Therapeutics™

DC-806: Phase 1 Topline Results

October 11, 2022

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Forward-looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. These factors, together with those that are described in under the heading “Risk Factors” contained in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (“SEC”) on August 11, 2022, and other documents we file from time to time with the SEC, may cause our actual results, performance or achievements to differ materially and adversely from those anticipated or implied by our forward-looking statements. Statements, including forward-looking statements, speak only to the date they are provided (unless an earlier date is indicated). We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this prospectus to conform these statements to actual results or to changes in our expectations, except as required by law. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements.

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Certain data in this presentation are based on cross-study comparisons and are not based on any head-to-head clinical trials. Cross-study comparisons are inherently limited and may suggest misleading similarities and differences. The values shown in the cross-study comparisons are directional and may not be directly comparable.

Ground-breaking: clinical demonstration of **direct inhibition of a cytokine with a small molecule**

Advancement to P2b: DC-806 appears to be **efficacious and well tolerated with a favorable safety and PK profile**; supports further development as potential best-in-class oral agent in psoriasis

Oral IL-17 opportunity: potential to expand a **$30+ billion market opportunity** across five approved indications[1]

Platform validation: opportunity to leverage DELSCAPE to develop oral small molecule medicines against **other validated protein-protein interactions** in immunology

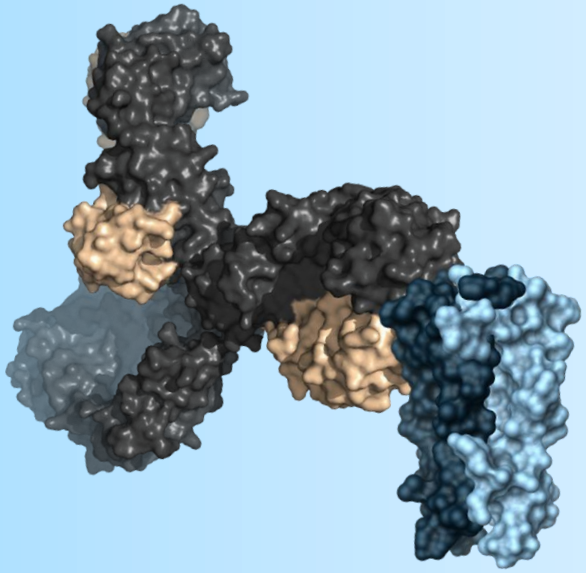
1. 2021 Sales Per Evaluate Pharma

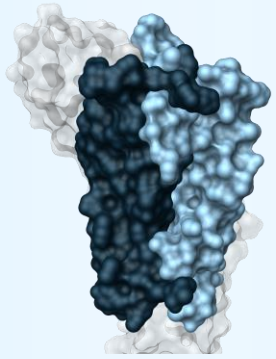
DC-806 allosterically blocks the *same biochemical step* as the anti-IL-17 antibodies

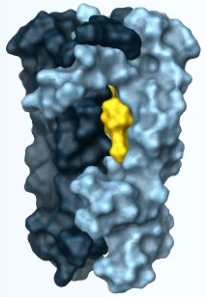
IL-17AA + ANTIBODY

IL-17 AA + RECEPTOR

IL-17 AA + DC-806







PRO-INFLAMMATORY SIGNAL

DC-806

Topline Phase 1 Results

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Chief Medical Officer

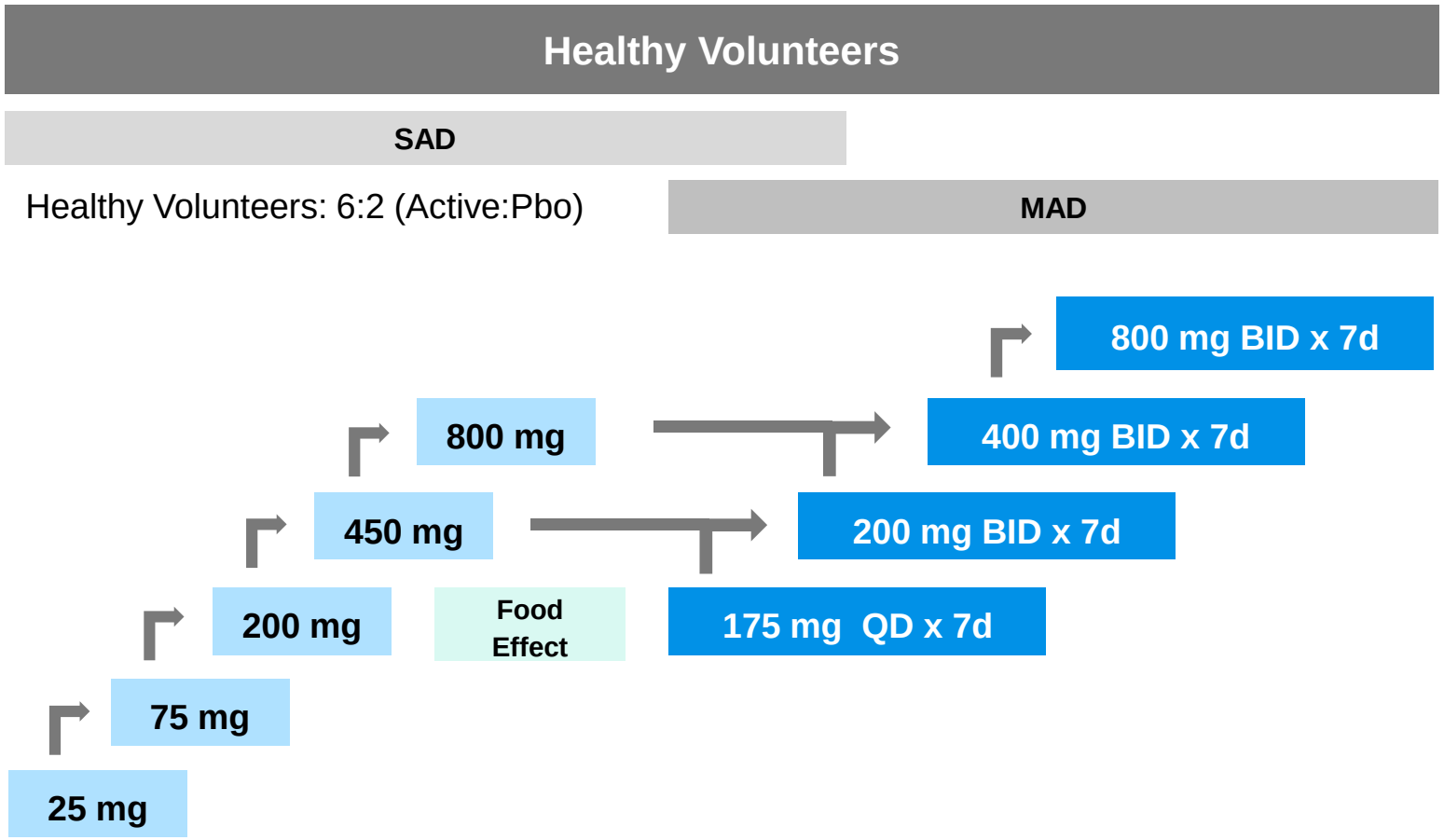
DICE Therapeutics™

DC-806: potential to be the best-in-class oral agent in psoriasis

Clean safety profile	✓ DC-806 exhibited a favorable safety and tolerability profile
Convenient dosing	✓ DC-806 PK profile enables commercially viable QD or BID dosing
Proof of concept to validate DC-806 and oral IL-17 Franchise	✓ DC-806 demonstrated clear benefit with improvement in PASI scores ✓ DC-806 showed target engagement and inhibition of IL-17 signaling

PASI: Psoriasis Area and Severity Index | QD: Once daily dosing | BID: Twice daily dosing

Phase 1 study design and dose rationale



Psoriasis Patients (4-weeks)

Phase 1c

800 mg BID x 28d (2:1 Active:Pbo)

4-fold above IC_{90} at trough

200 mg BID x 28d (2:1 Active:Pbo)

6-fold above IC_{50} at trough

- MAD data indicated that 175 mg QD and 400 mg BID would cover IC_{50} and IC_{90}, respectively
- In the P1c, we selected higher doses to explore safety margins and exceed PD targets

Safety Summary

DC-806 demonstrated a favorable safety and tolerability profile

- ✓ All treatment emergent adverse events (TEAEs) classified as **mild (>80%) or moderate; no severe AEs**
- ✓ **Only** three **mild** drug-related adverse events (AEs)
- ✓ **No** clinically significant or consistent alterations in clinical and safety lab parameters (including liver enzymes and hematology)
- ✓ **No** dose/exposure-dependent increases in AEs
- ✓ **No** treatment related discontinuations
- ✓ **No** serious adverse events (SAEs) reported

- Ability to achieve a **4-fold IC90 coverage at trough for at least 28 days** with **favorable safety** profile
- Overall safety profile to date suggests a well-tolerated oral drug that **should not require laboratory safety monitoring**

DC-806 demonstrated a favorable safety and tolerability profile in P1: TEAEs occurring in ≥ 2 subjects in SAD/MAD

No dose/exposure-dependent increases in number, severity or types of AEs

SAD Preferred Term, Subjects (%)	25 mg N=6	75 mg N=6	200 mg N=6	200 mg N=6 (Fed)	450 mg N=6	800 mg N=6	Overall DC-806 N=36	Placebo N=10
Headache	1 (16.7)	0	1 (16.7)	0	0	0	2 (6.7)	0
Medical device site reaction*	1 (16.7)	0	0 (16.7)	1 (16.7)	0	0	2 (6.7)	1 (10.0)

MAD Preferred Term, Subjects (%)	175 mg QD N=6	200 mg BID N=6	400 mg BID N=6	800 mg BID N=6	Overall DC-806 N=24	Placebo N=8
Headache	1 (16.7)	1 (16.7)	1 (16.7)	1 (16.7)	4 (16.7)	0
Medical device site reaction*	0	0	0	1 (16.7)	1 (4.2)	3 (37.5)
Nausea	0	0	1 (16.7)	1 (16.7)	2 (8.3)	0

