Achievement of Treat-to-Target Thresholds with Envudeucitinib, a Selective TYK2 Inhibitor, in Moderate-to-Severe Plaque Psoriasis: Results from STRIDE and OLE

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Background

- **Treat-to-target thresholds** in psoriasis (PsO) help to guide therapeutic decisions by defining clinically meaningful improvements in symptoms and quality of life (QoL).
- **Psoriasis Area Severity Index (PASI), body surface area (BSA), and Dermatology Life Quality Index (DLQI)** are validated scores used to define treatment success, with treat-to-target thresholds for PASI of 0, ≤1, ≤2, ≤3, and ≤5, BSA of ≤1% and ≤3%, and DLQI of 0 and 0/1 being recognized in clinical guidelines and real-world practice.[1,2,3,4]
- **Envudeucitinib*** (formerly known as ESK-001), a highly selective allosteric tyrosine kinase 2 (TYK2) inhibitor, has shown efficacy and a favorable safety profile in Phase 2 clinical trials, demonstrating its potential to achieve treat-to-target goals in moderate-to-severe plaque PsO.

**Envudeucitinib is investigational and has not been approved by any regulatory authority.*

Objectives

To assess the proportion of patients achieving clinically meaningful treat-to-target thresholds for PASI, BSA, and DLQI with envudeucitinib (envu) 40 mg twice daily (BID) in STRIDE and Open Label Extension (OLE).

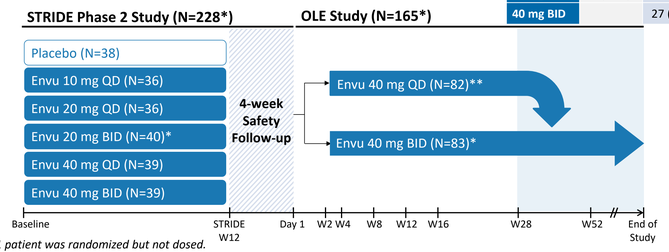
Methods

Study Design

- **STRIDE** is a 12-week randomized, double-blinded, placebo-controlled Phase 2 study of envudeucitinib in adults with moderate-to-severe plaque PsO *(NCT05600036)*.[5]
- **OLE study** is an ongoing open-label extension study with envudeucitinib *(NCT05739435)*.
  - This study enrolled 95% of eligible patients who completed the STRIDE study.

Dose Assignment from STRIDE to OLE

STRIDE Ph2 Dose	OLE Dose	
	40 mg QD	40mg BID
Placebo	17 (21%)	9 (11%)
10 mg QD	30 (37%)	
20 mg QD	26 (32%)	
20 mg BID		30 (36%)
40 mg QD	9 (11%)	17 (21%)
40 mg BID		27 (33%)



**1 patient was randomized but not dosed.*
***Upon identification of most beneficial dose (STRIDE, OLE Week 28), 40 mg QD patients switched to 40 mg BID between Week 40 and Week 64.*

Statistical Analyses

- Achievement of treat-to-target thresholds at Week 12 of STRIDE and Week 52 of OLE was performed as a post-hoc analysis. All p-values presented are nominal.
- Efficacy analyses were performed on the modified Intent-To-Treat (mITT) population that included all randomized patients who received at least one dose of study drug.
  - A non-responder imputation (NRI) was applied to analyses for STRIDE.
  - A modified NRI (mNRI) was applied to analyses for OLE where patients who discontinued due to adverse events or inadequate response were non-responders and last observation was carried forward (LOCF) for discontinuations due to other reasons.
  - LS Means and 95% confidence interval (CI) of percent change from baseline of PASI total score was based on a mixed model repeated measures (MMRM) analysis.

