VYN202 Phase 1b Moderate-to-Severe PsO

July 2025

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VYN202: A Novel BD2-Selective BET Inhibitor for Immune-Mediated Diseases

- **VYN202 is an innovative, oral BD2-selective BET inhibitor**
- **VYN202 is believed to be the most potent and BD2-selective BET Inhibitor in clinical development[1] which is designed to improve efficacy and tolerability**
- **Program supported by robust preclinical data across multiple diverse models of immune-mediated disease**
- **Phase 1 SAD and MAD studies in healthy volunteers complete:**
  - VYN202 demonstrated a favorable safety and tolerability profile with no drug-related adverse events historically associated with earlier generation, less selective BET inhibitors
  - Favorable PK profile demonstrated for VYN202, supporting once-daily dosing regimen
  - VYN202 demonstrated robust pharmacodynamic activity including evidence of target engagement and significant inhibition of inflammatory biomarkers relevant to several immune-mediated disorders in ex vivo stimulation assays, consistent with preclinical disease models
- **Phase 1b study in moderate-to-severe plaque psoriasis designed to serve as potential gateway to other strategically attractive indications**

1. Based on readily available public information such as clintrials.gov, academic publications and corporate websites/presentations.

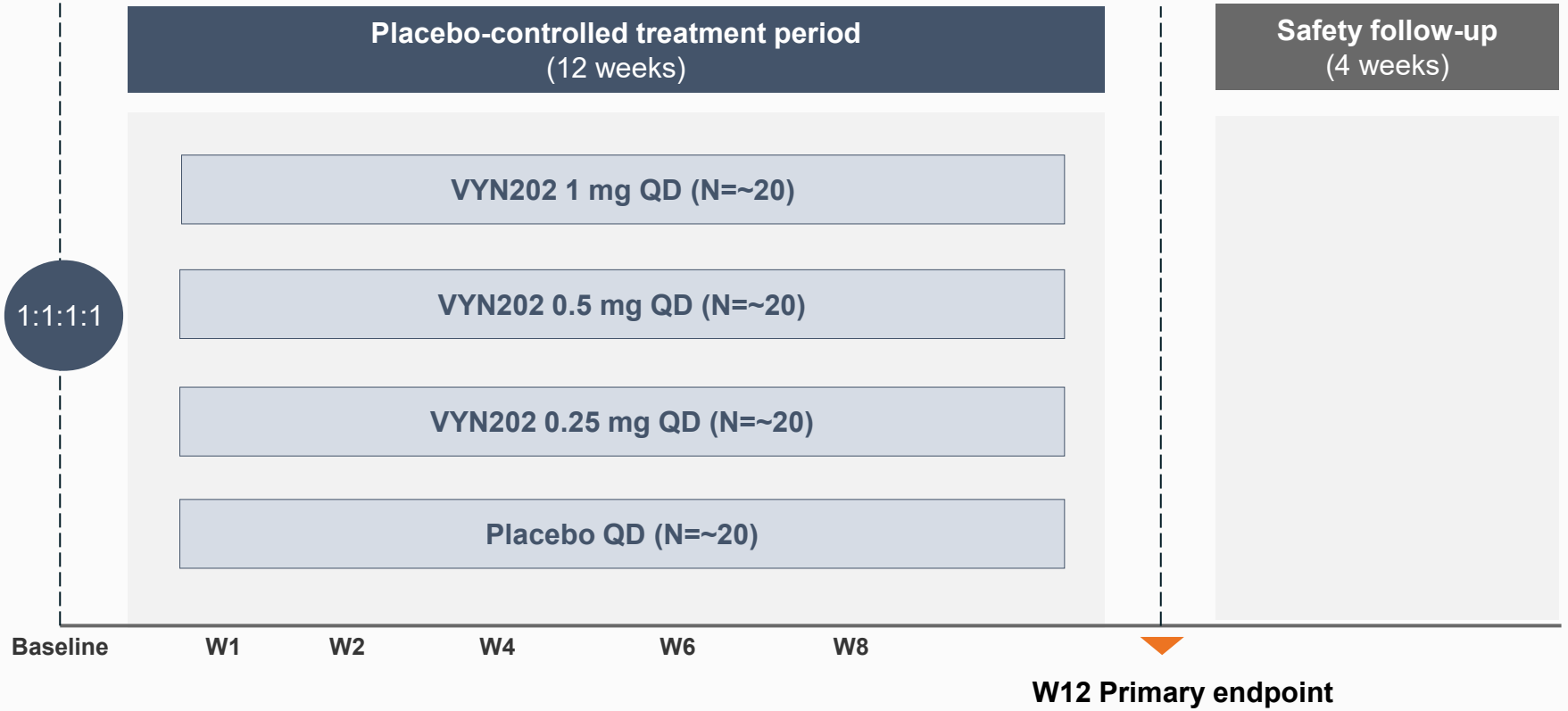
VYN202 Phase 1b Study Design in Moderate-to-Severe Plaque Psoriasis

N = up to 80 subjects with moderate-to-severe plaque psoriasis

Screening period
(30 days)

Key Inclusion Criteria
- 18-75 y
- BMI 18-40
- PASI ≥ 12
- sPGA≥ 3
- BSA ≥ 10%
- Biologic experienced capped at 30%

Key Exclusion Criteria
- Other forms of psoriasis
- Recent infections
- Concomitant immunomodulators



Key safety / PK assessments:

Treatment emergent adverse events

Physical exam/vitals

Clinical laboratory assessments

Cmin, Cave, AUC

Key efficacy endpoints: (exploratory)

Primary:
Change from baseline in PASI; PASI 75

Secondary:
PASI 90, PASI 100, sPGA 0/1, Scalp measures, DLQI

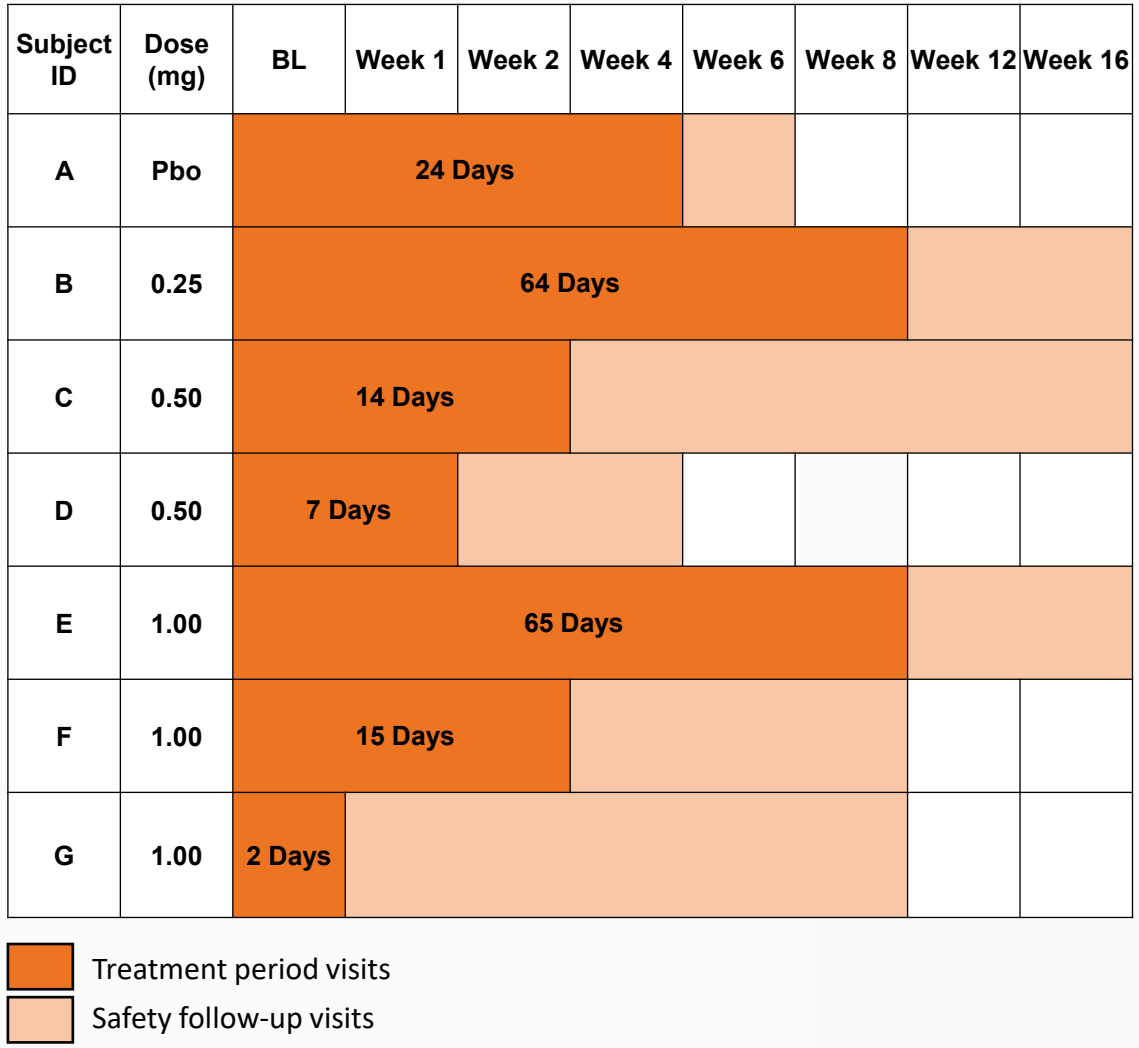
Biomarker Analysis

VYN202 Phase 1b Study: 7 Patients Enrolled

Demographic and Patient Characteristics

Parameter	Value
Mean Age, yr (min-max)	47.1 (30-59)
Sex, M/F	5/2
Race	White (7)
Ethnicity, HL / nHL	3/4
Mean PASI at Baseline (min-max)	18.3 (12.1-36.7)
Mean PSSI at Baseline (min-max)	20.0 (3-54)
Mean sPGA at Baseline (min-max)	3.1 (3-4)
Mean %BSA at Baseline (min-max)	20.8 (10-37)

Duration of treatment

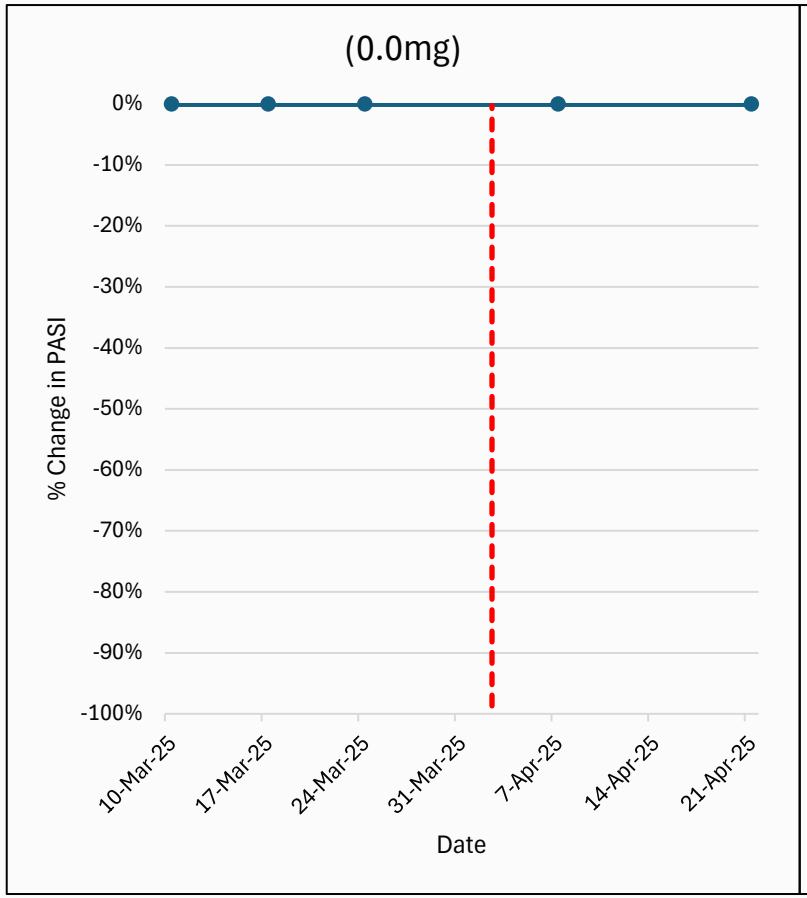


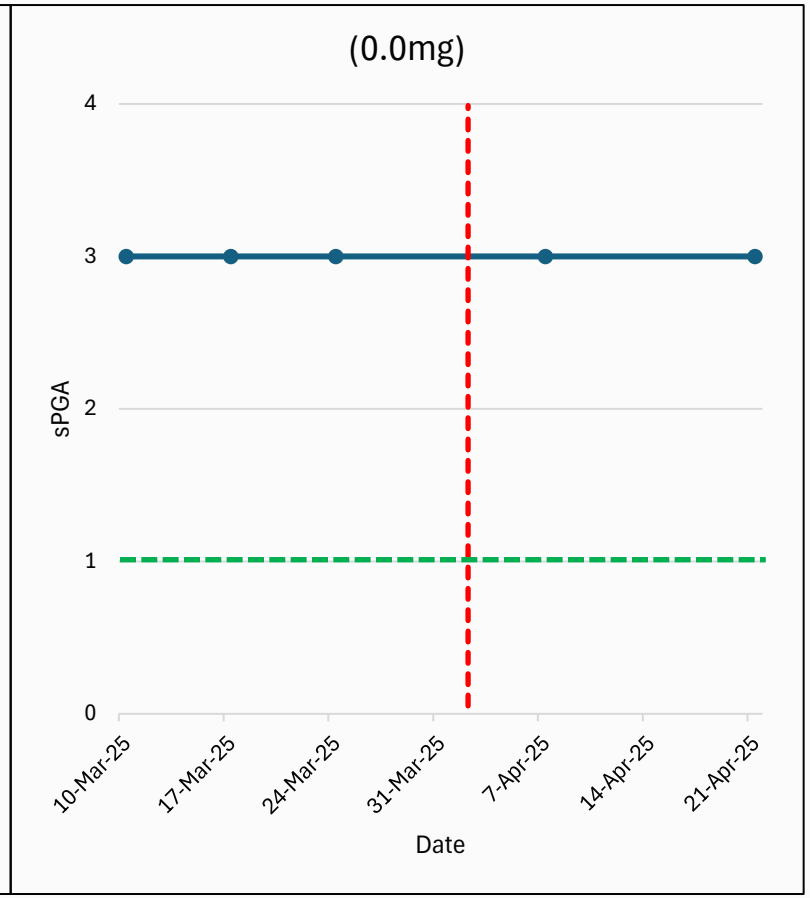
Preliminary Data available as of 6/20

HL - Hispanic or latino; nHL - not Hispanic or Latino

Subject A, Male (Placebo) - Efficacy

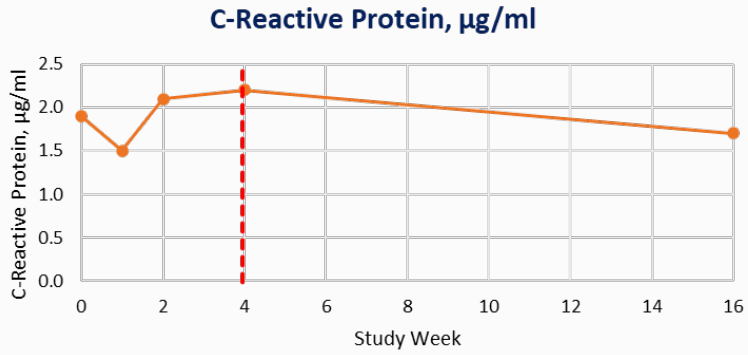
Visit	Baseline	Week 1	Week 2	Week 4	Week 6	Week 8	Week 12
Dosing Duration	10MAR			03APR (24 days)			
PASI Score	**26.7**	**26.7**	**26.7**	**26.7**	**26.7**	**-**	**-**
PSSI Score	24	24	24	24	24	-	-
sPGA Score	**3**	**3**	**3**	**3**	**3**	-	-
BSA	34	34	34	34	34	-	-
Itch NRS	8	10	9	9	9	-	-
Joint Pain NRS	8	8	8	9	9	-	-





Comments:

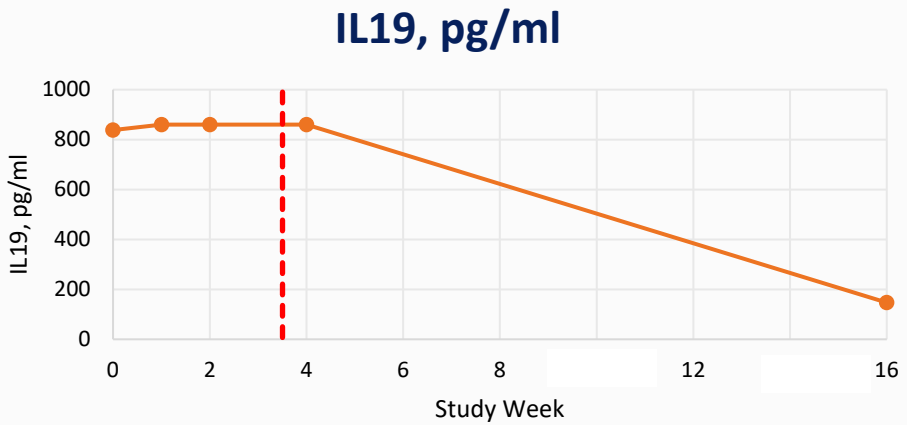
- Subject on placebo for 24 days
- No improvement in PASI, sPGA, Itch or Joint pain NRS

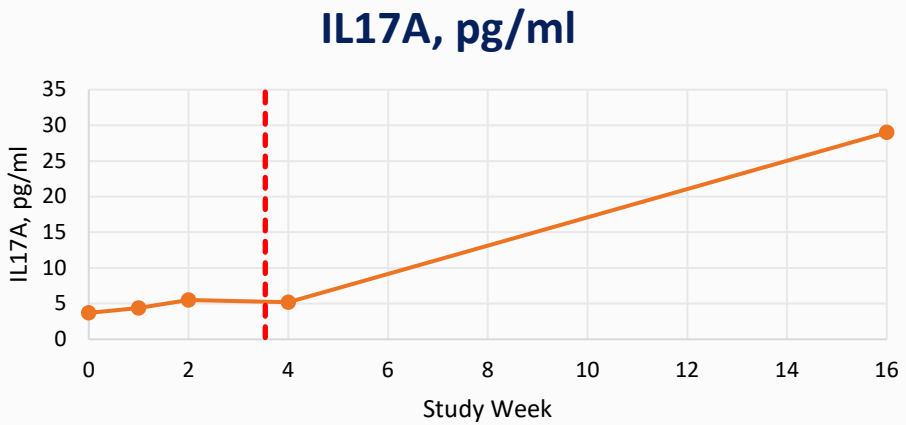


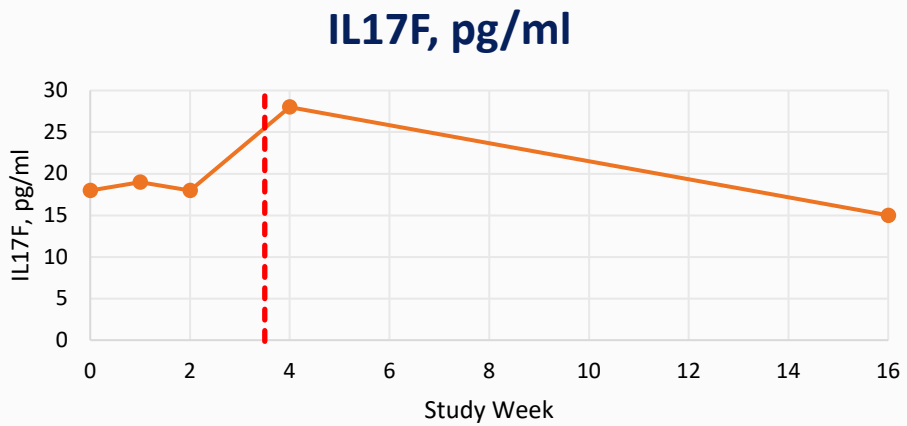
Treatment withdrawal date — Treatment success threshold by sPGA (Clear "0" or Almost clear "1")

