

Supplementary Material

Title: Efficacy of Apremilast in Patients with Psoriasis with Limited Skin Involvement, Including High-Impact Site Involvement: A Pooled Analysis of Six Trials

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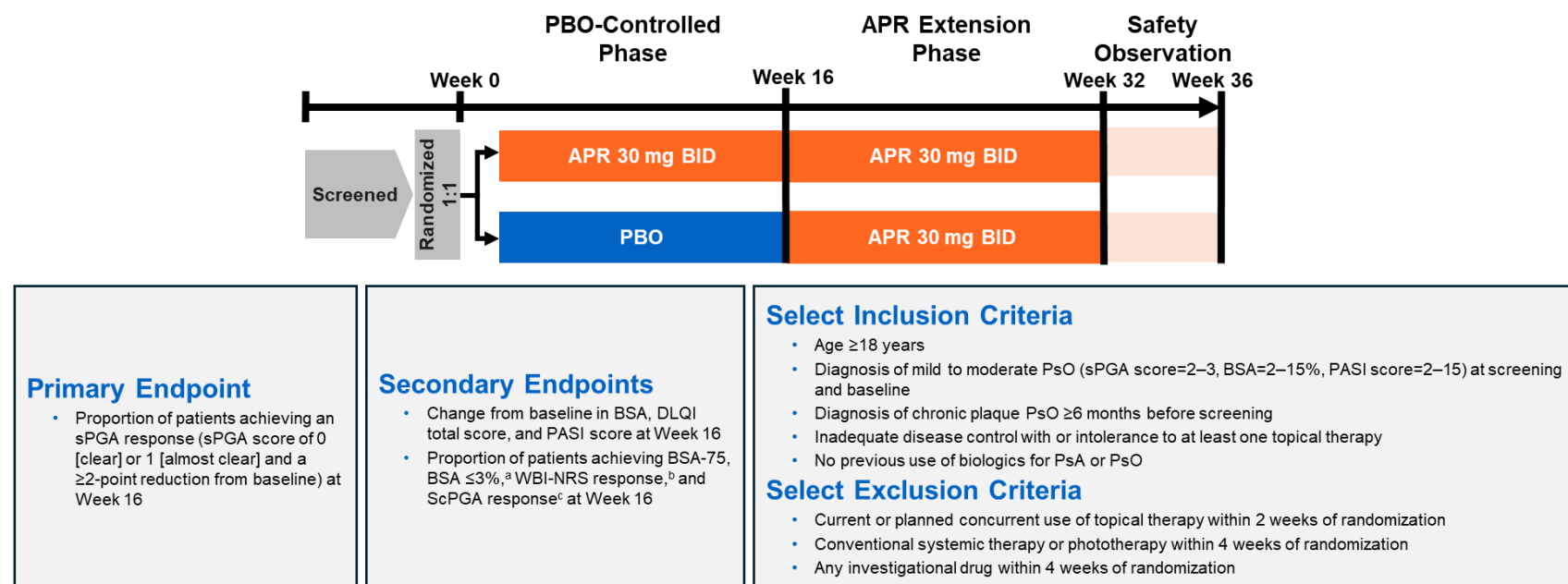
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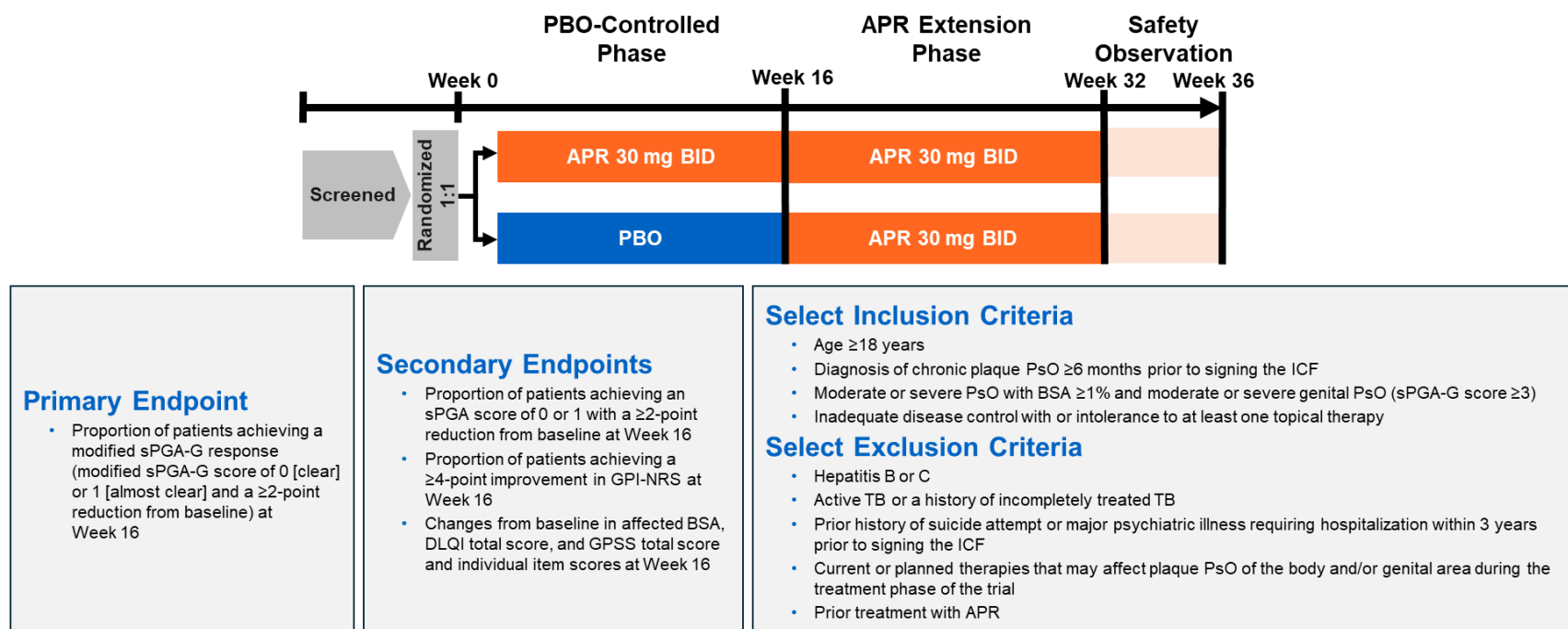
Supplementary Fig. S1. ADVANCE (NCT03721172) was a phase 3, multicenter, randomized, double-blind, PBO-controlled trial that evaluated the efficacy and safety of APR vs PBO in patients with mild to moderate plaque PsO who were biologic naïve.[1, 2]



