**Subset Analyses by Race of a Phase 2 Study of TAK-063 in Subjects With Acute Exacerbations of Psychotic Symptoms**

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**Background**

- **TAK-063** is a novel, potent, and selective inhibitor of phosphodiesterase 10A,1 an enzyme that mediates metabolism of second messengers in medium spiny neurons of the striatum.2
- **TAK-063** has shown potential antipsychotic effects in animal models of schizophrenia.1
- In phase 1 studies, TAK-063 has demonstrated favorable safety and tolerability profiles at doses up to 1000 mg in healthy volunteers.3
- We have previously reported results from a phase 2 trial of 20-mg TAK-063 versus placebo.4
- Although the study did not meet its primary endpoint (change from baseline in the Positive and Negative Syndrome Scale [PNSS] total score at week 6), there was some evidence of antipsychotic efficacy (p=0.115, effect size=0.303).
- These overall results may have been confounded by a relatively large change in baseline from the placebo group.
- We report findings from analyses of the efficacy and safety results from the phase 2 trial stratified by race.

**Methods**

**Study Design**

This was a phase 2, randomized, double-blind, placebo-controlled, parallel-group study with weekly efficacy visits during the 6-week treatment period.5 Key eligibility criteria included:
- PNSS total score of 80 at screening and day 1 and a score of 5 (moderate severity) or higher on 3 or more key positive/sympathetic symptoms of PNSS.
- Clinical Global Impression Severity (CGI-S) of 4 or 5 at screening and day 1.
- Exacerbation of psychotic symptoms within 60 days before screening.
- The primary endpoint was the least-squares (LS) mean change from baseline in total PNSS score at week 6.
- Secondary endpoints included change from baseline in CGI-S at screening and day 1.
- Non-black:
  - TAK-063: 20 mg
  - Placebo
  - Black:
  - TAK-063: 20 mg
  - Placebo

**Statistical Analyses**

Subset analyses were performed by dichotomous race group (black vs non-black).6
- Efficacy analyses were run separately for RACE="Black" and RACE="Non-Black" for the primary and secondary endpoints.
- Dichotomous race was also added as a covariate in the mixed model for repeated measures (MMMR) for the overall population.
- For the primary differences and p-values were calculated separately for black and non-black subgroups, and overall population after adjusting for dichotomous race effect.
- For the primary endpoint for the overall study analysis, all p-values presented here are nominal, with no adjustments made for multiplicity.

**Results**

- Of the 164 subjects enrolled, 108 were black (placebo: 43 black subjects of 81 placebo subjects; TAK-063: 65 black subjects of 83 TAK-063 subjects) (Table 1).
- Demographics and baseline characteristics for black and non-black groups were broadly comparable.

**Table 1. Demographic and Baseline Characteristics**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo (n=81)</th>
<th>TAK-063 (n=83)</th>
<th>Total (n=164)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs), mean (SD)</td>
<td>39 ± 17</td>
<td>39 ± 16</td>
<td>39 ± 17</td>
</tr>
<tr>
<td>Sex</td>
<td>35</td>
<td>39</td>
<td>74</td>
</tr>
<tr>
<td>Black</td>
<td>0</td>
<td>93</td>
<td>93</td>
</tr>
<tr>
<td>Non-black</td>
<td>47</td>
<td>0</td>
<td>47</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo (n=81)</th>
<th>TAK-063 (n=83)</th>
<th>Total (n=164)</th>
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</thead>
<tbody>
<tr>
<td>Race</td>
<td>35</td>
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<td>74</td>
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<tr>
<td>Black</td>
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<tr>
<td>Non-black</td>
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<td>93</td>
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</tbody>
</table>

**Disclosures**

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**References**