The Anti-TL1A Antibody PRA023 Demonstrated Proof-of-Concept in Crohn's Disease: **Phase 2a APOLLO-CD Study Results**

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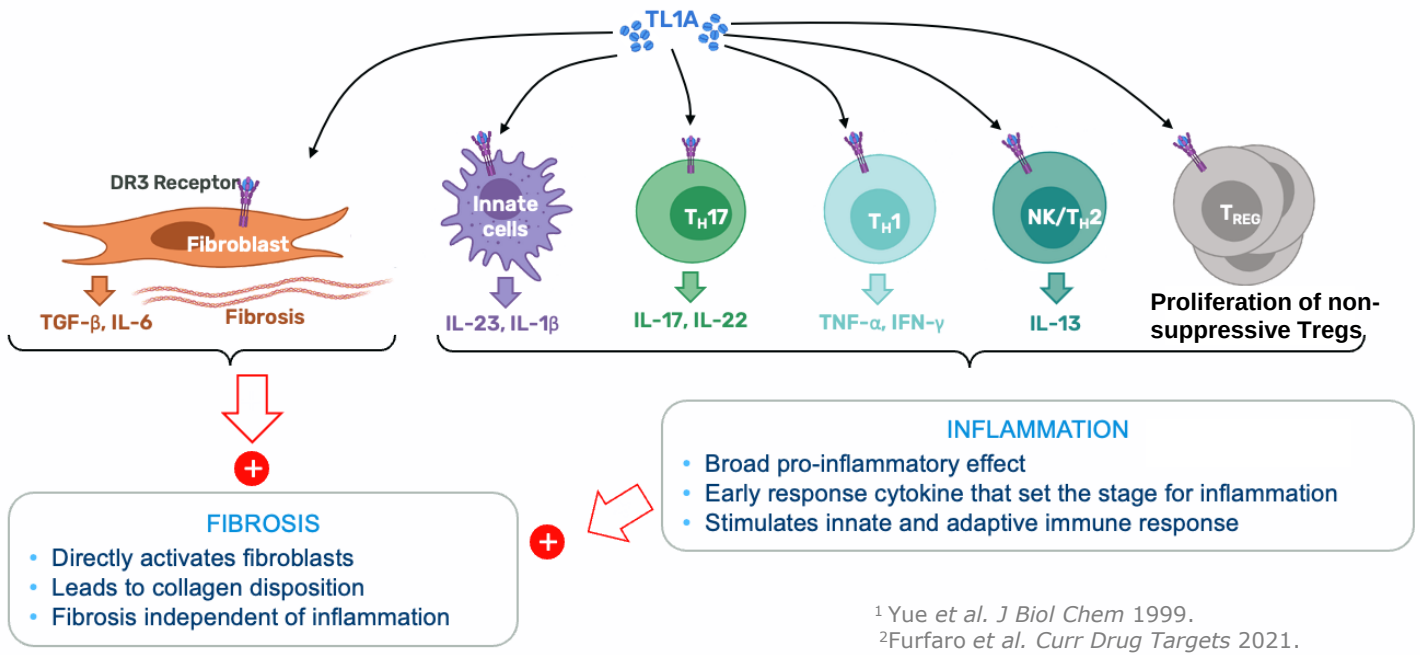
TL1A: First IBD Target That Mediates Inflammation & Fibrosis

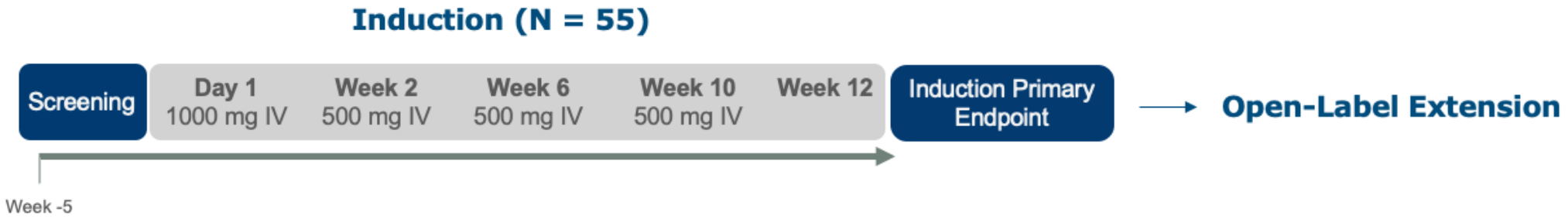
- TNF-like ligand 1A, member of the TNF superfamily[1]
- Expressed in antigen presenting cells, lymphocytes, and endothelial cells.
- Linked to multiple autoinflammatory & fibrotic diseases, including IBD[2,3]
- Mouse studies validate TL1A as relevant target to treat colitis and intestinal fibrosis[4-6]
- Variants in the TL1A-encoding gene (TNFSF15) are associated with increased IBD risk[7,8]
  - Genetically-based diagnostic (CDx) test being developed to identify patients with higher likelihood of response



