

Efficacy and Safety of Ruxolitinib Cream for the Treatment of Vitiligo: Week 24 Pooled Analysis of the TRuE-V Phase 3 Studies

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Introduction

- Vitiligo is a chronic autoimmune disease that targets melanocytes, resulting in patches of skin depigmentation¹ and reduced quality of life^{2,3}
- Disease pathogenesis is modulated by signaling through the Janus kinases (JAKs)⁴
- A cream formulation of ruxolitinib, a JAK1/JAK2 inhibitor, demonstrated substantial repigmentation over 52 weeks in a phase 2, dose-ranging, randomized study in adult patients with vitiligo (NCT03099304)⁵
- Following these promising results, two phase 3 Topical Ruxolitinib Evaluation in Vitiligo studies (TRuE-V1 and TRuE-V2) were conducted in larger patient populations

Objective

- To evaluate the efficacy and safety of ruxolitinib cream following 24 weeks of double-blind treatment using pooled data from two phase 3 studies of adults and adolescents with nonsegmental vitiligo (TRuE-V1 [NCT04052425], TRuE-V2 [NCT04057573])

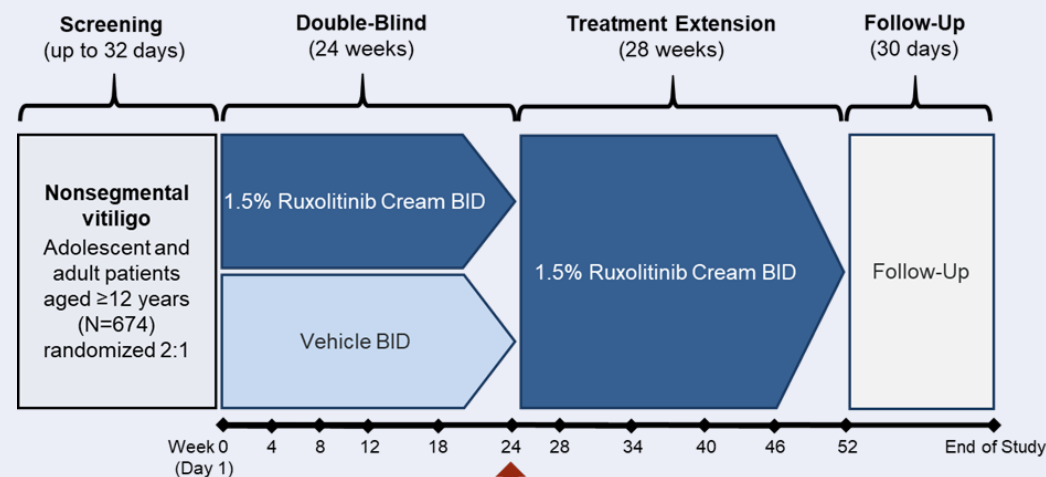
Methods

Patients and Study Design

- Eligible patients were aged ≥ 12 years with a diagnosis of nonsegmental vitiligo and depigmented areas covering $\leq 10\%$ total body surface area (BSA), including $\geq 0.5\%$ BSA on the face and $\geq 3\%$ BSA on non-facial areas, scores ≥ 0.5 on facial Vitiligo Area Scoring Index (F-VASI), and scores ≥ 3 on total VASI (T-VASI)

- Key exclusion criteria were the presence of complete leukotrichia within any facial lesions, dermatologic disease confounding vitiligo assessment, previous use of JAK inhibitor therapy, and use of the following therapies for vitiligo before baseline: any biological or experimental therapy within 12 weeks (or 5 half-lives), phototherapy within 8 weeks, immunomodulating treatments within 4 weeks, or topical treatments within 1 week
- Patients were stratified by geographic region (North America and Europe) and Fitzpatrick skin phototype (types I–II or types III–VI) and were randomized 2:1 to apply 1.5% ruxolitinib cream twice daily (BID) or vehicle BID for 24 weeks (**Figure 1**); pooled data per interim analyses at Week 24 are reported here
 - After completion of the Week 24 visit, all patients could apply 1.5% ruxolitinib cream BID for an additional 28 weeks in the open-label treatment extension

Figure 1. Study Design



BID, twice daily.

