

Efficacy and Safety of Half-Life Extended Antibodies SPY001, SPY002, and SPY003 for Induction Treatment of Moderately to Severely Active Ulcerative Colitis

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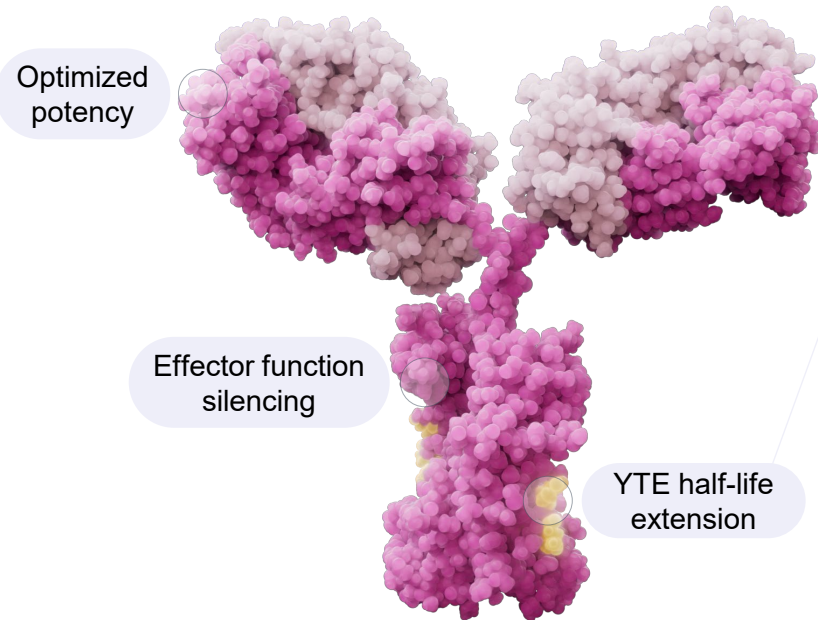
Disclosure of Conflicts of Interest

I, **Silvio Danese**, herewith declare the following paid or unpaid consultancies, business interests, or sources of honoraria payments for the past three years, and anything else which could potentially be viewed as a conflict of interest:

Consulting fees from AbbVie, Alimentiv, Allergan, Amgen, Applied Molecular Transport, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Eli Lilly, Entera, Ferring Pharmaceuticals Inc., Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, Morphic, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Spyre Therapeutics, Sublimity Therapeutics, Takeda, Teladoc Health, TiGenix, UCB Inc., Vial, and Vifor; and speaker's fees from AbbVie, Amgen, Ferring Pharmaceuticals Inc., Gilead, Janssen, Mylan, Pfizer, and Takeda.

Part A of the SKYLINE trial evaluated three molecules: SPY001 (anti- $\alpha 4\beta 7$), SPY002 (anti-TL1A), and SPY003 (anti-IL-23)

SPY001, SPY002, and SPY003 are monoclonal antibodies engineered for potency & half-life extension



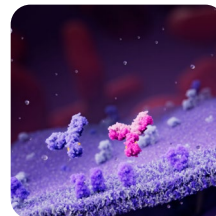
Antibodies are subject to degradation when internalized



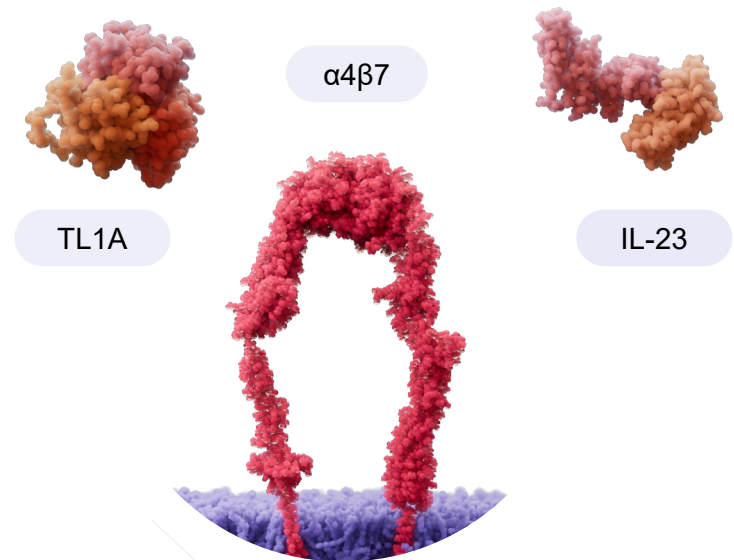
YTE modification increases internal binding to FcRn, avoiding degradation



FcRn binding promotes recycling of mAbs to circulation



SKYLINE is testing orthogonal MOAs rationally chosen based on attractive risk-benefit profiles



¹ Zhu, E. et al. A Novel Monoclonal Antibody Drug Candidate SPY001 Targeting Integrin $\alpha 4\beta 7$ for the Treatment of IBD: In Vitro Properties and Non-Human Primate Pharmacokinetics and Safety. UEGW, PP1103 (2024).