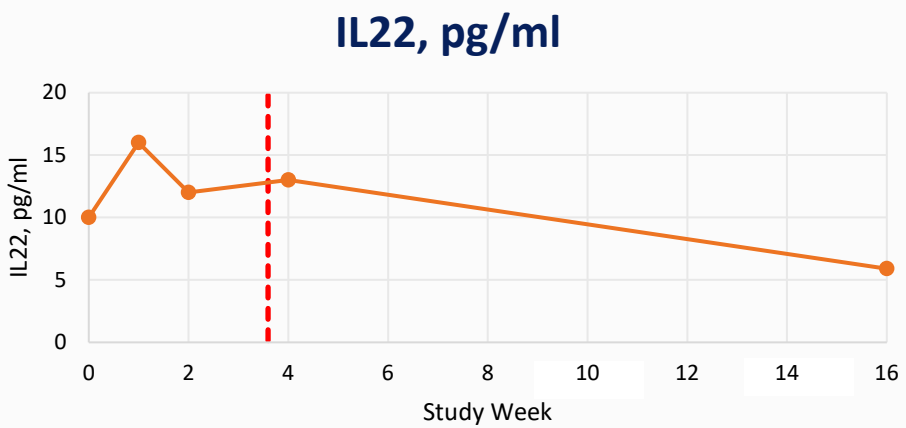
Preliminary Data available as of 6/20

Subject A, Male (Placebo) – Serum IL19, IL17A, IL17F & IL22 Biomarkers







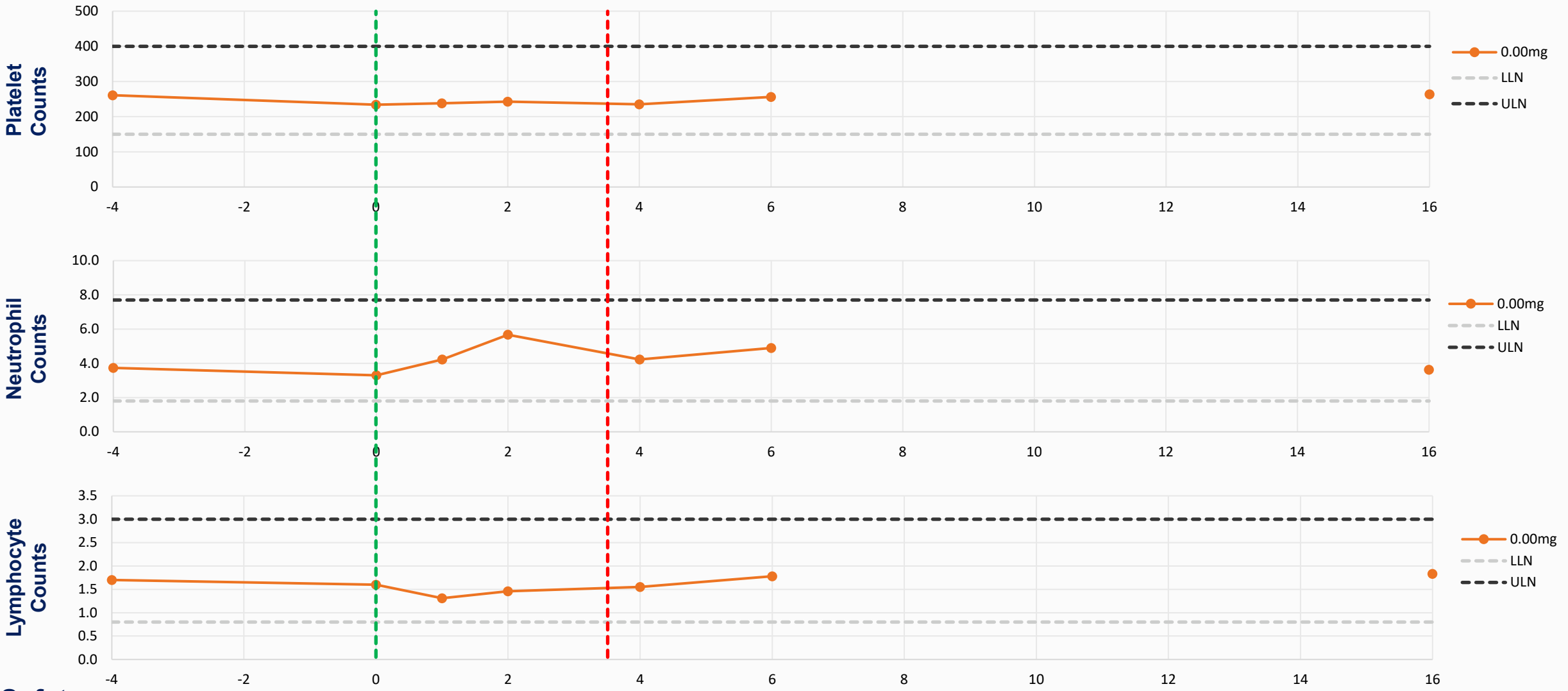


- No appreciable effect on any biomarkers during treatment

Treatment withdrawal date Percent change from baseline: 1-[Lowest value during treatment / Baseline value] * 100%

Preliminary Data available as of 6/30

Subject A, Male (Placebo) – Safety & Key Labs



Safety:

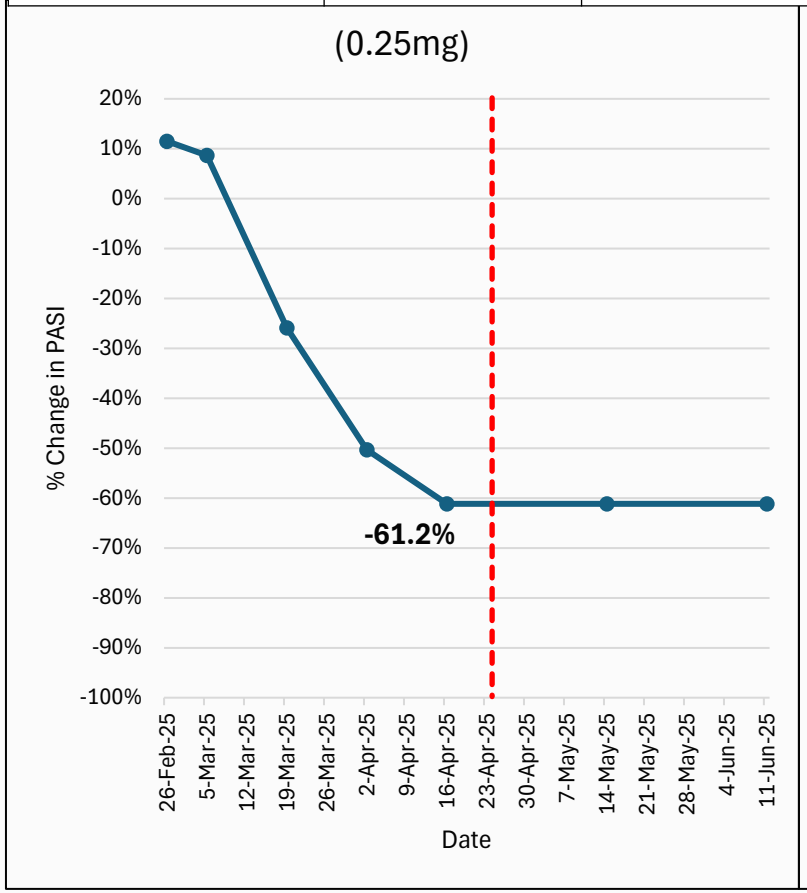
- Sinus infection, moderate severity, drug related, dose not changed, Augmentin (500mg), resolved.

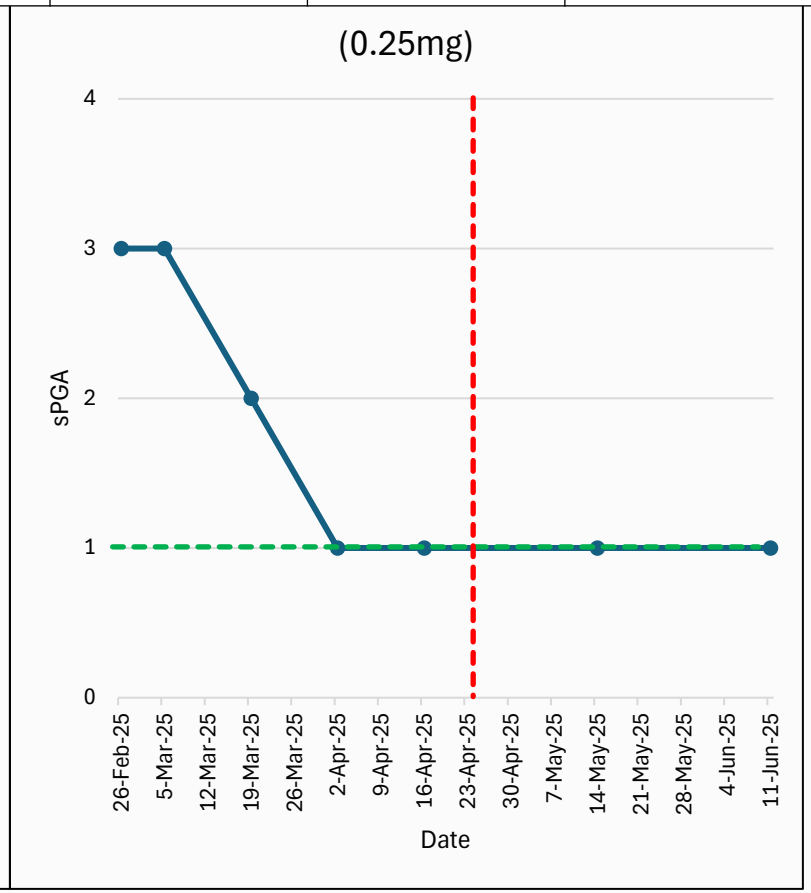
Treatment withdrawal date Baseline visit

Preliminary Data available as of 6/20

Subject B, Female (0.25mg) - Efficacy

Visit	Baseline	Week 1	Week 2	Week 4	Week 6	Week 8	Week 12	Week 16
Dosing Duration	26MARFEB					24APR (64 days)		
PASI Score	**13.9**	**15.5**	**15.1**	**10.3**	**6.9**	**5.4**	**5.4**	**5.4**
PSSI Score	14	14	14	8	4	4	4	4
sPGA Score	**3**	**3**	**3**	**2**	**1**	**1**	**1**	**1**
BSA	14	14	14	11	11	10	10	10
Itch NRS	9	7	7	6	5	7	4	3
Joint Pain NRS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	NA





Comments:

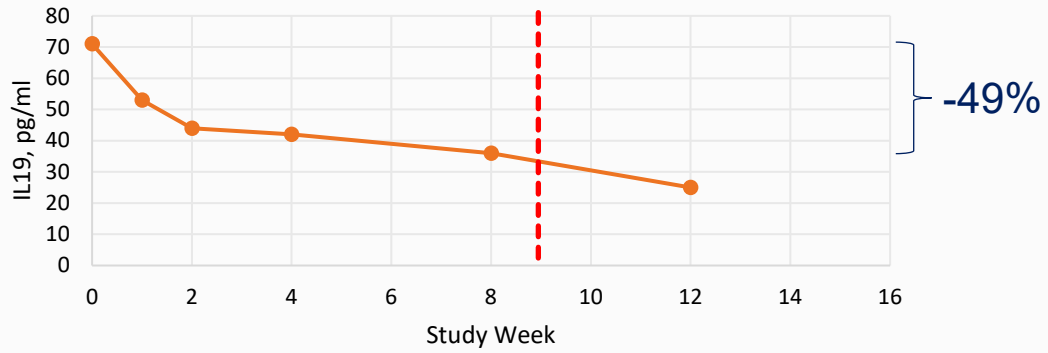
- Subject on active drug for 64 days
- Marked overall clinical response to treatment by PASI (>PASI60 at 2 months of treatment); Trending to PASI75
- Enduring treatment effect observed 1 month following last dose
- sPGA0/1 – treatment success reached.
- Positive impact on scalp psoriasis in addition to psoriasis on the body (>PSSI70 at Week 6).

Treatment withdrawal date Treatment success threshold by sPGA (Clear “0” or Almost clear “1”)

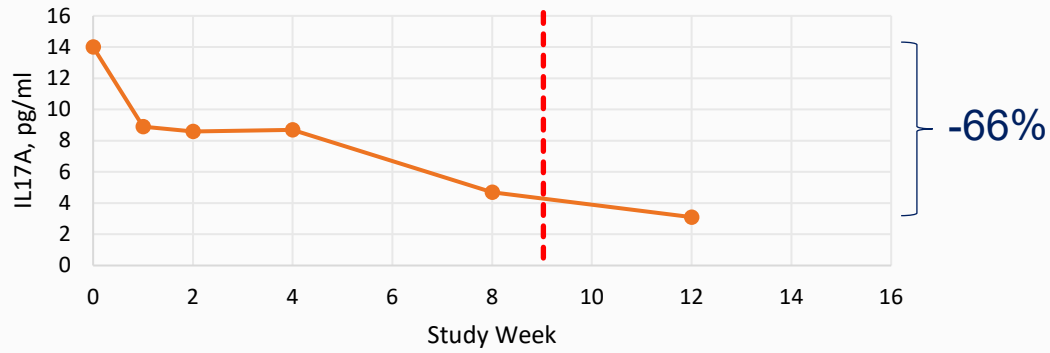
Preliminary Data available as of 6/20

Subject B, Female (0.25mg) - Serum IL19, IL17A, IL17F & IL22 Biomarkers

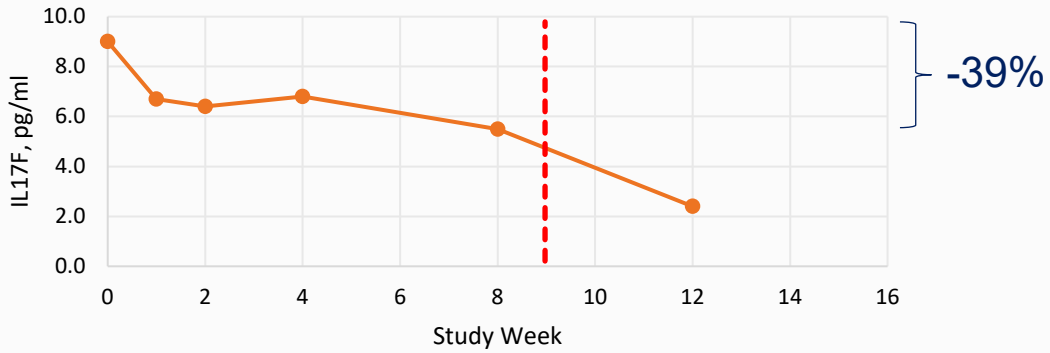
IL19, pg/ml



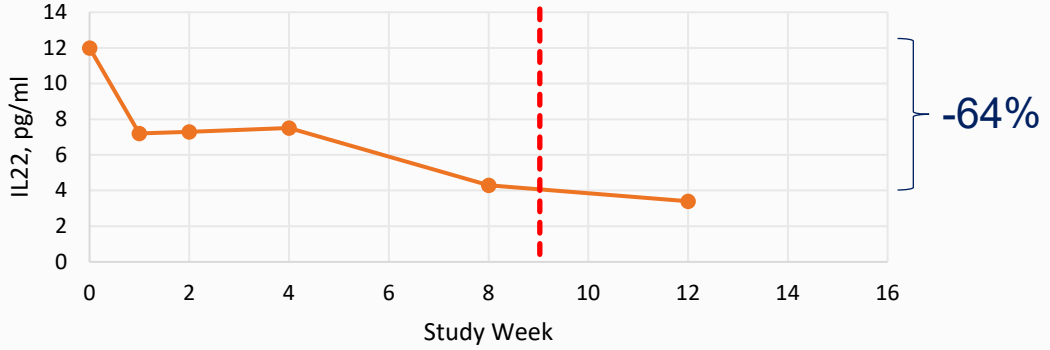
IL17A, pg/ml



IL17F, pg/ml



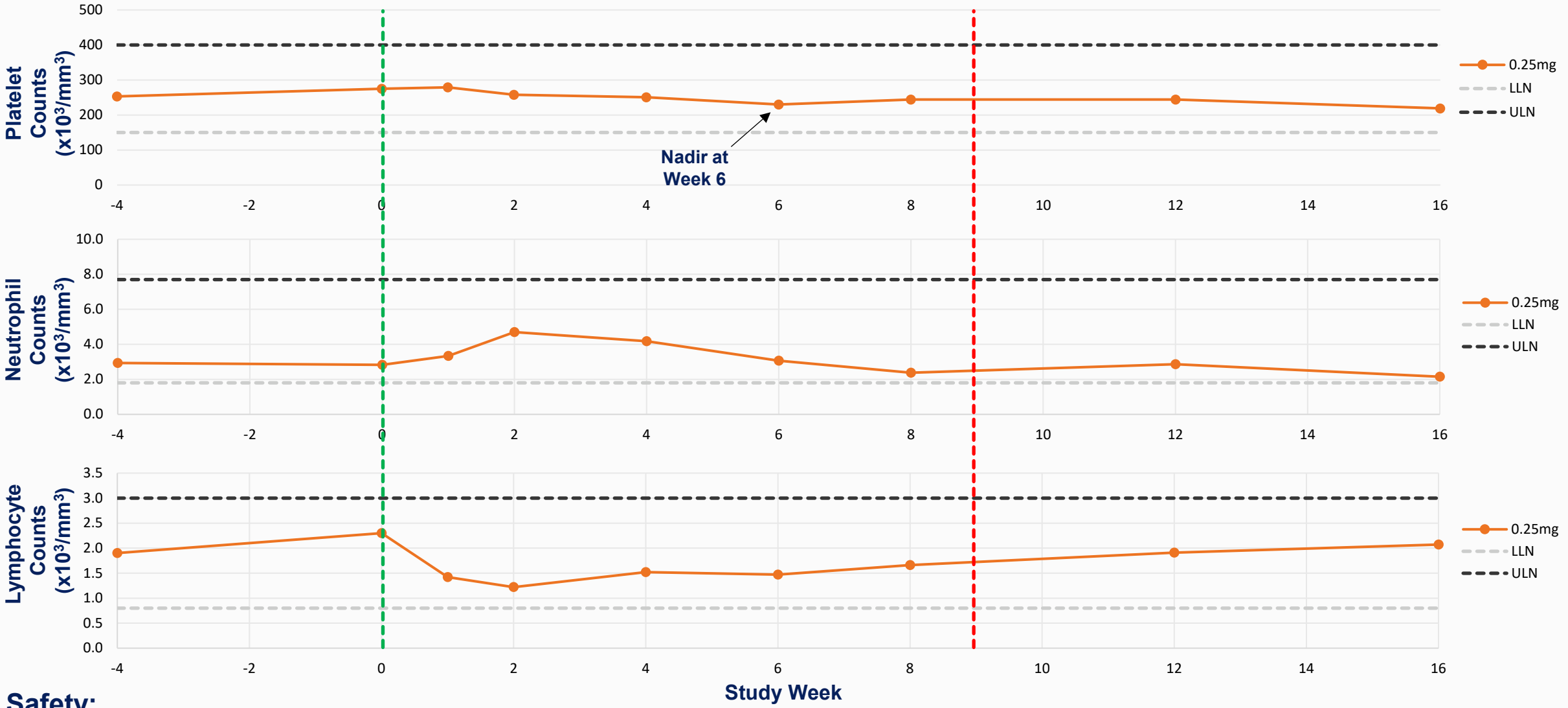
IL22, pg/ml



Treatment withdrawal date Percent change from baseline: 1-[Lowest value during treatment / Baseline value] * 100%

