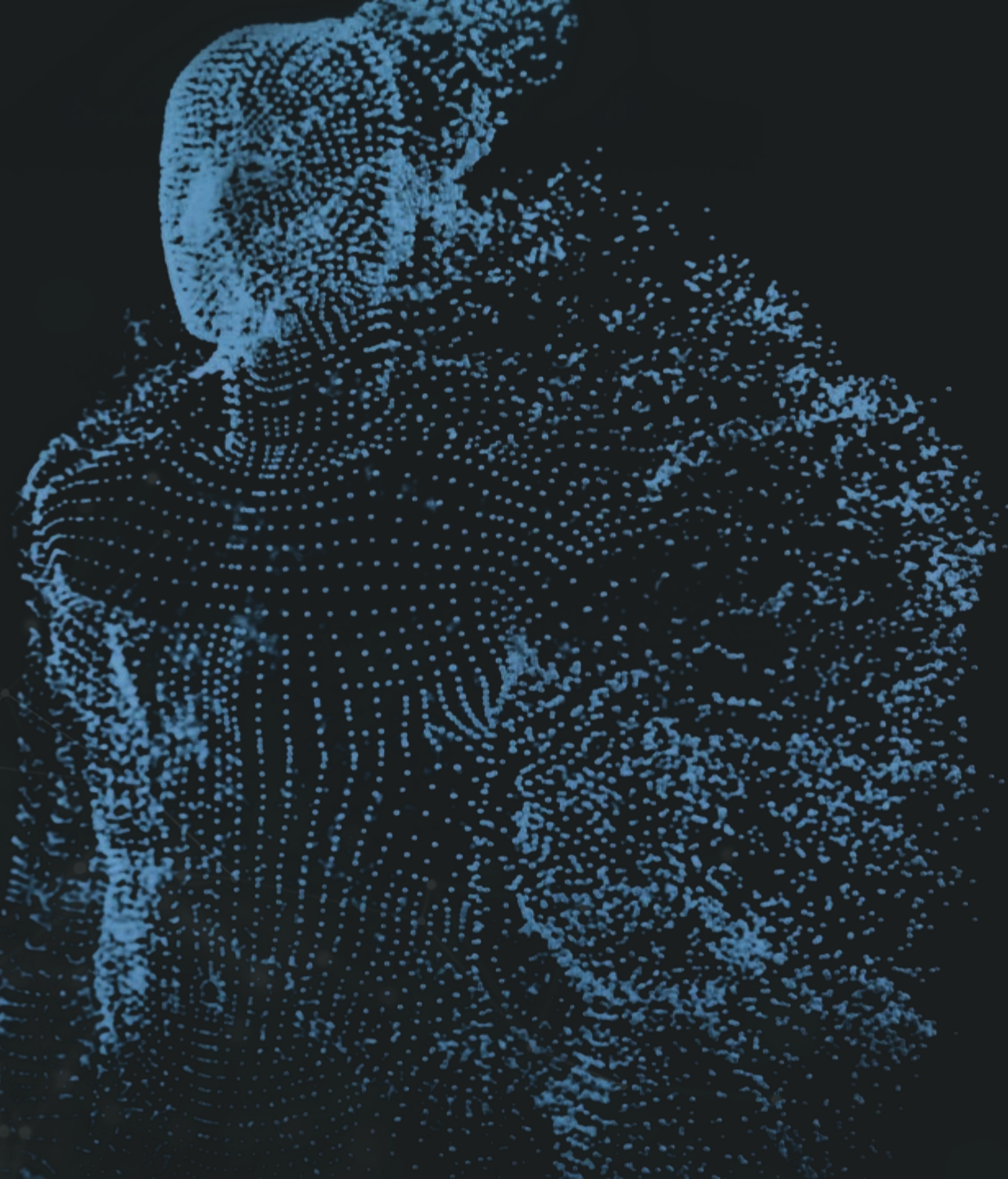
Prometheus Biosciences

Revolutionizing immunology with precision.



