DC-806, an oral IL-17A inhibitor:

Proof-of-concept in adults with mild-to-moderate psoriasis

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Disclosures

RB Warren: AbbVie, Almirall, Arena, Aristea, Amgen, Astellas, Avillion, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, DICE, Eli Lilly, GSK, Janssen, Lilly, Leo, Medac, Novartis, Pfizer, Sanofi, Sun Pharma, UCB and UNION.

HJA Hunter: AbbVie, Almirall, DICE Therapeutics, Eli Lilly, Janssen, La Roche-Posey, Leo, Pfizer, Janssen, Merck Serono, Novartis Regeneron, Sanofi Genzyme, UCB, UNION Therapeutics

KA Papp: AbbVie, Acelyrin, Akros, Amgen, Anacor, Aralez Pharmaceuticals, Arcutis, Avillion, Bausch Health/Valeant, Boehringer Ingelheim, Bristol-Myers Squibb, Can-Fite Biopharma, Celgene, Celltrion, Coherus, Dermavant, Dermira, DICE Therapeutics, Dow Pharma, Eli Lilly, Evelo, Forbion, Galderma, Gilead, GSK, Incyte, Janssen, Kyowa Hakko Kirin, Leo, Meiji Seika Pharma, Merck (MSD), Mitsubishi Pharma, Novartis, Pfizer, Regeneron, Reistone, Roche, Sanofi-Aventis/Genzyme, Sandoz, Sun Pharma, Takeda, UCB, vTv Therapeutics, Xencor

KB Gordon: AbbVie, Amgen, Arcutis, BMS, Boehringer Ingelheim, Dermavant, Incyte, Janssen, Lilly, Novartis, MoonLake, UCB, Union, DICE Therapeutics, Protagonist Therapeutics

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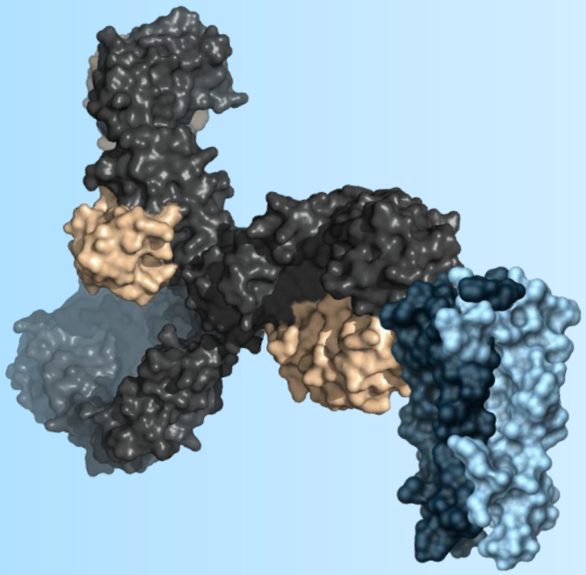
TT Lu: Employee of DICE Therapeutics

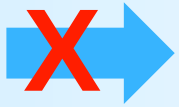
DC-806: blocking the *same step* as the antibodies via allosteric binding event

