ETP Pipeline Update Conference

Retigabine

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A first-in-class KCNQ (Kv7) channel opener in development for treatment of epilepsy.

RETIGABINE

N-(2-amino-4-(4-fluorobenzylamino)-phenyl) carbamic acid ethyl ester
Retigabine increases KCNQ channel activity, exerting a hyperpolarizing effect on neurons

...thus reducing hyperexcitability


Study 205: Median % Reduction and Responder Rate (≥ 50% reduction)
28-Day Total Partial-Seizure Frequency

<table>
<thead>
<tr>
<th></th>
<th>Double-blind period</th>
<th>Maintenance phase</th>
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</thead>
<tbody>
<tr>
<td>Median reduction (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>13%</td>
<td>16%</td>
</tr>
<tr>
<td>Retigabine 600 mg/d</td>
<td>23%</td>
<td>23%</td>
</tr>
<tr>
<td>Retigabine 900 mg/d</td>
<td>29% $^*$</td>
<td>29% $^*$</td>
</tr>
<tr>
<td>Retigabine 1200 mg/d</td>
<td>35% $^*$</td>
<td>44% $^*$</td>
</tr>
</tbody>
</table>

*Significant vs placebo. $P < 0.01$ for difference across all treatment arms. $P < 0.05$ for difference across retigabine 600, 900, and 1200 mg/d arms.

aITT population.
Study 301: Median % Reduction and Responder Rate (≥ 50% reduction) 28-Day Total Partial-Seizure Frequency

![Graph showing median reduction and responder rate](image)

- Placebo
- Retigabine 1200 mg/d

-P < 0.001.
- *P ≤ 0.01.

Study 302: Median % Reduction and Responder Rate (≥ 50% reduction) 28-Day Total Partial-SEizure Frequency

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median Reduction (%)</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retigabine 600 mg/d</td>
<td>35%*</td>
<td>35%*</td>
</tr>
<tr>
<td>Retigabine 900 mg/d</td>
<td>40%†</td>
<td>40%†</td>
</tr>
<tr>
<td>Placebo</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*P ≤ 0.01; †P < 0.001.

Conclusions

- Across 3 clinical trials, the efficacy of retigabine 600-1200mg/day vs. placebo as adjunctive treatment of patients with partial onset seizures has been demonstrated.
- Most adverse events were mild or moderate with CNS-associate AEs (dizziness, somnolence and fatigue) being most common.
- No clinically relevant changes in laboratory values, vital signs, or physical and neurological examinations were indicative of major safety issues.
- Few mild liver function test elevations were observed, which improved spontaneously or after discontinuation of study drug.
- Urinary retention, dysuria, and urinary hesitation were reported in small percentage of patients.