMT-061 (AAV5-Padua hFIX): Changes to the vector-transgene construct result in improvements in FIX activity

Baseline demographics:

Baseline demographics are shown in Table 1 (Table 1) Notably, all 3 had low titers of NABs to AAV5 at baseline.

Table 1. AMT-061 baseline demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Participant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1 2 3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>83 81 52</td>
</tr>
<tr>
<td>HIV Status</td>
<td>Negative</td>
</tr>
<tr>
<td>Hap B / Hap C</td>
<td>Hap C, Hap C, Hap C</td>
</tr>
<tr>
<td>Hemophilia B status</td>
<td>FIX 7%</td>
</tr>
<tr>
<td>Pre-screening FIX treatment</td>
<td>Prophylactic Prophylactic Prophylactic</td>
</tr>
<tr>
<td>Amnual bleeding rate 1-year prior to screening</td>
<td>3 1 5</td>
</tr>
<tr>
<td>Neutralizing antibody activity (AAV9)</td>
<td>Positive (1.48) Positive (1.44) Positive (1.25)</td>
</tr>
<tr>
<td>Liver function test</td>
<td>1 spontaneous (moderate) 0 0</td>
</tr>
</tbody>
</table>

AAV9-adenosine-associated virus, Factor IX, Hap B, Hap C, hepatitis B/C, human adenovirus-associated virus. Participants 2 & 3 were excluded from another AMT-based gene therapy trial for hemophilia B based on neutralizing antibody activity.

Mean FIX activity over 2 years was 7.4 IU/dL with AMT-060.

Liver-specific safety:

No clinically significant ALT elevations above upper limit of normal after dosing:

Participant 1 had an isolated, slight elevation in ALT at week 22 (44 UL), which resolved without intervention or loss of efficacy.

1 participant experienced two isolated elevations above the upper limit of normal in aspartate aminotransferase (AST):

43 UL (week 2) and 48 UL (week 4)

Resolved quickly without treatment or impact on FIX activity.

No participants required immunosuppression

CONCLUSION

AMT-061 resulted in increased FIX activity, with mean FIX of 47.1% at 26 weeks:

2 of 3 participants had FIX activity in the non- hemophiliac range.

AMT-061 was safe and well-tolerated, with no serious AEs.

Based on these favorable results, the efficacy and safety of AMT-061 will be further characterized in the pivotal HOPE-B study.

Figure 2. FIX activity post-AMT-061 treatment

<table>
<thead>
<tr>
<th>Bleeds</th>
<th>Participant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-AMT-061</td>
<td>Post-AMT-061</td>
</tr>
<tr>
<td>1</td>
<td>3 spontaneous (moderate) 0</td>
</tr>
<tr>
<td>1</td>
<td>1 spontaneous (mild) 0</td>
</tr>
<tr>
<td>1</td>
<td>6 spontaneous* (moderate [n=2] and mild [n=4])</td>
</tr>
</tbody>
</table>

Table includes all bleeds (treated and untreated). *1 bleed occurred after screening but prior to dosing.

For more information, please visit www.ClinicalTrials.gov NCT03246891 or contact unidure at uniQureHPE-B@uniQure.com

General safety:

AMT-061 was well tolerated:

1 participant experienced two adverse events (AE), possibly related to AMT-061, that resolved without intervention: 2 very transient, self-limiting headache and slightly elevated C-reactive protein

No loss of FIX activity

No FIX inhibitor development

No serious AE

DISCLOSURES

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REFERENCES