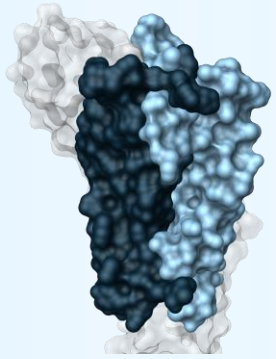
IL-17AA + ANTIBODY

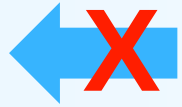
IL-17 AA + RECEPTOR

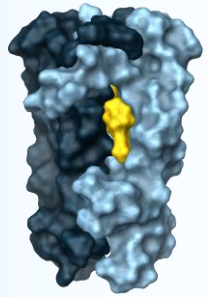
IL-17 AA + DC-806







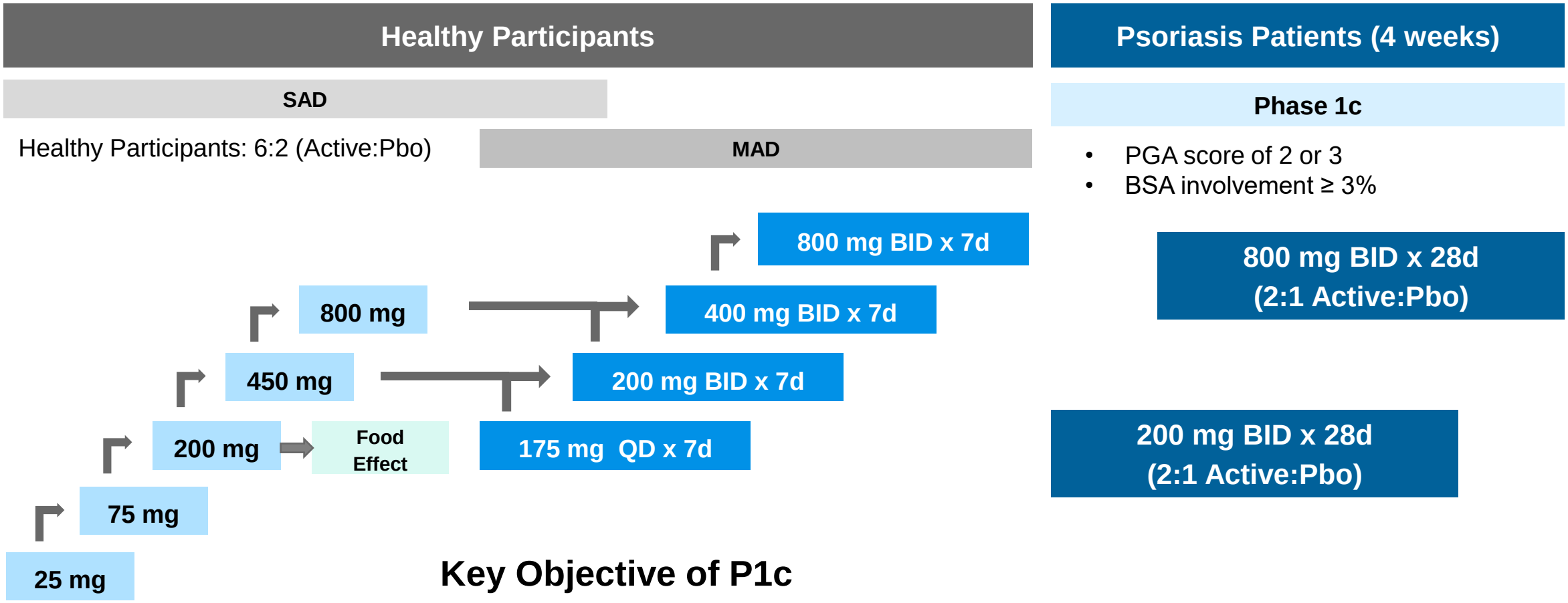




PRO-INFLAMMATORY SIGNAL

Phase 1 SAD/MAD in Healthy Participants and P1c in Psoriasis Patients

Safe and well tolerated in Healthy Participants



Key Objective of P1c

- Evaluate the safety, tolerability, and PK and explore preliminary clinical activity and pharmacodynamics of DC-806 in patients with psoriasis

Baseline demographics and disease characteristics

Mild – moderate patient population enrolled

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

BID = twice daily | PASI = Psoriasis Area and Severity Index | BSA = Body surface area

