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 Kim[4], Christopher G Bunick[5], Sarah S Chisolm[6,7#*], Sarina B Elmariah[8], Eric Wolf[9†], Yuri Klyachkin[9†], Grace Ma[9†], Elisa Muscianisi[9†], Gil Yosipovitch[10#*]

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

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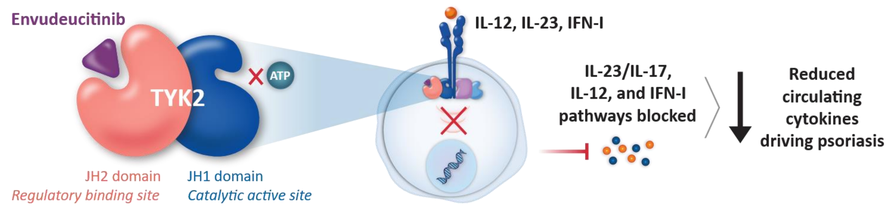
Contact: Eric Wolf; ewolf@alumis.com

Synopsis

- Itch is one of the most burdensome symptoms of plaque psoriasis and substantially impairs sleep, quality of life, work productivity, and daily functioning[1-3]
- 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 tolerability[6]

Figure 1. Envudeucitinib mechanism of action



IFN-I, interferon type I; 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.*

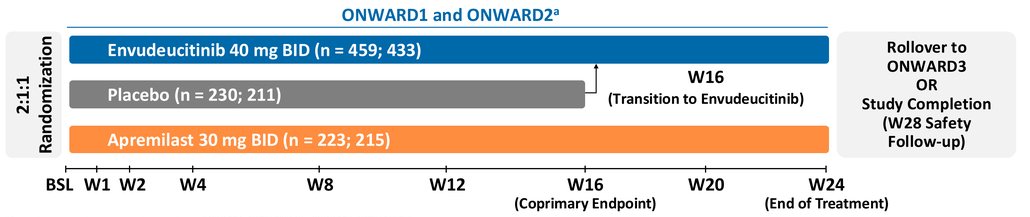
Objective

- 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



[a]*Replicate design; actual enrollment is reported as ONWARD1 (NCT06586112); ONWARD2 (NCT06588738).*
BID, bis in die (twice daily); BSL, baseline; W, week.

- Worst pruritus was assessed using a self-administered numeric rating scale (NRS, 0–10), reflective of the prior 24 hours[7]
- Endpoints
  - Clinically meaningful improvement (≥4-point reduction from baseline) in worst pruritus NRS
    - Among patients with baseline worst pruritus NRS ≥4
    - Among patients with baseline scalp-specific Physician's Global Assessment (ss-PGA) ≥3 and worst pruritus NRS ≥4
  - Worst pruritus NRS 0 with ≥1-point improvement
  - Worst pruritus NRS 0/1 with ≥1-point improvement
- Confidence intervals (CIs) were obtained using Clopper–Pearson methods, and the 95% CIs and *P*-values of the treatment differences were calculated using the Cochran–Mantel–Haenszel test adjusted for stratification factors with nonresponder imputation. *P*-values are nominal

