COMP360 psilocybin therapy for treatment-resistant depression

Phase IIb topline data

09 November 2021
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Our COMP360 psilocybin therapy

COMP360

- Investigational synthetic, high-purity, polymorphic crystalline formulation of psilocybin
- Oral capsules
- Designated Breakthrough Therapy for TRD (in 2018)

Psychological support

- COMP360 is combined with psychological support from specially trained therapists
- COMP360 psilocybin administration is preceded by preparation and followed up with integration

COMP360 psilocybin therapy: clinical status

- Preclinical genotoxicity and cardiotoxicity studies completed or underway
- Phase I trial completed: COMP360 generally well-tolerated in healthy participants (n=89)
- Phase IIb trial in TRD: recruitment completed (n=233). Topline results
- Phase II exploratory, open-label trial in TRD: adjunct to SSRI (n=20). Results expected late 2021
- Long-term follow up of phase II TRD patients ongoing
- Phase II trial in PTSD launched

Note: TRD = treatment-resistant depression; SSRI = selective serotonin reuptake inhibitor; PTSD = post-traumatic stress disorder

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COMP 001 study design and endpoints

Primary endpoint (to determine appropriate phase III dose)
Reduction of symptoms of depression as measured by change in MADRS total score from baseline to week 3

Note: MADRS = Montgomery-Åsberg Depression Rating Scale; EOS = end of study; TRD = treatment-resistant depression; D = day; V = visit
131 (56%) patients were from Europe, 102 (44%) from North America

219 (94%) patients had no prior psilocybin experience

Participant demographics (age, gender, race, BMI, baseline depression symptom severity) were well balanced across the three groups

Note: BMI = body mass index; n = number of participants; follow-up = post-COMP360 administration to week 12
Primary endpoint - change from baseline in MADRS total score

Statistically significant primary endpoint (p<0.001) at week 3 (25mg vs 1mg). There was a rapid onset of action and durable effects with treatment differences between the 25mg vs 1mg group apparent from the day after COMP360 psilocybin administration.

Baseline mean (SD): 25mg (n=79) = 31.9 (5.41); 10mg (n=75) = 33.0 (6.31); 1mg (n=79) = 32.7 (6.24)

Note: MADRS = Montgomery-Åsberg Depression Rating Scale; n = number observed; SE: Standard error; SD = standard deviation; LS = least squares; * = statistically significant treatment difference vs 1mg at visit; p = p-value
Key secondary endpoint - MADRS responders

25mg group demonstrated rapid response, with treatment differences from day 2 to week 3 compared with the 1mg group

Responders: ≥50% decrease in MADRS total score from baseline

Note: MADRS = Montgomery-Åsberg Depression Rating Scale; number of responders stated in bar
Participants who started new treatment for depression were assumed to be non-responders, hence decreasing numbers reflecting antidepressant use over time

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Key secondary endpoint - MADRS remitters

25mg group demonstrated rapid remission, with treatment differences from day 2 to week 3 compared with the 1mg group

Remitter: MADRS total score ≤ 10

<table>
<thead>
<tr>
<th>Day</th>
<th>COMP360 25mg</th>
<th>COMP360 10mg</th>
<th>COMP360 1mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>30</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>1</td>
<td>25</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>23</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>20</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>9</td>
<td>16</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>12</td>
<td>21</td>
<td>5</td>
<td>9</td>
</tr>
</tbody>
</table>

Note: MADRS = Montgomery-Åsberg Depression Rating Scale; number of remitters stated in bar.
Participants who started new treatment for depression were assumed to be non-remitters, hence decreasing numbers reflecting antidepressant use over time.

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MADRS sustained responders at week 12

Higher proportion of sustained responders found in the 25mg vs 1mg arm

Sustained responder* - patients meeting the MADRS response criteria at week 3 and at week 12, and at least at one visit out of week 6 and week 9, and who did not start any new treatments for depression

Note: MADRS = Montgomery-Åsberg Depression Rating Scale; number of sustained responders stated in bar

Statistical significance cannot be claimed on secondary endpoints due to hierarchical testing being broken for the 10mg vs 1mg dose on the primary endpoint

Participants who started new treatment for depression were assumed to be non-responders, hence decreasing numbers reflecting antidepressant use over time

*The protocol-defined sustained response up to week 12 was 20.3% of patients in the 25mg group vs 10.1% in the 1mg group

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Safety – treatment emergent adverse events (TEAEs) overview

• The vast majority of TEAEs (over 90%) were of mild or moderate severity

• The proportion of patients reporting a serious TEAE was comparable between the 25mg and 10mg groups:
  - 5 (6.3%) patients in the 25mg COMP360 arm
  - 6 (8.0%) patients in the 10mg COMP360 arm
  - 1 (1.3%) patient in the 1mg COMP360 arm

