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Envudeucitinib Provides Rapid and Sustained Itch Relief, Including Complete Itch Resolution, in Patients With Moderate-to-Severe Plaque Psoriasis: 24 Week Results From the Phase 3 ONWARD1 and ONWARD2 Trials

Jason E Hawkes^{1,2##}, Mark Lebwohl^{3##}, Brian S Kim⁴, Christopher G Bunick⁵, Sarah S Chisolm^{6,7##}, Sarina B Elmariah⁸, Eric Wolf^{9†}, Yuri Klyachkin^{9†}, Grace Ma^{9†}, Elisa Muscianisi^{9†}, Gil Yosipovitch^{10##}

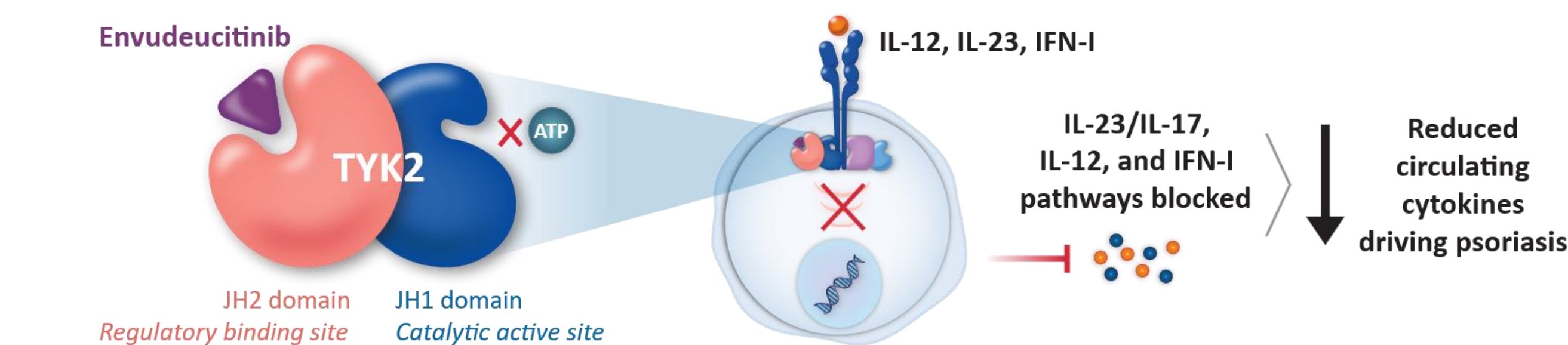
¹Oregon Medical Research Center, Portland, OR, USA; ²Department of Dermatology, Oregon Health & Science University, Portland, OR, USA; ³Kimberly and Eric J. Waldman Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, USA; ⁴Northwell Health, New Hyde Park, NY, USA; ⁵Department of Dermatology, Program in Translational Biomedicine, Institute for Global Health, Yale University School of Medicine, New Haven, CT, USA; ⁶Department of Dermatology, Emory University School of Medicine, Atlanta, GA, USA; ⁷VISN 7, Veterans Affairs Medical Center, Atlanta, GA, USA; ⁸Department of Dermatology, University of California San Francisco, San Francisco, CA, USA; ⁹Alumis Inc., South San Francisco, CA, USA; ¹⁰Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL, USA

Contact: Eric Wolf; ewolf@alumis.com

Synopsis

- Itch is one of the most burdensome symptoms of plaque psoriasis and substantially impairs sleep, quality of life, work productivity, and daily functioning¹⁻³
- Itch relief remains an important unmet need, particularly for patients with uncontrolled itch or significant scalp psoriasis^{2,4}
- **Envudeucitinib (ESK-001)* is a next-generation, oral, allosteric tyrosine kinase 2 (TYK2) inhibitor** that provides **maximal inhibition** over a 24-hour period in patients with psoriasis (**Figure 1**)⁵
- The **ONWARD1 and ONWARD2** Phase 3 trials of **envudeucitinib** in moderate-to-severe psoriasis met both coprimary and all key secondary endpoints and maintained favorable tolerability⁶

Figure 1. Envudeucitinib mechanism of action



IFN-γ, interferon type γ; IL-12/17/23, interleukin 12/17/23; JH1/2, Janus kinase homology 1/2.
*Envudeucitinib is an investigational therapy not reviewed or approved by any regulatory agency.