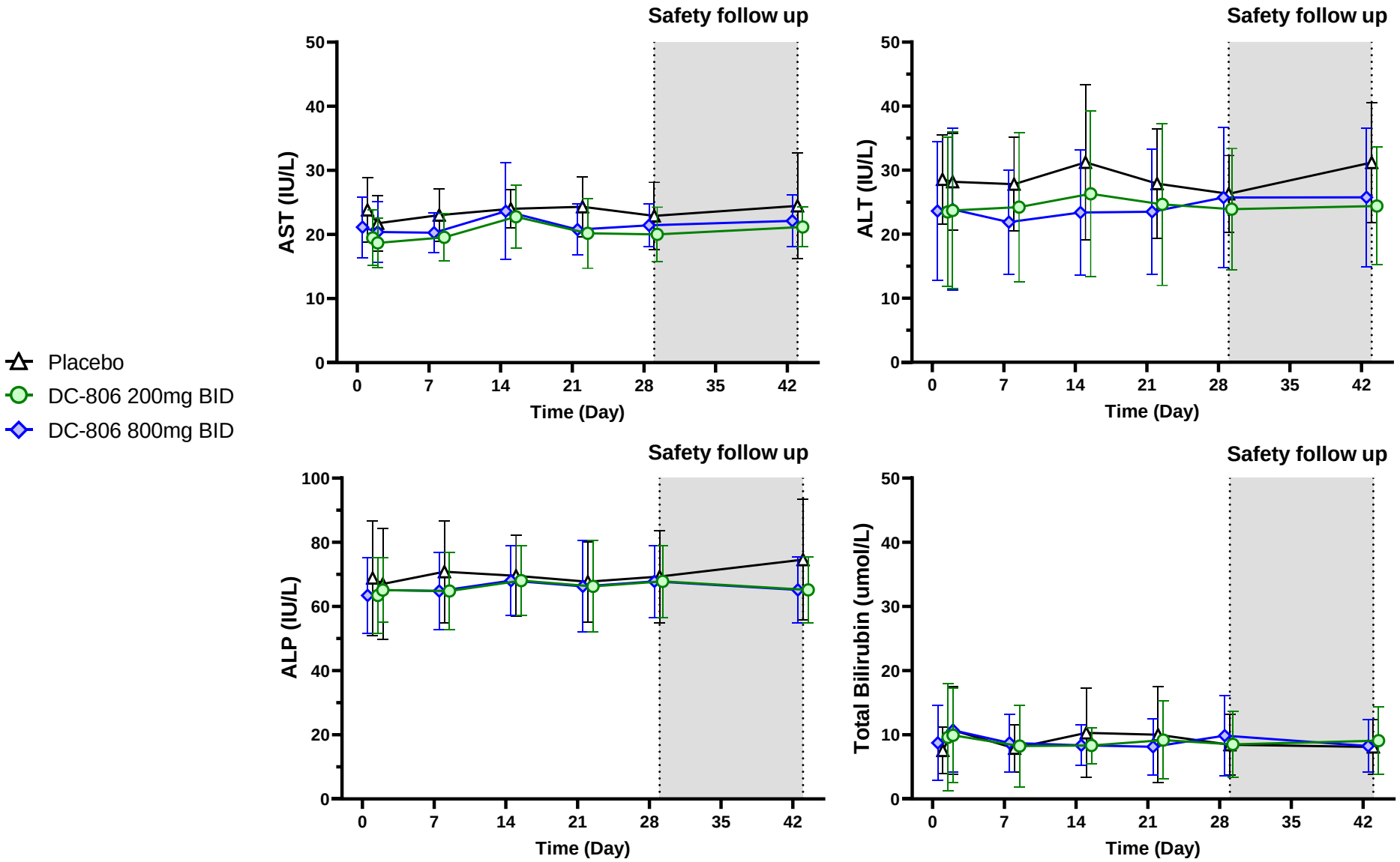
*rash due to Holter/ECG electrode placement

DC-806 demonstrated a favorable safety and tolerability profile in P1: TEAEs occurring in ≥ 2 patients in Phase 1c

No dose/exposure-dependent increases in number, severity or types of AEs

Preferred Term, Subjects (%)	DC-806 200 mg BID N=13	DC-806 800 mg BID N=8	Overall DC-806 N=21	Placebo N=11
Headache	4 (30.8)	2 (25.0)	6 (28.6)	1 (9.1)
Abdominal discomfort	1 (7.7)	1 (12.5)	2 (9.5)	0
COVID-19	2 (15.4)	1 (12.5)	3 (14.3)	0
Tonsillitis	0	0	0	2 (18.2)
Skin abrasion	2 (15.4)	0	2 (9.5)	0

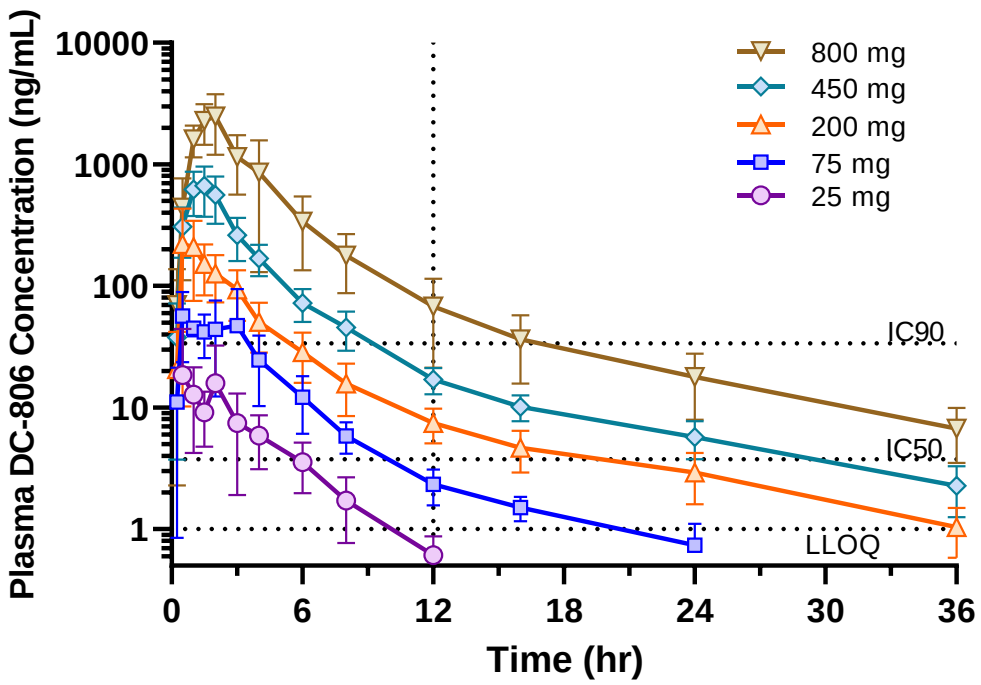
All hepatic enzymes remained within normal limits throughout 28-day treatment period