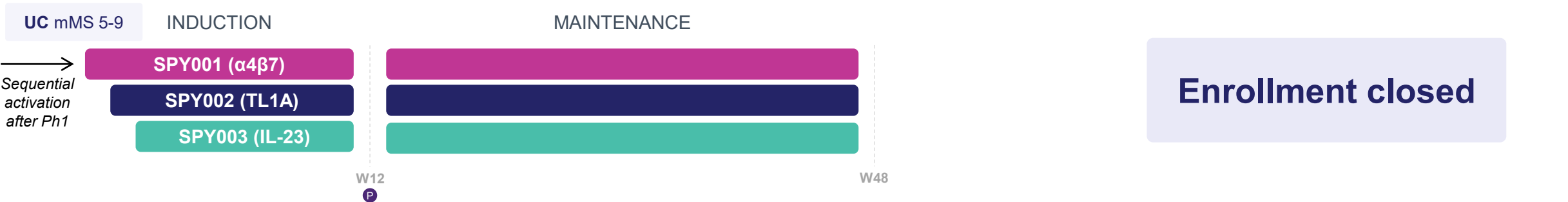
² Zhu, E. et al. Characterization of Two Novel Extended Half-life Monoclonal Antibody Drug Candidates Targeting TL1A for the Treatment of IBD. UEGW, MP450 (2024).

³ Kwan, B.. et al. Development and Characterization of SPY003, a Novel Extended Half-Life Monoclonal Antibody Drug Candidate Targeting IL-23 for the Treatment of IBD. UEGW, MP118 (2024).

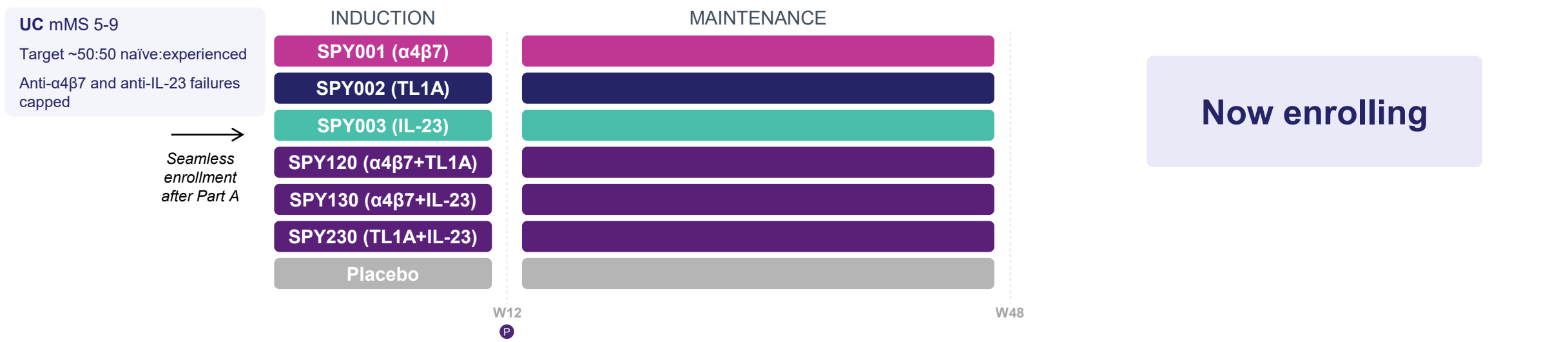
SKYLINE is a two-part platform study, with Part B now enrolling



Part A: Open-label monotherapy evaluation (N = ~130)



Part B: PBO-controlled factorial combination evaluation (N = ~550)



Today's presentation describes Part A Week 12 induction results for SPY001, SPY002, and SPY003

 SKYLINE

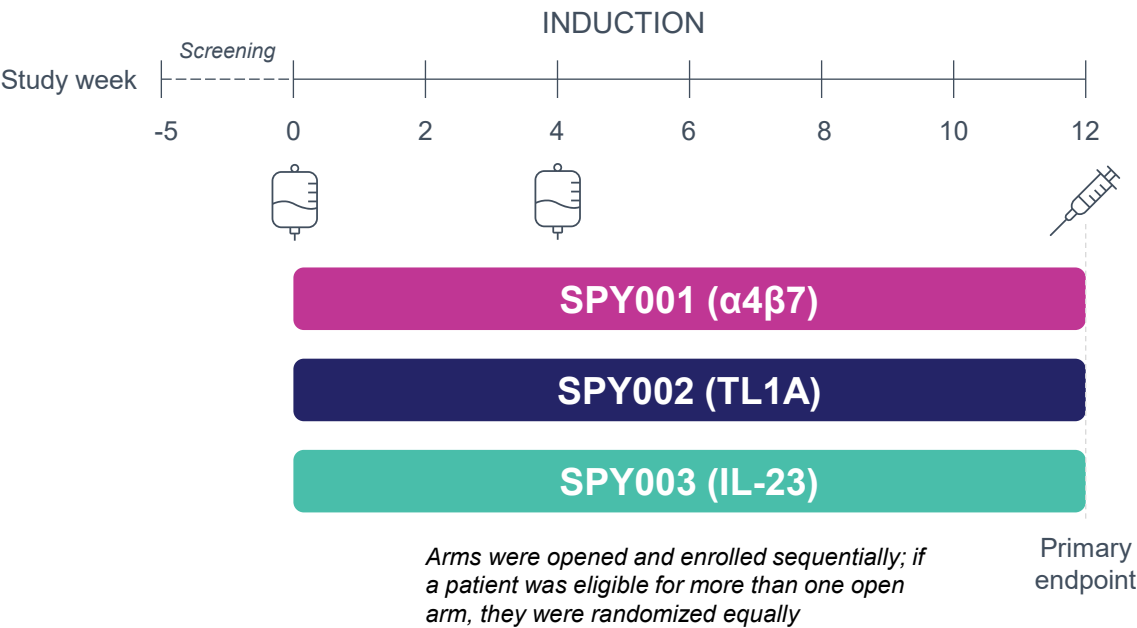
Part A: Open label monotherapy evaluation