Preliminary Data available as of 6/30

Subject B, Female (0.25mg) – Safety & Key Labs



Safety:

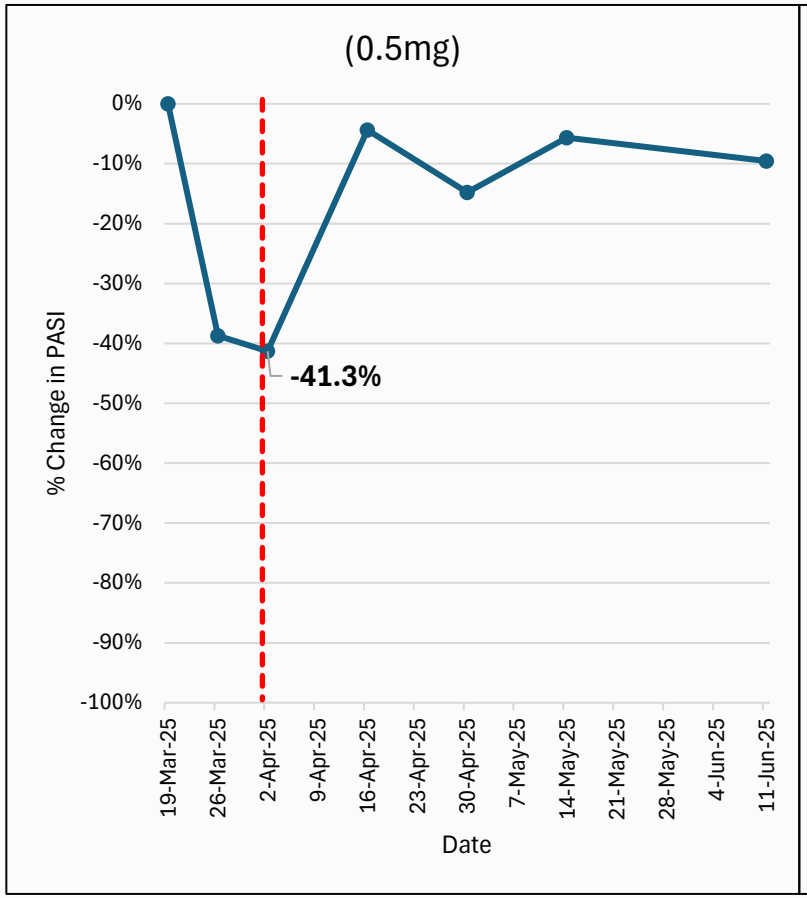
- Urinary tract infection, moderate severity, not drug related, dose not changed, Ciprofloxacin (500mg), resolved prior to treatment discontinuation.

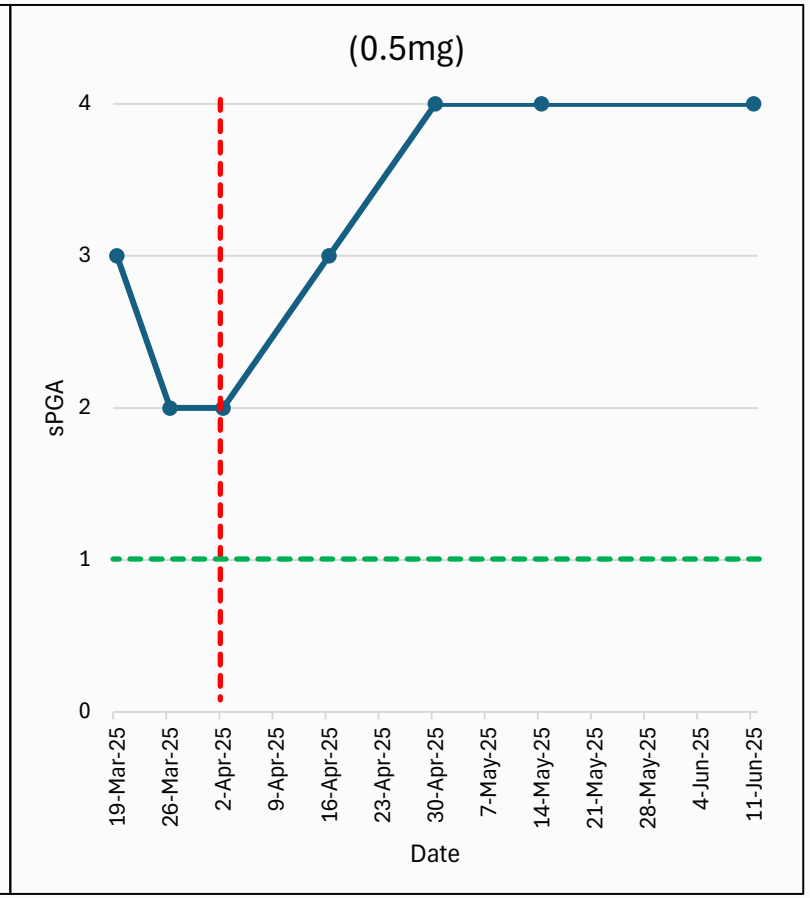
Treatment withdrawal date Baseline visit

Preliminary Data available as of 6/20

Subject C, Male (0.5mg) - Efficacy

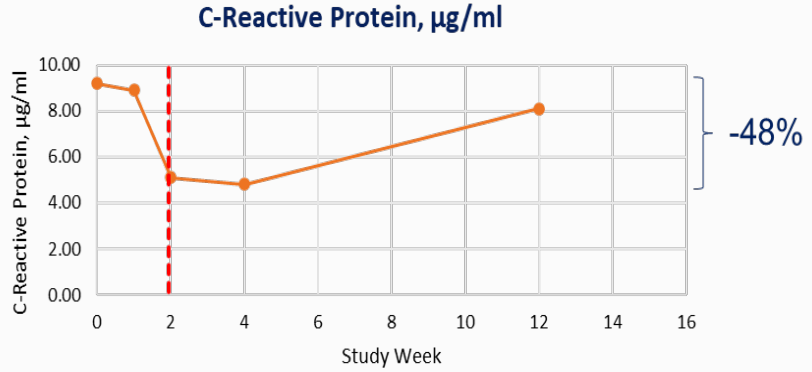
Visit	Baseline	Week 1	Week 2	Week 4	Week 6	Week 8	Week 12
Dosing Duration	19MAR		02APR (14 days)				
PASI Score	**23**	**14.1**	**13.5**	**22**	**19.6**	**21.7**	**20.8**
PSSI Score	12	3	3	10	10	10	10
sPGA Score	**3**	**2**	**2**	**3**	**4**	4	4
BSA	37	27	26	29	28.5	34	35
Itch NRS	6	3	3	3	5	8	8
Joint Pain NRS	7	5	3	3	7	8	8





Comments:

- Subject on active drug for 14 days
- Clear positive response to treatment followed by a worsening of disease after treatment withdrawal. >PASI40 at Week 2.
- 4-point improvement in joint pain NRS scale by week 2 which corresponded with a -48% reduction in serum c-reactive protein level.

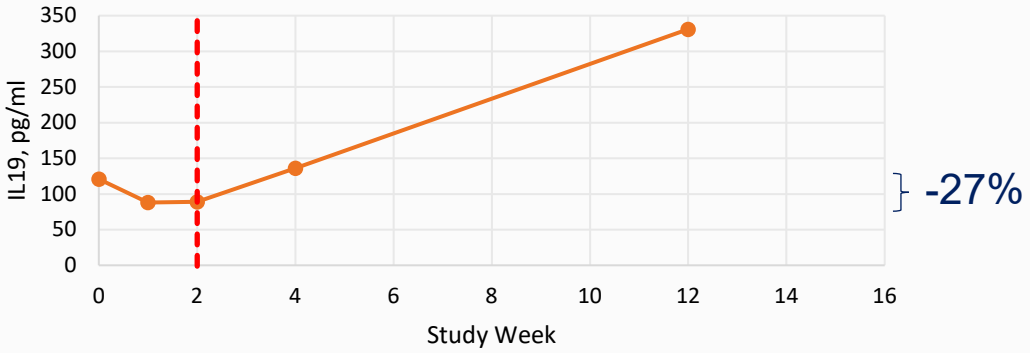


Treatment withdrawal date — Treatment success threshold by sPGA (Clear "0" or Almost clear "1")

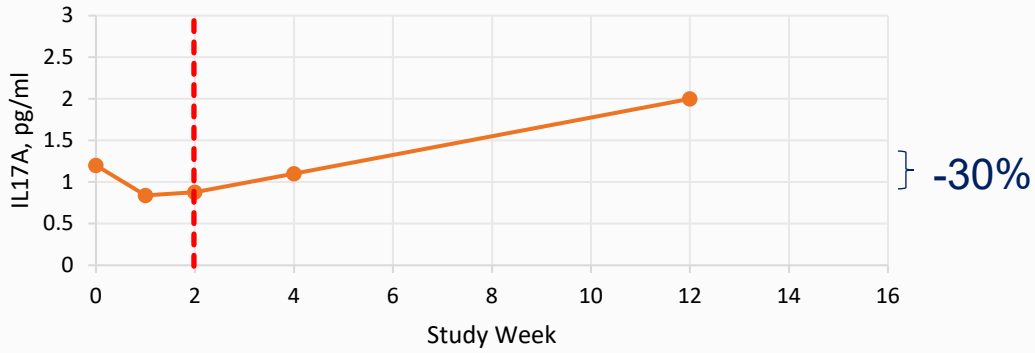
Preliminary Data available as of 6/20

Subject C, Male (0.5mg) - Serum IL19, IL17A, IL17F & IL22 Biomarkers

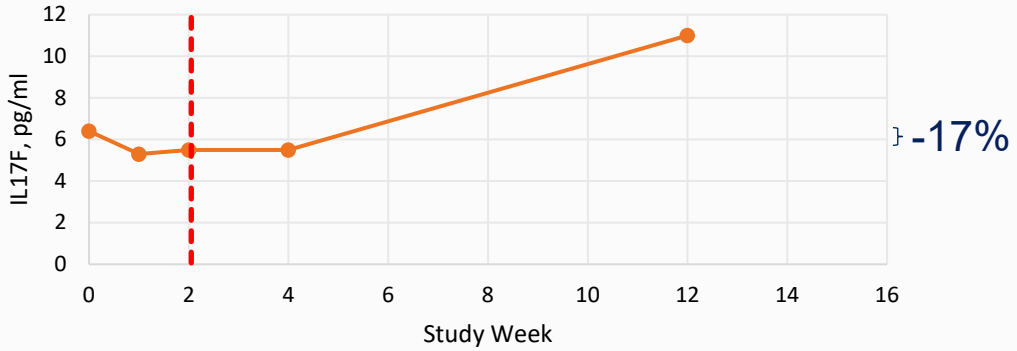
IL19, pg/ml



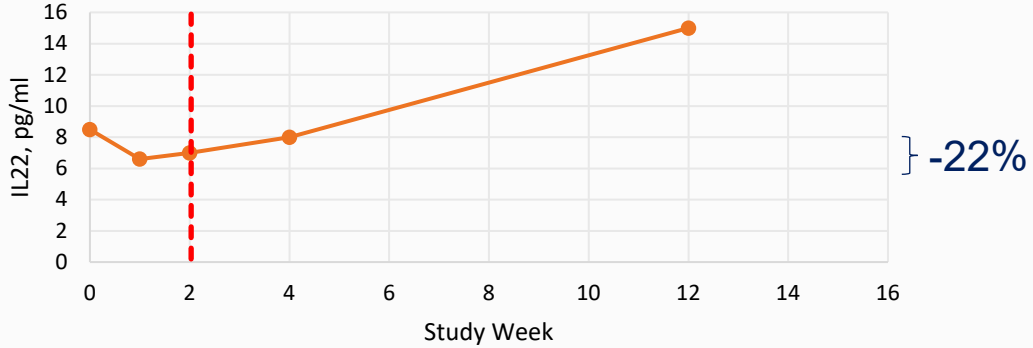
IL17A, pg/ml



IL17F, pg/ml



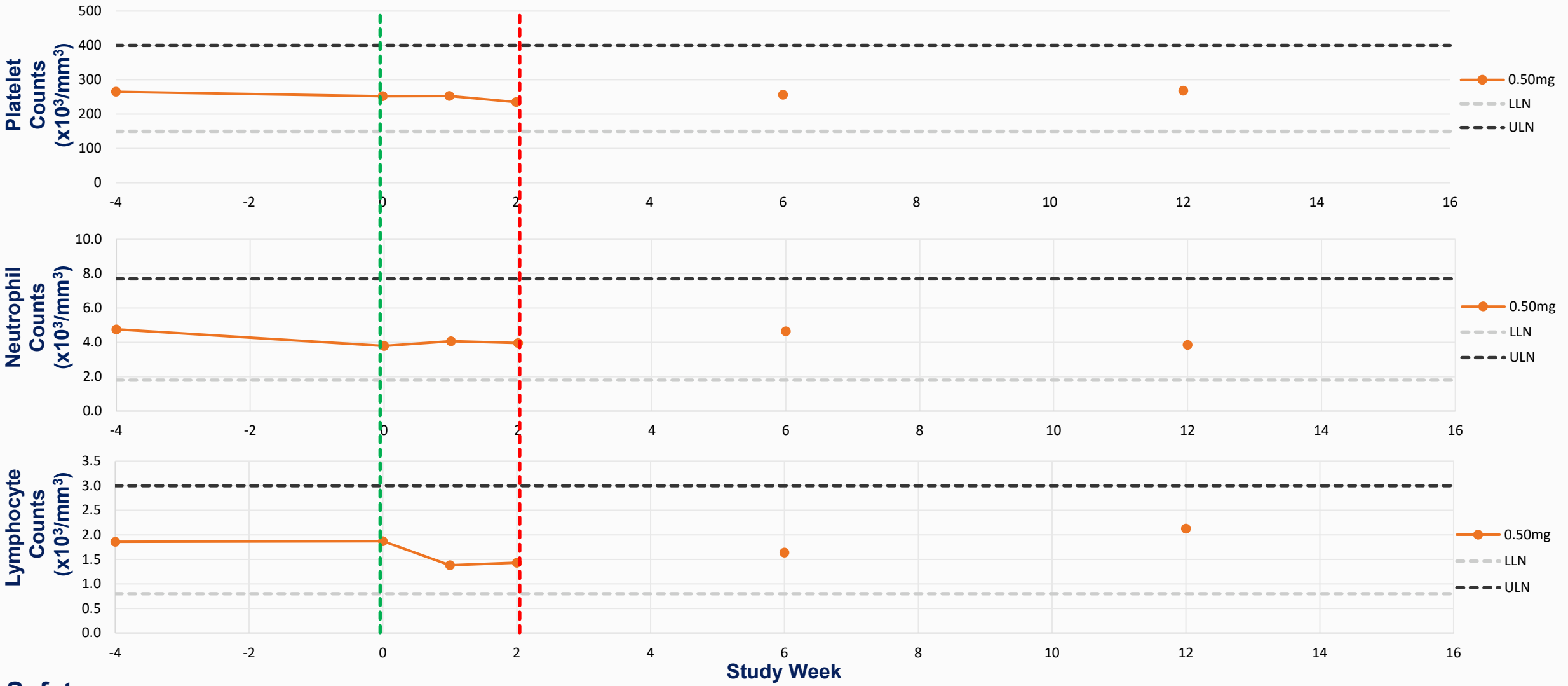
IL22, pg/ml



Treatment withdrawal date Percent change from baseline: 1-[Lowest value during treatment / Baseline value] * 100%

Preliminary Data available as of 6/30

Subject C, Male (0.5mg) – Safety & Key Labs



Safety:

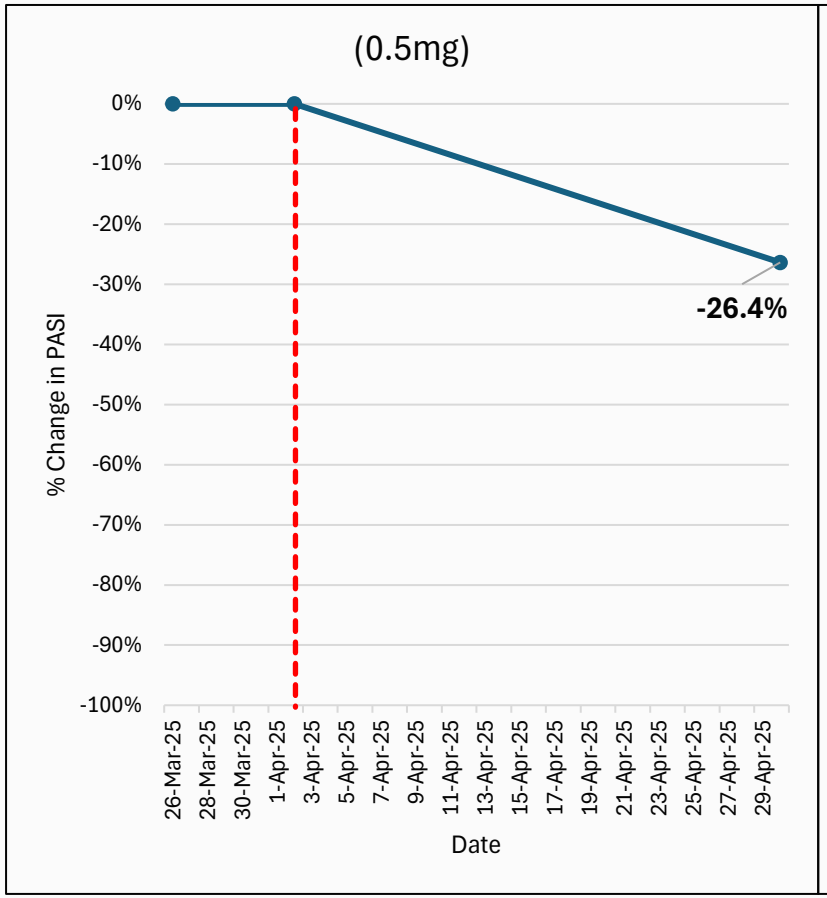
- No AEs

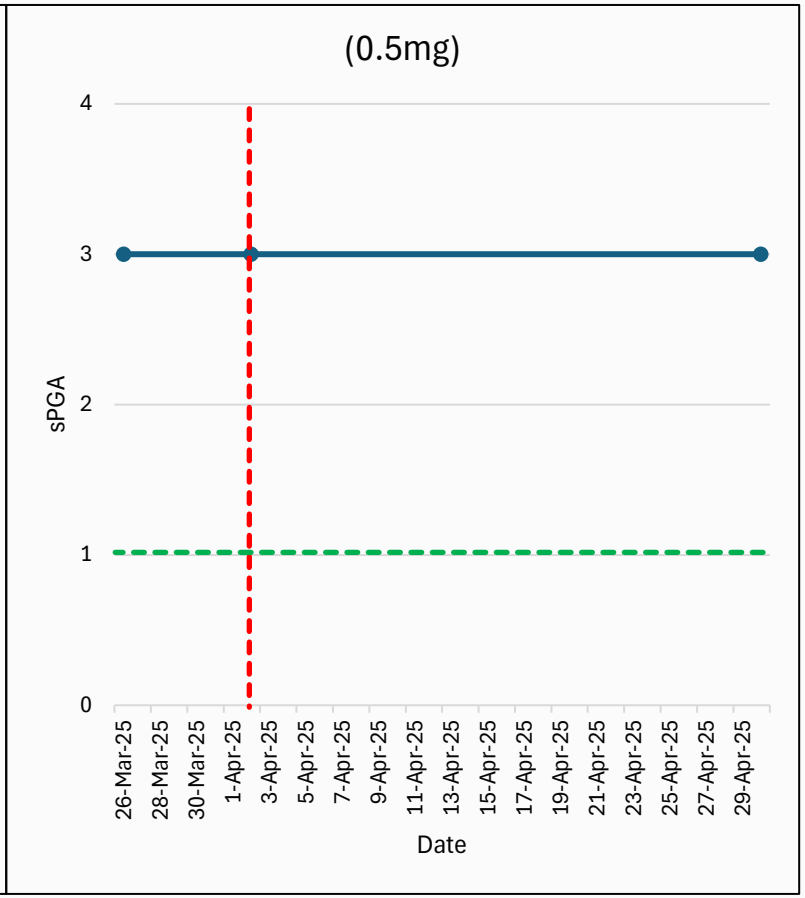
Treatment withdrawal date Baseline visit

