SPYRE THERAPEUTICS

CORPORATE OVERVIEW

APRIL 2026

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Certain information set forth in this presentation contains "forward-looking statements" within the meaning of applicable United States securities legislation. Except for statements of historical fact, certain information contained herein constitutes forward-looking statements which include but are not limited to statements regarding: our business strategy, including our ability to develop best-in-class and first-in-class therapeutics for inflammatory bowel disease (IBD), rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthritis (axSpA) and other immune-mediated diseases that meaningfully improve both efficacy and convenience compared to today's standard of care; our ability to achieve the expected benefits or opportunities with respect to our product candidates, including their potential commercialization; the potential consistency of the SPY001, SPY002, SPY072 and SPY003 Phase 1 trial and Phase 2 trial final data readouts with previously disclosed data for our programs; the potential for combination therapies to break the therapeutic ceiling with respect to IBD; expectations regarding the drug delivery of our product candidates, including in the form of a subcutaneous injection; the efficacy, safety profile, dosing regime, convenience, commercial viability and tolerability of SPY001, SPY002, SPY072 and SPY003, including combinations thereof; expected competitors and competing products; Spyre's non-clinical and clinical development activities, including clinical trial designs, our plans for and timing of cohort initiation and data readouts for the ongoing SKYWAY Phase 2 basket trial and SKYLINE Phase 2 platform trial, enrollment of clinical trials and, the inclusion of each rational combination in Part B of the SKYLINE Phase 2 platform trial and the number of data readouts expected to be delivered in 2026 and 2027; our ability to provide anticipated readouts ahead of any disclosed bispecific approaches against our targets; the induction and maintenance dosing regimen for SPY001 and our other product candidates and combinations thereof, including the potential for a Q3M-Q6M dosing profile; the potential therapeutic benefits and economic value of our product candidates as monotherapies or in combinations and their extended half-life, including their expected benefits in comparison to expected competitor products and potential best-in-indication product profiles; expected timing for regulatory feedback; estimated market sizes and potential growth opportunities; the length of time that the Company believes its existing cash resources will fund its operations; statements regarding the Company's cash guidance; and management's assessment of future plans and operations which are based on current internal expectations, estimates, projections, assumptions and beliefs, which may prove to be incorrect. 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Industry Information

This presentation also contains or references certain industry data that is based upon information from independent industry publications, market research, and surveys and other publicly available sources. Although the Company believes these sources to be generally reliable, such information is subject to interpretation and cannot be verified with complete certainty due to limits on the availability and reliability of data, the voluntary nature of the data gathering process and other inherent limitations and uncertainties. The Company has not independently verified any of the data from third party sources referred to in this presentation and accordingly, the Company makes no representation or warranty as to the origin, validity, accuracy, completeness, currency or reliability of the information in this presentation.

Spyre is pioneering long-acting antibodies and combinations to redefine standard of care in IBD and rheumatic diseases

Inflammatory bowel disease

Potential **best-in-class** monotherapies

SPY001	α4β7
SPY002	TL1A
SPY003	IL-23

Enable potential **paradigm changing** combinations

SPY120	α4β7 + TL1A
SPY130	α4β7 + IL-23
SPY230	TL1A + IL-23

Target 2-4 doses per year

After loading doses

Rheumatic disease

Potential **first-in-class & best-in class** anti-TL1A

SPY072 TL1A → RA, PsA, axSpA

Target 2-4 doses per year

After loading doses

Two innovative trials provide six expected Ph2 readouts in ’26

6 expected POC readouts

in ’26

Trial	Readout	Anticipated Milestones
SKYLINE	SPY001 α4β7 Ph2 POC in UC	Q2 ✓
	SPY002 TL1A Ph2 POC in UC	Mid-year
	SPY003 IL-23 Ph2 POC in UC	Q3
SKYWAY	SPY072 TL1A Ph2 POC in RA	Q3
	SPY072 TL1A Ph2 POC in PsA	Q4
	SPY072 TL1A Ph2 POC in axSpA	Q4

POC=proof of concept; UC=ulcerative colitis; RA=rheumatoid arthritis; PsA=psoriatic arthritis; axSpA=axial spondyloarthritis

Advancing a robust I&I pipeline with exceptional financial strength

Trial	Indication	Program	Target	Phase 1	Phase 2	Phase 3	Anticipated Milestones
SKYLINE	**UC**	SPY001	α4β7				**Q2 2026: Ph2 open label POC**
		SPY002	TL1A				**Mid 2026: Ph2 open label POC**
		SPY003	IL-23				**Q3 2026: Ph2 open label POC**
		SPY120	α4β7 + TL1A				**2027: Ph2 pbo-controlled POC**
		SPY130	α4β7 + IL-23				
		SPY230	TL1A + IL-23				
SKYWAY	**RA**	SPY072	TL1A				**Q3 2026: Ph2 POC**
	PsA						**Q4 2026: Ph2 POC**
	axSpA						**Q4 2026: Ph2 POC**

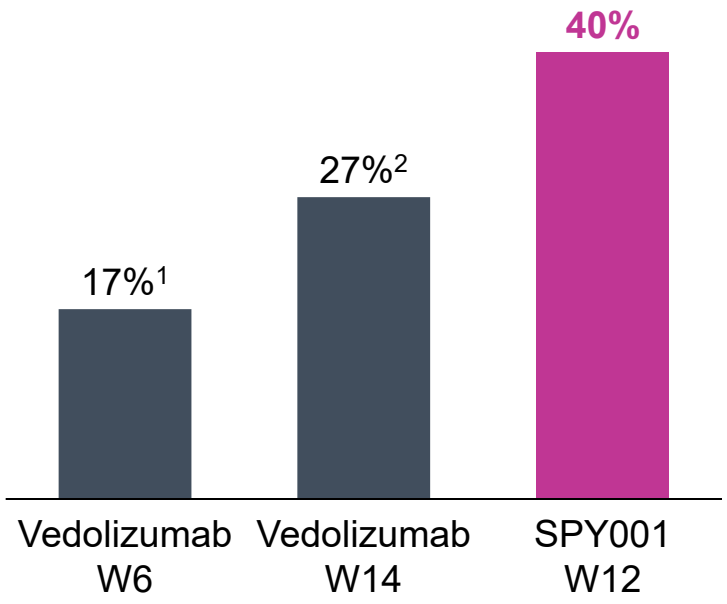
$1.2 billion proforma cash as of March 31, 2026[1], with expected runway into 2H 2029

Milestones expected as of the date of this presentation. [1]Reflects preliminary and unaudited cash, cash equivalents, & marketable securities as of 3/31/26 of $741.5 million plus $435.3 million in estimated net proceeds from the recently closed April 2026 underwritten public offering of common stock. Pipeline chart does not include preclinical research and development programs.

Next-generation antibodies designed to match or exceed the efficacy of first-generation molecules

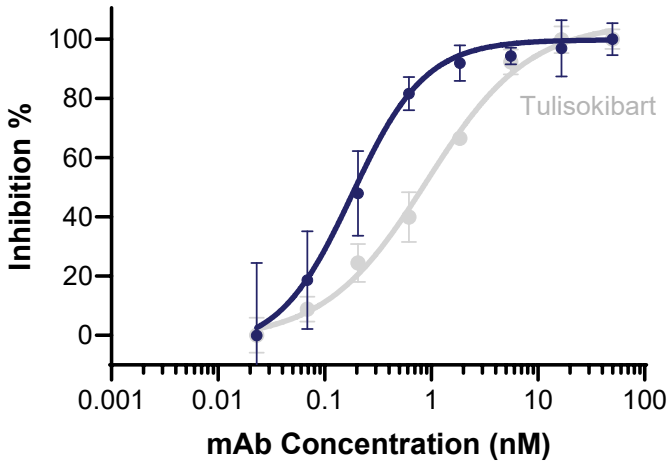
SPY001 (α4β7) POC efficacy

Clinical remission rate



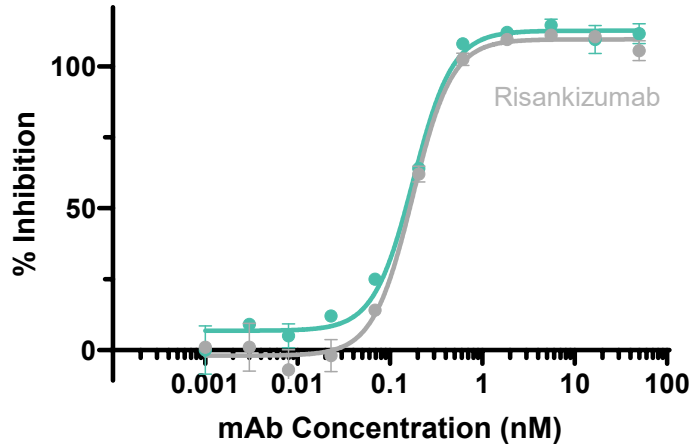
SKYLINE Part A POC achieved
2Q 2026

SPY002 (TL1A) potency



SKYLINE Part A POC data
Mid-2026

SPY003 (IL-23) potency

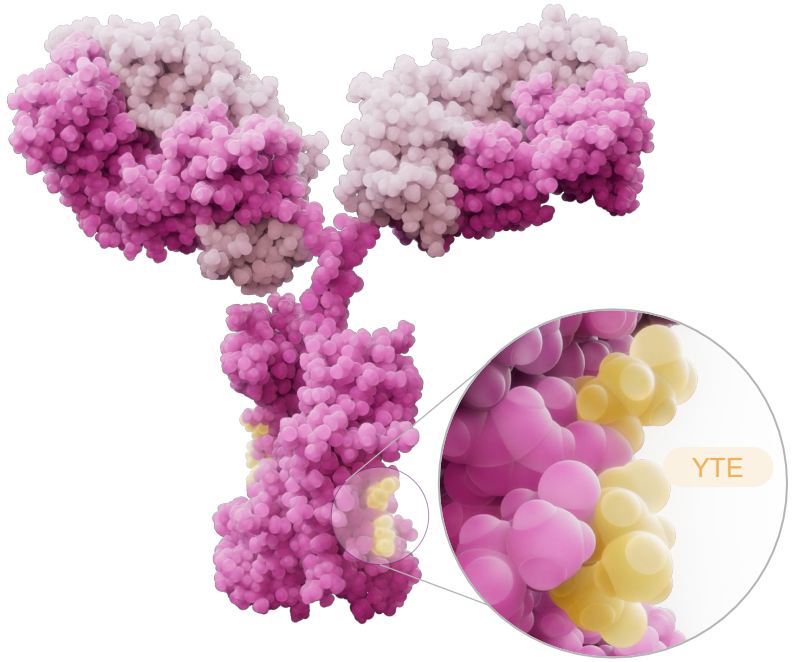


SKYLINE Part A POC data
3Q 2026

Data on file. [1]*GEMINI trial, endoscopy not centrally read,* Feagan, Brian G., et al. New England Journal of Medicine 369.8 (2013): 699-710 (N=374); [2]VARSITY trial, Sands, Bruce E., et al. New England Journal of Medicine 381.13 (769): 1215-1226 (N=394). *Potency refers to in vitro potency: SPY002 assay reports inhibition of TL1A-induced apoptosis in TF-1 cells. SPY003 assay reports inhibition of cellular STAT3 signaling. Vedolizumab, tulisokibart, and risankizumab are synthesized comparator antibodies.*
Trial designs differ and no head-to-head clinical trials have been conducted. Efficacy data pertain to Induction Treatment Period.

Engineered to be long-acting via YTE modification

YTE modification

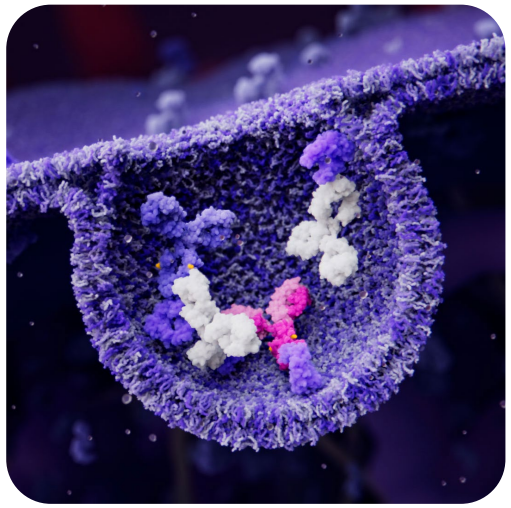


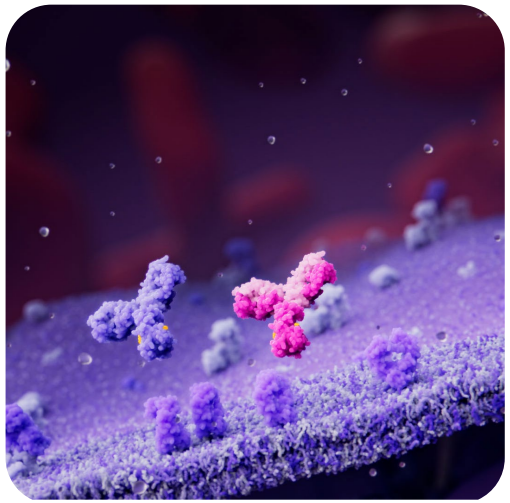
YTE-modified mAbs are returned to circulation for continued activity

Antibodies are subject to degradation when internalized

YTE modification increases internal binding to FcRn, avoiding degradation

FcRn binding promotes recycling of mAbs to circulation

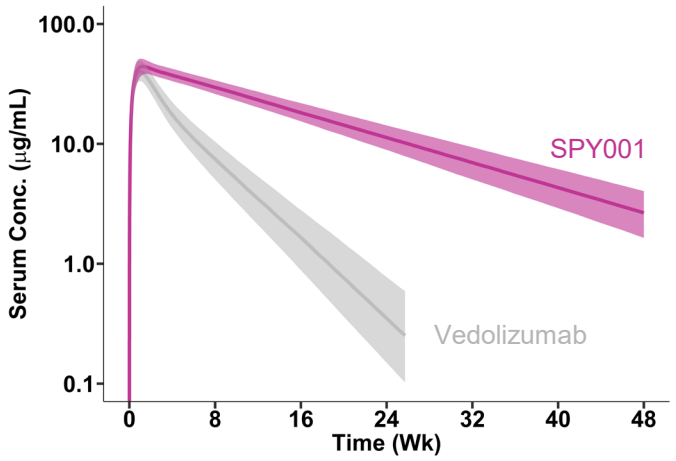




mAb=monoclonal antibody; FcRn=neonatal Fc receptor

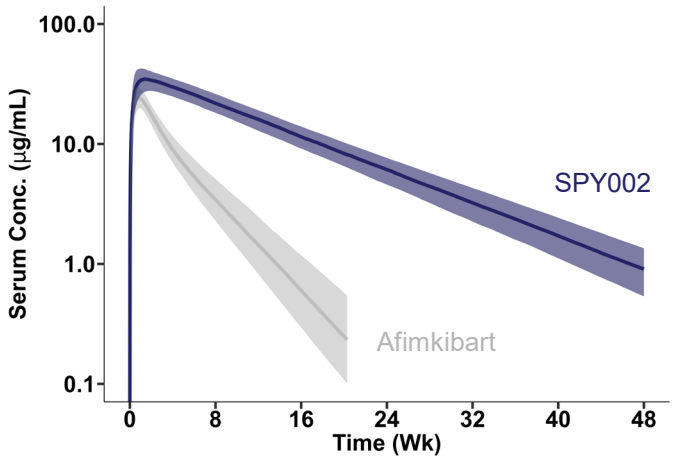
Demonstrated half-life extension for potential quarterly or twice-annual dosing

