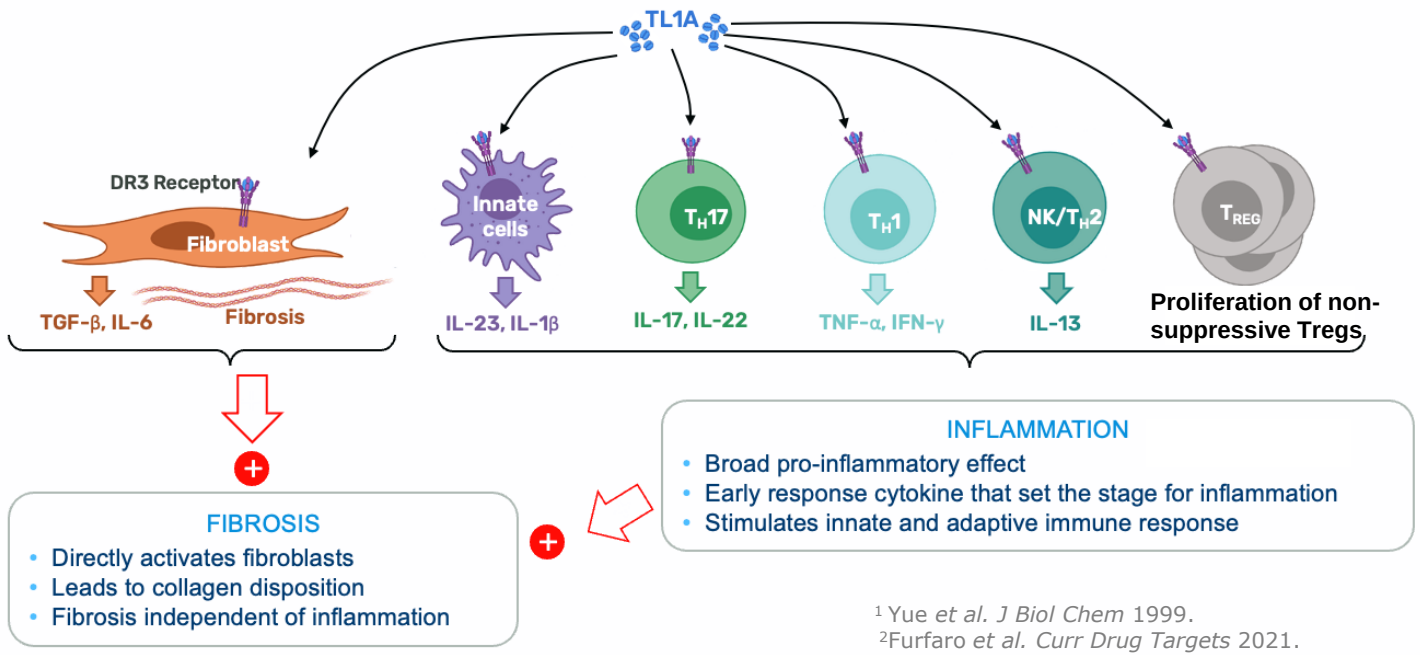
PRA023 Demonstrated Efficacy and Favorable Safety as Induction Therapy for Moderately to Severely Active UC: **Phase 2 ARTEMIS-UC Study Results**

Bruce E. Sands[1], Laurent Peyrin-Biroulet[2], Silvio Danese[3], David T. Rubin[4], Séverine Vermeire[5], Olivier Laurent[6], Allison Luo[6], Deanna D. Nguyen[6], JD Lu[6], Anna Wiechowska-Kozlowska[7], Jaroslaw Leszczyszyn[8], Radosław Kempiński[9], Jaroslaw Kierkus[10], Christopher Ma[11], Timothy E. Ritter[12], Brian G. Feagan[13], Stephan Targan[14]

[1]Icahn School of Medicine at Mount Sinai, New York, New York, USA; [2]Last Inserm U954 and CHU de Nancy, Lorraine University, Nancy, France; [3]Gastroenterology and Gastrointestinal Endoscopy Unit, IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milano, Italy; [4]University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, IL, USA; [5]University Hospitals Leuven, Department of Gastroenterology and Hepatology, Leuven, Belgium; [6]Prometheus Biosciences, Inc., San Diego, CA, USA; [7]Endoscopy Unit, SONOMED Medical Center, Szczecin, Poland; [8]Department of Gastroenterology, Melita Medical, Wroclaw, Poland; [9]Wroclaw Medical University, Department of Gastroenterology and Hepatology, Wroclaw, Poland; [10]Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, The Children's Memorial Health Institute, Warsaw, Poland; [11]Alimentiv Inc., London, ON, Canada Division of Gastroenterology & Hepatology, Department of Medicine and Community Health Sciences, University of Calgary, Calgary, AB, Canada; [12]GI Alliance, Southlake, Texas, USA; [13]Department of Medicine, Division of Gastroenterology, Western University, London, ON, Canada; [14]Division of Gastroenterology and Hepatology and F. Widjaja IBD Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA.