^aIn patients with baseline BSA $> 3\%$. ^bWBI-NRS (itch) response was defined as a ≥ 4 -point reduction from baseline in WBI-NRS score in patients with a baseline score ≥ 4 . ^cScPGA (scalp) response was defined as an ScPGA score of 0 (clear) or 1 (almost clear) with a ≥ 2 -point reduction from baseline in patients with a baseline score ≥ 2 .

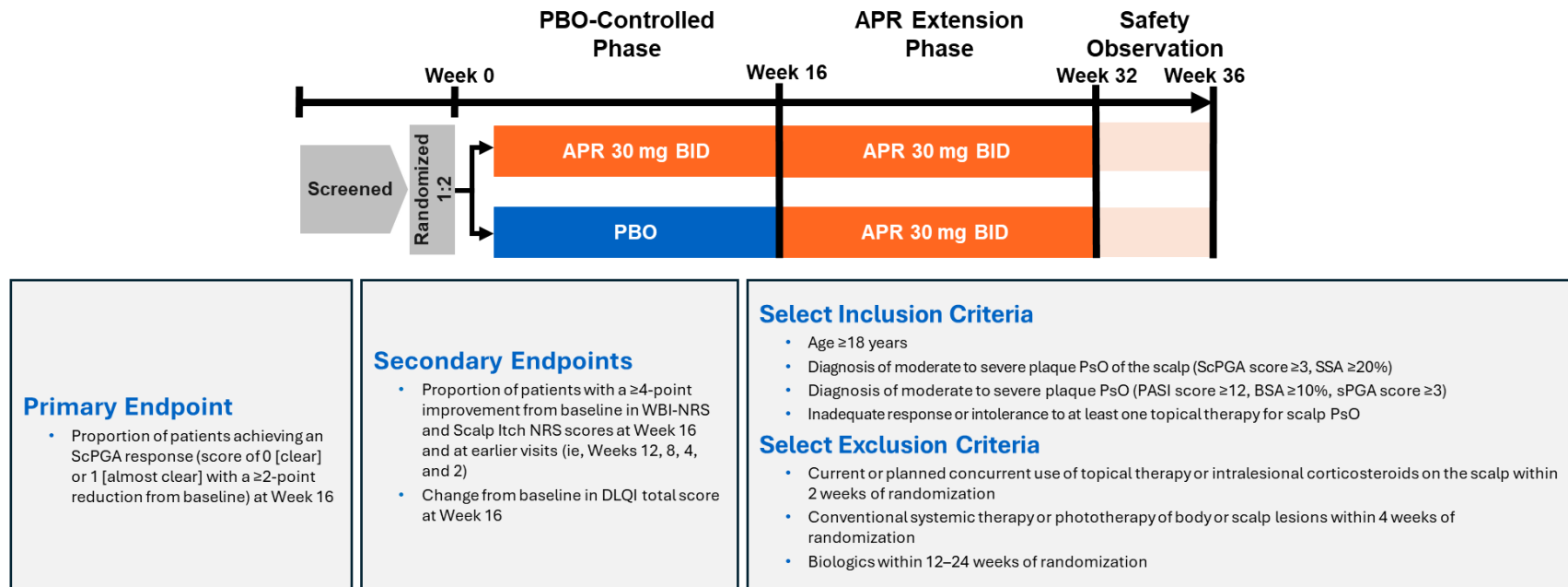
APR apremilast, BID twice daily, BSA body surface area, BSA-75 a $\geq 75\%$ reduction in BSA from baseline, DLQI Dermatology Life Quality Index, NRS Numeric Rating Scale, PASI PsO Area and Severity Index, PBO placebo, PsA psoriatic arthritis, PsO psoriasis, ScPGA Scalp Physician's Global Assessment, sPGA static Physician's Global Assessment, WBI Whole Body Itch.