SPY001 human PK simulation



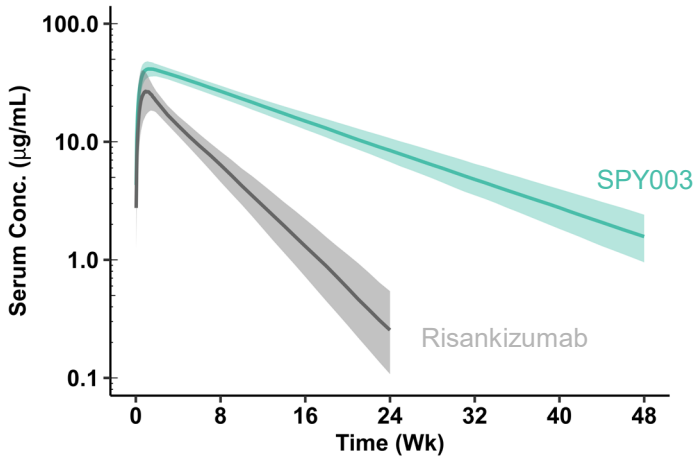
2-4
Doses per year

SPY002 human PK simulation



2-4
Doses per year

SPY003 human PK simulation



2-4
Doses per year

Target Profiles

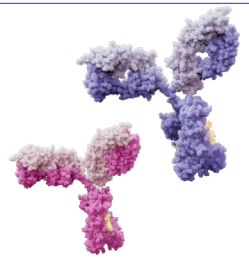
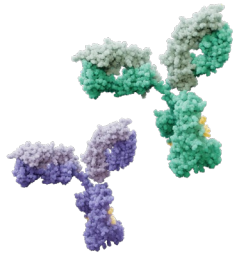
After loading doses

SPY001 PK simulation based on PK data as of 03/19/2025 cutoff; SPY002 PK simulation based on PK data from 5/31/2025 cutoff; SPY003 PK simulation based on PK data from 9/15/2025 cutoff. Vedolizumab, Afimkibart, and Risankizumab simulations based on published data (Rosario, M, et. al. (2015); Danese, Silvio, et al. (2024) Thakre, Neha et. al. (2024)*; no head-to-head clinical trials have been conducted. Concept image of drug delivery device shown for illustrative purposes only.*

Potential paradigm-changing combination therapies in IBD

Inflammatory bowel disease

Rational combinations targeting diverse disease drivers

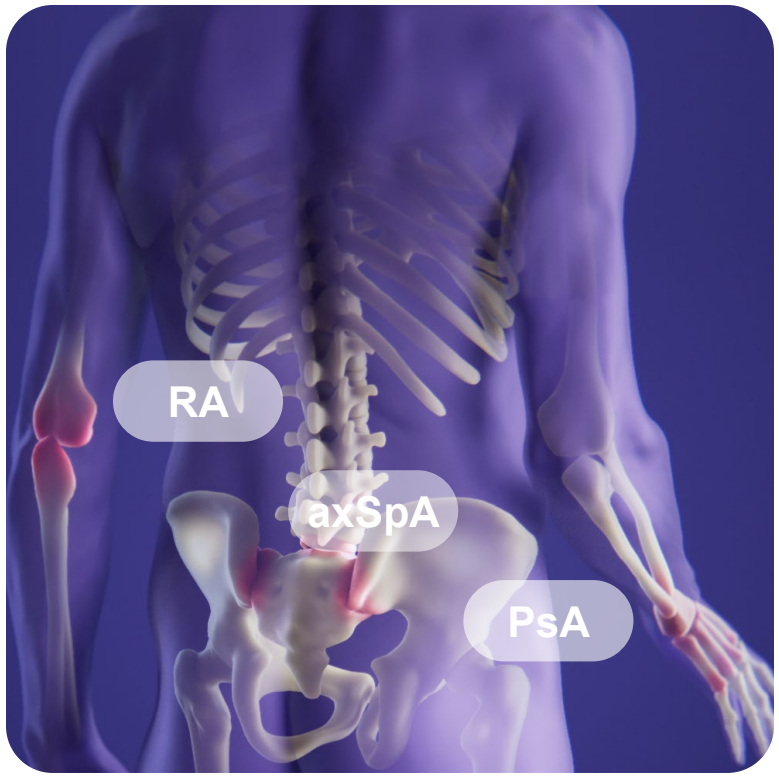
SPY120		TL1A + α4β7	❱	
SPY130		IL-23 + α4β7	❱	
SPY230		IL-23 + TL1A	❱	

Target 2-4 doses per year

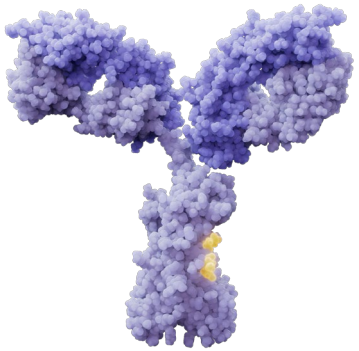
Potential Q3M-Q6M maintenance dosing interval based on PK modeling. Concept image of drug delivery device shown for illustrative purposes only.

Potential first-in-class & best-in-class anti-TL1A in rheumatic diseases

Rheumatic diseases



Distinct anti-TL1A targeting quarterly or twice-annual dosing



SPY072

- Rheumatoid arthritis
- Psoriatic arthritis
- Axial spondyloarthritis

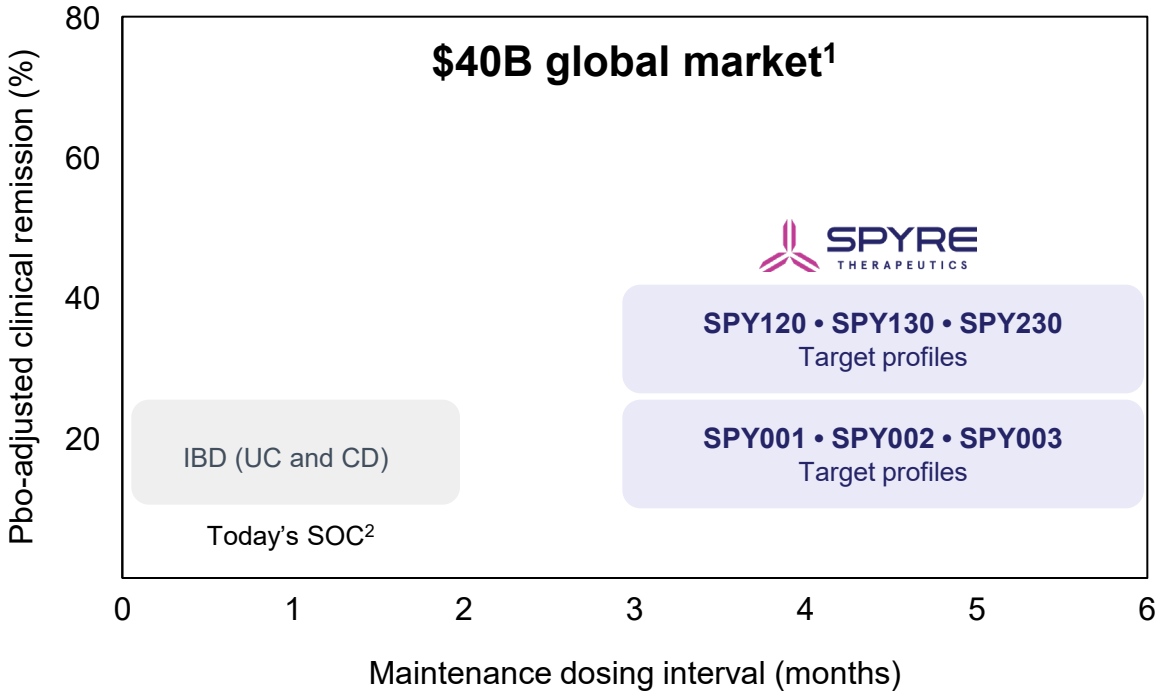
Target 2-4 doses per year

Potential Q3M-Q6M maintenance dosing interval based on PK modeling.

Spyre is uniquely positioned to enable superior product profiles in IBD and rheumatic diseases

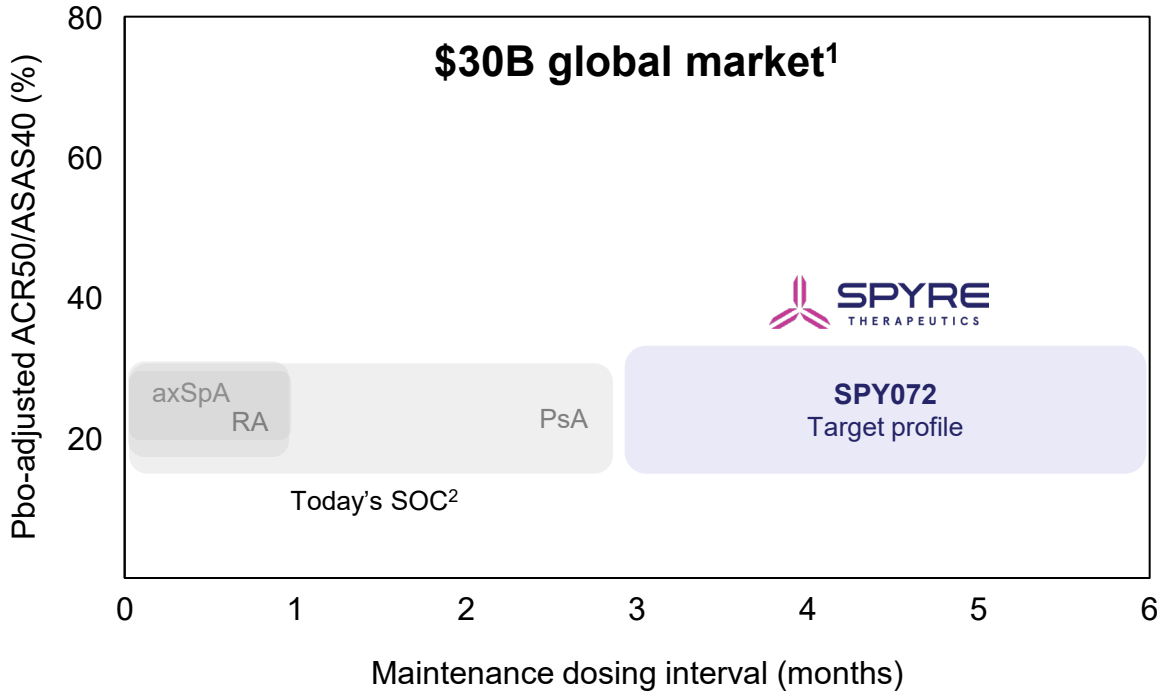
Inflammatory bowel disease

Advancing potential **best-in-class** monotherapies
Enabling potential **paradigm changing** combinations



Rheumatic disease

Advancing potential **first-in-class & best-in-class** anti-TL1A



Positioning of Spyre programs is illustrative and based on Phase 1 results and illustrates what we believe we can potentially achieve. Placebo-adjusted clinical remission data are derived from different clinical trials conducted at different times, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted. [1]Evaluate Pharma 2030 Global Sales Forecast; Barclays Immunology Deep Dive (2023); [2]Oral and SC administered advanced therapies.

Ph2 trials ongoing in IBD and rheumatic diseases

SKYLINE

Ph2 *platform* trial evaluating SPY001, SPY002, SPY003 and pairwise combinations in ulcerative colitis

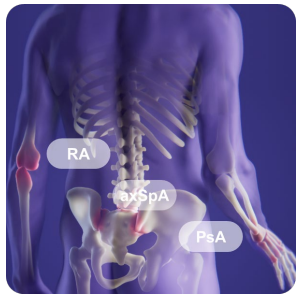
6
INTERVENTIONS

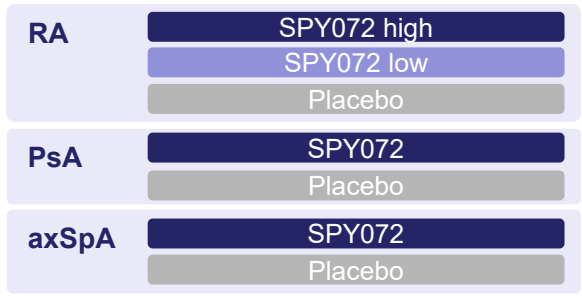
1
INDICATION

’26-’27
EXPECTED READOUTS*

SKYWAY

Ph2 *basket* trial evaluating SPY072 in rheumatoid arthritis, psoriatic arthritis, and axial spondyloarthritis



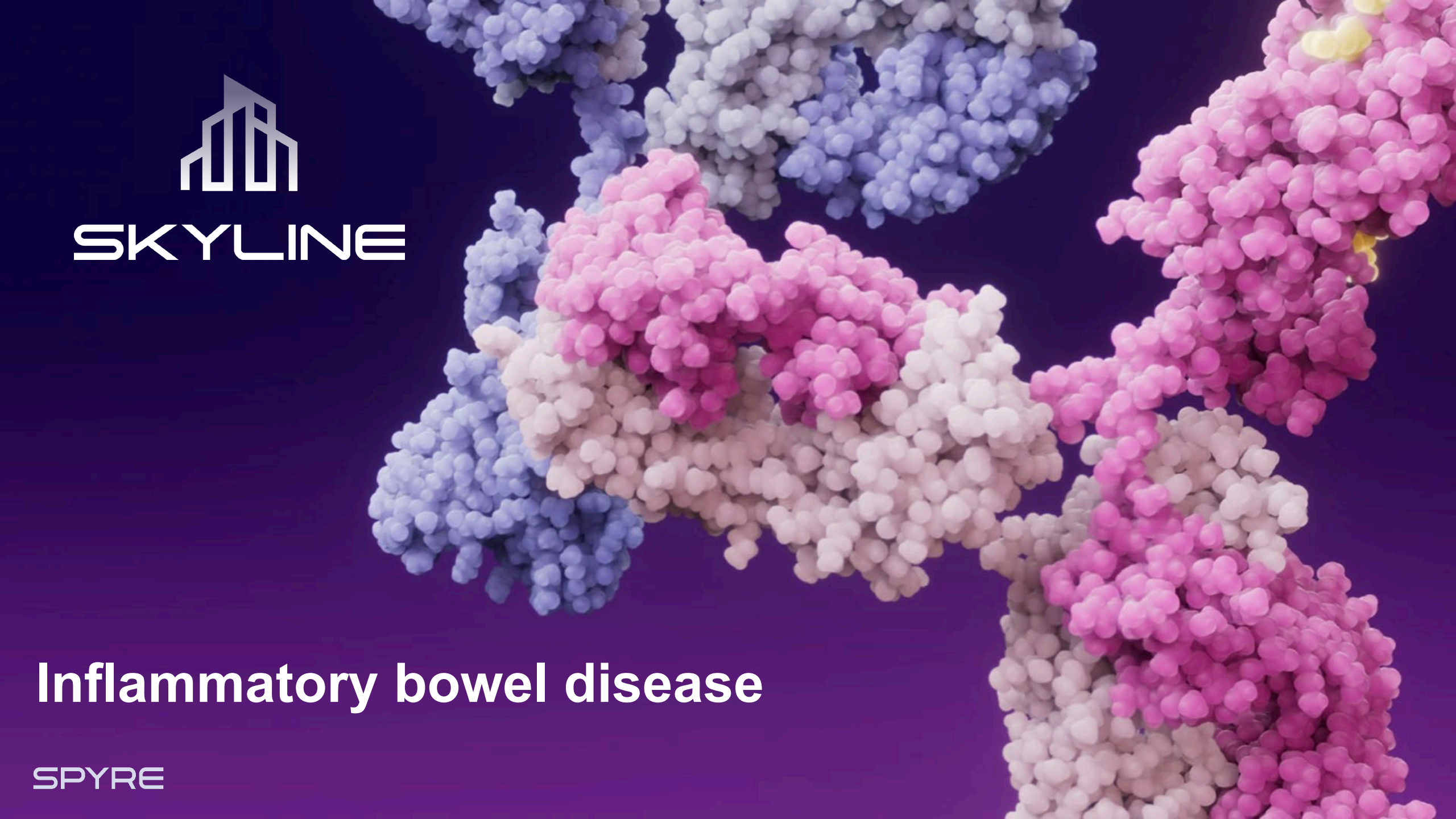


1
INTERVENTION

3
INDICATIONS

Q3-Q4’26
EXPECTED READOUTS

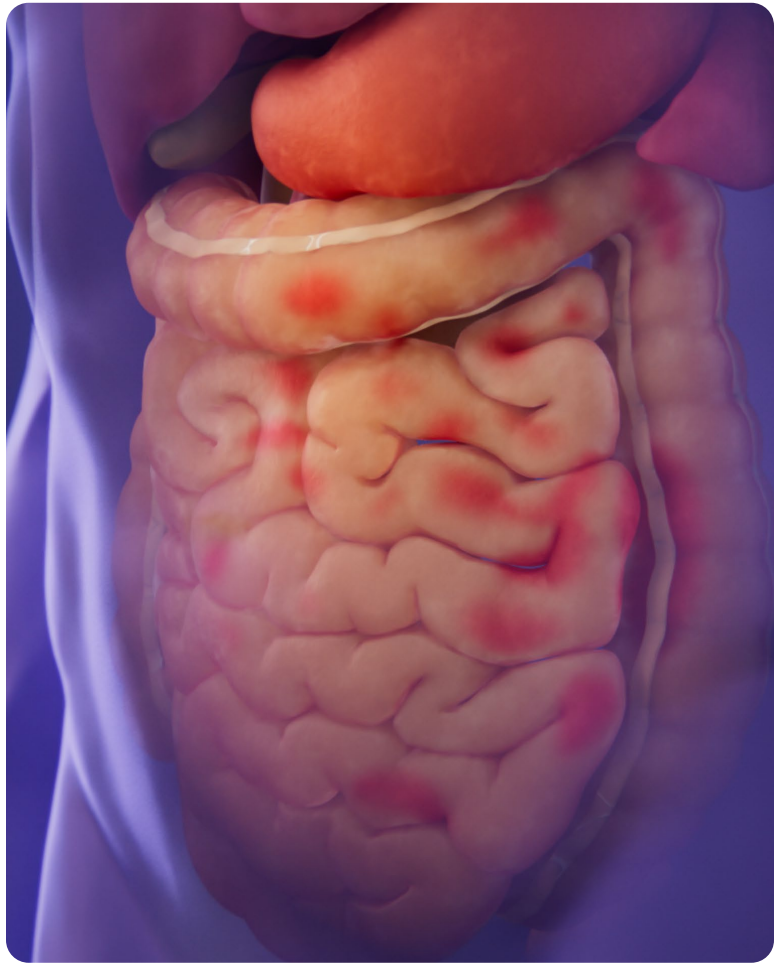
**Part A open-label monotherapy readouts: SPY001 (Q2 2026), SPY002 (mid-year 2026), SPY003 (Q3 2026); Part B (2027)*



