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One-year safety and efficacy of tapinarof cream for the treatment of plaque psoriasis: Results from the PSOARING 3 trial

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One-year safety and efficacy of tapinarof cream for the treatment of plaque psoriasis: Results from the PSOARING 3 trial

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Background: Tapinarof cream 1% once daily, an aryl hydrocarbon receptor-modulating agent, was significantly more efficacious than vehicle and well tolerated in two 12-week phase 3 trials in adults with mild to severe plaque psoriasis.

Objective: To assess long-term safety, efficacy, remittive effect, durability of response, and tolerability of tapinarof.

Methods: Patients completing the 12-week trials were eligible for 40-weeks' open-label treatment and 4-weeks' follow-up. Treatment was based on the Physician Global Assessment (PGA) score. Patients entering with PGA≥1 received tapinarof until PGA = 0. Patients with PGA = 0 discontinued tapinarof and were monitored for remittive effect. Patients with PGA≥2 were re-treated until PGA = 0.

Results: Overall, 91.6% (n = 763) of eligible patients enrolled; 40.9% of patients achieved complete disease clearance (PGA = 0), and 58.2% entering with PGA≥2 achieved PGA = 0 or 1. Mean duration of off therapy remittive effect for patients achieving PGA = 0 was 130.1 days. No new safety signals were observed. Most frequent adverse events were folliculitis (22.7%), contact dermatitis (5.5%), and upper respiratory tract infection (4.7%).

Limitations: Open-label; no control; may not be generalizable to all forms of psoriasis; remittive effect/response rate potentially underestimated.

Conclusions: Efficacy improved beyond the 12-week trials, with a 40.9% complete disease clearance rate, ~4-month off therapy remittive effect, durability on therapy, and consistent safety. (J Am Acad Dermatol 2022;87:800-6.)

Key words: plaque psoriasis; PSOARING 3 trial; remittive effect; tapinarof; therapeutic aryl hydrocarbon receptor (AhR)-modulating agent.

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INTRODUCTION

Topical therapies remain the mainstay for most patients with psoriasis across the spectrum of disease severity.[1] Existing topicals are efficacious and are routinely used alone and in combination therapy,[2-4] but most have restrictions on duration, extent, and sites of application due to potential adverse events (AEs).[1] Although controversial, tachyphylaxis (loss of effectiveness) is often reported after extended use of corticosteroids (>12 weeks).[4] Furthermore, psoriasis can recur after cessation of therapy, including corticosteroids or biologics.[4,5] No topicals with novel mechanisms of action had been approved by the Food and Drug Administration (FDA) for over 25 years, highlighting a need for efficacious topical therapies that address these limitations.[1,4] Tapinarof (VTAMA®; Dermavant Sciences, Inc) is a novel, first-in-class, small-molecule topical therapeutic aryl hydrocarbon receptor (AhR) agonist, FDA approved for the treatment of psoriasis[6] and under investigation for atopic dermatitis.[1] Tapinarof specifically binds and activates AhR, a ligand-dependent transcription factor that downregulates proinflammatory cytokines, including interleukin (IL)-17A and IL-17F, normalizes skin barrier protein expression, and increases antioxidant activity.[1] In a phase 2 trial, tapinarof cream 1% demonstrated limited systemic exposure under maximal-use conditions in patients with extensive psoriasis, up to 46% body surface area (%BSA) affected, indicating low potential for systemic AEs following topical application.[7] In 2 identically designed, phase 3, randomized, double-blind, vehicle-controlled, multicenter trials (PSOARING 1 and 2), tapinarof cream 1% once daily (QD) demonstrated clinically meaningful and statistically significant efficacy over 12 weeks in adults with mild to severe plaque psoriasis.[8] All primary and secondary endpoints were achieved with statistical significance and clinically meaningful improvements. In addition, tapinarof significantly and consistently improved patient-reported outcomes.[9] Furthermore, a remittive effect warranting further investigation was observed in a 12-week phase 2b trial, where efficacy was maintained for 4 weeks after discontinuation of tapinarof.[10]

Here, we report the results of PSOARING 3, the long-term, open-label, multicenter (US, Canada) extension trial of tapinarof cream 1% QD in adults with mild to severe plaque psoriasis.