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



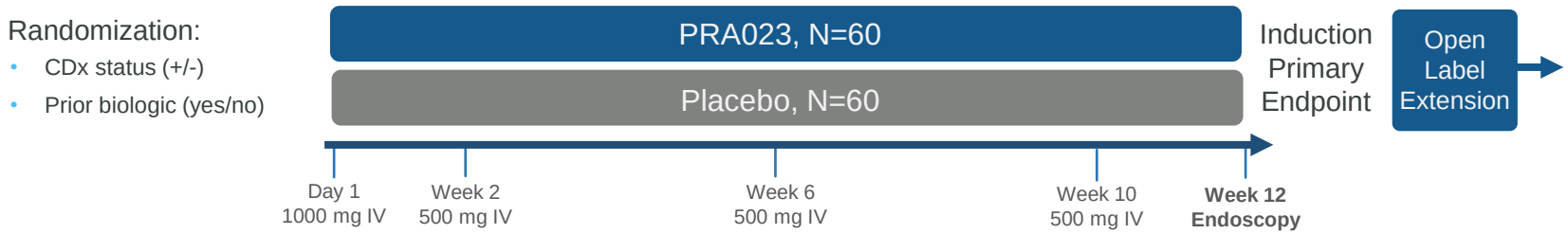
[1] Yue *et al. J Biol Chem* 1999.
[2] Furfaro *et al. Curr Drug Targets* 2021.
[3] Xu et *al. Front Immunol* 2022.
[4] Barrett *et al. Am J Pathol* 2012.
[5] Takedatsu *et al. Gastroenterol* 2008.
[6] Shih *et al. Muc Immunol* 2014.
[7] Yamazaki *et al. Hum Mol Genet* 2005.
[8] Jostins *et al. Nature*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

ARTEMIS-UC Phase 2 Study Design

Cohort 1 to Demonstrate Efficacy of PRA023

Inclusion Criteria:

- Moderately to severely active UC (modified Mayo Score 4-9)
- No/insufficient response, loss of response, and/or intolerance to conventional or advanced therapies
- Permitted prior medications
  - ≤ 4 approved advanced therapies (biologics & small molecule)
  - ≤ 3 classes of advanced therapies



Primary Endpoint:

- Clinical remission at Week 12 defined by Modified Mayo Score

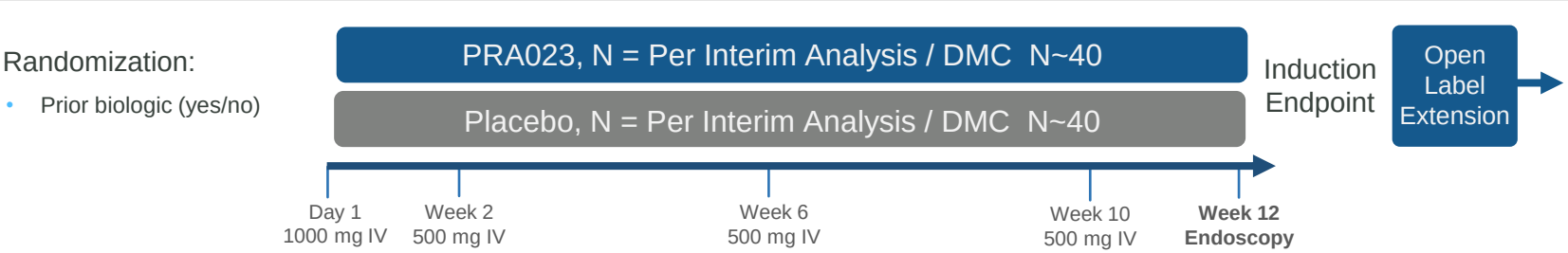
Secondary Endpoints (α-controlled):

