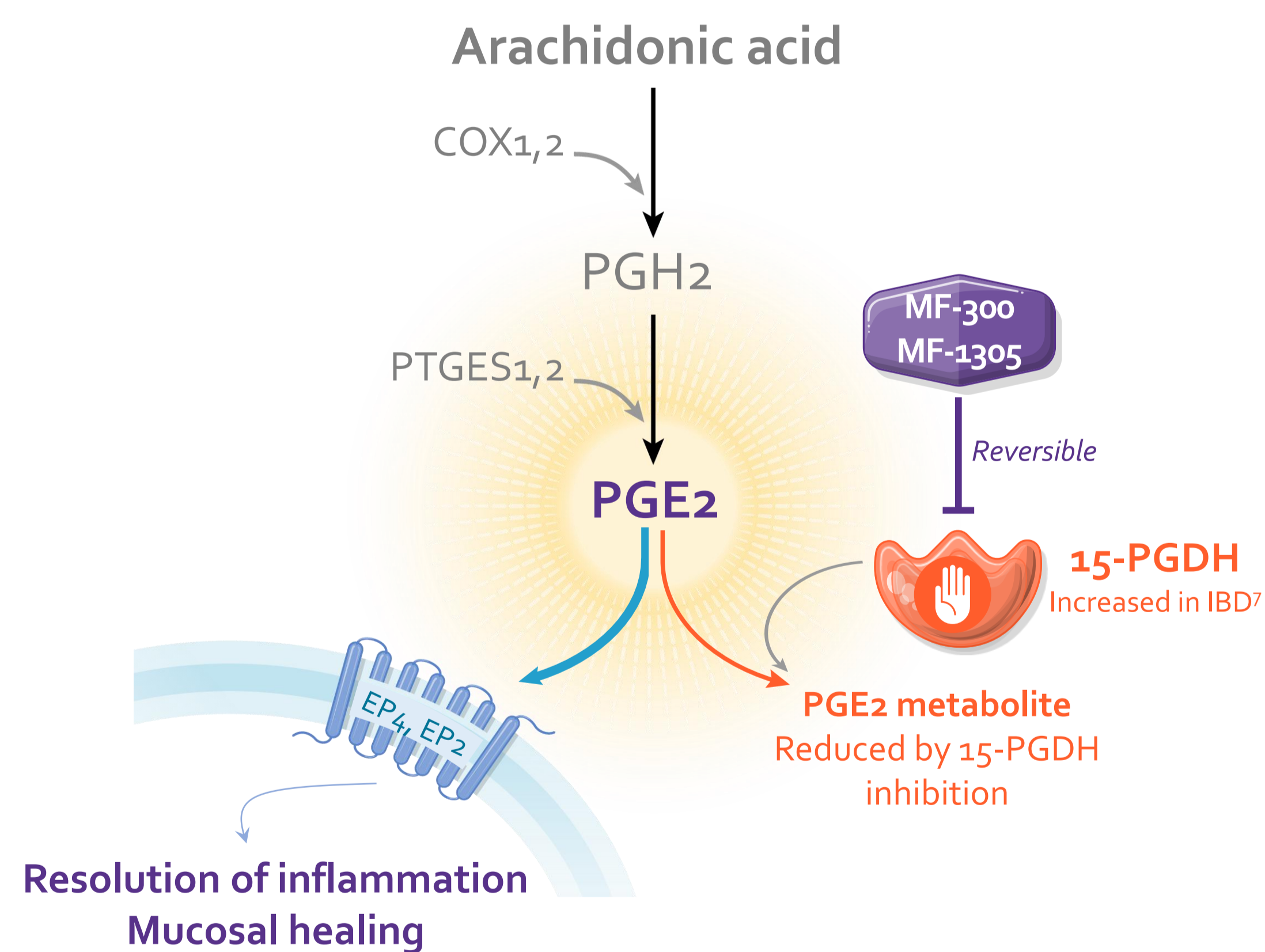


## BACKGROUND

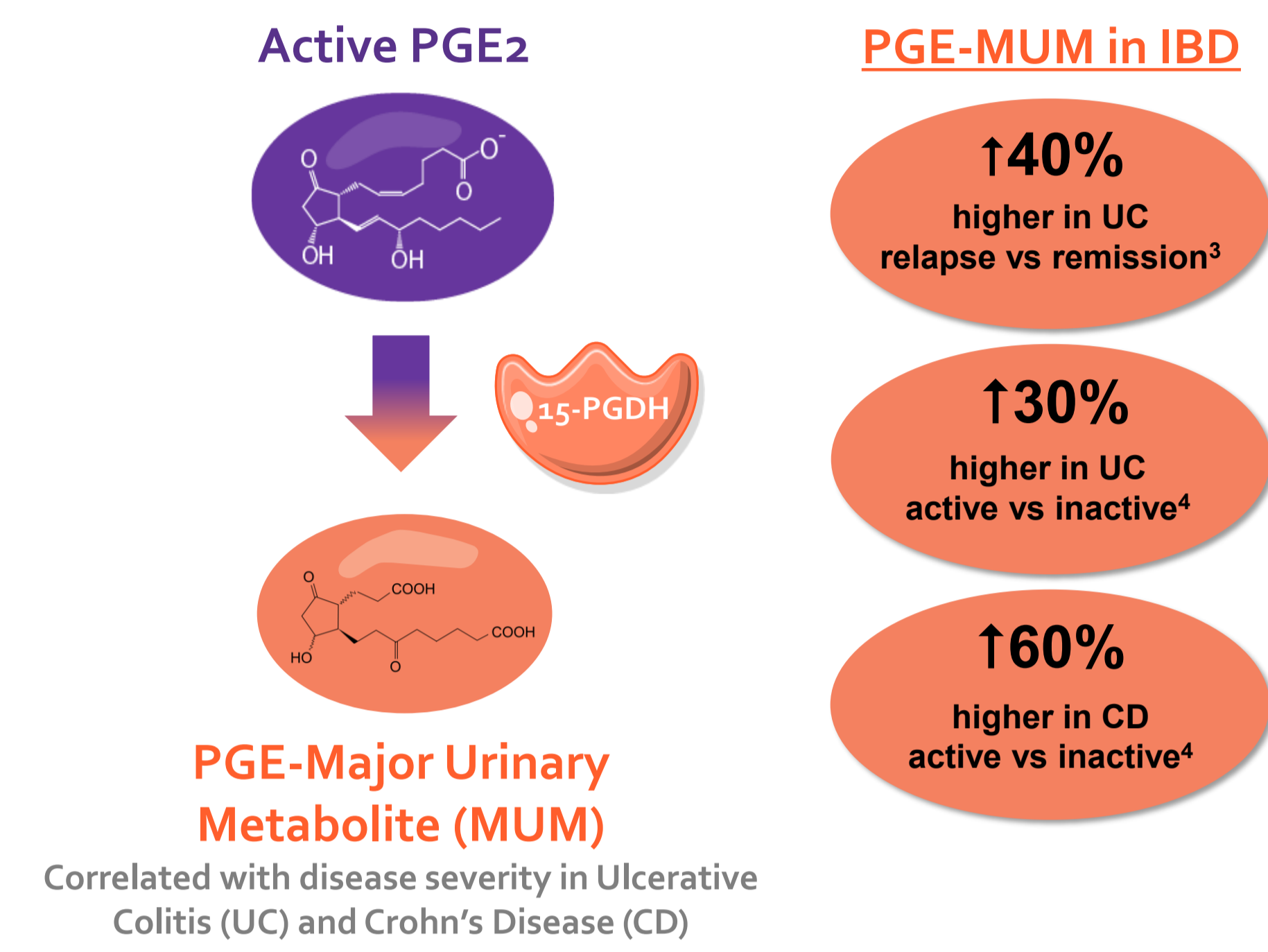
- Inflammatory bowel disease (IBD) a chronic, relapsing inflammation of the GI tract driven by dysregulated innate and adaptive immune responses, impaired epithelial barrier integrity, and disrupted mucosal repair.
- Though many treatment options are available, rates of relapse remain high - need for novel agents that support mucosal healing in IBD.
- Prostaglandin E2 (PGE2) plays a key role in maintaining barrier integrity by promoting resolution of inflammation and epithelial repair<sup>1,2</sup>.
- Pharmacologic inhibition of 15-PGDH (15-hydroxyprostaglandin dehydrogenase), an enzyme that metabolically degrades PGE2, is a novel strategy to increase physiological levels of PGE2.