Key Inclusion Criteria

- Adults with moderately to severely active UC (mMS 5-9)
- Rectal bleeding subscore ≥1
- Mayo endoscopic subscore ≥ 2
- Prednisone ≤ 20mg/day, budesonide ≤ 9mg/day, or beclomethasone ≤ 5 mg/day, stable for ≥ 2 weeks before Day 1
- Fecal calprotectin ≥ 250 µg/g

Key Exclusion Criteria

- Failure of 4+ advanced therapy classes
- Failure of 2 or more of these classes: anti-α4β7, anti-TL1A, anti-IL-23
- Use of immunomodulators



Topline endpoints

- PRIMARY**
- ΔRHI from baseline
- SECONDARY**
- % Clinical remission
 - % Endoscopic improvement
 - Δ modified Mayo Score
 - Incidence of treatment-emergent adverse events

mMS=modified Mayo Score; RHI=Robarts Histopathology Index. Data pertain to SPY001, SPY002, and SPY003 Induction Treatment Period. Primary endpoint of ΔRHI was analyzed using per protocol analysis set, and t-test was applied to test against the null hypothesis of ΔRHI =0; Secondary endpoints including Clinical Remission and Endoscopic Improvement rates were analyzed using full analysis set.

Baseline characteristics were consistent with expectations

	SPY001 (α4β7)	SPY002 (TL1A)	SPY003 (IL-23)
Enrolled / completed ITP (n)	43 / 41 ¹	48 / 47 ²	44 / 44
Age (years, mean)	44	45	42
Sex (% female)	28	42	39
Weight (kg, mean)	76	74	74
Duration of UC (years, mean)	4.5	7.0	7.1
RHI (mean ± SD)	15.6 ± 8.6	16.9 ± 8.5	17.2 ± 8.3
Baseline mMS (mean ± SD)	6.8 ± 1.1	6.9 ± 1.0	6.9 ± 1.2
Mayo Endoscopy Score (MES) (n, %)			
2	19 (44%)	21 (44%)	18 (41%)
3	24 (56%)	27 (56%)	26 (59%)
Fecal calprotectin (mg/kg, median (IQR))	2123 (759–4570)	1152 (629–2772)	3179 (1089–7614)
Concomitant corticosteroid use (n, %)	18 (42%)	20 (42%)	19 (43%)
Number of prior advanced therapy classes (n, %)			
Naïve	35 (81%)	31 (65%)	26 (59%)
1	7 (16%)	12 (25%)	9 (20%)
≥2	1 (2%)	5 (10%)	9 (20%)
Prior anti-IL-12/23 or anti-IL-23 exposure (n, %)	1 (2.3%)	4 (8.3%)	5 (11.4%)
Prior JAK inhibitor exposure (n, %)	2 (4.7%)	2 (4.2%)	6 (13.6%)

¹Two subjects withdrew consent; ²One subject received both induction doses of SPY002 and subsequently discontinued treatment due to an adverse event (UC exacerbation).

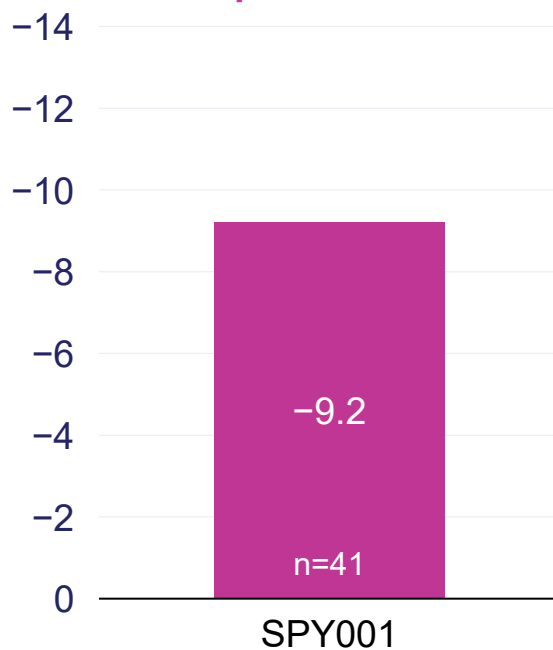
Source: Data on file. Percentages may not sum to 100% due to rounding.

SKYLINE Part A Week 12 primary and secondary endpoints SPY001 (anti- $\alpha 4\beta 7$)