Double-blind efficacy and safety analyses (pooled)

Endpoints and Assessments

- The primary endpoint was the proportion of patients achieving $\geq 75\%$ improvement from baseline in F-VASI (F-VASI75) at Week 24
- Key secondary endpoints were
 - Proportion of patients achieving $\geq 50\%$ and $\geq 90\%$ improvement from baseline in F-VASI (F-VASI50 and F-VASI90, respectively) at Week 24
 - Proportion of patients achieving $\geq 50\%$ improvement from baseline in T-VASI (T-VASI50) at Week 24
 - Proportion of patients achieving a Vitiligo Noticeability Scale (VNS) rating of “a lot less noticeable” or “no longer noticeable” (VNS response) at Week 24
 - Percentage change from baseline in facial BSA (F-BSA) at Week 24
- The safety and tolerability of ruxolitinib cream were also assessed

Statistical Analyses

- For the primary and key secondary endpoints, ruxolitinib cream and vehicle were compared using exact logistic regression for binary outcomes and analysis of covariance for F-BSA
 - Multiple imputation was applied to account for missing values
 - All randomized patients were included in the efficacy analyses (intent-to-treat population)
- Safety analyses were summarized using descriptive statistics
 - All patients who applied ≥ 1 dose of ruxolitinib cream or vehicle were included in the safety analyses (safety population)

Results

Patients

- TRuE-V1/TRuE-V2 randomized 674 patients (ruxolitinib cream, n=450; vehicle, n=224; **Table 1**)
 - Mean (SD) age was 39.6 (15.1) years; 67.5% of patients had skin phototypes III–VI
 - Baseline mean F-VASI and T-VASI values were 0.92 and 6.69, respectively

Table 1. Patient Demographics and Baseline Clinical Characteristics (Intent-to-Treat Population)

Characteristic	Vehicle (n=224)	Ruxolitinib Cream (n=450)	Total (N=674)
Age, mean (SD), y	39.7 (14.5)	39.5 (15.4)	39.6 (15.1)
Female, n (%)	110 (49.1)	248 (55.1)	358 (53.1)
White, n (%)	189 (84.4)	363 (80.7)	552 (81.9)
Fitzpatrick skin phototype, n (%)			
I	4 (1.8)	12 (2.7)	16 (2.4)
II	72 (32.1)	131 (29.1)	203 (30.1)
III	88 (39.3)	179 (39.8)	267 (39.6)
IV	40 (17.9)	89 (19.8)	129 (19.1)
V	17 (7.6)	28 (6.2)	45 (6.7)
VI	3 (1.3)	11 (2.4)	14 (2.1)
Geographic region, n (%)			
North America	156 (69.6)	308 (68.4)	464 (68.8)
Europe	68 (30.4)	142 (31.6)	210 (31.2)
Baseline F-VASI, mean (SD)	0.92 (0.56)	0.92 (0.55)	0.92 (0.56)
Baseline T-VASI, mean (SD)	6.73 (2.09)	6.66 (2.05)	6.69 (2.06)
Facial BSA,* mean (SD), %	1.03 (0.65)	1.02 (0.63)	1.02 (0.64)
Total BSA, mean (SD), %	7.46 (2.03)	7.36 (2.02)	7.39 (2.03)
Duration of disease, median (range), y	12.1 (0–59.5)	11.8 (0–60.5)	12.0 (0–60.5)
Diagnosed in childhood, n (%)	77 (34.4)	168 (37.3)	245 (36.4)
Disease stability,† n (%)			
Stable	168 (75.0)	331 (73.6)	499 (74.0)
Progressive	56 (25.0)	119 (26.4)	175 (26.0)
Other autoimmune disorders, n (%)	36 (16.1)	90 (20.0)	126 (18.7)
Prior therapy,‡ n (%)	137 (61.2)	274 (60.9)	411 (61.0)
Topical corticosteroids	56 (25.0)	133 (29.6)	189 (28.0)
Topical calcineurin inhibitors	68 (30.4)	146 (32.4)	214 (31.8)
Phototherapy§	77 (34.4)	138 (30.7)	215 (31.9)

BSA, body surface area; F-VASI, facial Vitiligo Area Scoring Index; NB-UVB, narrow-band ultraviolet-B; PUVA, psoralen ultraviolet A; T-VASI, total Vitiligo Area Scoring Index.

* Percentage of total BSA.

† Determination of disease stability was based on investigator judgment.

