Tapinarof cream 1% once daily: significant efficacy in the treatment of atopic dermatitis in two pivotal phase 3 trials in adults and children down to 2 years of age

Authors: Jonathan I. Silverberg¹, Lawrence F. Eichenfield², Adelaide A. Hebert³, Eric Simpson⁴, Linda Stein Gold⁵, Robert Bissonnette⁶, Kim A. Papp⁷,⁸, John Browning⁹, Pearl Kwong¹⁰, Neil J. Korman¹¹, Philip M. Brown¹², David S. Rubenstein¹², Stephen C. Piscitelli¹², Matthew C. Somerville¹², Anna M. Tallman¹², Leon Kircik¹³,¹⁴

Affiliations:

¹The George Washington University School of Medicine and Health Sciences, Washington, DC, USA;
²University of California San Diego and Rady Children’s Hospital, San Diego, CA, USA;
³UTHealth McGovern School of Medicine and Children’s Memorial Hermann Hospital, Houston, TX, USA;
⁴Oregon Health & Science University, Portland, OR, USA;
⁵Henry Ford Health System, Detroit, MI, USA;
⁶Innovaderm Research Inc., Montreal, QC, Canada;
⁷Probitiy Medical Research Inc. and Alliance Clinical Trials, Waterloo, ON, Canada; ⁸University of Toronto, Toronto, ON, Canada;
⁹UT Health San Antonio, TX, USA;
¹⁰Solutions through Advanced Research, Jacksonville, FL, USA;
¹¹University Hospitals Cleveland Medical Center, Cleveland, OH, USA;
¹²Dermavant Sciences, Inc., Morrisville, NC, USA;
¹³Icahn School of Medicine at Mount Sinai, New York, NY, USA;
¹⁴Indiana University School of Medicine, Indianapolis, IN, USA
Abstract word count (excl. title, authors, author affiliations, references, or disclosures) = 494/600

Introduction: Tapinarof cream 1% once daily (QD) demonstrated efficacy versus vehicle and was well tolerated in adults and adolescents with moderate to severe atopic dermatitis (AD) in a previously reported phase 2 trial.

Objective: Here, we report pivotal phase 3 efficacy and safety results for tapinarof cream 1% QD in the treatment of adults and children down to 2 years of age with AD.

Materials and Methods: ADORING 1 and 2 were two identical phase 3, randomized, double-blind, vehicle-controlled trials. Eligibility criteria included a Validated Investigator Global Assessment for Atopic Dermatitis™ (vIGA-AD™) score of ≥3, Eczema Area and Severity Index (EASI) score of ≥6, and body surface area (BSA) involvement of 5–35%. Patients were randomized 2:1 to receive tapinarof cream 1% or vehicle cream QD for 8 weeks. The primary efficacy endpoint was vIGA-AD™ response, defined as a score of clear (0) or almost clear (1) and ≥2-grade improvement from baseline at Week 8. Secondary efficacy endpoints included ≥75% improvement in EASI score (EASI75) and proportion of patients (aged ≥12 years) with a baseline Peak Pruritus-Numerical Rating Scale (PP-NRS) score of ≥4 who achieved a ≥4-point reduction at Week 8. Adverse events (AEs) included rates of AEs of special interest (AESIs): contact dermatitis, follicular event, and headache.

Results: 407 and 406 patients aged 2–81 years were randomized in ADORING 1 and 2, respectively. At baseline, 84.0–89.9% of patients had a vIGA-AD™ score of 3 (moderate), mean EASI score of 12.5–13.3, and mean BSA affected of 16.7–16.9% across trials. At Week 8, both the primary and all secondary efficacy endpoints were met with statistical significance in the tapinarof groups versus vehicle: vIGA-AD™ response rates were 45.4% vs 13.9% and 46.4% vs 18.0% (both P<0.0001); EASI75 response rates were 55.8% vs 22.9% and 59.1% vs 21.2% (both P<0.0001); and a ≥4-point reduction in PP-NRS was achieved by 55.8% vs 34.2%
(P=0.0366) and 52.8% vs 24.1% (P=0.0015), in ADORING 1 and 2, respectively. AEs were mostly mild or moderate; the most frequent (≥5% in any group) were folliculitis, headache, and nasopharyngitis. Trial discontinuation rates due to AEs were lower with tapinarof versus vehicle (ADORING 1: 1.9% vs 3.6%; ADORING 2: 1.5% vs 3.0%, respectively). Rates of AESIs with tapinarof versus vehicle were: contact dermatitis 1.5% vs 2.2% and 1.1% vs 1.5%; follicular events 10.0% vs 0.7% and 8.9% vs 1.5%; and headache 7.0% vs 2.2% and 1.5% vs 0%, in each trial, respectively.

**Conclusions:** Tapinarof cream 1% QD demonstrated statistically significant efficacy compared with vehicle for primary and secondary efficacy endpoints in adults and children down to 2 years of age with AD. Tapinarof was well tolerated, with no new safety or tolerability signals. AEs were mostly mild to moderate and led to low rates of trial discontinuation, demonstrating the predictable safety profile of tapinarof cream 1% QD.

**Keywords (max 5):** tapinarof cream 1% QD, phase 3, efficacy, adults and children, well tolerated

**Funding Support:** Research was funded by Dermavant Sciences, Inc.