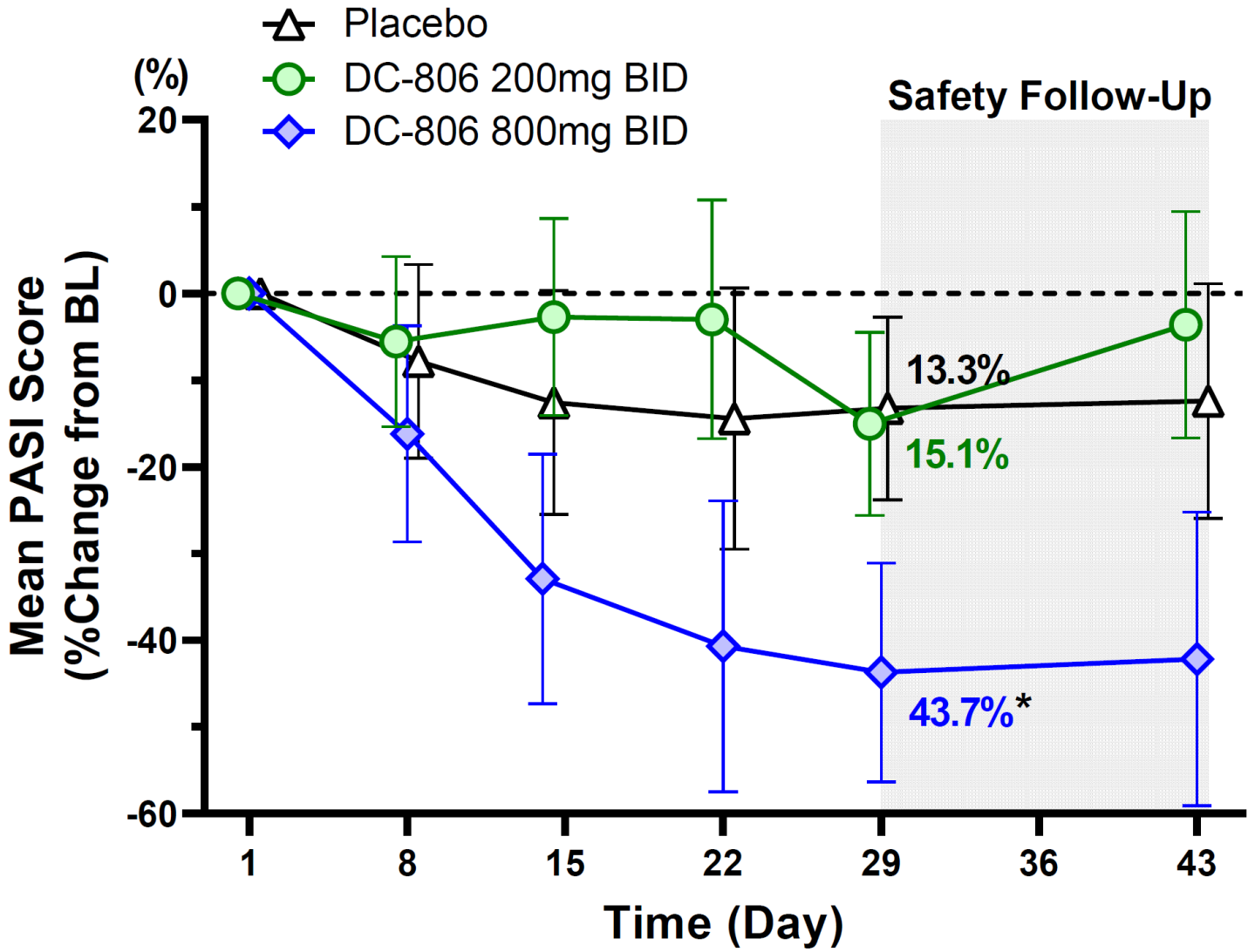
Disposition of Psoriasis Patients in P1c

No discontinuations due to treatment-related AEs or lack of efficacy/worsening of psoriasis in DC-806 treatment arms