Primary endpoint

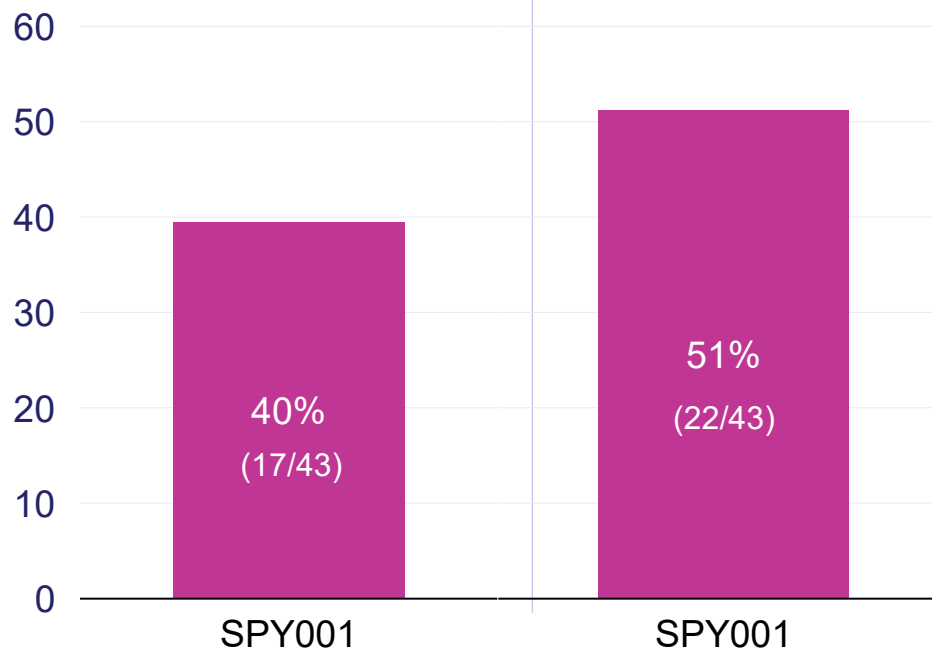
Mean Δ RHI at W12 from baseline

$p < 0.0001$

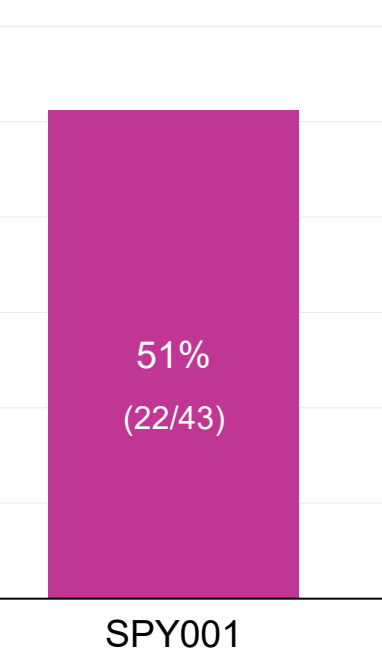


Secondary endpoints

% with clinical remission at W12



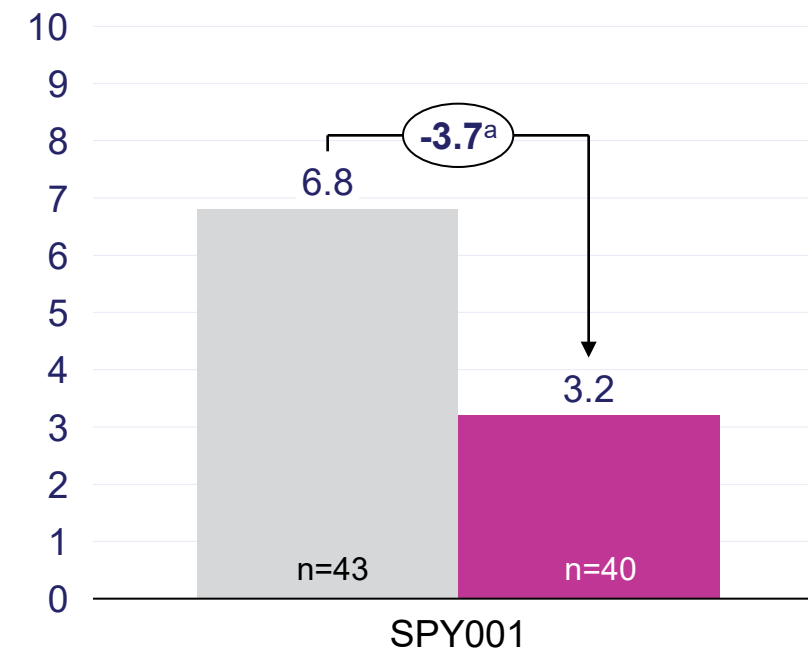
% with endoscopic improvement at W12



Mean modified Mayo Score at baseline and at W12

Baseline

SPY001
($\alpha 4\beta 7$)



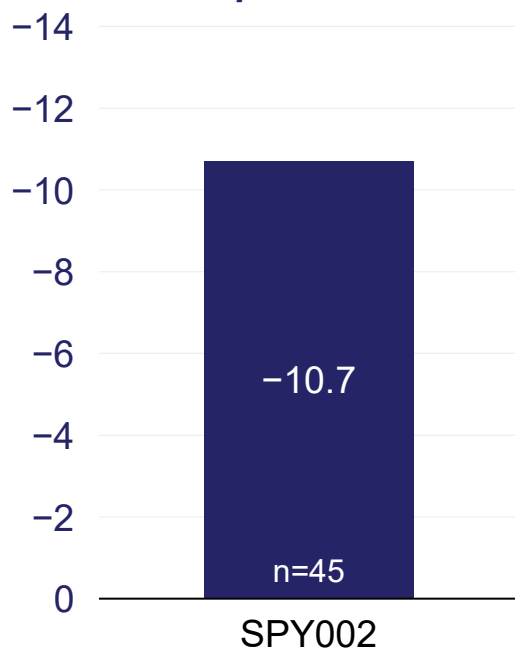
Source: Data on file. Primary endpoint of Δ RHI was analyzed using the per-protocol analysis set and t-test was applied to test against the null hypothesis of Δ RHI = 0 (N=41). Secondary endpoints including Clinical Remission and Endoscopic Improvement were analyzed using the full analysis set (N=43); participants with missing W12 data were imputed as non-responders. ^a Change from baseline calculated in participants with both baseline and W12 assessments (n=40). Clinical remission: SF ≤ 1 , RB = 0, ES ≤ 1 ; endoscopic improvement: ES ≤ 1 . ES, endoscopic subscore; RB, rectal bleeding; RHI, Robarts Histopathology Index; SF, stool frequency; W12, Week 12.