CAPSULE SUMMARY

- Tapinarof cream 1% once daily was safe, well tolerated, and durably efficacious in patients with mild to severe psoriasis for up to 1 year, with 40.9% complete disease clearance rate, ~4-month remittive effect, and no tachyphylaxis.
- Tapinarof may represent a novel nonsteroidal topical therapy that addresses limitations of current therapies.

METHODS

Trial design

PSOARING 3 assessed the safety, efficacy, tolerability, durability of response on therapy (absence of tachyphylaxis), and duration of remittive effect off therapy of tapinarof cream 1% QD. Patients with plaque psoriasis received up to 40 weeks of open-label treatment, followed by 4-weeks' off treatment follow-up (Supplementary Fig 1, available via Mendeley at https://doi.org/10.17632/sgdn2s5yfc.2). Patients could receive tapinarof for up to 52 weeks from PSOARING 1 and 2 baseline through PSOARING 3 completion.

The trial was conducted according to Good Clinical Practice and the Declaration of Helsinki. Approval was obtained from local ethics committees/institutional review boards at each center. All patients provided written informed consent.

Trial participants

In PSOARING 3, eligible patients had completed 12-weeks treatment with tapinarof or vehicle in PSOARING 1 or 2 before enrolling. Patients were aged 18−75 years with chronic plaque psoriasis, were stable for at least 6 months before randomization, had %BSA affected of ≥3% and ≤20% (excluding scalp, palms, soles, fingernails, toenails), and had the Physician Global Assessment (PGA) score of 2 (mild), 3 (moderate), or 4 (severe) at screening. Full inclusion and exclusion criteria, previously reported for PSOARING 1 and 2,[8] are provided in Supplementary Table I, available via Mendeley at https://doi.org/10.17632/sgdn2s5yfc.2.

Trial treatment

In PSOARING 3, patients were treated based on their PGA score. Patients entering the trial having achieved complete disease clearance (PGA = 0 [clear]) after the 12-week pivotal trials discontinued treatment and were monitored for remittive effect, defined as maintenance of PGA score of 0 (clear) or 1 (almost clear) while off therapy.

Abbreviations used:

AE: adverse events
AhR: aryl hydrocarbon receptor
BSA: body surface area
IL: interleukin
PASI: Psoriasis Area and Severity Index
PGA: Physician Global Assessment

Patients entering with PGA≥1 were instructed to apply a thin layer of tapinarof 1% QD to all affected areas, including newly appearing lesions. During trial visits, patients applied tapinarof under supervision. Visits occurred every 4 weeks with a follow-up visit at Week 44 or 4 weeks after the last visit. Patients entering with, or achieving, PGA = 0 discontinued treatment and were observed for off-therapy remittive effect. If disease worsening occurred, defined as PGA≥2, tapinarof was restarted and continued until PGA = 0. This pattern of treatment, discontinuation upon PGA = 0, and retreatment continued until trial end. Therefore, patients could receive tapinarof continuously or intermittently.

Adherence was evaluated based on patient diaries and weight of tapinarof tubes used; the actual number of doses administered was compared with expected exposure. Patients were permitted, but not required, to treat fingernail, toenail, palm, sole, and scalp lesions; however, these areas were not assessed for efficacy.

Outcome measures and statistical analysis

Safety. Safety and tolerability assessments included incidence and frequency of AEs, patient- and investigator-assessed local tolerability, vital signs, physical examinations, and laboratory tests. AEs were assessed using Common Terminology Criteria for Adverse Events, version 5.0, where grade 1 corresponds to "mild" and grade 5 to "fatal." AEs of special interest based on previous trials were folliculitis, contact dermatitis, and headache.[8,10,11] Local tolerability was evaluated using a patient-reported 5-point scale of 0 (none) to 4 (strong/severe) for burning/stinging and itching and an investigator-assessed 5-point scale of 0 (no irritation) to 4 (very severe) for dryness, erythema, and peeling.

