## SUPPLEMENTARY MATERIALS

*Eligibility criteria*

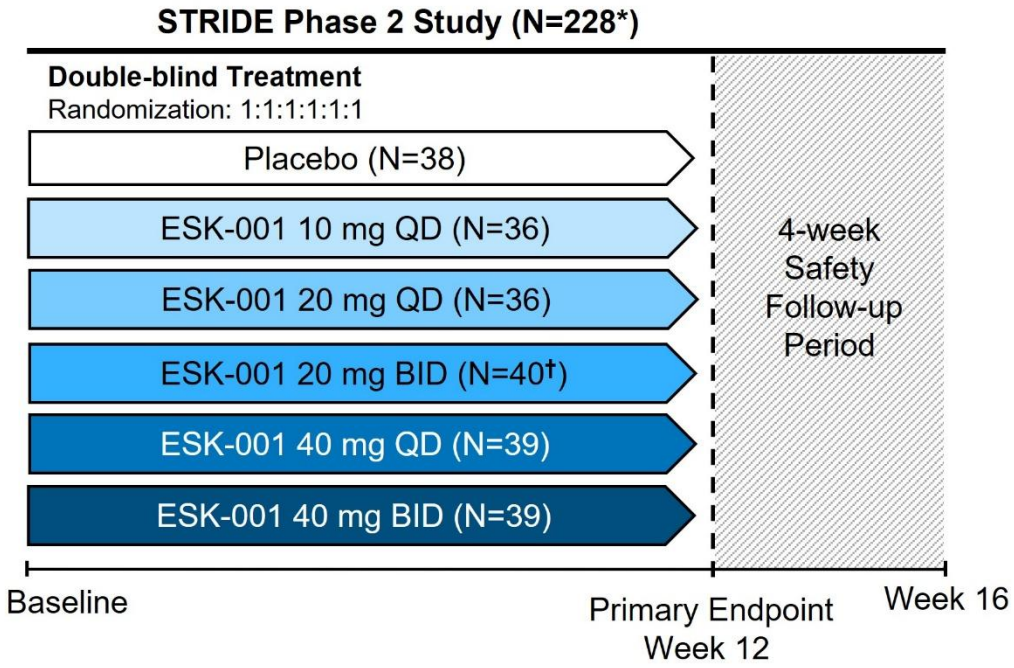
Eligible patients were adults with plaque psoriasis between the ages of 18-75 years with a total body weight >40 kg (88 lb), a diagnosis of plaque psoriasis for ≥6 months, body surface area (BSA) ≥10%, Psoriasis Area and Severity Index (PASI) ≥12 and static Physician's Global Assessment (sPGA) score ≥3 at baseline. Patients agreed to adhere to highly effective methods of contraception for the entirety of the study, and for 30 days or 90 days after the last dose of study drug for eligible females and males, respectively. Key patient exclusion criteria included presence of unstable medical conditions, active viral infections, active or untreated latent tuberculosis, or current malignancy. Prohibited treatments included systemic immunomodulatory medications and topical medications that could affect psoriasis evaluation. Patients who had been previously unresponsive to agents targeting IL-12, IL-23, or IL-17, patients who had failed more than 2 biologics, or patients who had received any investigational treatment within 30 days or 5 half-lives of treatment with study drug were excluded from the study.