Supplementary Fig. S2. DISCREET (NCT03777436) was a phase 3, multicenter, randomized, double-blind, PBO-controlled trial that evaluated the efficacy and safety of APR vs PBO in patients with moderate to severe genital PsO and moderate to severe plaque PsO.[3, 4]



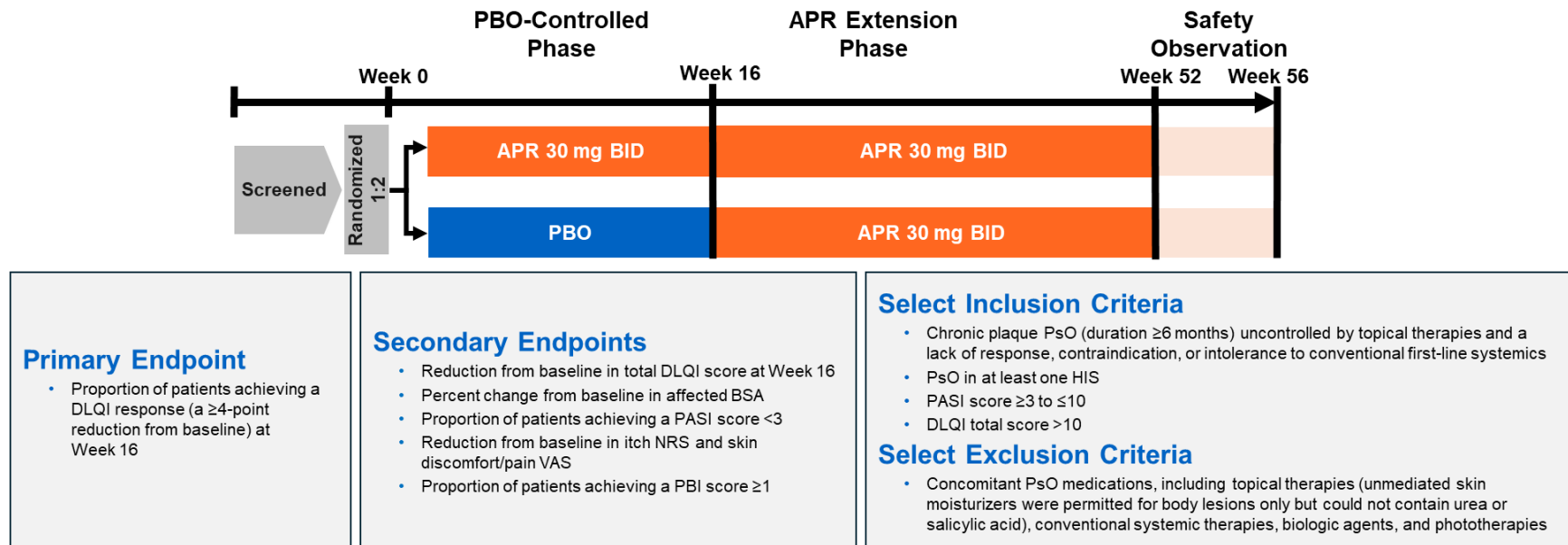
APR apremilast, BID twice daily, BSA body surface area, DLQI Dermatology Life Quality Index, GPI Genital PsO Itch, GPSS Genital PsO Symptoms Scale, ICF informed consent form, NRS Numeric Rating Scale, PBO placebo, PsO psoriasis, sPGA static Physician's Global Assessment, sPGA-G sPGA of Genitalia, TB tuberculosis.