SKYLINE Part A Week 12 primary and secondary endpoints SPY002 (anti-TL1A)

Primary endpoint

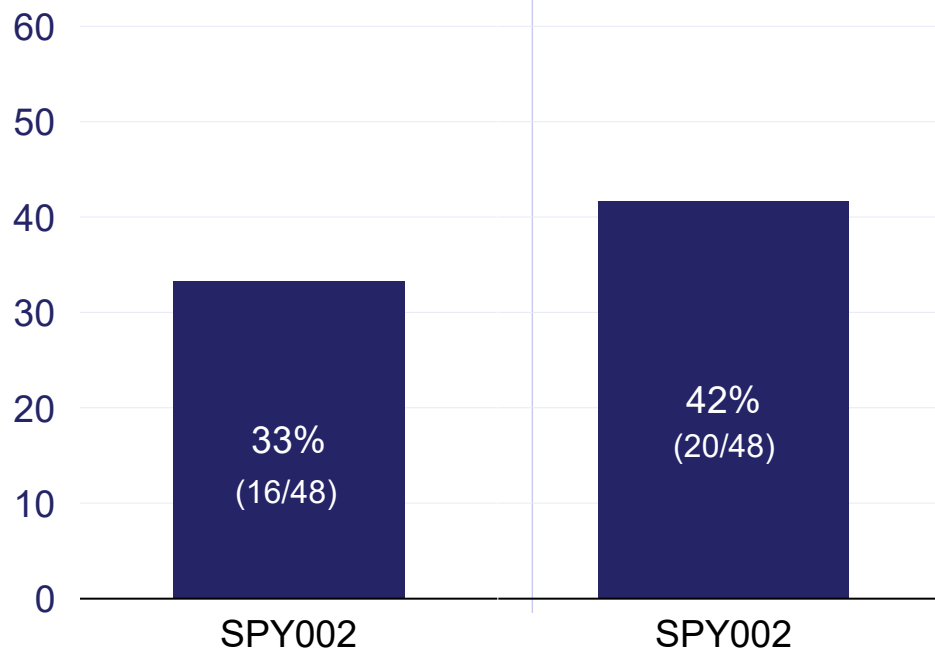
Mean Δ RHI at W12 from baseline

$p < 0.0001$

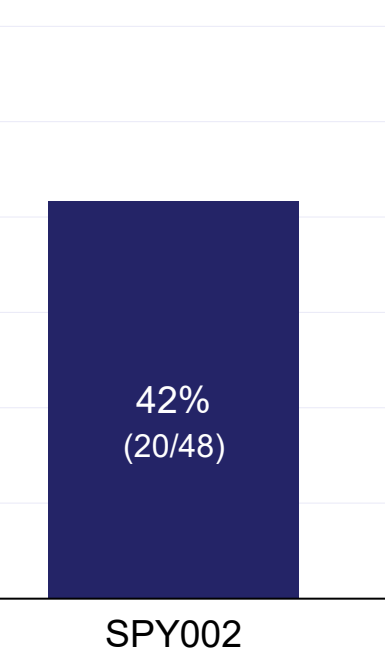


Secondary endpoints

% with clinical remission at W12



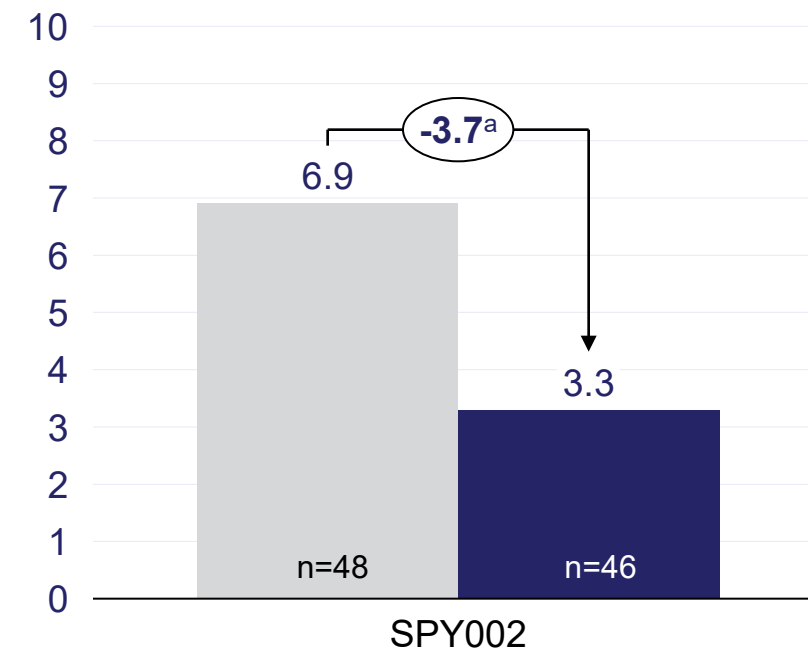
% with endoscopic improvement at W12



Mean modified Mayo Score at baseline and at W12

Baseline

SPY002 (TL1A)



