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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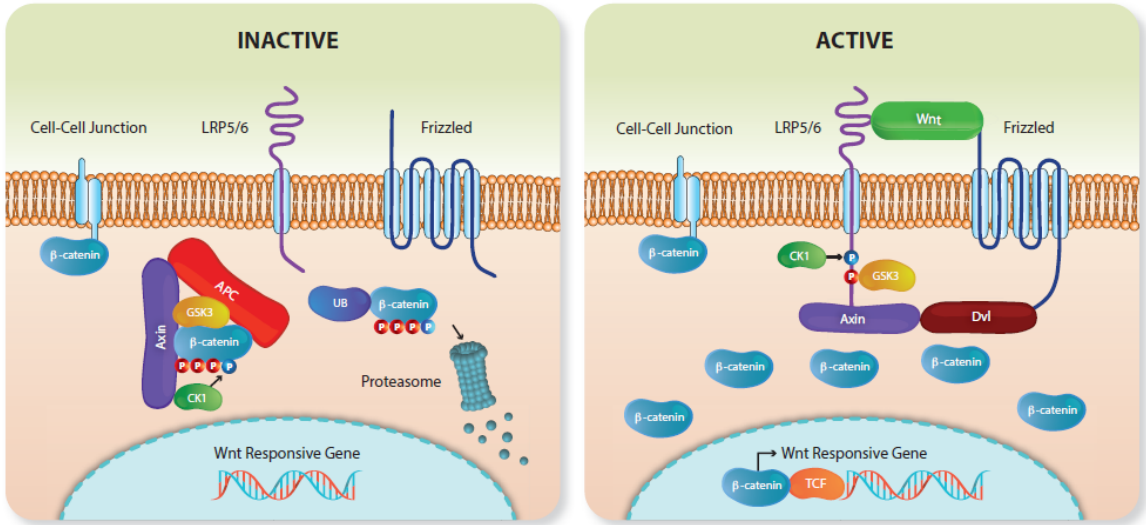
Wnt Signaling Pathway

The Wnt (wingless & int1) Pathway

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



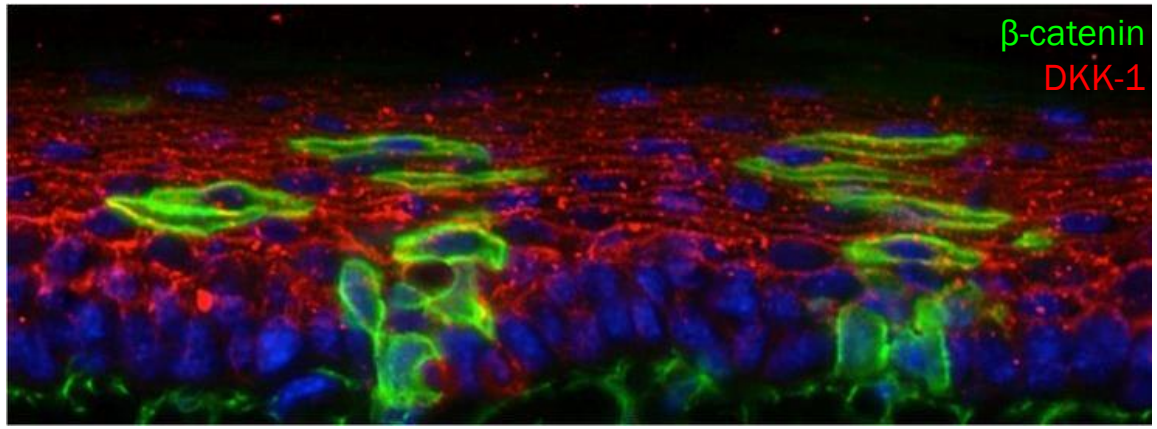


Image from Lim, et al. *Science.* 2013;342:1226-30.

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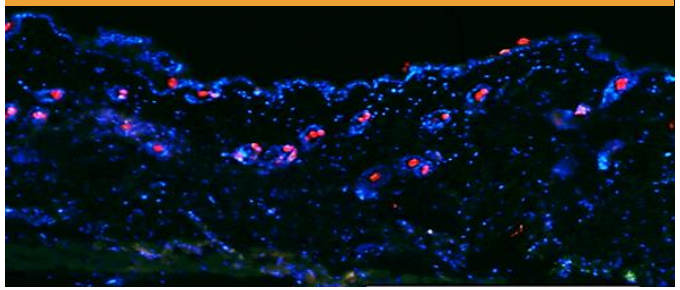
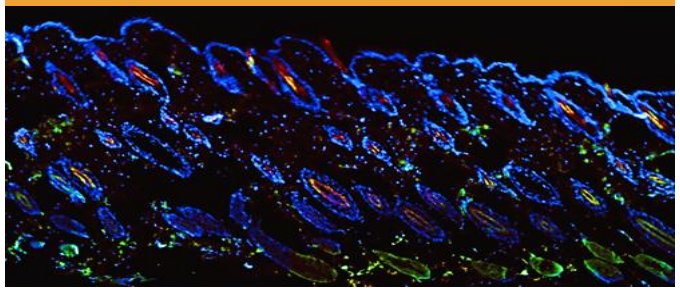
SM04554 Increases the Number of Follicles/mm^2 in Mice