Epirium Bio is developing oral small molecule inhibitors of 15-PGDH

**MF-300: Phase 2-ready**  
**MF-1305: Preclinical development**



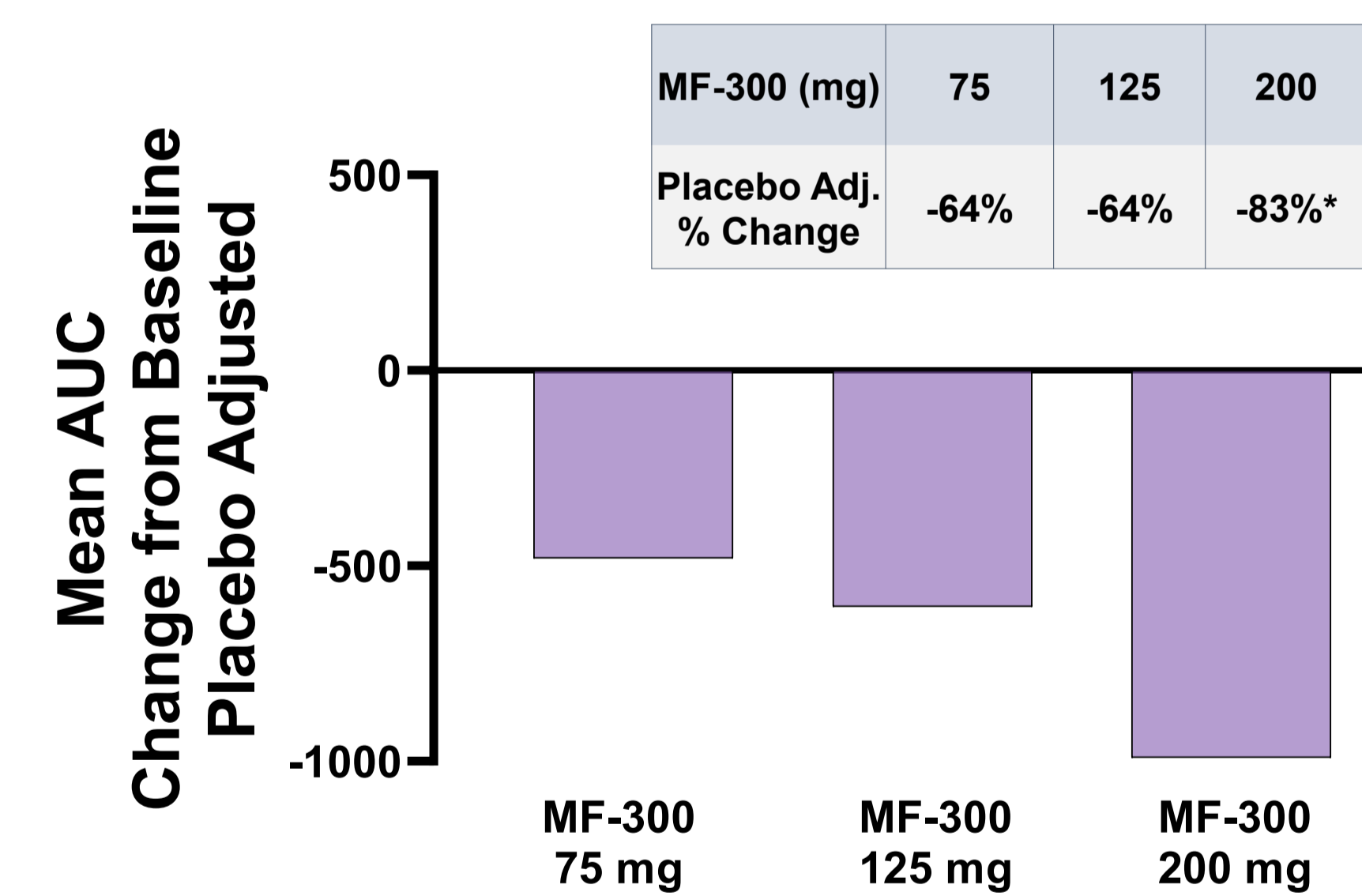
## PGE-MUM correlates with disease activity in IBD<sup>3-6</sup>



