**Results (continued)**

### Table 1: Demographics and Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Flexible Dose</th>
<th>OLE</th>
<th>OLE (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (median)</td>
<td>42 (35–49)</td>
<td>42 (35–49)</td>
<td>42 (35–49)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>3 (12%)</td>
<td>3 (12%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td>3 (12%)</td>
<td>3 (12%)</td>
<td>3 (12%)</td>
</tr>
</tbody>
</table>

### Figure 3: AAR and Annualized Hemin Doses in the OLE

- **A) Givosiran-treated**
  - Run-in: 8.7 ± 0.6 mg/kg AAR (n=16)
  - Placebo cross-over: 5 ± 0.6 mg/kg AAR (n=5)

- **B) Placebo cross-over**
  - Run-in: 5 ± 0.6 mg/kg AAR (n=5)
  - Placebo cross-over: 5 ± 0.6 mg/kg AAR (n=5)

- **C) OLE (N=12)**
  - Run-in: 8.7 ± 0.6 mg/kg AAR (n=12)

### Figure 4: Average Number of Attacks* per Patient per Month

- **A) Givosiran-treated**
  - Before treatment: 24 ± 11.6 attacks per month
  - During treatment: 2.3 ± 2.1 attacks per month

- **B) Placebo cross-over**
  - Before treatment: 24 ± 11.6 attacks per month
  - During treatment: 11 ± 5.8 attacks per month

### Sustained Reduction of Attack Rate Over Time

- **Ongoing monthly dosing at 2.5 mg/kg maintained the reduction in mean attack rate to Month 37** (Fig. 4)

### Summary

- These data represent patients with the longest treatment experience with givosiran to date, with a mean time in the Phase 1/2 OLE of 27.9 months and up to a total of 41.0 months of treatment in the combined Phase 1 and Phase 2 studies.
- **Long-term treatment with givosiran demonstrated**
  - Maintenance, and potential enhancement, of clinical activity with continuous monthly dosing at 2.5 mg/kg
  - Consistent and durable AAR and PBG reductions of 86% at Month 30 and reductions in AAR and annualized hemin use of >90%.
  - An acceptable and consistent safety profile, with no new safety findings.
- These long-term results are consistent with the results of the ENVISION Phase 3, global, placebo-controlled study (NCCT03308616) -6 month double-blind period and 12-month interim OLE period.

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**Note:**
- All patients received givosiran 2.5 mg/kg for a median 26.7 (range, 2.1–35.7) months with a cumulative 33.2 patient-years of exposure.
- The 2.5 mg/kg dose was maintained in patients who had received a dose increase to 5.0 mg/kg q3M → 2.5 mg/kg up to 12 months.
- The 5.0 mg/kg qM dose was maintained in patients who had received a dose increase to 10 mg/kg qM up to 12 months.
- **Accreditation**
  - The ENVISION study is funded by Alnylam Pharmaceuticals, Inc. (Cambridge, MA) under a master agreement with Horizon Discovery Group. The study is conducted in accordance with the principles of Good Clinical Practice and the Declaration of Helsinki. All authors have been involved in the design of the study, the collection, analysis, and interpretation of the data, the writing of the report, and the decision to submit the report for publication.