Efficacy. Efficacy endpoints included: the proportion of patients achieving complete disease clearance (PGA = 0) at any time during the trial; the total duration of remittive effect during the 44-week trial, defined as duration of efficacy maintenance (PGA = 0 or 1) while off therapy; the median duration of remittive effect in patients entering with PGA = 0; and the proportion of patients entering the trial with PGA≥2 who achieved a response, defined as PGA = 0 or 1 at any time during the trial. Due to the intermittent treatment regimen, patients could achieve PGA = 0 or a response more than once during the trial. Durability of response (absence of tachyphylaxis) with intermittent treatment over time was evaluated using independent measures of response while on treatment, including PGA score, %BSA, and Psoriasis Area and Severity Index (PASI) over the 40-week treatment period. PASI and % BSA assessments were modified, as patients were permitted, but not required, to treat fingernail, toenail, palm, sole, and scalp lesions; however, PASI and %BSA analyses did not include assessment of psoriasis in these areas.

Statistical analyses. Sample size was based on the International Council for Harmonization's E1 guideline on the extent of population exposure to assess clinical safety for drugs for long-term treatment of non-life-threatening conditions.[12] Approximately 850 patients were planned to be enrolled. Efficacy endpoints were summarized descriptively using observed cases and last observation carried forward in the intention-to-treat population. The time-to-event parameters were summarized using the Kaplan-Meier (KM) product limit method, using observed cases. Safety assessments were summarized descriptively in the intention-to-treat population.

RESULTS

Patient disposition and baseline characteristics

Of 833 eligible patients from PSOARING 1 and 2, 763 (91.6%) elected to enroll in PSOARING 3. Supplementary Table II, available via Mendeley at https://doi.org/10.17632/sgdn2s5yfc.2 reports patient disposition in PSOARING 3. At PSOARING 3 baseline, the mean age was 50.7 years, 58.7% were male, and 84.3% were White. At baseline, 10.4% of patients had PGA = 0, 21.1% had PGA = 1, 32.4% had PGA = 2, 32.6% had PGA = 3, and 3.0% had PGA = 4. Patients previously treated with tapinarof had lower baseline PGA scores than those treated with vehicle, reflecting the significant efficacy of tapinarof in the pivotal trials.

Mean %BSA was 4.7%, and the mean PASI was 4.8. Baseline disease characteristics are summarized in Supplementary Table III, available via Mendeley at https://doi.org/10.17632/sgdn2s5yfc.2, including by prior treatment in the pivotal trials. Baseline disease scores were lower in patients previously treated with tapinarof than in those treated with vehicle. Mean baseline %BSA was 3.3% in patients previously treated with tapinarof and 7.3% in patients previously treated with vehicle. At baseline, 42.9% of

patients previously treated with tapinarof had PGA = 0 or 1 compared with 8.6% of those who had received vehicle.

Safety, tolerability, and adherence

AEs were consistent with previous trials,[8,10] with no new safety signals identified during long-term treatment (Supplementary Table IV, available via Mendeley at https://doi.org/10.17632/sgdn2s5yfc.2). The most frequent treatment-emergent AEs included folliculitis (22.7%), contact dermatitis (5.5%), and upper respiratory tract infection (4.7%). The incidence and severity of folliculitis and contact dermatitis neither increased nor worsened with long-term treatment compared with the pivotal trials, and most of these AEs were mild or moderate. Trial discontinuation rates due to folliculitis or contact dermatitis were low (1.2% and 1.4%, respectively) and were similar to rates observed in the pivotal trials.[8]

Investigators assessed that >90% of patients had no irritation (score of 0) at all visits over the 40-week trial. Favorable tolerability was also demonstrated when tapinarof was applied on sensitive and intertriginous skin (Supplementary Fig 2, available via Mendeley at https://doi.org/10.17632/sgdn2s5yfc.2). Patient-reported burning/stinging and itching were rated as low (none, slight, or mild) by 86% to 92% of patients over 40 weeks. The number of doses administered compared with expected exposure (adherence) was approximately 90%.

Efficacy

Complete disease clearance (PGA = 0). At baseline, 10.4% (79/763) of patients had PGA = 0 (14.6% [74/508] of patients previously treated with tapinarof; 2.0% [5/255] of patients previously treated with vehicle). Overall, 40.9% (312/763) achieved complete disease clearance (PGA = 0) at least once during the trial. For patients entering with PGA≥1, 34.3% (233/680) achieved PGA = 0 at least once.