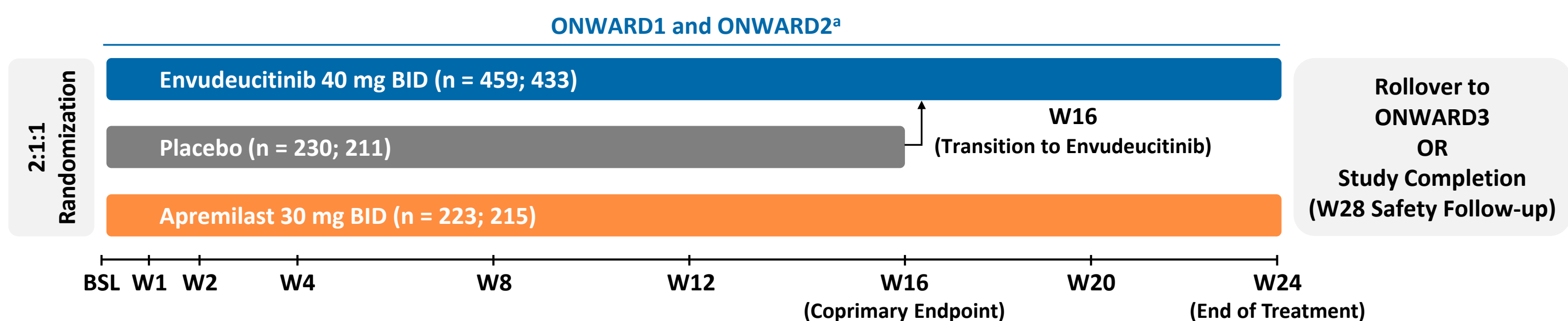
Objective

- To evaluate the onset, magnitude, and durability of itch improvement with envudeucitinib, including among patients with scalp involvement, in ONWARD1 and ONWARD2

Methods

- ONWARD1 and ONWARD2 were randomized, double-blinded, placebo- and active comparator–controlled, Phase 3 trials (**Figure 2**)

Figure 2. ONWARD1 and ONWARD2 study designs



^aReplicate design; actual enrollment is reported as ONWARD1 (NCT06586112); ONWARD2 (NCT06588738).
BID, bis in die (twice daily); BSL, baseline; W, week.

Conclusion

- **Envudeucitinib** provided rapid, substantial, and sustained itch relief in patients with moderate-to-severe plaque psoriasis
- Clinically meaningful improvement was evident as early as **Week 2**, and increasing proportions of patients achieved complete or near-complete itch resolution through **Week 24**

Results

Baseline demographics and disease characteristics

- Baseline demographics and disease characteristics were balanced across treatment arms and representative of a typical moderate-to-severe population (**Table 1**)