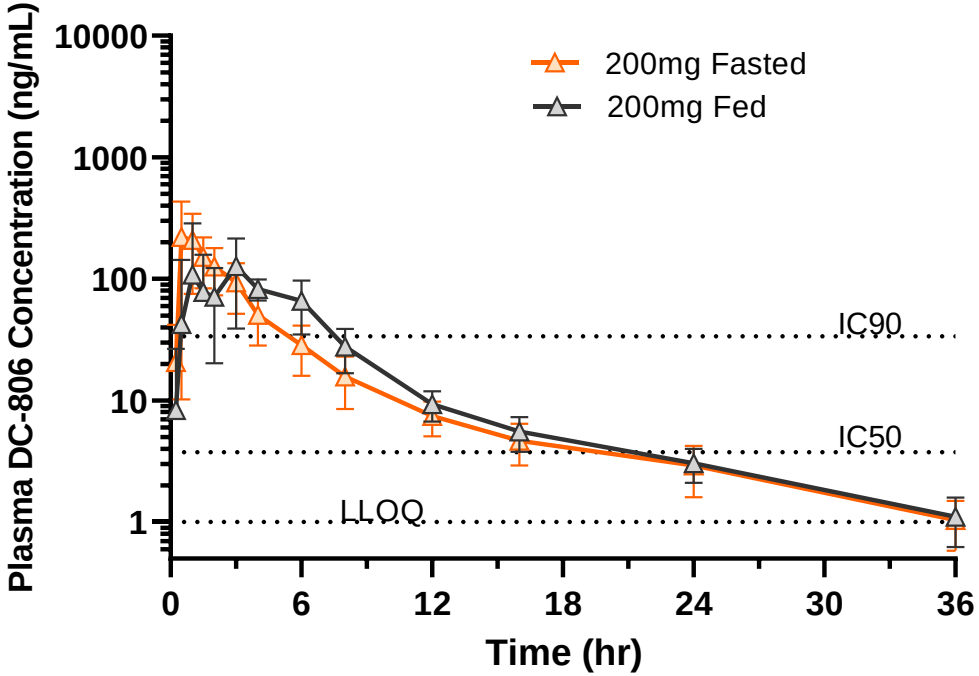


PK Summary: SAD / MAD / Phase 1c

DC-806 PK profile enables commercially viable dosing

Summary of single ascending dose data

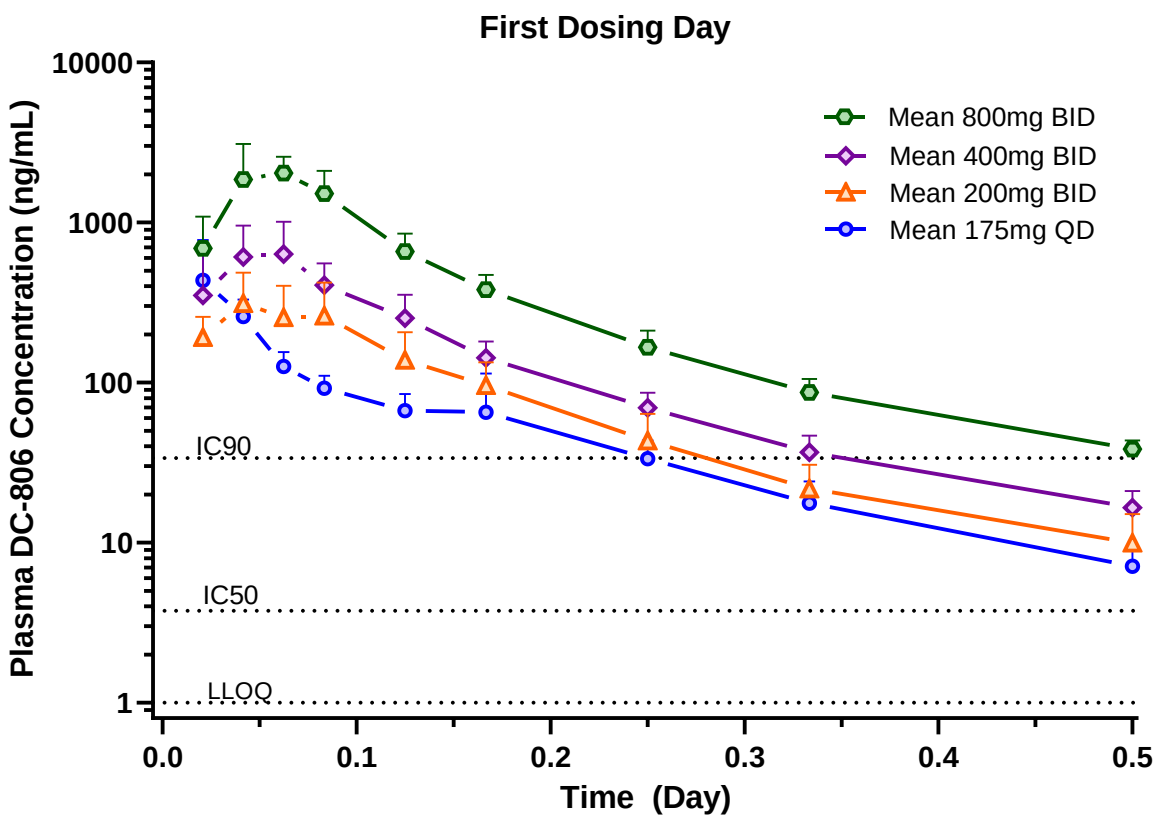


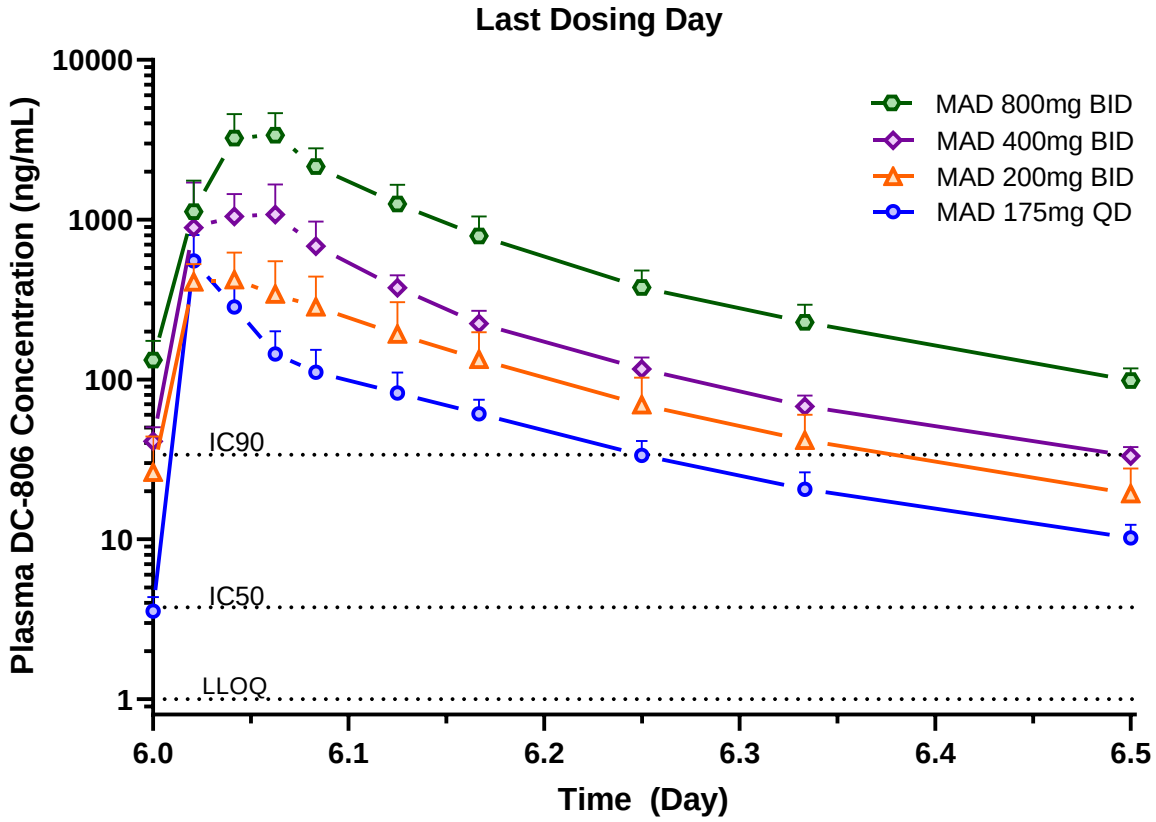


- DC-806 is rapidly absorbed, peak plasma concentrations ~0.5-2hrs
- PK was approximately dose proportional
- Minimal food effect, enabling flexible dosing for outpatient treatment

DC-806 PK profile enables commercially viable dosing:

Summary of multiple ascending dose data

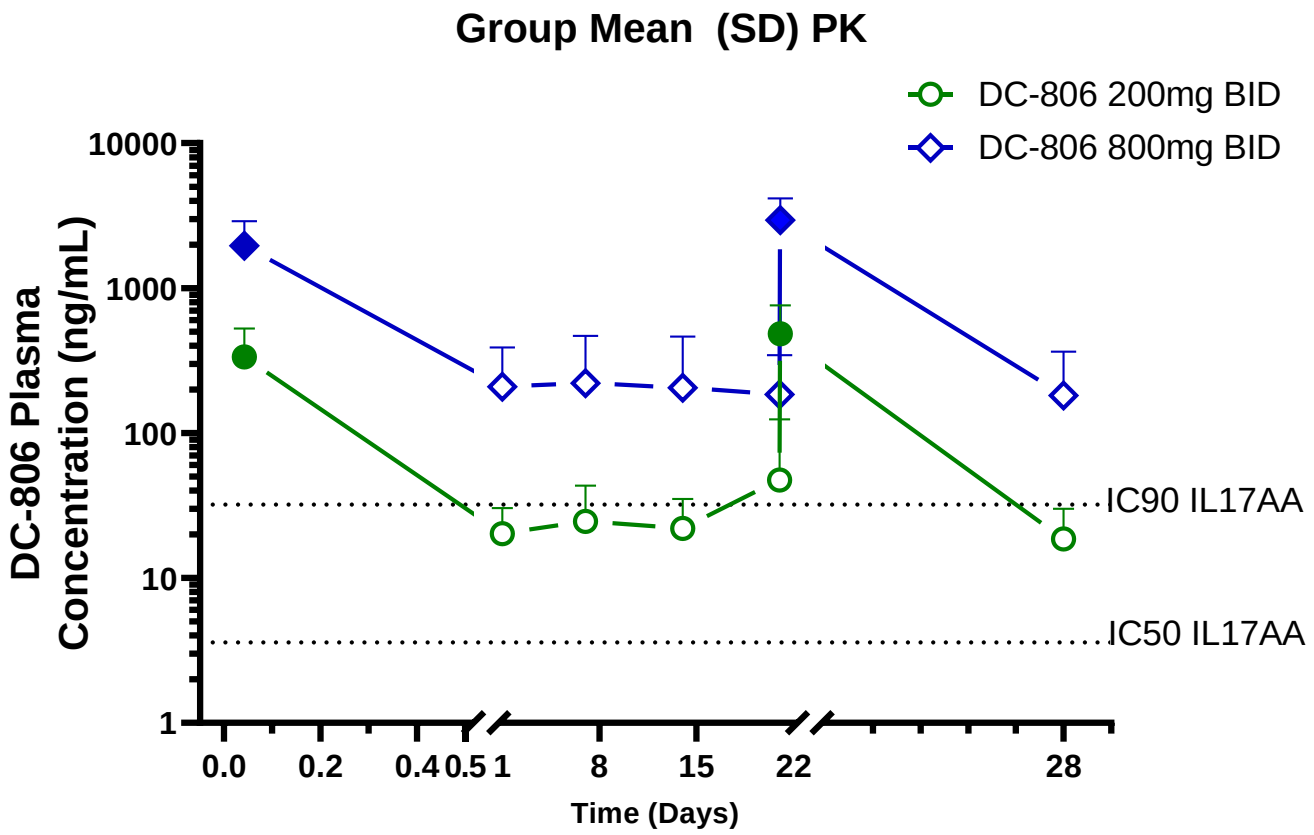




- Low PK variability within cohorts
- P1c cohorts evaluated 200mg BID (6x IC_{50} at trough) and 800mg BID (4x IC_{90} at trough)

DC-806 PK profile enables commercially viable dosing

Summary of Phase 1c data in patients



- PK in psoriasis patients was comparable to healthy volunteer PK, with consistent trough levels over 28 days after achievement of steady state around day 3

PK profile of DC-806 supports commercially viable dosing

Daily target coverage of IL-17 AA (hours) at steady state (MAD day 7)		
Dose Regimen	**IC_{50}**	**IC_{90}**
175mg QD	24	12
200mg BID	24	18
400mg BID	24	24
800mg BID	24	24