March 2023

Disclaimer: Forward Looking Statements & Market Data

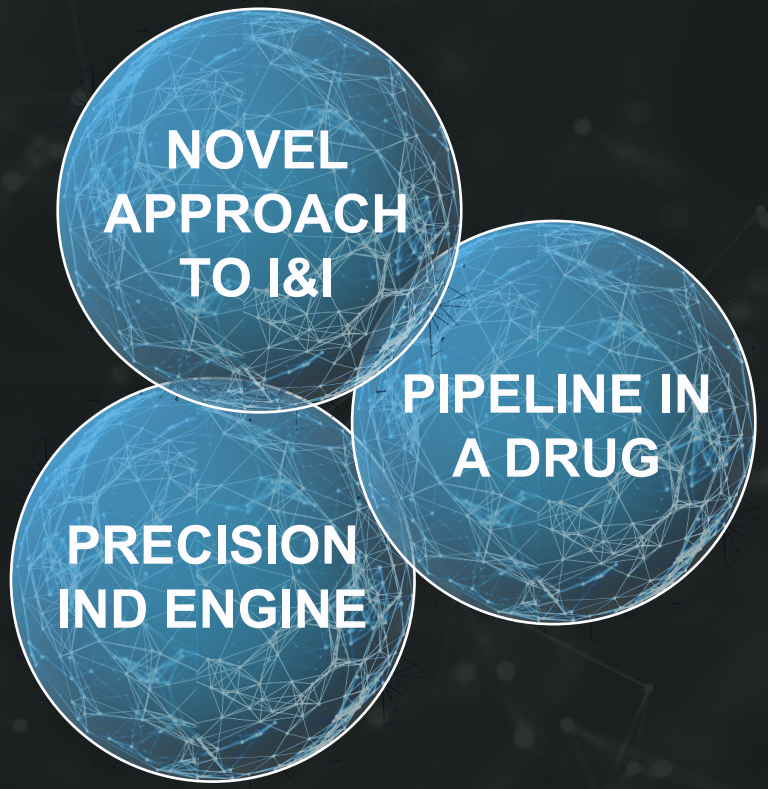
We caution you that this presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, including statements regarding our future results of operations and financial position, business strategy, research and development plans, the anticipated timing, costs, design and conduct of our ongoing and planned preclinical studies and clinical trials for our product candidates and diagnostics, the potential of PRA023 to improve IBD treatment and to be both a first-in-class and best-in-class anti-TL1A mAb, the timing of results from Cohort 2 of the ARTEMIS-UC trial, plans to advance PRA023 into registrational studies in UC and CD and the timing thereof, as well as plans to use an alternative algorithm in our diagnostic candidate for CD, the timing of results from the ATHENA-SSc trial, as well as the timing to announce a fourth indication for PRA023 and the potential future revenue from such additional indications, the timing of our Phase 1 clinical trial of PRA052, our ability to advance new INDs and the timing thereof, the potential benefits from our current or future collaboration arrangements with third parties, the timing and likelihood of success, prospective products, product approvals, plans and objectives of management for future operations, and future results of anticipated product development efforts, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions. The inclusion of forward-looking statements should not be regarded as a representation by us that any of our plans will be achieved.

Actual results may differ from those set forth in this presentation due to the risks and uncertainties inherent in our business, including, without limitation: topline results we report are based on preliminary analysis of key efficacy and safety data, and such data may change following a more comprehensive review of the data related to the clinical trial and such topline data may not accurately reflect the complete results of a clinical trial; our approach to the discovery and development of precision medicines based on Prometheus360 is unproven; interim results of a clinical trial, such as with cohort 1 analysis our our diagnostic candidate, do not predict final results and the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, as follow-up on the outcome of any particular patient continues and as more patient data become available; potential delays in the commencement, enrollment and completion of clinical trials and preclinical studies; the results of clinical trials are not necessarily predictive of future results; our dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; our ability to develop companion or complementary diagnostics for our therapeutic product candidates; unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval and/or commercialization, or may result in recalls or product liability claims; planned future trials of PRA023 may not support regulatory registration; regulatory developments in the United States and foreign countries; our ability to maintain undisrupted business operations due to the COVID-19 pandemic, including delaying or otherwise disrupting its preclinical studies, clinical trials, manufacturing and supply chain, and other risks described in our filings with the SEC, including under the heading “Risk Factors” in our Form 10-K filed with the SEC on February 28, 2023 and any subsequent filings with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