• TEAE incidence was slightly higher in the 25mg group than in the 10mg and 1mg groups

• Further analysis on the onset and duration of TEAEs is underway

• TEAE incidence includes all events, including those thought to be related to the psychedelic experience on the day of COMP360 psilocybin administration in the therapeutic setting

Note: TEAE = treatment emergent adverse event
Most frequent TEAEs ordered by the 25mg arm (at least 5% in any treatment group)

<table>
<thead>
<tr>
<th>MedDRA TEAE preferred term</th>
<th>COMP360 25mg</th>
<th>COMP360 10mg</th>
<th>COMP360 1mg</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=79</td>
<td>N=75</td>
<td>N=79</td>
<td>N=233</td>
</tr>
<tr>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>27 (34.2)</td>
<td>16 (21.3)</td>
<td>20 (25.3)</td>
<td>63 (27.0)</td>
</tr>
<tr>
<td>Nausea</td>
<td>18 (22.8)</td>
<td>7 (9.3)</td>
<td>4 (5.1)</td>
<td>29 (12.4)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>12 (15.2)</td>
<td>5 (6.7)</td>
<td>7 (8.9)</td>
<td>24 (10.3)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>8 (10.1)</td>
<td>11 (14.7)</td>
<td>14 (17.7)</td>
<td>33 (14.2)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>7 (8.9)</td>
<td>13 (17.3)</td>
<td>3 (3.8)</td>
<td>23 (9.9)</td>
</tr>
<tr>
<td>Mood altered</td>
<td>7 (8.9)</td>
<td>3 (4.0)</td>
<td>1 (1.3)</td>
<td>11 (4.7)</td>
</tr>
<tr>
<td>Back pain</td>
<td>6 (7.6)</td>
<td>0</td>
<td>3 (3.8)</td>
<td>9 (3.9)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>6 (7.6)</td>
<td>1 (1.3)</td>
<td>1 (1.3)</td>
<td>8 (3.4)</td>
</tr>
<tr>
<td>Suicidal ideation</td>
<td>5 (6.3)</td>
<td>5 (6.7)</td>
<td>4 (5.1)</td>
<td>14 (6.0)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>5 (6.3)</td>
<td>2 (2.7)</td>
<td>1 (1.3)</td>
<td>8 (3.4)</td>
</tr>
<tr>
<td>Euphoric mood</td>
<td>4 (5.1)</td>
<td>5 (6.7)</td>
<td>4 (5.1)</td>
<td>13 (5.6)</td>
</tr>
<tr>
<td>Depression</td>
<td>4 (5.1)</td>
<td>6 (8.0)</td>
<td>5 (6.3)</td>
<td>15 (6.4)</td>
</tr>
<tr>
<td>Abdominal pain upper</td>
<td>4 (5.1)</td>
<td>2 (2.7)</td>
<td>1 (1.3)</td>
<td>7 (3.0)</td>
</tr>
<tr>
<td>Irritability</td>
<td>4 (5.1)</td>
<td>2 (2.7)</td>
<td>1 (1.3)</td>
<td>7 (3.0)</td>
</tr>
<tr>
<td>Panic reaction</td>
<td>4 (5.1)</td>
<td>1 (1.3)</td>
<td>1 (1.3)</td>
<td>6 (2.6)</td>
</tr>
<tr>
<td>Depressed mood</td>
<td>3 (3.8)</td>
<td>5 (6.7)</td>
<td>4 (5.1)</td>
<td>12 (5.2)</td>
</tr>
<tr>
<td>Paraesthesia</td>
<td>3 (3.8)</td>
<td>4 (5.3)</td>
<td>1 (1.3)</td>
<td>8 (3.4)</td>
</tr>
<tr>
<td>Thinking abnormal</td>
<td>0</td>
<td>4 (5.3)</td>
<td>0</td>
<td>4 (1.7)</td>
</tr>
</tbody>
</table>

Note: MedDRA = Medical Dictionary for Regulatory Activities; TEAE = treatment emergent adverse event; N = number of participants in the population; n = number observed

TEAE incidence is higher in the 25mg group overall

Key mood-related TEAEs (euphoric mood, depression, depressed mood, suicidal ideation) do not have a higher incidence in the 25mg arm
Treatment emergent serious adverse events (TESAEs) ordered by 25mg arm