## MF-300 reduced levels of PGE-MUM in a Phase 1 healthy volunteer study

**Phase 1: Multiple Ascending Dose**

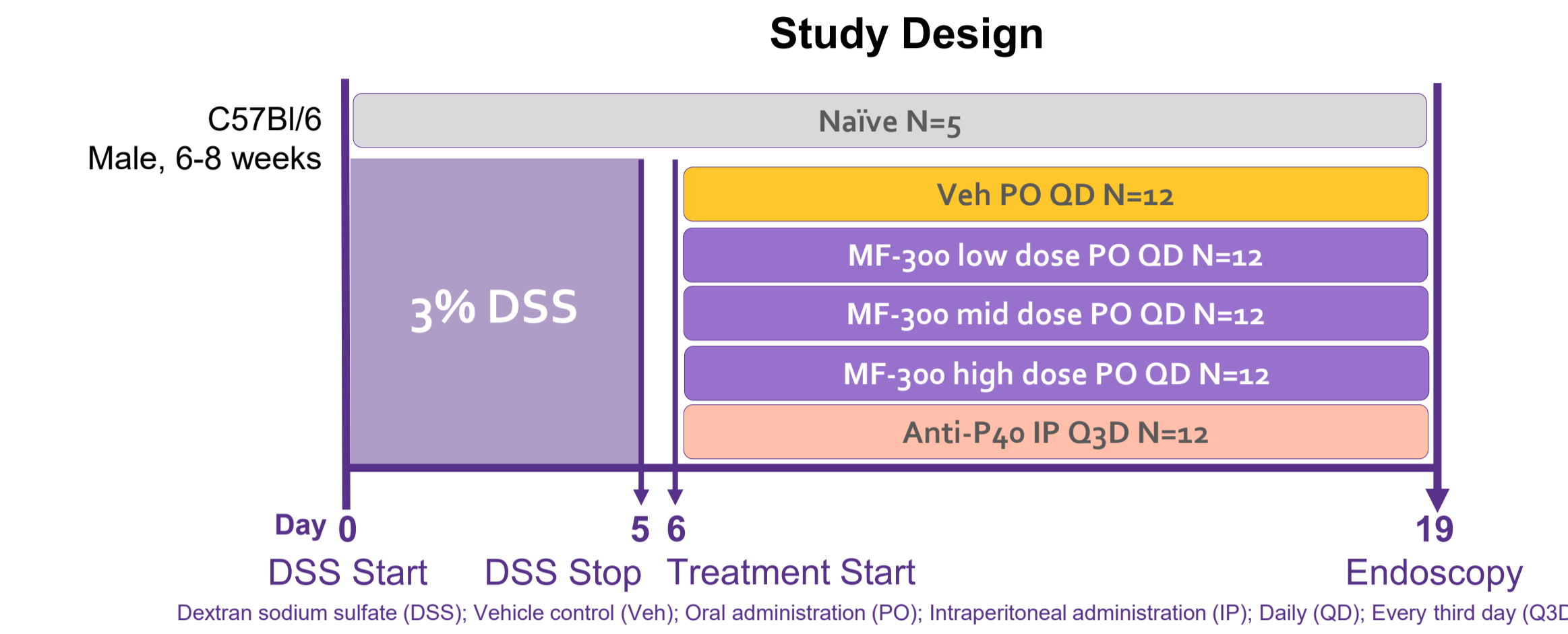
- 3 adult cohorts (<65 y.o.)
- N=10 per cohort (2 pbo, 8 MF-300)
- QD dosing for 5 days
- Doses: 75mg, 125mg, 200mg
- Urinary PGE-MUM analyzed by LC-MS/MS



\*p<0.05 versus placebo (95% CI does not include 0)

