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Tapinarof: Therapeutic AhR Modulating Agent (TAMA)

- Tapinarof is a topical, small molecule TAMA that directly binds to and activates AhR transcription factor¹
- AhR activation via tapinarof in vitro and animal models leads to:
  - Reduction of Th17 cytokine expression¹
  - Reduction of Th2 cytokine expression¹,²
  - Decreased oxidative stress¹
  - Increased skin barrier proteins¹

AhR pathway


AhR, aryl hydrocarbon receptor; ARNT, aryl hydrocarbon receptor nuclear translocator; TAMA, therapeutic aryl hydrocarbon receptor modulating agent; Th, T helper cell.
Tapinarof Phase 2b Study in Atopic Dermatitis
IGA 0 or 1 and ≥2-grade Improvement†

Primary endpoint: Assessed in ITT population (NRI Analysis)

- Tapinarof resulted in higher IGA response† at all timepoints beyond Week 2 compared with vehicle

*Difference vs vehicle is statistically significant at α=0.05 level (the 95% confidence interval excludes 0). †IGA response: IGA score of 0 (clear) or 1 (almost clear) and ≥2-grade improvement from baseline.

The Safety and Efficacy of Roflumilast Cream 0.15% and 0.05% in Atopic Dermatitis: Phase 2 Proof-of-Concept Study


¹SKiN Centre for Dermatology, Probity Medical Research and Queen’s University, Peterborough, ON, Canada; ²Icahn School of Medicine at Mount Sinai, NY; Indiana Medical Center, Indianapolis, IN; Physicians Skin Care, PLLC, Louisville, KY; and Skin Sciences, PLLC, Louisville, KY, USA; ³Dermatologists of the Central States, Probity Medical Research, and Ohio University, Bexley, OH, USA; ⁴Progressive Clinical Research, San Antonio, Texas, USA; ⁵Minnesota Clinical Study Center, Fridley, MN, USA; ⁶Dermatology Consulting Services, PLLC, High Point, NC, USA; ⁷University of Pittsburgh, Department of Dermatology, Pittsburgh, PA, USA; ⁸US Dermatology Partners, Bryan, TX, USA; ⁹Innovaderm Research, Montreal, QC, Canada; ¹⁰Therapeutics Clinical Research, San Diego, CA, USA; ¹¹The Dermatology Center of Indiana, PC; The Indiana Clinical Trials Center, PC, Plainfield, IN, USA; ¹²Clinical Trials Management, LLC, Metairie, LA, USA; Tulane University School of Medicine in New Orleans, LA, USA; ¹³Arcutis Biotherapeutics, Inc., Westlake Village, CA, USA
Secondary and Exploratory Endpoints Showed Significant Improvement With Roflumilast Cream Over Vehicle

Data presented for intent-to-treat population. Only significant P-values (P<0.05) shown. CI: confidence interval; EASI: eczema area and severity index; LS: least squares; vIGA-AD: validated investigator global assessment–atopic dermatitis.

Week 4

- **EASI Percent Change From Baseline**
  - Roflumilast 0.15% (n=45)
  - Roflumilast 0.05% (n=46)
  - Vehicle (n=45)
  - Statistic: P=0.049

- **EASI-75 Responder Rate**
  - Roflumilast 0.15% (n=45)
  - Roflumilast 0.05% (n=46)
  - Vehicle (n=45)
  - Statistic: P=0.045

- **vIGA-AD Score of Clear or Almost Clear**
  - Roflumilast 0.15% (n=45)
  - Roflumilast 0.05% (n=46)
  - Vehicle (n=45)
  - Statistic: P=0.009

Week 8

- **EASI Percent Change From Baseline**
  - Roflumilast 0.15% (n=45)
  - Roflumilast 0.05% (n=46)
  - Vehicle (n=45)
  - Statistic: P=0.049

- **EASI-75 Responder Rate**
  - Roflumilast 0.15% (n=45)
  - Roflumilast 0.05% (n=46)
  - Vehicle (n=45)
  - Statistic: P=0.045

- **vIGA-AD Score of Clear or Almost Clear**
  - Roflumilast 0.15% (n=45)
  - Roflumilast 0.05% (n=46)
  - Vehicle (n=45)
  - Statistic: P=0.009
Roflumilast Cream Improved Severity of AD

<table>
<thead>
<tr>
<th>Roflumilast 0.15%</th>
<th>Roflumilast 0.05%</th>
<th>Vehicle</th>
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</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>vIGA-AD = 3</td>
<td>vIGA-AD = 2</td>
<td>vIGA-AD = 3</td>
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<tr>
<td><strong>Week 4</strong></td>
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<tr>
<td>vIGA-AD = 2</td>
<td>vIGA-AD = 2</td>
<td>vIGA-AD = 3</td>
</tr>
<tr>
<td>EASI CFB = -77%</td>
<td>EASI CFB = -85%</td>
<td>EASI CFB = -27%</td>
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</tbody>
</table>

CFB: change from baseline; EASI: eczema area and severity index; vIGA-AD: validated investigator global assessment—atopic dermatitis.