[1] Yue *et al. J Biol Chem* 1999.
[2] Furfaro *et al. Curr Drug Targets* 2021.
[3] Xu et *al. Front Immunol* 2022.
[4] Barrett *et al. Am J Pathol* 2012.
[5] Takedatsu *et al. Gastroenterol* 2008.
[6] Shih *et al. Muc Immunol* 2014.
[7] Yamazaki *et al. Hum Mol Genet* 2005.
[8] Jostins *et al. Nature* 2012.

APOLLO-CD Study Design

Phase 2a, Multi-Center, Open-Label Study to Evaluate the Safety, Efficacy, and Pharmacokinetics of PRA023 in Subjects with Moderately to Severely Active Crohn's Disease



Inclusion Criteria

- Moderately to severely active CD by CDAI
- Endoscopically active disease by SES-CD (≥4 points for isolated ileal disease; otherwise, ≥6 points)
- No/insufficient response and/or intolerance to conventional or biologic therapy (capped biologic-exposed stratum at 70%)
- Permitted prior medications
  - ≤ 4 approved biologics
  - ≤ 3 classes of advanced therapies approved biologics

Objectives

Primary

- Safety and tolerability
- Endoscopic response at Week 12

Secondary

- Clinical remission at Week 12
- Clinical response at Week 12
- Endoscopy and clinical improvement at Week 12
- Biomarker and clinical improvement at Week 12
- Normalization of C-reactive protein (among subjects with elevated concentrations at Baseline) at Week 12
- Normalization of fecal calprotectin (among subjects with elevated concentrations at Baseline) at Week 12

Placebo Estimates and Sample Size Rationale

Null hypothesis of an endoscopic response[1] rate =12%

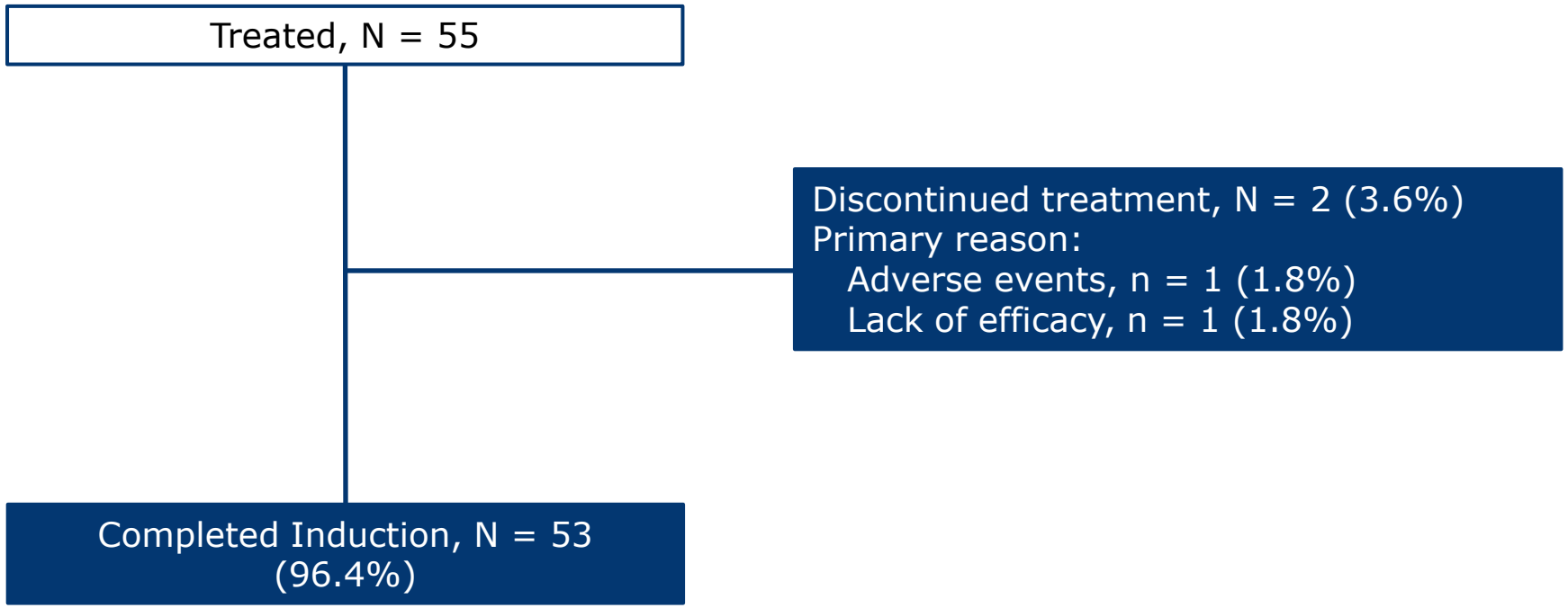
- Based on a meta-analysis estimate of the upper limit of 95% CI of observed placebo rate (95% CI) of 9.5% (7.1, 11.9) from trials below