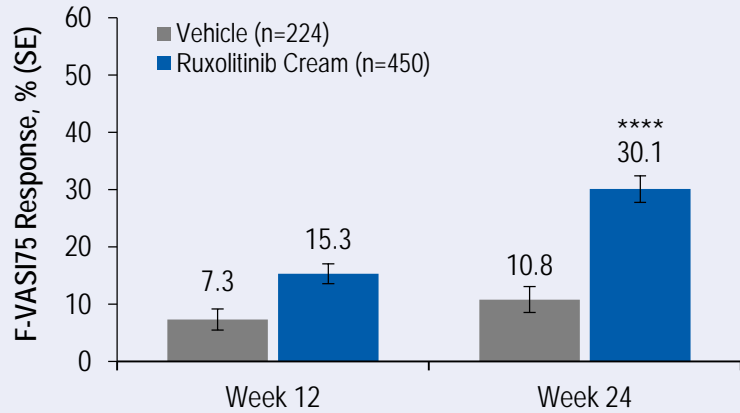
‡ Patients could have used multiple previous lines of therapy.

§ Phototherapy includes NB-UVB phototherapy, excimer laser, and PUVA photochemotherapy.

Efficacy

- At Week 24, F-VASI75 was achieved by a significantly greater proportion of patients applying ruxolitinib cream vs vehicle (30.1% vs 10.8%; $P < 0.0001$; **Figure 2**)

Figure 2. F-VASI75 Response



- The proportion of patients achieving F-VASI50 and F-VASI90 responses were significantly higher with ruxolitinib cream than vehicle at Week 24 (both $P \leq 0.0001$; **Figure 3**)

Figure 3A. F-VASI50 Response

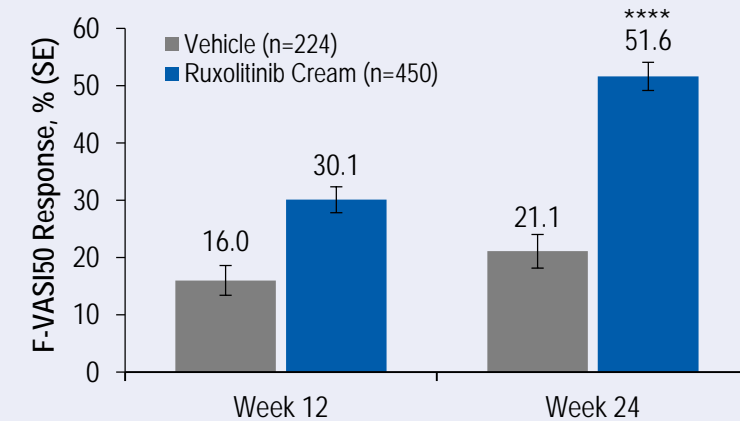
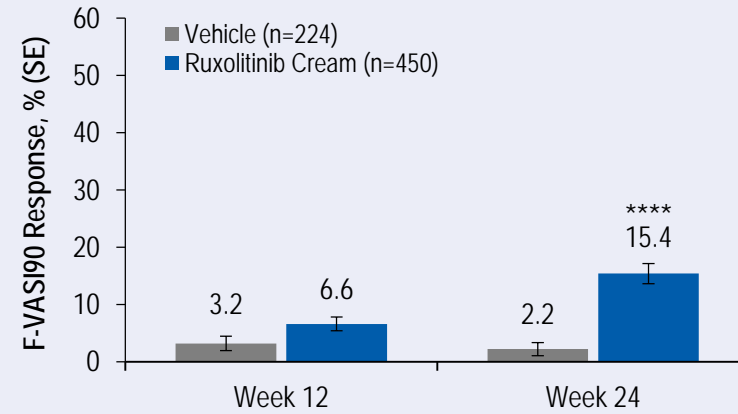
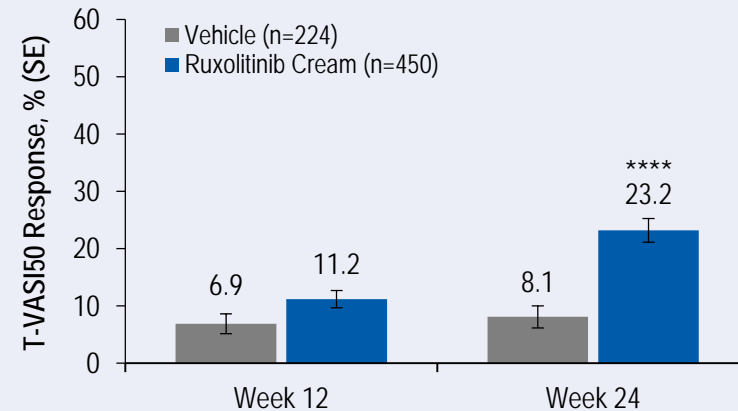