Inflammatory bowel disease

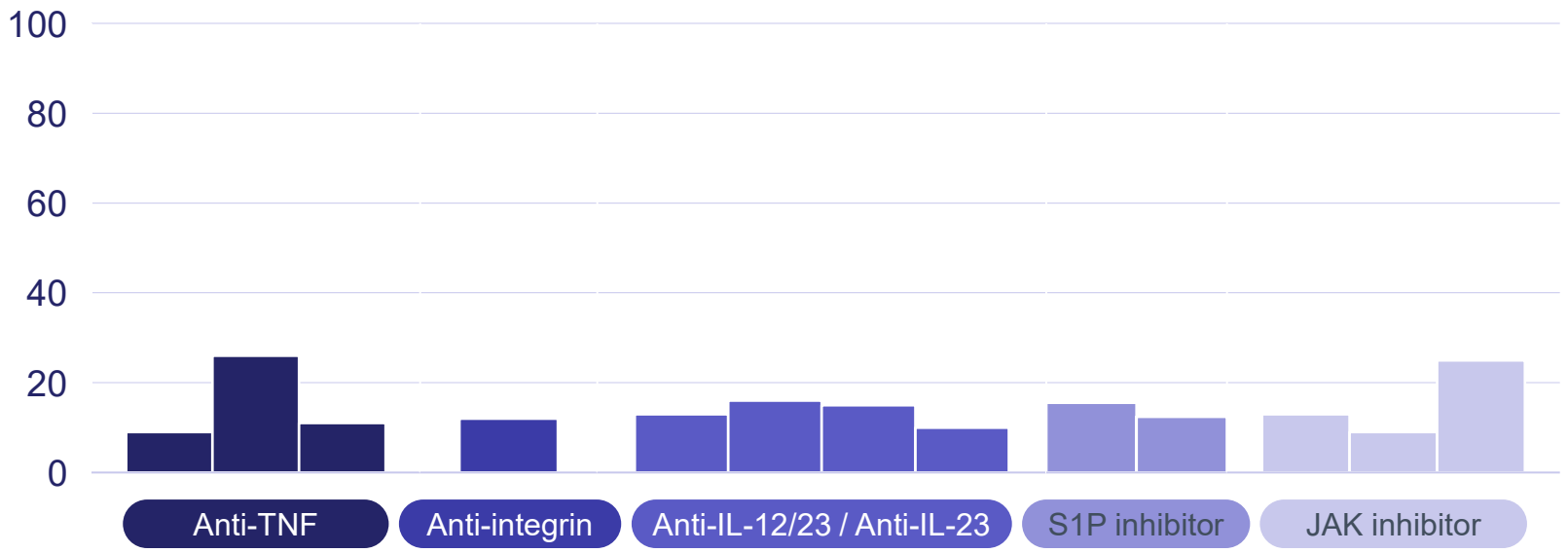
SPYRE

Substantial unmet need remains for the millions of individuals living with IBD



- ~2.4M individuals in the U.S. are diagnosed with IBD (~1.3M UC and ~1.0M CD)[1]
- Substantial unmet need remains due to:
  - Minority remission rates and lack of durability with existing therapies
  - Side effects and safety concerns associated with certain treatments
  - Poor adherence to frequent and/or inconvenient dosing regimens

UC placebo-adjusted clinical remission rates by MOA (Induction)

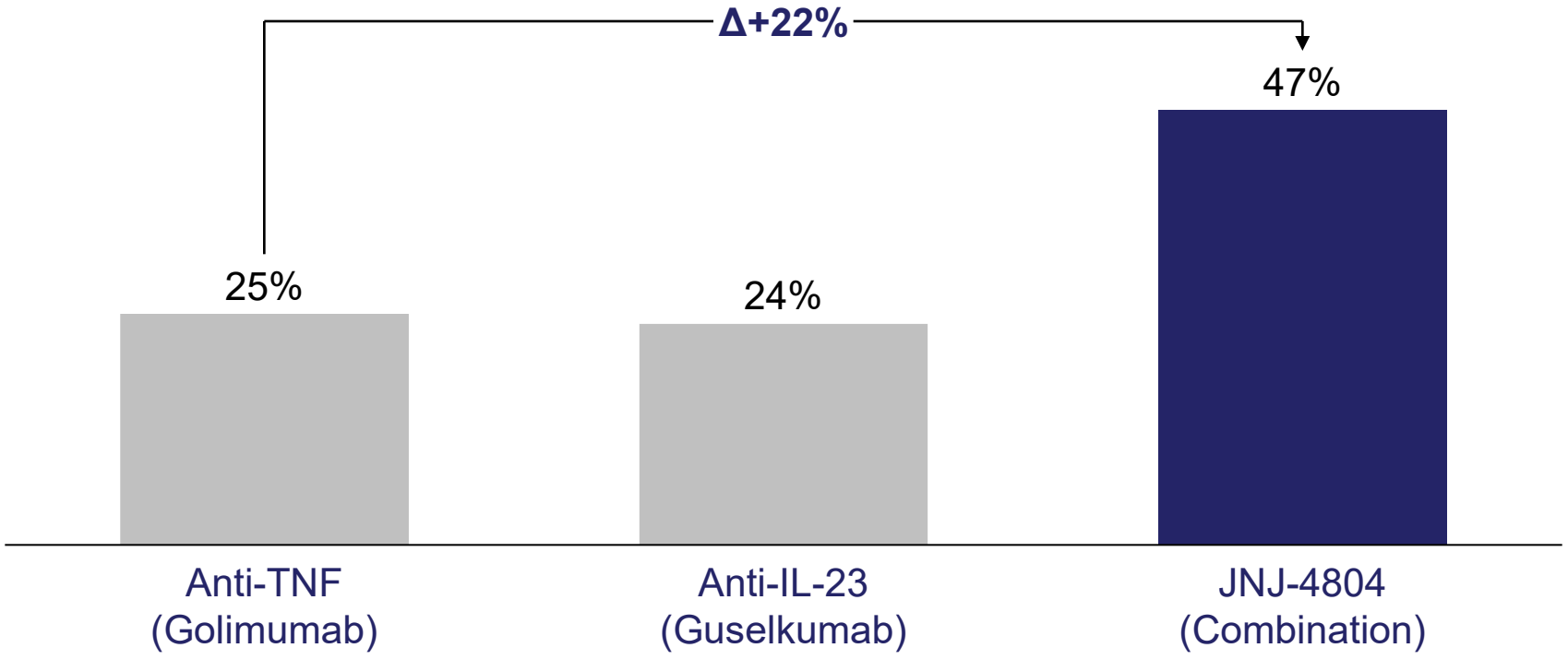


[1]*Lewis, James D., et al. Gastroenterology (2023). Estimate includes patients identified with indeterminate IBD. Clinical remission rates from product labels.*

JNJ's VEGA study demonstrated the power of combination therapy to break the efficacy ceiling in IBD

VEGA combination study • Ulcerative colitis

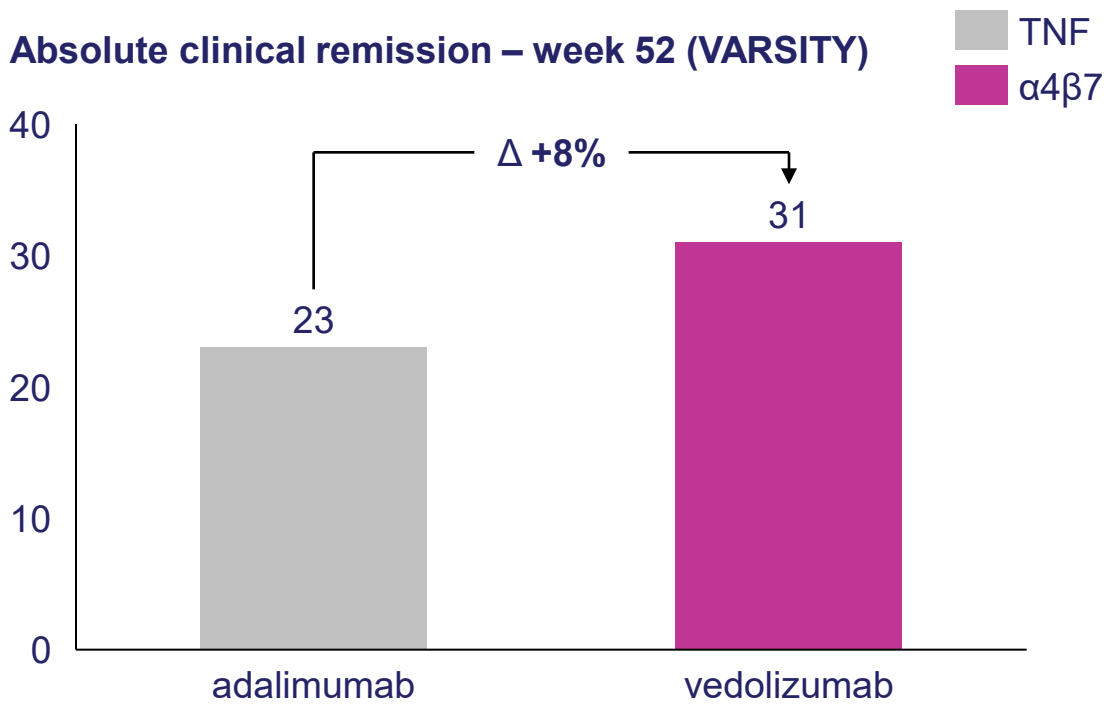
~Additive absolute W12 mMS clinical remission rates



Feagan, B. G. et al. Lancet Gastroenterol. Hepatol. 8, 307–320 (2023). mMS=modified mayo score

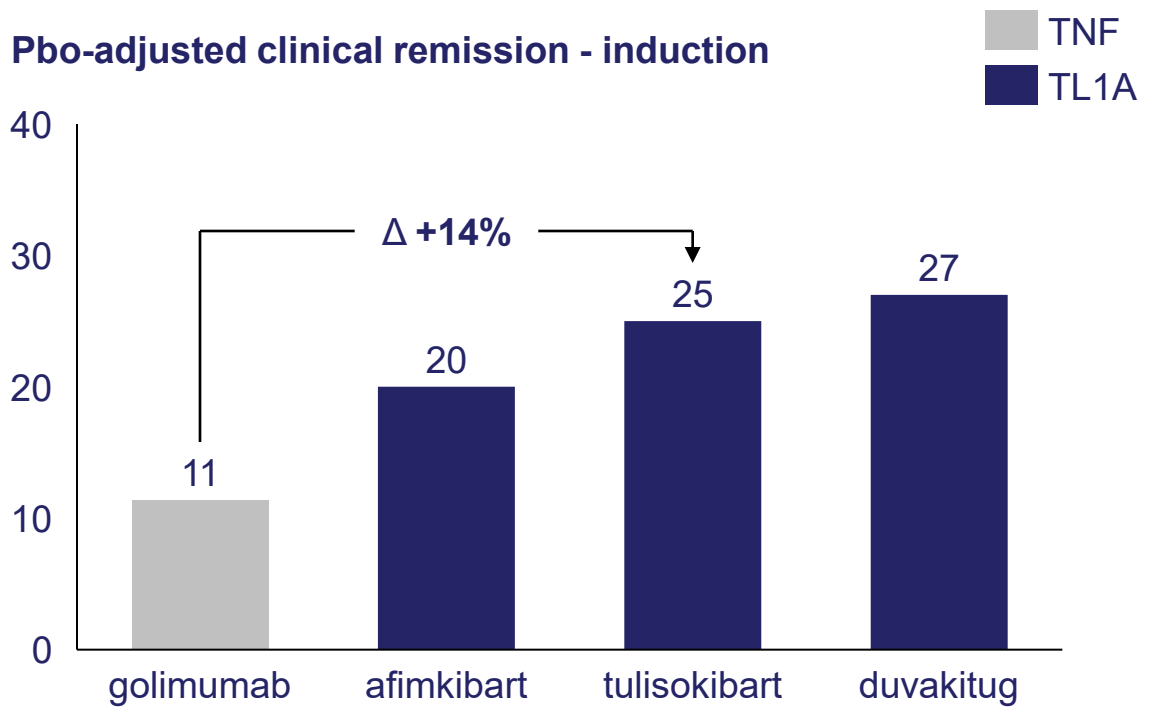
Replacing anti-TNF with anti-α4β7 or anti-TL1A may yield combinations with improved safety and efficacy

anti-α4β7 was superior to anti-TNF in H2H UC study



Established α4β7 long-term safety profile and gut-restrictive MOA

anti-TL1A exceeds anti-TNF on cross-trial comparison

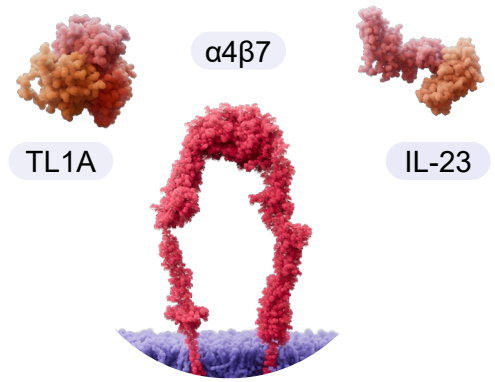


TL1A safety is encouraging to date

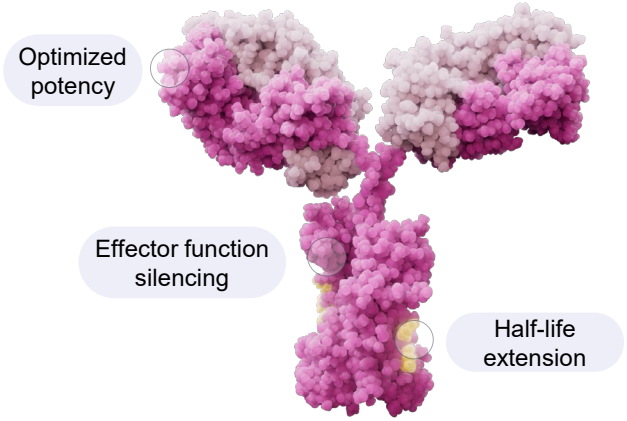
Product labels, Sands BE. et al. N Engl J Med. 2019; Roivant corporate presentation January 2023; Sands, Bruce E., et al. New England Journal of Medicine 391.12 (2024); Teva corporate presentation February 2025.