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

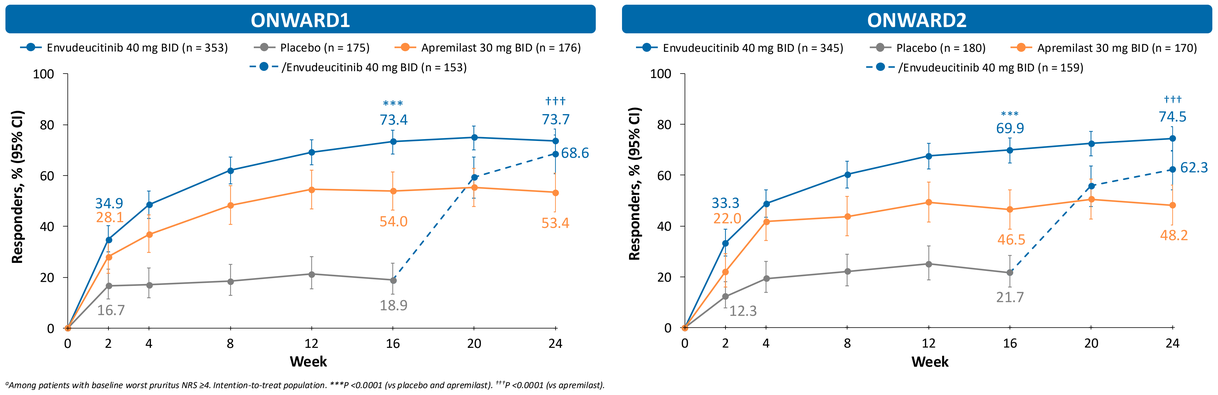
	ONWARD1			ONWARD2		
	Envudeucitinib 40 mg BID N = 459	Placebo N = 230	Apremilast 30 mg BID N = 223	Envudeucitinib 40 mg BID N = 433	Placebo N = 211	Apremilast 30 mg BID N = 215
Age, years, mean (SD)	49.1 (13.4)	49.2 (13.3)	47.7 (11.8)	48.3 (13.1)	49.5 (13.3)	48.0 (12.8)
Sex, male, n (%)	300 (65.4)	156 (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)

[a]*Includes 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

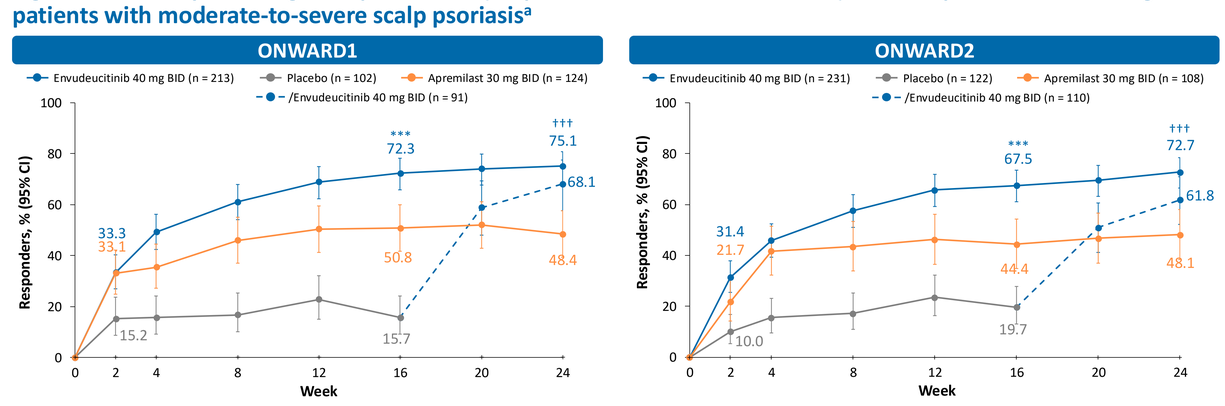
- Approximately one-third of patients receiving envudeucitinib reported a clinically meaningful ≥4-point improvement in worst pruritus NRS at Week 2 (**Figure 3**)
  - Patients transitioning from placebo to envudeucitinib at Week 16 also reported rapid improvements in their worst pruritus NRS
  - Improvements 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]