Clinical Trial	N	Placebo Endoscopic Response Rate (%)
Feagan et al. 2017	39	13
Vermeire et al. 2017	44	14
Sands et al. 2019	64	10.9
Selinger et al. 2018	59	3.4
ADVANCE Study 2021 (later published as D'Haens et al. 2022)	175	12
MOTIVATE Study 2021 (later published as D'Haens et al. 2022)	187	11
Average		10.7
Sample-size Weighted Average	568	9.5

Sample size of 50 provided 80% power to detect a difference of 15% with 2-sided p value of 0.05

[1]decrease in SES-CD ≥ 50%

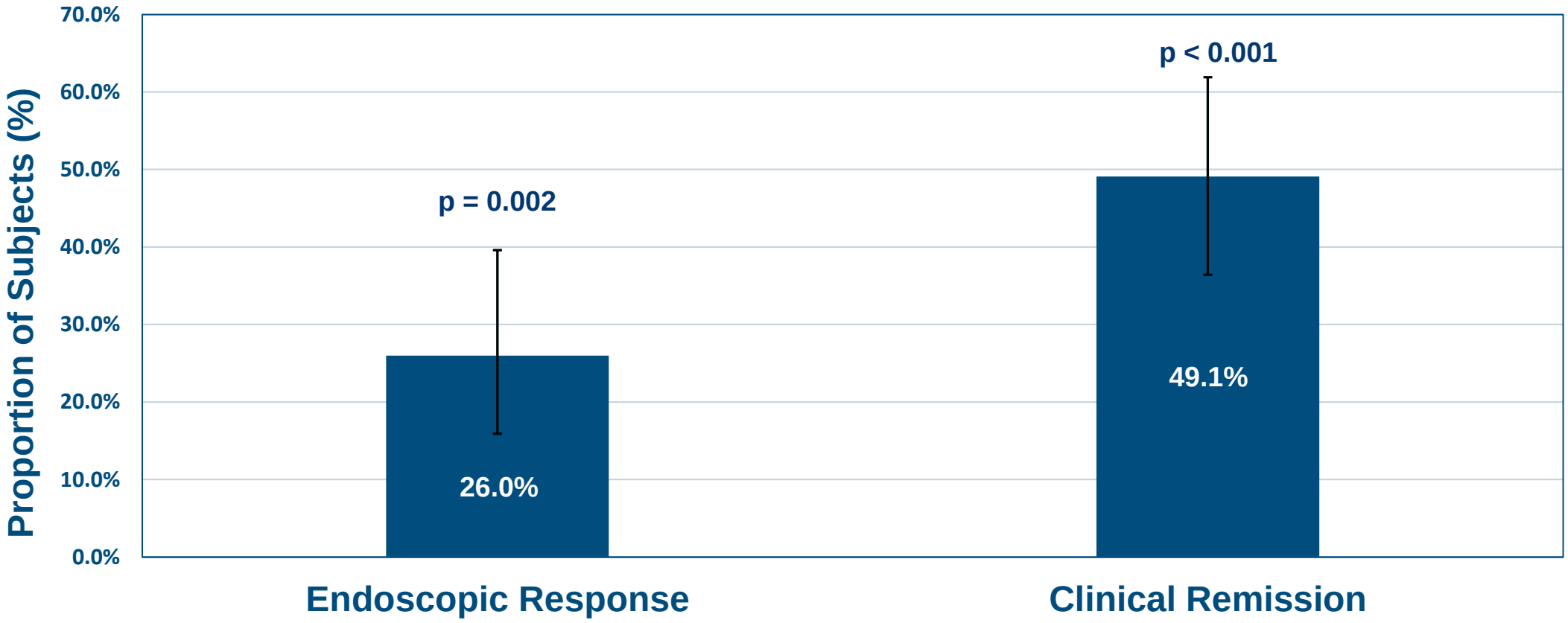
Subject Disposition



Baseline Characteristics and Demographics

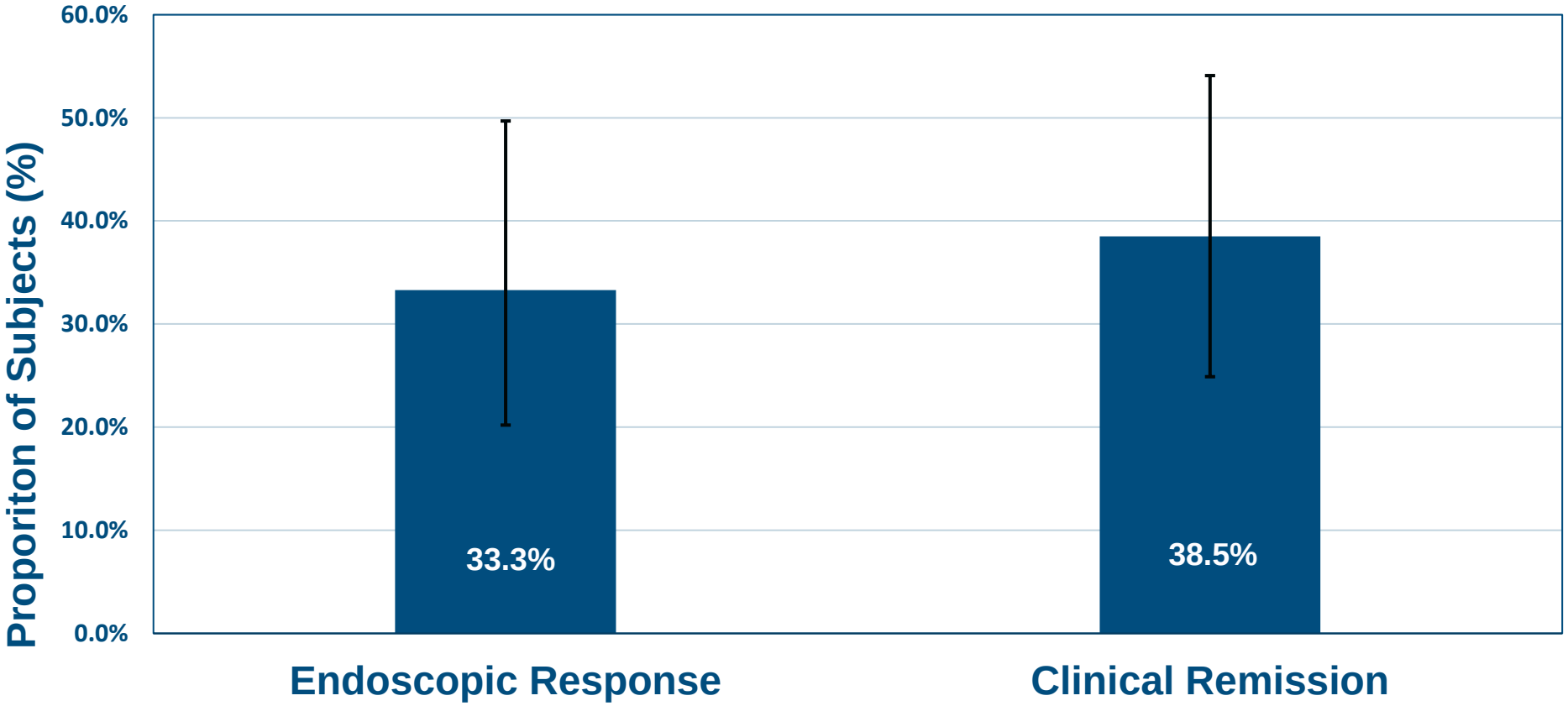
	PRA023 (N = 55)
Age, years, mean (SD)	39.1 (15.7)
Female, n (%)	21 (38.2%)
Weight, kg, mean (SD)	77.6 (20.6)
Geographic region, n (%) North America Eastern Europe Western Europe Rest of world (Australia)	 33 (60%) 13 (23.6%) 7 (12.7%) 2 (3.6%)
Duration of disease, years, mean (SD)	10.3 (9.3)
Extent of disease, n (%) Ileal Colonic Ileocolonic	 8 (14.5%) 15 (27.3%) 32 (58.2%)
Baseline CDAI Score, mean (SD)	317.9 (67.2)
Baseline SES-CD, mean (SD)	13.4 (6.7)
Concomitant immunomodulator use, n (%)	8 (14.5%)
Concomitant corticosteroid use, n (%)	22 (40%)
Number of prior exposure to biologic therapy, n (%) 0 1 2 ≥3	 16 (29.1%) 10 (18.2%) 10 (18.2%) 19 (34.5%)