Figure 3B. F-VASI90 Response



- A significantly greater proportion of patients applying ruxolitinib cream achieved T-VASI50 at Week 24 compared with vehicle (23.2% vs 8.1%; $P < 0.0001$; **Figure 4**)

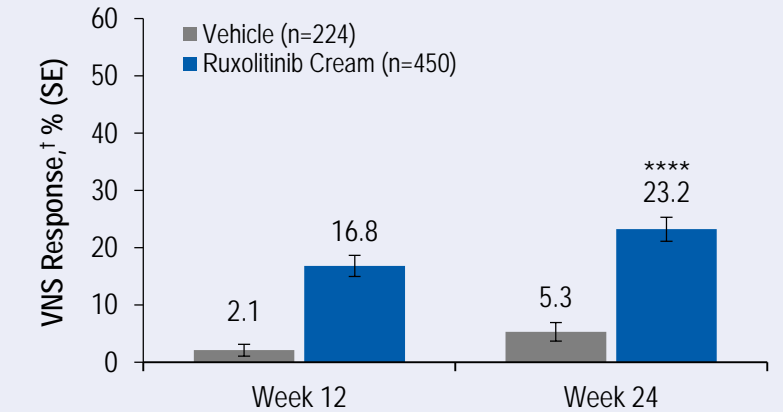
Figure 4. T-VASI50 Response



ANCOVA, analysis of covariance; F-BSA, facial body surface area; F-VASI50/75/90, $\geq 50\%/75\%/90\%$ improvement in facial Vitiligo Area Scoring Index; LSM, least squares mean; T-VASI50, $\geq 50\%$ improvement in total Vitiligo Area Scoring Index; VNS, Vitiligo Noticeability Scale.
 **** $P \leq 0.0001$ for response rate difference for ruxolitinib cream vs vehicle at Week 24.
 † VNS response was defined as achieving a rating of “a lot less noticeable” or “no longer noticeable.”
 ‡ At Week 24, an ANCOVA model was applied to determine LSM, LSM difference, and P value.
 Data per interim analyses at Week 24 are reported.

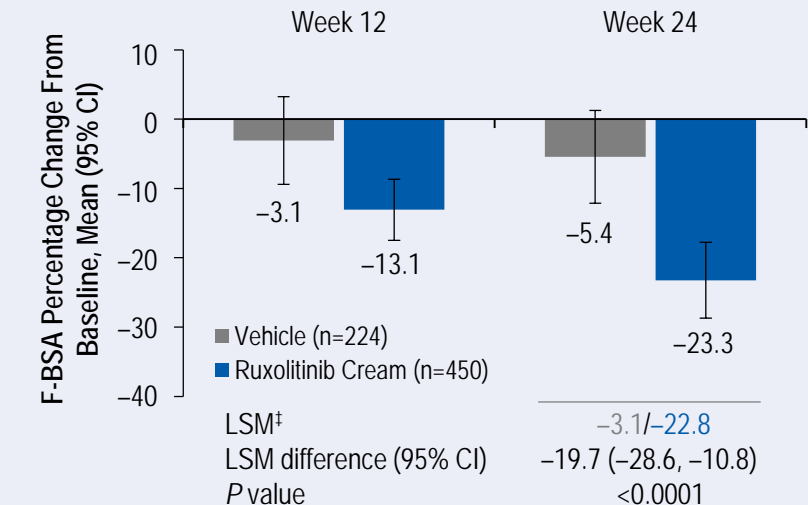
- The proportion of patients who achieved a VNS response at Week 24 with ruxolitinib cream vs vehicle was 23.2% vs 5.3%, respectively ($P < 0.0001$; **Figure 5**)