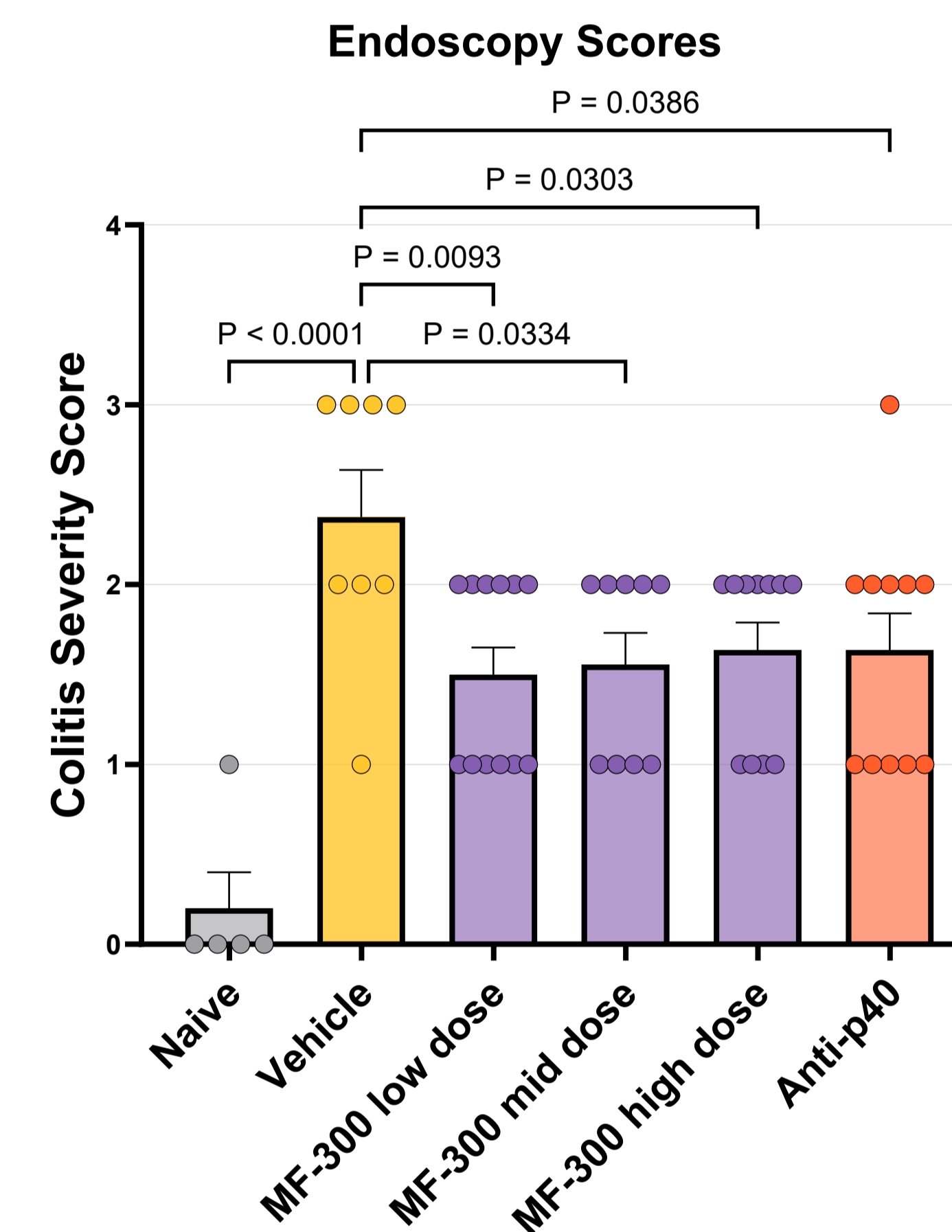
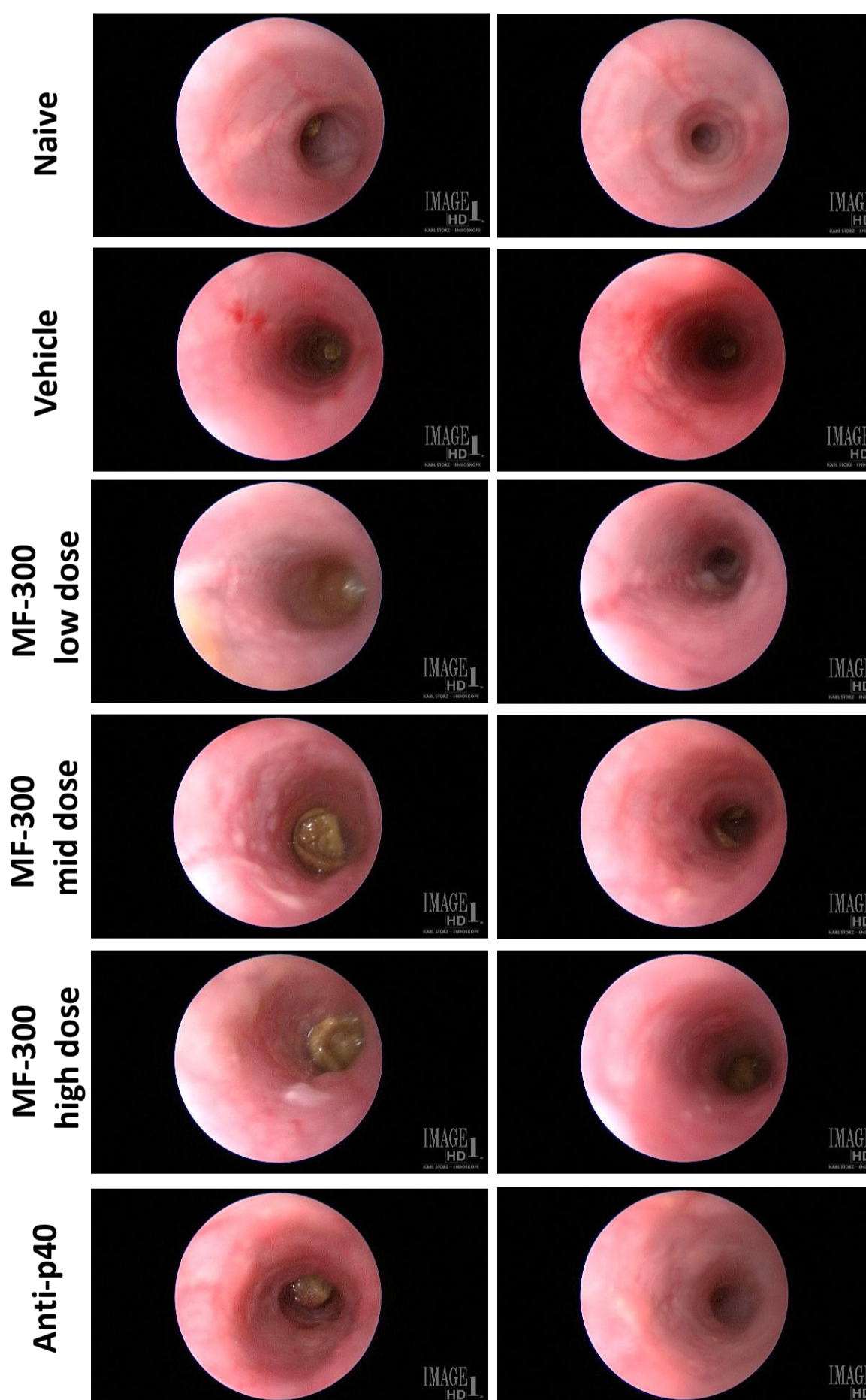
## RESULTS