Spyre is unique in developing uncompromising combinations from first principles

Orthogonal MOAs rationally chosen based on attractive risk-benefit profiles



Next-generation molecules engineered for best-in-class potential

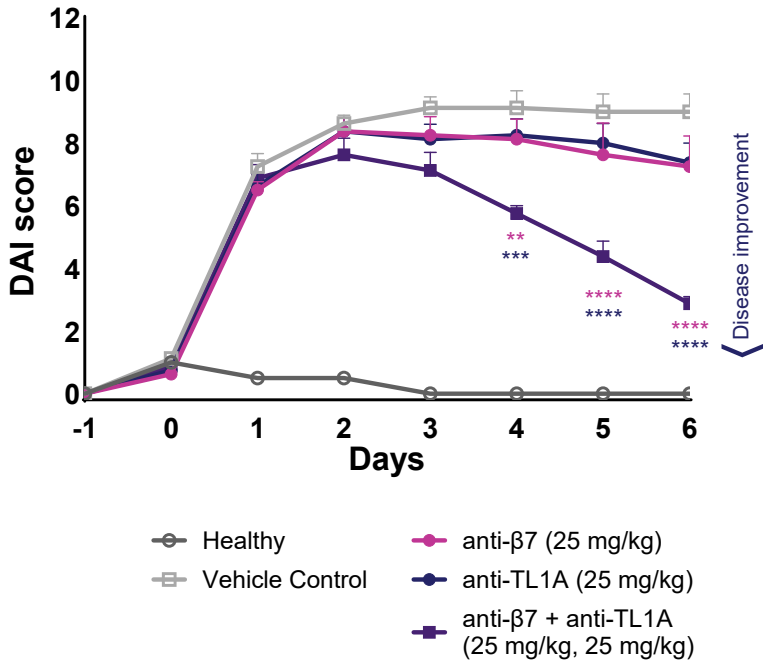


Coformulations optimized for convenient, SC delivery (Q3-6M)[1]

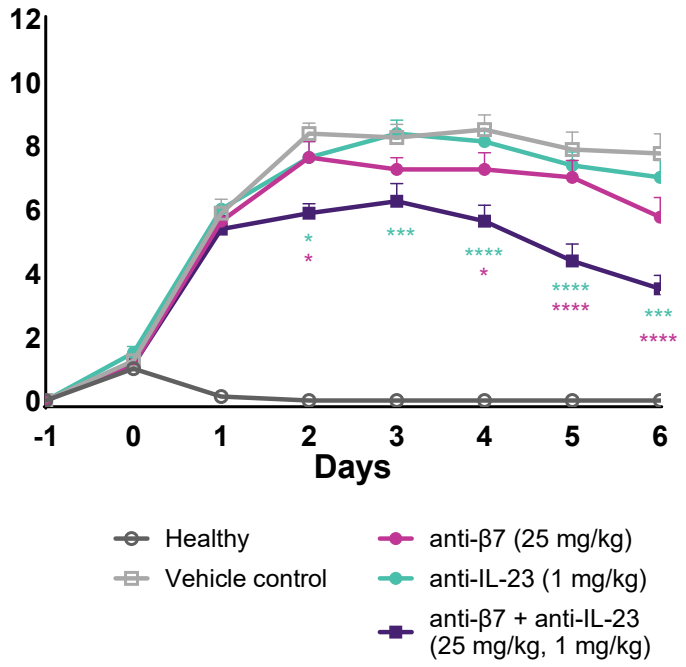
1After loading doses, concept image of drug delivery device shown for illustrative purposes only.

Combination therapy results in additive-to-superior efficacy in mouse TNBS colitis model

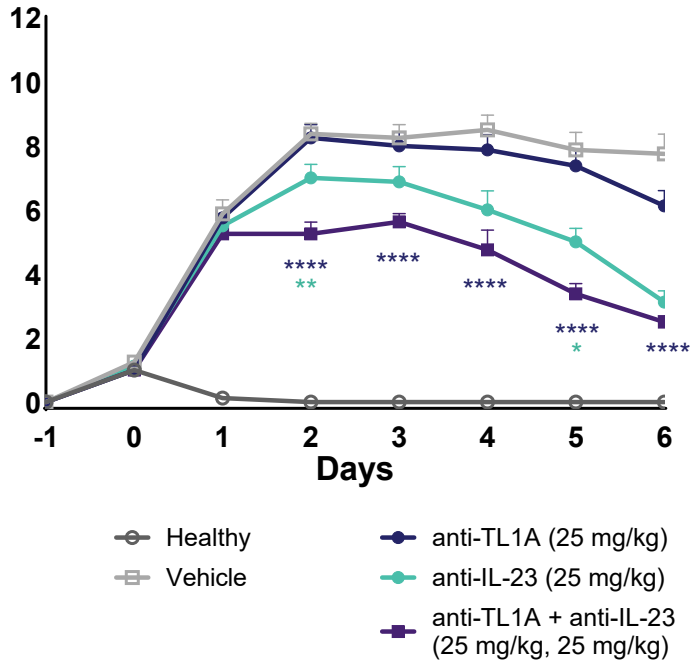
α4β7 + TL1A



α4β7 + IL-23



TL1A + IL-23



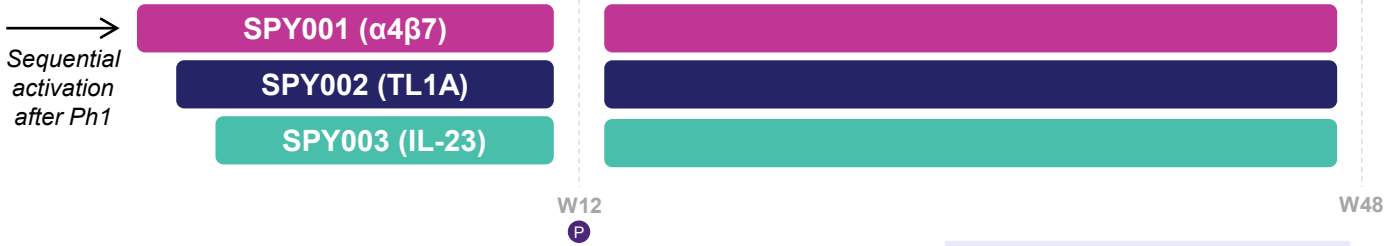
*Data on file. Preclinical models utilized surrogate antibodies. *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001 vs. vehicle (2-way ANOVA with Dunnett's correction). N=8 per group. TNBS=trinitrobenzene sulfonic acid.*

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

SKYLINE

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

UC mMS 5-9



OBJECTIVES

- Monotherapy POC

KEY ENDPOINTS

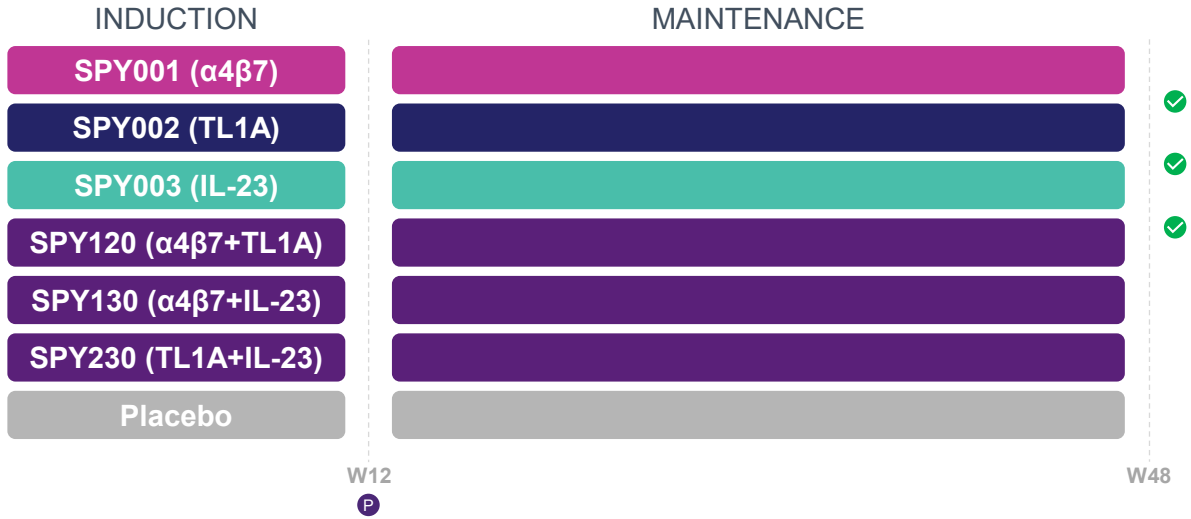
- P Change in RHI at W12
- S Clinical remission at W12
- S Endoscopic improvement at W12
- S Change in mMS at W12

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

UC mMS 5-9

~50:50 naïve:experienced

α4β7 and IL-23 failures capped



- Monotherapy dose optimization
- Combination POC
- Contribution of components

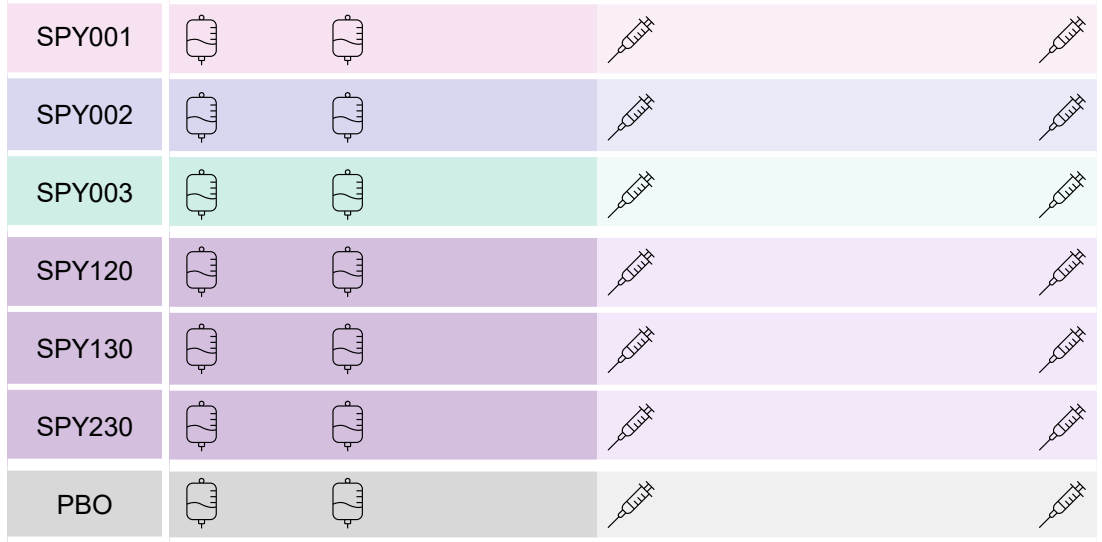
- P Clinical remission at W12
- S Endoscopic improvement at W12
- S Clinical response at W12
- S Histological improvement at W12
- S HEMI at W12
- S Clinical remission at W48

SPYRE

mMS=modified mayo score; RHI=Robarts Histopathology Index; HEMI=Histo-Endoscopic Mucosal Improvement; P=primary endpoint; S=secondary endpoint
Initiation of each cohort subject to regulatory clearance.

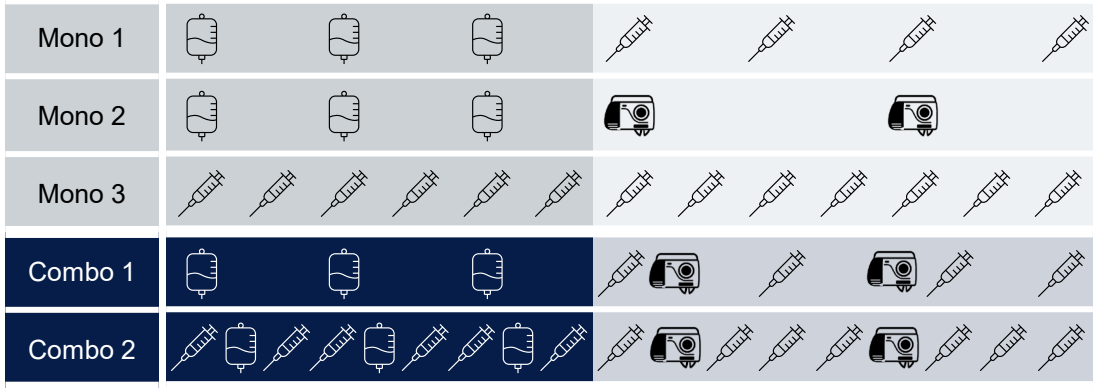
Comparison to other trials highlights advantage of designing a portfolio from the ground up w/ unified dosing

SKYLINE



- ✓ Unified dosing intervals and formats enables blinded trial
- ✓ Two IV induction doses, Q3M-Q6M SC chronic dosing
- ✓ Clear approach to advance coformulation for Ph3

TARGET-CD[1]

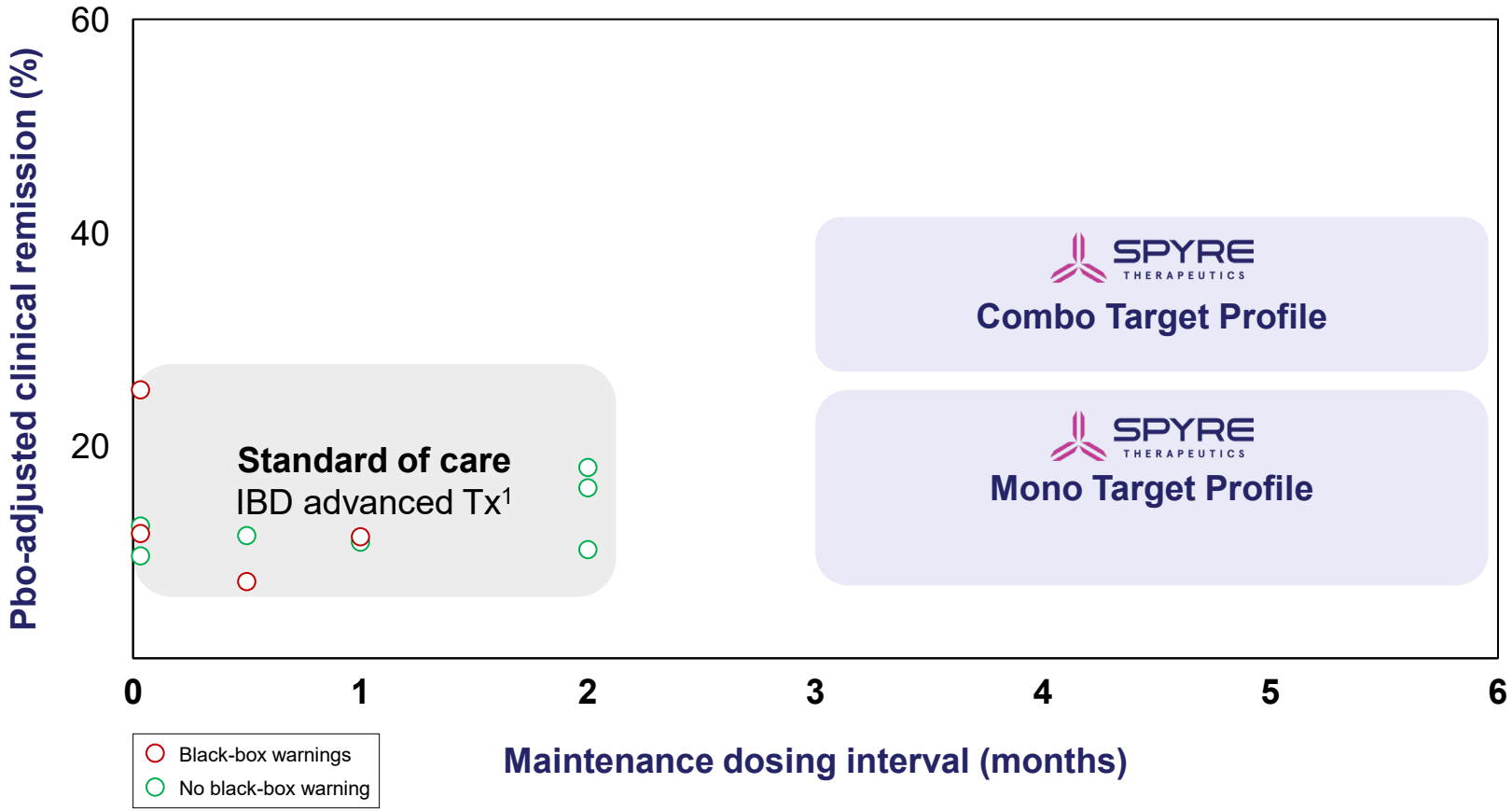


- × Mix of IV, SC, and OBI routes of administration; open label trial
- × Combos default to highest dosing frequency (Q2W or Q4W)
- × Unclear strategy to single product combination for Ph3