*List of Investigators*

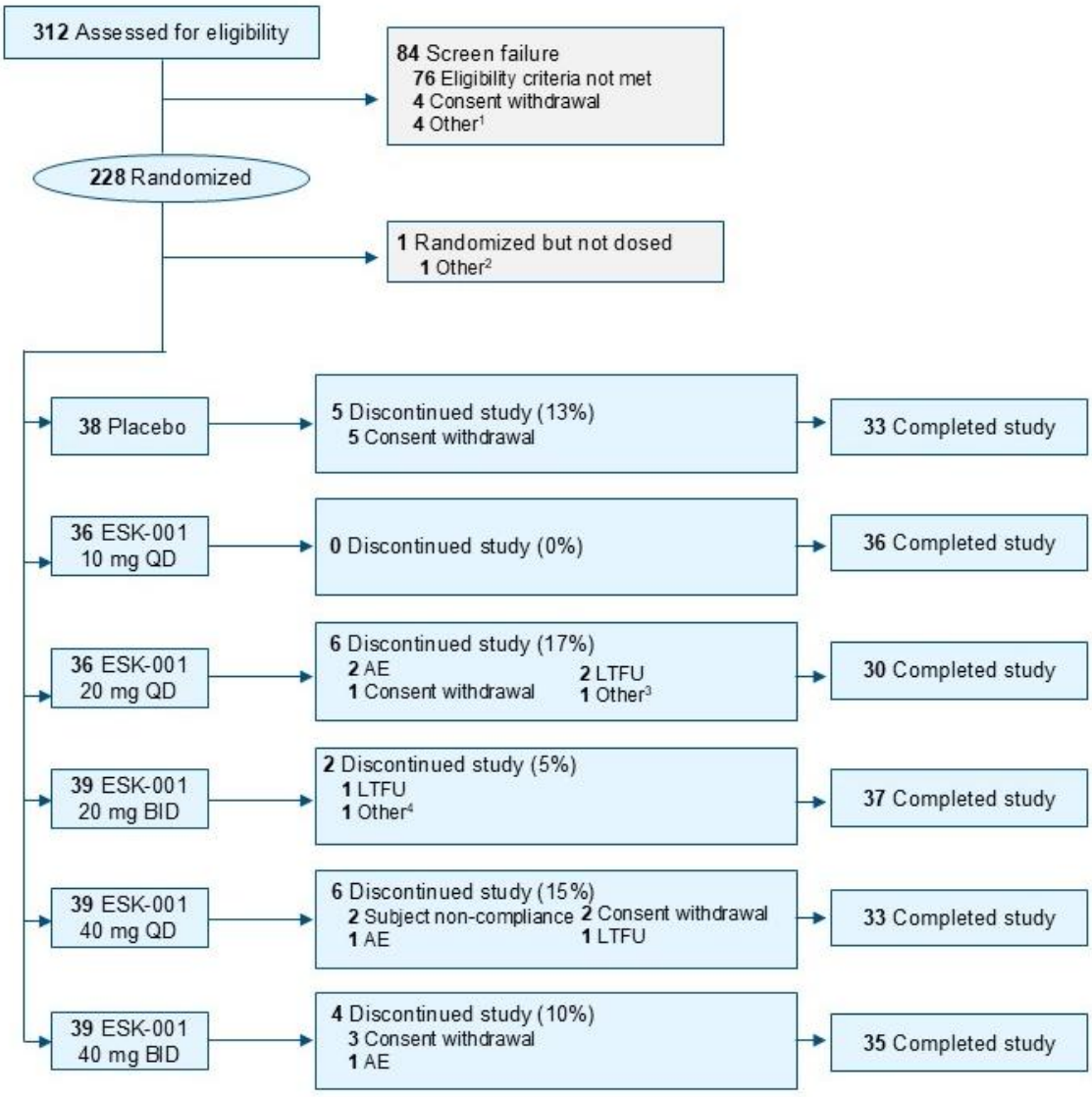
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| United States | Wiltz, Hector |
| Canada | Wiseman, Marni |
