**Title**: Safety and Efficacy of a Topical Treatment (SM04554) for Androgenetic Alopecia (AGA): Results from a Phase 1 Trial

**Introduction**: AGA, a form of hair loss impacting approximately 35 million men in the US, has received only two US drug approvals in the last 15 years. SM04554 is a novel small molecule, topical scalp treatment for AGA targeting the Wnt pathway, a pathway known to regulate hair growth. This abstract summarizes the analysis of a randomized, double-blind, placebo-controlled, single-center trial assessing safety and efficacy of SM04554 in treating AGA.

**Methods**: Male subjects were treated topically once daily for 14 days with either 0.05%, 0.15% or 0.45% SM04554 solution or vehicle; subjects returned 14 days post--treatment for final evaluation. Safety data, including pharmacokinetics (PK), electrocardiogram (ECG), laboratory parameters, application site assessments and vital signs, were collected throughout treatment, with subject--reported efficacy outcomes[1] collected at end of study.

**Results**: 29 subjects (0.05% n=7, 0.15% n=8, 0.25% n=8, vehicle n=6, average age 44.6) were enrolled; 13 (45%) had a Norwood--Hamilton score of 5 (range 4-7). 15 treatment--emergent adverse events (TEAEs) were reported by 11 (38%) subjects; 4 (67%) of the vehicle group reported TEAEs, compared to 1 (14%) in the 0.05% group, 4 (50%) in the 0.15% group, and 2 (25%) in the 0.45% group. The most frequently reported TEAE was eye irritation / hyperaemia (N=2 [7%]). ECGs, labs and vital signs were unremarkable with no clinically significant changes from baseline reported in any subject. One vehicle subject presented with minimal scalp erythema; no other subject reported application site irritation. No serious adverse events were reported. Day 14 PK was dose--dependent. No subjects had detectable SM04554 concentration in the 0.05% group; 3 (38%) subjects had systemic exposure in 0.15% group (Tmax = 9 hours) and 7 (88%) had systemic exposure in 0.45% group (Tmax = 15 hours). In the 0.05% group, 4 (57%) reported slowing of hair loss and 2 (29%) reported hair growth; in the 0.15% group, 6 (75%) subjects reported slowing of hair loss and 3 (37%) reported hair growth; in the 0.45% group, 2 (25%) reported slowing of hair loss and 3 (37%) reported hair growth, compared to zero (P=0.01 for 0.15% group) and 1 (17%) of vehicle subjects, respectively, at end of study.

**Conclusions**: SM04554 appears to be safe, well--tolerated, and potentially efficacious. These results will help guide future AGA trials using this treatment.

References: 1. Barber BI. J Dermatolog Treat 1998; 9:181-6.

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