Vehicle



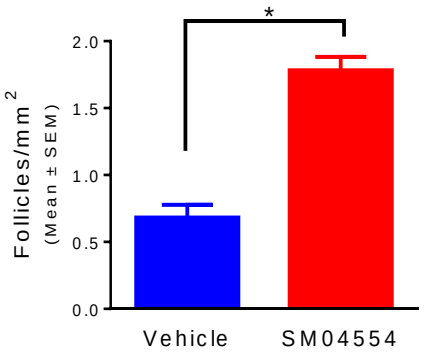
SM04554



Vehicle

SM04554

Alopecia-Hair Growth Study
3 Day Post Treatment Start



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

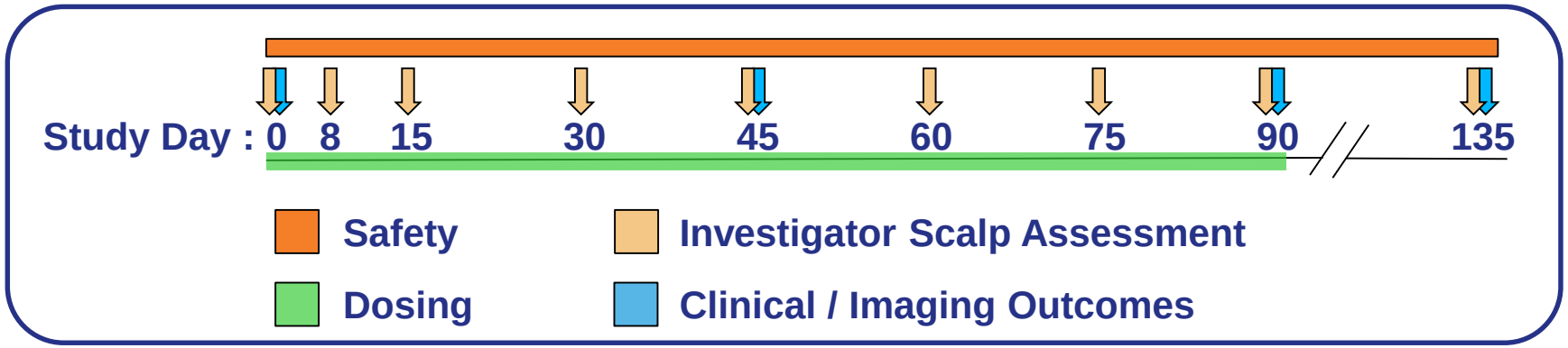
SM04554 Phase 2 Study – Trial Design

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

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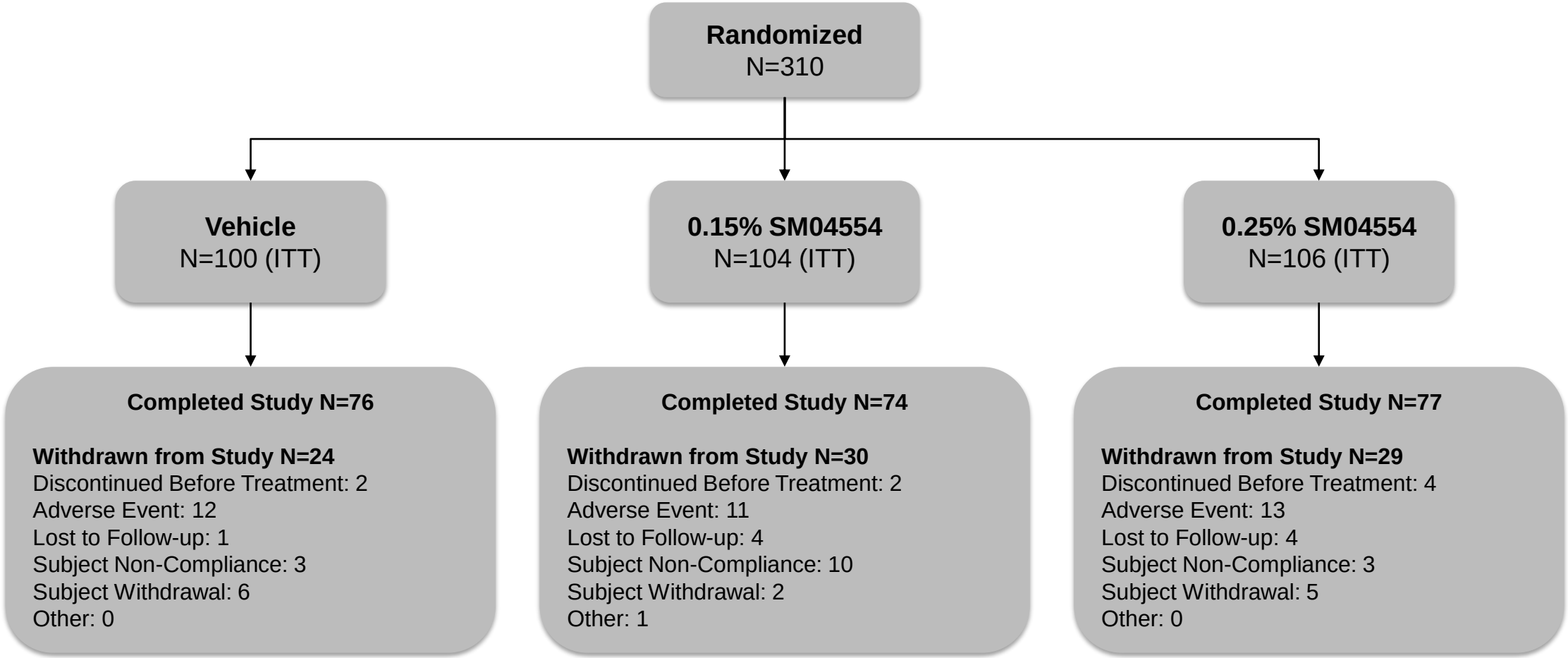
SM04554 Phase 2 Study – Disposition



SM04554 Phase 2 Study – Baseline Demographics and Characteristics

	Vehicle	0.15% SM04554	0.25% SM04554
N (Safety Population)	98	102	102
Age at Consent (Years) [Mean (SD)]	45.0 (8.6)	44.2 (8.2)	44.7 (8.8)