| United States | Yamauchi, Paul |
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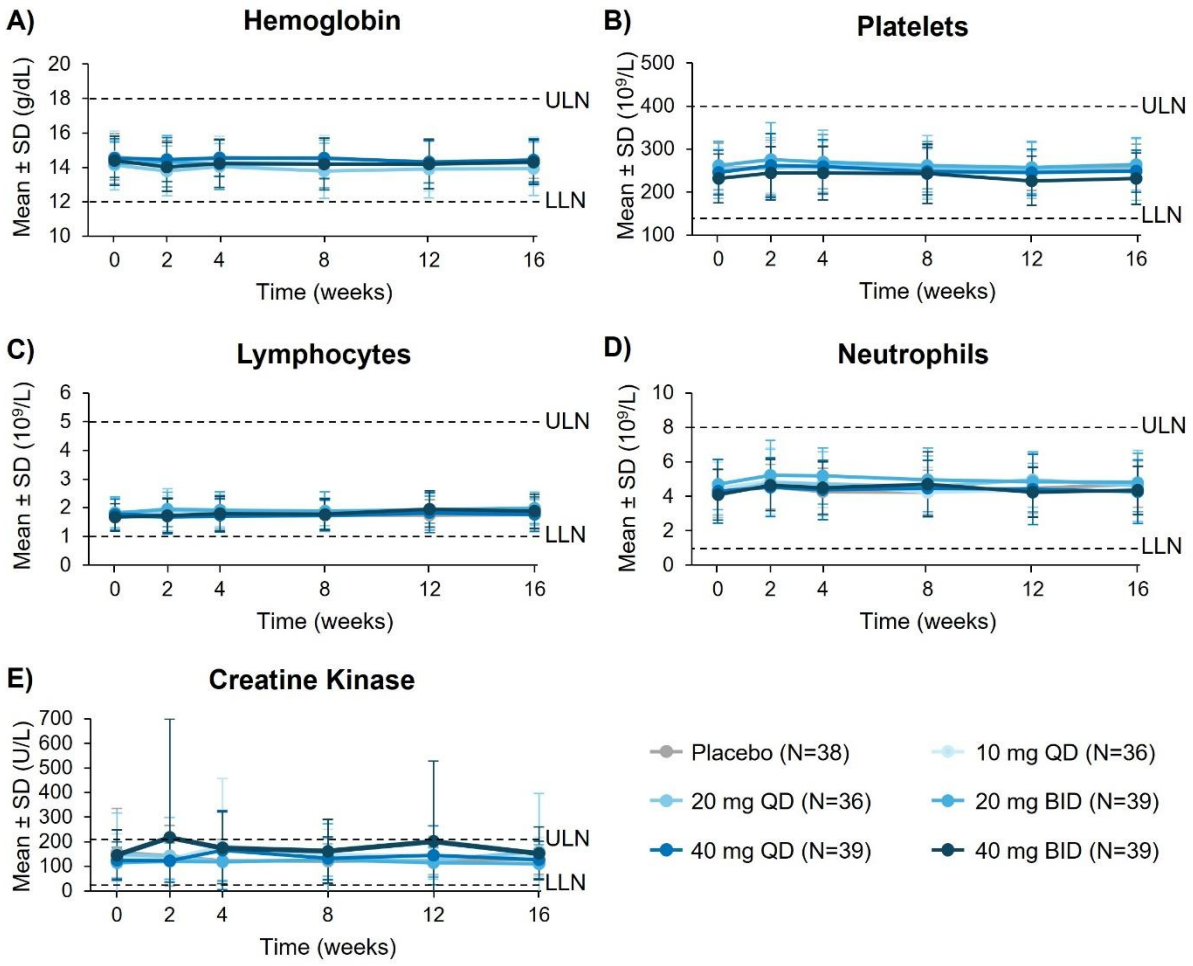
*Supplementary Figures*