- *One pill, once a day to cover IC_{50}*
- *One pill, twice a day to cover IC_{90}*

Phase 1c: Clinical Proof of Concept

Phase 1c patient disposition

No treatment-related discontinuations

	Placebo N=11	DC-806 200mg BID N=13	DC-806 800mg BID N=8
Subjects who completed the study, n (%)	10 (90.9)	10 (76.9)	7 (87.5)
Subjects who prematurely discontinued study, n (%)	1 (9.1)	3 (23.1)	1 (12.5)
Reason, n (%)			
Adverse Event/Other Medical Condition/COVID	0	2 (15.4)[b,c]	0
Withdrawal of Informed Consent	1 (9.1)[a]	0	1 (12.5)[e]
Investigator Decision	0	1 (7.7)[d]	0

[a] Withdrew consent due to psoriasis exacerbation (Day 7)
[b] Withdrew due to left leg cellulitis (Day 22, not treatment related)
[c] Withdrew due to COVID19 (Day 21, not treatment related)
[d] Non-compliance with study drug (Day 23)
[e] Withdrew consent due to COVID19 (Day 29, not treatment related) – unable to continue with study visits

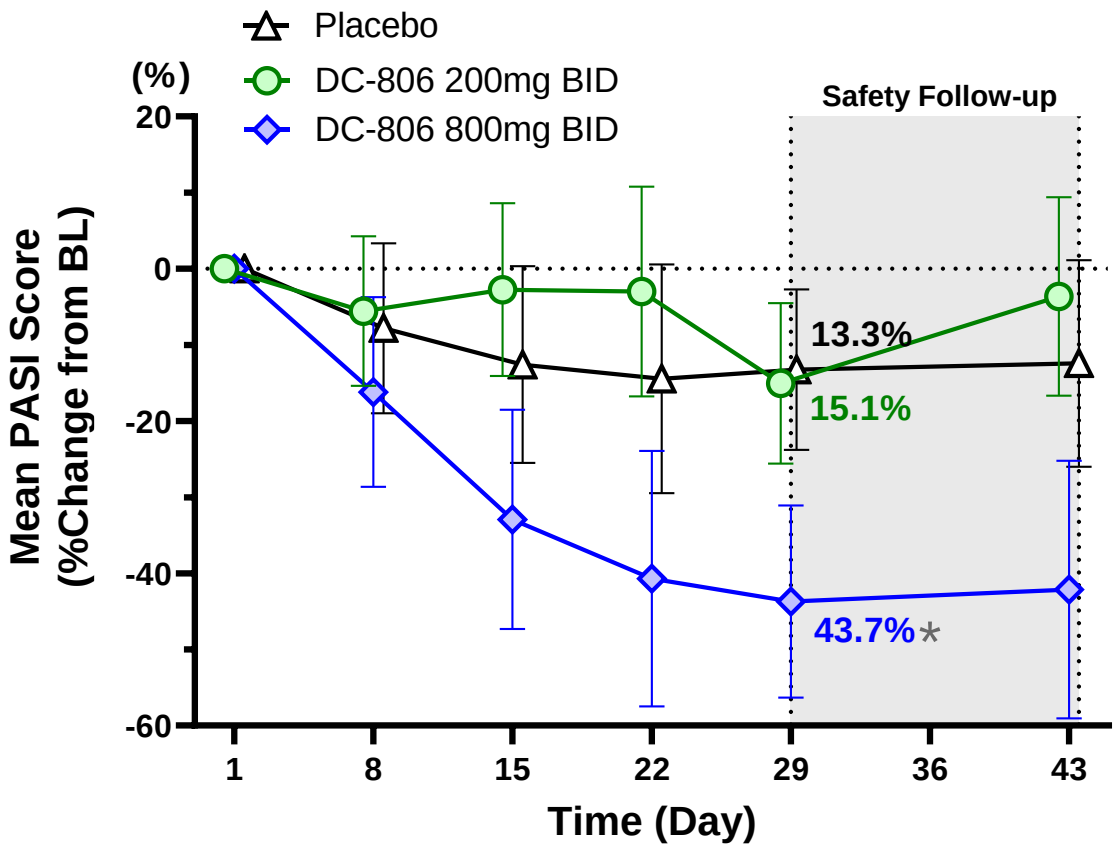
Baseline demographics and disease characteristics

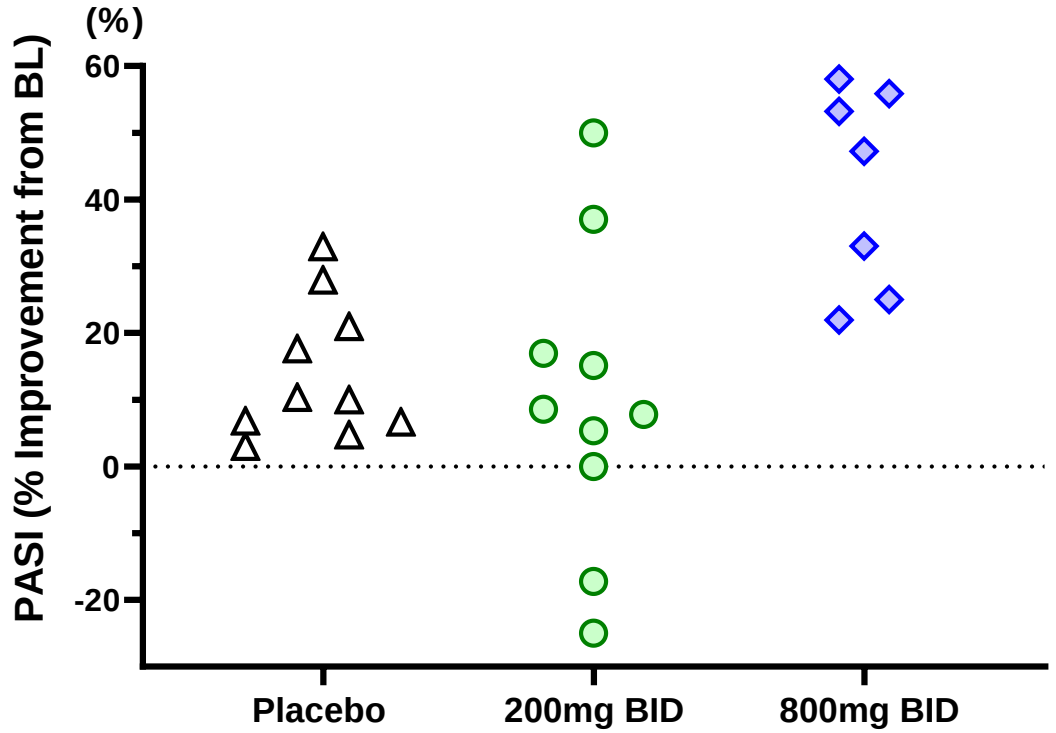
Mild – moderate patient population enrolled

	Placebo N=11	DC-806 200mg BID N=13	DC-806 800mg BID N=8
Age in years, mean (SD)	38.5 (10.9)	41.8 (12.8)	47.0 (13.3)
Male, n (%)	9 (81.8)	9 (69.2)	8 (100)
Race, n (%)			
White	11 (100)	10 (76.9)	8 (100)
Asian	0	3 (23.1)	0
Weight in kg, mean (SD)	88.8 (18.3)	88.9 (17.0)	82.2 (15.0)
PASI Score, mean (SD)	7.15 (1.6)	6.08 (3.0)	6.74 (2.2)
Percent BSA involvement, mean % (SD)	8.52 (4.3)	6.98 (4.5)	8.49 (7.0)

BID = twice daily | PASI = Psoriasis Area and Severity Index | BSA = Body surface area | PGA = Physician Global Assessment