Figure 5. VNS Response



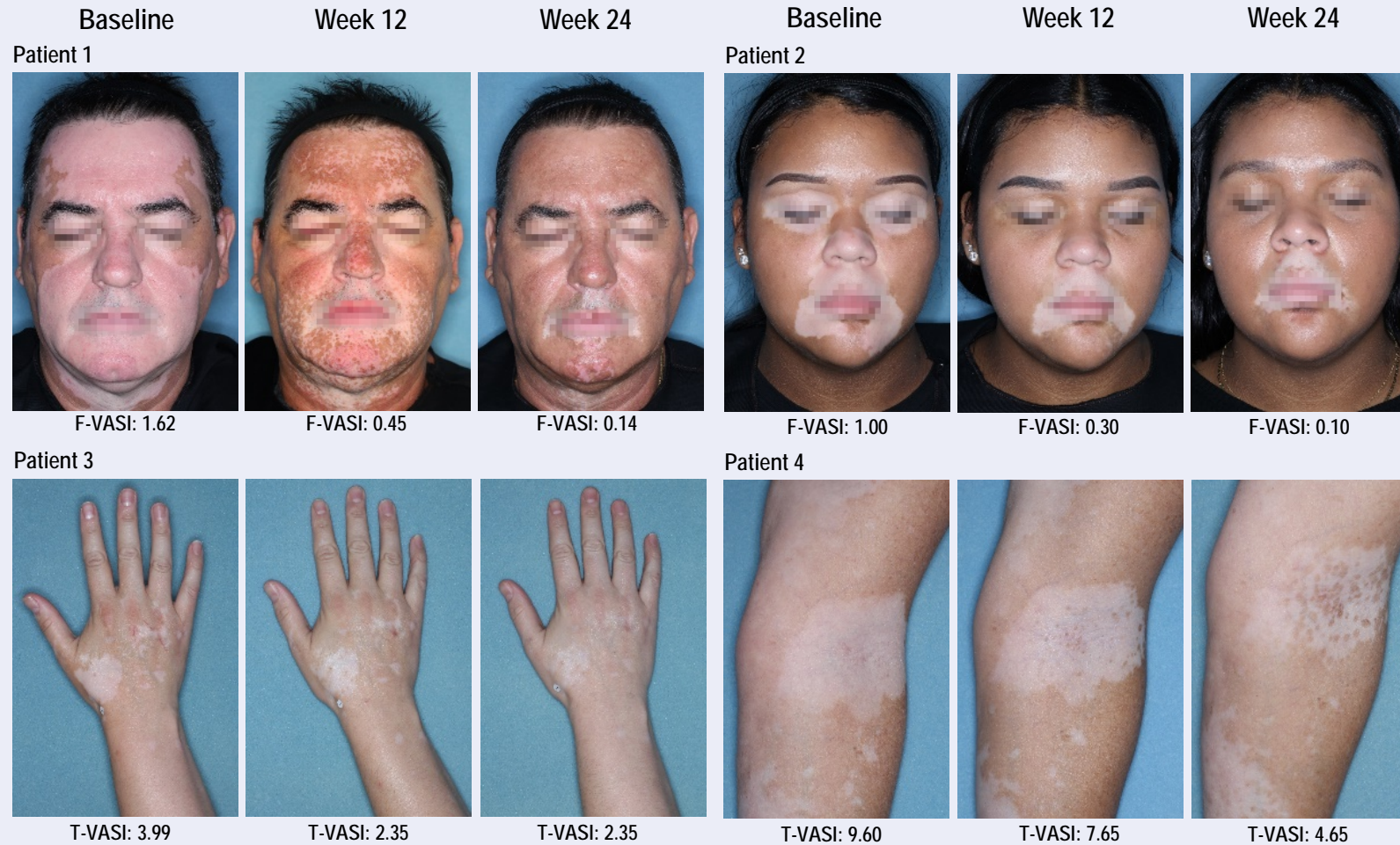
- At Week 24, the least squares mean percentage change from baseline in F-BSA was -22.8 with ruxolitinib cream vs -3.1 with vehicle ($P < 0.0001$; **Figure 6**)

Figure 6. Percentage Change From Baseline in F-BSA



- Visible improvement in repigmentation of facial and non-facial lesions was seen in patients who applied ruxolitinib cream (Figure 7)

Figure 7. Representative Clinical Images of Patients Who Applied Ruxolitinib Cream During the Double-Blind Period



F-VASI, facial Vitiligo Area Scoring Index; T-VASI, total Vitiligo Area Scoring Index.