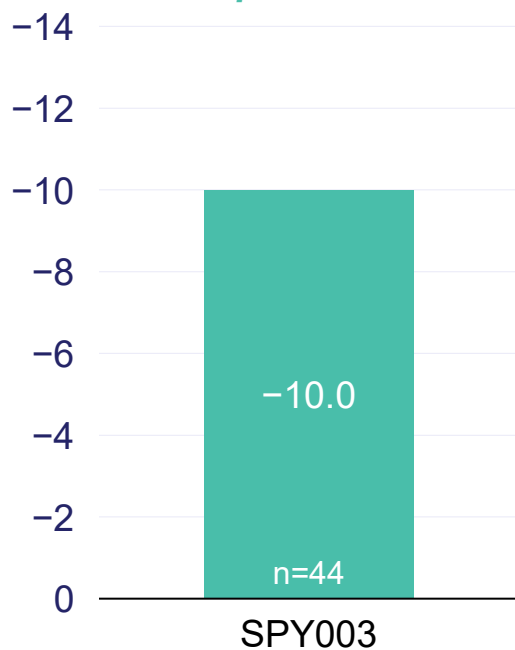
Source: Data on file. Primary endpoint of Δ RHI was analyzed using the per-protocol analysis set and t-test was applied to test against the null hypothesis of Δ RHI = 0 (N=45). Secondary endpoints including Clinical Remission and Endoscopic Improvement were analyzed using the full analysis set (N=48); participants with missing W12 data were imputed as non-responders. ^a Change from baseline calculated in participants with both baseline and W12 assessments (n=46). Clinical remission: SF $\leq$ 1, RB = 0, ES $\leq$ 1; endoscopic improvement: ES $\leq$ 1. ES, endoscopic subscore; RB, rectal bleeding; RHI, Robarts Histopathology Index; SF, stool frequency; W12, Week 12.

SKYLINE Part A Week 12 primary and secondary endpoints SPY003 (anti-IL-23)

