RPT193, an oral CCR4 inhibitor: Efficacy results from a randomized, placebo-controlled Phase 1b monotherapy trial in patients with moderate-to-severe atopic dermatitis

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Disclosures

- R Bissonnette is an Advisory Board Member, Consultant, Speaker and/or Investigator for and receives honoraria and/or grant from AbbVie, Arcutis, Arena Pharma, Arista, Asana BioSciences, Bellus Health, Bluefin Biomedicine, Boehringer-Ingelheim, CARA, Dermavant, Eli Lilly, EMD Serono, Evidera, Galderma, GSK, Inmagene Bio, Incyte, Kiniksa, Kyowa Kirin, LEO Pharma, Novan, Pfizer, Ralexar, RAPT, Regeneron, Respivant, Sanofi-Genzyme, Sienna and Target RWE. R Bissonnette is also an employee and shareholder of Innovaderm Research.
RPT193 Targets Th2 Activity Responsible for Allergic Inflammation in Atopic Dermatitis, Asthma, and Other Diseases

Epithelial Barrier Surface

Allergen, Microbes

CCL17 (TARC)
CCL22 (MDC)

CCR4

Signaling via CCR4 regulates Th2 cell migration into inflamed tissues and can enhance cytokine secretion of activated T cells

Cytokines

IL-5  IL-4  IL-13

Inflammation Thickening Itch
RPT193 Targets Th2 Activity Responsible for Allergic Inflammation in Atopic Dermatitis, Asthma, and Other Diseases

Epithelial Barrier Surface

Allergen, Microbes

CCR4

Signaling via CCR4 regulates Th2 cell migration into inflamed tissues and can enhance cytokine secretion of activated T cells

CCL17 (TARC)
CCL22 (MDC)

RPT193 is a potent and selective oral CCR4 antagonist that specifically inhibits Th2 cell migration, function, and activation.

Th2

Cytokines

IL-5  IL-4  IL-13

Inflammation Thickening Itch
Phase 1b trial part of a broader study conducted in healthy volunteers (HV) to investigate single and multiple doses of RPT193.

- 400 mg dose selected based on safety, tolerability, PK and PD data from HV.
- Double-blind, randomized, monotherapy study.
- Primary and secondary endpoints were safety and PK, respectively.
  - Trial was not powered for any specific endpoint.
  - Modified Intent to Treat (mITT) dataset with arithmetic means and standard error for continuous endpoints presented.

**Phase 1b Trial Explored RPT193 Activity in Patients with Moderate-to-Severe Atopic Dermatitis**

- ≥12-month history of AD
- 18-65 years of age (inclusive)
- BMI ≥18 and <40 kg/m²
- BSA ≥10%
- EASI ≥12
- vIGA ≥3

**Obtain Informed Consent**

- Screening (Up to 35 days)
- Treatment (28 days)
- Follow-up (14 days)

**Study Assessments (Day 1 to 43)**

- Day -35
- Day -1
- Day 1
- Day 8
- Day 15
- Day 29
- Day 43

- RPT193 400 mg once daily
- Placebo

**Screening Assessments**

- ≥12-month history of AD
- 18-65 years of age (inclusive)
- BMI ≥18 and <40 kg/m²
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- vIGA ≥3