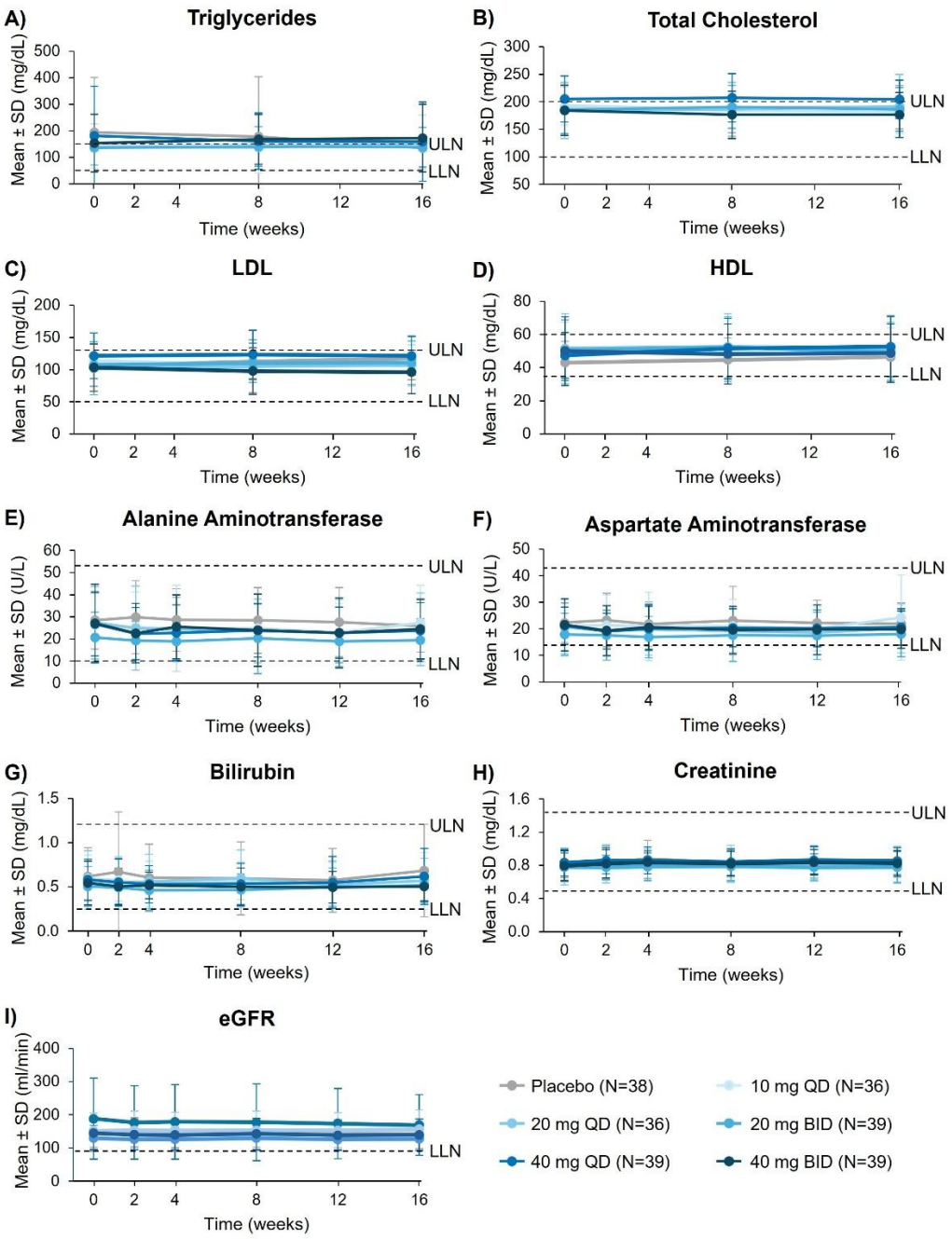

**Supplementary Figure 1. Design of the STRIDE Phase 2 study of ESK-001 in patients with moderate-to-severe plaque psoriasis.** *BID*, twice daily; *N*, number of patients; *OLE*, open-label extension; *QD*, once daily. *Eligible patients rolled over to OLE study. †One patient randomized but not dosed.



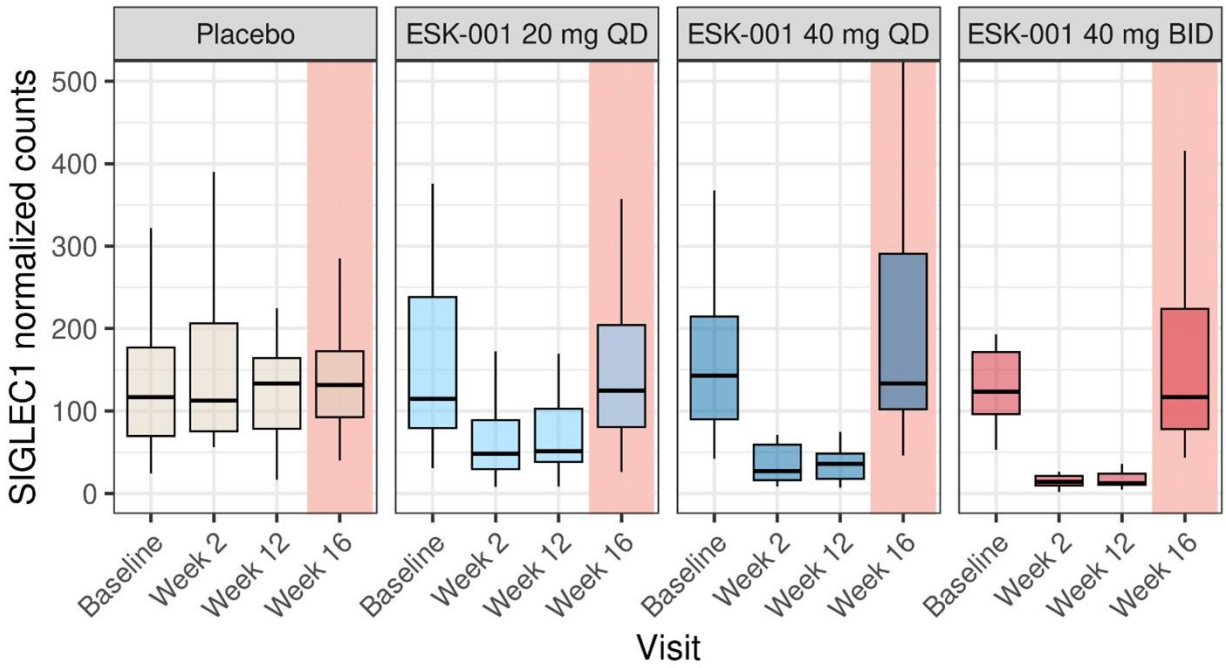

**Supplementary Figure 2. Patient disposition of STRIDE Phase 2 study in patients with moderate-to-severe plaque psoriasis.** *AE*, adverse event; *BID*, twice daily; *BMI*, body mass index; *LTFU*, loss to follow-up; *QD,* once daily. [1]LTFU (n=2); enrollment closed by Sponsor (n=1), BMI too high and LTFU (n=1); [2]Subject randomized to 20 mg BID dose discontinued prior to dosing due to blood sample logistics; [3]At Sponsor's discretion; [4]Subject refused to comply with protocol.