<table>
<thead>
<tr>
<th>MedDRA preferred term</th>
<th>COMP360 25mg</th>
<th>COMP360 10mg</th>
<th>COMP360 1mg</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=79</td>
<td>N=75</td>
<td>N=79</td>
<td>N=233</td>
</tr>
<tr>
<td>Number of patients per category (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with a TESAE</td>
<td>5 (6.3)</td>
<td>6 (8.0)</td>
<td>1 (1.3)</td>
<td>12 (5.2)</td>
</tr>
<tr>
<td>Any TESAE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suicidal behaviour</td>
<td>3 (3.8)</td>
<td>0</td>
<td>0</td>
<td>3 (1.3)</td>
</tr>
<tr>
<td>Intentional self-injury</td>
<td>2 (2.5)</td>
<td>2 (2.7)</td>
<td>1 (1.3)</td>
<td>5 (2.1)</td>
</tr>
<tr>
<td>Suicidal ideation</td>
<td>2 (2.5)</td>
<td>2 (2.7)</td>
<td>0</td>
<td>4 (1.7)</td>
</tr>
<tr>
<td>Drug withdrawal syndrome</td>
<td>1 (1.3)</td>
<td>0</td>
<td>0</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Adjustment disorder with anxiety</td>
<td>1 (1.3)</td>
<td>0</td>
<td>0</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Adjustment disorder with mixed</td>
<td>1 (1.3)</td>
<td>0</td>
<td>0</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>anxiety and depressed mood</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>0</td>
<td>1 (1.3)</td>
<td>0</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Hospitalisation</td>
<td>0</td>
<td>1 (1.3)</td>
<td>0</td>
<td>1 (0.4)</td>
</tr>
</tbody>
</table>

19 TESAEs were reported in total, experienced by 12 patients (note: two patients had the same TESAE twice)

All suicidal behaviours were experienced at least one month after COMP360 administration

**Note:** MedDRA = Medical Dictionary for Regulatory Activities; TESAE = treatment emergent serious adverse event; N = number of participants in the population

1 = These were cases of non-suicidal self-injury (including) superficial cutting, scratching and punching which, although not meeting criteria for a TESAE, were classed as TESAEs in this study due to the protocol specifying that any behaviours on the Columbia-Suicide Severity Rating Scale, completed by participants at every study visit, be reported as a TESAE

2 = Codeine withdrawal

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Largest, randomised, controlled double-blind psilocybin therapy trial shows rapid and sustained response for COMP360 psilocybin therapy

Key conclusions

- Largest, randomised, controlled, double-blind psilocybin therapy study ever completed shows rapid and sustained response for patients receiving a single 25mg dose of COMP360 psilocybin with psychological support
  - Multicentre, robust study of well characterised patients with treatment-resistant depression; 94% of patients had no prior psilocybin experience
  - Topline data, along with comprehensive secondary analyses to follow, provides the springboard for phase III development

Primary endpoint

- Study achieved its primary endpoint with 25mg demonstrating a statistically significant treatment difference of \(-6.6\) points on change from baseline in MADRS total scores vs the 1mg dose at week 3 (\(p<0.001\))
  - The 10mg vs 1mg dose did not show a statistically significant difference at week 3 (numerical difference of \(-2.5\) points)
  - The 25mg group demonstrated statistically significant efficacy from the day after the COMP360 psilocybin administration
  - At week 3, the 25mg group showed a 12 point reduction from baseline in MADRS total score

Secondary endpoints

- At least double the number of MADRS responders\(^1\), remitters\(^2\), and sustained responders\(^3\) with 25mg vs 1mg; rapid response and remission from day 2 to week 3
  - 36.7% (29 patients) in 25mg group showed response at week 3
  - 29.1% (23 patients) in 25mg group were in remission at week 3
  - 24.1% (19 patients) in 25mg group were sustained responders at week 12

Safety

- COMP360 was generally well-tolerated
  - Vast majority of TEAEs were mild or moderate in severity
  - The most frequent TEAEs were headache, nausea, fatigue and insomnia
  - There were 12 patients who reported serious TEAEs, including suicidal behaviour, intentional self-injury, and suicidal ideation, which are often observed in a treatment-resistant depression population

Note: MADRS = Montgomery-Åsberg Depression Rating Scale; TEAE = treatment emergent adverse events

1. Response: \(\geq 50\%\) decrease in MADRS total score from baseline; 2. Remission: MADRS total score \(\leq 10\); 3. Sustained response: patients meeting the MADRS response criteria at week 3 and at week 12, and at least one visit out of week 6 and week 9; the protocol-defined sustained response up to week 12 was 20.3% of patients in the 25mg group vs 10.1% in the 1mg group

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COMP360 psilocybin therapy development moving forward

• Complete final analysis of all data and endpoints to further inform path forward

• Hold an end-of-phase II meeting with FDA to discuss topline data and continue discussions around development path and phase III design
  – Meeting anticipated Q1 2022

• Pending FDA meeting outcome, we anticipate advancing to phase III by Q3 2022

• Continue expanding our pipeline of indications beyond treatment-resistant depression and post-traumatic stress disorder

• Additional indications are currently being researched via investigator initiated studies which may provide signal generation for future COMP360 psilocybin therapy studies
Thank you for your time

Any questions?