Supplementary Fig. S3. STYLE (NCT03123471) was a phase 3b, multicenter, randomized, double-blind, PBO-controlled trial that evaluated the efficacy and safety of APR vs PBO in patients with moderate to severe plaque PsO of the scalp.[5, 6]



APR apremilast, BID twice daily, BSA body surface area, DLQI Dermatology Life Quality Index, NRS Numeric Rating Scale, PASI PsO Area and Severity Index, PBO placebo, PsO psoriasis, ScPGA Scalp Physician's Global Assessment, sPGA static Physician's Global Assessment, SSA scalp surface area, WBI Whole Body Itch.

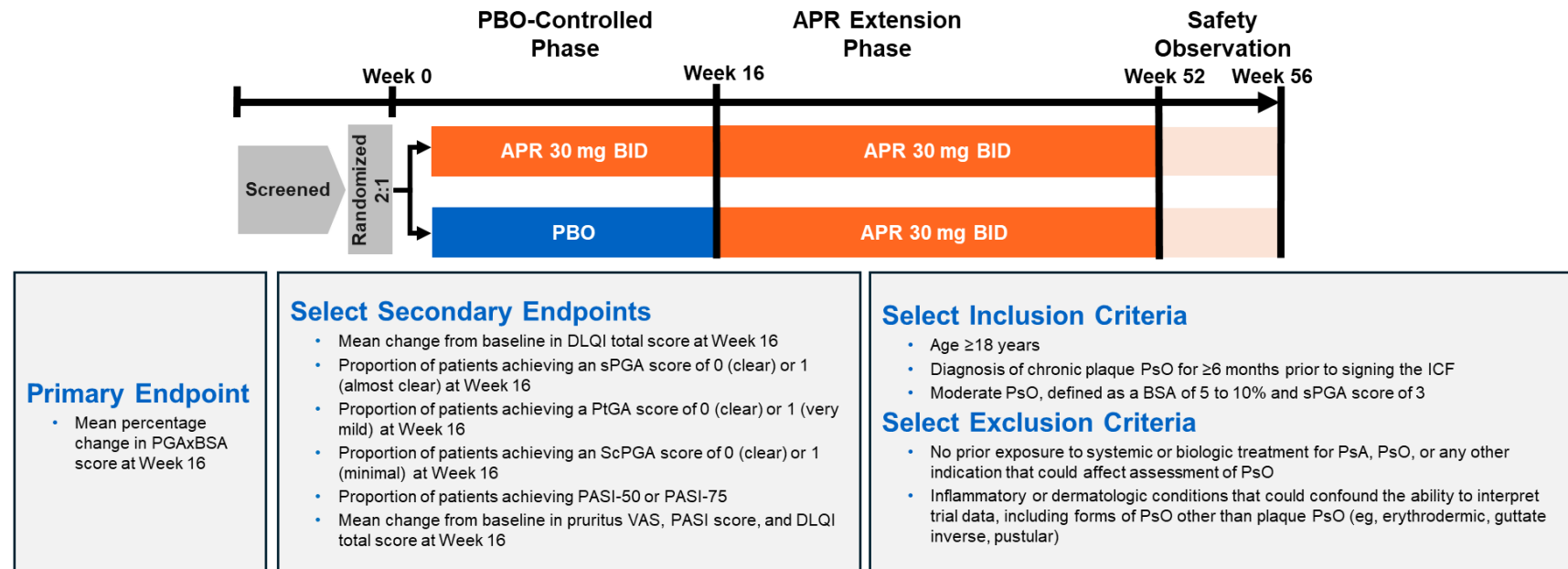
Supplementary Fig. S4. EMBRACE (NCT03774875) was a phase 4, multicenter, randomized, double-blind, parallel-group, PBO-controlled trial that evaluated the efficacy and safety of APR vs PBO in patients with limited skin involvement with chronic plaque PsO manifestations in at least one HIS and impaired QOL.[7, 8]