### MF-300 accelerated colon repair in a DSS mouse model



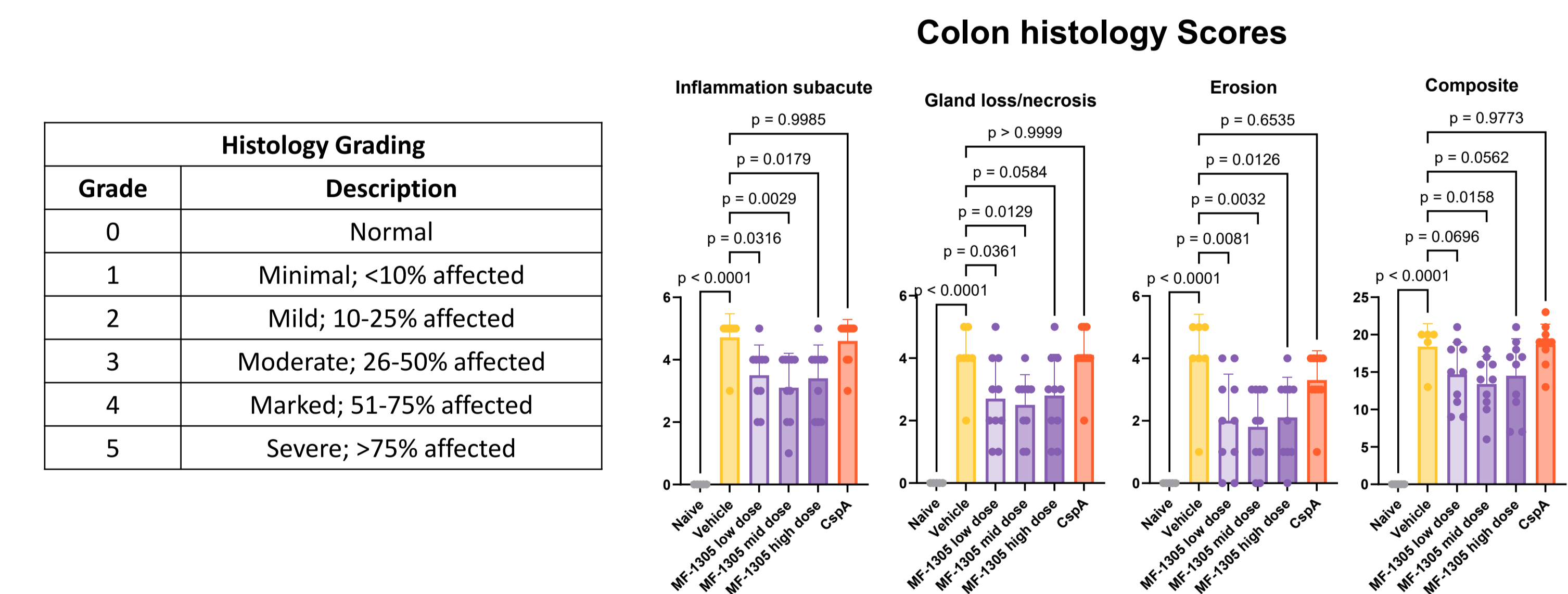
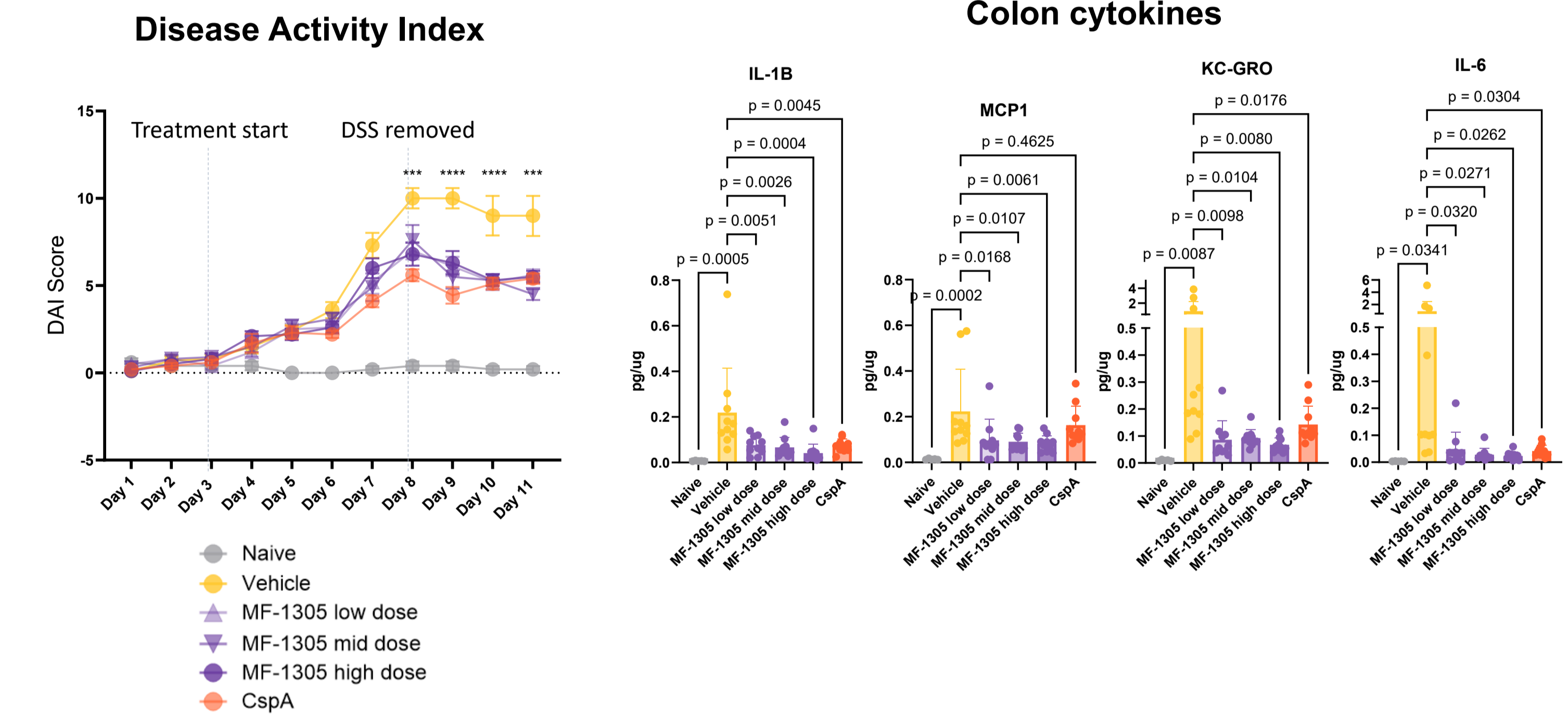
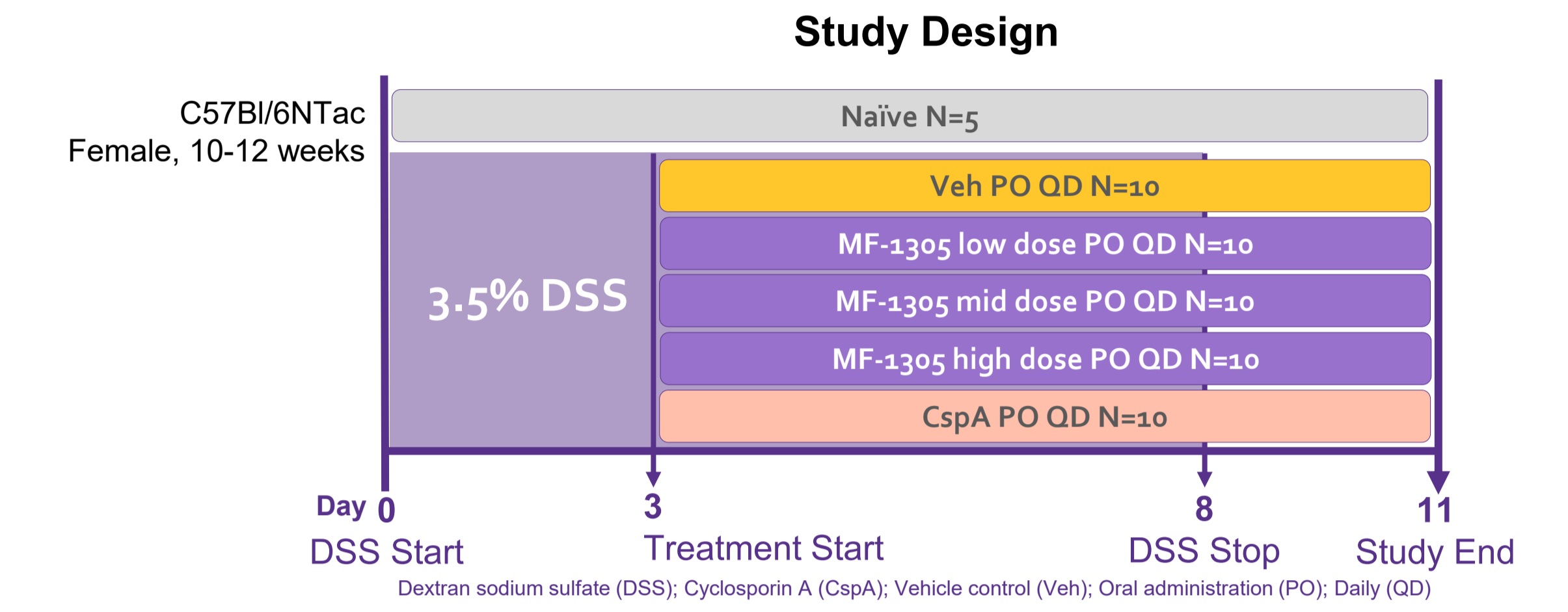
Endoscopy Scoring	
Score	Description
0	Normal
1	Loss of vascularity
2	Loss of vascularity & friability
3	Friability % erosions
4	Ulcerations & bleeding