Table 1. Baseline demographics and disease characteristics

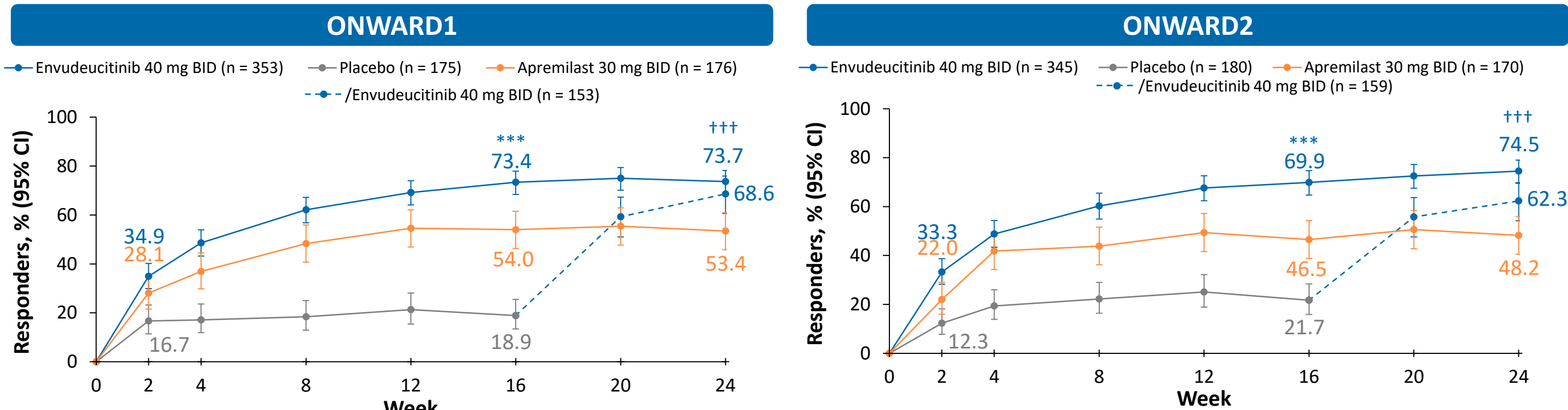
	ONWARD1			ONWARD2		
	Envudeucitinib 40 mg BID N = 459	Placebo N = 230	Apremilast 30 mg BID N = 223	Envudeucitinib 40 mg BID N = 433	Placebo N = 211	Apremilast 30 mg BID N = 215
Age, years, mean (SD)	49.1 (13.4)	49.2 (13.3)	47.7 (11.8)	48.3 (13.1)	49.5 (13.3)	48.0 (12.8)
Sex, male, n (%)	300 (65.4)	156 (67.8)	152 (68.2)	283 (65.4)	135 (64.0)	135 (62.8)
Race, n (%)						
White	358 (78.0)	182 (79.1)	177 (79.4)	388 (89.6)	181 (85.8)	193 (89.8)
Asian	68 (14.8)	28 (12.2)	30 (13.5)	10 (2.3)	10 (4.7)	7 (3.3)
Other ^a	33 (7.2)	20 (8.7)	16 (7.2)	35 (8.1)	20 (9.5)	15 (7.0)
Duration of disease, years, mean (SD)	19.9 (13.5)	19.5 (13.3)	17.2 (11.8)	19.0 (13.5)	20.2 (14.5)	18.7 (14.5)
PASI, mean (SD)	20.4 (8.0)	19.9 (7.5)	20.3 (6.9)	20.6 (8.3)	21.8 (9.0)	20.4 (8.4)
DLQI, mean (SD)	10.6 (6.5)	10.1 (6.7)	10.8 (6.8)	10.8 (7.0)	10.8 (6.8)	9.7 (7.1)
Worst pruritus NRS						
Mean (SD)	6.1 (2.7)	6.0 (2.7)	6.3 (2.6)	6.4 (2.6)	6.4 (2.4)	6.0 (2.7)
≥1, n (%)	420 (91.5)	210 (91.3)	210 (94.2)	400 (92.4)	200 (94.8)	199 (92.6)
≥4, n (%)	353 (76.9)	175 (76.1)	176 (78.9)	345 (79.7)	180 (85.3)	170 (79.1)
ss-PGA ≥3, n	274	135	150	285	140	134
Worst pruritus NRS ≥4 and ss-PGA ≥3, n (%)	213 (77.7)	102 (75.6)	124 (82.7)	231 (81.1)	122 (87.1)	108 (80.6)

^aIncludes Black or African American, Native Hawaiian or Other Pacific Islander, American Indian or Alaska Native, and Other or not reported.
DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; SD, standard deviation.