Race [N(%)]			
White	90 (91%)	89 (87%)	88 (86%)
Black	6 (6%)	10 (10%)	10 (10%)
Norwood-Hamilton [N(%)]			
4	35 (36%)	29 (28%)	36 (35%)
5	17 (17%)	9 (9%)	14 (14%)
5A	22 (22%)	18 (18%)	11 (11%)
5V	14 (14%)	26 (26%)	22 (22%)
6	10 (10%)	20 (20%)	19 (19%)

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

Dose Limiting Toxicity	Vehicle	0.15% SM04554	0.25% SM04554
Sinusitis	3	0	1
Upper Respiratory Infection	0	1	2
Hyperglycemia	2	0	1
Diarrhea	1	1	0
Bronchitis	1	1	0
ALT increased	1	1	0
AST increased	1	0	1

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

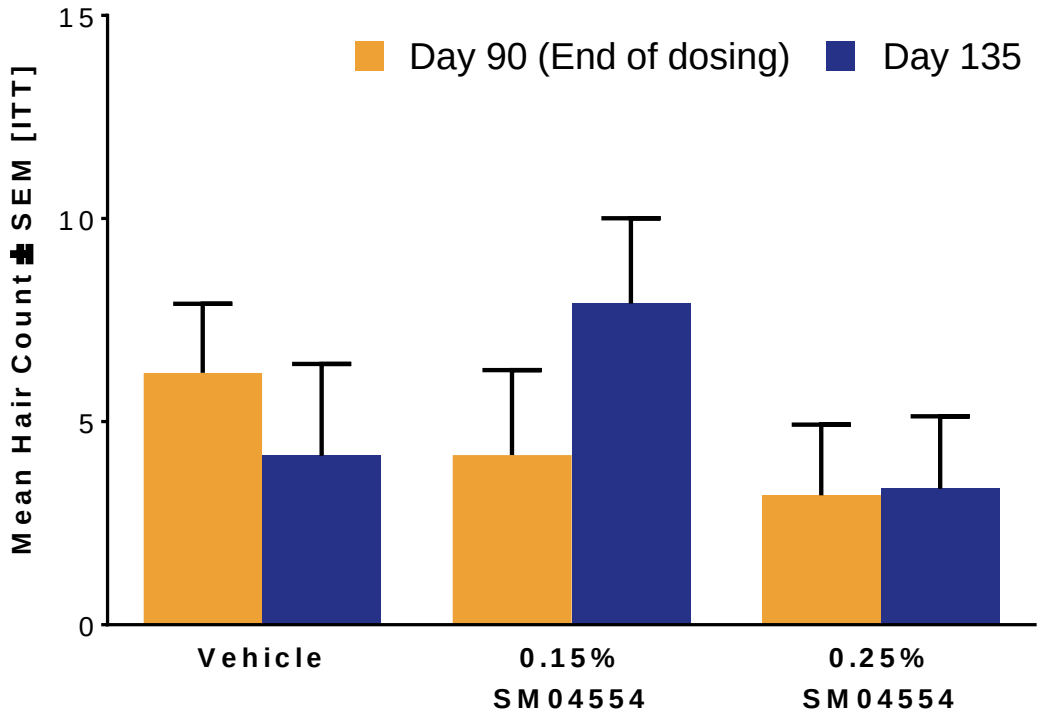
SM04554 Phase 2 Study – Hair Count and Density (ITT)