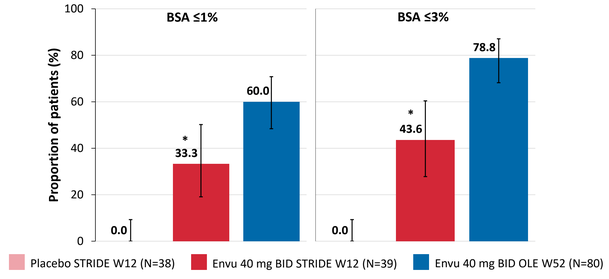
Results

Demographics and baseline disease characteristics were distributed similarly across dosing arms, both in STRIDE and OLE study

	STRIDE		OLE	
	Placebo (N=38)	Envu 40 mg BID (N=39*)	Envu 40 mg QD (N=82)	Envu 40 mg BID* (N=83)
Age (years), mean (SD)	49.1 (11.7)	47.9 (14.2)	47.5 (12.7)	50.8 (12.1)
Male, n (%)	31 (81.6)	26 (66.7)	56 (68.3)	61 (73.5)
Race, n (%)				
White	27 (71.1)	33 (84.6)	63 (76.8)	70 (84.3)
Asian	4 (10.5)	2 (5.1)	7 (8.5)	4 (4.8)
Black/African American	3 (7.9)	1 (2.6)	5 (6.1)	1 (1.2)
Other/not reported	4 (10.5)	3 (7.7)	7 (8.5)	8 (9.6)
BMI (kg/m^2), mean (SD)	31.9 (6.8)	31.6 (7.1)	33.1 (8.8)	31.7 (7.4)
Psoriasis duration (years), mean (SD)	19.8 (11.6)	21.5 (15.5)	17.2 (10.9)	22.3 (14.3)
PASI, mean (SD)	18.0 (4.5)	17.5 (4.9)	10.2 (7.2)	6.8 (7.0)
DLQI, mean (SD)	9.6 (7.2)	10.8 (6.8)	5.8 (5.8)	4.5 (4.8)
BSA involvement (%), mean (SD)	22.9 (12.1)	21.5 (15.1)	12.9 (13.4)	8.7 (11.1)
Previously exposed to biologics or JAK inhibitors, n (%)	13 (34.2)	13 (33.3)	38 (46.3)	42 (50.6)

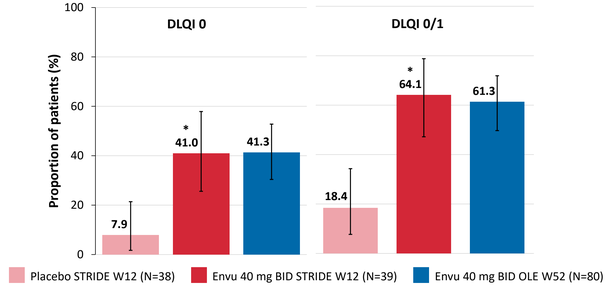
*ITT analysis population. *Based on original dose assignment at start of OLE.*

At Week 52, 60% of patients on envudeucitinib 40 mg BID achieved BSA ≤1%



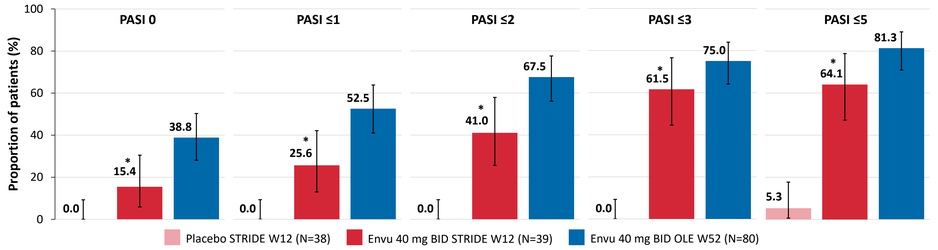
*Error bars represent the 95% CI. * p<0.0001 versus placebo (STRIDE).*

At Week 12 and 52, >60% of patients on envudeucitinib 40 mg BID reported minimal or no impact on QoL



