Safety, Tolerability and Efficacy of a Topical Treatment (SM04554) for Androgenetic Alopecia (AGA): Results from a Phase 2 Trial

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Disclosure of Relationships with Industry

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F065 - Late-breaking Research - Procedural Dermatology

**Disclosures**

All authors are employees of Samumed, LLC

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The Wnt (wingless & int1) Pathway

- Highly conserved across all animals
- Controls stem cell differentiation
- Implicated in tissue development & regeneration

SM04554 Increases the Number of Follicles/mm\(^2\) in Mice

Vehicle

Vehicle

SM04554

SM04554

Vehicle

SM04554

Alopecia-Hair Growth Study
3 Day Post Treatment Start

Follicles/mm\(^2\) (Mean ± SEM)

Vehicle

SM04554

n=4 mice/group, 6 sections/mouse
* p<0.05 (t-test)

Samumed Data on File
Primary subject characteristics
- Men age 18 to 55 years
- Androgenetic Alopecia (AGA)
- NH Classification score 4, 5, 5A, 5V, or 6

Treatment Groups
- Vehicle (n=100)
- 0.15% SM04554 (n=100)
- 0.25% SM04554 (n=100)

Safety: Vital signs, ECGs, Clinical lab sampling, Scalp safety assessment, Physical exam, AEs
Clinical/Imaging Outcomes: Macro photography, Scalp assessment for hair growth (Investigator), Subject quality of life assessed by KAP, Subject MHGQ
SM04554 Phase 2 Study – Disposition

Randomized
N=310

Vehicle
N=100 (ITT)
Completed Study N=76
Withdrawn from Study N=24
Discontinued Before Treatment: 2
Adverse Event: 12
Lost to Follow-up: 1
Subject Non-Compliance: 3
Subject Withdrawal: 6
Other: 0

0.15% SM04554
N=104 (ITT)
Completed Study N=74
Withdrawn from Study N=30
Discontinued Before Treatment: 2
Adverse Event: 11
Lost to Follow-up: 4
Subject Non-Compliance: 10
Subject Withdrawal: 2
Other: 1

0.25% SM04554
N=106 (ITT)
Completed Study N=77
Withdrawn from Study N=29
Discontinued Before Treatment: 4
Adverse Event: 13
Lost to Follow-up: 4
Subject Non-Compliance: 3
Subject Withdrawal: 5
Other: 0

Samumed Data on File
# SM04554 Phase 2 Study – Baseline Demographics and Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Vehicle</th>
<th>0.15% SM04554</th>
<th>0.25% SM04554</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (Safety Population)</td>
<td>98</td>
<td>102</td>
<td>102</td>
</tr>
<tr>
<td>Age at Consent (Years)</td>
<td>45.0 (8.6)</td>
<td>44.2 (8.2)</td>
<td>44.7 (8.8)</td>
</tr>
<tr>
<td>Race [N(%)]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>90 (91%)</td>
<td>89 (87%)</td>
<td>88 (86%)</td>
</tr>
<tr>
<td>Black</td>
<td>6 (6%)</td>
<td>10 (10%)</td>
<td>10 (10%)</td>
</tr>
<tr>
<td>Norwood-Hamilton [N(%)]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>35 (36%)</td>
<td>29 (28%)</td>
<td>36 (35%)</td>
</tr>
<tr>
<td>5</td>
<td>17 (17%)</td>
<td>9 (9%)</td>
<td>14 (14%)</td>
</tr>
<tr>
<td>5A</td>
<td>22 (22%)</td>
<td>18 (18%)</td>
<td>11 (11%)</td>
</tr>
<tr>
<td>5V</td>
<td>14 (14%)</td>
<td>26 (26%)</td>
<td>22 (22%)</td>
</tr>
<tr>
<td>6</td>
<td>10 (10%)</td>
<td>20 (20%)</td>
<td>19 (19%)</td>
</tr>
</tbody>
</table>
SM04554 Phase 2 Study – Adverse Events Definitions

• All events identified by Investigator Scalp Assessment with an increase in score were to become adverse events (AEs)
  – Investigators actively assessed all subjects for erythema, scaling, pruritus/itching, and burning/stinging, each on a 5 point scale

• Dose limiting Toxicities (DLTs) were defined as a subset of AEs and recorded as follows:
  – Any new onset systemic AE ≥ Grade 2
  – Any new onset local AE ≥ Grade 3
  – A systemic AE does not occur in the treatment area; a local AE occurs in the treatment area
  – All such events were to be deemed related to study medication
  – All subjects with a DLT were withdrawn from the study
SM04554 Phase 2 Study – Adverse Event Summary

- 240 AEs were experienced by 137 subjects
  - 94 in the Vehicle group
  - 75 in the 0.15% SM04554 group
  - 71 in the 0.25% SM04554 group