- Endoscopic improvement
- Clinical response
- Symptomatic remission
- Mucosal Healing
- Histologic improvement
- Histologic-endoscopic mucosal improvement
- IBDQ response

Cohort 2 Expansion to Enrich for CDx+ (includes CDx+ from initial cohort)

Inclusion Criteria:

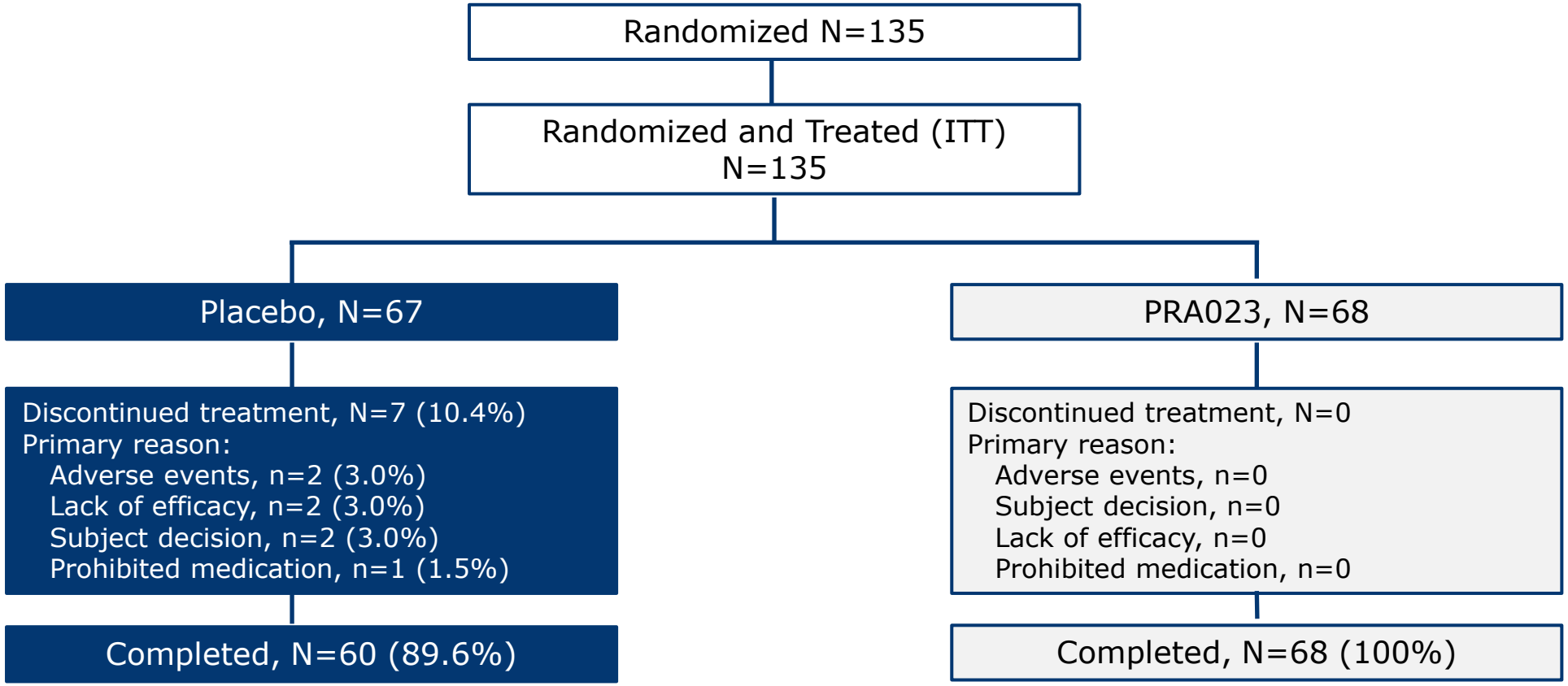
- As in Cohort 1
- Must also be CDx+



CDx: companion diagnostic

Expansion Cohort enrollment completed

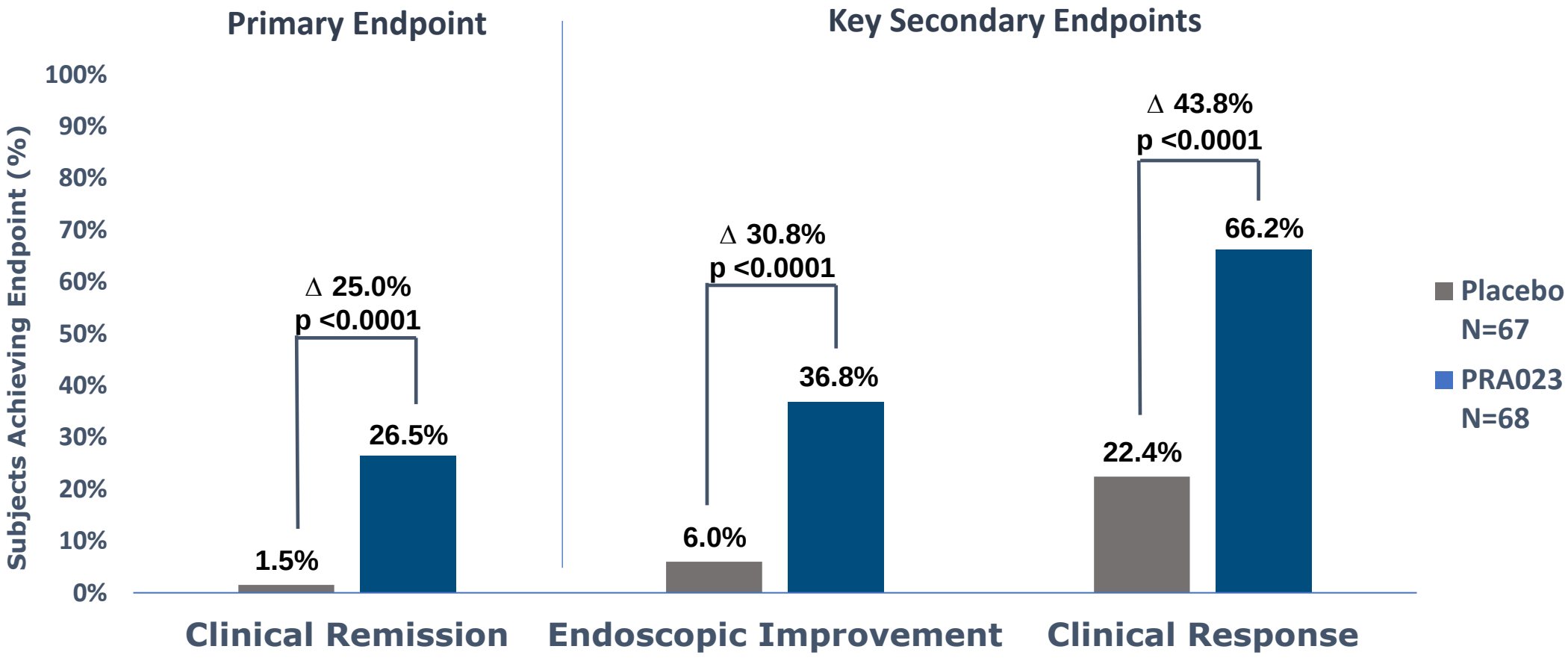
Subject Disposition: Cohort 1



Baseline Disease Characteristics and Demographics

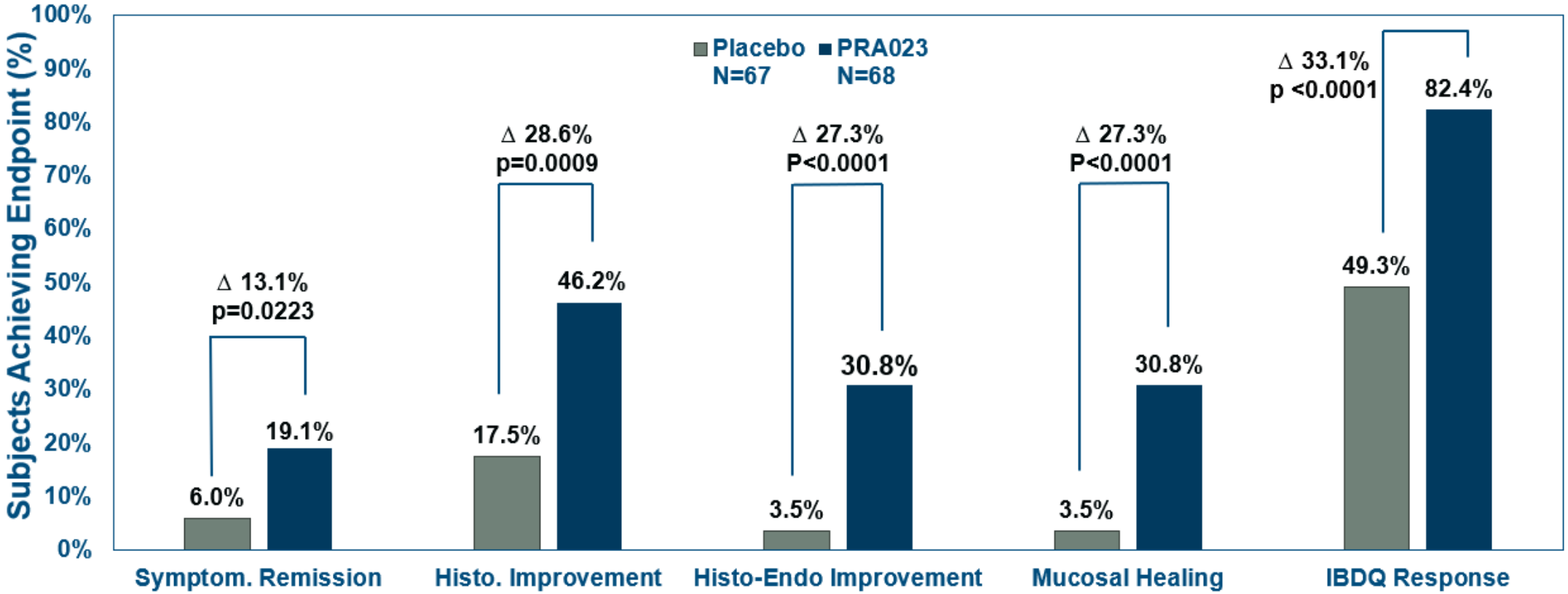