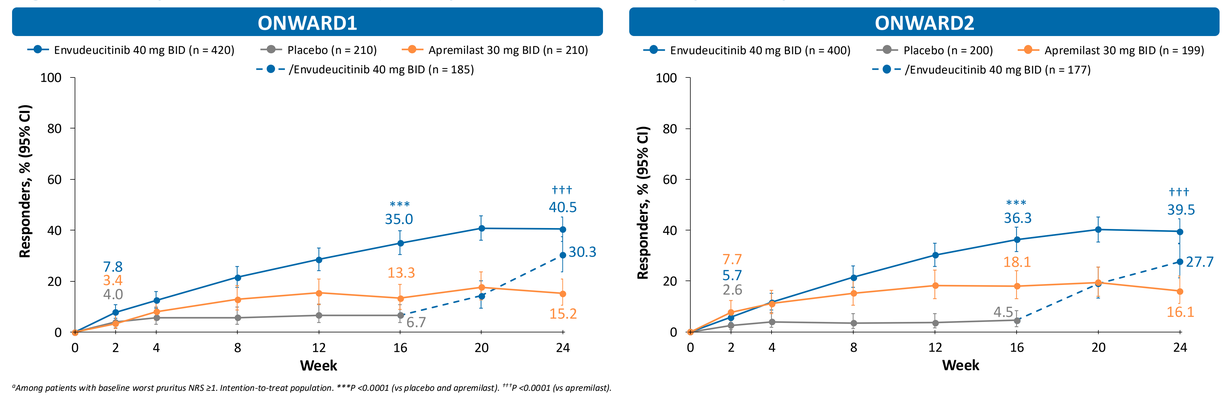
[a]*Among patients with baseline worst pruritus NRS ≥4. Intention-to-treat population. ***P <0.0001 (vs placebo and apremilast). †††P <0.0001 (vs apremilast).*

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



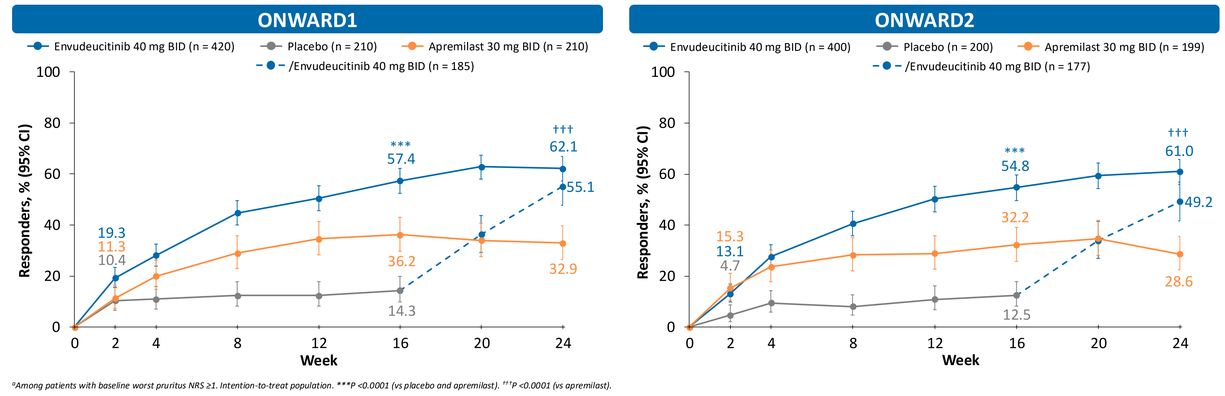
[a]*Among patients with baseline worst pruritus NRS ≥4 and ss-PGA ≥3. Intention-to-treat population. ***P <0.0001 (vs placebo and apremilast). †††P <0.0001 (vs apremilast).*

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



[a]*Among 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]



[a]*Among patients with baseline worst pruritus NRS ≥1. Intention-to-treat population. ***P <0.0001 (vs placebo and apremilast). †††P <0.0001 (vs apremilast).*

References

1. Jaworecka K, et al. *J Clin Med*. 2022;11(19):5553. 2. Taliercio VL, et al. *J Clin Aesthet Dermatol*. 2021;14(6):42-8. 3. Korman NJ, et al. *Dermatol Online J*. 2015;21(10):13030. 4. Greene RK, et al. *JAAD Reviews*. 2026;8:173-6. 5. Armstrong AW, et al. *Dermatol Ther (Heidelb)*. 2026;16(6):2661-73. 6. Blauvelt A, et al. Envudeucitinib (ESK-001) in moderate-to-severe plaque psoriasis: 24-week results from the randomized, double-blind, active comparator- and placebo-controlled, phase 3 ONWARD 1 and 2 studies. Presented at American Academy of Dermatology; March 27-31, 2026. 7. Verweyen E, et al. *Acta Derm Venereol*. 2019;99(7):657-63.

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