APR apremilast, BID twice daily, BSA body surface area, DLQI Dermatology Life Quality Index, HIS high-impact site, NRS Numeric Rating Scale,

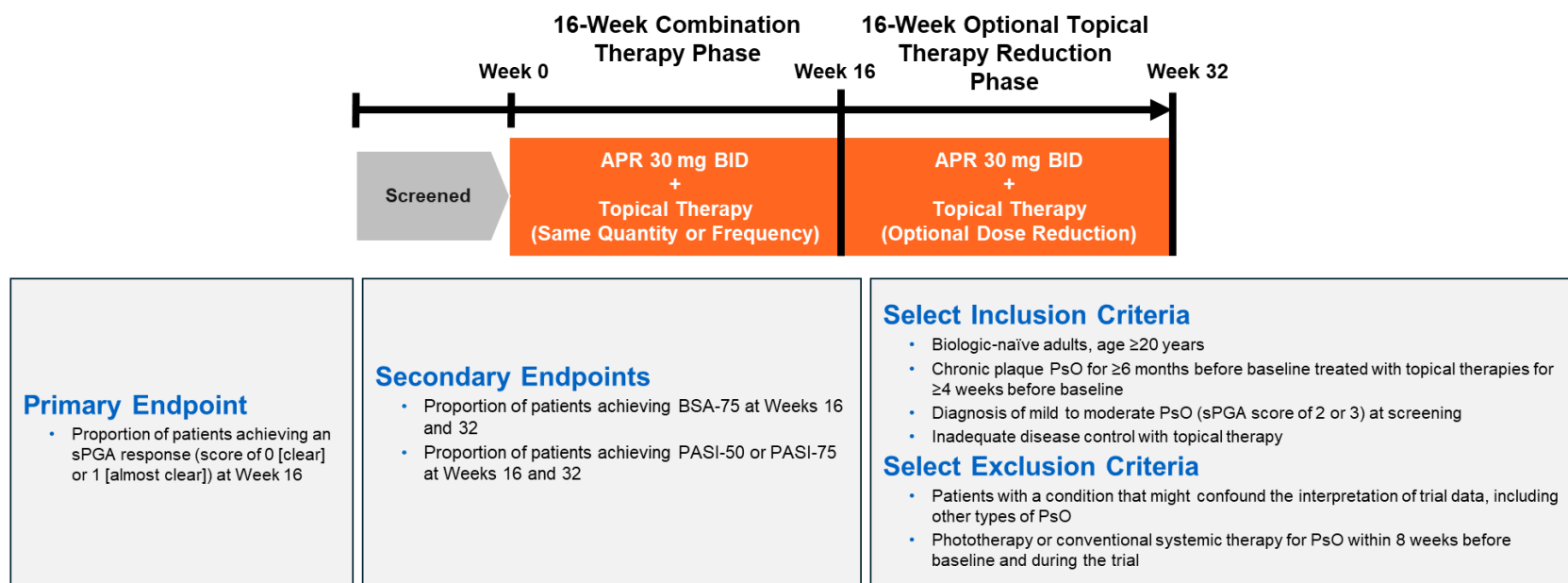
PASI PsO Area and Severity Index, PBI Patient Benefit Index, PBO placebo, PsO psoriasis, QOL quality of life, VAS visual analog scale.