	Placebo (N = 67)	PRA023 (N = 68)	Overall (N = 135)
Age, years, mean (SD)	42.2 (16.3)	40.4 (14.4)	41.3 (15.3)
Female, n (%)	29 (43%)	34 (50%)	63 (47%)
Weight, kg, mean (SD)	77 (18.5)	74 (19.7)	75 (19.1)
Geographic region, n (%)			
Eastern Europe	39 (58%)	39 (57%)	78 (58%)
North America	17 (25%)	20 (29%)	37 (27%)
Western Europe	8 (12%)	7 (10%)	15 (11%)
Australia	3 (4%)	2 (3%)	5 (4%)
Duration of disease, years, mean (SD)	6.3 (6.2)	6.7 (6.4)	6.5 (6.3)
Extent of disease, n (%)			
Proctosigmoiditis	7 (10%)	2 (3%)	9 (7%)
Left-sided colitis	28 (42%)	35 (51%)	63 (47%)
Pancolitis	32 (48%)	31 (46%)	63 (47%)
Modified Mayo Score (mMS), mean (SD)	7.1 (1.1)	6.9 (1.2)	7.0 (1.2)
Mayo Endoscopy Subscore (MES), n (%)			
2	14 (21%)	22 (32%)	36 (27%)
3	**53 (79%)**	**46 (68%)**	99 (73%)
Concomitant immunomodulator use, n (%)	11 (16%)	7 (10%)	18 (13%)
Concomitant corticosteroid use, n (%)	39 (58%)	35 (52%)	74 (55%)
Number of prior advanced therapies exposed, n (%)			
0	35 (52%)	36 (53%)	71 (53%)
1	8 (12%)	12 (18%)	20 (15%)
2	12 (18%)	14 (21%)	26 (19%)
≥3	**12 (18%)**	**6 (9%)**	**18 (13%)**

Primary and Key Secondary Endpoints with PRA023 Treatment Compared to Placebo at Week 12



