A Responder Analysis of Tarenflurbil (MPC-7869), a Selective Aβ42-Lowering Agent, in Mild Alzheimer's Disease (AD): Analysis from a Phase 2 Study of up to 24 months of Treatment

Kenton Zavitov, Suzanne Hendrix, Mark Laughlin, Edward Swabb, Myriad Pharmaceuticals, Inc., Salt Lake City, UT, USA

**Tarenflurbil Clinical Rationale**
- Novel antiamyloid treatment strategy for AD
- Selective Aβ-Lowering Agent (SALAs) in vivo & in vitro
- Abolishes neurtic filaments
- Reduces insoluble amyloid in mouse brain
- Improves spatial reference learning and memory performance in transgenic mice
- Effective concentrations in animal models achievable in humans at doses that have been well tolerated
- Phase 3 studies of tarenflurbil (800 mg BID) in subjects with mild AD (MMSE 20-24) are ongoing

**Methodology**
- Randomized, Double-Blind, Placebo-Controlled Phase 2 study
- Subjects with mild to moderate AD (MMSE 15-26) at 31 sites in UK and Canada
- Treatment: Tarenflurbil 400 mg BID vs. Placebo (1:1) for 24 months
- Primary end point: Neurtic filaments
- Secondary end points: Cognition (MMSE), Activities of Daily Living (ADCS-ADL), Global Function (CDR-sb), ADAS-cog
- Safety assessments: A plasma concentration response was observed with all treatment groups

**Primary Efficacy**
- Cognition (MMSE): Percentage of Mild Patients Improved or with Zero Decline After 24 Months
- Activities of Daily Living (ADCS-ADL)
- Global Function (CDR-sb)
- ADAS-cog

**Safety and Tolerability**
- Overall, MPC-7869 appeared very well tolerated
- 0% of patients in each treatment group experienced a serious adverse event
- 11% of patients in each treatment group experienced at least one adverse event
- No serious adverse reactions or unexpected AEs

**Conclusions**
- Using a very conservative definition of "responder" (improvement or no decline (change of 0) in ADAS-cog ADCS-ADL CDR-sb MMSE at month 24), 21% of patients treated with tarenflurbil vs. placebo (1:1) showed improvement or no decline
- Over 80% of the eligible patients elected to continue in this blinded study in which placebo patients were randomized into one of the two treatment groups
- These long-term and increasing response rates have not, to our knowledge, been observed previously in clinical studies of drugs in Alzheimer's disease
- Patients treated with tarenflurbil may slow the underlying biological progression of AD

**Demographics by Treatment Group**

<table>
<thead>
<tr>
<th>Group</th>
<th>Placebo (n=32)</th>
<th>400 mg BID (n=32)</th>
<th>800 mg BID (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age/years</td>
<td>75.0 / 26.0</td>
<td>73.0 / 26.0</td>
<td>75.0 / 26.0</td>
</tr>
<tr>
<td>AChE Use</td>
<td>97% / 95%</td>
<td>94% / 93%</td>
<td>95% / 93%</td>
</tr>
<tr>
<td>MMSE</td>
<td>22.9 / 21.8</td>
<td>23.2 / 21.8</td>
<td>22.8 / 23.2</td>
</tr>
<tr>
<td>ADAS-cog</td>
<td>27.5 / 26.8</td>
<td>28.1 / 27.5</td>
<td>28.1 / 27.5</td>
</tr>
<tr>
<td>ADCS-ADL</td>
<td>58.7 / 58.4</td>
<td>58.8 / 58.5</td>
<td>59.7 / 59.8</td>
</tr>
<tr>
<td>CDR-sb</td>
<td>5.7 / 5.0</td>
<td>6.0 / 5.7</td>
<td>6.0 / 5.7</td>
</tr>
</tbody>
</table>

**Absolute Risk Reduction =**

- Month 12: 21% (p=0.063) 32% (p=0.020)
- Month 24: 25% (p=0.000) 35% (p=0.000)

**Tarenflurbil (MPC-7869), a Selective Aβ42-Lowering Agent, in Mild Alzheimer's Disease (AD): Analysis from a Phase 2 Study of up to 24 months of Treatment**

Kenton Zavitov, Suzanne Hendrix, Mark Laughlin, Edward Swabb, Myriad Pharmaceuticals, Inc., Salt Lake City, UT, USA

**Summary**
- Defining "responder" as an improvement or 0 decline from baseline over 12 or 24 months, subjects with mild AD treated with 800 mg BID tarenflurbil showed an increasing response rate over time (absolute risk reduction, Fisher’s Exact p-value)

**Safety and Tolerability Summary**
- 0% of patients treated with tarenflurbil improved or had no further decline
- AEs are difficult to assess – improvement not common
- AIAA combination response was observed with all three primary outcome measures

**Drug Concentration Response**
- Subjects who achieved a higher plasma concentration (C_{max}) had a significantly better response

**References:**
- Wilcock GK et al. 2006
- JAMA 295: 611-618
- Alzheimer's and Dementias 6 (3): Supplement 1, pS81
- PDF copies of this poster will be available at www.myriad.com