DC-806 demonstrated clear benefit with reductions in PASI scores



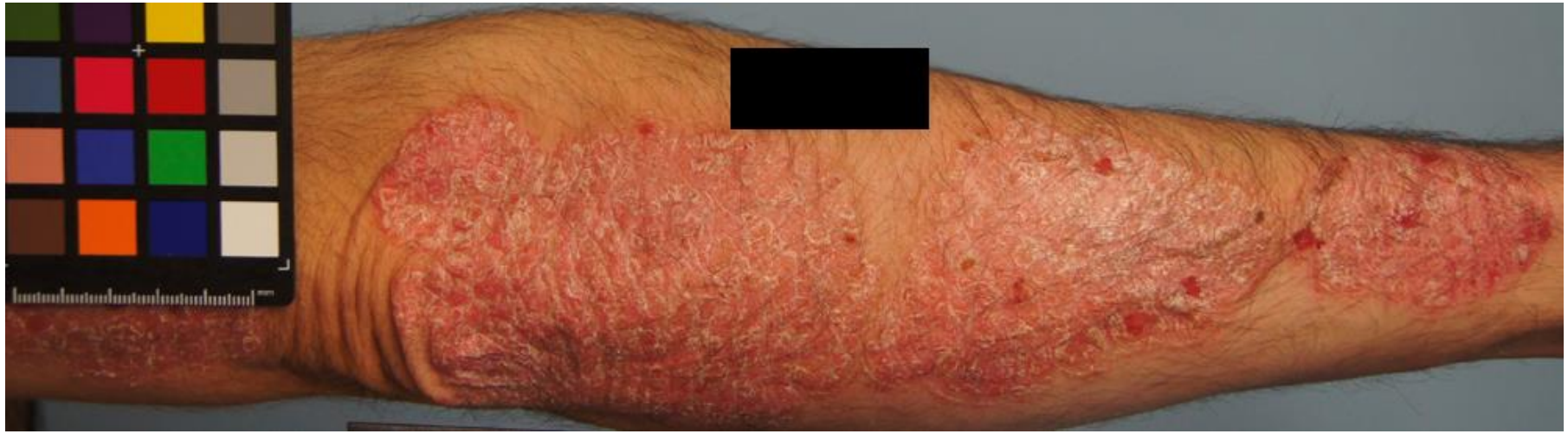


*Exploratory p = 0.0008

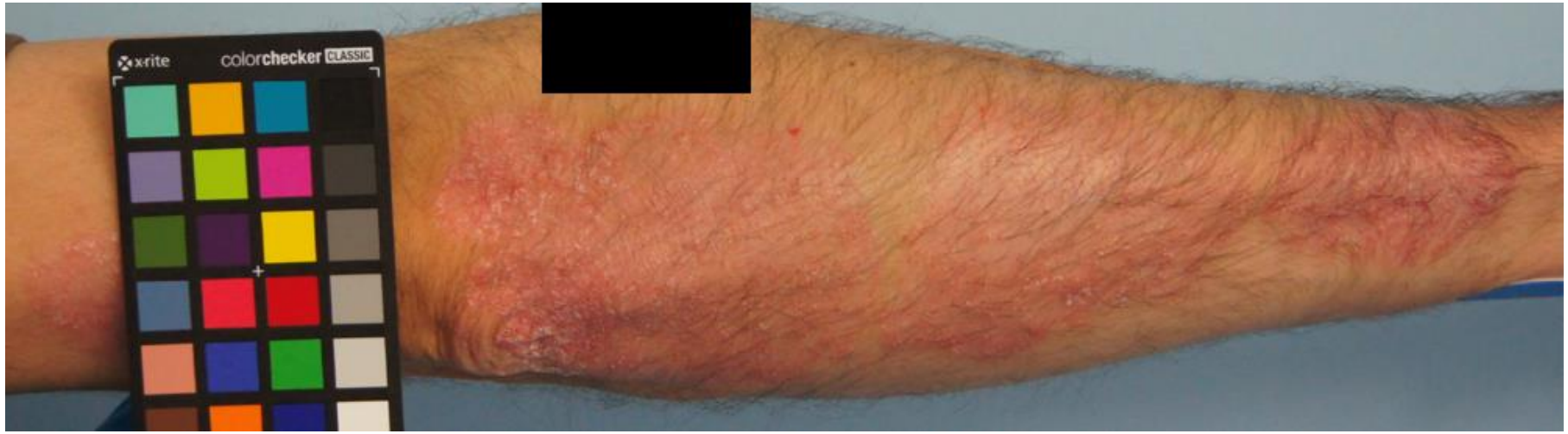
Visual improvements in psoriasis

PASI 6.8 to 3 in 28 days

Baseline

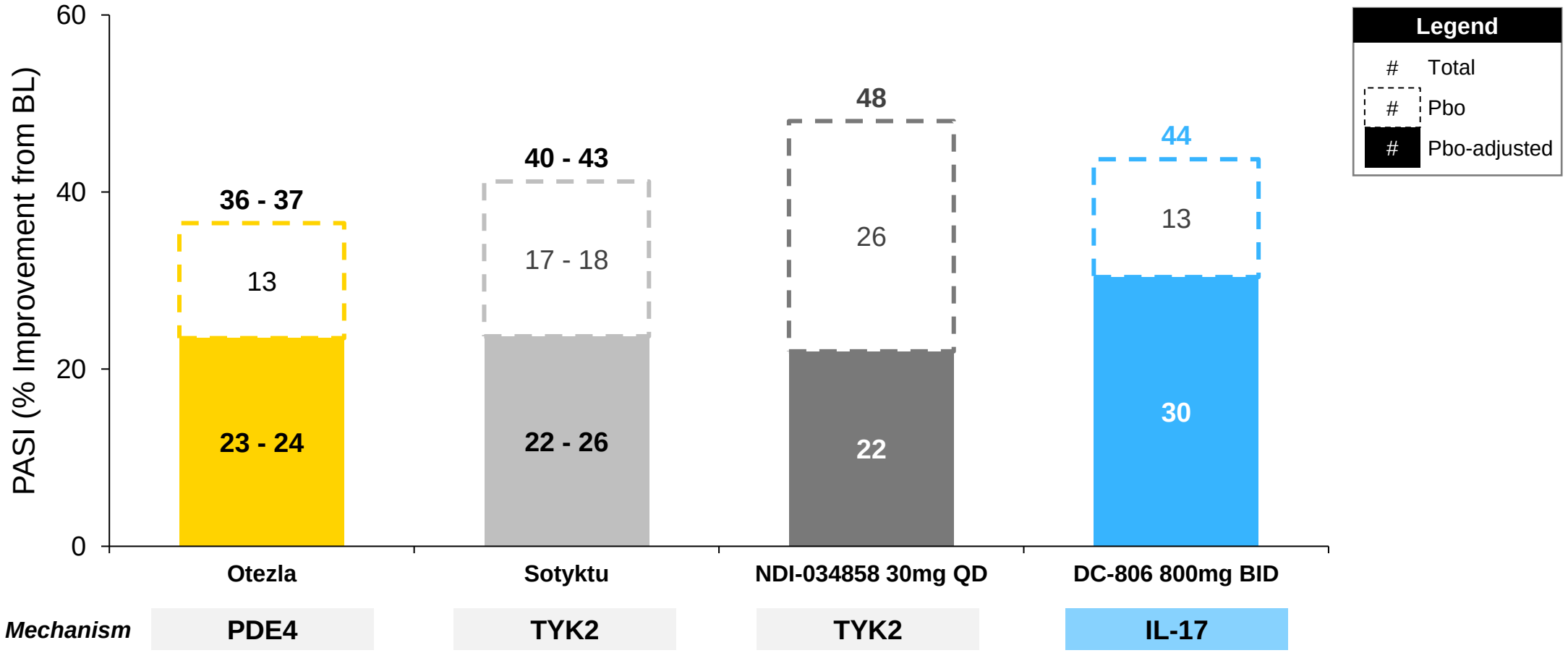


Day 29



DC-806 demonstrated competitive efficacy profile at 4-weeks

4-Week PASI Improvement by Oral Agent [1]



1. OTEZLA P3 trials (ESTEEM-1 & ESTEEM-2; N=834), SOTYKTU P3 trials (POETYK PSO-1 & POETYK PSO-2; N=843), NDI-034858 P1 trial (AAD 2022; N=5), DC-806 P1 trial (N=7)

Phase 1c: Biomarker Analysis

Biomarkers confirmed dose-dependent target engagement and biological activity

- Well established IL-17 biomarkers are more sensitive and quantitative than clinical endpoints
- Changes in IL-17 biomarkers can precede changes in clinical endpoints

IL-17A Serum Levels

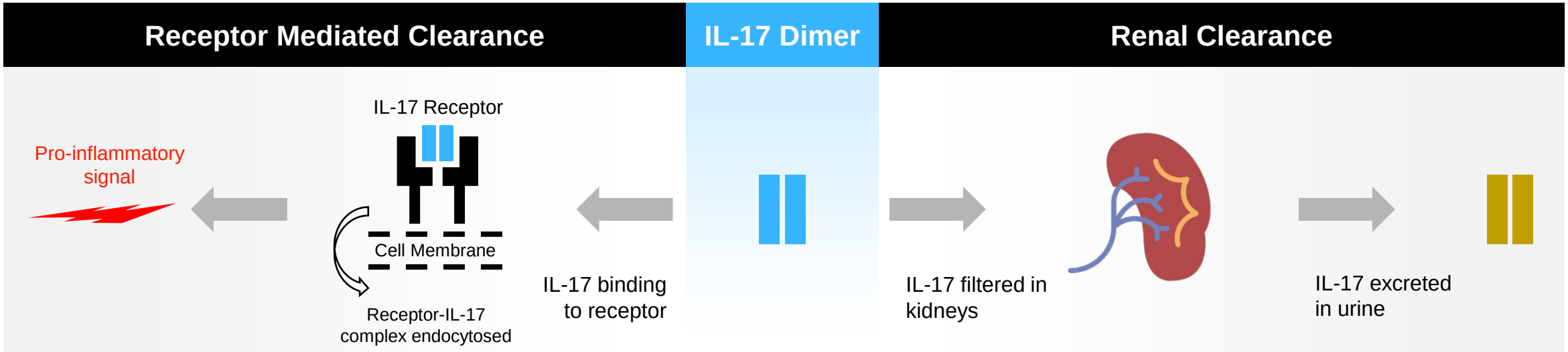
- An increase in IL-17A serum levels demonstrate target engagement, and are associated with effective treatment with anti-IL-17 antibodies

Beta Defensin-2[1]

- Psoriasis patients have elevated levels of BD-2, an antimicrobial peptide secreted by keratinocytes in inflamed skin
- A decrease in BD-2 levels have been shown to correlate with biological activity