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

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

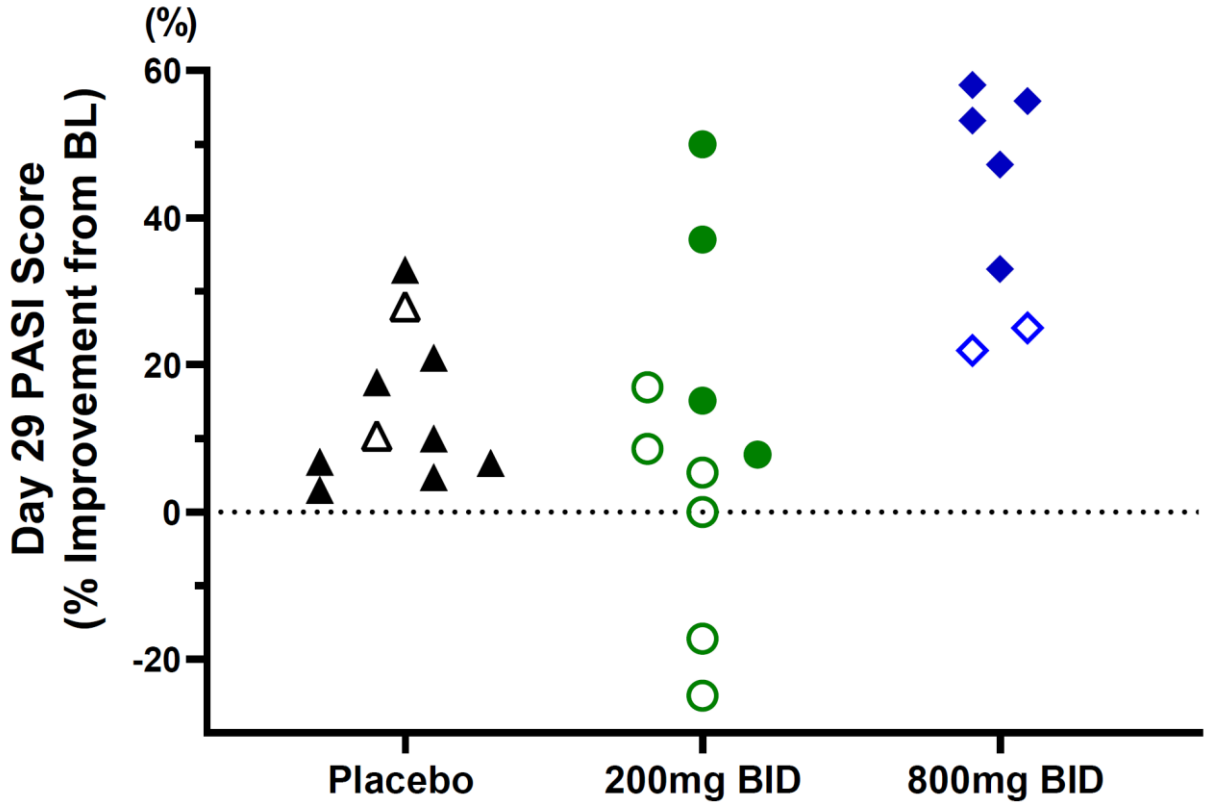
DC-806 demonstrated clear benefit with reductions in PASI scores