Primary and Key Secondary Endpoints at Week 12



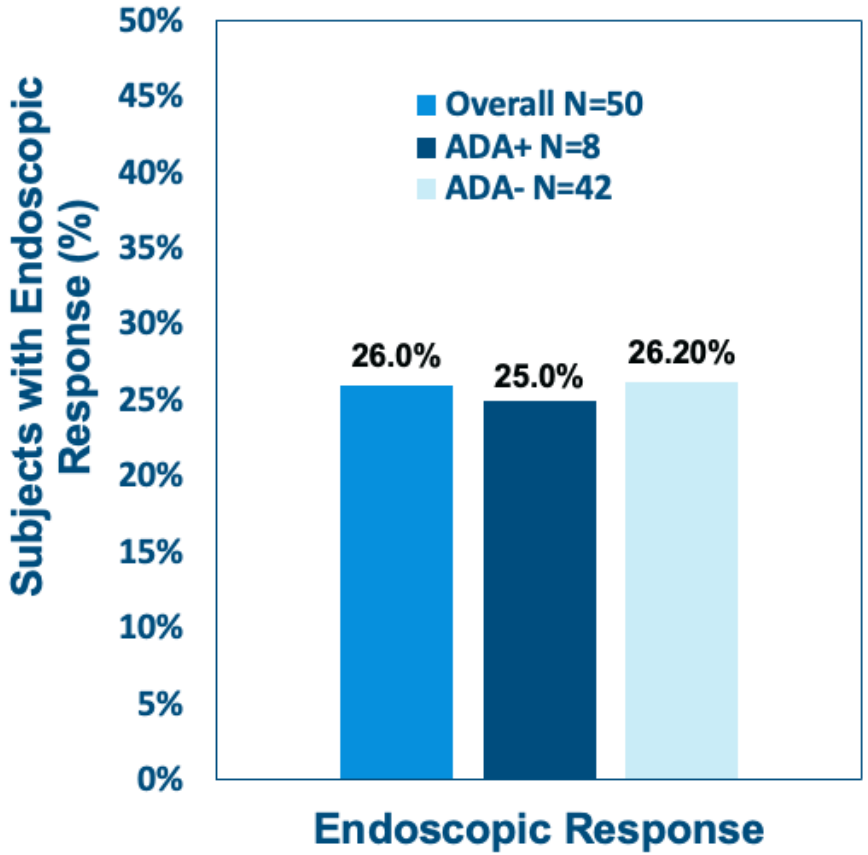
P-values (two-sided) were computed for the testing of the null hypothesis of 12% for endoscopic response in the per-protocol population (N=50) and 16% for clinical remission at Week 12 for the full analysis set (N=55); Endoscopic response was defined as reduction of SES-CD by ≥ 50% (pre-specified using data from the per protocol population [eligible participants who received at least 2/4 planned doses and had a final colonoscopy at Week 12]); Clinical remission was defined as CDAI ≤ 150 points (full analysis set).