1. Kolbinger et al., *JACI* 2017

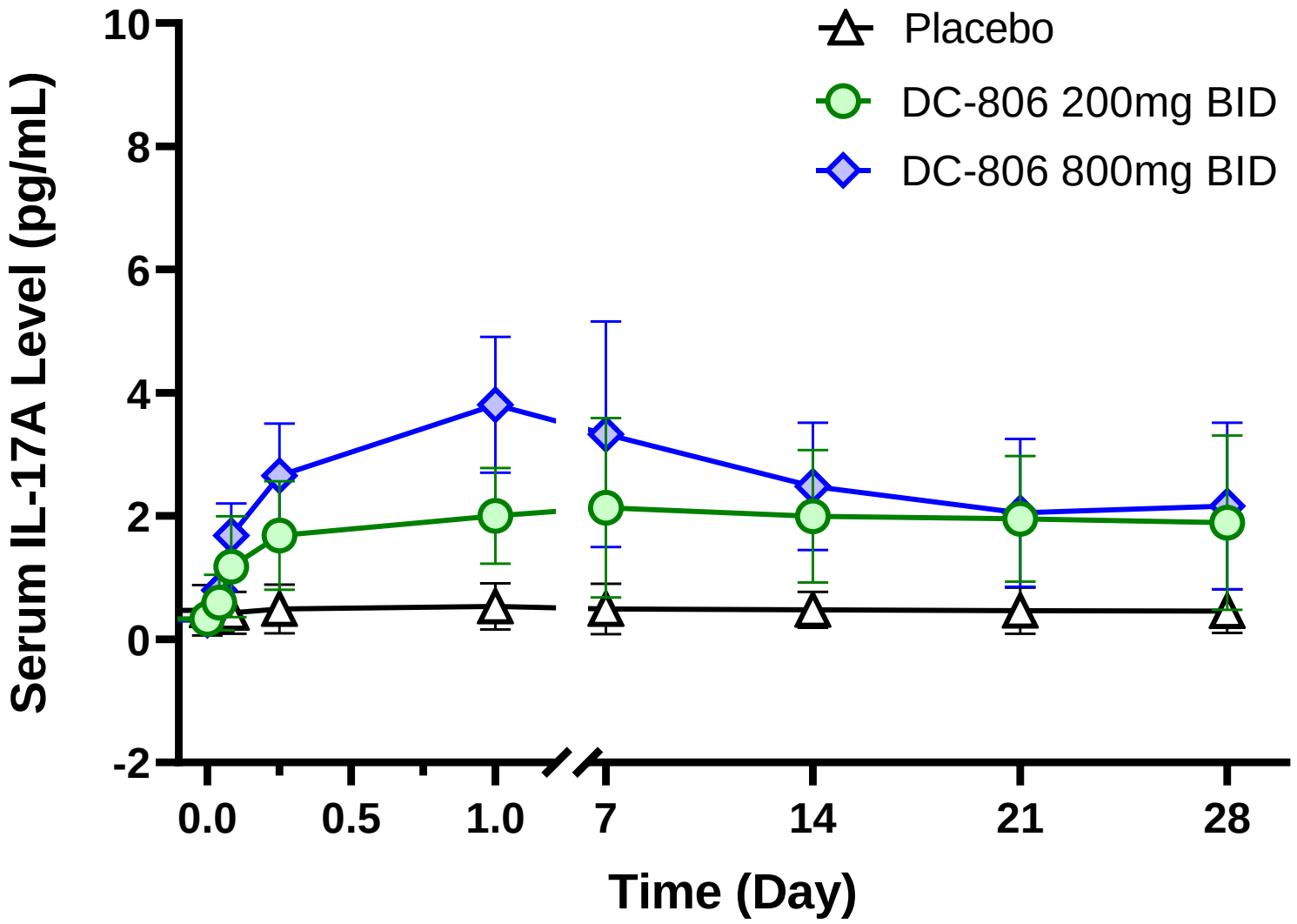
Counterintuitive increases in serum IL-17A is a measure of target engagement



Therapeutic Agent	IL-17 Complex	Receptor Mediated Clearance	Renal Clearance	IL-17A Serum Buildup
Secukinumab (Binds to cytokine)	IL-17 + mAb	↓	↓	↑↑↑
Brodalumab (Binds to receptor)	IL-17	↓	—	↑
DC-806	IL-17 + SM	↓	—	↑

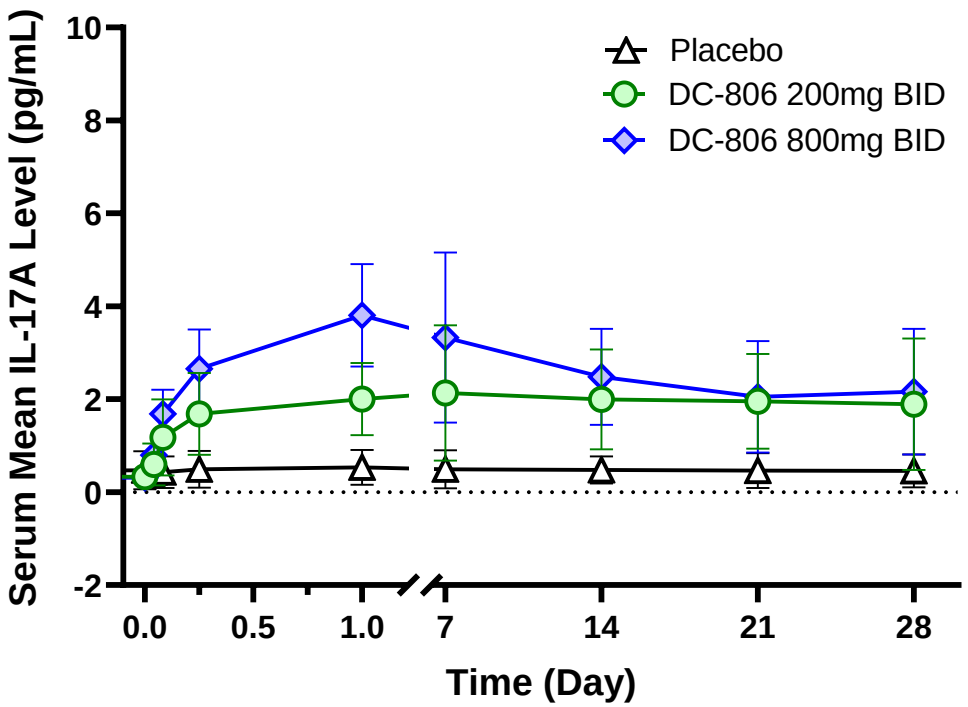
Dose-dependent increases in serum IL-17A

Confirmed target engagement at both doses

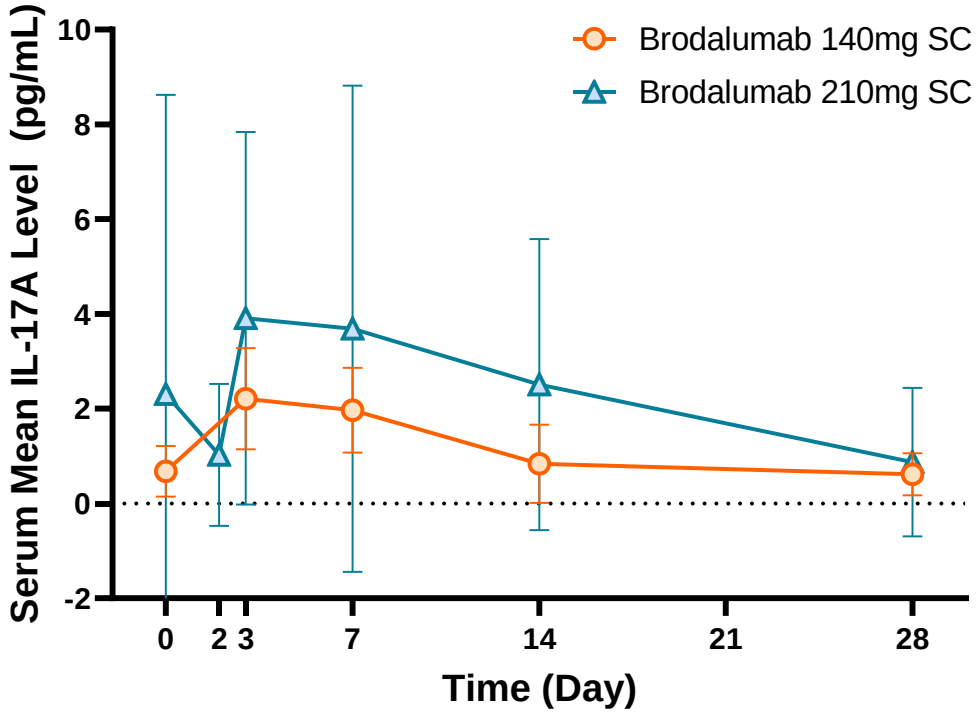


DC-806 increased serum IL-17A to levels comparable to brodalumab

DC-806 Treatment



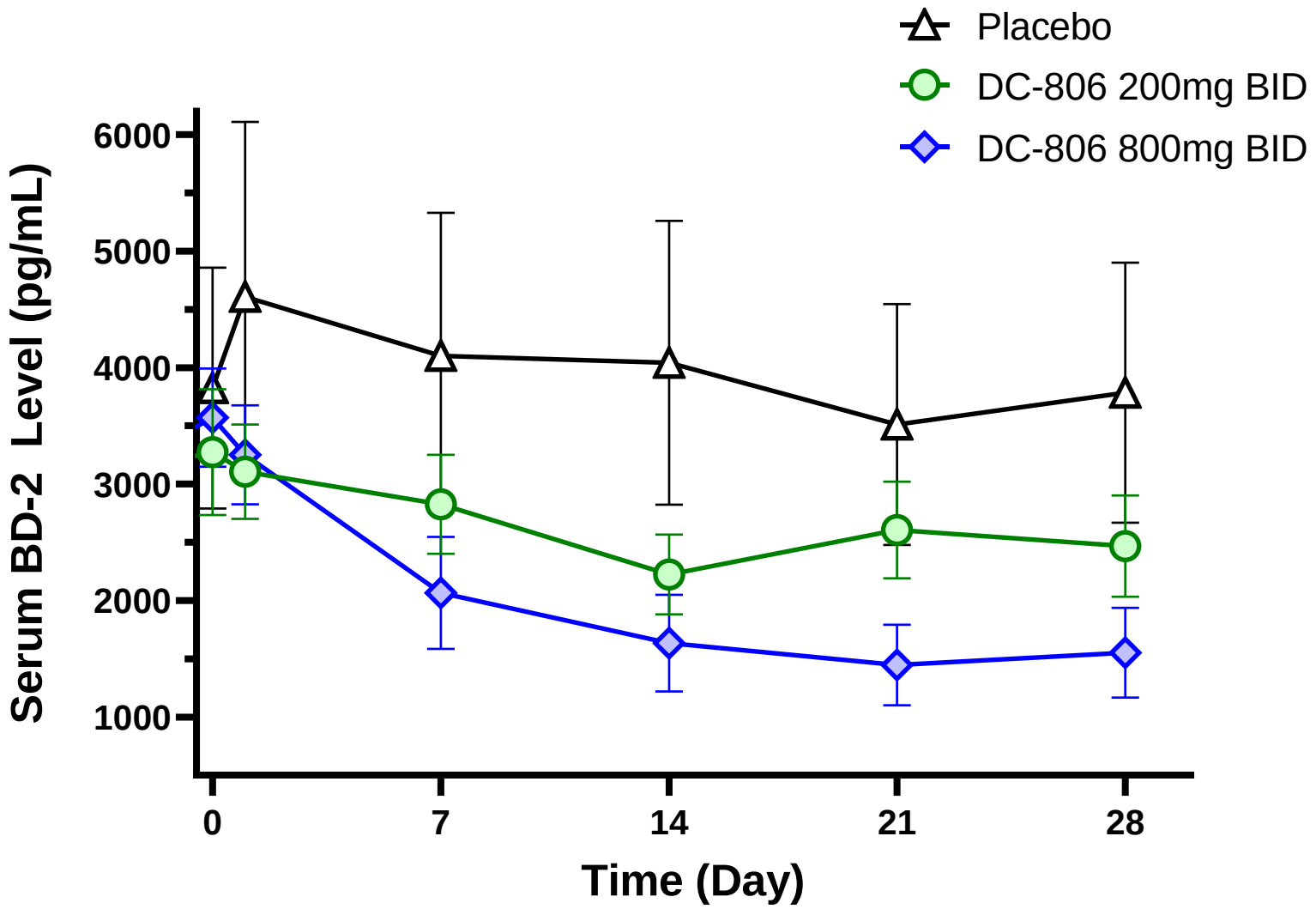
Brodalumab Treatment[1]