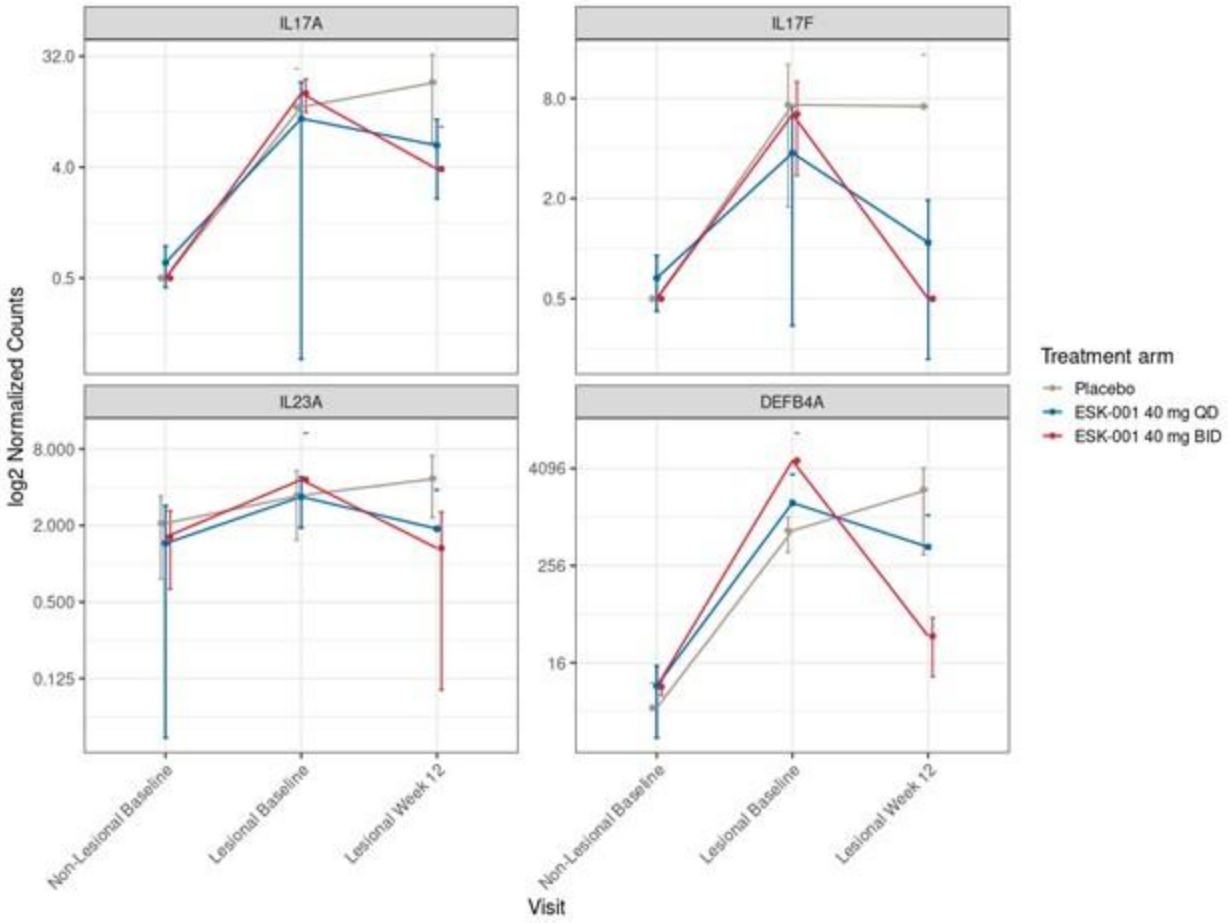

**Supplementary Figure 3. Hematologic laboratory parameters and creatine kinase over time following ESK-001 treatment in patients with moderate-to-severe plaque psoriasis in STRIDE Phase 2 study.** Dashed lines represent the ULN and LLN reference range for each parameter. *BID*, twice daily; *LLN,* lower limit of normal; *QD*, once daily; *SD*, standard deviation; *ULN*, upper limit of normal.