Pending regulator feedback; [1]Inferred dosing regimen based on Clinicaltrials.gov posting and dosing regimens of individual agents in commercial or prior monotherapy clinical trial settings. OBI=on body injector

Best-in-class monotherapies provide foundation for paradigm-changing combinations for IBD

Potential for best-in-indication positioning (UC example)



Target product profiles

Monos: Comparable-to-better efficacy vs. standard of care

Combos: Meaningfully improved efficacy vs. standard of care

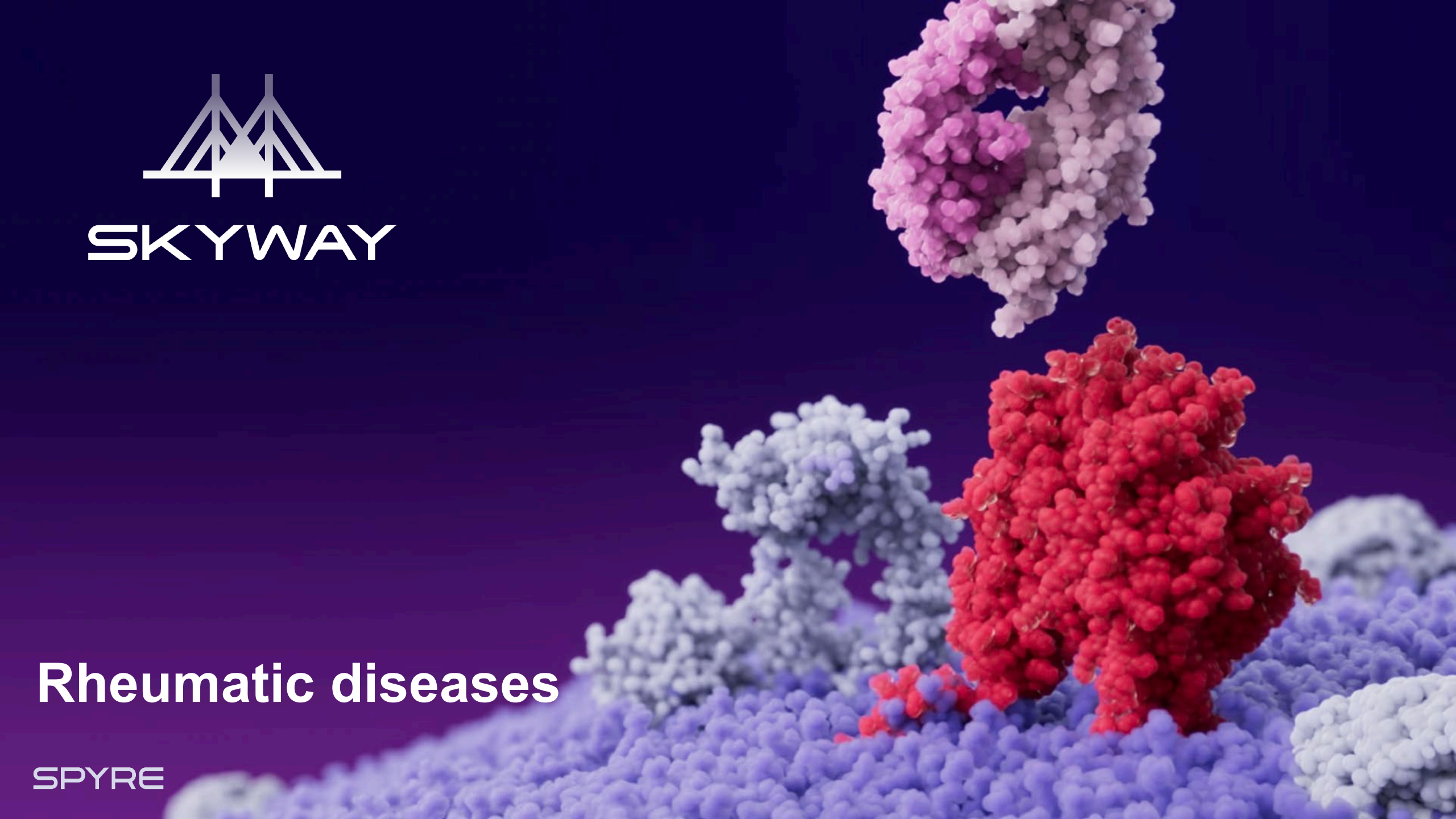
Favorable safety profile

No black box warning

2-4 doses per year

Positioning of Spyre programs is illustrative and based on Phase 1 results and illustrates what we believe we can potentially achieve. Placebo-adjusted clinical remission data are derived from different clinical trials conducted at different times, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted. [1]Oral and SC administered products

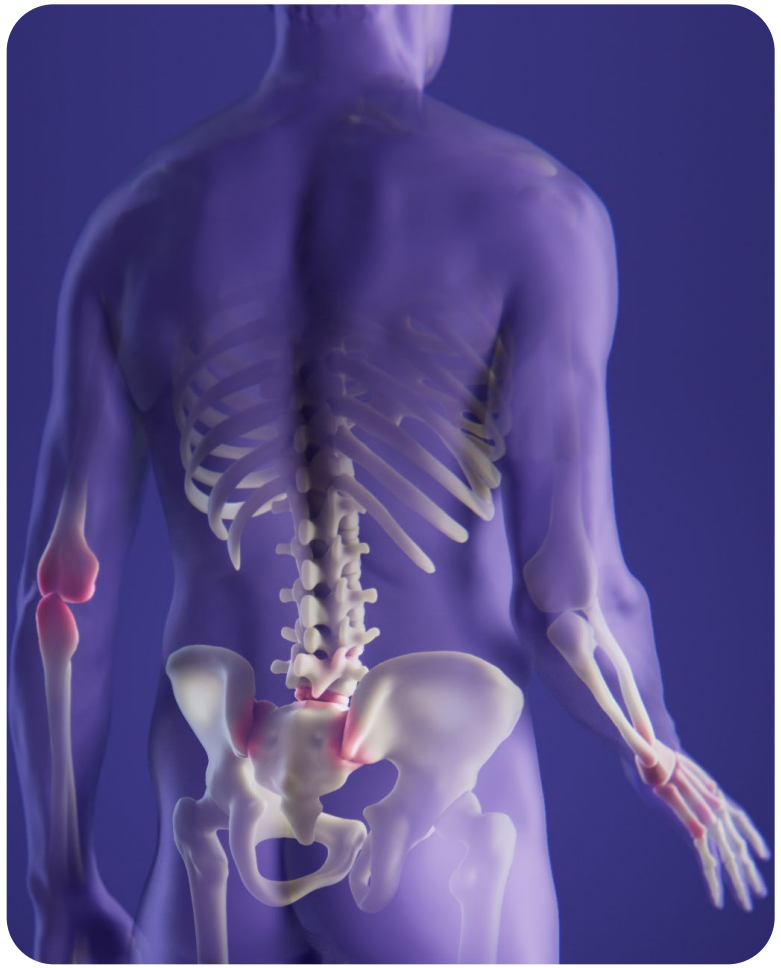
SKYWAY



Rheumatic diseases

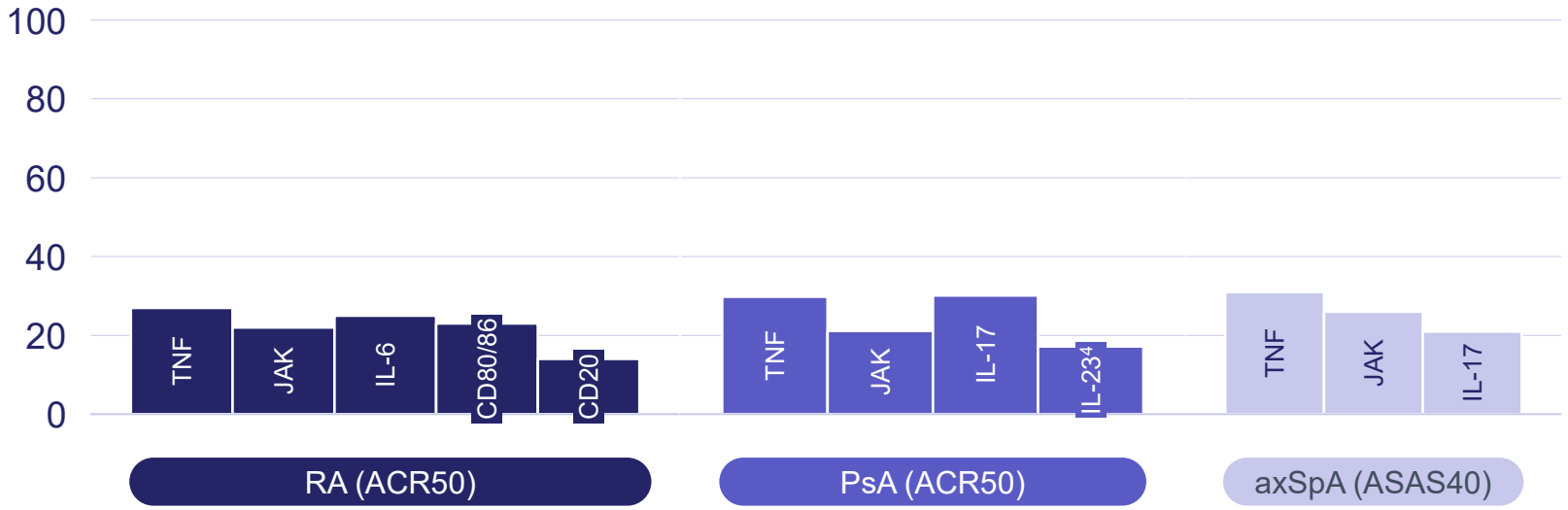
SPYRE

Substantial unmet need remains for the millions of individuals living with RA, PsA, and axSpA



- >3M individuals in the U.S. diagnosed with RA (>1.5M[1]), PsA (~1M[2]), and axSpA (~1M[2])
- Substantial unmet need remains due to:
  - Minority remission rates, inability to control multiple aspects of disease, and lack of durability with existing therapies
  - Limited MOAs to cycle through following incomplete responses
  - Poor adherence to frequent and/or inconvenient dosing regimens

Placebo-adjusted efficacy rates by MOA (W24[3])

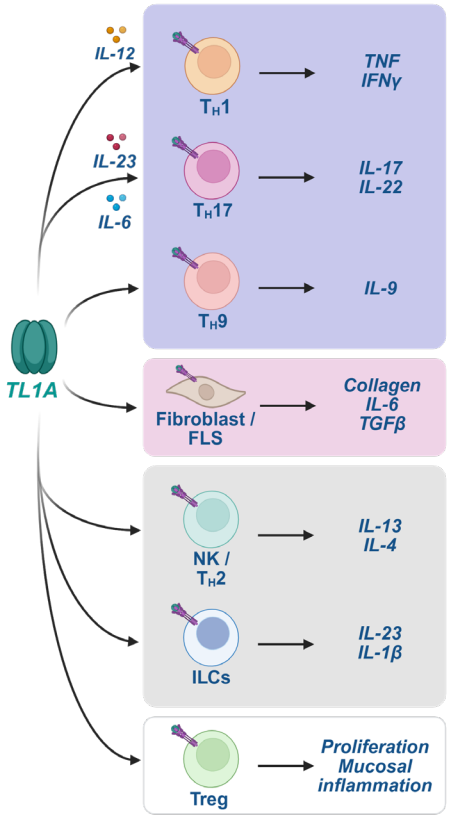


SPYRE

[1]Hunter, Theresa M., et al. Rheumatol Int (2017); [2]Ogdie, Alexis, et al. Rheumatol Ther (2021); Danve, Abhijeet, and Atul Deodhar. *Clinical rheumatology* 38.3 (2019). *Efficacy rates by MOA from product labels. Note:* [3]*Week 24 data when available, otherwise data is Week 12 or 16;* [4]*Includes IL-12/23 and IL-23*

TL1A has been implicated in several inflammatory and fibrotic diseases, with strong rationale in rheumatic diseases

TL1A exacerbates inflammation and fibrosis



Target rheumatic diseases share mechanistic pathways with IBD, where POC is established

Increasing overlap with clinically validated biology

	POC studies[1]	T_H1 | T_H17 | T_H9	Fibroblasts FLS | osteoclasts	NK | T_H2 | ILCs
Ulcerative colitis (UC)	✓	●		
Crohn's disease (CD)	✓	●	●	
Rheumatoid arthritis (RA)	Roche	●	●	
Psoriatic arthritis (PsA)		●		
Axial spondyloarthritis (axSpA)		●		
Psoriasis (PsO)		●		
Hidradenitis suppurativa (HS)		●	●	
Primary biliary cholangitis (PBC)		●	●	
Pulmonary sarcoidosis		●		
Interstitial lung disease (SSc-ILD)			●	
Metabolic steatohepatitis (MASH)	Roche		●	
Atopic dermatitis (AD)	Roche			●
Asthma	✘			●

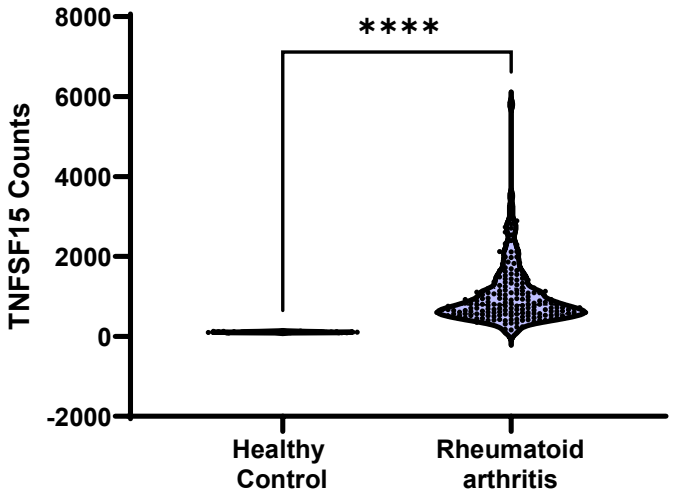
Figure created with BioRender.com. [1] Logos indicate active clinical POC studies.

Hisamoto, T. et al. Int. J. Mol. Sci. 24, 1813 (2023); Herro, R. et al. J. Immunol. 205(9), 2414-2422 (2020); Ma, C. et al. Int. Immunopharm. 137, 112360 (2024); Richard, A. et al. JLB 3(98), 333-345 (2015); Song, Y. et al. Arthritis Research & Therapy 22, 106 (2020); Xu, W. et al. Frontiers in Immunology 13, 891328 (2022).