*Exploratory p = 0.0008

Subgroup analysis in patients with baseline PASI ≥ 6

High dose arm effect maintained; Low dose arm shows trend of benefit



Solid symbols: Baseline PASI ≥ 6
Open symbols: Baseline PASI < 6

Mean % change from Baseline PASI	Placebo	200mg BID	800mg BID
Total Population	**13.3%**	**15.1%**	**43.7%**
Baseline PASI ≥ 6	**11.0%**	**31.4%**	**47.0%**

Biomarkers confirmed dose-dependent target engagement and biological activity

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

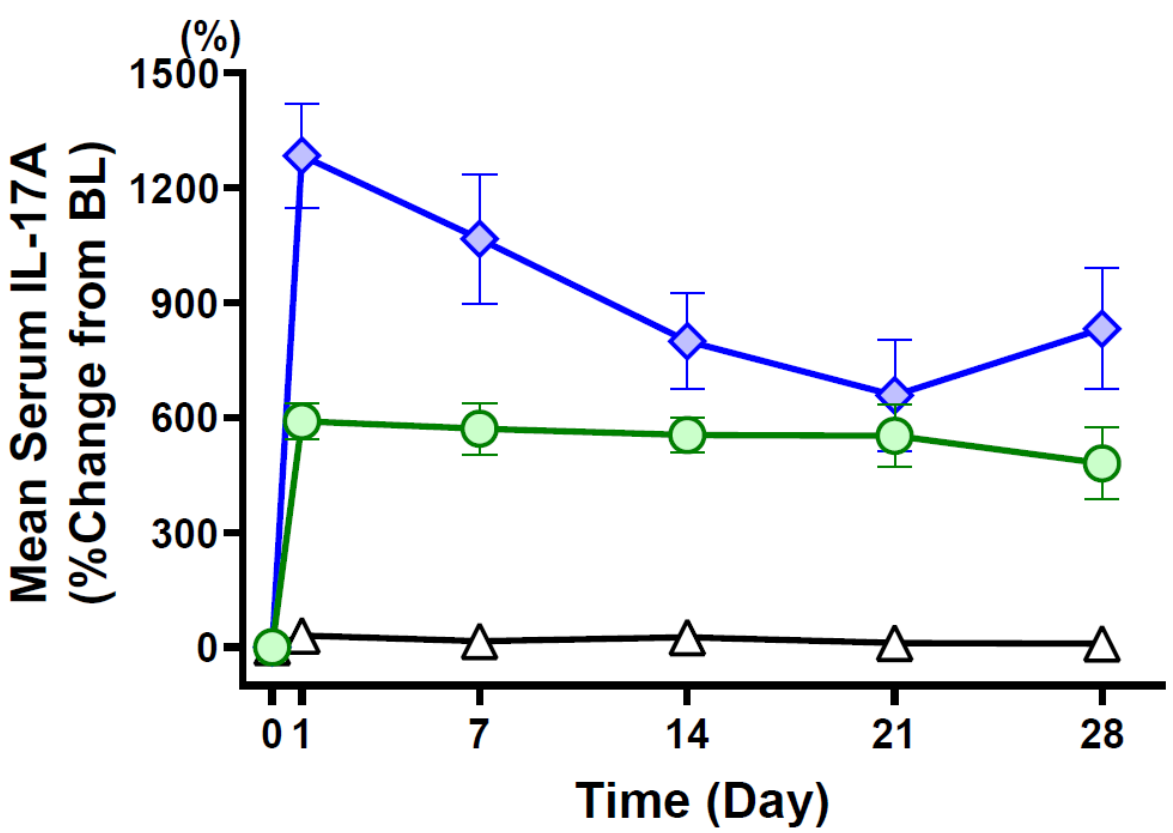
Beta Defensin-2

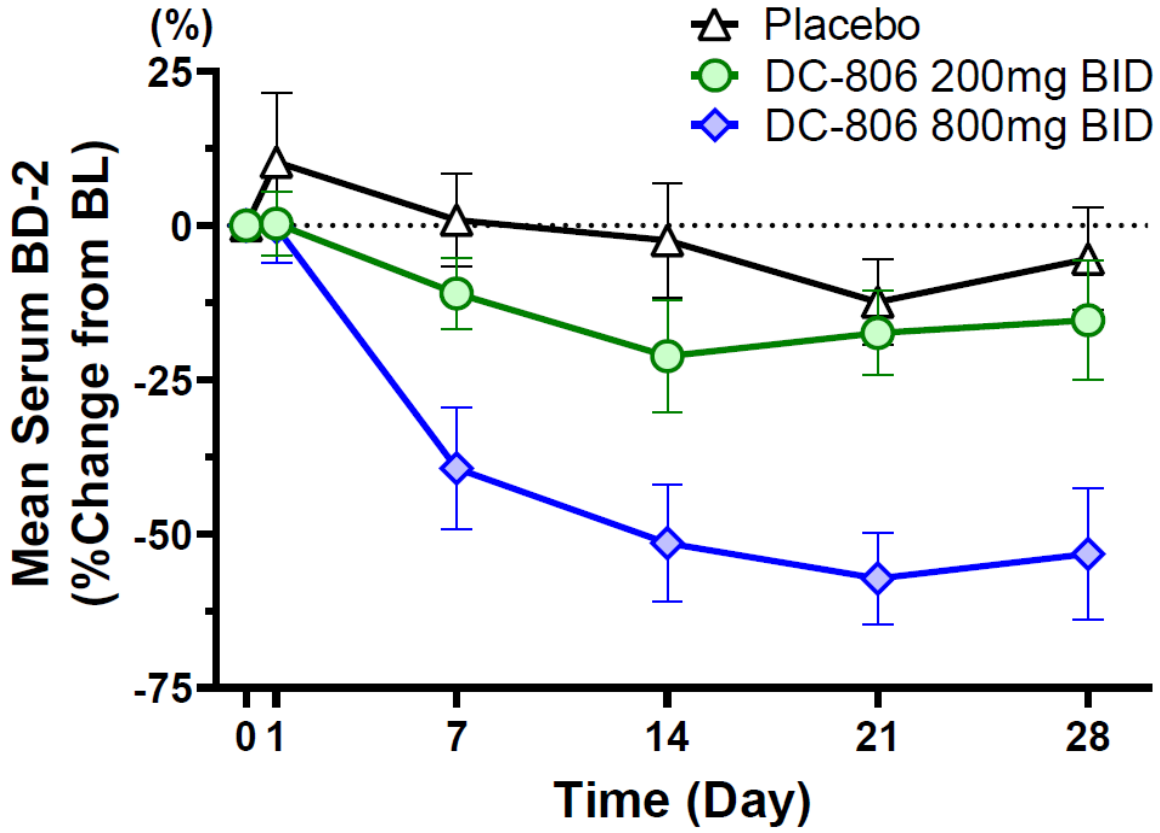
- Psoriasis patients have elevated levels of BD-2, an antimicrobial peptide secreted by keratinocytes in inflamed skin
- A ***decrease*** in BD-2 levels has been shown to correlate with biological activity