Preliminary Data available as of 6/20

Subject D, Male (0.5mg) - Efficacy

Visit	Baseline	Week 1	SFU
Dosing Duration	26MAR	02APR (7 days)	30APR
PASI Score	**20.1**	**20.1**	**14.8**
PSSI Score	3	-	-
sPGA Score	**3**	**3**	**3**
BSA	31	31	32
Itch NRS	9	10	10
Joint Pain NRS	N/A	N/A	N/A





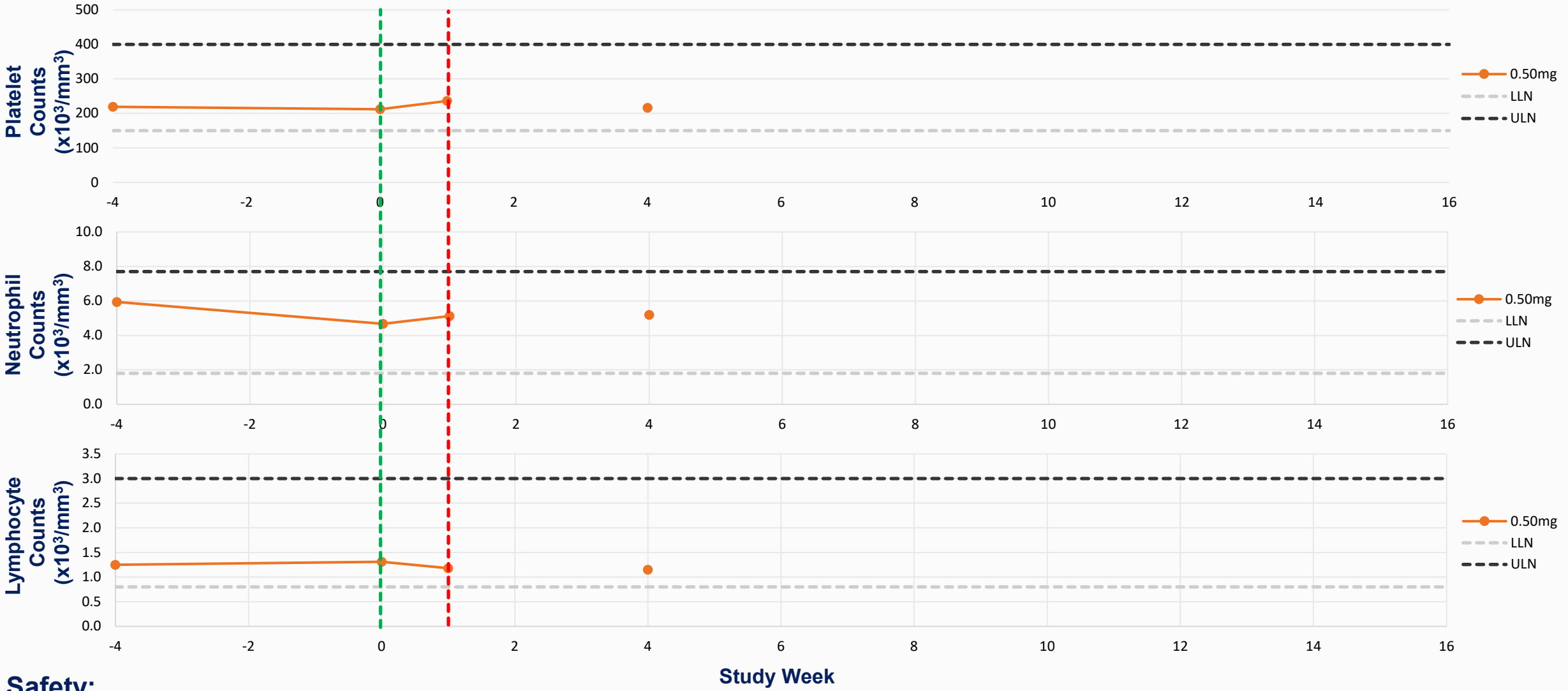
Comments:

- Subject on active drug for 7 days
- Safety follow up visit 4-weeks post-last dose showing improvement in PASI score
- Inflammatory biomarkers pending

Treatment withdrawal date — Treatment success threshold by sPGA (Clear “0” or Almost clear “1”)

Preliminary Data available as of 6/20

Subject D, Male (0.5mg) – Safety & Key Labs



Safety:

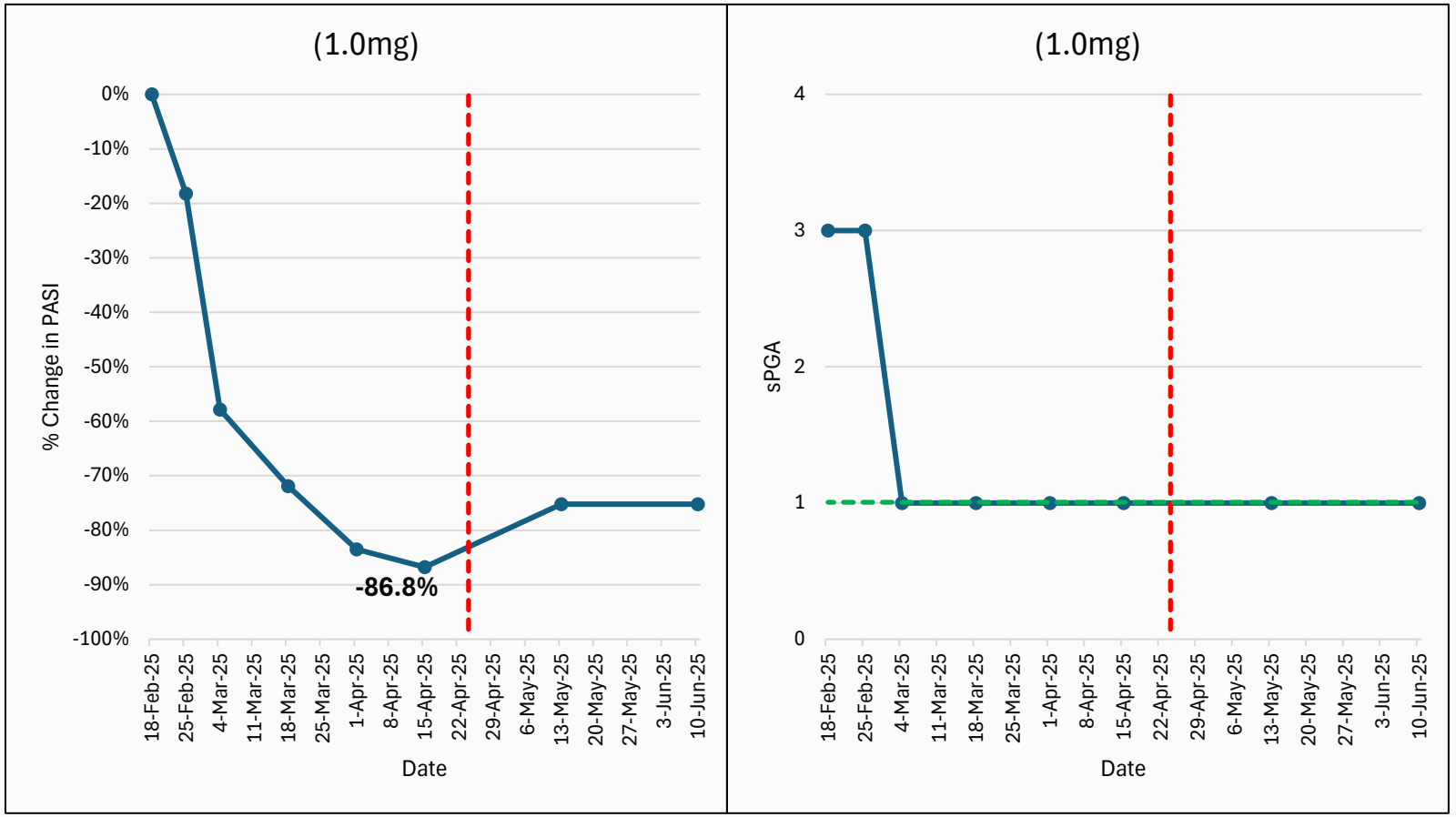
- No AEs

Treatment withdrawal date — Baseline visit

Preliminary Data available as of 6/20

Subject E, Female (1.0mg) - Efficacy

Visit	Baseline	Week 1	Week 2	Week 4	Week 6	Week 8	Week 12	Week 16
Dosing Duration	18FEB					24APR (65 days)		
PASI Score	**12.1**	**9.9**	**5.1**	**3.4**	**2**	**1.6**	**3**	**3**
PSSI Score	21	18	6	0	0	0	0	0
sPGA Score	**3**	**3**	**1**	**1**	**1**	**1**	1	1
BSA	10	10	6	4	3	3	4	4
Itch NRS	3	0	2	0	1	2	3	6
Joint Pain NRS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A



Comments:

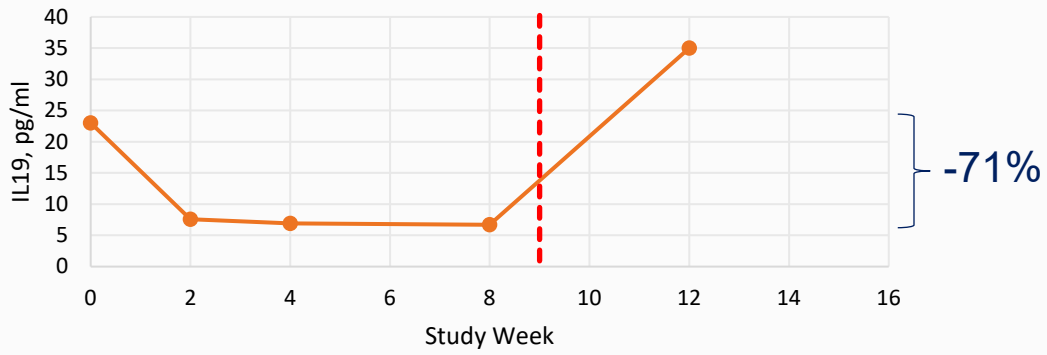
- Subject on active drug for 65 days
- Marked overall clinical response to treatment by PASI (Approx. PASI90 at 2 months of treatment) followed by worsening of disease after treatment withdrawal.
- sPGA0/1 – treatment success.
- Positive impact on scalp psoriasis in addition to psoriasis on the body (PSSI100, fully resolved).

Treatment withdrawal date Treatment success threshold by sPGA (Clear “0” or Almost clear “1”)

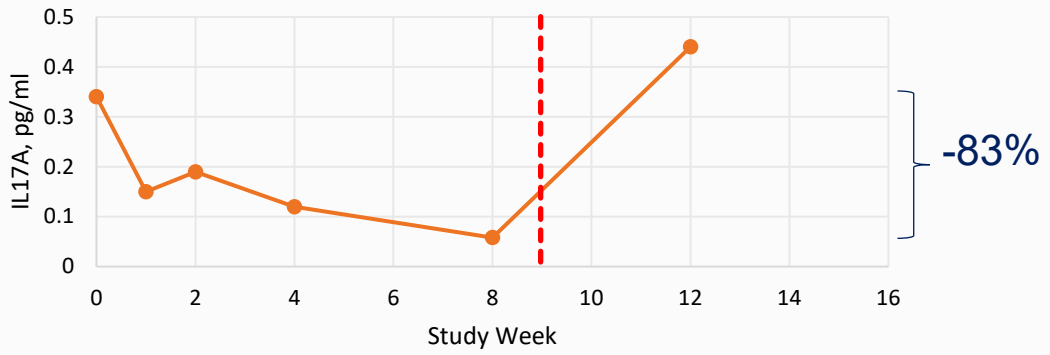
Preliminary Data available as of 6/20

Subject E, Female (1.0mg) - Serum IL19, IL17A, IL17F & IL22 Biomarkers

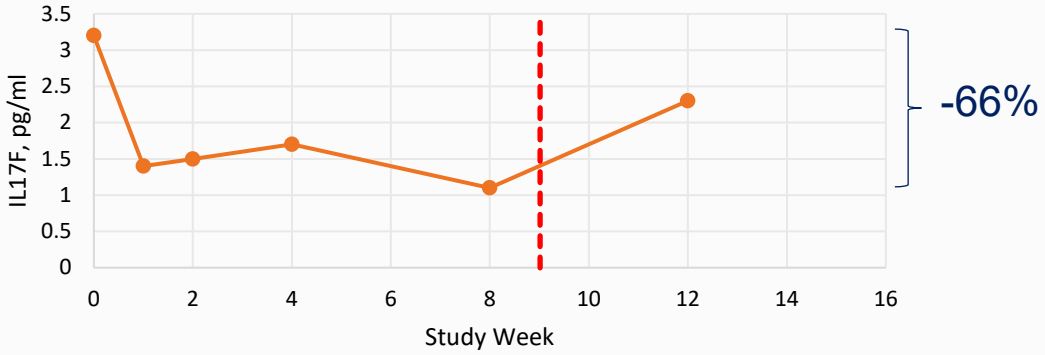
IL19, pg/ml



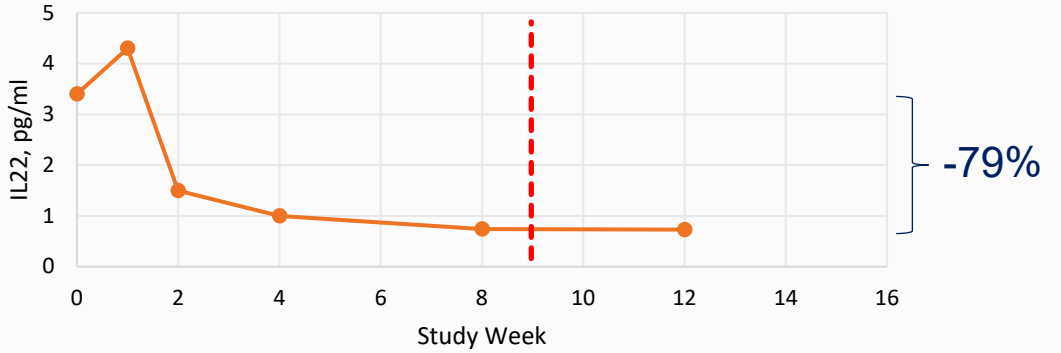
IL17A, pg/ml



IL17F, pg/ml



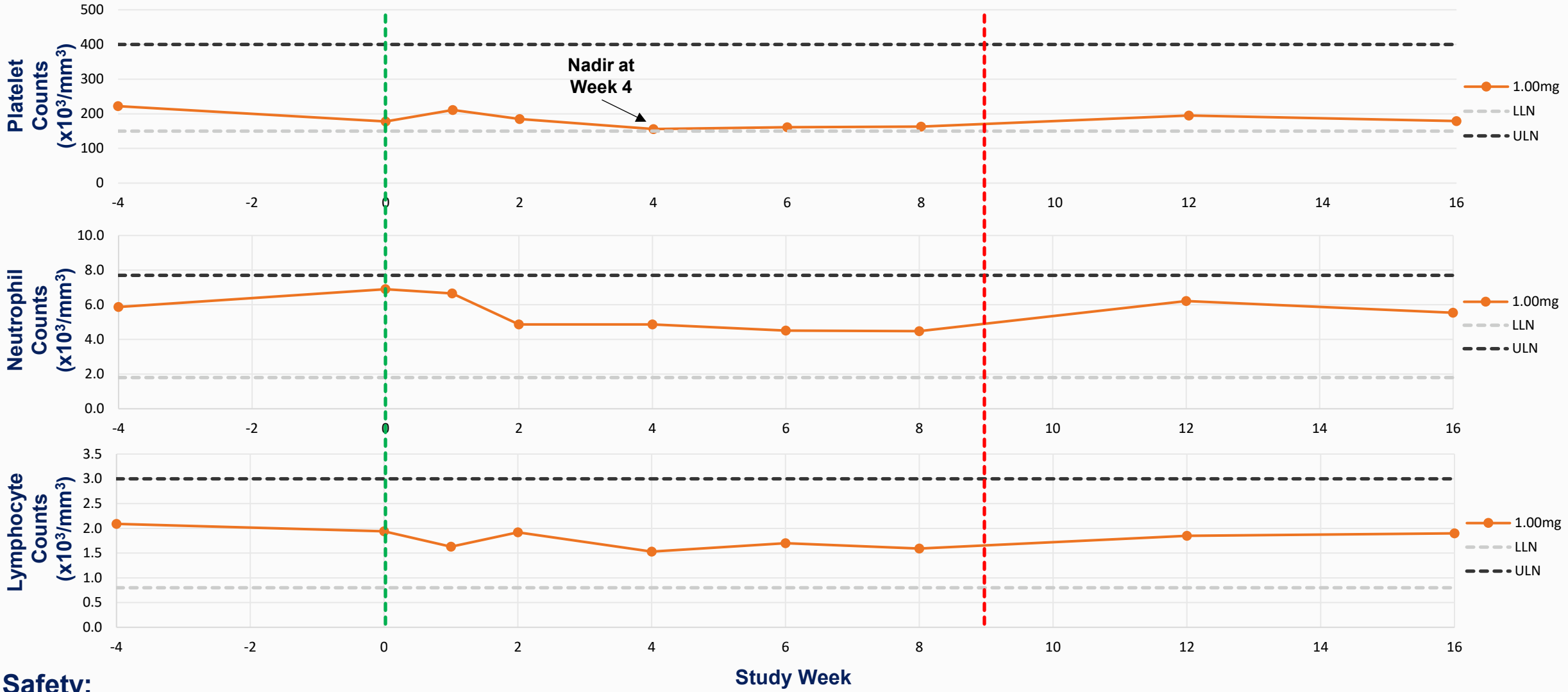
IL22, pg/ml



Treatment withdrawal date Percent change from baseline: 1-[Lowest value during treatment / Baseline value] * 100%