Safety

- Ruxolitinib cream was generally well tolerated in TRuE-V1/TRuE-V2
- Treatment-emergent adverse events considered by investigators to be treatment related were mild or moderate (grades 1 or 2) in severity and occurred in 14.7% of patients who applied ruxolitinib cream and 7.6% who applied vehicle (Table 2)
 - Serious adverse events occurred in 1.8% and 0.4% of patients, respectively; none were considered related to treatment

Table 2. TEAEs Through 24 Weeks of Double-Blind Treatment (Safety Population)

Parameter, n (%)	Vehicle (n=224)	Ruxolitinib Cream (n=449)*
Patients with TEAE	79 (35.3)	214 (47.7)
Most common TEAEs [†]		
Application site acne	2 (0.9)	26 (5.8)
Application site pruritus	6 (2.7)	23 (5.1)
Nasopharyngitis	5 (2.2)	19 (4.2)
Headache	6 (2.7)	17 (3.8)
COVID-19	6 (2.7)	13 (2.9)
Upper respiratory tract infection	5 (2.2)	13 (2.9)
Sinusitis	5 (2.2)	10 (2.2)
Patients with treatment-related TEAE	17 (7.6)	66 (14.7)
Most common treatment-related TEAEs [†]		
Application site acne	2 (0.9)	22 (4.9)
Application site pruritus	6 (2.7)	21 (4.7)
Patients with serious TEAE [‡]	1 (0.4)	8 (1.8)
Patients with TEAE leading to discontinuation	1 (0.4)	2 (0.4)

TEAE, treatment-emergent adverse event.

* 1 patient who did not apply ≥ 1 dose of ruxolitinib cream was excluded from the safety population.

[†] Occurring in $\geq 2\%$ of patients in either treatment group.

[‡] No serious TEAEs were considered by investigators to be related to treatment. Data per interim analyses at Week 24 are reported.

Conclusions

- **Ruxolitinib cream demonstrated clinically meaningful superiority to vehicle for the primary and all key secondary endpoints in the pooled analysis of the TRuE-V1/TRuE-V2 phase 3 studies, confirming phase 2 findings**
- **Adolescent and adult patients with nonsegmental vitiligo achieved substantial facial and total body repigmentation at 24 weeks**
- **Ruxolitinib cream was well tolerated, and no serious adverse events were considered related to treatment**

Disclosures

DR has received honoraria as a consultant for AbbVie, Abcuro, AltruBio, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Concert, Dermavant Sciences, Dermira, Incyte Corporation, Janssen, Kyowa Kirin, Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals, Sanofi, Sun Pharmaceuticals, UCB, and Viela Bio; has received research support from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Dermira, Galderma, Incyte Corporation, Janssen, Lilly, Merck, Novartis, Pfizer, and Regeneron Pharmaceuticals; and has served as a paid speaker for AbbVie, Amgen, Celgene, Janssen, Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals, and Sanofi. KE is a consultant for AbbVie, Incyte Corporation, La Roche-Posay, Pfizer, Pierre Fabre, Sanofi, and Viela Bio. SRD has received fees and/or honoraria as a consultant for Almirall, Avita, Bristol Myers Squibb, Cassiopea SpA, Dermira, EPI Health, Ferndale Laboratories, Foamix, Galderma Laboratories LP, Incyte Corporation, Ortho Dermatologics, Pfizer, Scientis, Sente Labs, SkinCeuticals LLC, UCB, and Verrica Pharmaceuticals; has received stock options as a consultant for Gore Range Capital; has received honoraria as a speaker for Almirall, Galderma, and Ortho Dermatologics; has received grants/research funding as an investigator for AbbVie, AOBiome LLC, Atacama Therapeutics, Brickell Biotech, Dermavant Sciences, and Incyte Corporation; has served as an advisory board member for Dermavant Sciences and the Foundation for Research & Education of Dermatology; and is a stockholder of Gore Range Capital. JS has received grants and/or honoraria from AbbVie, Bristol Myers Squibb, Calypso Biotech, Eli Lilly, Incyte Corporation, LEO Pharma, Novartis, Pfizer, Pierre Fabre, Sanofi, Sun Pharmaceuticals, and Viela Bio; and has patents on MMP9 inhibitors and uses thereof in the prevention or treatment of a depigmenting disorder and three-dimensional model of depigmenting disorder. DK, KS, and KB are employees and shareholders of Incyte Corporation. TP has received grants and/or honoraria from AbbVie, ACM Pharma, Almirall, Amgen, Astellas, Bristol Myers Squibb, Celgene, Eli Lilly, Galderma, Genzyme/Sanofi, GlaxoSmithKline, Incyte Corporation, Janssen, LEO Pharma, Novartis, Pfizer, Sun Pharmaceuticals, and UCB; is the cofounder of YUKIN Therapeutics; and has patents on WNT agonists or GSK3b antagonist for repigmentation of vitiligo and on the use of CXCR3B blockers in vitiligo.

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