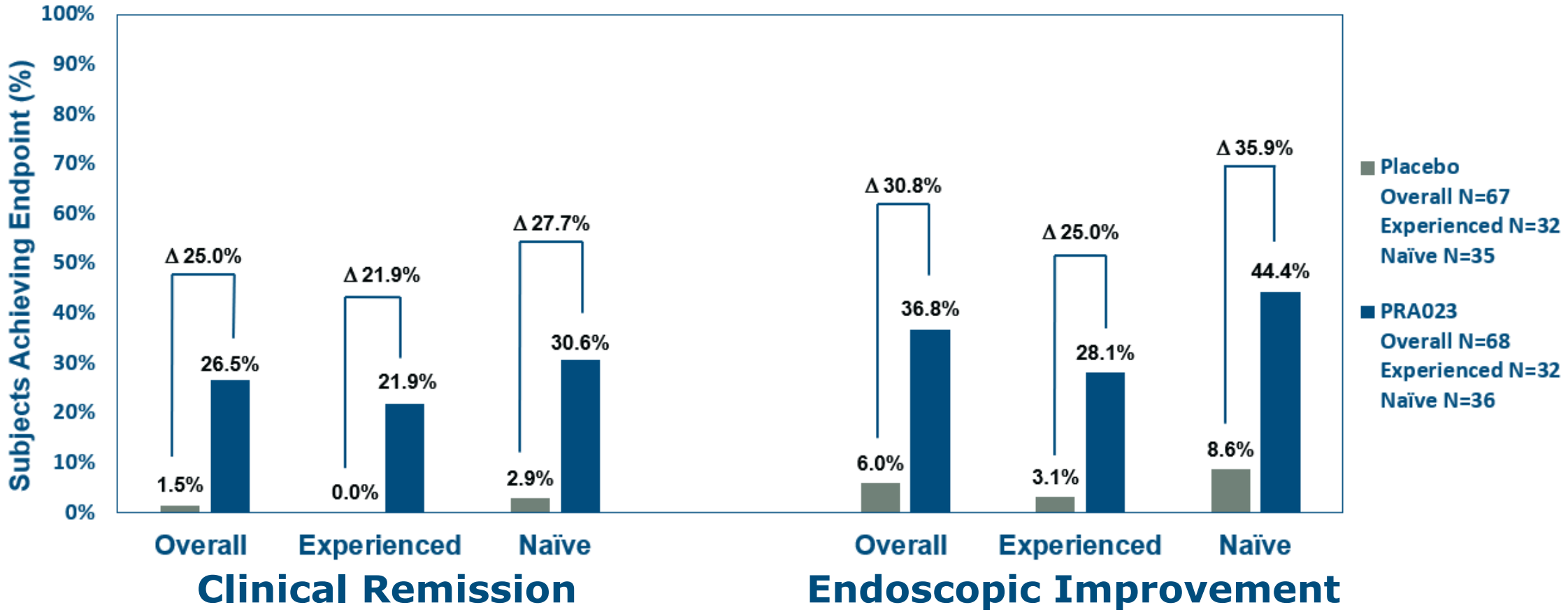
Clinical remission per mMS is defined as endoscopic subscore of 0 or 1, rectal bleeding subscore of 0, and stool frequency subscore of 0 or 1 and not greater than Baseline; Endoscopic improvement is defined as endoscopy subscore ≤ 1 with no friability; Clinical response per mMS is defined as reduction from Baseline ≥ 2 points and ≥ 30% in 3-component Modified Mayo Score, accompanied by a reduction ≥ 1 in rectal bleeding subscore or absolute rectal bleeding subscore ≤ 1. P-values for testing the treatment difference are based on Cochran-Mantel-Haenszel test adjusted for prior biologic exposure status and CDx status. All endpoints are statistically significant according to multiplicity controlled 2-sided alpha of 0.05.