Preliminary Data available as of 6/30

Subject E, Female (1.0mg) - Safety & Key Labs



Safety:

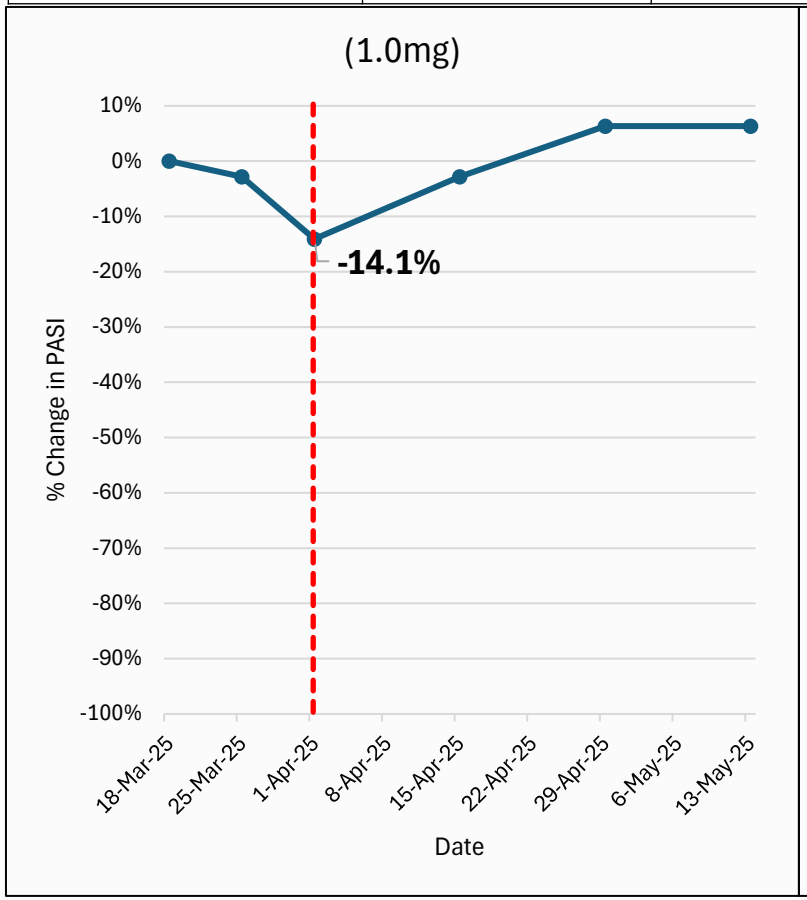
- Sinus infection, moderate severity, not drug related, dose not changed, Doxycycline (200mg)/Mucinex DM, resolved prior to treatment discontinuation; Diarrhea, moderate severity, drug related, dose not changed, Imodium/peptobismol, resolved

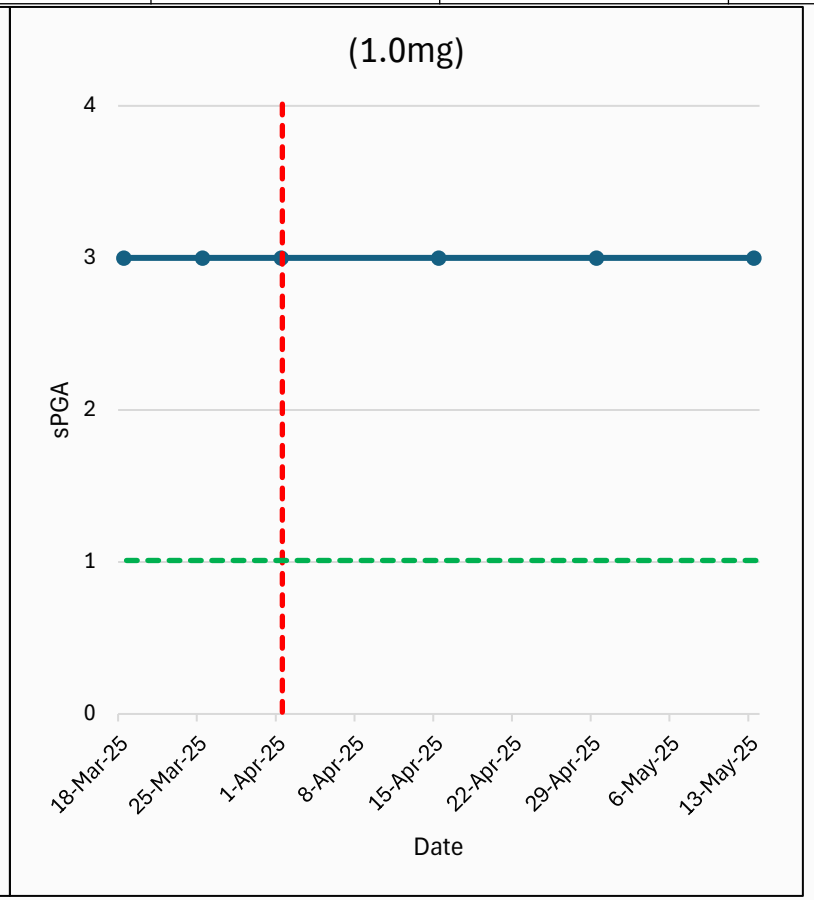
Treatment withdrawal date Baseline visit

Preliminary Data available as of 6/20

Subject F, Male (1.0mg) - Efficacy

Visit	Baseline	Week 1	Week 2	Week 4	Week 6	Week 8	Week 12
Dosing Duration	18MAR		02APR (14 days)				
PASI Score	**14.2**	**13.8**	**12.2**	**13.8**	**15.1**	**15.1**	**-**
PSSI Score	54	54	30	30	30	35	-
sPGA Score	**3**	**3**	**3**	**3**	**3**	3	-
BSA	18	18	16	18	18	18	-
Itch NRS	7	1	1	5	1	1	-
Joint Pain NRS	N/A	N/A	N/A	N/A	N/A	N/A	-





Comments:

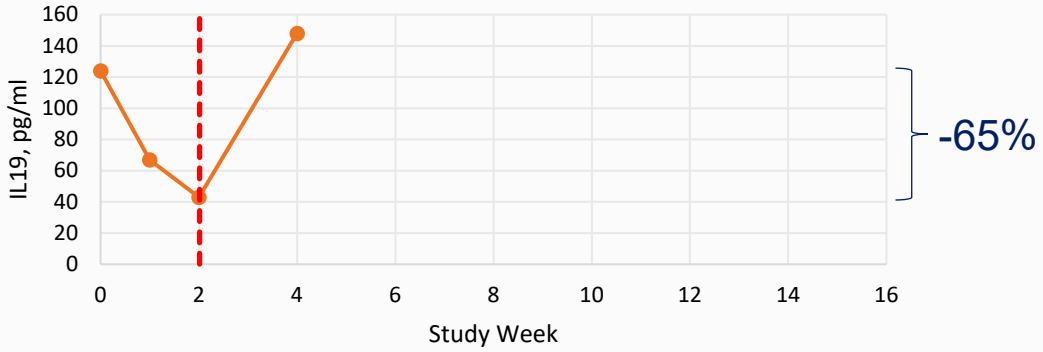
- Subject on active drug for 15 days
- Initial response to treatment followed by a worsening of disease after treatment withdrawal.
- Positive impact on scalp psoriasis (>PSSI40 at Week 2).

Treatment withdrawal date — Treatment success threshold by sPGA (Clear "0" or Almost clear "1")

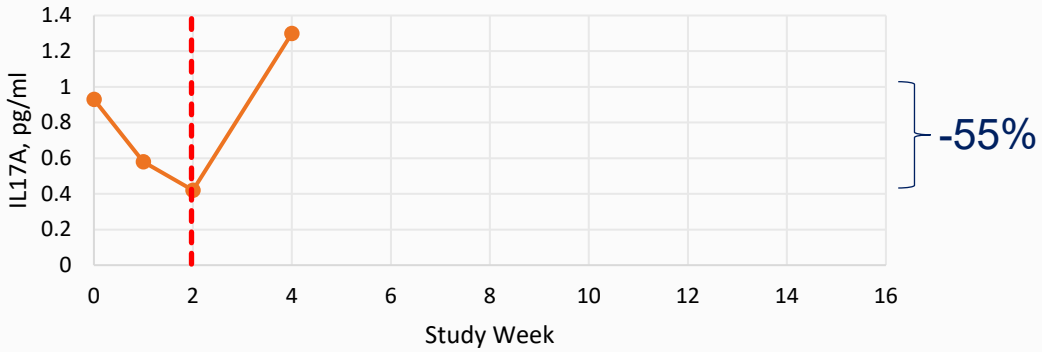
Preliminary Data available as of 6/20

Subject F, Male (1.0mg) - Serum IL19, IL17A, IL17F & IL22 Biomarkers

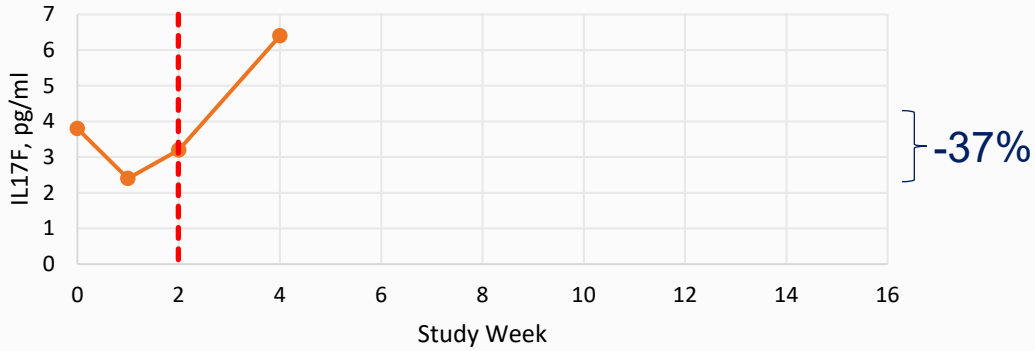
IL19, pg/ml



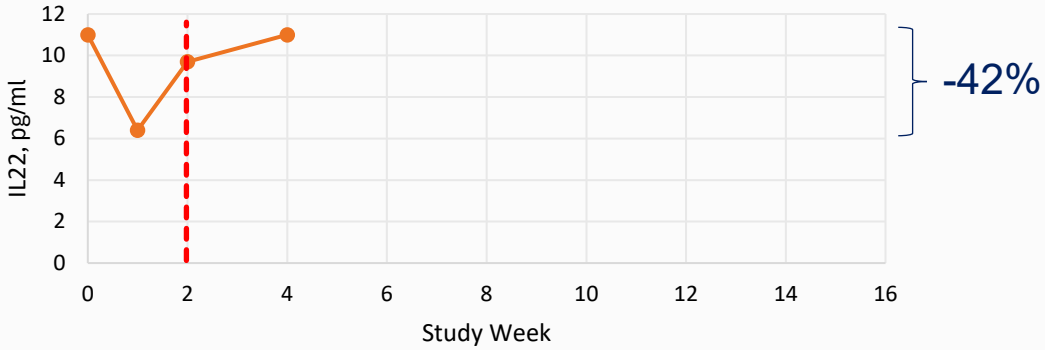
IL17A, pg/ml



IL17F, pg/ml



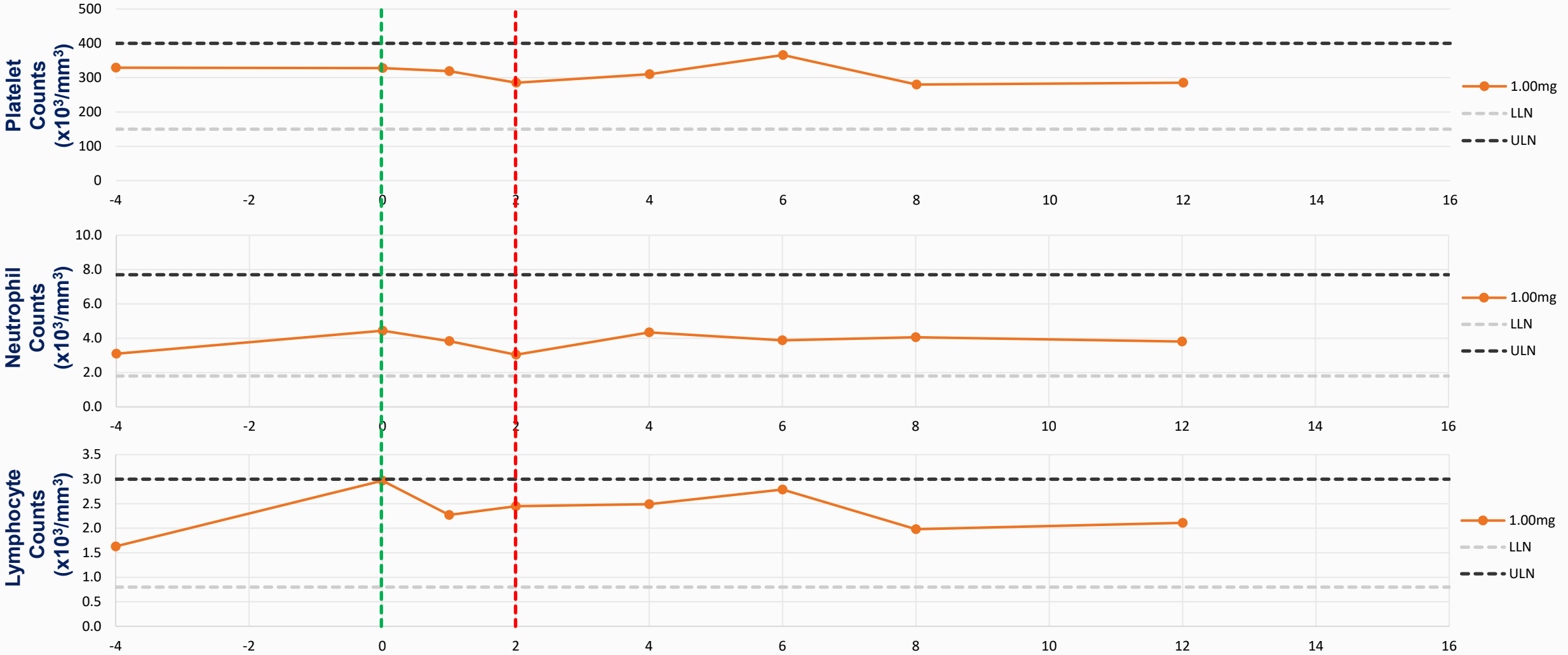
IL22, pg/ml



Treatment withdrawal date Percent change from baseline: 1-[Lowest value during treatment / Baseline value] * 100%

Preliminary Data available as of 6/30

Subject F, Male (1.0mg) - Safety & Key Labs



Safety:

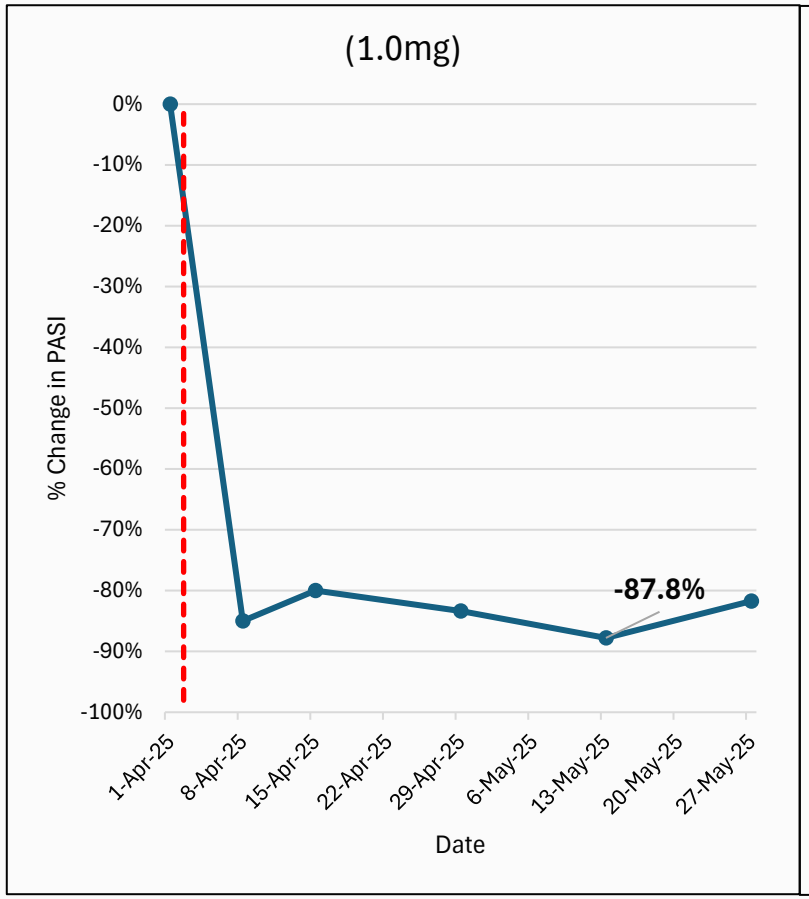
- No AEs.

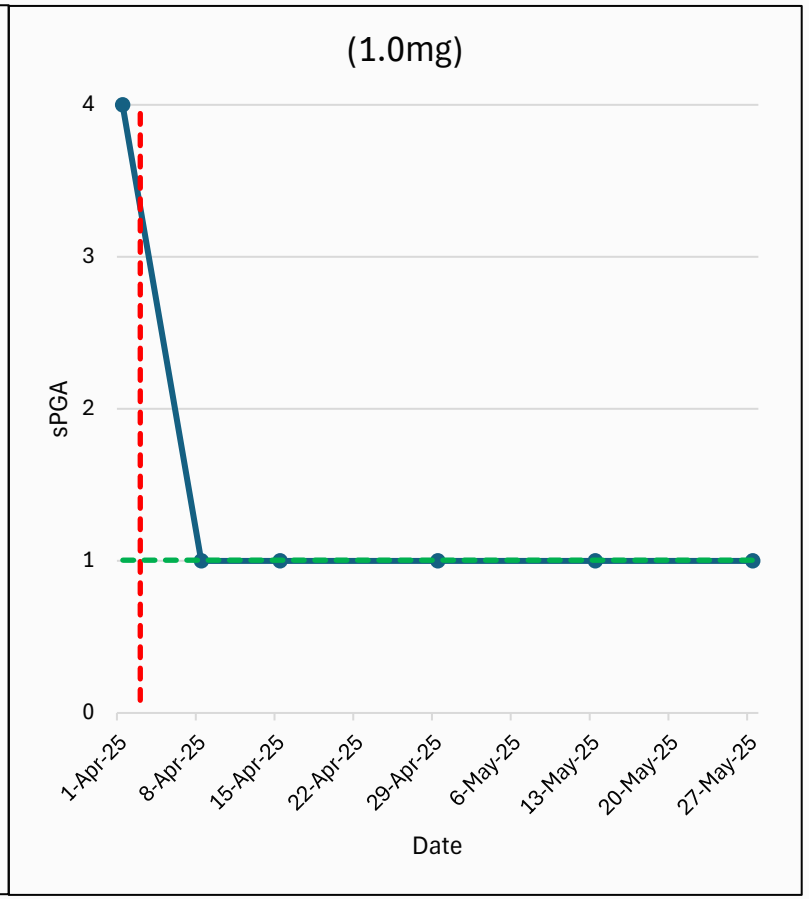
Treatment withdrawal date Baseline visit

Preliminary Data available as of 6/20

Subject G, Male (1.0mg) - Efficacy

Visit	Baseline	Week 1	Week 2	Week 4	Week 6	Week 8	Week 12
Dosing Duration	01APR	02APR (2 days)					
PASI Score	**18**	**2.7**	**3.6**	**3**	**2.2**	**3.3**	**-**
PSSI Score	12	-	-	-	-	-	-
sPGA Score	**4**	**1**	**1**	**1**	**1**	1	-
BSA	11.5	3.5	3.5	2	3	3	-
Itch NRS	6	7	7	7	5	7	-
Joint Pain NRS	N/A	N/A	N/A	N/A	N/A	N/A	-





Comments:

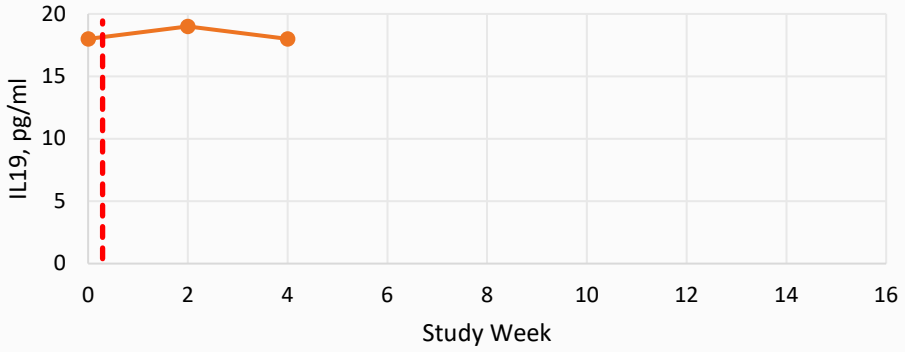
- Subject on active drug for 2 days
- Marked overall clinical response to treatment by PASI (Approx. PASI90 after 1.5 months)
- sPGA0/1 – treatment success.