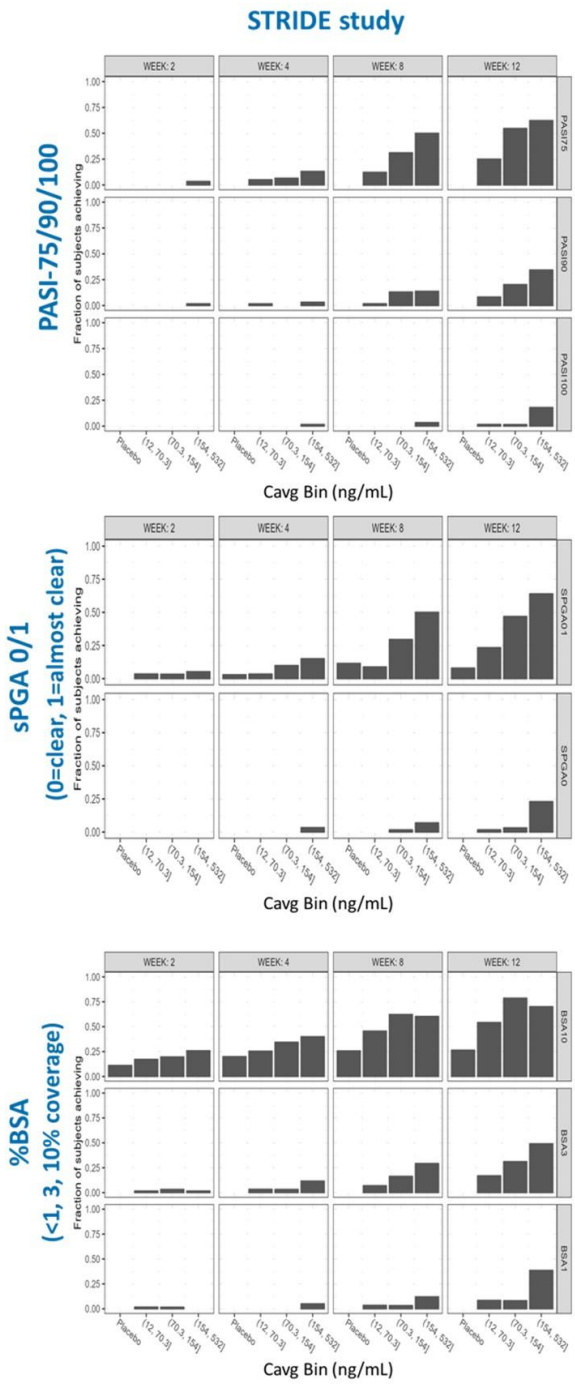

**Supplementary Figure 4. Lipid, hepatic, and renal laboratory parameters over time following ESK-001 treatment in patients with moderate-to-severe plaque psoriasis in STRIDE Phase 2 study.** Dashed lines represent the ULN and LLN reference range for each parameter. *BID*, twice daily; *eGFR*, estimated glomerular filtration rate; *LDL*, low density lipoprotein; *LLN,* lower limit of normal; *HDL*, high density lipoprotein; *QD*, once daily; *SD*, standard deviation; *ULN*, upper limit of normal.




**Supplementary Figure 5. Median SIGLEC1 gene counts by ESK-001 treatment in patients in STRIDE Phase 2 study.** Pink-shaded bars reflect samples collected at end of drug washout period (Week 12 to Week 16). *BID*, twice daily*, QD*, once daily; *SIGLEC1;* sialic acid binding immunoglobulin (Ig)-like lectin 1; *SD*, standard deviation.




**Supplementary Figure 6. Median log2 normalized gene counts in skin biopsies by ESK-001 treatment in patients in STRIDE Phase 2 study.** *BID*, twice daily; *DEFB4A,* defensin beta 4A (encodes for hBD2 protein)*; IL,* interleukin; *QD*, once daily.




**Supplementary Figure 7. Exploratory exposure response analysis results between primary and secondary efficacy endpoints and exposure.** *BSA*, body surface area; *PASI*, Psoriasis Area and Severity Index; *PASI-75*, ≥75% reduction from baseline in; *PASI-90*, ≥90% reduction from baseline in PASI; *PASI-100*, 100% reduction from baseline in PASI; *sPGA-0/1*, static Physician's Global Assessment score of 0 or 1.