This presentation also includes data, results and attributes from PRA023, Roivant/Pfizer’s product candidate, and other approved therapies, which are generated from separate, independent studies and do not come from head-to-head analysis. Differences exist between study or trial designs and subject characteristics, and caution should be exercised when comparing data across studies. Data from Roivant/Pfizer’s product candidate is based on information publicly disclosed by Roivant/Pfizer and certain preclinical results and attributes are based on our own internal experiments.

Pioneering Precision Medicine in Immunology, Beginning with IBD



Novel precision medicine approach to immune-mediated diseases, starting with IBD

Powered by Prometheus360™ Platform, one of world's largest precision GI biobanks

Lead Rx candidate PRA023 with unique dual anti-inflammatory & anti-fibrotic MOA

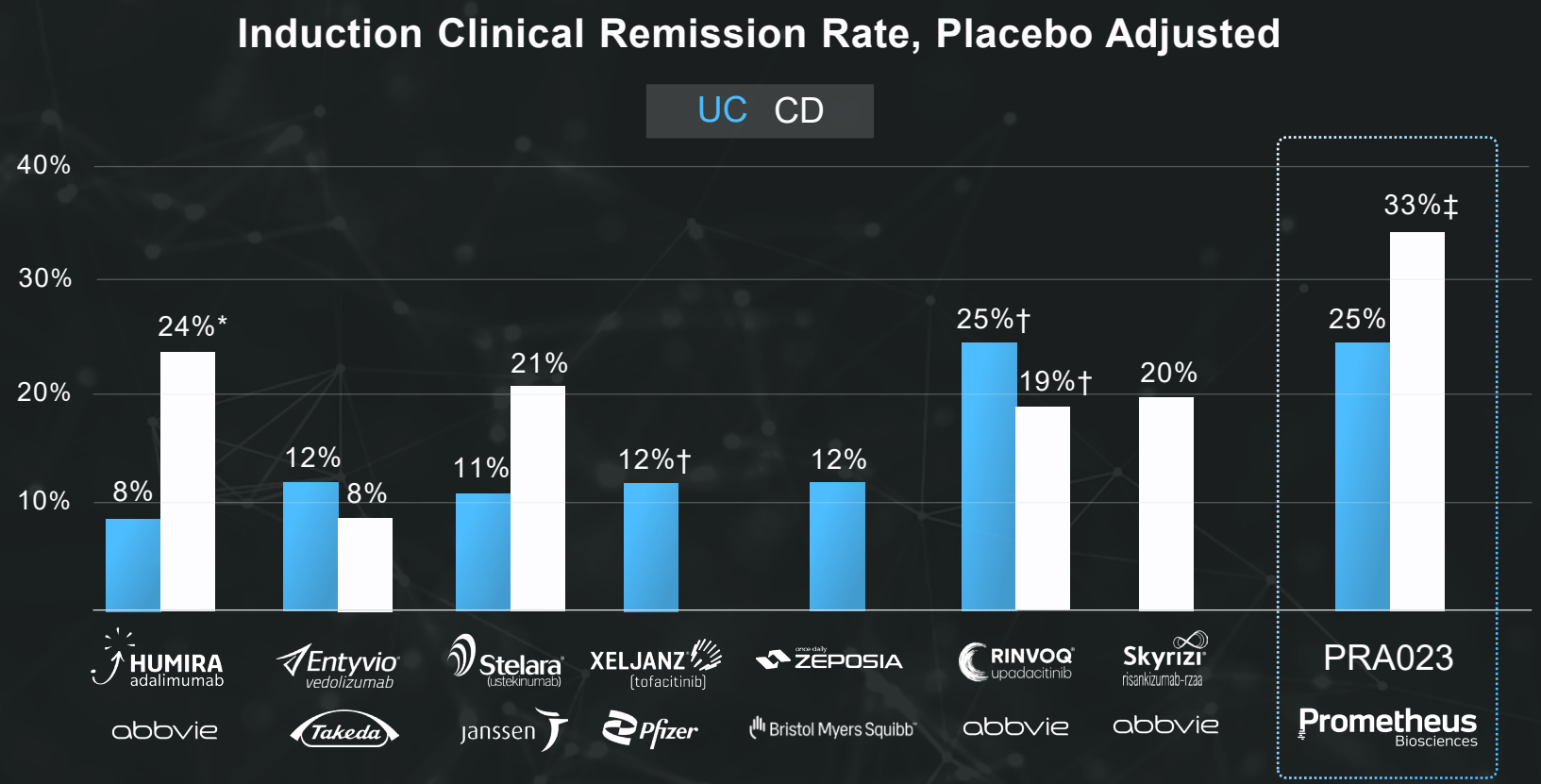
PRA023 showed class-leading Ph2 data in UC & CD; registrational studies begin 2023