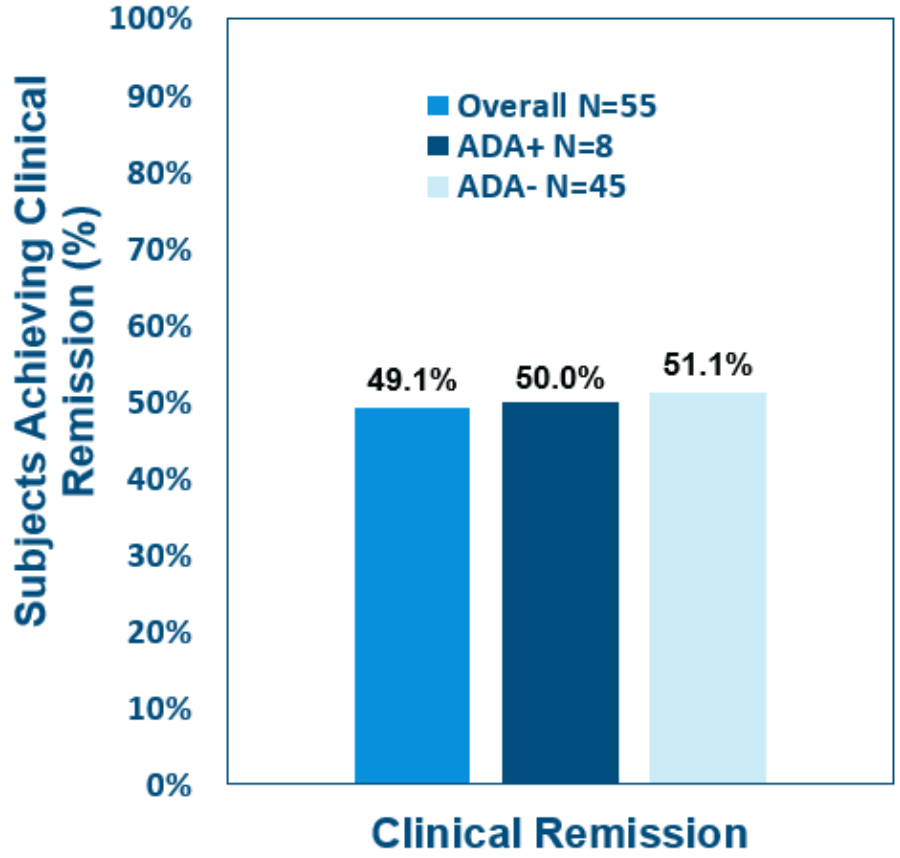
Endoscopic Response and Clinical Remission Rates in Biologic-Experienced Subjects at Week 12



N=36 for endoscopic response and 39 for clinical remission; Endoscopic response was defined as reduction of SES-CD by ≥ 50% (pre-specified using data from the per protocol population [eligible participants who received at least 2/4 planned doses and a final colonoscopy at Week 12]); Clinical remission was defined as CDAI ≤ 150 points (full analysis set).