Response. In PSOARING 3, continued efficacy was observed with tapinarof 1% QD beyond that seen in the pivotal trials, indicating that maximal effect may not have been achieved by Week 12 in PSOARING 1 and 2. Overall, 58.2% (302/519) of patients entering PSOARING 3 with PGA≥2 achieved PGA = 0 or 1 at least once during the trial. Durability of response on therapy (no tachyphylaxis) was demonstrated for up to 52 weeks across the trials. With intermittent use of tapinarof, the proportion of patients achieving a PGA = 0 or 1 was consistent over time (Supplementary Fig 3, available via Mendeley at https://doi.org/10.17632/sgdn2s5yfc.2), with continued improvements in % BSA and PASI also observed (Supplementary Fig 4, available via Mendeley at https://doi.org/10.17632/sgdn2s5yfc.2). Patients previously randomized to vehicle in PSOARING 1 or 2 achieved similar responses in PSOARING 3 to those previously randomized to tapinarof.

PGA score by visit. In PSOARING 1 and 2, most tapinarof-treated patients (74.5-80.3%) achieved at least a 1-grade improvement in PGA score compared with 30.6-35.6% of vehicle-treated patients. In PSOARING 3, 73.3% of patients previously treated with vehicle achieved at least a 1-grade improvement in PGA score.

Remittive effect (duration of efficacy maintenance while off therapy). For the 79 patients entering PSOARING 3 with PGA = 0, the median duration of off-therapy remittive effect was 115 days (KM estimate; 95% confidence intervals, 85.0; 168.0) (Fig 1). The 25th and 75th KM-estimated percentiles were 57 and 222 days, respectively, indicating that 75% of patients entering the trial with PGA = 0 were likely to maintain efficacy off therapy for at least 57 days, while 25% of patients entering with PGA = 0 were likely to maintain efficacy off therapy for at least 222 days. Among patients entering PSOARING 3 with PGA = 0, 24.1% (19/79) did not require retreatment.

Among patients achieving PGA = 0 at any time during the trial (n = 312), the total duration of remittive effect off therapy was approximately 4 months (mean: 130.1 days [SD: 89.4]). For patients entering the trial with PGA = 0 (n = 79), the total duration of remittive effect was 188.3 (92.8) days. For patients entering the trial with PGA = 1 and achieving PGA = 0 at any time during the trial (n = 88), the total duration of remittive effect was 134.1 (86.5) days. Clinical images of tapinarof-treated patients across the pivotal trials and PSOARING 3 demonstrate an off-therapy remittive effect that persisted for 24 weeks during PSOARING 3 (Fig 2; Supplementary Fig 5, available via Mendeley at https://doi.org/10.17632/sgdn2s5yfc.2).

DISCUSSION

In PSOARING 3, tapinarof cream 1% QD demonstrated continued improvement in efficacy beyond that observed in the pivotal trials and was well tolerated with long-term use of up to 52 weeks. A high rate of complete disease clearance (40.9%), durability of response over time, and a remittive effect of ~4 months off therapy were demonstrated. Tachyphylaxis, which has been reported with topical corticosteroids and biologics,[4,13,14] was not observed with tapinarof for up to 52 weeks. The findings were consistent with those of previous phase 2 and 3 trials.[7,8,10]