**Treatment Assessments**

- RPT193 400 mg once daily
- Placebo

**Follow-up Assessments**

- (14 days)
## Phase 1b Patient Demographics and Baseline AD Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>RPT193</th>
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</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>10</td>
<td>21</td>
</tr>
<tr>
<td><strong>Age, Mean (Range)</strong></td>
<td>35.8 (22-64)</td>
<td>41.1 (19-63)</td>
</tr>
<tr>
<td><strong>Female, n (%)</strong></td>
<td>4 (40.0%)</td>
<td>12 (57.1%)</td>
</tr>
<tr>
<td><strong>Hispanic or Latino Ethnicity, n (%)</strong></td>
<td>3 (30.0%)</td>
<td>3 (14.3%)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>White, n (%)</strong></td>
<td>5 (50.0%)</td>
<td>12 (57.1%)</td>
</tr>
<tr>
<td><strong>Asian, n (%)</strong></td>
<td>0 (0%)</td>
<td>2 (9.5%)</td>
</tr>
<tr>
<td><strong>Black or African American, n (%)</strong></td>
<td>5 (50.0%)</td>
<td>7 (33.3%)</td>
</tr>
<tr>
<td><strong>Baseline AD Characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total SCORAD (Range)</strong></td>
<td>56.62 (41.0-81.4)</td>
<td>56.98 (36.6-82.4)</td>
</tr>
<tr>
<td><strong>SCORAD Subj (Range)</strong></td>
<td>10.77 (2.0-16.3)</td>
<td>11.99 (5.0-18.0)</td>
</tr>
<tr>
<td><strong>EASI, Mean (Range)</strong></td>
<td>21.07 (13.6-45.5)</td>
<td>18.49 (12-30)</td>
</tr>
<tr>
<td><strong>BSA, Mean (Range)</strong></td>
<td>24.50 (10-61)</td>
<td>23.29 (11-55)</td>
</tr>
<tr>
<td><strong>vIGA 3, n (%)</strong></td>
<td>8 (80.0%)</td>
<td>18 (85.7%)</td>
</tr>
</tbody>
</table>
RPT193: Previously Reported Phase 1b Data

**Clinical Safety**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>RPT193</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects with treatment emergent AE (TEAE), n (%)</td>
<td>2 (20.0%)</td>
<td>9 (42.9%)</td>
</tr>
<tr>
<td>Number of SAEs reported, n (%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>TEAEs observed in 2 or more subjects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea, n (%)</td>
<td>0 (0.0%)**</td>
<td>3 (14.3%)</td>
</tr>
</tbody>
</table>

*Once-daily, oral RPT193 was generally well tolerated after 28 days of dosing*

**Improvement compared to Placebo in EASI and vIGA at Day 29 with further deepening of the response at Day 43**

*P<0.05; post-hoc analysis

**Nausea also observed in 12.5% of HV in the placebo arm of the MAD portion of the Phase 1**
SCORAD Background

- Developed in 1993
- Score range from 0-103 with objective, investigator-assessed and subjective, patient-reported elements
- Objective
  - Six criteria signs are used to assess Intensity or lesion severity
  - Extent of BSA affected by AD
- Subjective
  - Sleep loss and pruritus assessed individually
  - Patients rate average for each over the past 3 days using a visual analog scale
RPT193: Percent Change in Total SCORAD

*\textsuperscript{p}<0.05 (post-hoc analysis)
RPT193: Percent Change in SCORAD Extent Area Involved

Percent Change from Baseline

* *p<0.05 (post-hoc analysis)
RPT193: Percent Change in SCORAD Intensity (Lesion Severity)

* *p<0.05 (post-hoc analysis)
RPT193: Percent Change in Subjective SCORAD

**Sleep Loss + Pruritus**

- Day 1: Baseline
- Day 8: Treatment
- Day 15: Follow-up
- Day 29: Day 43

*Percent Change from Baseline

**Sleep Loss**

- Day 1
- Day 8
- Day 15
- Day 29
- Day 43

*Percent Change from Baseline

**Pruritus**

- Day 1
- Day 8
- Day 15
- Day 29
- Day 43

*Percent Change from Baseline

*\( p < 0.05 \) (post-hoc analysis)
Conclusions

- This is the first reported study of a CCR4 antagonist that showed a positive efficacy signal on both the signs and symptoms of AD.
- Once-daily, oral RPT193 was generally well tolerated after 28 days of dosing.
- At the End of Treatment (Day 29) and compared to Placebo, RPT193 showed greater decrease in total SCORAD and all sub-domains.
- At the End of Study (Day 43), RPT193 showed further decreases in total SCORAD and sub-domains, including pruritus and sleep loss, compared to Day 29.
  - Change in total SCORAD and all sub-domains at Day 43 demonstrated statistical significance in a post-hoc analysis.
- Further improvement after cessation of dosing could be consistent with unique kinetics associated with targeting Th2 cell migration and activation through CCR4 inhibition.
- A dose-ranging Phase 2b trial is planned to further investigate RPT193’s efficacy and safety in patients with AD.

For additional details, please refer to the Poster for Abstract 88.
Acknowledgments

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