DRM04 for the treatment of axillary hyperhidrosis: Primary results from the ATMOS-1 and ATMOS-2 Phase 3 randomized controlled trials

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- **D. Pariser**: Investigator and Consultant for Dermira, Inc.

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- **L. Green**: Investigator for Dermira, Inc.

- **H. Hofland**: Employee of Dermira, Inc.

- **J. Drew**: Employee of Dermira, Inc.

- **J. Quiring**: Biostatistical consultant for Dermira, Inc.

- **D. A. Glaser**: Investigator and Consultant for Dermira, Inc.

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Background

- Hyperhidrosis, which is excessive sweating beyond that physiologically required to maintain normal thermal regulation, affects an estimated 2.8% (7.8 million) of the US population.¹

- The impact on quality of life is reported as comparable to, or greater than, psoriasis and eczema.²

- Currently there are limited treatment options for patients suffering from hyperhidrosis.

- DRM04 is a cholinergic receptor antagonist developed for topical application for the treatment of primary axillary hyperhidrosis.

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OBJECTIVE: The efficacy and safety of DRM04 as a treatment of primary axillary hyperhidrosis was assessed in two parallel, randomized, double-blind, vehicle-controlled, Phase 3 trials (ATMOS-1 & ATMOS-2).

ATMOS-1 and ATMOS-2 Trial Design

Co-primary efficacy endpoints at Week 4:
- ASDD response (≥4 point improvement from baseline)
- Absolute change from baseline in axillary sweat production†

Other pre-specified efficacy endpoint at Week 4:
- DLQI change from baseline

ASDD: Axillary Sweating Daily Diary; DLQI: Dermatology Life Quality Index. *Over 80% of patients completing ATMOS-1 or ATMOS-2 elected to enter the open-label extension. †Average of both axillae, measured gravimetrically.
ATMOS-1 and ATMOS-2 Key Inclusion Criteria

- Eligible patients, aged ≥9 years, were required to have primary axillary hyperhidrosis, defined as:
  - ≥6 months duration
  - Sweat production of ≥50 mg/5 min in each axilla, measured gravimetrically
  - Axillary Sweating Daily Diary (ASDD) score ≥4 on an 11-point scale
  - Hyperhidrosis Disease Severity Scale (HDSS) grade 3 or 4 on a 4-point scale
ATMOS-1 and ATMOS-2 Key Exclusion Criteria

- Known history of a condition that could cause secondary hyperhidrosis
- Prior surgical procedure for hyperhidrosis
- Inadequate washout or discontinuation of any other hyperhidrosis product
- Other treatments having systemic anticholinergic activity or conditions which could be exacerbated by study medication
ATMOS-1 and ATMOS-2 Patient Disposition

**ATMOS-1**

- **Randomized**
  - VEH: n=115
  - DRM04: n=229
  - Completed: n=112 (97.4%)
  - Discontinued: n=3 (2.6%)

**ATMOS-2**

- **Randomized**
  - VEH: n=119
  - DRM04: n=234
  - Completed: n=113 (95.0%)
  - Discontinued: n=16 (6.8%)

VEH: Vehicle
# ATMOS-1 and ATMOS-2 Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>ATMOS-1</th>
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<th>ATMOS-1</th>
<th>ATMOS-2</th>
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<tbody>
<tr>
<td></td>
<td>VEH (n=115)</td>
<td>DRM04 (n=229)</td>
<td></td>
<td>VEH (n=119)</td>
<td>DRM04 (n=234)</td>
</tr>
<tr>
<td><strong>Patient demographics</strong></td>
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<td><strong>Patient demographics</strong></td>
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</tr>
<tr>
<td>Age, mean (SD) years</td>
<td>34.0 (13.2)</td>
<td>32.1 (11.2)</td>
<td>Age, mean (SD) years</td>
<td>32.8 (11.2)</td>
<td>32.6 (10.9)</td>
</tr>
<tr>
<td>Sex, n (%) male</td>
<td>55 (47.8)</td>
<td>99 (43.2)</td>
<td>Sex, n (%) male</td>
<td>59 (49.6)</td>
<td>113 (48.3)</td>
</tr>
<tr>
<td>Race, n (%) white</td>
<td>94 (81.7)</td>
<td>182 (79.5)</td>
<td>Race, n (%) white</td>
<td>102 (85.7)</td>
<td>192 (82.1)</td>
</tr>
<tr>
<td>BMI, mean (SD) kg/m²</td>
<td>27.2 (4.9)</td>
<td>27.6 (5.8)</td>
<td>BMI, mean (SD) kg/m²</td>
<td>28.4 (5.5)</td>
<td>27.3 (5.0)</td>
</tr>
<tr>
<td><strong>Disease characteristics</strong></td>
<td></td>
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<td><strong>Disease characteristics</strong></td>
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<tr>
<td>Sweat production, mean (SD), mg/5 min</td>
<td>170.3 (164.2)</td>
<td>182.9 (266.9)</td>
<td>Sweat production, mean (SD), mg/5 min</td>
<td>181.9 (160.1)</td>
<td>162.3 (149.5)</td>
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<tr>
<td>ASDD, mean (SD)</td>
<td>7.1 (1.7)</td>
<td>7.3 (1.6)</td>
<td>ASDD, mean (SD)</td>
<td>7.2 (1.6)</td>
<td>7.3 (1.6)</td>
</tr>
<tr>
<td>HDSS 3, n(%)</td>
<td>84 (73.0)</td>
<td>133 (58.1)</td>
<td>HDSS 3, n(%)</td>
<td>71 (59.7)</td>
<td>144 (61.5)</td>
</tr>
<tr>
<td>HDSS 4, n(%)</td>
<td>31 (27.0)</td>
<td>96 (41.9)</td>
<td>HDSS 4, n(%)</td>
<td>47 (39.5)</td>
<td>90 (38.5)</td>
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</tbody>
</table>