Additional Secondary Endpoints at Week 12



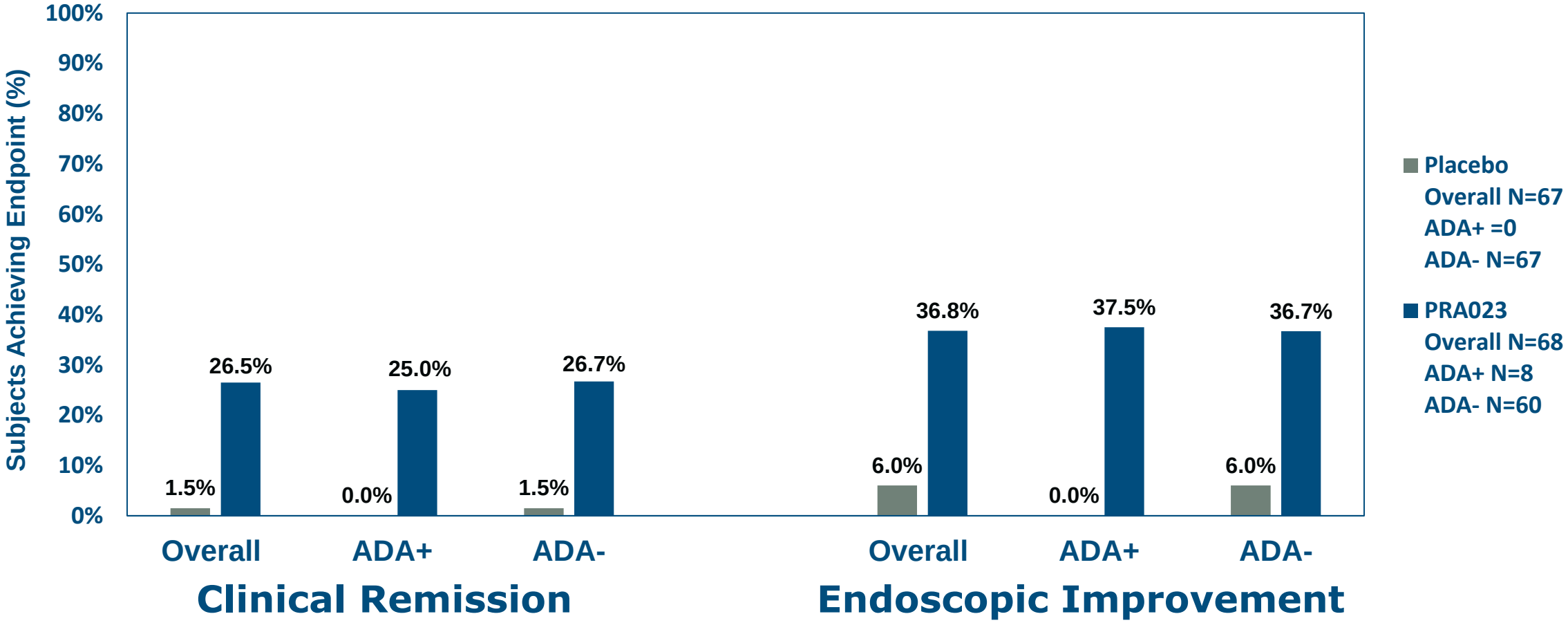
Symptomatic remission is defined as stool frequency subscore of 0 and rectal bleeding subscore of 0; Histologic improvement is defined as Geboes score ≤ 3.1; Histologic-endoscopic mucosal improvement is defined as Geboes score ≤ 3.1 and endoscopy subscore ≤ 1; Mucosal healing is defined as Geboes score ≤ 2B.1 and endoscopy subscore ≤ 1; IBD response is defined as IBD score increase of ≥ 16 points from Baseline. P-values for testing the treatment difference are based on Cochran-Mantel-Haenszel test adjusted for prior biologic exposure status and CDx status. All endpoints are statistically significant according to multiplicity controlled 2-sided alpha of 0.05. For histology endpoints: n=57 for placebo and n-65 for PRA023; final analysis of histology data includes mapping to raw histology scores of '0' when "Segment image(s) contains entirely normal mucosa" was indicated by the central readers.

Clinical Remission and Endoscopic Improvement Rates at Week 12 in Advanced Therapy-Experienced and Naïve Subgroups



Clinical remission per mMS is defined as endoscopic subscore of 0 or 1, rectal bleeding subscore of 0, and stool frequency subscore of 0 or 1 and not greater than Baseline; Endoscopic improvement is defined as endoscopy subscore ≤ 1 with no friability; Advanced therapy-experienced includes prior exposure to approved biologics, S1P1 modulators, and/or JAK inhibitors.