Pipeline-in-a-drug potential via indication expansion; Ph2 SSc-ILD data expected 1H24

Second program PRA052 targeting CD30L in Phase 1; results expected 4Q23

Prometheus360™ IND engine equipped to produce a new IND every 12-18 months

PRA023 Phase 2 Results Demonstrate Potential for Best-in-Class Efficacy & Safety in IBD



- Uniquely favorable combination of efficacy *and* safety in UC & CD
- Induction efficacy comparable or superior to leading approved agents
- Safety profile comparable to safest approved agents with no Phase 2 safety signal observed

Source: Study publications | * Tested in largely biologic-naïve patients, which can inflate efficacy numbers | † JAK inhibitor class has a black box warning for risk of fatal cardiovascular events | ‡ Ph 2a APOLLO-CD study was open label, so the absolute clinical remission rate of 49.1% was adjusted using a historical placebo rate of 16% to yield a 33% delta a | Figures reflect cross-trial comparison and not results from a head-tohead study. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies. Data for comparators come from respective Phase 3 studies.

Prometheus360™ Powers Target Discovery and Dx Development

Our uniquely robust dataset and machine learning approaches enable us to link genetics to biology for precision drug discovery and patient stratification

UNMATCHED DATA ASSETS ENABLING NOVEL INSIGHTS

Our data platform builds on the IBD biobank our partners at **Cedars Sinai** have created over the past 20+ years