Treatment withdrawal date — Treatment success threshold by sPGA (Clear “0” or Almost clear “1”)

Preliminary Data available as of 6/20

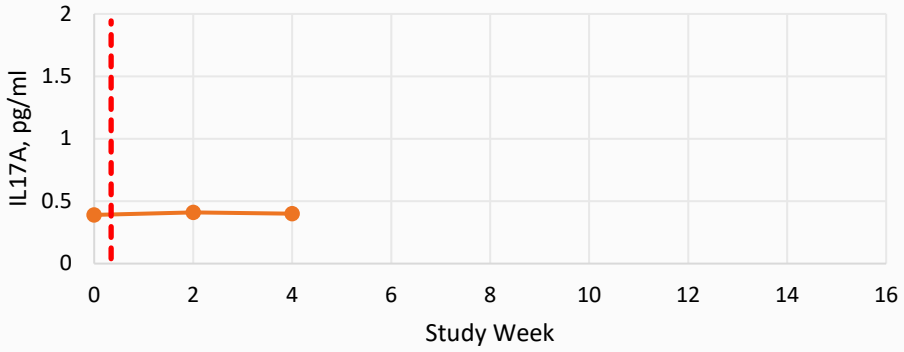
Subject G, Male (1.0mg) - Serum IL19, IL17A, IL17F & IL22 Biomarkers

IL19, pg/ml



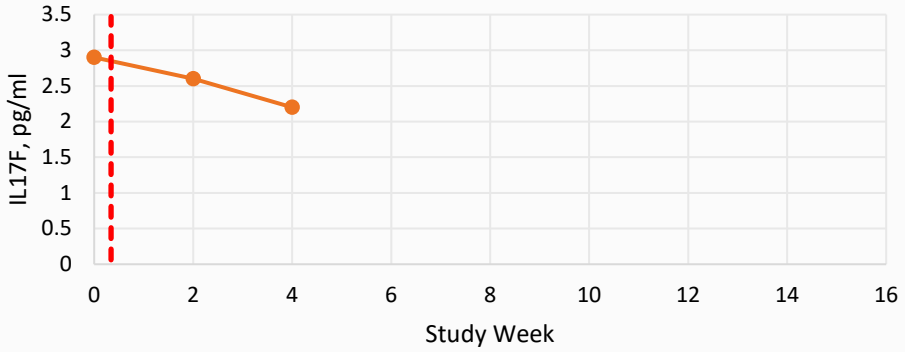
No change

IL17A, pg/ml



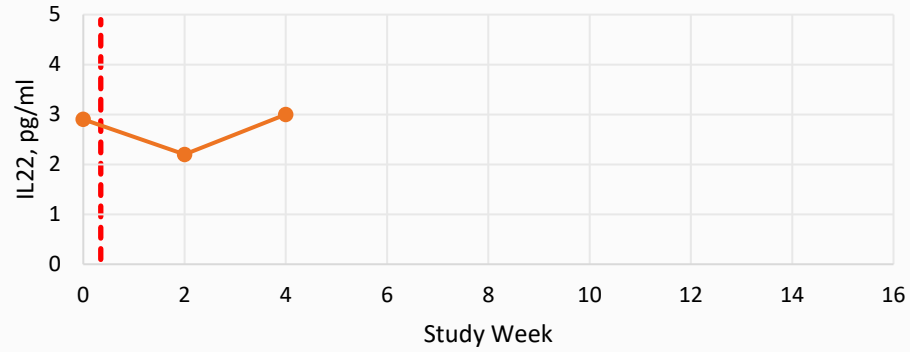
No change

IL17F, pg/ml



No change

IL22, pg/ml

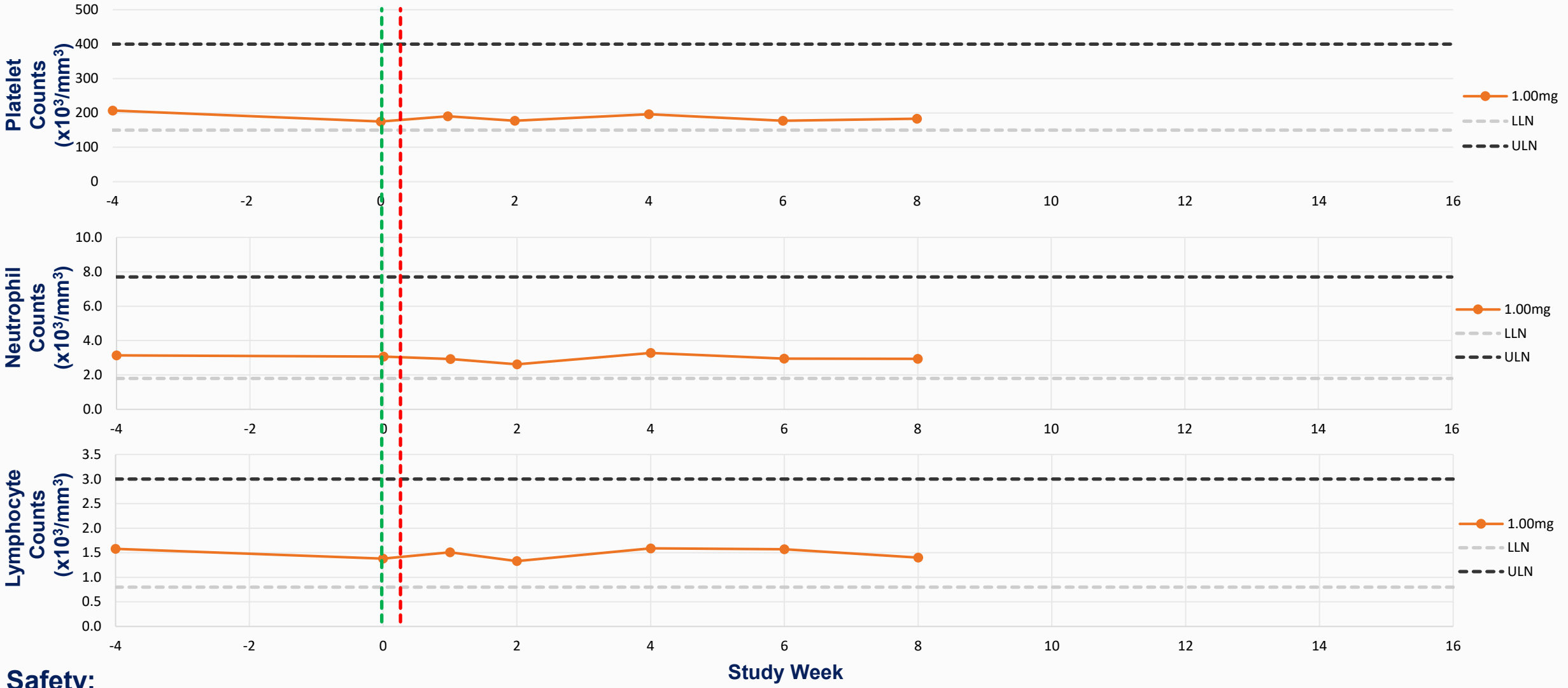


No change

Treatment withdrawal date Percent change from baseline: 1-[Lowest value during treatment / Baseline value] * 100%

Preliminary Data available as of 6/30

Subject G, Male (1.0mg) - Safety & Key Labs



Safety:

- No AEs.

Treatment withdrawal date Baseline visit

Preliminary Data available as of 6/20

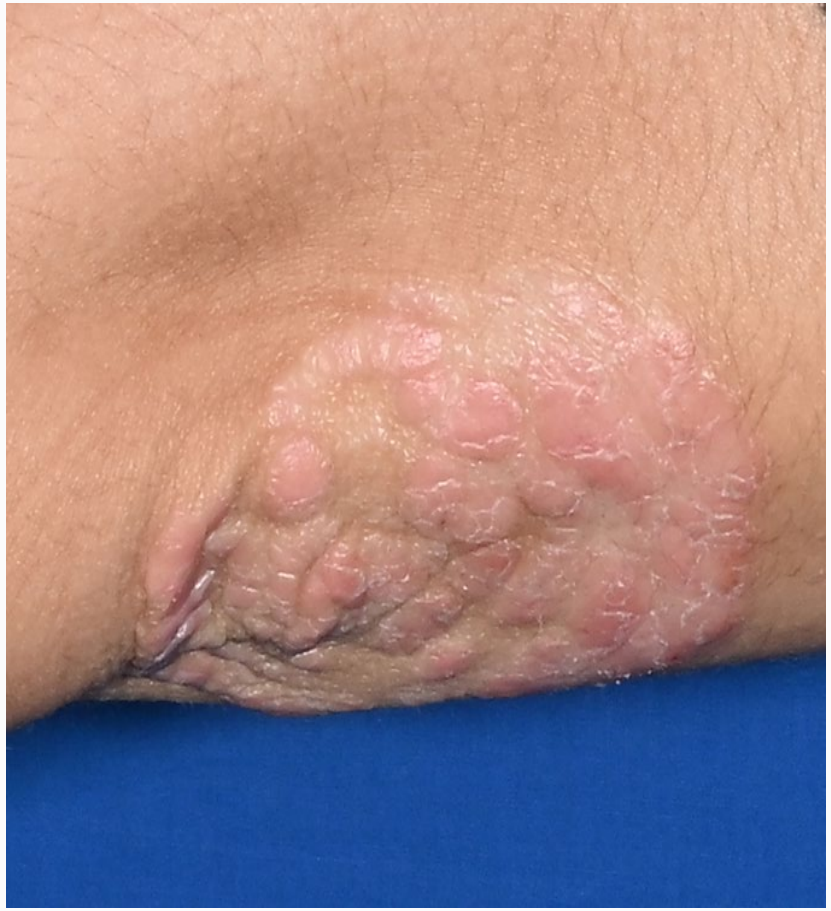
Visual Improvements in Psoriasis in 6 weeks

Subject B (0.25mg)

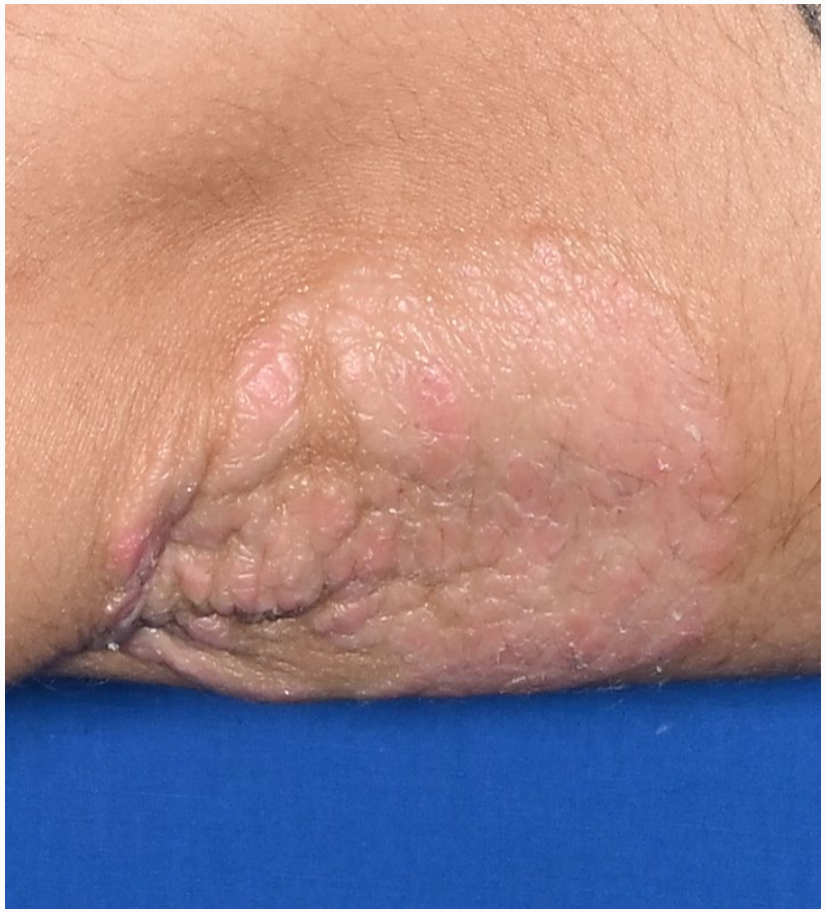
Last Dose Administered Day 64

Right Elbow

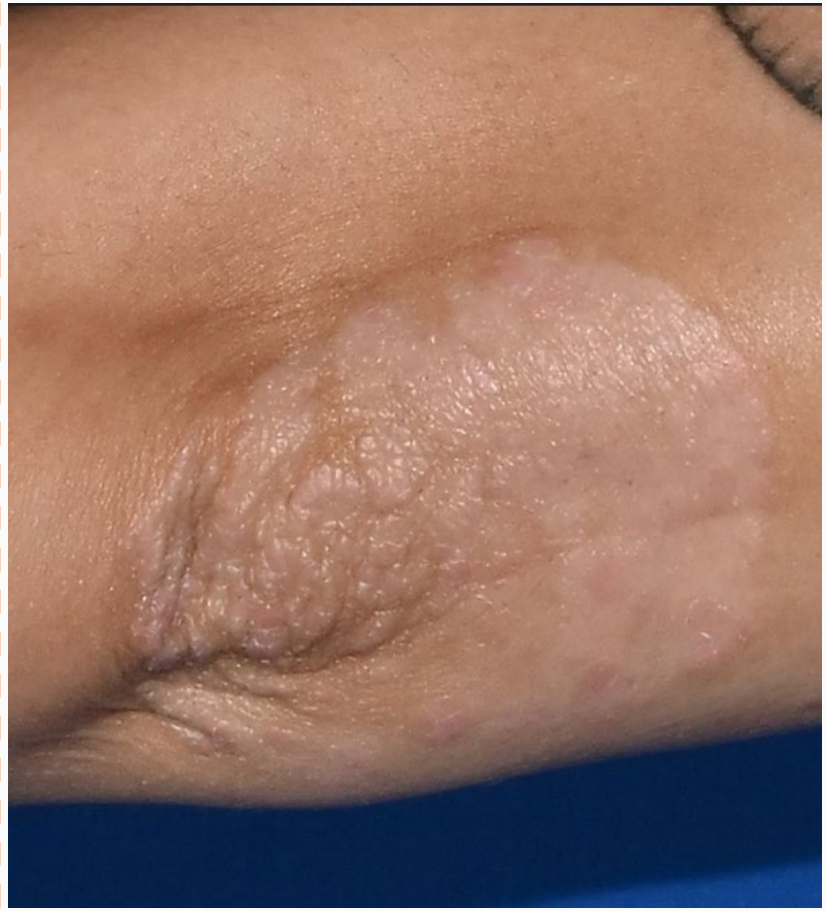
Day 1
(PASI 13.9)



Week 6
(PASI 6.9)



Week 12
(PASI 5.4)



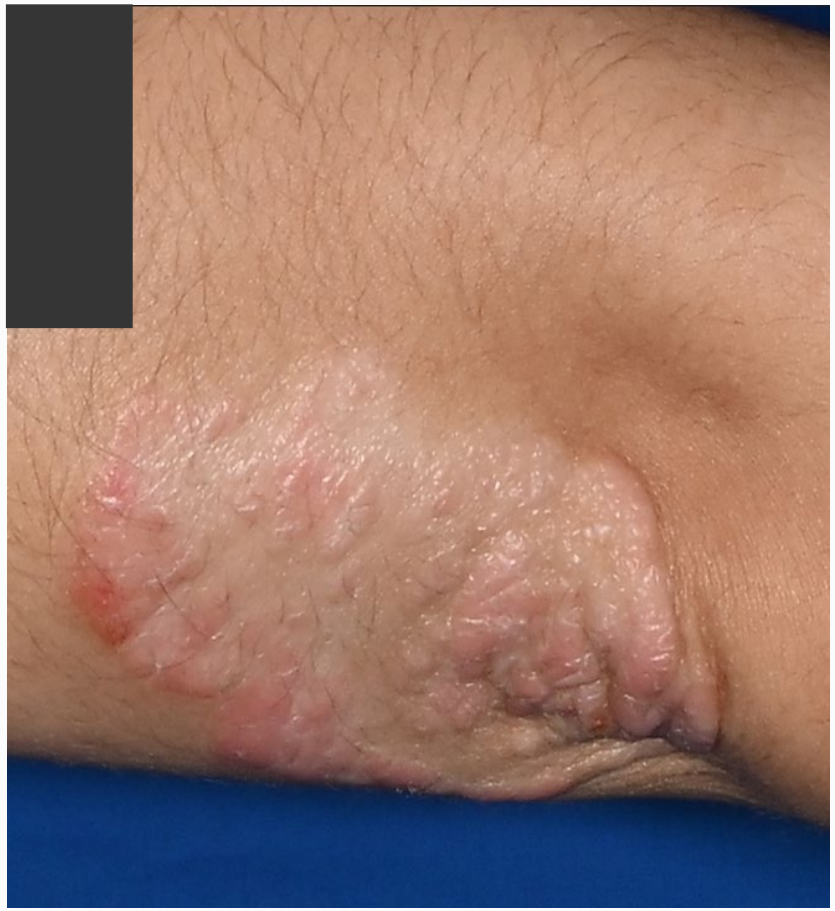
Visual Improvements in Psoriasis in 6 weeks

Subject B (0.25mg)