Envudeucitinib provided rapid and sustained improvements in itch through Week 24

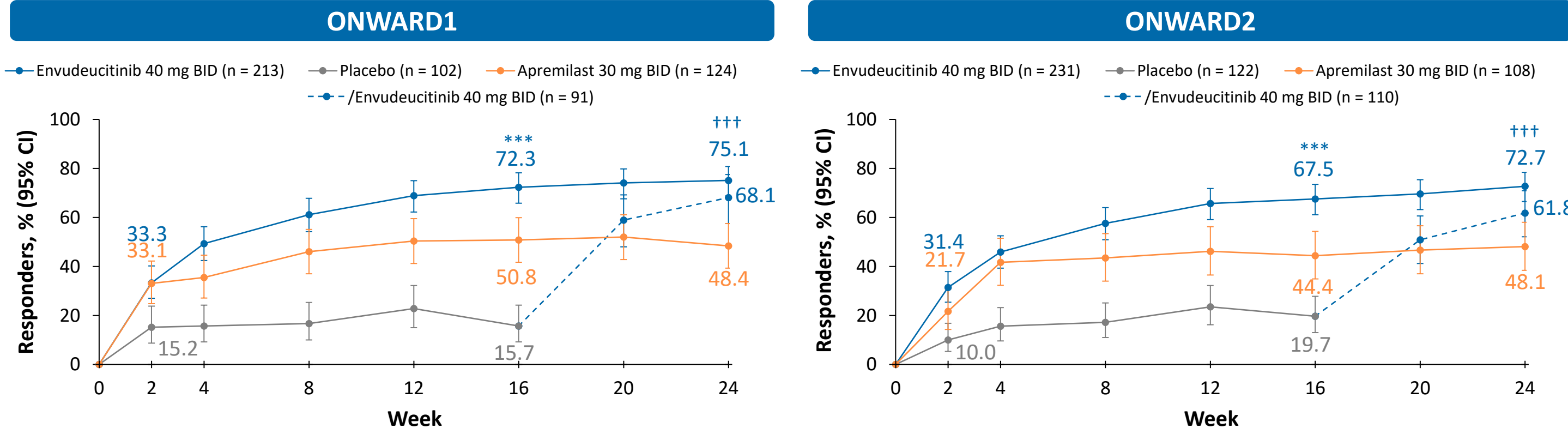
- Approximately one-third of patients receiving envudeucitinib reported a clinically meaningful ≥4-point improvement in worst pruritus NRS at Week 2 (**Figure 3**)
- Patients transitioning from placebo to envudeucitinib at Week 16 also reported rapid improvements in their worst pruritus NRS
- Improvements in patients with moderate-to-severe scalp psoriasis were consistent with improvements observed in the overall population (**Figure 4**)
- By Week 16, over one-third of patients receiving envudeucitinib achieved complete itch resolution (NRS 0; **Figure 5**) and more than half achieved minimal itch (NRS 0/1; **Figure 6**)
- All reported itch responses continued to improve with envudeucitinib treatment through Week 24 (**Figures 3–6**)

Figure 3. Clinically meaningful improvement (≥4-point reduction from baseline) in worst pruritus NRS^a



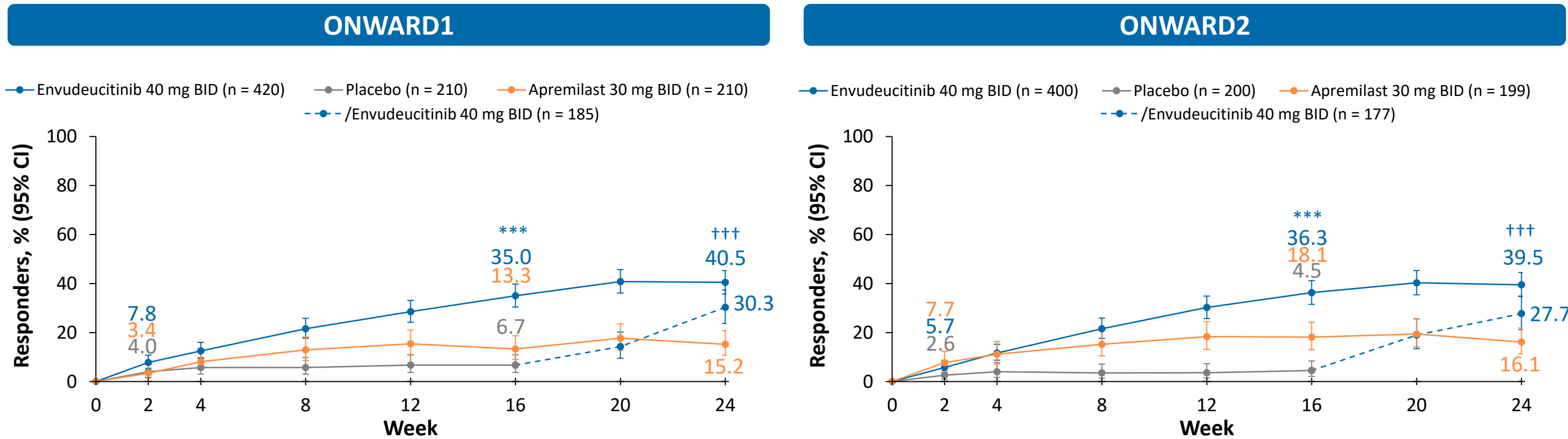
^aAmong patients with baseline worst pruritus NRS ≥4. Intention-to-treat population. ***P < 0.0001 (vs placebo and apremilast). ****P < 0.0001 (vs apremilast).