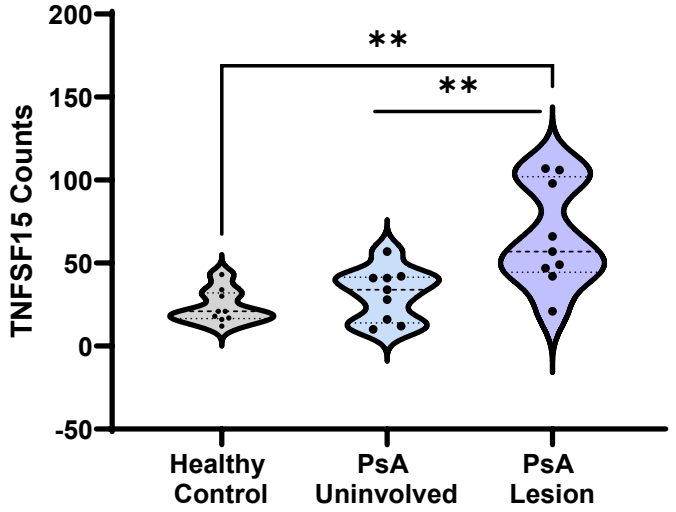
SPYRE

TL1A is upregulated in RA, PsA, and axSpA relative to healthy controls

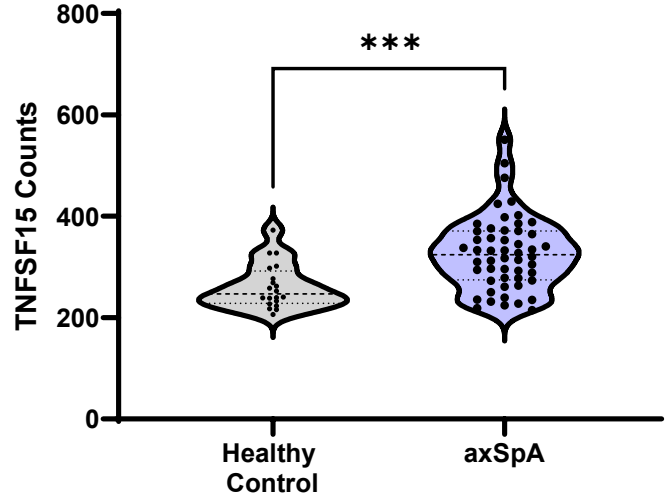
Rheumatoid arthritis



Psoriatic arthritis



Axial spondyloarthritis



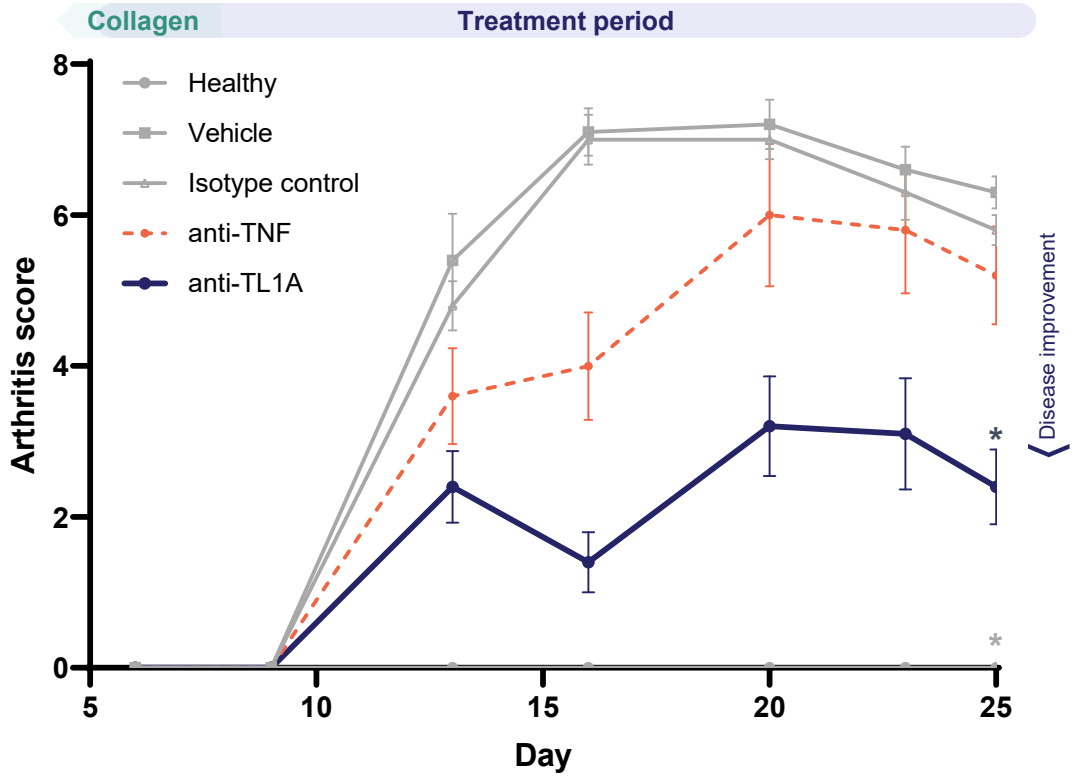
Source	Whole blood	Skin biopsy	Whole blood
Sequencing	Microarray	Bulk RNA seq	Microarray
Sample size	N=192 RA, 30 HC	N=9 per cohort	N=52 axSpA, 20 HC

SPYRE

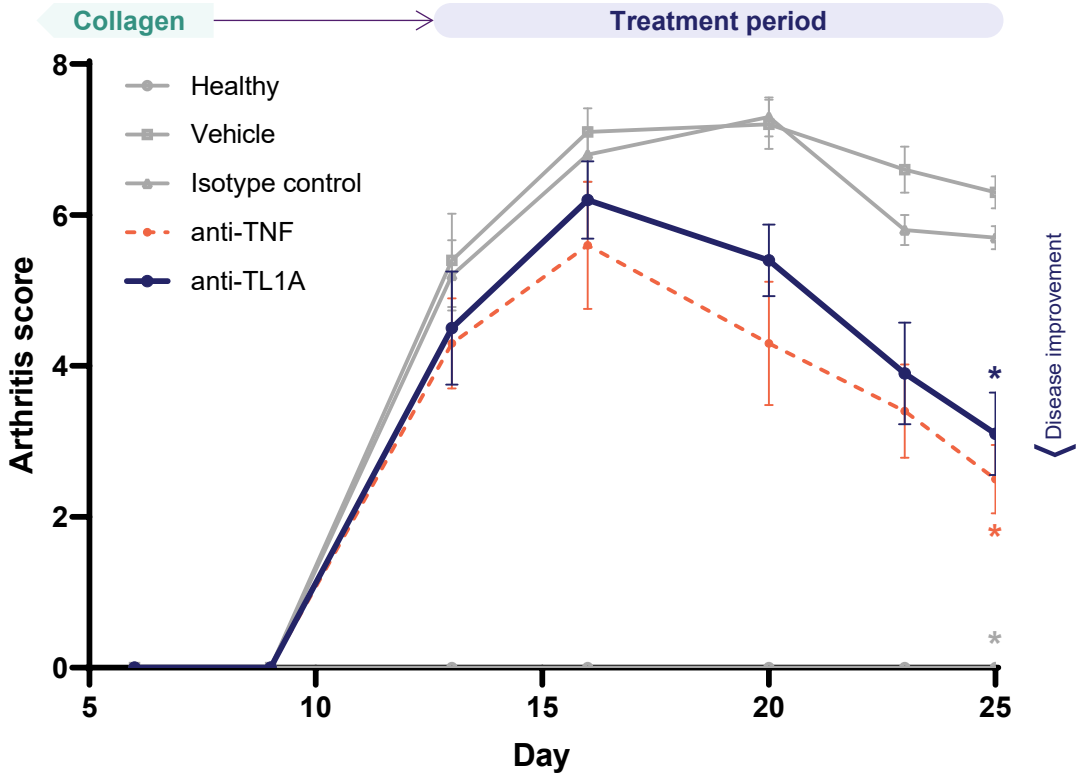
Spyre analysis of RA-MAP, Li, Sifang, et al. BMC Musculoskeletal Disorders 25.1 (2024), and Johnsson, Hanna, et al. Arthritis Research & Therapy.
*** P≤0.01, *** P ≤0.001, **** P ≤0.0001. Unpaired tailed t-test used for RA and axSpA analysis, One-way ANOVA used in PsA.*
RA=rheumatoid arthritis; PsA=psoriatic arthritis; axSpA=axial spondyloarthritis; HC=healthy controls.

Spyre anti-TL1A antibody meets or exceeds the efficacy of etanercept (anti-TNF) in rat models of arthritis

Superior efficacy in semi-preventative model



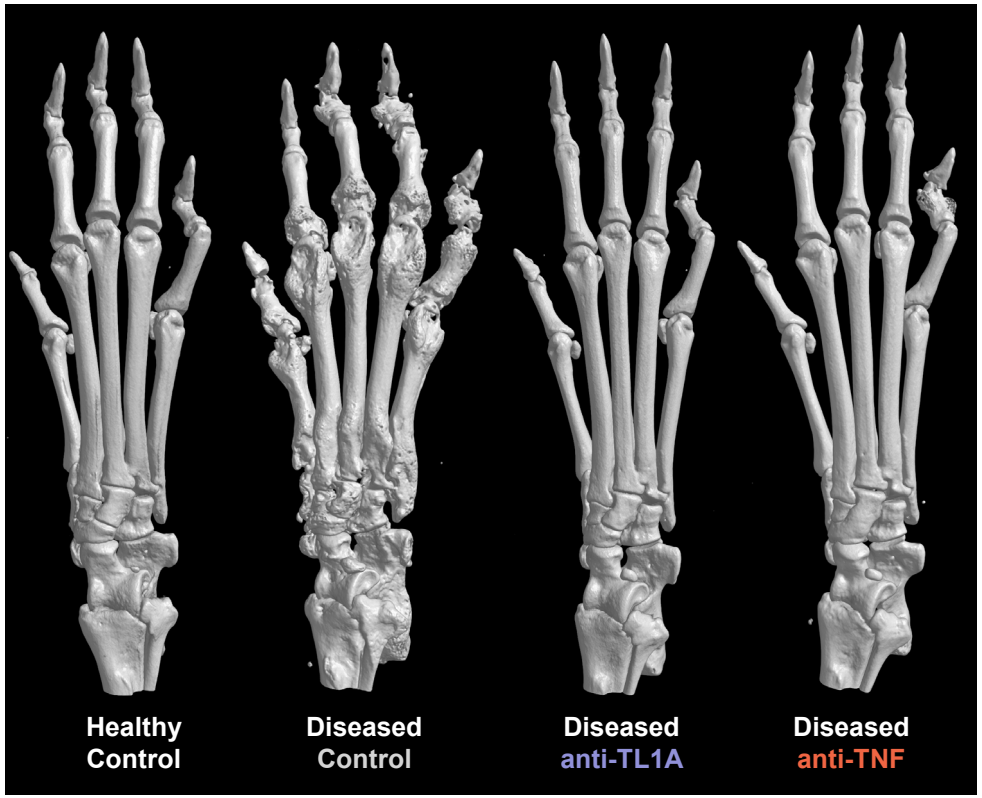
Comparable efficacy in therapeutic model



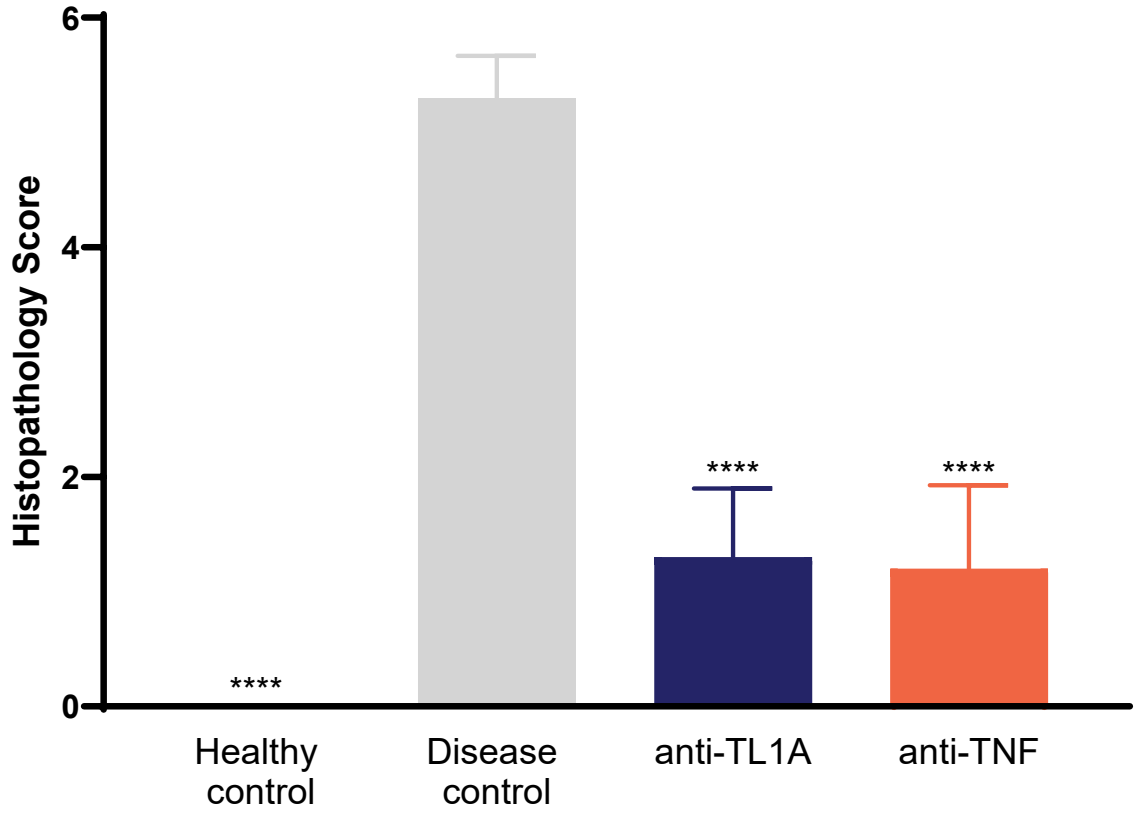
** P< 0.0001 vs. isotype control; 2-way ANOVA using Dunnett's correction for multiple comparisons. Data on file.*

Robust anti-TL1A activity further replicated in mouse models of arthritis

Anti-TL1A prevents disease and bone erosion



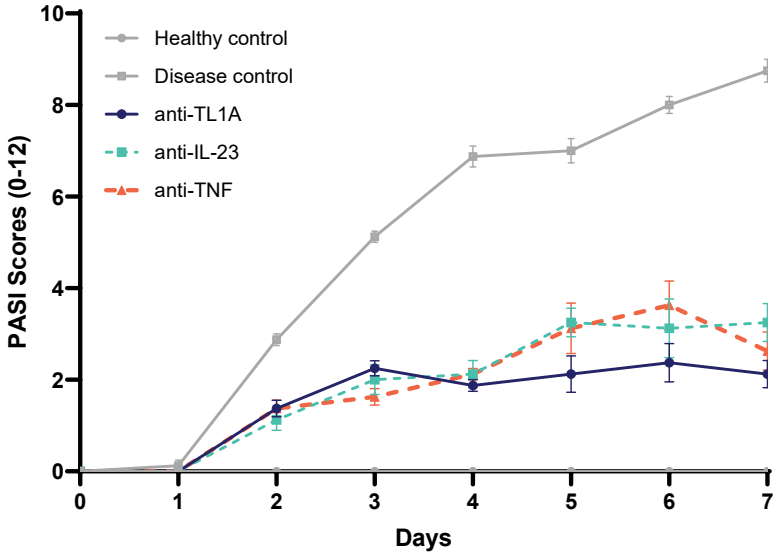
Comparable efficacy to anti-TNF



*Data on file. **** P ≤0.0001*

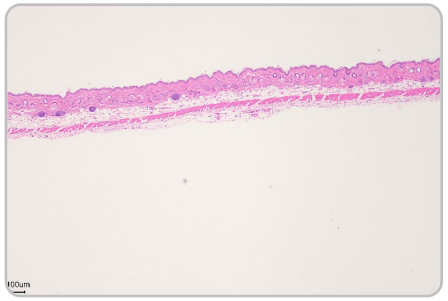
Additionally, anti-TL1A treatment led to comparable improvements in psoriatic skin lesions in mouse IMQ model

Anti-TL1A reduces skin lesions

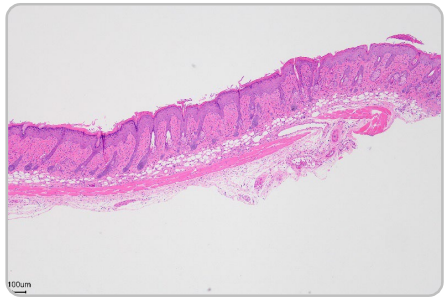


Potential for robust skin clearance in PsA

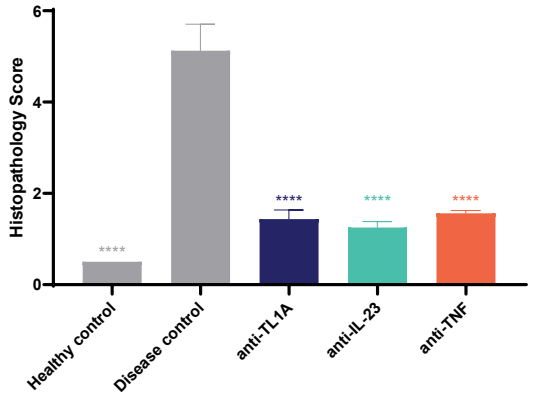
Comparable efficacy to anti-IL-23 and anti-TNF