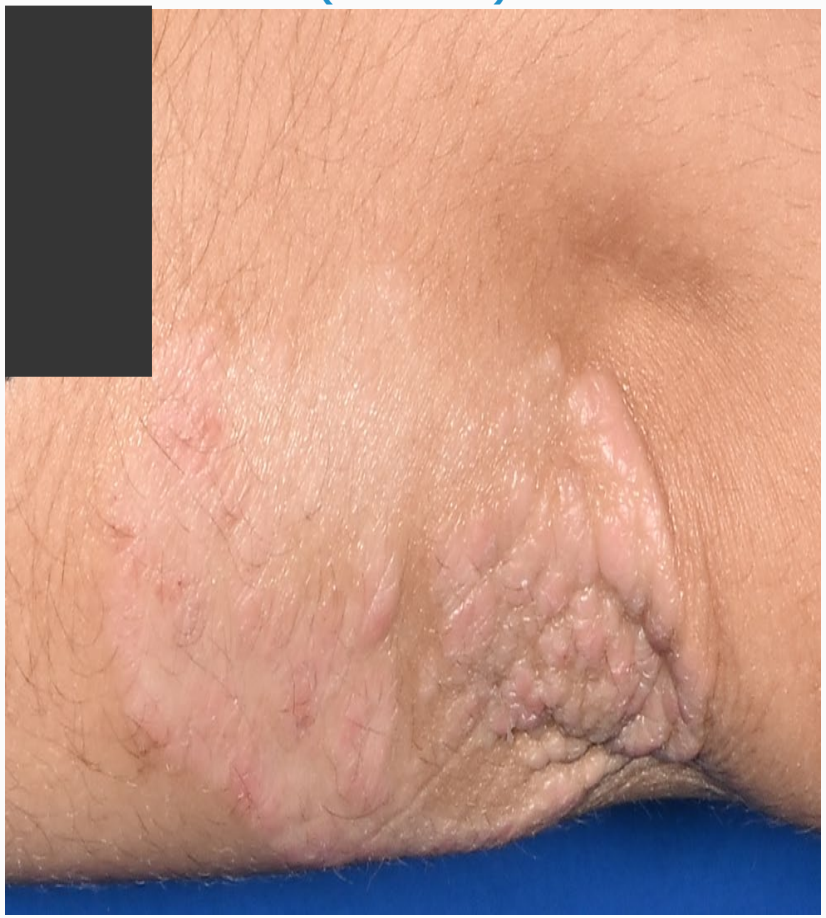
Last Dose Administered Day 64

Left Elbow

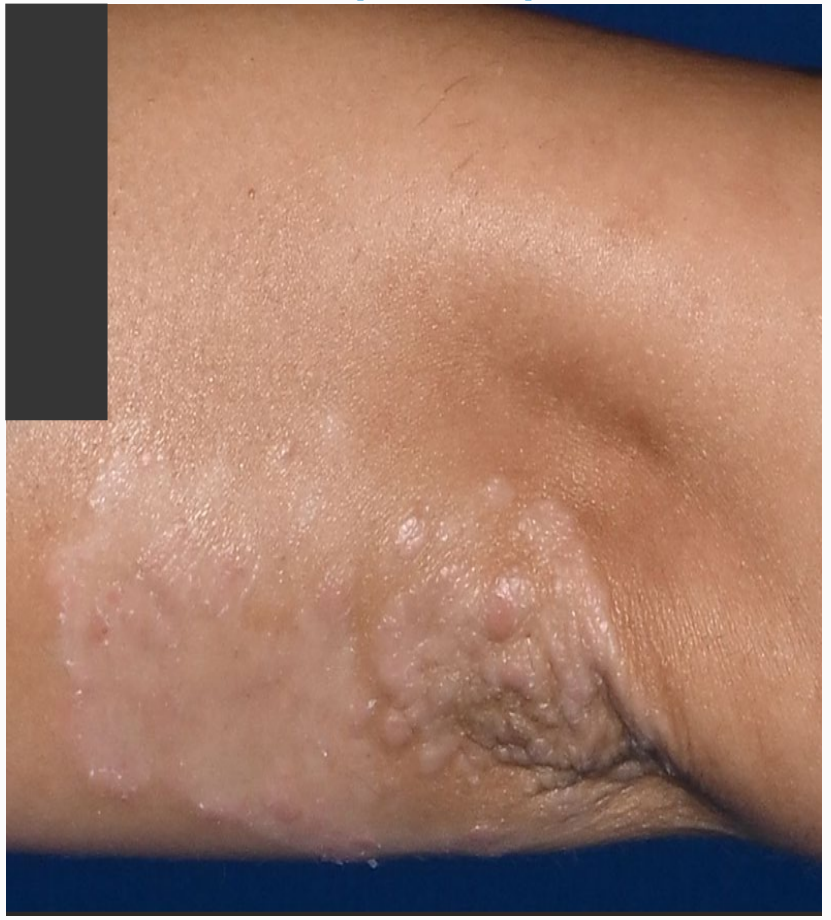
Day 1
(PASI 13.9)



Week 6
(PASI 6.9)



Week 12
(PASI 5.4)



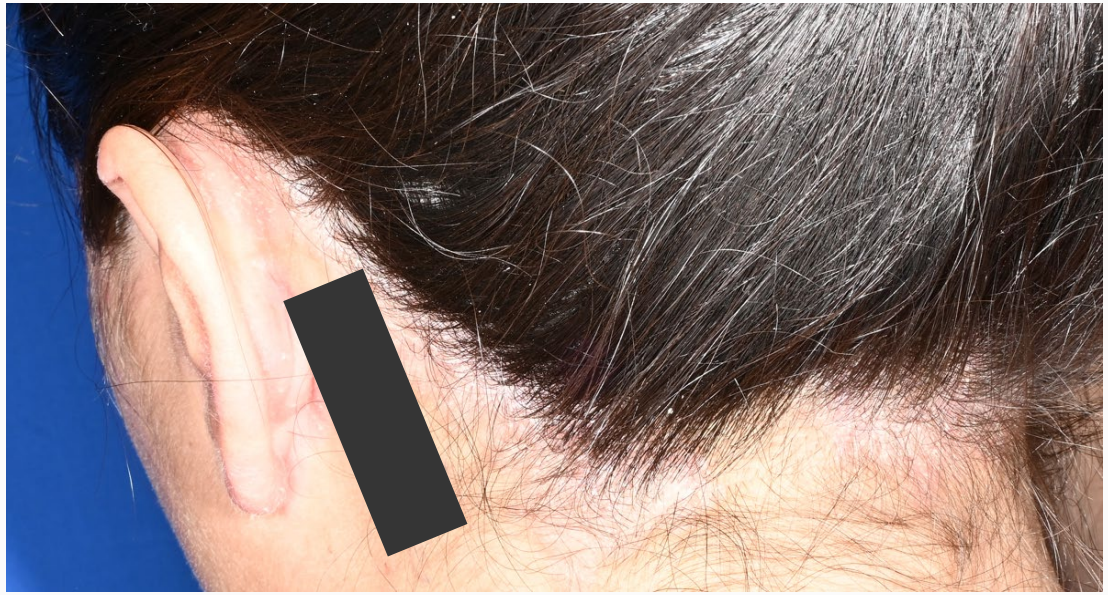
Visual Improvements in Psoriasis in 6 weeks

Subject B (0.25mg)

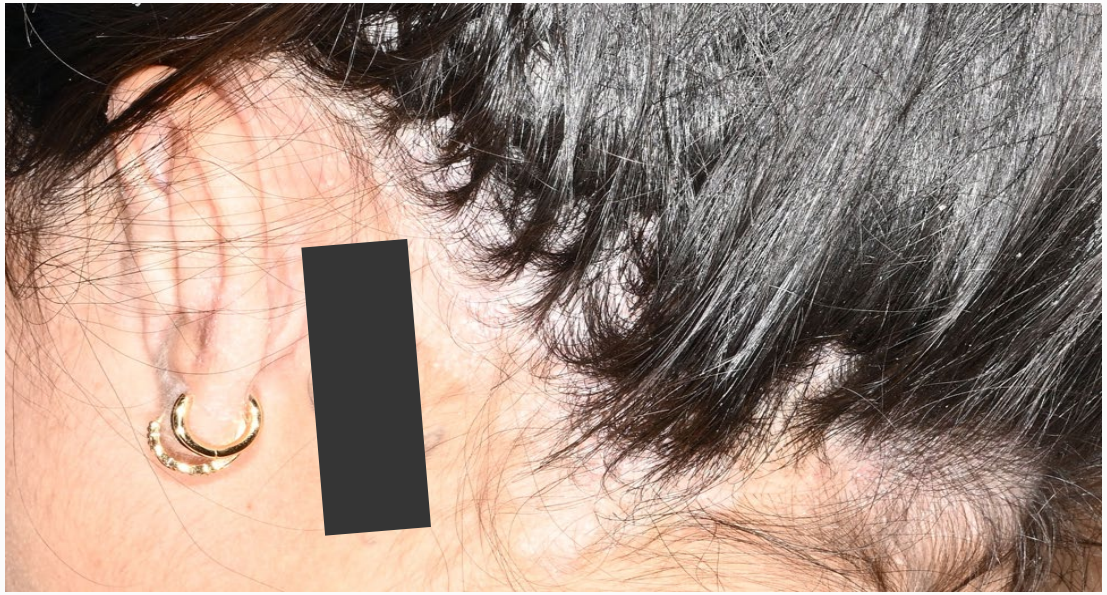
Back Scalp

Day 1
(PSSI 14)

Week 6
(PSSI 4)



Week 12
(PSSI 1)



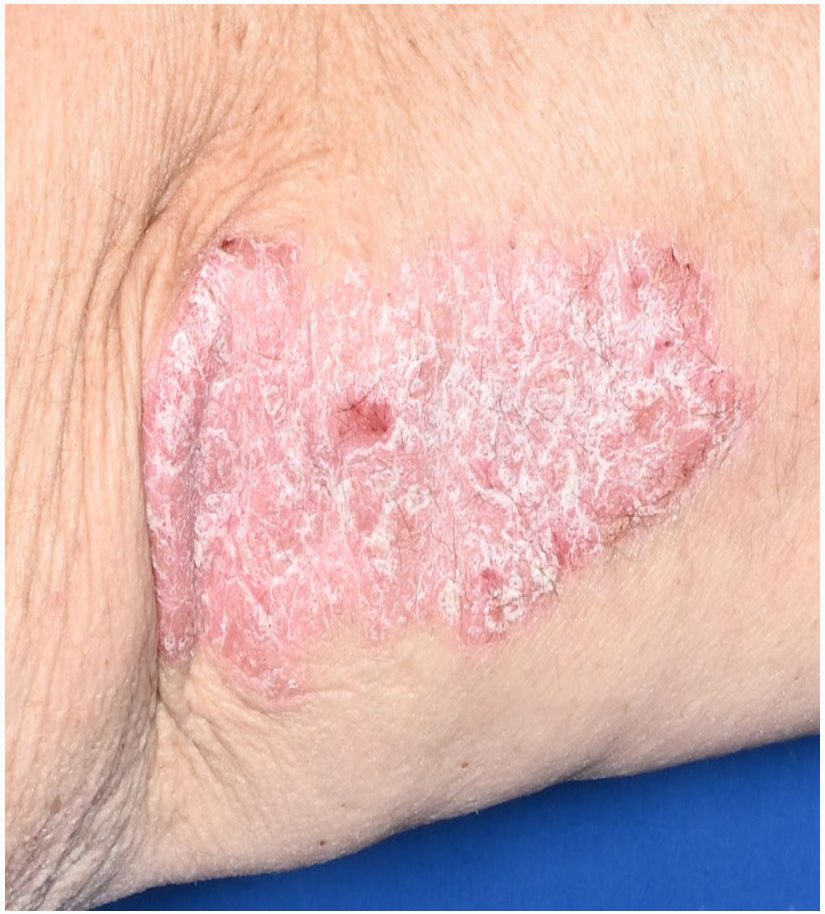
Visual Improvements in Psoriasis in 6 weeks

Subject E (1mg)

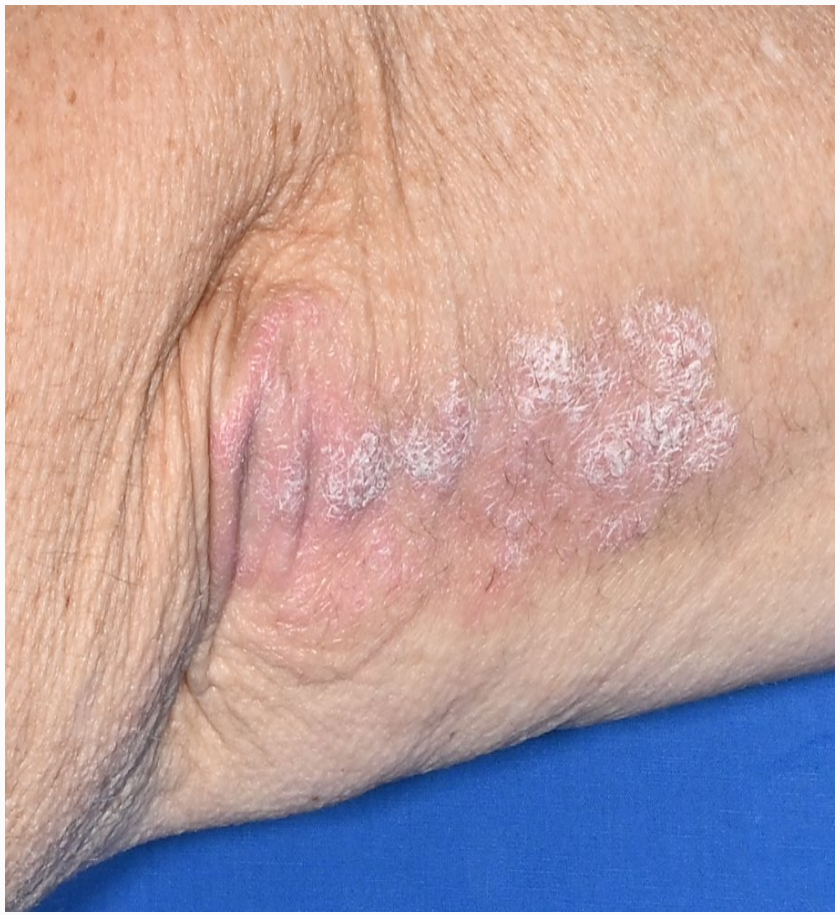
Last Dose Administered Day 65

Right Elbow

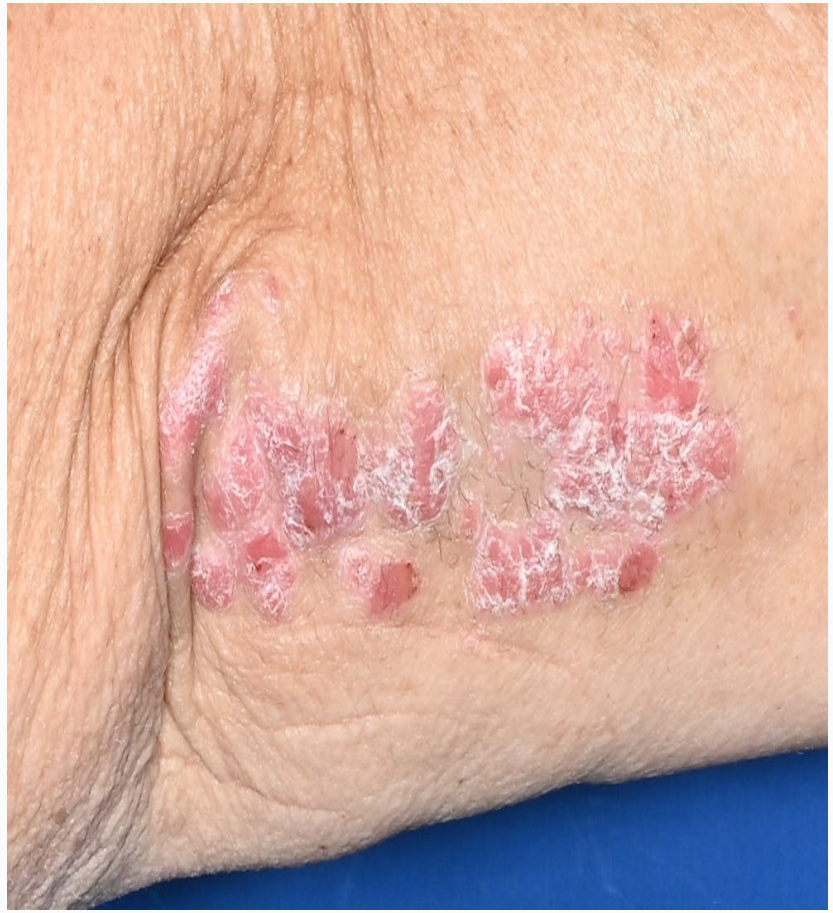
Day 1
(PASI 12.1)



Week 6
(PASI 2.0)



Week 12
(PASI 3.0)



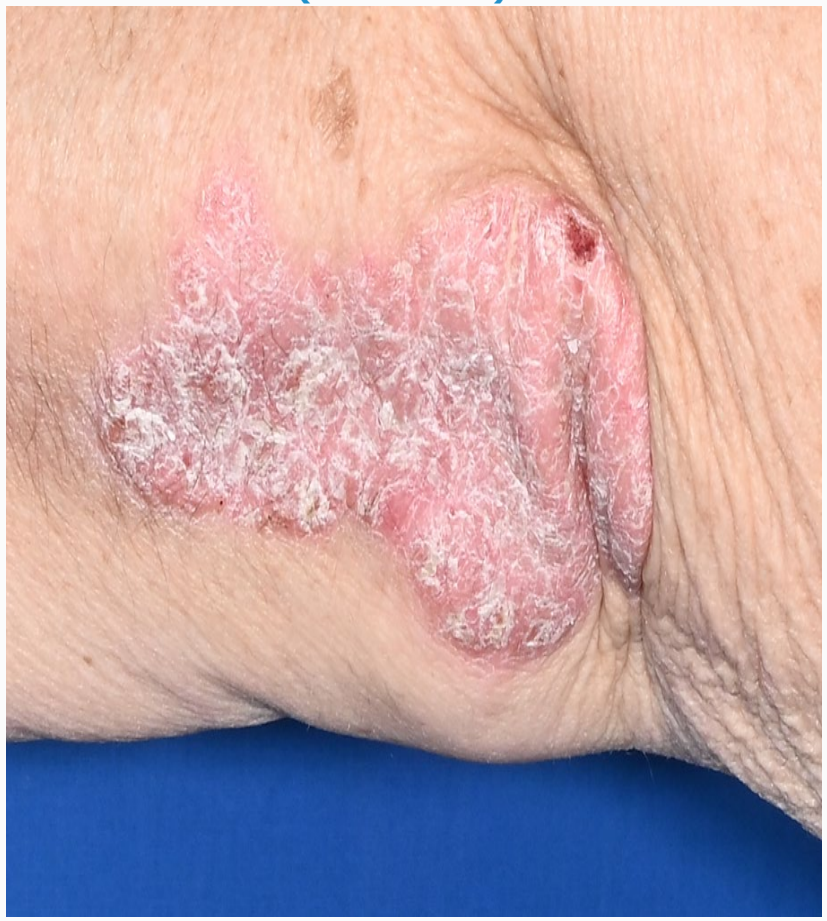
Visual Improvements in Psoriasis in 6 weeks

Subject E (1mg)

