Factor IX Gene Therapy Phase 1/2 Trial Update*

- BAX 335 is a novel liver-directed scAAV8 vector from Baxalta that delivers a codon optimized hyperactive F9 transgene (FIXR338Lopt)\(^1\)

- First-in-human safety and single ascending dose-finding trial ongoing in adults with severe hemophilia B

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Dose (vector genomes [vg]/kg)</th>
<th># subjects dosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.0 x 10(^{11})</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>1.0 x 10(^{12})</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>3.0 x 10(^{12})</td>
<td>2</td>
</tr>
</tbody>
</table>

*Preliminary data*

\(^1\)Monahan PE, et al Hum Gene Ther 2015

Update on a phase 1/2 open-label trial of BAX335, an adeno-associated virus 8 (AAV8) vector-based gene therapy program for hemophilia B. ISTH 2015 Congress, Toronto, June 20–25
BAX335 Phase 1/2 Study: 1st and 2nd dose cohorts

- Dose-dependent FIX expression in both cohorts
- Sustained FIX expression of 20–25% in one subject in Cohort 2 with no bleeding and no exogenous FIX infusions

Subject #5 – Cohort 2

Weeks

% FIX Activity

ALT (IU/L)

BL 1 2 3 4 5 6 7 8 9 10 11 12 14 17 22 26 38 52 (M12)

0 5 10 15 20 25 30

0 20 40 60 80 100

↑ = FIX infusion

* = Bleeding Episode (BE)

Update on a phase 1/2 open-label trial of BAX335, an adeno-associated virus 8 (AAV8) vector-based gene therapy program for hemophilia B. ISTH 2015 Congress, Toronto, June 20–25
BAX335 Phase 1/2 Study: 3rd dose cohort – enrollment ongoing

- Dose-dependent FIX expression observed with peak levels >50% in 3rd dose cohort
- T-cell mediated immune response and liver enzyme elevations observed in two patients, with declining FIX expression triggering immunosuppression with corticosteroids

Subject #6 – Cohort 3

![Graph showing % FIX Activity and ALT levels over weeks with FIX infusion and bleeding episode markers.](image-url)
Summary

• The ongoing BAX 335 Phase 1/2 study has escalated to 3rd dose cohort. An additional 5 patients will be dosed
• Sustained expression of 20–25% for 1 year was observed in cohort 2
• Peak FIX activity level >50% achieved in Cohort 3 but persistent, stable expression was not achieved in the first two patients in this cohort
• Dose-dependent immune responses were observed in two patients in cohort 3 and treated with corticosteroid. FIX expression has subsequently declined in both subjects, likely due to delayed start of corticosteroid
• No inhibitors observed in any of the subjects treated to date
• Conclusion: Hemostatically effective plasma FIX activity levels were achieved in cohort 2 and 3 with sustained high level expression in one patient (20–25%)