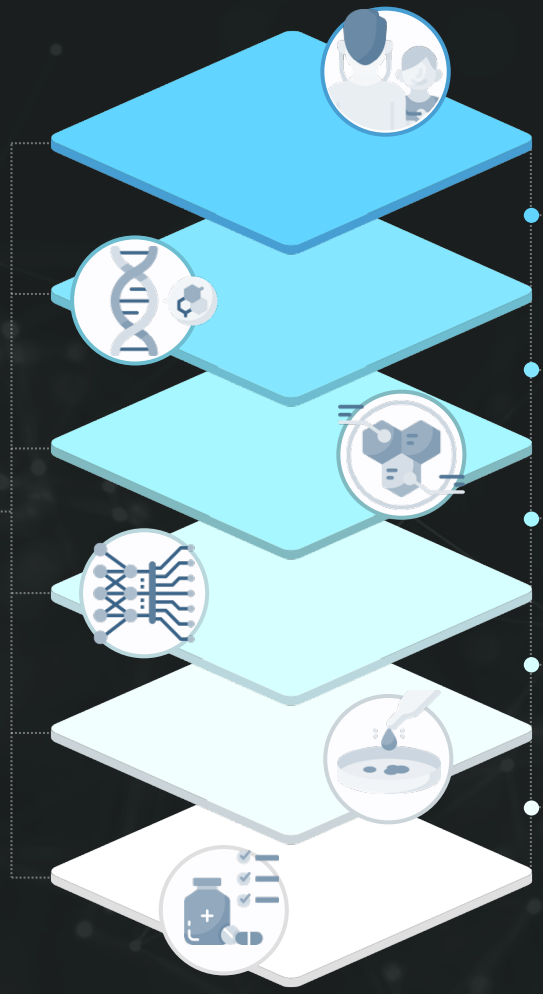
> 20,000 Patients

> 200,000 Specimens

Multimodal Analyses

Clinical Metadata

Longitudinal Insights



CLINICAL INSIGHTS

Clinical Metadata • Historical Rx Response Pathway Effects • Novel Mechanisms

GENETIC ANALYTICS

Phenotypic/Genomic Association • Disease Stratification • Mechanistic Interpretation

MULTIOMICS INSIGHTS

Single cell & bulk RNA-seq • Transcriptomics Deconvolution • Proteomics • Metabolomics

MACHINE LEARNING

Supervised & Unsupervised Learning Bayesian Modeling • Feature Encoding

FUNCTIONAL VALIDATION

Tissue Explants • Druggability • in vitro and in vivo Pharmacology • De-risking

Novel therapeutic target discovery

Higher probability of clinical success

Rx

BETTER MEDICINES
BETTER MATCHING
BETTER OUTCOMES

Dx

Predictive SNPs linking genetics & biology

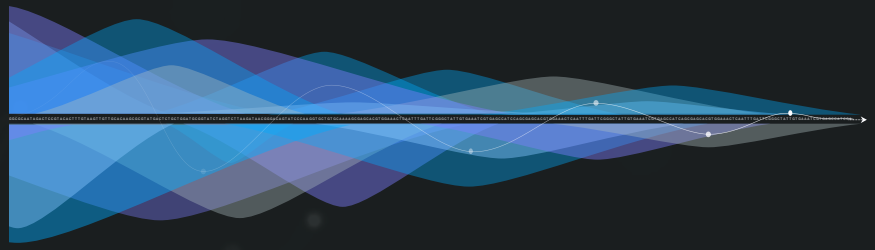
Tested on hundreds of patient samples

Genetics-based Precision Medicine Increases Probability of Success

Prometheus uses large multi-modal datasets to power target selection and co-diagnostic development

DECODE THE GENETICS OF INFLAMMATORY DISEASES

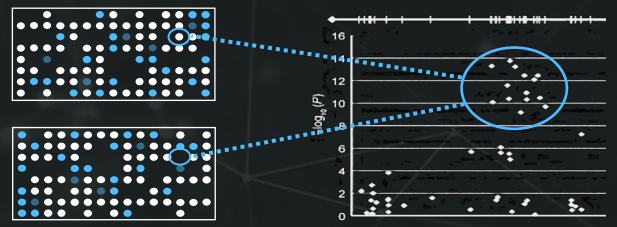
We use ML and AI to identify the patterns that connect genetics to clinical phenotypes and tissue dysfunction



DISEASE DRIVERS

RISK ALLELES

SELECT THE RIGHT TARGETS



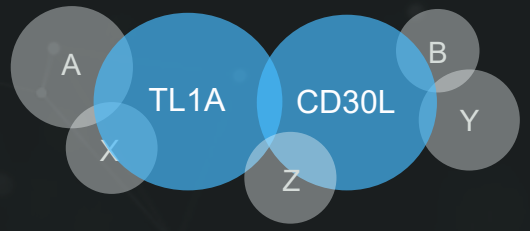
Targets genetically associated with diseases have a higher probability of clinical success[1]

Risk alleles connecting targets and disease provide the starting point for co-diagnostic genetic assays

SELECT THE RIGHT PATIENTS

Genetic risk signatures are validated using multiple functional genomic approaches and converted into co-diagnostic assays

Co-diagnostic selects patients with an increased chance of responding to a specific drug