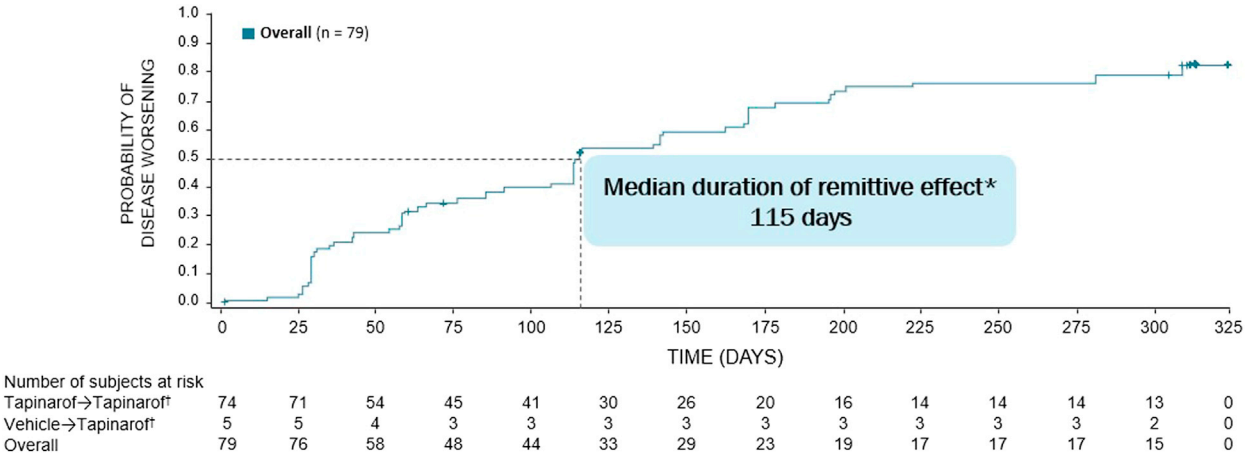

Fig 1. Duration of remittive effect among patients entering PSOARING 3 with a PGA score of 0 (clear): Maintenance of a PGA of 0 or 1 (almost clear) while off therapy. Intention-to-treat population, observed cases. *Duration of remittive effect defined as the duration of efficacy maintenance (PGA = 0 or 1) while off therapy (patients with disease worsening [PGA≥2] were retreated with tapinarof 1% QD until PGA = 0 was achieved). †Tapinarof→tapinarof, patients previously assigned to tapinarof in the pivotal trials who received tapinarof in PSOARING 3 based on PGA score; Vehicle→tapinarof, patients previously assigned to vehicle in the pivotal trials who received tapinarof in PSOARING 3 based on PGA score. For the total number of patients who entered with, or achieved, a PGA of 0 at any time during the trial (n = 312), the mean total duration of remittive effect while off therapy was 130.1 days. *PGA*, Physician Global Assessment; *QD*, once daily.