Hair Count (in 1 cm^2)		Vehicle	0.15% SM04554	0.25% SM04554
Baseline	Mean *(SE; n)*	114.3 (*5.8; 90*)	104.9 (*5.7; 92*)	110.8 (*6.4; 97*)
Day 90	Mean *(SE; n)*	115.7 (*6.8; 77*)	110.5 (*6.6; 74*)	117.3 (*8.0; 82*)
Day 135	Mean (*SE; n*)	111.5 (*7.0; 71*)	115.0 (*6.8; 74*)	118.5 (*8.0; 79*)

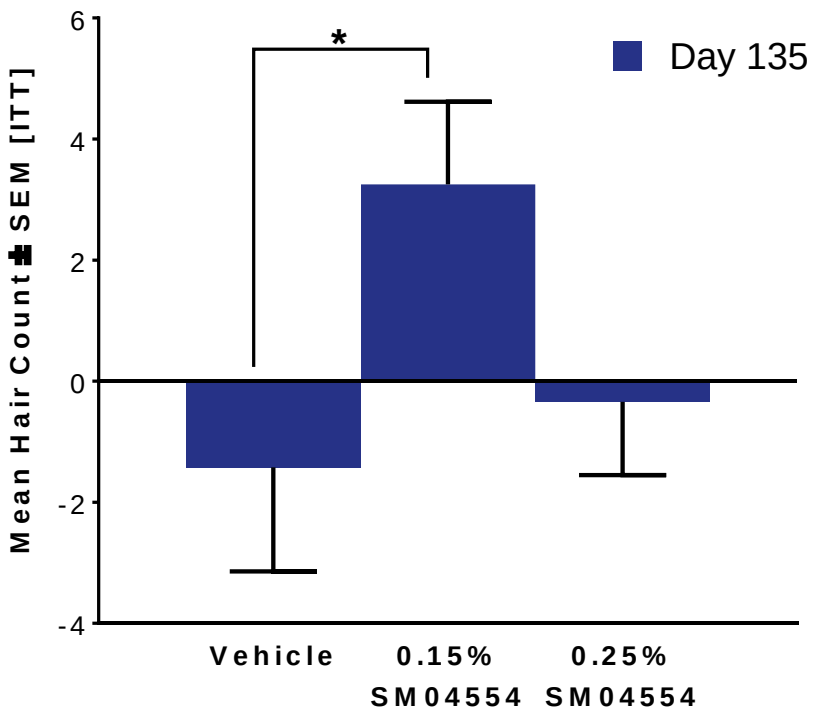
Hair Density (µm in 1 cm^2)		Vehicle	0.15% SM04554	0.25% SM04554
Baseline	*Mean (SE; n)*	6141.2 (*327.6; 90*)	5656.0 (*337.4; 92*)	6055.7 (*392.1; 97*)
Day 90	*Mean (SE; n)*	6014.5 (*370.7; 77*)	5774.5 (*372.4; 74*)	6277.6 (*453.0; 82*)
Day 135	*Mean (SE; n)*	5722.5 (*375.2; 71*)	5992.4 (*381.5; 74*)	6337.4 (*459.3; 79*)

SM04554 Phase 2 Study – Change in Mean Hair Count

Change from Baseline



Change from Day 90



* 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 cm^2)
ITT analysis; analysis not powered for efficacy and comparison to Vehicle