Primary endpoint

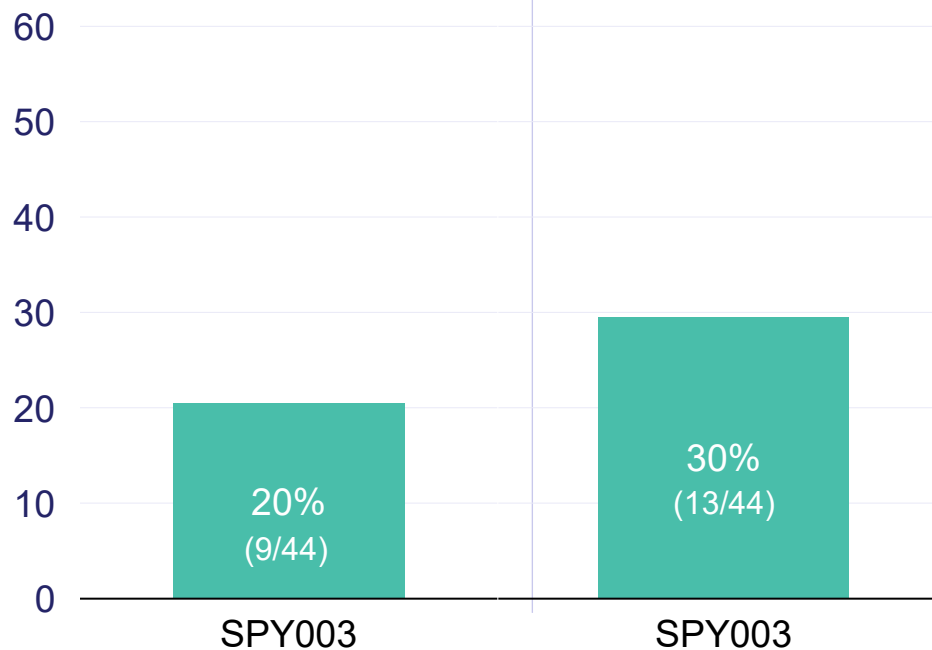
Mean Δ RHI at W12 from baseline

$p < 0.0001$

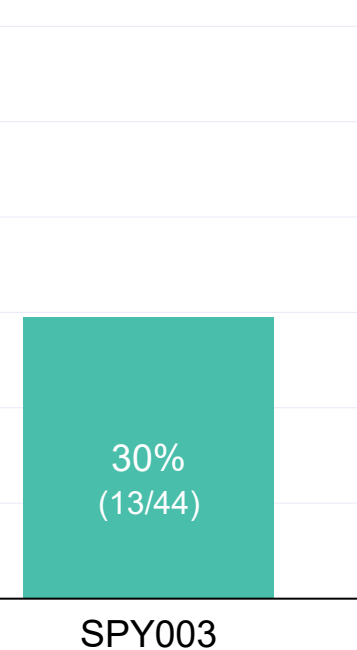


Secondary endpoints

% with clinical remission at W12



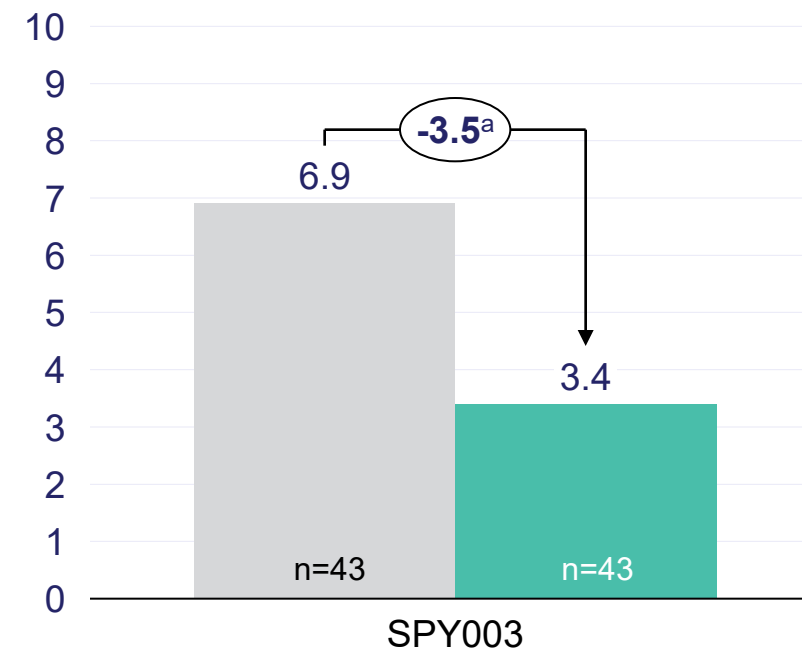
% with endoscopic improvement at W12



Mean modified Mayo Score at baseline and at W12

Baseline

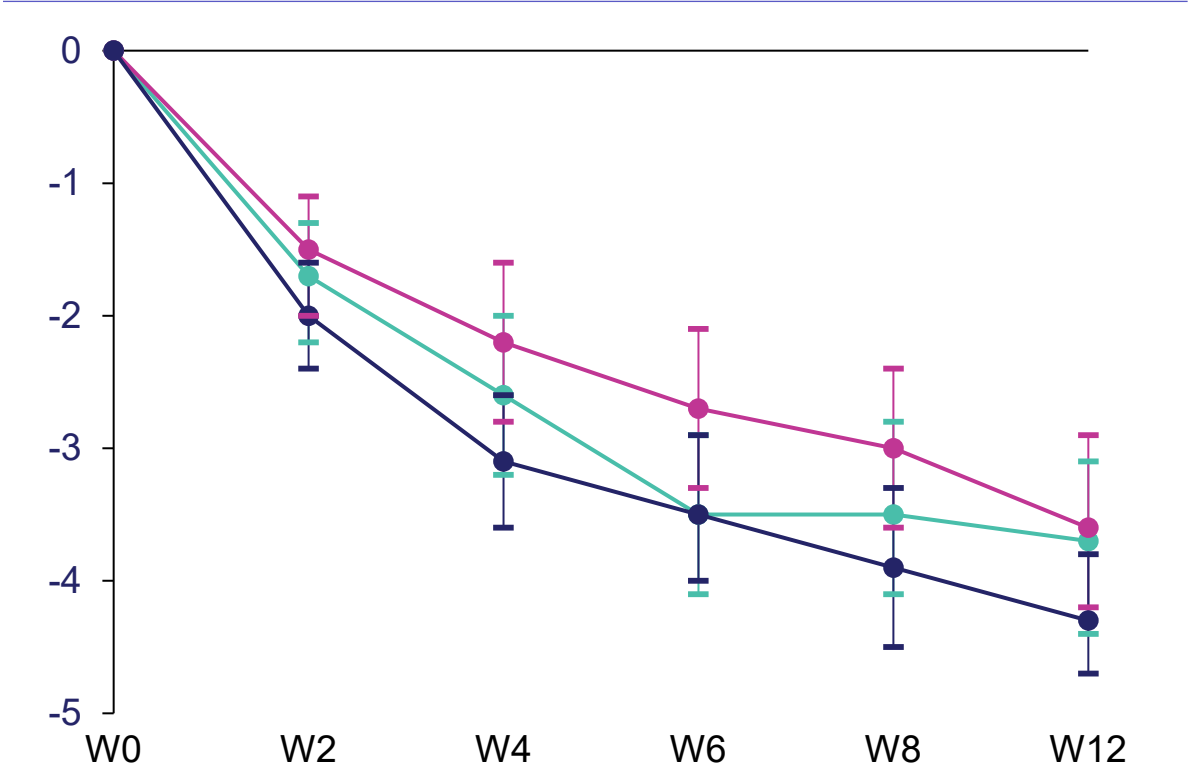
SPY003
(IL-23)