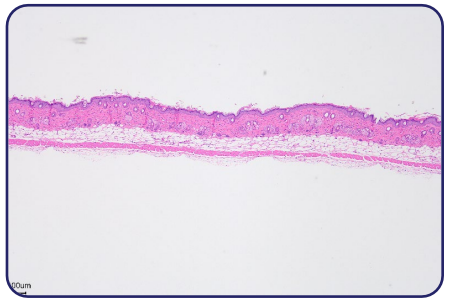


Healthy control

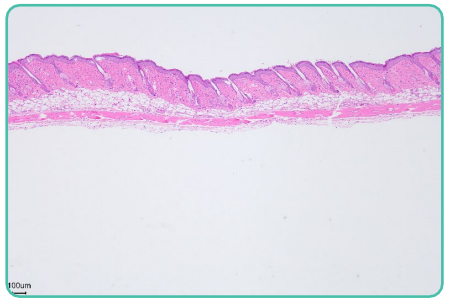


Disease control

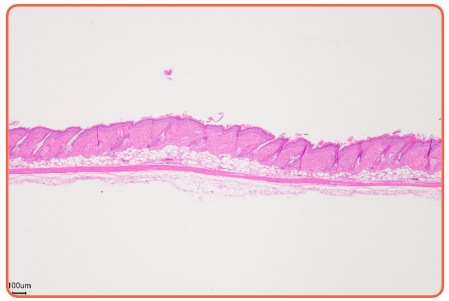




anti-TL1A



anti-IL-23



anti-TNF

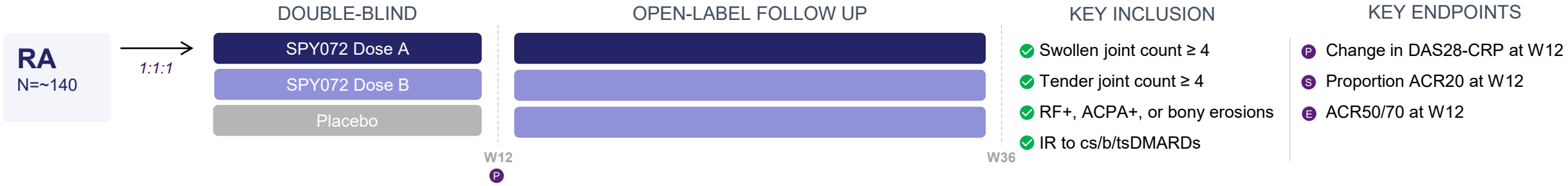
SPYRE

*Data on file. **** P ≤0.0001*

SKYWAY: Phase 2 *basket* study evaluating SPY072 (anti-TL1A) in RA, PsA, and axSpA

SKYWAY

Sub-study A: SPY072 in moderate-to-severely active rheumatoid arthritis (RA) **Enrollment complete**



Sub-study B: SPY072 in moderate-to-severely active psoriatic arthritis (PsA)

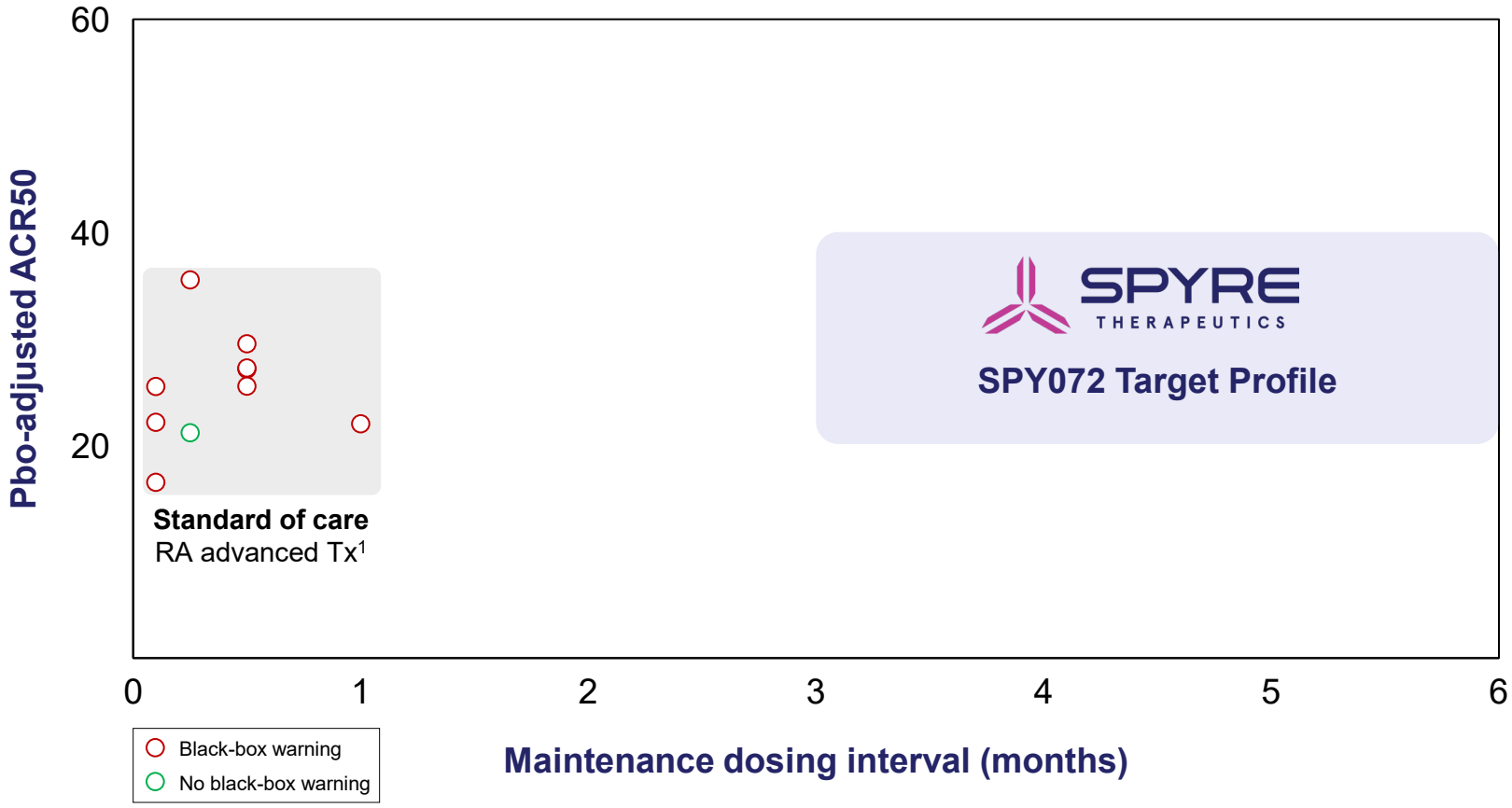
Sub-study C: SPY072 in moderate-to-severely active axial spondyloarthritis (axSpA)

SPYRE

RF=rheumatoid factor; ACPA= Anti-citrullinated protein antibodies; cs/b/tsDMARD=conventional synthetic, biologic, or targeted synthetic disease modifying antirheumatic drugs; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; P=primary endpoint; S=secondary endpoint; E=exploratory endpoint. IR=inadequate response

SPY072 is a potential first-in-class & best-in-class therapy for rheumatic diseases with quarterly or twice-annual dosing

Potential for best-in-indication positioning (RA example)



SPY072 target product profile

- First-in-class anti-TL1A
- Comparable-to-better efficacy
- Favorable safety profile
- No black box warning
- 2-4 doses per year

Positioning of Spyre programs is illustrative and based on Phase 1 interim results. Placebo-adjusted clinical data are derived from different clinical trials conducted at different times, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted. [1]Oral and SC administered products.

Catalysts & capitalization

SPYRE

Capitalized to deliver one of the industry's most compelling catalyst maps

Trial	2026	2027
SKYLINE Part A (Open-label)	☑ SPY001 α4β7 Ph2 UC induction POC ❑ SPY002 TL1A Ph2 UC induction POC (mid-2026) ❑ SPY003 IL-23 Ph2 UC induction POC (3Q 2026)	❑ SPY001 α4β7 Ph2 UC maintenance data ❑ SPY002 TL1A Ph2 UC maintenance data ❑ SPY003 IL-23 Ph2 UC maintenance data
SKYLINE Part B (Pbo-controlled)	☑ Initiate enrollment of Part B cohorts	❑ SPY120 α4β7 + TL1A Ph2 UC induction POC ❑ SPY130 α4β7 + IL-23 Ph2 UC induction POC ❑ SPY230 TL1A + IL-23 Ph2 UC induction POC ❑ SPY001 α4β7 Ph2 UC induction POC ❑ SPY002 TL1A Ph2 UC induction POC ❑ SPY003 IL-23 Ph2 UC induction POC
SKYWAY	❑ SPY072 TL1A Ph2 W12 POC in RA (3Q 2026) ❑ SPY072 TL1A Ph2 W16 POC in PsA (4Q 2026) ❑ SPY072 TL1A Ph2 W16 POC in axSpA (4Q 2026)	❑ SPY072 TL1A Ph2 maintenance data in RA ❑ SPY072 TL1A Ph2 maintenance data in PsA ❑ SPY072 TL1A Ph2 maintenance data axSpA

$1.2 billion proforma cash as of March 31, 2026[1], with expected runway into 2H 2029

Milestones expected as of the date of this presentation. [1]Reflects preliminary and unaudited cash, cash equivalents, & marketable securities as of 3/31/26 of $741.5 million plus $435.3 million in net proceeds from the recently closed April 2026 underwritten public offering of common stock

Cash and shares outstanding

$1.2B pro forma cash as of March 31, 2026[1]

Expected runway into 2H 2029

		Number of shares (M)
Common stock	Shares outstanding	86.3
Common stock equivalents	• Series A preferred stock	13.8
	• Series B preferred stock	0.7
Common stock and common stock equivalents[2]	**Total outstanding**	**100.8**

[1]Reflects preliminary and unaudited cash, cash equivalents, & marketable securities as of 3/31/26 of $741.5 million plus $435.3 million in estimated net proceeds from the recently closed April 2026 underwritten public offering of common stock; [2]Shares outstanding on a pro forma and as-converted basis as of 3/31/26, inclusive of the April 2026 financing, which (i) gives effect to the full conversion of the Company's preferred stock, and (ii) disregards beneficial ownership limitations that may limit the ability of certain holders of preferred stock to convert into common stock

SPYRE

THANK YOU

Engineering for new heights in the treatment of IBD and beyond

Scientific illustrations by Visual Sciences

Appendix

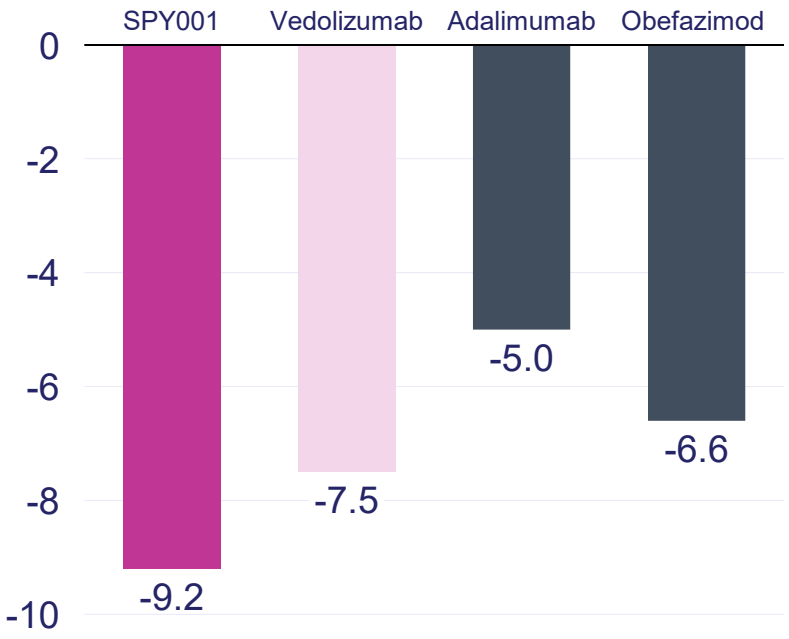
2026 Milestone Aims

SPY001 Part A Induction Data

2026 Part A readout: Aiming for comparable safety and efficacy as in-class comparators

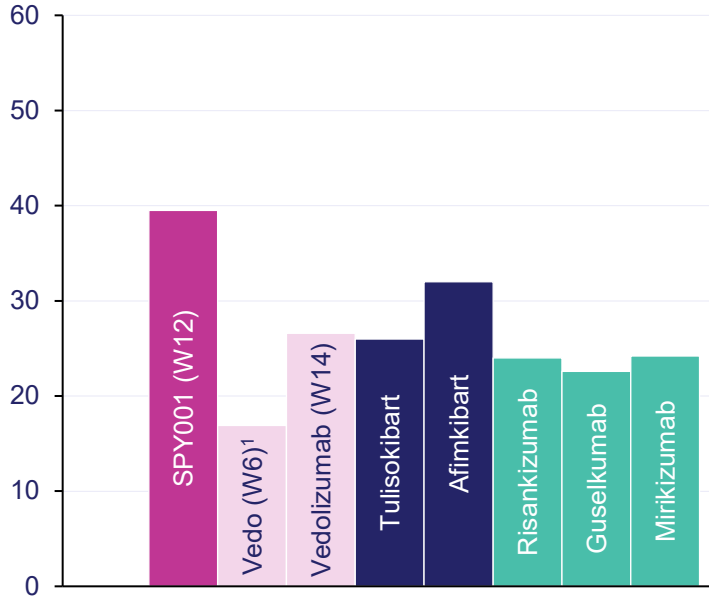
Primary endpoint

ΔRHI from baseline (W8-14)

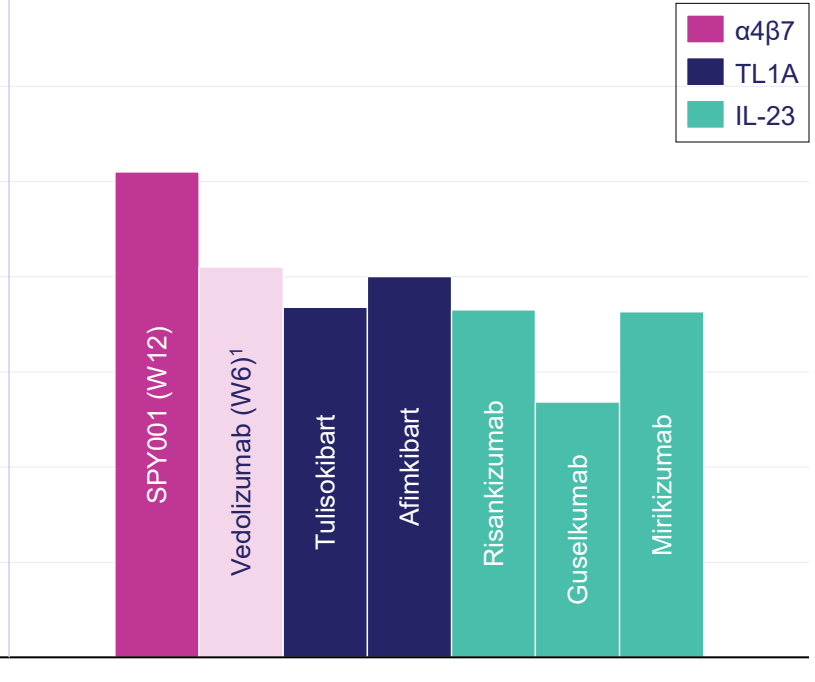


Secondary endpoints

Absolute % clinical remission (W6-14)



Absolute % endoscopic improvement (W6-14)



Source: Vedolizumab (VARSITY, GEMINI I), adalimumab (VARSITY), obefazimod (Ph2b – 25 mg and 50 mg pooled), tulisokibart (ARTEMIS-UC), afimkibart (TUSCANY-2), risankizumab (INSPIRE), guselkumab (QUASAR), mirikizumab (LUCENT 1); Duvakitug not shown given outlier placebo response rate. Trial designs differ and no head-to-head clinical trials have been conducted. [1]GEMINI endoscopies not centrally read

2026 RA readout: Aiming for ΔDAS28-CRP and ACRs comparable-to-better than SOC analogs

Primary endpoint

Placebo-adjusted ΔDAS28-CRP (W12-26)[1]

Secondary & exploratory endpoints

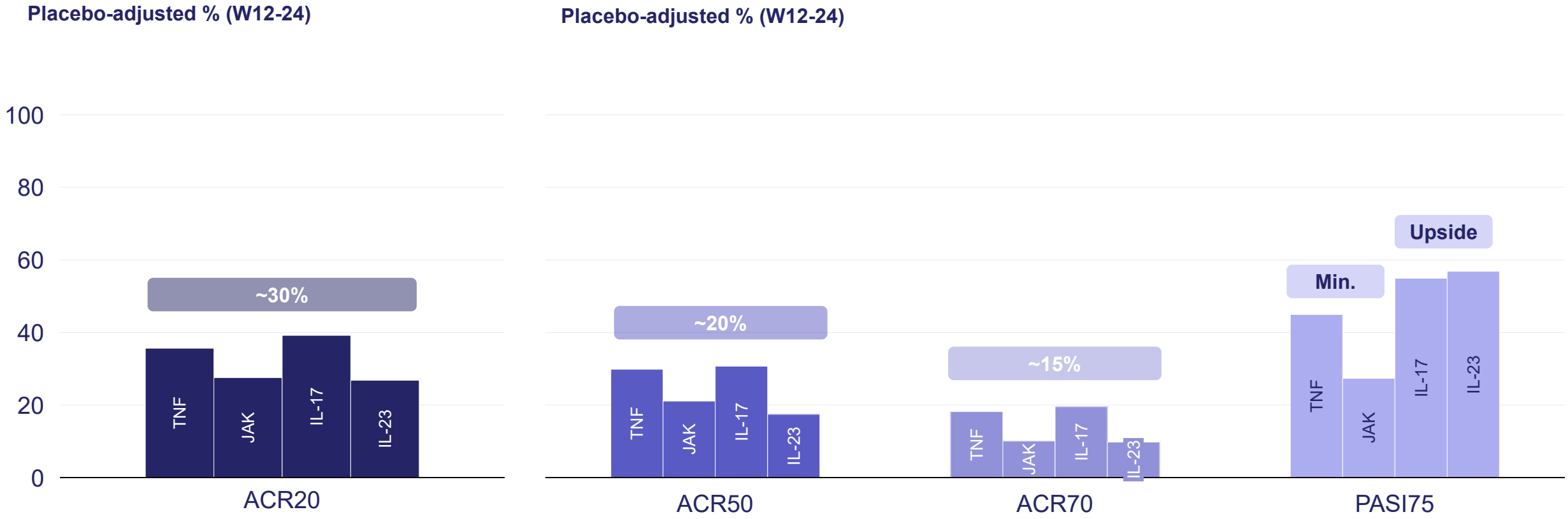
Placebo-adjusted % (W12-26)[2]

Notes: [1]Results from studies in mixed populations or weighted average of naïve and inadequate response (IR) trial results. [2]Average ACR values from pivotal studies of approved products within each class. Data on file.