Treatment Effects at Week 12 by Presence by Anti-Drug Antibody Status

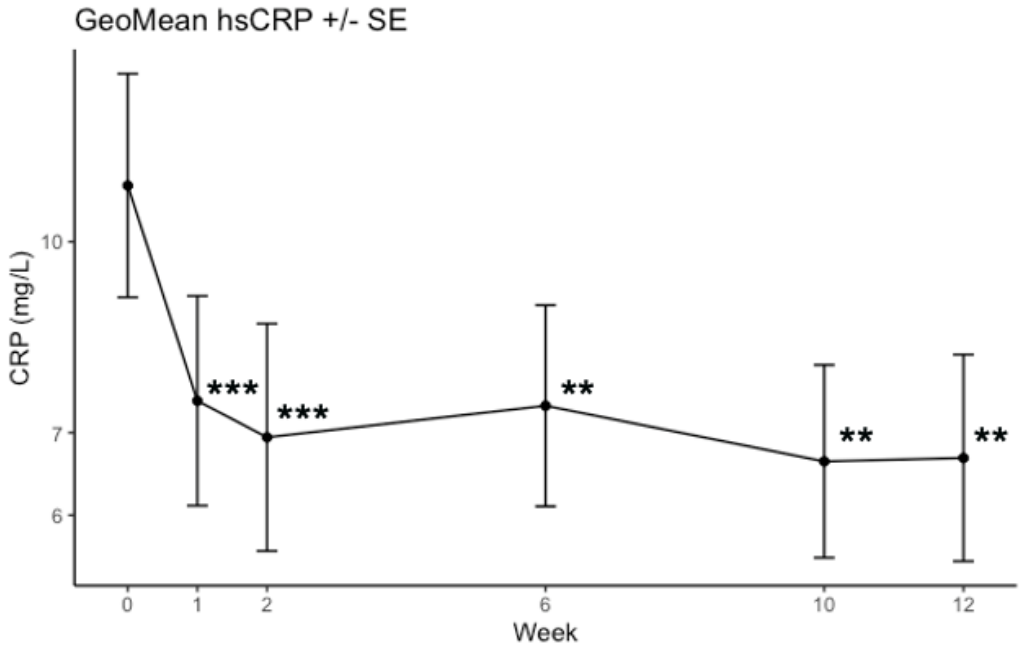




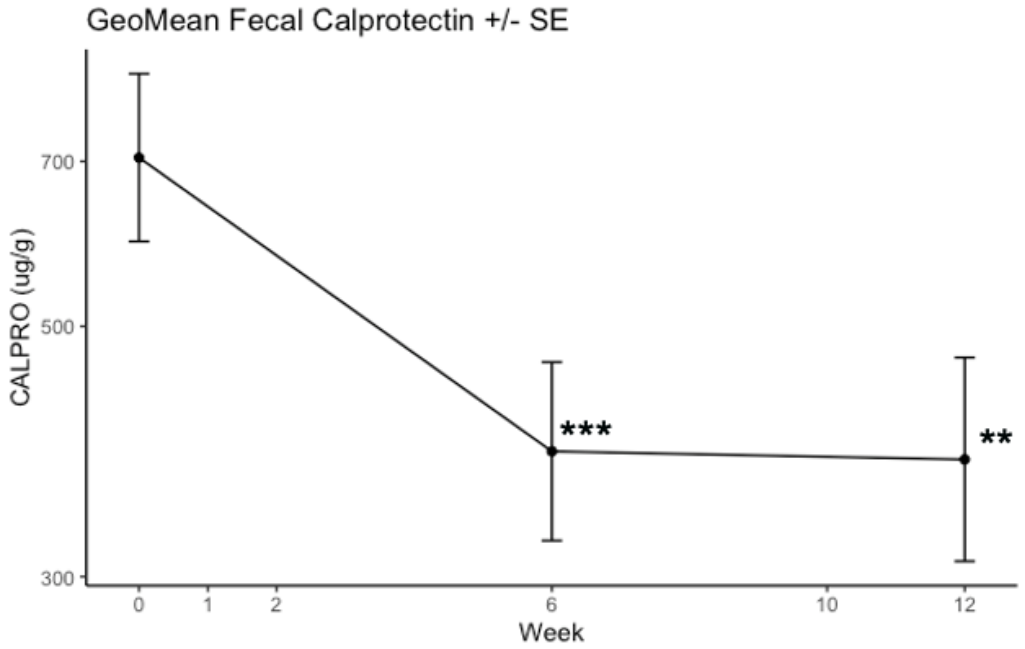
ADA: anti-drug antibody

Effect of PRA023 Treatment on Disease Surrogate Biomarkers

Change in hs-CRP Over Time

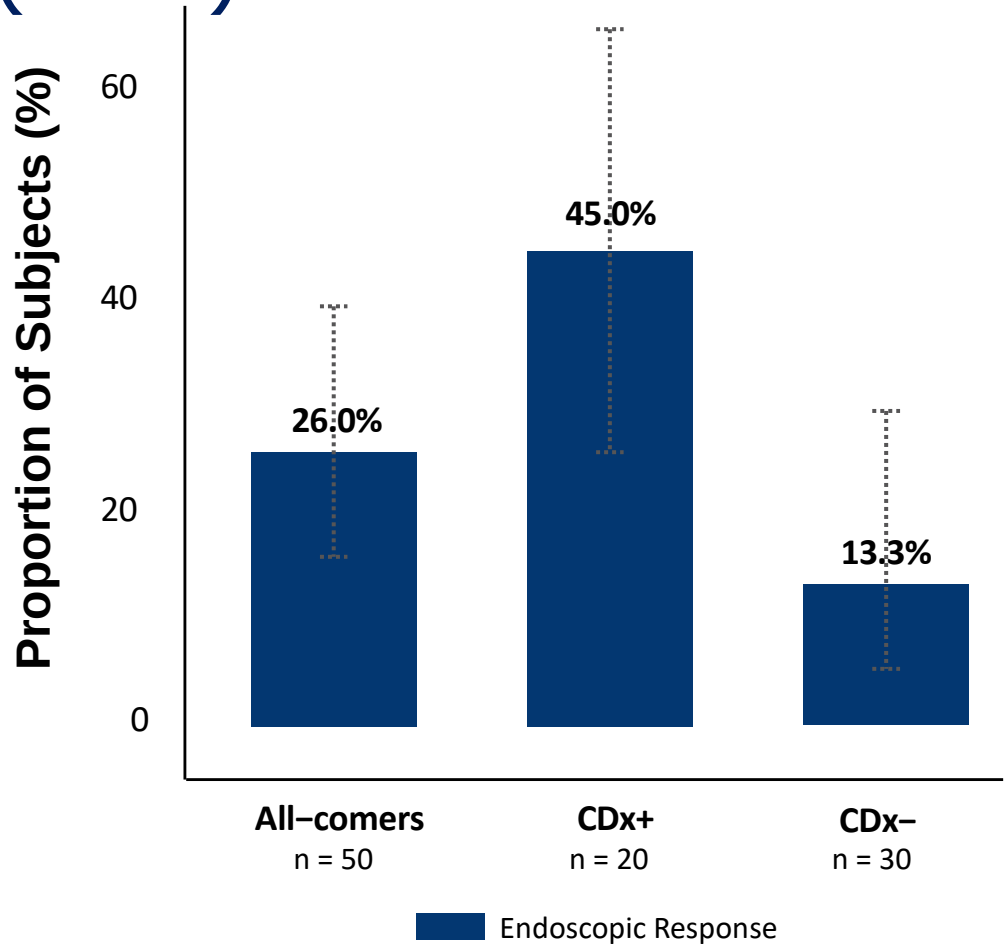


Change in Fecal Calprotectin Over Time



Nominal p-values, * p<0.05, ** p<0.01, ***p<0.001. Error bars depict Standard Error.

Endoscopic Response Treatment Effects in CDx+ Subjects with Alternative Algorithm for Companion Diagnostic (CDx)



Safety Summary

	All-causality TEAEs (N = 55)	Treatment-related TEAEs (N = 55)
Subjects with any AE	**43 (78.2%)**	**4 (7.3%)**
Subjects with any Serious AE(s)	**8 (14.5%)**	**0 (0%)**
Subjects with any Severe (Grade ≥ 3) AE(s)	**3 (5.5%)**	**0 (0%)**
Subjects with an AE Leading to Study Drug Discontinuation	**2 (3.6%)**	**0 (0%)**
Death	**0 (0%)**	**0 (0%)**
Subjects with any AE of Special Interest		
Acute Infusion Reaction*	**0 (0%)**	**0 (0%)**
Peri-Infusion Reaction^	**0 (0%)**	**0 (0%)**
Infection and Infestation	**25 (45.5%)**	**1 (1.8%)**

No clinically meaningful changes in ECG, vital signs, or laboratory values were noted.

TEAE: treatment-emergent adverse events