1. Brodalumab BLA

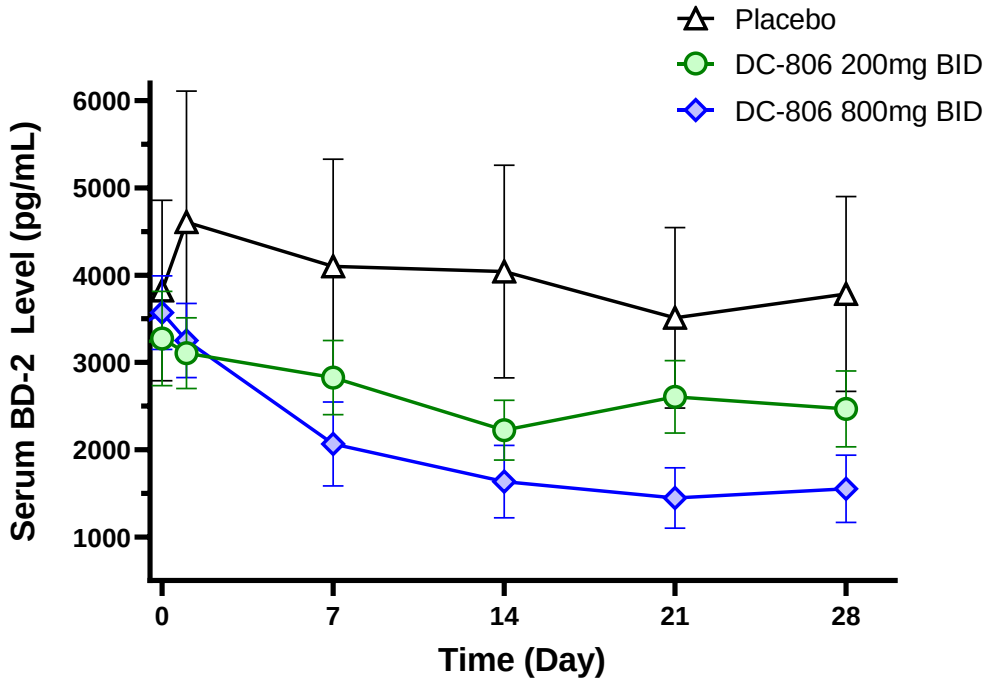
Dose-dependent reductions in beta defensin-2

Confirmed inhibition of IL-17 signaling

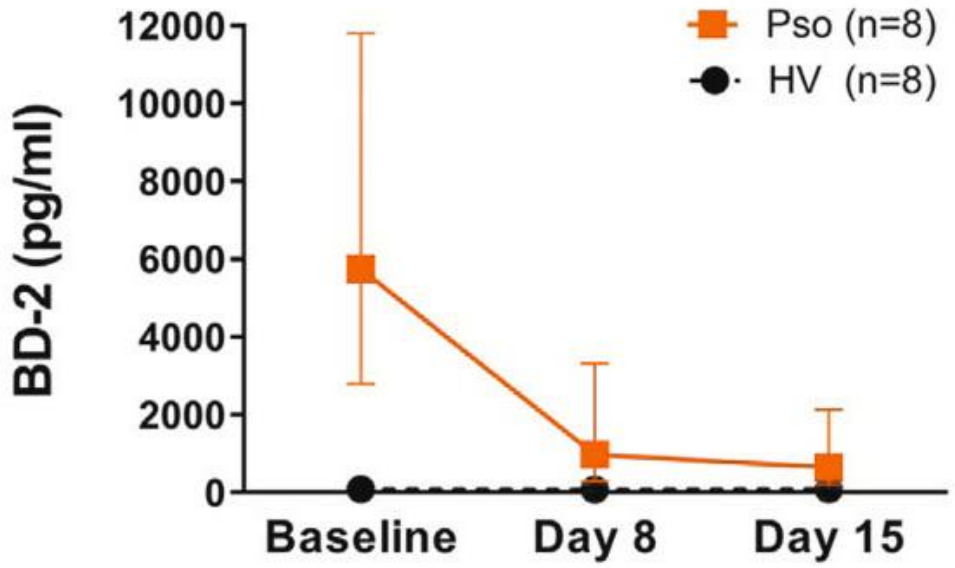


DC-806 demonstrated a reduction in beta defensin-2 comparable to secukinumab

DC-806 Treatment



Secukinumab Treatment[1]



- Both DC-806 and secukinumab rapidly decrease beta defensin-2 levels within one to two weeks

1. Kolbinger et al., 2017

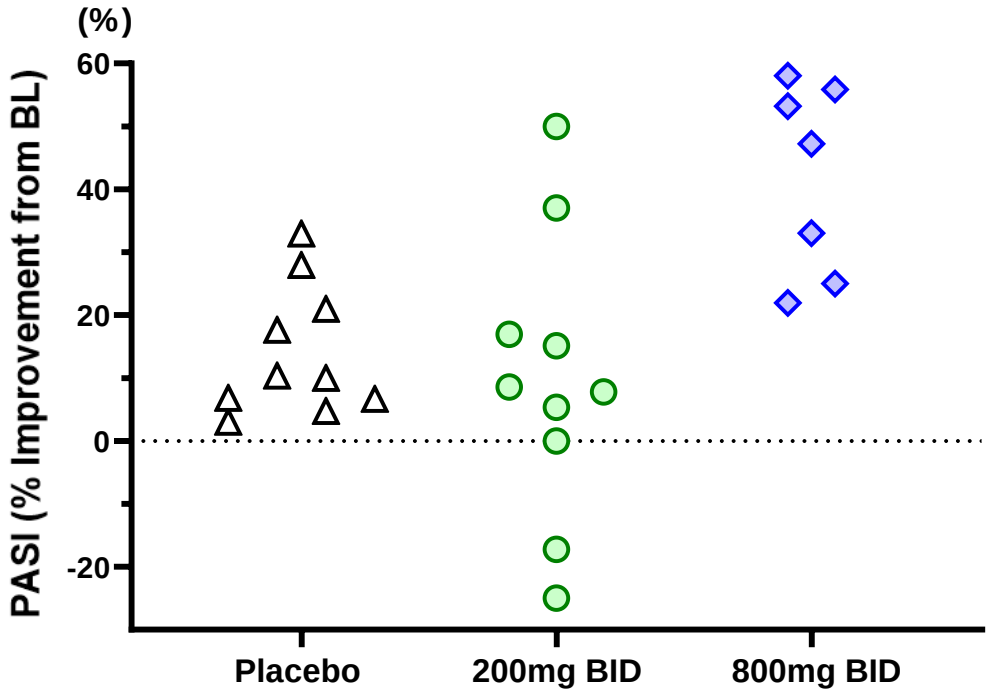
Key takeaways from DC-806 Phase 1c efficacy results

PoC
Achieved

- ✓ *Clinical demonstration of a small molecule blocking a cytokine; same mechanism of action as marketed antibodies*
- ✓ *Both doses are biologically active and show comparable biomarker activity to IL-17 antibodies*
- ✓ *4-week efficacy data suggests potential to be best oral in psoriasis*
- ✓ *Validated mechanism of action provides confidence that efficacy will continue to improve in a 12-week study*
- ? *What will DC-806 look like in a Phase 2 population with higher disease burden?*

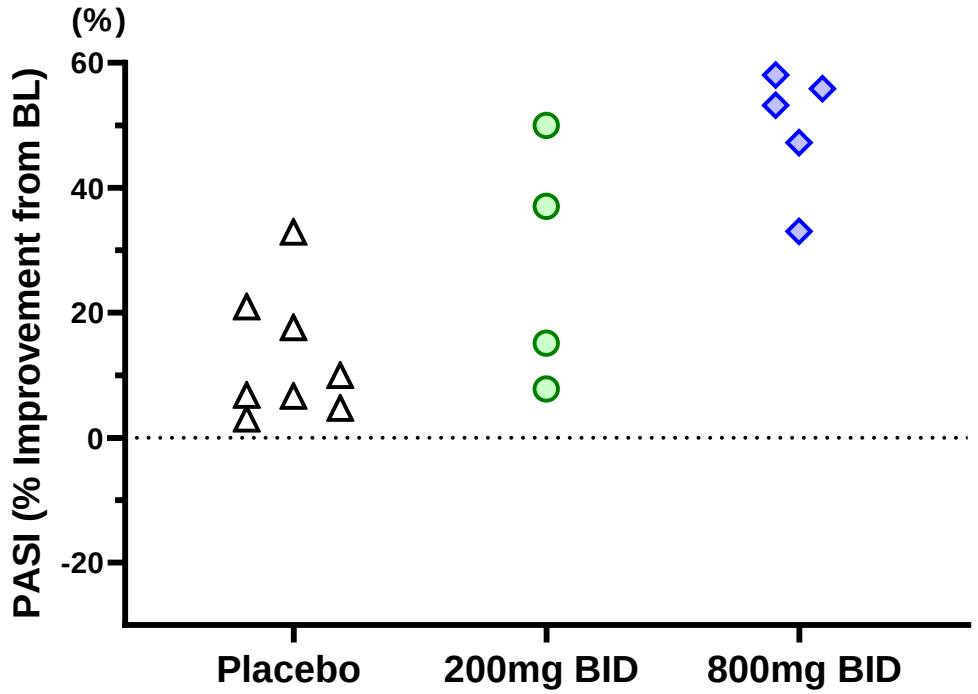
Clinical response maintained in patients with higher disease burden