Supplementary Fig. S5. UNVEIL (NCT02425826) was a phase 4, multicenter, randomized, double-blind, PBO-controlled trial that evaluated the efficacy and safety of APR vs PBO in patients with moderate plaque PsO who were systemic and biologic naïve.[9, 10]



APR apremilast, BID twice daily, BSA body surface area, DLQI Dermatology Life Quality Index, ICF informed consent form, PASI PsO Area and Severity Index, PASI-50 a $\geq 50\%$ reduction in PASI score from baseline, PASI-75 a $\geq 75\%$ reduction in PASI score from baseline, PBO placebo, PGABSA product of the sPGA and PsO-involved BSA, PsA psoriatic arthritis, PsO psoriasis, PtGA patient global assessment, ScPGA Scalp Physician's Global Assessment, sPGA static Physician's Global Assessment, VAS visual analog scale.

Supplementary Fig. S6. PROMINENT (NCT03930186) was a phase 3b, open-label, single-arm trial in Japan that evaluated the efficacy and safety of APR in combination with topical therapy in patients with mild to moderate plaque PsO not adequately controlled by topical therapy.[11, 12]



APR apremilast, BID twice daily, BSA-75 a $\geq 75\%$ reduction in body surface area from baseline, PASI PsO Area and Severity Index, PASI-50 a $\geq 50\%$ reduction in PASI score from baseline, PASI-75 a $\geq 75\%$ reduction in PASI score from baseline, PsO psoriasis, sPGA static Physician's Global Assessment.

Supplementary Table S1: : List of institutional review boards and ethics committee

Study	Ethics committees / IRBs
ADVANCE	Approved by applicable IRBs/ethics committees across participating sites in the United States and Canada, including Advarra Institutional Review Board, University of Utah Institutional Review Board, Western Institutional Review Board, Henry Ford Health System Institutional Review Board, Research Review Board Inc., Health Research Ethics Board of Alberta–Clinical Trials Committee, and other local review boards.
DISCREET	Approved by applicable IRBs/ethics committees across North America and Europe, including Advarra Institutional Review Board, Advarra Canada IRB, Research Review Board Inc., Western Institutional Review Board, Oregon Health & Science University IRB, UZ Leuven Ethics Committee, and other local ethics committees.
STYLE	Approved by applicable IRBs/ethics committees. The primary reviewing board for most participating sites was Advarra IRB d/b/a Schulman IRB, with additional local institutional review boards at participating institutions.
EMBRACE	Approved by applicable ethics committees across participating sites in France, Germany, Italy, Spain, Switzerland, and the United Kingdom, including national and institutional ethics committees.
PROMINENT	Approved by applicable institutional review boards across participating sites in Japan, including Sapporo Skin Clinic Institutional Review Board, Iwate Medical University Institutional Review Board, Tokyo Medical University Hospital Institutional Review Board, The University of Tokyo Hospital Institutional Review Board, and other local institutional review boards.
UNVEIL	The study protocol was approved by the institutional review boards of participating medical centers, and all patients provided written informed consent before study-related procedures

Supplementary Table S2. Endpoints assessed in this pooled analysis.[2, 4, 6, 8, 10, 12]

