JAK Inhibitor CTP-543 Achieves Primary Endpoint in Phase 2 Trial in Alopecia Areata

An interim analysis of 4 and 8 mg BID

James Cassella, PhD; Colleen Hamilton; Jana von Hehn, PhD; Virginia Braman
Concert Pharmaceuticals, Lexington, MA 02421, USA

ClinicalTrials.gov Identifier: NCT03137381
Disclosures of Relationship with Industry

James V. Cassella, PhD

S034 - Late-breaking Research: Clinical Trials

DISCLOSURES

• Concert Pharmaceuticals: Employee; Salary and Stock Received
Alopecia Areata: A Serious Medical Disease

• A devastating and poorly treated autoimmune disease

• Up to 650,000 patients affected with alopecia areata (AA) in the U.S. at any given time*

• Chronic condition affecting women, men and children of all ages

• Disease profoundly impacts patients; associated with anxiety, depression and other autoimmune conditions

• No FDA-approved treatment options

*Fricke M. Clinical, Cosmetic and Investigational Dermatology, 2015.
CTP-543: Phase 2 Dose Ranging Trial Design

• Double-blind, randomized, placebo-controlled trial in adult patients with moderate-to-severe alopecia areata
• Entry criteria of at least 50% hair loss as measured by Severity of Alopecia Tool (SALT)
• Patients sequentially randomized to receive one of three doses of CTP-543 (4, 8 and 12 mg BID) or placebo for 24 weeks
• 4 mg BID and 8 mg BID Cohorts completed; 12 mg BID Cohort is currently ongoing
  – Interim analysis: 4 mg BID and 8 mg BID Cohorts
• Primary Endpoint: 50% relative reduction in SALT between Week 24 and baseline
## Interim Analysis

### Key Demographics and Baseline Alopecia Areata Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>CTP-543 4 mg BID</th>
<th>CTP-543 8 mg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy Population (N)</td>
<td>35</td>
<td>28</td>
<td>38</td>
</tr>
<tr>
<td>Age: Yrs</td>
<td>37</td>
<td>36</td>
<td>37</td>
</tr>
<tr>
<td>Females, N (%)</td>
<td>24 (67%)</td>
<td>22 (73%)</td>
<td>26 (68%)</td>
</tr>
<tr>
<td>Episode Duration: Yrs</td>
<td>3.6</td>
<td>6</td>
<td>3.8</td>
</tr>
<tr>
<td>SALT score, Mean (SD)</td>
<td>85.0 (19.4)</td>
<td>88.8 (16.2)</td>
<td>89.1 (16.4)</td>
</tr>
<tr>
<td>AA Patchy, N(%)</td>
<td>19 (52.8%)</td>
<td>16 (53.3%)</td>
<td>16 (42.1%)</td>
</tr>
<tr>
<td>AA Totalis, N(%)</td>
<td>5 (13.9%)</td>
<td>2 (6.7%)</td>
<td>6 (15.8%)</td>
</tr>
<tr>
<td>AA Universalis, N(%)</td>
<td>12 (33.3%)</td>
<td>12 (40.0%)</td>
<td>14 (36.8%)</td>
</tr>
<tr>
<td>AA Ophiasis, N(%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (5.3%)</td>
</tr>
</tbody>
</table>
### Interim Analysis

#### Most Common Treatment Emergent Adverse Events by Patient

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Placebo</th>
<th>CTP-543 4 mg BID</th>
<th>CTP-543 8 mg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Headache</strong></td>
<td>4 (11.1%)</td>
<td>5 (17.2%)</td>
<td>10 (26.3%)</td>
</tr>
<tr>
<td><strong>Nausea</strong></td>
<td>4 (11.1%)</td>
<td>4 (13.8%)</td>
<td>4 (10.5%)</td>
</tr>
<tr>
<td><strong>Acne</strong></td>
<td>2 (5.6%)</td>
<td>4 (13.8%)</td>
<td>4 (10.5%)</td>
</tr>
<tr>
<td><strong>Cough</strong></td>
<td>0</td>
<td>4 (13.8%)</td>
<td>1 (2.6%)</td>
</tr>
<tr>
<td><strong>Diarrhoea</strong></td>
<td>3 (8.3%)</td>
<td>3 (10.3%)</td>
<td>1 (2.6%)</td>
</tr>
<tr>
<td><strong>Nasopharyngitis</strong></td>
<td>1 (2.8%)</td>
<td>3 (10.3%)</td>
<td>3 (7.9%)</td>
</tr>
<tr>
<td><strong>Folliculitis</strong></td>
<td>0</td>
<td>3 (10.3%)</td>
<td>2 (5.3%)</td>
</tr>
<tr>
<td><strong>Blood creatine phosphokinase increased</strong></td>
<td>1 (2.8%)</td>
<td>3 (10.3%)</td>
<td>2 (5.3%)</td>
</tr>
<tr>
<td><strong>Oropharyngeal pain</strong></td>
<td>0</td>
<td>3 (10.3%)</td>
<td>1 (2.6%)</td>
</tr>
<tr>
<td><strong>Upper respiratory tract infection</strong></td>
<td>6 (16.7%)</td>
<td>2 (6.9%)</td>
<td>2 (5.3%)</td>
</tr>
<tr>
<td><strong>Discontinuations Due to AE</strong></td>
<td>3 (37.5%)</td>
<td>0 (0%)</td>
<td>2 (25%)</td>
</tr>
</tbody>
</table>
Interim Analysis
Primary Analysis: Responders at Week 24