ASDD: Axillary Sweating Daily Diary; BMI: Body Mass Index; HDSS: Hyperhidrosis Disease Severity Scale; SD: Standard Deviation; VEH: Vehicle
ASDD Response Rate (≥4-point Improvement) at Week 4
Primary Endpoint

ATMOS-1

VEH (n=115)
28.3

DRM04 (n=229)
p<0.001
52.8

ATMOS-2

VEH (n=119)
26.9

DRM04 (n=234)
p<0.001
66.1

ITT population; MCMC multiple imputation; p-value calculated DRM04 vs vehicle using Cochran-Mantel-Haenszel test stratified by analysis center; VEH: Vehicle
Absolute Change in Sweat Production at Week 4
Primary Endpoint

**ATMOS-1**

- **VEH (n=115)**
  - Mean absolute change from baseline: -91.9 mg/5 min
  - P-value: 0.065

- **DRM04 (n=229)**
  - Mean absolute change from baseline: -104.9 mg/5 min

**ATMOS-2**

- **VEH (n=119)**
  - Mean absolute change from baseline: -92.2 mg/5 min
  - P-value: <0.001

- **DRM04 (n=234)**
  - Mean absolute change from baseline: -110.3 mg/5 min

ITT population; MCMC multiple imputation; p-value calculated DRM04 vs vehicle using ANCOVA model with factors of treatment group and analysis center and a covariate of baseline gravimetrically-measured sweat production. ATMOS-1 analysis based on rank transformed data; VEH: Vehicle.
Absolute Change in Sweat Production at Week 4
ATMOS-1 sensitivity analysis

As outlined in the pre-specified statistical analysis plan, a sensitivity analysis was conducted that led to the exclusion of an analysis center with extreme outlier data for the gravimetric measurement of sweat.

The excluded analysis center consisted of 14 patients:
- 9 DRM04 3.75%
- 5 vehicle only

ITT population excluding analysis center with extreme outlier data; MCMC multiple imputation; p-value calculated DRM04 vs vehicle using ANCOVA model with factors of treatment group and analysis center and a covariate of baseline gravimetrically-measured sweat production; VEH: Vehicle
Change in DLQI from Baseline at Week 4
Other pre-specified efficacy endpoint

**ATMOS-1**

<table>
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<tr>
<th></th>
<th>VEH (n=115)</th>
<th>DRM04 (n=229)</th>
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<tbody>
<tr>
<td>Mean change from baseline</td>
<td>-4.3</td>
<td>-8.1</td>
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<tr>
<td>p-value</td>
<td>p&lt;0.001</td>
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**ATMOS-2**

<table>
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<th>DRM04 (n=234)</th>
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<tbody>
<tr>
<td>Mean change from baseline</td>
<td>-5.0</td>
<td>-8.6</td>
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<tr>
<td>p-value</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
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ITT population; no imputation for missing data; p-value calculated DRM04 vs vehicle using ANCOVA model with factors of treatment group and analysis center and a covariate of baseline DLQI score; VEH: Vehicle
### ATMOS-1 and ATMOS-2 Adverse Events to Week 4