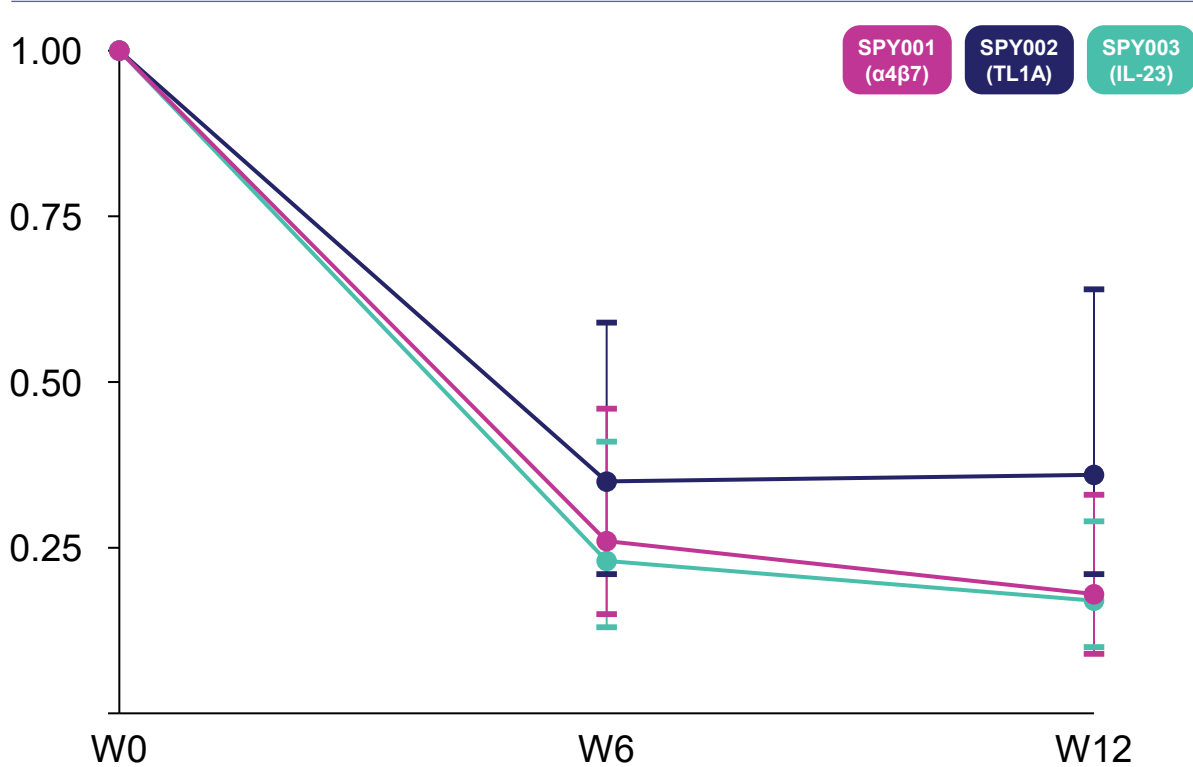
Source: Data on file. Primary endpoint of Δ RHI was analyzed using the per-protocol analysis set and t-test was applied to test against the null hypothesis of Δ RHI = 0 (N=44). Secondary endpoints including Clinical Remission and Endoscopic Improvement were analyzed using the full analysis set (N=44); participants with missing W12 data were imputed as non-responders. ^a Change from baseline calculated in participants with both baseline and W12 assessments (n=42). Clinical remission: SF $\leq$ 1, RB = 0, ES $\leq$ 1; endoscopic improvement: ES $\leq$ 1. ES, endoscopic subscore; RB, rectal bleeding; RHI, Robarts Histopathology Index; SF, stool frequency; W12, Week 12.

SKYLINE Part A exploratory endpoints for SPY001, SPY002, and SPY003 over time during ITP

Partial Mayo score ($\Delta \pm 95\%$ CI)



Fecal calprotectin (fold $\Delta \pm 95\%$ CI)



SPY001, SPY002, and SPY003 were well tolerated during ITP

	SPY001 (α4β7), N=43	SPY002 (TL1A), N = 48	SPY003 (IL-23), N = 44
Subjects with any Treatment-Emergent Adverse Event (n, %)	6 (14%)	20 (41.7%)	19 (43.2%)
Severe (Grade ≥ 3) AE	1 (2%) ¹	2 (4.2%) ²	5 (11.4%) ⁵
Drug-Related AE	0	3 (6.3%) ³	1 (2.3%) ⁶
AE Leading to Drug Discontinuation	0	2 (4.2%) ⁴	0
Serious Adverse Event (SAE)	1 (2%) ¹	2 (4.2%) ²	3 (6.8%) ⁷
Drug-Related SAE	0	0	0
AEs of Special Interest	0	0	0
Death	0	0	0
TEAEs in ≥2 patients (n, %)	Back pain (2, 4.7%)	Arthralgia (2, 4.2%), hypertension (3, 6.3%), nausea (2, 4.2%), ulcerative colitis (2, 4.2%), viral respiratory tract infection (2, 4.2%)	Arthralgia (2, 4.5%), nasopharyngitis (2, 4.5%), urinary tract infection (2, 4.5%)

¹ Chest pain in a 68-year-old male with history of coronary artery disease and angina pectoris, type 2 diabetes mellitus, hypertension, and hypercholesterolemia who presented with chest pain. ECG and cardiac enzymes did not show signs of a myocardial infarction. Data on file. ² Hospitalization for exacerbation of UC in one subject, deemed not drug-related; hospitalization for worsening heart failure in one 68-year-old subject with history of heart failure, moderate aortic valve stenosis and atrial fibrillation, on diuretics, who was later diagnosed with worsening aortic stenosis, deemed not drug related. ³ One case each of nausea (Grade 1), hypertension (Grade 2), arthralgia (Grade 1). ⁴ The same participant who was hospitalized for worsening heart failure was later diagnosed with worsening aortic stenosis, deemed not drug related; ulcerative colitis exacerbation in one subject, deemed not drug-related. ⁵ UC flare (serious), intervertebral disc protrusion, anaemia, urinary tract infection, and acute cholecystitis (serious), each in one subject; all deemed not drug-related. ⁶ Pruritus (Grade 1) that resolved without intervention or treatment interruption. ⁷ Hospitalization for UC flare, hemorrhoid thrombosis, and acute cholecystitis, each in one subject; all deemed not drug-related. Data pertain to the induction treatment period (through Week 12), with a data cutoff of July 27, 2026 and database lock on August 27, 2026.

Conclusions

- Efficacy
 - SPY001, SPY002, and SPY003 each met the primary endpoint with statistically significant reductions from baseline at Week 12 in Robart's Histopathology Index (RHI) score
 - Participants receiving SPY001, SPY002, or SPY003 experienced meaningful clinical remission and endoscopic improvement outcomes
- Safety
 - SPY001, SPY002, and SPY003 were each well tolerated with safety profiles consistent with the $\alpha 4\beta 7$, TL1A, and IL-23 mAb classes, respectively
- SKYLINE Part B with 3 investigational monotherapies and 3 combinations (actively enrolling)
 - SPY120 (anti-a4b7 & anti-TL1A)
 - SPY130 (anti-a4b7 & anti-IL-23)
 - SPY230 (anti-TL1A & anti-IL-23)