2026 PsA readout: Aiming for ACRs and PASI comparable-to-better than SOC analogs

Primary endpoint

Secondary & exploratory endpoints

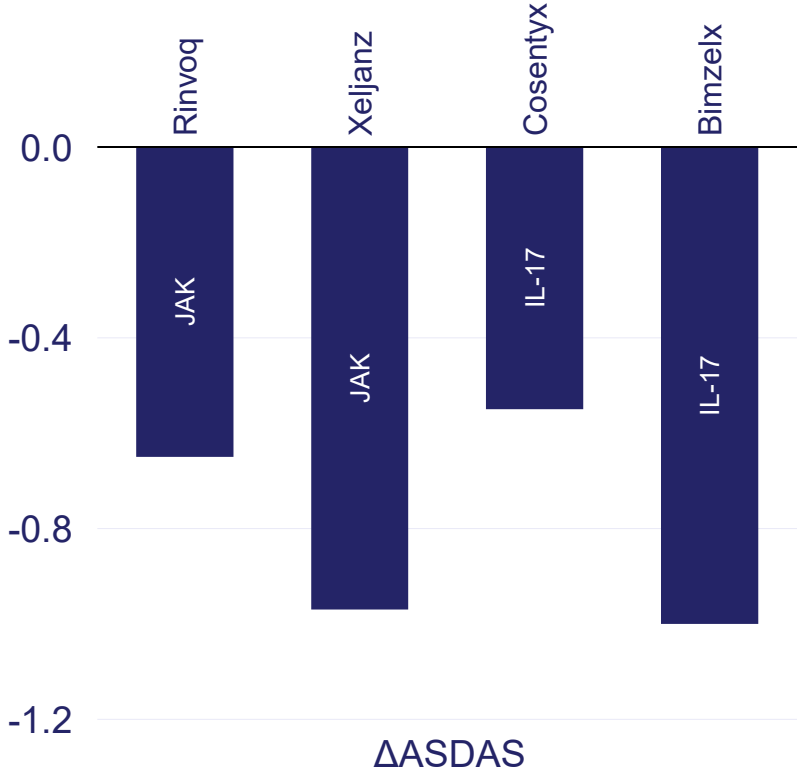


Average ACR and PASI values from pivotal studies of approved products within each class. IL-23 includes IL-12/23. Data on file.

2026 axSpA readout: Aiming for ΔASDAS and ASAS comparable-to-better than SOC analogs

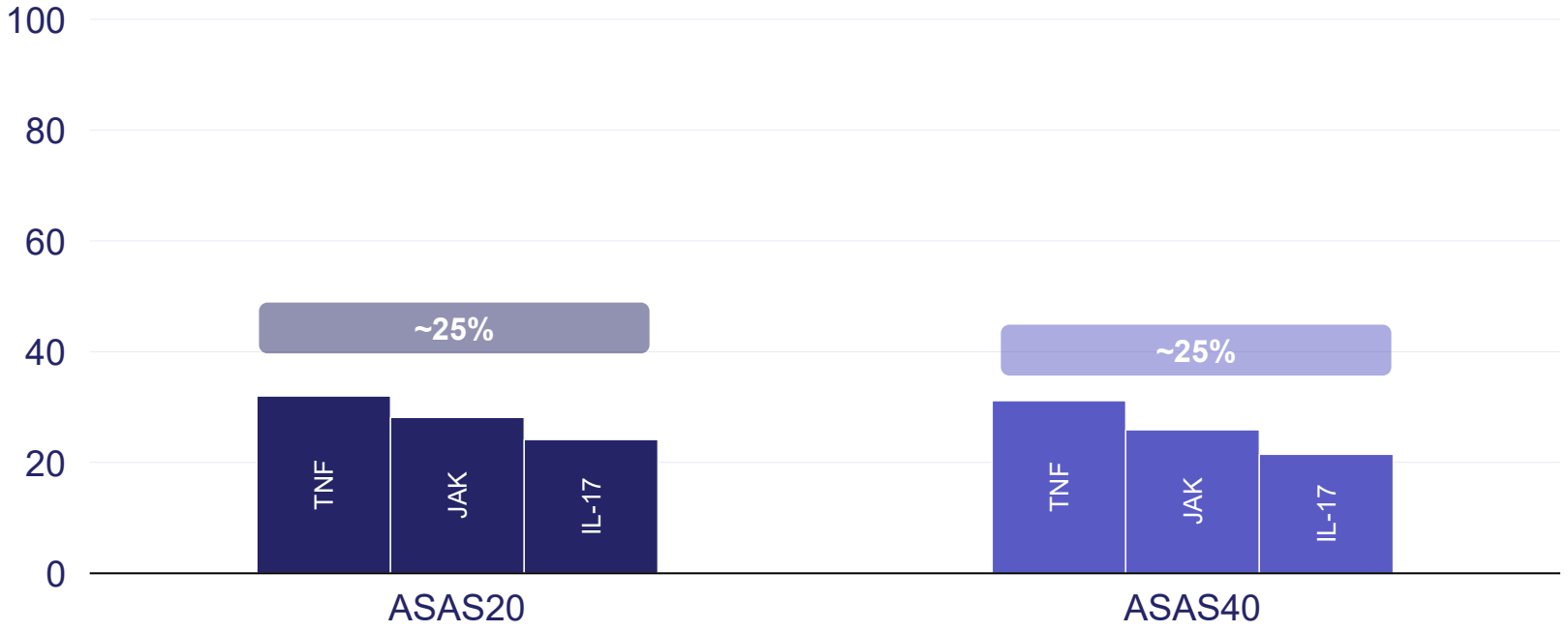
Primary endpoint

Placebo-adjusted ΔASDAS (W12-16)[1]



Secondary & exploratory endpoints

Placebo-adjusted % (W12-16)[2]



[1]Results from studies in mixed populations [2]Average ASAS values from pivotal studies of approved products within each class. Data on file.

Appendix

2026 Milestone Aims

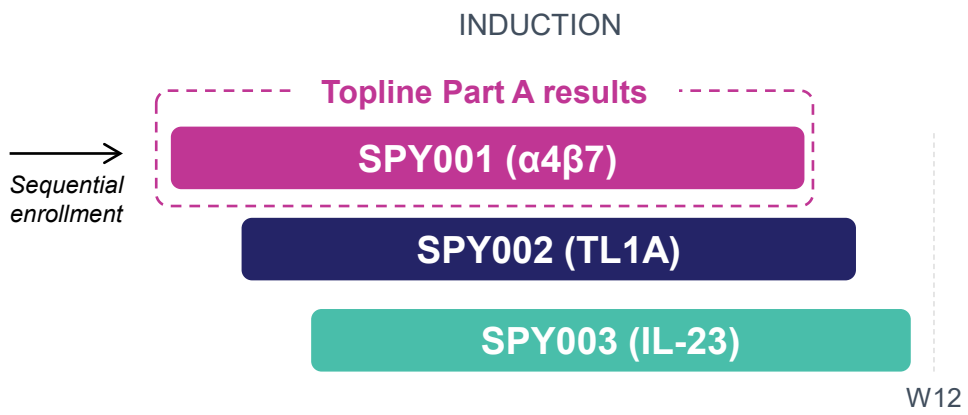
SPY001 Part A Induction Data

SPY001 topline induction results from SKYLINE Part A

SKYLINE Part A: Open label monotherapy evaluation

Patient characteristics

- Adults with moderately to severely active UC (mMS 5-9)
- Rectal bleeding subscore ≥1
- Mayo endoscopic subscore ≥ 2



Key topline endpoints

PRIMARY

ΔRHI from baseline

SECONDARY

% Clinical remission

% Endoscopic improvement

Incidence of treatment-emergent adverse events

mMS=modified Mayo Score; RHI=Robarts Histopathology Index. Data pertain to SPY001 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

Patient disposition

Screened
(N=91)

↓

Dosed
(N=43)

↓

Completed Induction Period[1]
(N=41)

	SPY001 (α4β7), N = 43
Age (years, mean)	44
Sex (% female)	28
Weight (kg, mean)	76
Geographic region Europe North America	 88% 12%
Duration of UC (years, mean)	4.5
RHI (mean ± SD)	15.6 ± 8.6
RHI ≥ 10 (n, %)	34 (79%)
Baseline mMS (mean ± SD)	6.8 ± 1.1
Mayo Endoscopy Score (MES) (n, %) 2 3	 19 (44%) 24 (56%)
Concomitant immunomodulator use (n, %)	0
Concomitant corticosteroid use (n, %)	18 (42%)
Number of prior advanced therapies (n, %) Naïve 1 ≥2	 35 (81%) 7 (16%) 1 (2%)

[1]*Two subjects withdrew consent*
Source: Data on file.

SPY001 was well tolerated with a favorable safety profile

	SPY001 (α4β7), N=43
Subjects with any Adverse Event (n, %)	**6 (14%)**
Severe (Grade ≥ 3) AE	1 (2%)*
Drug-Related AE	0
AE Leading to Drug Discontinuation	0
Serious Adverse Event (SAE)	1 (2%)*
Drug-Related SAE	0
AEs of Special Interest	0
Death	0

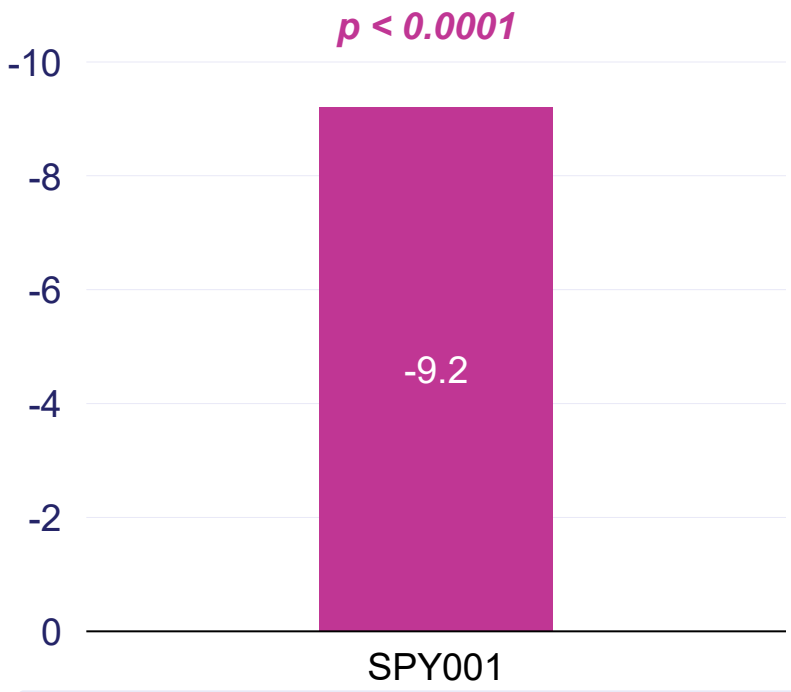
Most common AE (≥2 patients) was back pain (n=2)

**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.*
Data pertain to SPY001 Induction Treatment Period (through Week 12) with a data cut-off date of Feb 23, 2026.

SPY001 met its primary endpoint and outperformed our expectations on key secondary endpoints

Primary endpoint

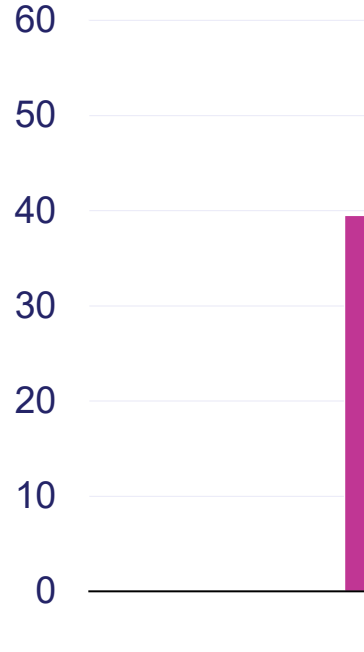
Mean ΔRHI at W12 from baseline



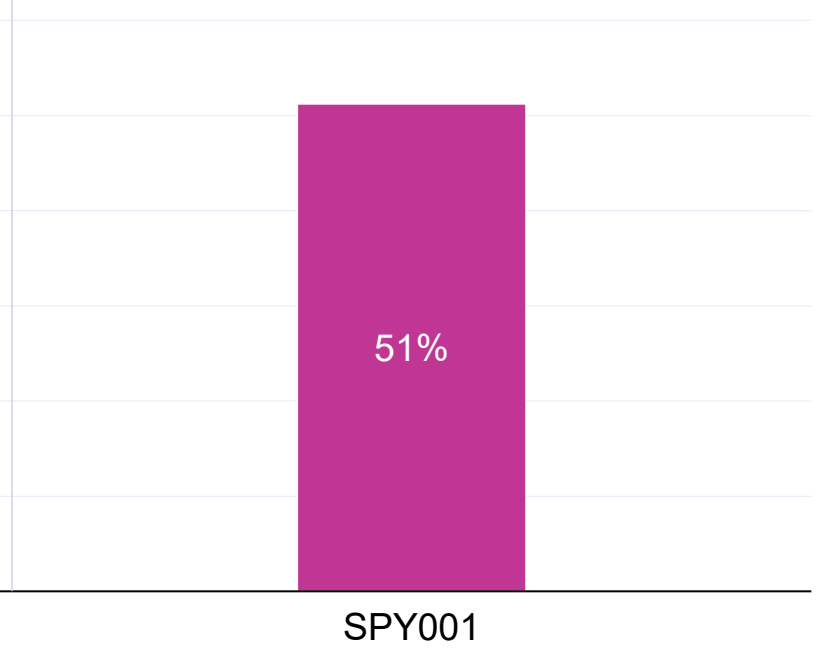
Pre-specified sensitivity analysis:
-10.6 for participants with a baseline RHI ≥ 10

Key secondary endpoints

Proportion with clinical remission at W12



Proportion with endoscopic improvement at W12



SPYRE

Source: Data on file. 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 (N=41); Secondary endpoints including Clinical Remission and Endoscopic Improvement rates were analyzed using full analysis set (N=43).