- Most Common Related AEs
  - Application Site Erythema*: 19 events; 5 in Vehicle, 6 in 0.15% and 8 in 0.25%
  - Application Site Pruritus*: 18 events; 6 in Vehicle, 7 in 0.15% and 5 in 0.25%
  - Application Site Paresthesia* [burning/stinging and tingling]: 16 events; 6 in Vehicle, 7 in 0.15% and 3 in 0.25%

- Laboratory parameters, ECGs and vital signs were unremarkable during the study and no clinically significant values or changes from baseline were reported in any of the subjects

*AEs identified by Investigator Scalp Assessment
SM04554 Phase 2 Study – Dose Limiting Toxicities

- 44 systemic DLTs reported by 37 subjects
  - 17 DLTs reported by 12 subjects in the Vehicle group
  - 11 DLTs reported by 11 subjects in the 0.15% SM04554 group
  - 16 DLTs reported by 14 subjects in the 0.25% SM04554 group

- No local DLTs reported

- 1 SAE of ‘small bowel obstruction’ in the Vehicle group, recorded as related per DLT definition
# SM04554 Phase 2 Study – Dose Limiting Toxicities

## DLTs reported more than once in aggregate

<table>
<thead>
<tr>
<th>Dose Limiting Toxicity</th>
<th>Vehicle</th>
<th>0.15% SM04554</th>
<th>0.25% SM04554</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinusitis</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Upper Respiratory Infection</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>ALT increased</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>AST increased</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

## DLTs reported once

- **Vehicle**: abdominal pain, constipation, small intestinal obstruction, gastroenteritis, influenza, laryngitis, localized infection, hyperlipidemia
- **0.15% SM04554**: conjunctivitis, tooth impacted, toothache, pharyngitis, skin infection, tooth abscess, basal cell carcinoma
- **0.25% SM04554**: nausea, gingival infection, orchitis, tooth infection, clavicle fracture, muscle strain, arthralgia, headache, renal pain, rhinitis allergic, skin mass
### SM04554 Phase 2 Study – Hair Count and Density (ITT)

#### Hair Count (in 1 cm$^2$)

<table>
<thead>
<tr>
<th></th>
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<th>0.25% SM04554</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td>Mean (SE; n)</td>
<td>114.3 (5.8; 90)</td>
<td>104.9 (5.7; 92)</td>
</tr>
<tr>
<td><strong>Day 90</strong></td>
<td>Mean (SE; n)</td>
<td>115.7 (6.8; 77)</td>
<td>110.5 (6.6; 74)</td>
</tr>
<tr>
<td><strong>Day 135</strong></td>
<td>Mean (SE; n)</td>
<td>111.5 (7.0; 71)</td>
<td>115.0 (6.8; 74)</td>
</tr>
</tbody>
</table>

#### Hair Density (µm in 1 cm$^2$)

<table>
<thead>
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<th>0.25% SM04554</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td>Mean (SE; n)</td>
<td>6141.2 (327.6; 90)</td>
<td>5656.0 (337.4; 92)</td>
</tr>
<tr>
<td><strong>Day 90</strong></td>
<td>Mean (SE; n)</td>
<td>6014.5 (370.7; 77)</td>
<td>5774.5 (372.4; 74)</td>
</tr>
<tr>
<td><strong>Day 135</strong></td>
<td>Mean (SE; n)</td>
<td>5722.5 (375.2; 71)</td>
<td>5992.4 (381.5; 74)</td>
</tr>
</tbody>
</table>
SM04554 Phase 2 Study – Change in Mean Hair Count

Change from Baseline

Day 90 (End of dosing)  Day 135

Mean Hair Count ± SEM [ITT]

Vehicle  0.15% SM04554  0.25% SM04554

Change from Day 90

Day 135

Mean Hair Count ± SEM [ITT]

Vehicle  0.15% SM04554  0.25% SM04554

* P=0.025 [ANCOVA adjusting for Day 90, Medication Use (%), Age, and Norwood-Hamilton 5A, 5V and 6 at screening]

Count = the total number of hairs in the target area (1 cm²)

ITT analysis; analysis not powered for efficacy and comparison to Vehicle
Density = the total width of all detected/measured hairs in the target area (1 cm$^2$)

ITT analysis; analysis not powered for efficacy and comparison to Vehicle
SM04554 Phase 2 Study – Summary

- SM04554 appeared to be safe, well-tolerated, and potentially efficacious
  - 302 subjects were exposed
  - 77 related AEs, 44 DLTs and 1 SAE (Vehicle) were reported

- At Day 135, when compared to day 90, significant differences were observed between the 0.15% SM04554 and Vehicle groups for:
  - Change in mean hair count (P=0.025)
  - Change in mean hair density (P=0.011)

- Further studies are being conducted to evaluate safety, efficacy, and appropriate dosing regimen
Thank you