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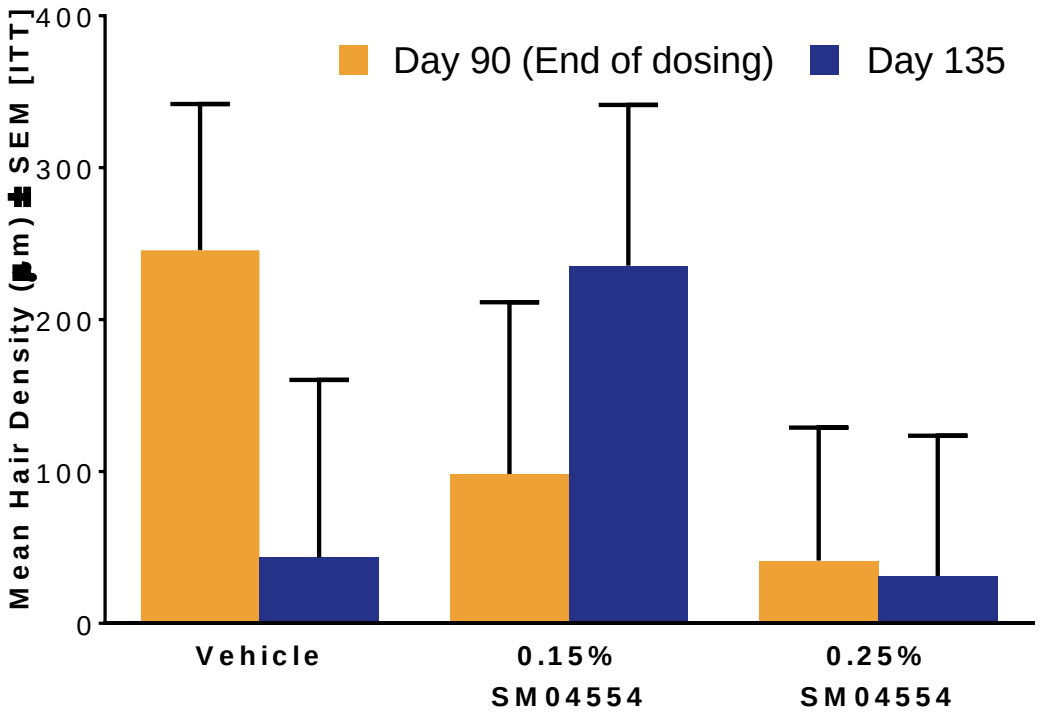
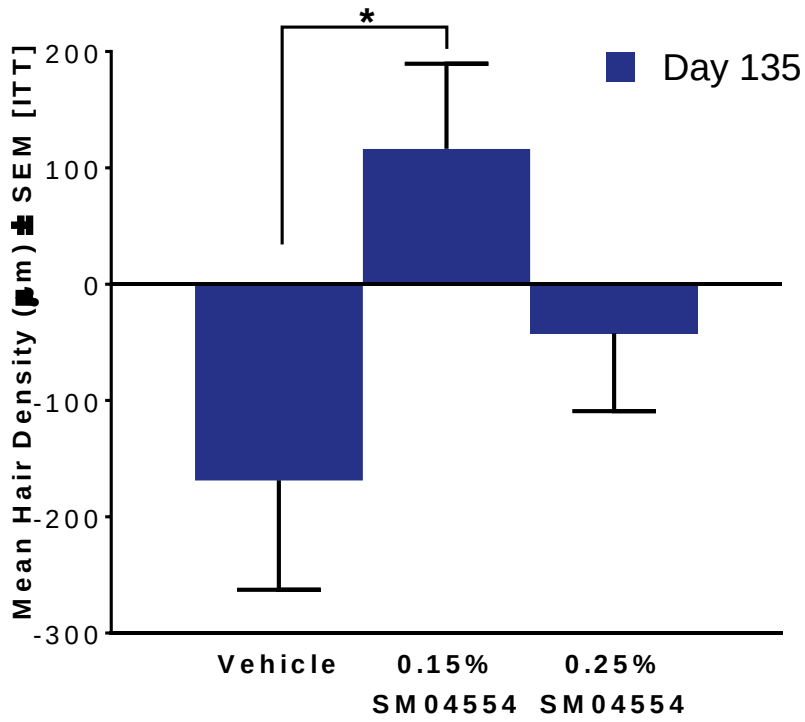
SM04554 Phase 2 Study – Change in Mean Hair Density

Change from Baseline



Change from Day 90



* P=0.011 [ANCOVA adjusting for Day 90, Medication Use (%), Age, and Norwood-Hamilton 5A, 5V and 6 at screening]

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

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