#### Summary

<table>
<thead>
<tr>
<th></th>
<th>ATMOS-1</th>
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<th>ATMOS-2</th>
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<tbody>
<tr>
<td></td>
<td>VEH (n=114)</td>
<td>DRM04 (n=227)</td>
<td>VEH (n=118)</td>
<td>DRM04 (n=232)</td>
</tr>
<tr>
<td>Any TEAE, n(%)</td>
<td>33 (28.9)</td>
<td>123 (54.2)</td>
<td>42 (35.6)</td>
<td>134 (57.8)</td>
</tr>
<tr>
<td>Drug-related TEAE</td>
<td>18 (15.8)</td>
<td>77 (33.9)</td>
<td>20 (16.9)</td>
<td>102 (44.0)</td>
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<td>TEAE by intensity</td>
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<td></td>
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<tr>
<td>Mild</td>
<td>22 (19.3)</td>
<td>79 (34.8)</td>
<td>31 (26.3)</td>
<td>91 (39.2)</td>
</tr>
<tr>
<td>Moderate</td>
<td>11 (9.6)</td>
<td>43 (18.9)</td>
<td>11 (9.3)</td>
<td>40 (17.2)</td>
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<tr>
<td>Severe</td>
<td>0</td>
<td>1 (0.4)</td>
<td>0</td>
<td>3 (1.3)</td>
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<td>Discontinuations due to TEAE</td>
<td>1 (0.9)</td>
<td>8 (3.5)</td>
<td>0</td>
<td>9 (3.9)</td>
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<tr>
<td>Serious TEAE</td>
<td>0</td>
<td>1 (0.4)</td>
<td>0</td>
<td>1* (0.4)</td>
</tr>
</tbody>
</table>

* Considered not related to study drug.

Serious TEAEs: ATMOS 1: Moderate unilateral mydriasis, considered related to study drug; ATMOS:2: Moderate dehydration, considered not related to study drug. TEAE: Treatment Emergent Adverse Events; VEH: Vehicle.
### ATMOS-1 and ATMOS-2 Adverse Events to Week 4

**Anticholinergic Related TEAE reported in >2% patients**

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<td>33 (28.9)</td>
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<td>134 (57.8)</td>
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<tr>
<td>Anticholinergic Related TEAE reported in &gt;2% patients</td>
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<tr>
<td>Dry mouth</td>
<td>4 (3.5)</td>
<td>43 (18.9)</td>
<td>9 (7.6)</td>
<td>68 (29.3)</td>
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<tr>
<td>Mydriasis</td>
<td>0</td>
<td>15 (6.6)</td>
<td>0</td>
<td>16 (6.9)</td>
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<td>Urinary hesitation</td>
<td>0</td>
<td>5 (2.2)</td>
<td>0</td>
<td>11 (4.7)</td>
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<td>Dry eye</td>
<td>0</td>
<td>2 (0.9)</td>
<td>1 (0.8)</td>
<td>9 (3.9)</td>
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<td>Vision blurred</td>
<td>0</td>
<td>8 (3.5)</td>
<td>0</td>
<td>8 (3.4)</td>
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<td>Nasal dryness</td>
<td>1 (0.9)</td>
<td>5 (2.2)</td>
<td>0</td>
<td>7 (3.0)</td>
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<td>Constipation</td>
<td>0</td>
<td>4 (1.8)</td>
<td>0</td>
<td>5 (2.2)</td>
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<tr>
<td>Urinary retention</td>
<td>0</td>
<td>1 (0.4)</td>
<td>0</td>
<td>6 (2.6)</td>
</tr>
</tbody>
</table>

*Table represents n(%) of patients experiencing one or more incidences of each TEAE. TEAE: Treatment Emergent Adverse Events; VEH: Vehicle.*
Conclusions

• Topically applied DRM04 demonstrated clinically meaningful improvements in disease severity and reductions in sweat production.

• A 4-week daily application of DRM04 was well-tolerated in patients with primary axillary hyperhidrosis.
Acknowledgments

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Back-up slides
ATMOS-1 and ATMOS-2 Prohibited Treatments

- The following medications and treatments were prohibited during the study:
  - Concomitant treatment for axillary hyperhidrosis (e.g. iontophoresis)
  - Non-prescription or prescription antiperspirants containing aluminum chloride or other metallic salts
  - Initiation of or change in dose of medications with topical or systemic anticholinergic effects, centrally acting alpha 2 adrenergic agonists (e.g. clonidine, guanabenz, methyldopa), or beta-blockers
  - IV, oral or topical glycopyrrolate treatment
  - Agents that promote axillary drying (e.g. powders)