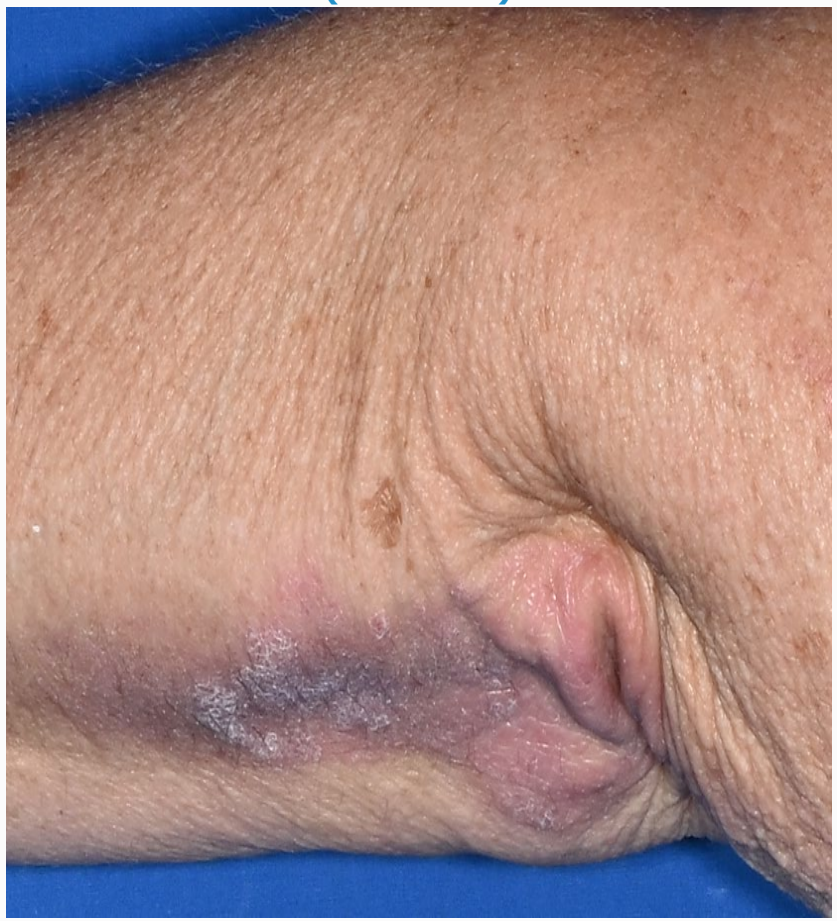
Last Dose Administered Day 65

Left Elbow

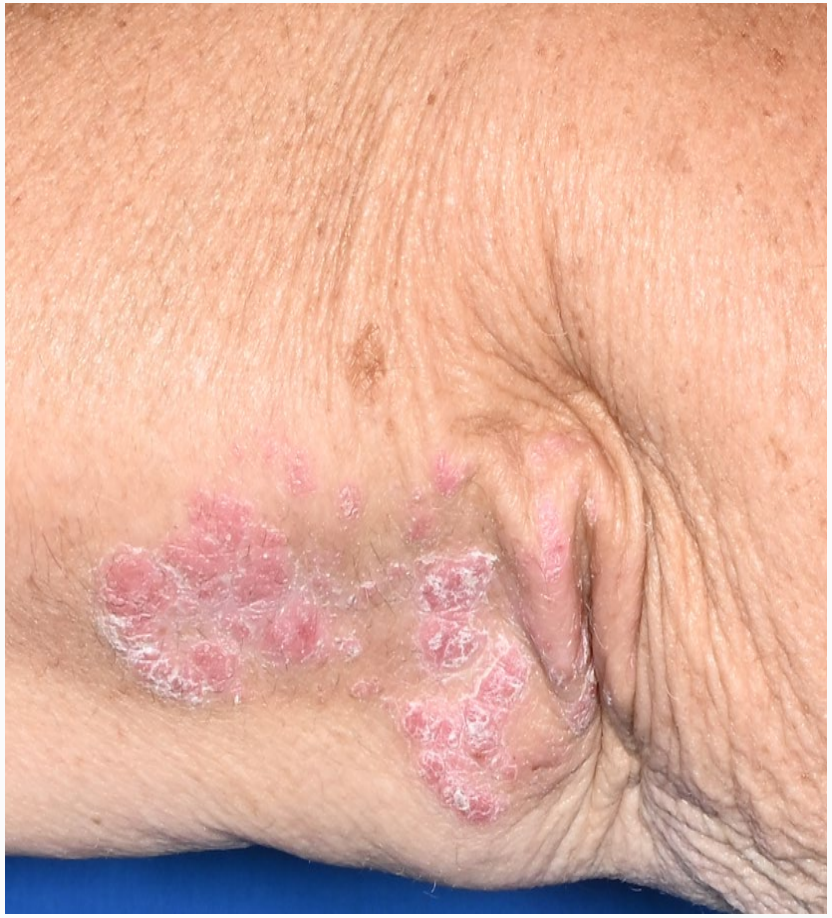
Day 1
(PASI 12.1)



Week 6
(PASI 2.0)



Week 12
(PASI 3.0)



Data Summary

Safety and Tolerability

- No TESAEs or discontinuation due to a clinical TEAE
- No treatment interruptions due to a clinical TEAE
- No grades of thrombocytopenia, neutropenia or lymphocytopenia

Exploratory Efficacy

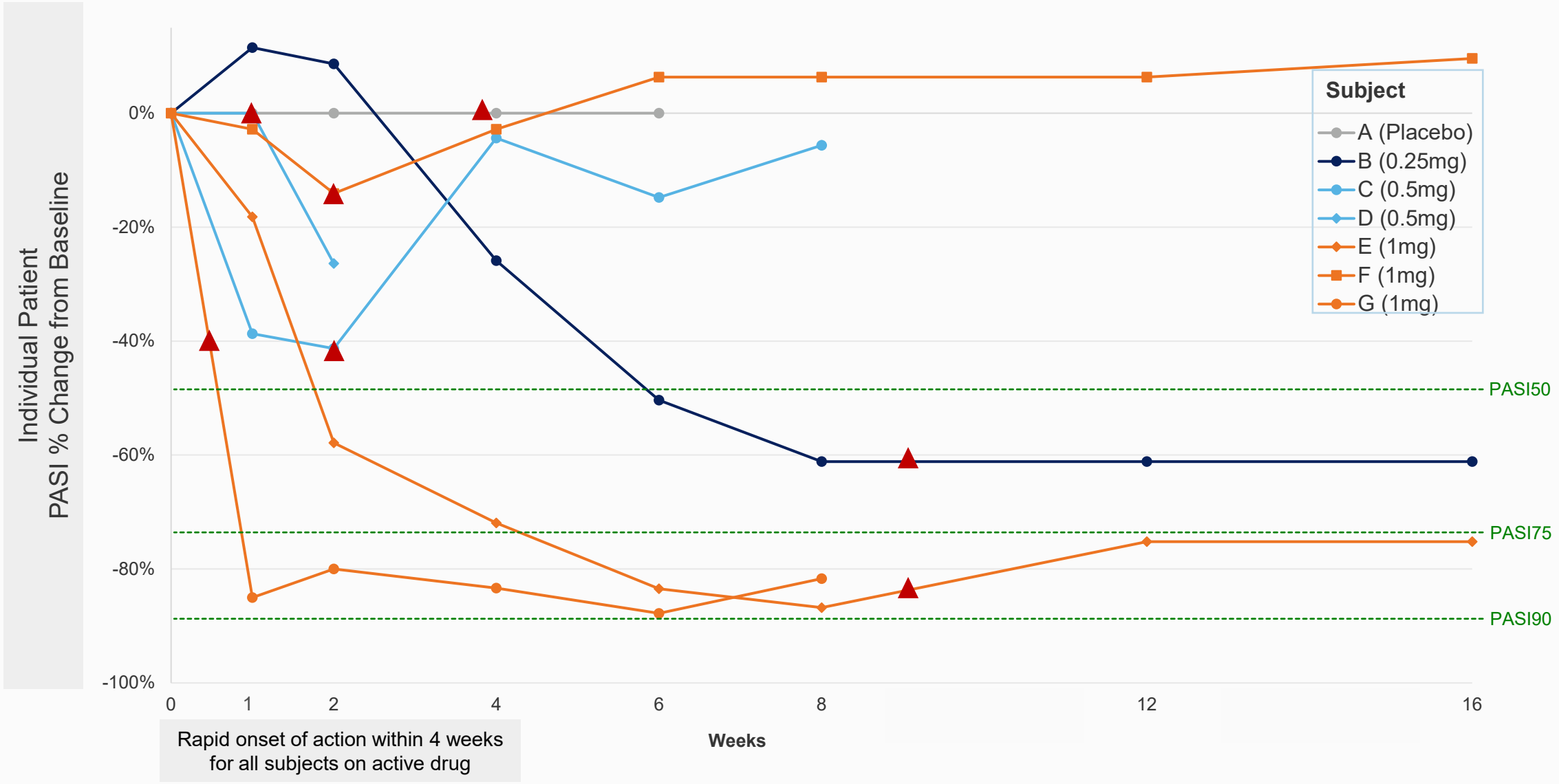
- All subjects receiving VYN202 had an improvement in signs and symptoms of disease, including scalp psoriasis:
  - Improvement in PASI scores ranged from ~27% reduction after 1 week of treatment to ~90% reduction at week 8
- Improvements (reduction) in serum cytokine levels observed in subjects treated with VYN202 for greater than 1 week, including IL17A, IL17F, IL19, and IL22 ranging from -17% to -83%. There was no change in these serum cytokines for the subject receiving placebo.
- Two subjects enrolled co-presented with psoriatic arthritis (n=1 treated with VYN202 0.5 mg; n=1 treated with placebo)
  - Subject treated with VYN202 0.5 mg reported a four-point improvement in joint pain NRS scale by week 2 which corresponded with a -48% reduction in serum c-reactive protein level, a biomarker associated with psoriatic arthritis and other rheumatic diseases.
  - Subject treated with placebo had no improvement in joint pain NRS and no change in serum c-reactive protein levels.

Preliminary data available as of 6/20 and 6/30

Appendix

VYNE™ THERAPEUTICS

Individual PASI Score Changes



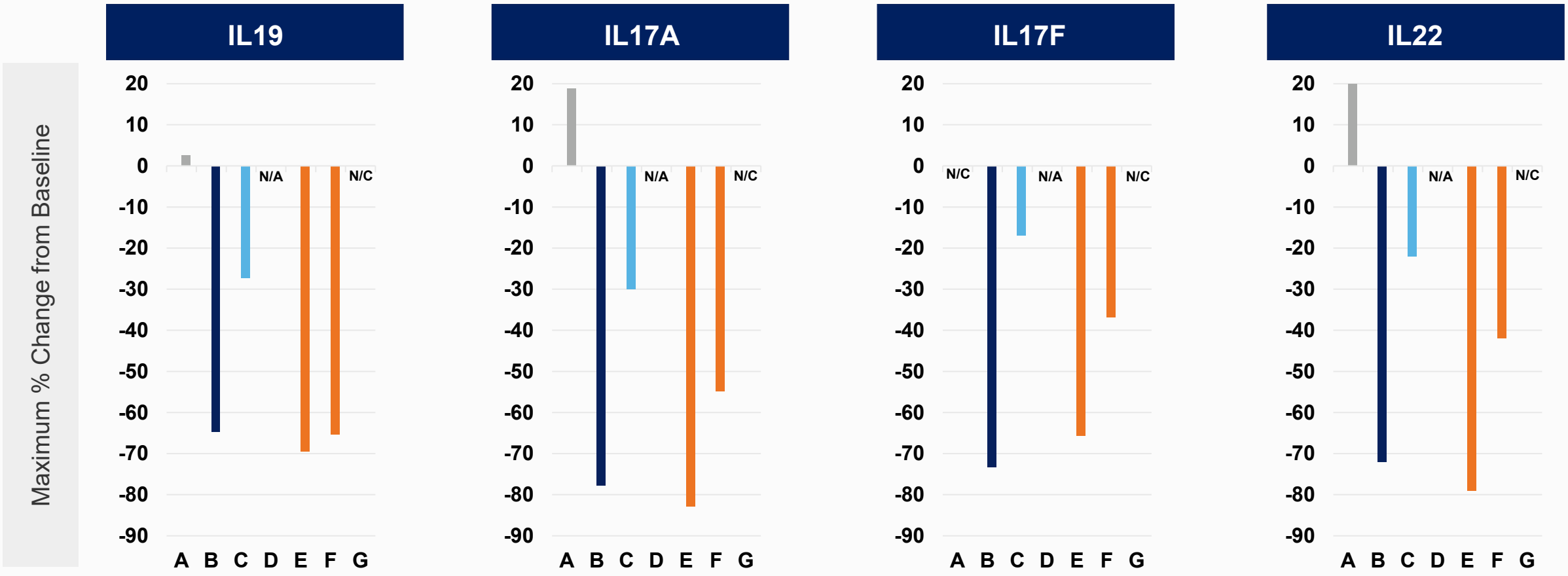
Rapid onset of action within 4 weeks for all subjects on active drug

▲ Last dose

Letters A-G represent Patient ID

Preliminary Data available as of 6/20

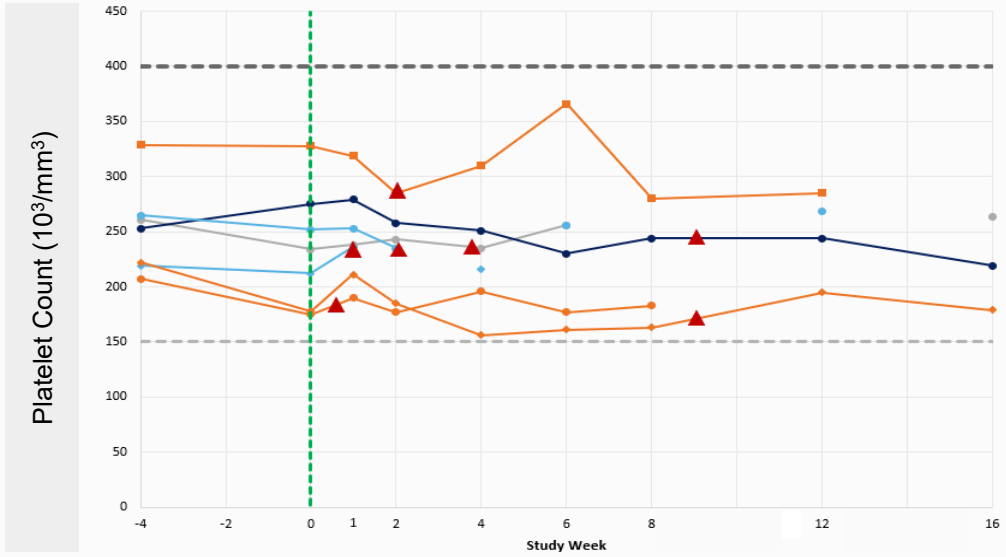
Serum Inflammatory Biomarkers



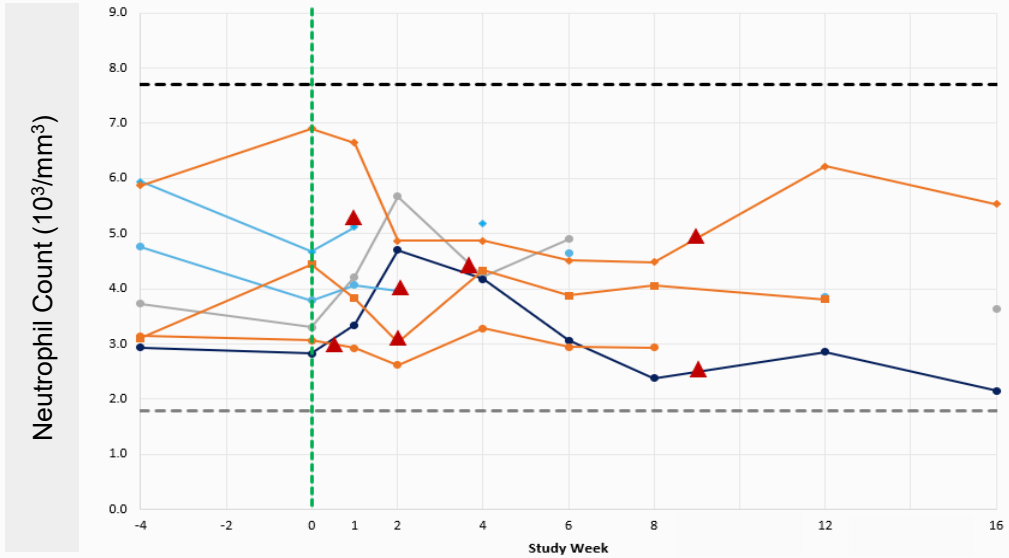
- Reduction in serum cytokine levels observed in subjects treated with VYN202 for greater than 1 week ranging from -17%to -83%. No change in these serum cytokines for the subject receiving placebo (Subj. A).
- Subject C treated with VYN202 0.5 mg with a medical history of psoriatic arthritis reported a four-point improvement in joint pain NRS scale by week 2 corresponding with a -48% reduction in serum c-reactive protein level. Subject A treated with placebo with a medical history of psoriatic arthritis had no improvement in joint pain NRS and no change in serum c-reactive protein levels.

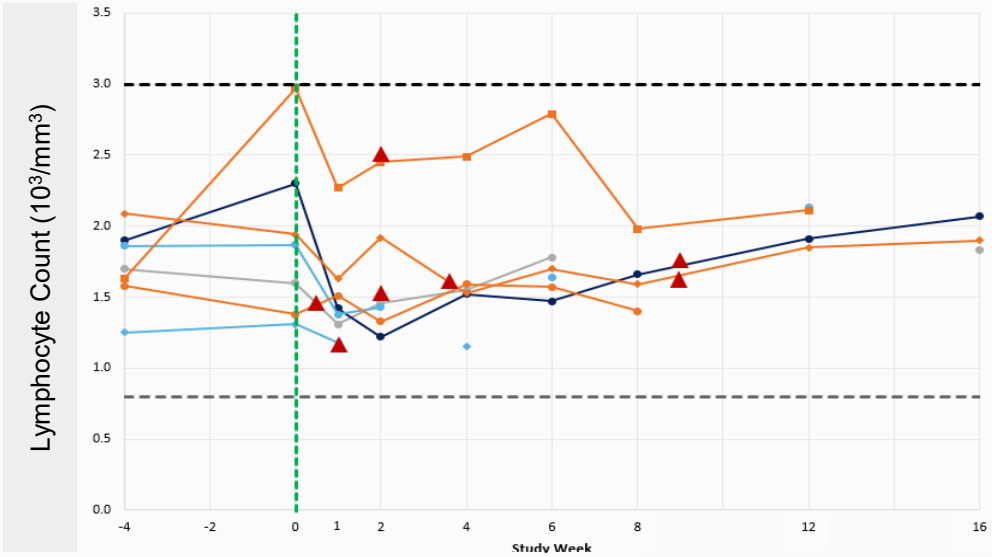
Preliminary Data available as of 6/30; N/A – Data not available; N/C – No change; Percent change from baseline: 1-[Lowest value during treatment / Baseline value] * 100%

Selected Laboratory Data



- All data within Upper and Lower Limits of Normal (ULN/LLN)
- No grades of thrombocytopenia and trends in platelet counts reach a nadir between 4 and 6 weeks and increase during treatment
- No grades of Neutropenia
- No grades of lymphopenia





Baseline visit ▲ Last dose ----- Upper/Lower limit of normal

A (Placebo) B (0.25mg) C (0.5mg) D (0.5mg) E (1mg) F (1mg) G (1mg)