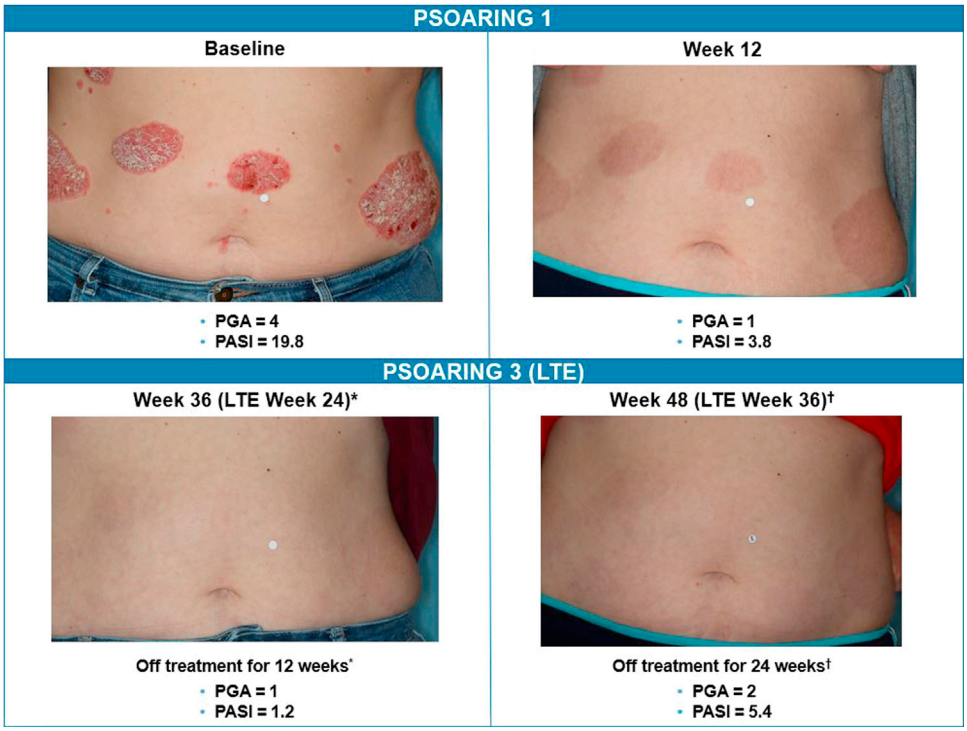

Fig 2. Clinical response, remittive effect, and durability in a patient with plaque psoriasis treated with tapinarof cream 1% QD: representative target lesions on a patient's torso. PGA and PASI are global efficacy assessments. Examples of representative target lesions of 1 tapinarof-treated patient from PSOARING 1 and 3 trials. Individual results may vary. *PSOARING 3 (LTE) Week 24: Off treatment for 12 weeks. Patient achieved PGA = 0 at Week 12 and tapinarof treatment was discontinued. †PSOARING 3 (LTE) Week 36: Off treatment for 24 weeks; re-treatment at PSOARING 3 (LTE) Week 36 due to disease worsening. *LTE*, Long-term extension; *PASI*, Psoriasis Area and Severity Index; *PGA*, Physician Global Assessment; *QD*, once daily.

The mechanism for the remittive effect with tapinarof may be explained by its specific binding and activation of AhR, a ligand-dependent transcription factor.[1] AhR activation has been shown to inhibit T-cell expansion and T helper 17 (Th17) cell differentiation and reduce IL-17 production in T-cell assays.[15] Ligand-dependent AhR activation has also been demonstrated to result in epigenetic modification of both the forkhead box P3 (FoxP3) and IL-17 gene promoters, leading to preferential differentiation of regulatory T cells and inhibition of Th17 cells.[16] Long-term persistence of tissue-resident memory T cells has also been shown to be AhR dependent,[17] and the remittive effect observed with tapinarof may additionally result from reduction in activity of these cells.[18]

With long-term treatment of up to 52-weeks duration, the incidence and severity of AEs, particularly folliculitis and contact dermatitis, were consistent with that previously reported in the 12-week pivotal trials and led to low trial discontinuation rates. Folliculitis was generally mild, with no severe events reported, leading to trial discontinuation in 1.2% of patients. Contact dermatitis was generally mild or moderate, with no severe events, leading to trial discontinuation in 1.4% of patients. Headache was reported with low frequency, with no trial discontinuations. Both patients and investigators reported a favorable local tolerability profile, even when tapinarof was applied to sensitive and intertriginous skin areas.

To characterize the long-term impact of tapinarof and provide real-world evidence on disease management, PSOARING 3 employed a unique forced-withdrawal design that resulted in intermittent treatment (treatment withdrawal when patients achieved PGA = 0). The forced-withdrawal design of this trial may have led to undertreatment, underestimating the percentage of patients who could have achieved a PGA of 0 or 1 at Week 40, had they received continuous treatment. Furthermore, right censoring of data may have resulted in underestimation of the duration of off-therapy remittive effect because trial end, rather than disease worsening, curtailed the duration of evaluation for some patients.

Other trial limitations include the open-label design and lack of a control group. As is possible with all extension trials, patients who opted to enroll might represent a self-selected, enriched population, with improved response and tolerability to treatment. Finally, while this trial assessed adults with mild to severe plaque psoriasis based on the PGA score, patients with %BSA <3% or >20% were excluded, and the results may not be generalizable to all forms or severities of psoriasis, or to children. A separate phase 3 trial (NCT05172726) evaluates tapinarof in children.

In summary, continuous and intermittent use of tapinarof cream 1% QD was safe and efficacious for up to 1 year in patients with mild to severe psoriasis. Durable efficacy on therapy and a substantial remittive effect of at least 4 months off therapy were demonstrated. Consequently, tapinarof cream 1% QD may represent a novel, nonsteroidal topical therapy for patients with plaque psoriasis that is effective and well tolerated with long-term use.