* Acute infusion reaction: events as defined by the MedDRA hypersensitivity SMQ occurring within 1 hour of completion of infusion.
^ Peri-infusion reaction: events as defined by the MedDRA hypersensitivity SMQ occurring within 24 hours of completion of infusion.

Most Common (>2 Subjects) Treatment-Emergent Adverse Events During Induction

Adverse Events, n (%)	PRA023 N = 55
COVID-19	**6 (10.9%)**
Urinary Tract Infection	**5 (9.1%)**
Crohn's disease	**5 (9.1%)**
Anemia	**4 (7.3%)**
Nasopharyngitis	**3 (5.5%)**
Fatigue	**3 (5.5%)**

Conclusions

- In APOLLO-CD, 12-week PRA023 induction treatment led to statistically significant improvements in clinical & endoscopic endpoints compared to historical placebo rates in subjects with moderately to severely active Crohn's disease.
  - Efficacy in biologic-experienced subjects consistent with overall population
  - Efficacy consistent across subgroups and irrespective of presence of ADA
  - Early, robust, and persistent reductions in disease surrogate biomarkers levels from baseline consistent with clinical & endoscopic observation
- Positive trend for enhanced endoscopic response and clinical remission rates using next generation CDx algorithm.
- PRA023 was well tolerated with no safety signal identified.
- Confirmatory studies planned to be initiated later this year