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



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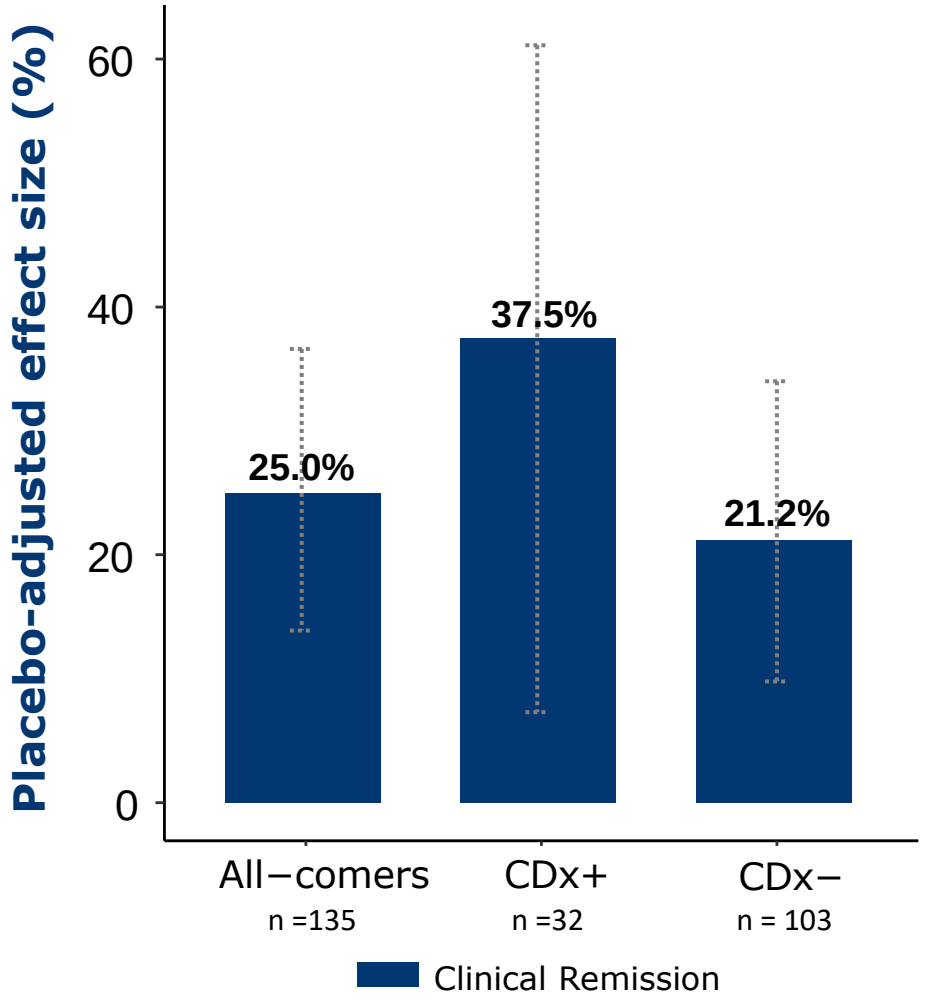
Interim Analysis of the CDx+ Subgroup



ARTEMIS-UC CDx Expansion Cohort continues to enroll

Safety Summary

Treatment Emergent Adverse Events, n (%)	Placebo N = 67	PRA023 N = 68
Subjects with any AE (n, %)	27 (40.3%)	28 (41.2%)
Subjects with any Severe (Grade ≥ 3) AE	3 (4.5%)	0
Subjects with any Drug-Related AE	1 (1.5%)	3 (4.4%)@
Subjects with an AE Leading to Study Drug Discontinuation	3 (4.5%)	0
Subjects with any SAE	5 (7.5%)	0
Subjects with any Drug-Related SAE	0	0
Death	0	0
Subject with any AE of Special Interest	12 (17.9%)	10 (14.7%)
Acute Infusion Reaction*	0	0
Peri-Infusion Reaction^	1 (1.5)	0
Infection and Infestation	11 (16.4%)	10 (14.7%)

Database lock when all subjects completed Week 12 or early terminated during the Induction Period. * 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 hour of completion of infusion | @ All mild to moderate AEs; all resolved as study drug continued

Most Common (>2 Subjects in Any Group) Treatment-Emergent Adverse Events

Adverse Events, n (%)	Placebo N = 67	PRA023 N = 68
COVID-19	3 (4.5%)	5 (7.4%)
Upper respiratory tract infection	3 (4.5%)	1 (1.5%)
Headache	3 (4.5%)	3 (4.4%)
Colitis ulcerative	6 (9.0%)	1 (1.5%)

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

Conclusions

- In ARTEMIS-UC, 12 weeks of PRA023 induction treatment led to **statistically significant increases** in clinical remission, endoscopic improvement, mucosal healing, and patient-reported outcome measures compared to placebo in subjects with moderately to severely active UC
  - Efficacy was consistent across subgroups and irrespective of presence of ADA
- **All** ranked secondary **endpoints** for Cohort 1 were **met**
- Interim analysis indicated **positive trend** for enhanced treatment effects in CDx+ subjects.
- PRA023 was well tolerated with no safety signal identified
- Limitations: small sample size and short treatment duration
- Phase 3 study to be initiated later this year to confirm findings