Figure 4. Clinically meaningful improvement (≥4-point reduction from baseline) in worst pruritus NRS among patients with moderate-to-severe scalp psoriasis^a



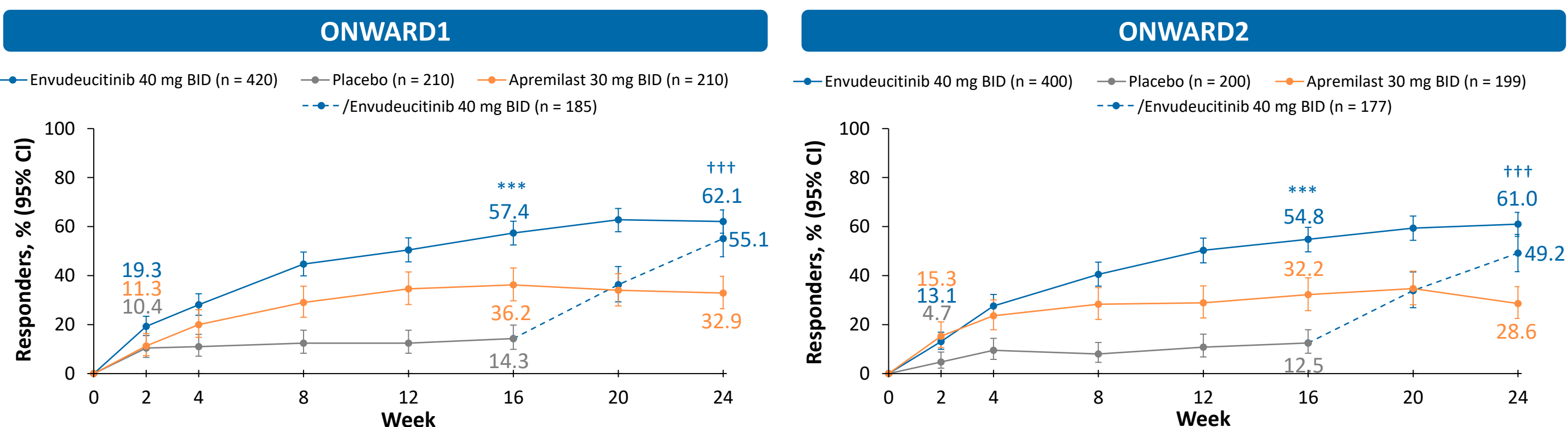
^aAmong patients with baseline worst pruritus NRS ≥4 and ss-PGA ≥3. Intention-to-treat population. ***P < 0.0001 (vs placebo and apremilast). ****P < 0.0001 (vs apremilast).

Figure 5. Complete itch resolution (worst pruritus NRS 0 with ≥1-point improvement)^a



^aAmong patients with baseline worst pruritus NRS ≥1. Intention-to-treat population. ***P < 0.0001 (vs placebo and apremilast). ****P < 0.0001 (vs apremilast).

Figure 6. No or minimal itch (worst pruritus NRS 0/1 with ≥1-point improvement)^a



^aAmong patients with baseline worst pruritus NRS ≥1. Intention-to-treat population. ***P < 0.0001 (vs placebo and apremilast). ****P < 0.0001 (vs apremilast).

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Disclosures

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