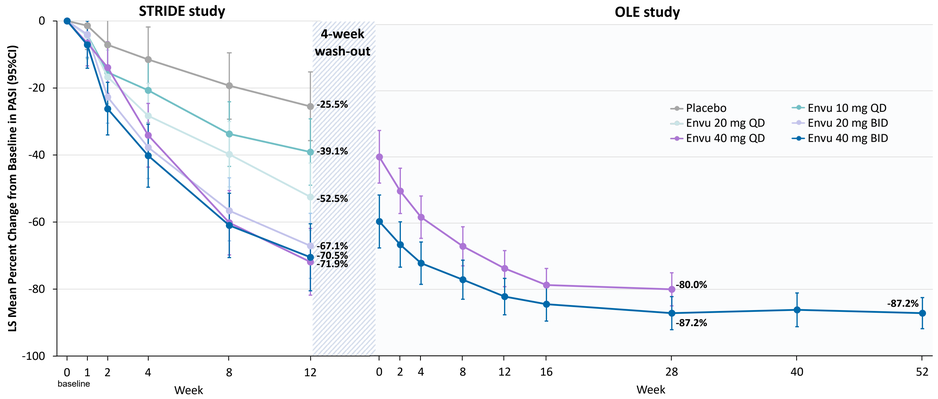
*Error bars represent the 95% CI. * p≤0.001 versus placebo (STRIDE).*

Consistent improvement in absolute PASI thresholds over time with envudeucitinib through 52 weeks



*Error bars represent the 95% CI. * p<0.013 versus placebo (STRIDE).*

Nearly 90% PASI improvement from baseline at 52 weeks with envudeucitinib 40 mg BID



Patients on 40 mg QD in OLE received placebo, 10 mg QD, 20 mg QD and 40 mg QD in STRIDE.
Patients on 40 mg BID in OLE received placebo, 20 mg BID, 40 mg QD, 40 mg BID in STRIDE.

Conclusions

- **Safety profile at 52 weeks remained consistent with that observed in the placebo-controlled treatment period, with upper respiratory tract infection, nasopharyngitis, headache, and COVID-19 being the most common adverse events.[6]**
- **Treatment with envudeucitinib 40 mg BID led to rapid and sustained achievement of stringent treat-to-target thresholds in patients with moderate-to-severe plaque PsO.**
- **Progressive improvements in skin clearance were observed from Week 12 through Week 52, accompanied by QoL gains that were maintained, reflecting consistent benefits across clinical and patient-reported outcomes.**
- **These results demonstrated sustained efficacy over time, reinforcing envudeucitinib's potential as a differentiated next-generation oral TYK2 inhibitor.**

References

1. Armstrong AW et al. From the Medical Board of the National Psoriasis Foundation: Treatment targets for plaque psoriasis. J Am Acad Dermatol. 2017;76(2):290-298.
2. Mahil SK et al. Psoriasis treat to target: defining outcomes in psoriasis using data from a real-world, population-based cohort study (the British Association of Dermatologists Biologics and Immunomodulators Register, BADBIR). Br J Dermatol. 2020;182(5):1158-1166.
3. Gisondi P et al. Treat-to-Target Approach for the Management of Patients with Moderate-to-Severe Plaque Psoriasis: Consensus Recommendations. Dermatol Ther (Heidelb). 2021;11(1):235-252.
4. Golbari NM et al. Psoriasis severity: commonly used clinical thresholds may not adequately convey patient impact. J Eur Acad Dermatol Venereol. 2021;35(2):417-421.
5. Blauvelt A et al. Highly selective, allosteric inhibition of TYK2 with oral ESK-001 in patients with moderate-to-severe plaque psoriasis: Results from STRIDE, a 12-week, randomized, double-blinded, placebo-controlled, dose-ranging phase 2 study. J Am Acad Dermatol. 2025:S0190-9622(25)02466-1.
6. Blauvelt et al. EADV2025 Poster Presentation. https://www.alumis.com/file.cfm/18/docs/eadv_late_breaker_presentation_final.pdf

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† Author is employed by Alumis Inc.