Total Enrolled Population



PASI (% Change)	13.3%	15.1%	43.7%

Patients with Baseline PASI ≥ 6



PASI (% Change)	11.0%	31.4%	47.0%

DC-806: potential to be the best-in-class oral agent in psoriasis

Clean safety profile	✓ DC-806 exhibited a favorable safety and tolerability profile
Convenient dosing	✓ DC-806 PK profile enables commercially viable QD or BID dosing
Proof of concept to validate DC-806 and oral IL-17 Franchise	✓ DC-806 demonstrated clear benefit with improvement in PASI scores ✓ DC-806 showed target engagement and inhibition of IL-17 signaling

PASI: Psoriasis Area and Severity Index | QD: Once daily dosing | BID: Twice daily dosing

Next Steps and Differentiation

Next steps: continue to execute against our stated oral IL-17 franchise strategy

Phase 1 Psoriasis

PoC Achieved

DC-806 Strategy

- P2b start anticipated 1H 2023
- Adults with moderate-to-severe psoriasis (PASI ≥ 12)
- 12-week dosing period
- Multiple doses exploring QD and BID dosing vs. placebo
- Goal: Evaluate efficacy and safety at 12-weeks; determine optimal dose for Phase 3 trials

DC-853 (Fast-Follower) Strategy

- P1 data anticipated in 2H23
- PoC from DC-806 will allow us to accelerate development of DC-853 and skip P1c in psoriasis patients

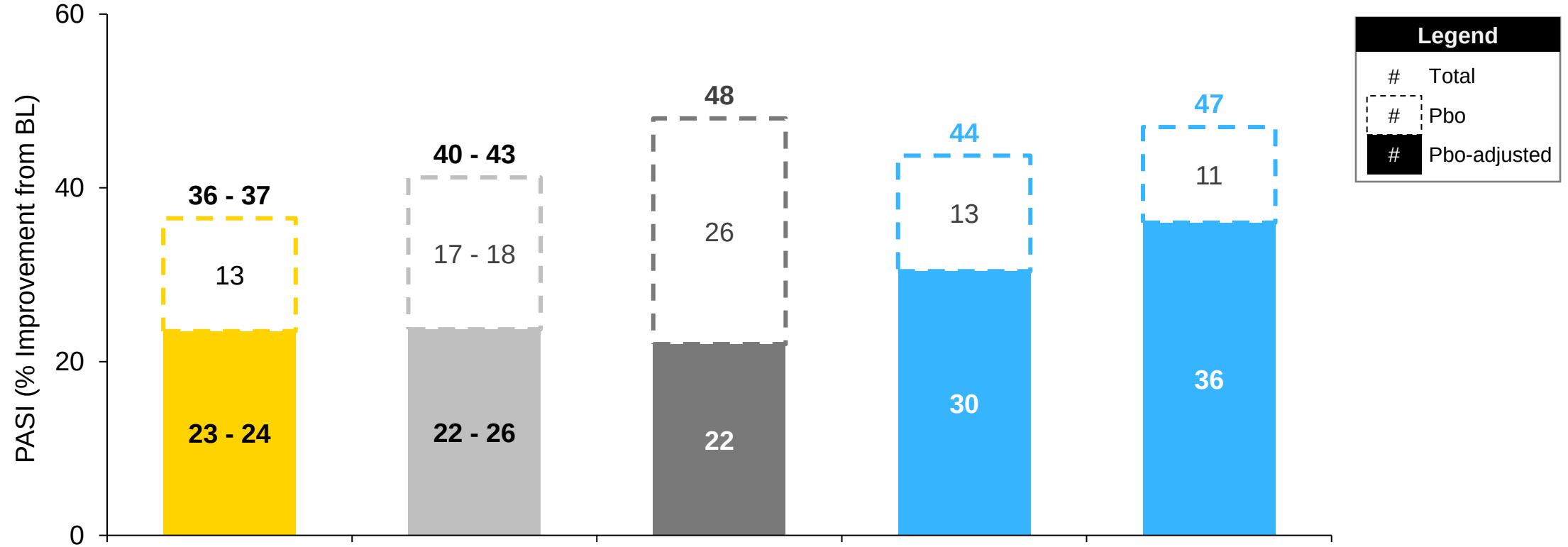
PK profile of DC-806 supports commercially viable dosing

Daily target coverage of IL-17 AA (hours) at steady state (MAD day 7)		
Dose Regimen	**IC_{50}**	**IC_{90}**
175mg QD	24	12
200mg BID	24	18
400mg BID	24	24
800mg BID	24	24

- *One pill, once a day to cover IC_{50}*
- *One pill, twice a day to cover IC_{90}*

DC-806 demonstrated improved PASI response in patients with higher disease burden

4-Week PASI Improvement by Oral Agent[1]



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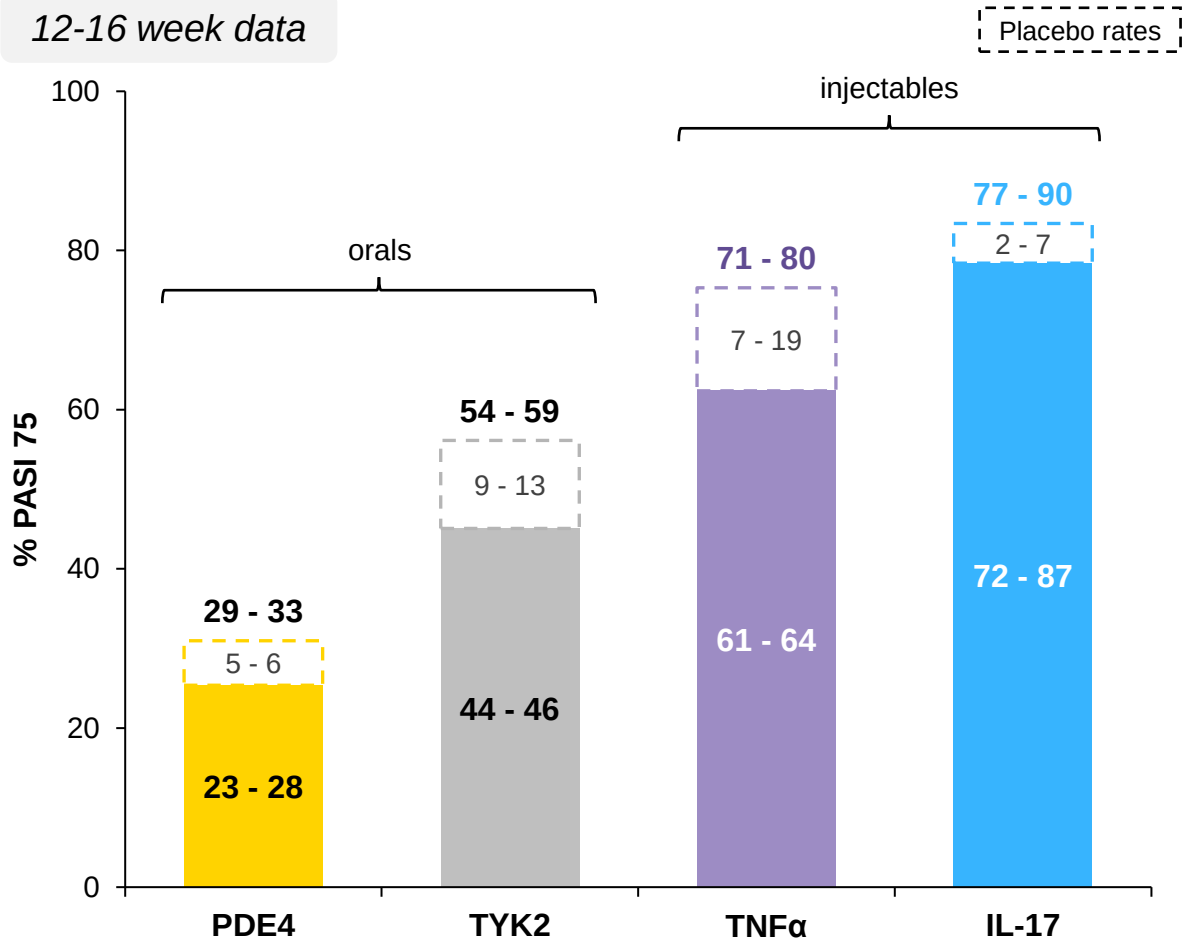
Oral IL-17 inhibition: potential to combine best modality with best mechanism

Potential for Superior Efficacy[1]

12-16 week data



Potential for Broadest Use[2,3]

Rx Considerations	Sotyktu (oral)	Cosentyx (injectable)
Target	TYK2	IL-17
Tuberculosis	Screen for TB (Observed active TB)	Screen for TB (TB not observed)
Lab Monitoring	Monitor liver enzymes, serum triglycerides, CPK	--
Other	JAK warning language	IBD Contraindication

1. IL-17 P3 trials (FIXTURE & UNCOVER-2; N=1306), TNF-α P3 trials (REVEAL & CHAMPION; N=1483), TYK2 P3 trials (POETYK PSO-1 & POETYK PSO-2; N=1686), PDE4 P3 trials (ESTEEM-1 & ESTEEM-2; N=1257)
2. SOTYKTU label, COSENTYX label
3. Kelsey et al. *Dermatology Online Journal*. 2018

DICE Therapeutics™

Q&A

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