IL-19 Plasma Levels

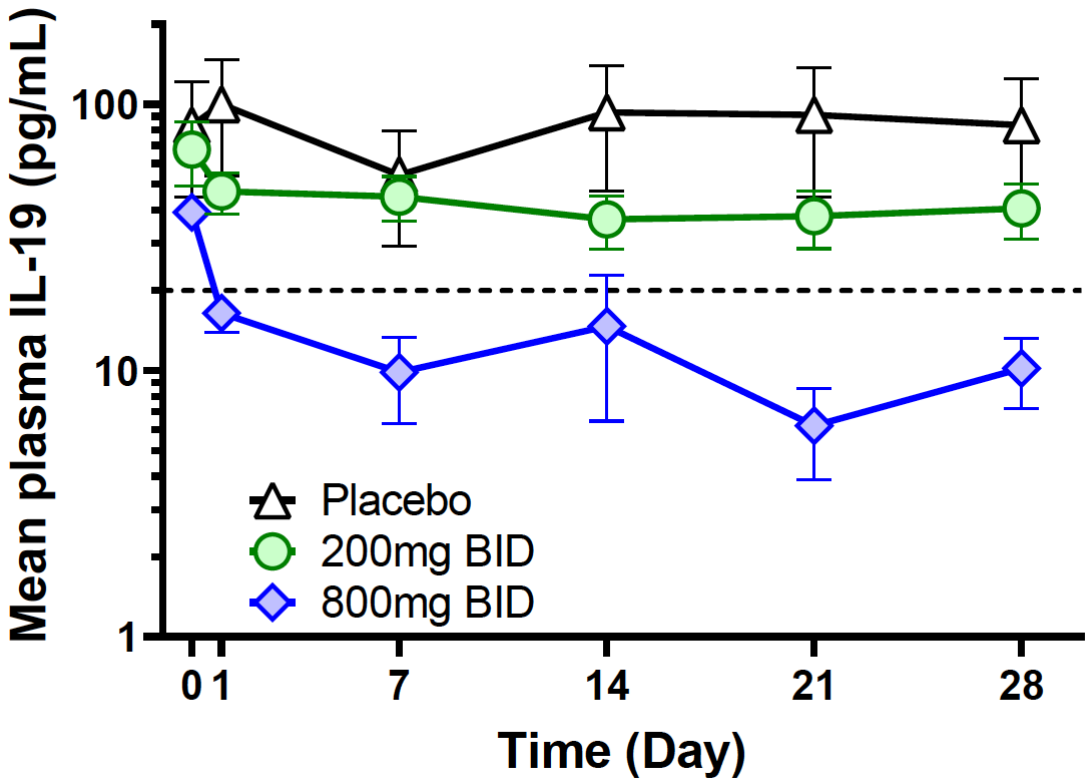
- A ***decrease*** in IL-19 plasma levels **demonstrate effective blockade of IL-17** mediated signaling, and has been shown to correlate with clinical improvement

Dose-dependent increases in IL-17A and decreases in BD-2 confirmed target engagement and reduction in IL-17 signaling





Reductions in systemic IL-19 by DC-806 suggest potential for significant long term PASI responses



2 weeks of treatment with DC-806		
Cohort	**[IL-19] < 21 pg/mL[1]**	**[IL-19] pg/mL**
Placebo	0/9 pts (0%)	93.1
200 mg BID	3/8 pts (38%)	37.0
800 mg BID	6/7 pts (86%)	14.7

IL-19 reductions below ~20 pg/ml after 2 weeks of treatment are associated with PASI90/100 at week 16[2]

1. In patients with baseline IL-19 > 21 pg/ml [*Lower limit of quantification (LLOQ): 7.8 pg/mL]*
2. Konrad, et. al. *Scientific Reports* (2019) 9:521

DC-806 demonstrated a favorable safety and tolerability profile in psoriasis patients

- **35 total TEAEs in 20 patients** (16 DC-806-treated and 4 placebo patients)
  - 27 **mild** in severity and 8 **moderate** in severity
- **No** severe AEs, SAEs, or AESIs
- **2 Treatment-related AEs:** Nausea and abdominal discomfort in 1 patient (800mg BID)
- **No** clinically significant or consistent alterations from baseline across all clinical and safety lab parameters (including liver enzymes)

AEs occurring in ≥ 2 patients Preferred Term, Patients (%)	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

Key takeaways from DC-806 Phase 1c efficacy results

- ***Clinical demonstration of a small molecule blocking a cytokine, opens new approaches to develop oral immunological therapeutics***
- ***Both doses demonstrate biological activity and show robust biomarker activity***
- ***4-week efficacy and IL-19 data suggest potential for significant long term clinical benefit***
- ***Preliminary safety and efficacy data support further clinical development***

Questions

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