### Representative Endoscopy Images Day 19



Colitis Severity Score % Reduction Relative to Vehicle	
Group	Day 19
Naive	-92%
Vehicle	--
MF-300 low dose	-37%
MF-300 mid dose	-35%
MF-300 high dose	-31%
Anti-p40	-27%

### MF-1305 reduced disease activity index, colon cytokines, and improved histological endpoints in a DSS mouse model



Histology Grading	
Grade	Description
0	Normal
1	Minimal; <10% affected
2	Mild; 10-25% affected
3	Moderate; 26-50% affected
4	Marked; 51-75% affected
5	Severe; >75% affected

## METHODS

- Dextran sulfate sodium (DSS) was administered in drinking water.
- MF-300 or MF-1305 were administered orally once daily beginning after DSS administration.
- Disease activity index: composite of body weight, fecal blood, stool consistency.
- Colon cytokines were measured with Luminex MAGPIX.
- Statistics: 2way ANOVA w/ Holm-Šidák's multiple comparisons test.

## CONCLUSIONS

- 15-PGDH inhibition is a novel therapeutic strategy for leveraging the pro-resolution of inflammation and tissue repair biology of PGE2 to address unmet need in IBD.
- MF-300, a Phase 2-ready oral small molecule 15-PGDH inhibitor that reduced PGE-MUM in a Phase 1 study, accelerated colon repair at clinically relevant exposures with an effect magnitude similar to an anti-p40 positive control in a DSS mouse colitis model.
- MF-1305, a preclinical oral small molecule 15-PGDH inhibitor, improved disease activity index, reduced colon cytokines, and improved histological endpoints in a DSS mouse colitis model.
- These results support advancing 15-PGDH inhibitors to improve mucosal healing in IBD.

## REFERENCES

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