Patients with ≥ 50% Change in SALT Relative to Baseline

- **Placebo**: 8.6%
- **4 mg BID**: 21%
- **8 mg BID**: 47% ± ***

**Statistical Significance**:
- *** P < 0.001 vs PBO
- ± P < 0.05 vs 4 mg
Interim Analysis
Responders by Visit

Patients with ≥ 50% Change in SALT Relative to Baseline

% Patients per Treatment

- Placebo
- 4 mg BID
- 8 mg BID

Week 4  Week 8  Week 12  Week 16  Week 20  Week 24

8.6%  21%  47%

*** P < 0.001 vs PBO
** P < 0.01 vs PBO
* P < 0.05 vs PBO
± P < 0.05 vs 4 mg
# Interim Analysis

## Responders by Alopecia Areata Subtype at Week 24

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>CTP-543 4 mg BID</th>
<th>CTP-543 8 mg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Responders by Subtype per Treatment, N%</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alopecia patchy</td>
<td>3 (8.6%)</td>
<td>3 (10.7%)</td>
<td>8 (21.1%)</td>
</tr>
<tr>
<td>Alopecia ophiasis</td>
<td>0</td>
<td>0</td>
<td>1 (2.6%)</td>
</tr>
<tr>
<td>Alopecia totalis</td>
<td>0</td>
<td>0</td>
<td>2 (5.3%)</td>
</tr>
<tr>
<td>Alopecia universalis</td>
<td>0</td>
<td>3 (10.7%)</td>
<td>7 (18.4%)</td>
</tr>
</tbody>
</table>

Responder: ≥ 50% relative reduction in SALT between Week 24 and Baseline
Interim Analysis

Responders by Alopecia Areata Subtype by Visit

Week of Treatment

% of Patients in Treatment

- PBO AA
- PBO AU/AT
- 8 mg AA
- 8 mg AU/AT
Interim Analysis
CTP-543 Phase 2: Patient SALT Improvement

Relative Change in SALT from Baseline to Week 24

% of Patients per Treatment

≥ 50%

≥ 75%

≥ 90%

Placebo
4 mg BID
8 mg BID

*** P < 0.001 vs PBO
* P < 0.05 vs PBO
± P < 0.05 vs 4 mg
Interim Analysis

Response Over Treatment Period

Baseline

Week 12

Week 24
Interim Analysis

Response Over Treatment Period

Baseline

Week 12

Week 24
Phase 2 interim analysis showed:

• 4 mg BID and 8 mg BID CTP-543 generally well-tolerated

• Primary endpoint met with 8 mg BID cohort
  – 8 mg BID dose group was significantly different from Placebo and 4 mg BID dose groups
  – 8 mg BID determined to be the minimally effective dose
  – Response did not appear to have plateaued at Week 24
    • Significant changes in SALT score were observed starting at 12 weeks

• Similar overall scalp regrowth response rate between patchy AA and AU/AT
Thank You

- To the Alopecia Areata Patients volunteering for participation in clinical studies

- To the Investigators and clinical study teams:
  
  Wilma Bergfeld  
  Suzanne Bruce  
  Maria Colavincenzo  
  Emma Guttman  
  Timothy Jochen  
  Steven Kempers  
  Brett King  
  Justin Ko  
  Amy McMichael  
  Natasha Mesinkovska  
  Paradi Mirmirani  
  Janet Roberts  
  Julian MacKay-Wiggan