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Conflicts of interest

Dr Strober is a consultant (honoraria) for AbbVie, Alumis, Almirall, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Immunic Therapeutics, Bristol Myers Squibb, Connect Biopharma, Dermavant Sciences, Inc, EPI Health, Evelo Biosciences, Janssen, Leo, Eli Lilly, Maruho, Meiji Seika Pharma, Mindera Health, Novartis, Ono, Pfizer, UCB Pharma, Sun Pharma, Regeneron, Sanofi-Genzyme, Union Therapeutics, Ventyxbio, and vTv Therapeutics; a speaker for AbbVie, Eli Lilly, Incyte, Janssen, Regeneron, and Sanofi-Genzyme; an investigator for AbbVie, CorEvitas (formerly Corrona) Psoriasis Registry, Dermavant Sciences, Inc, Dermira, Cara, and Novartis; a scientific co-director (receiving consulting fee) for CorEvitas Psoriasis Registry; an Editor-in-chief (honorarium) for the *Journal of Psoriasis and Psoriatic Arthritis*; and owns stock options in Connect Biopharma and Mindera Health. Dr Stein Gold has served as a consultant and/or has received payment for the development of educational presentations and/or has received grants from Arcutis, Amgen, Bristol Myers Squibb, Dermavant Sciences, Inc, Eli Lilly, LEO Pharma, Ortho Dermatologics, Pfizer, and UCB Biopharma. Dr Bissonnette has served as a consultant/investigator/advisory board member for AbbVie, Alumis, Almirall, Amgen, AnaptysBio, Arcutis, Aristea, Bausch Health, Boehringer Ingelheim, Boston, Bristol Myers Squibb, Dermavant Sciences, Inc, Eli Lilly, Escalier, Janssen, Kyowa Kirin, LEO Pharma, Nimbus, Novartis, Pfizer, Regeneron, Sienna, and UCB; and is an employee and shareholder of Innovaderm Research. Dr Armstrong has served as a research investigator and/or scientific advisor to AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant Sciences, Inc, Dermira, EPI, Incyte, Janssen, LEO Pharma, Lilly, Modmed, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun, and UCB. Dr Kircik has served as a consultant/speaker/investigator/advisory board member for Abbott

Laboratories, AbbVie, Ablynx, Aclaris, Acambis, Allergan, Inc, Almirall, Amgen, Inc, Anacor Pharmaceuticals, Anaptys, Arcutis, Arena, Assos Pharma, Astellas Pharma US, Inc, Asubio, Bausch Health, Berlex Laboratories (Bayer HealthCare Pharmaceuticals), Biogen-Idec, Biolife, Biopelle, Bristol Myers Squibb, Boehringer Ingelheim, Breckinridge Pharma, Cassiopea, Centocor, Inc, Cellceutix, Cipher, Coherus, Colbar, Combinatrix, Connetics Corporation, Coria, Dermavant Sciences, Inc, Dermira, Dermik Laboratories, Dow Pharmaceutical Sciences, Inc, Dr Reddy's Lab, Dusa, Embil Pharmaceuticals, Eli Lilly, EOS, Exeltis, Ferndale Laboratories, Inc, Foamix, Ferrer, Galderma, Genentech, Inc, GlaxoSmithKline, PLC, Glenmark, Health Point, LTD, Idera, Incyte, Intendis, Innocutis, Innovail, Isdin, Johnson & Johnson, Kyowa Kirin, Laboratory Skin Care, Inc, LEO Pharma, L'Oréal, 3M, Maruho, Medical International Technologies, Merck, Medicis Pharmaceutical Corp., Merz, Nano Bio, Novartis AG, Noven Pharmaceuticals, Nucryst Pharmaceuticals Corp, Obagi, Onset, OrthoNeutrogena, PediaPharma, Pfizer, Promius, PuraCap, PharmaDerm, QLT, Inc, Quinnova, Quatrix, Regeneron, Sanofi, Serono (Merck Serono International SA), SkinMedica, Inc, Stiefel Laboratories, Inc, Sun Pharma, Taro, TolerRx, Triax, UCB, Valeant Pharmaceuticals Intl, Warner-Chilcott, XenoPort, and ZAGE. Dr Tyring has been an investigator for Dermavant Sciences, Inc. Drs Piscitelli, Brown, Rubenstein, and Tallman are employees of Dermavant Sciences Inc, with stock options. Dr Lebwohl has received grants and/or is a consultant for AbbVie, Amgen, Aditum Bio, Almirall, AltruBio Inc, AnaptysBio, Arcutis, Aristea Therapeutics, Arrive Technologies, Avotres, BiomX, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant Sciences, Inc, Dr Reddy's Laboratories, Eli Lilly, Evelo Biosciences, Evommune, Inc, Facilitation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Helsinn Therapeutics, Hexima Ltd, Incyte, Janssen Research & Development, LEO Pharma, LLC, Meiji Seika Pharma, Mindera, Ortho Dermatologics, Pfizer, Regeneron, Seanergy, UCB, Inc, and Verrica.

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