Assessments		Score Range	Eligibility Criteria Components	Population
BSA	BSA $\leq 1\%$	0 to 100%	• ADVANCE: BSA 2 to 15% • DISCREET: BSA $\geq 1\%$ in a nongenital area • STYLE: BSA $\geq 10\%$ • EMBRACE: N/A • UNVEIL: BSA 5 to 10% • PROMINENT: N/A	• Patients with BSA of 3–10% at baseline
	BSA $\leq 3\%$	0 to 100%	• ADVANCE: BSA 2 to 15% • DISCREET: BSA $\geq 1\%$ in a nongenital area • STYLE: BSA $\geq 10\%$ • EMBRACE: N/A • UNVEIL: BSA 5 to 10% • PROMINENT: N/A	• Patients with BSA of 3–10% at baseline
	BSA-75	0 to 100%	• ADVANCE: BSA 2 to 15% • DISCREET: BSA $\geq 1\%$ in a nongenital area • STYLE: BSA $\geq 10\%$ • EMBRACE: N/A • UNVEIL: BSA 5 to 10% • PROMINENT: N/A	• Patients with BSA of 3–10% at baseline
PASI score < 3		0 to 72, with a higher score indicating worse disease activity	• ADVANCE: PASI score 2 to 15 • DISCREET: N/A • STYLE: PASI score ≥ 12 • EMBRACE: PASI score ≥ 3 to ≤ 10 • UNVEIL: N/A • PROMINENT: N/A	• Patients with BSA of 3–10% at baseline
sPGA score of 0 or 1		5-point scale 0=clear 1=almost clear 2=mild	• ADVANCE: sPGA score 2 to 3 • DISCREET: sPGA score ≥ 3 • STYLE: sPGA score ≥ 3 • EMBRACE: N/A	• Patients with BSA of 3–10% at baseline

	3=moderate 4=severe	• UNVEIL: sPGA score of 3 • PROMINENT: sPGA score of 2 or 3	
DLQI reduction ≥ 4	0 to 30, with a higher score indicating worse health-related quality of life	• ADVANCE: N/A • DISCREET: N/A • STYLE: N/A • EMBRACE: DLQI total score >10 • UNVEIL: N/A • PROMINENT: N/A	• Patients with BSA of 3–10% at baseline
DLQI score of 0 or 1	0 to 30, with a higher score indicating worse health-related quality of life	• ADVANCE: N/A • DISCREET: N/A • STYLE: N/A • EMBRACE: DLQI total score >10 • UNVEIL: N/A • PROMINENT: N/A	• Patients with BSA of 3–10% at baseline
ScPGA score of 0 or 1	5-point scale 0=clear 1=almost clear 2=mild 3=moderate 4=severe	• ADVANCE: N/A • DISCREET: N/A • STYLE: ScPGA ≥ 3 • EMBRACE: patients had involvement of ≥ 1 HIS • UNVEIL: N/A • PROMINENT: N/A	• Patients with BSA of 3–10% at baseline and an ScPGA score ≥ 2 at baseline
sPGA-G score of 0 or 1	5-point scale 0=clear 1=almost clear 2=mild 3=moderate 4=severe	• ADVANCE: N/A • DISCREET: sPGA-G score ≥ 3 • STYLE: N/A • EMBRACE: patients had involvement of ≥ 1 HIS • UNVEIL: N/A • PROMINENT: N/A	• Patients with BSA of 3–10% at baseline and an sPGA-G score ≥ 2 at baseline
NAPSI score percent change from baseline	0 to 8, scored for the most affected nail as the sum of ratings for nail matrix (0 to 4) and nail bed (0 to 4) involvement 0=none 1=present in 1/4 of most affected nail	• ADVANCE: N/A • DISCREET: N/A • STYLE: N/A • EMBRACE: patients had involvement of ≥ 1 HIS • UNVEIL: N/A	• Patients with BSA of 3–10% at baseline and a NAPSI score >0 at baseline

	2=present in 2/4 of most affected nail 3=present in 3/4 of most affected nail 4=present in 4/4 of most affected nail	PROMINENT: N/A	
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BSA body surface area, *BSA-75* a $\geq 75\%$ reduction in BSA from baseline, *DLQI* Dermatology Life Quality Index, *HIS* high-impact site, *N/A* not

applicable, *NAPSI* Nail Psoriasis Severity Index, *PASI* Psoriasis Area and Severity Index, *ScPGA* Scalp Physician's Global Assessment, *sPGA* static

Physician's Global Assessment, *sPGA-G* sPGA of Genitalia.

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