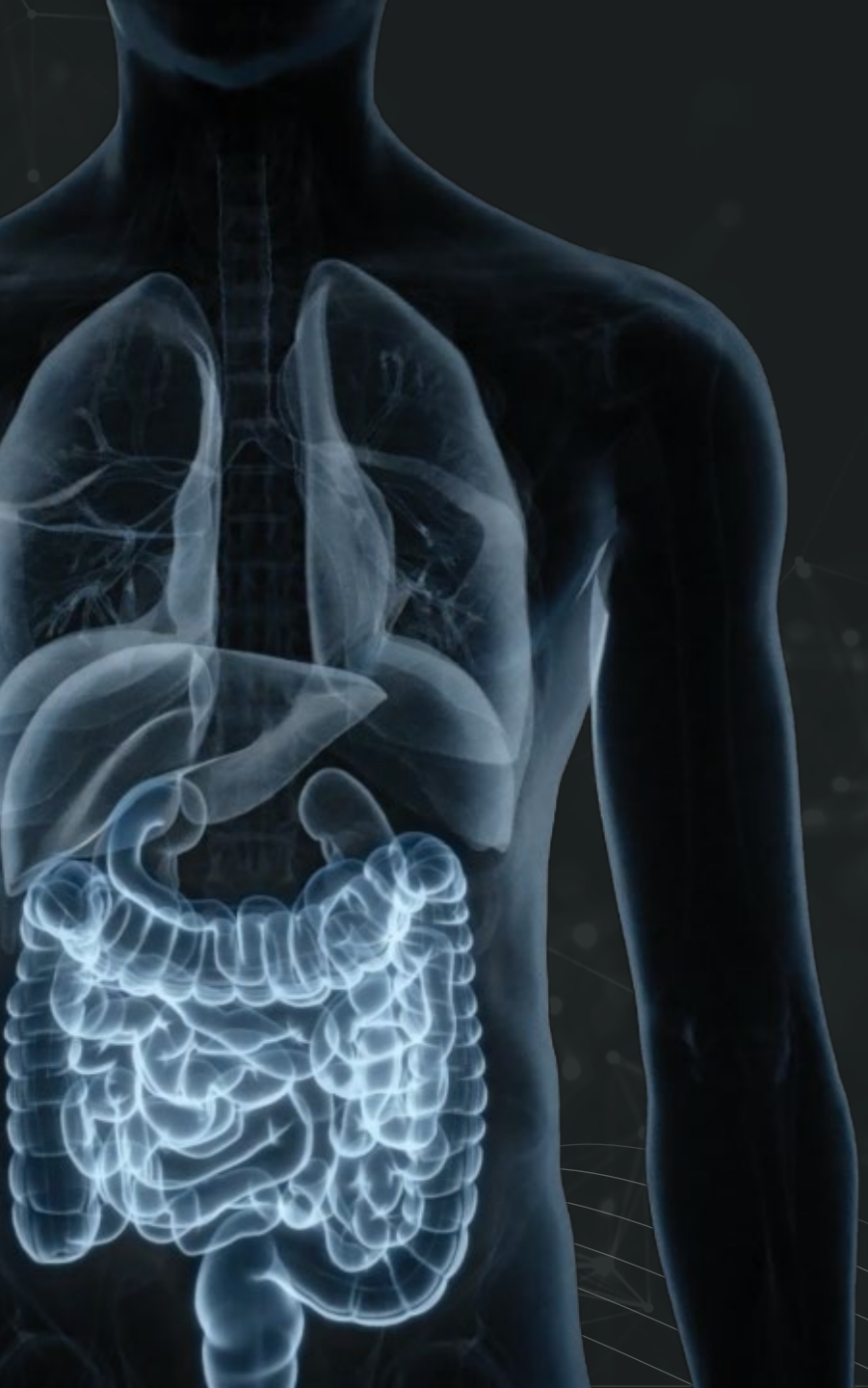
1. King *et al.* Plos Genet. 2019.

Building the Premier Pipeline for Immune-Mediated Diseases

PROGRAM	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	ANTICIPATED MILESTONES
PRA023 *TL1A mAb*	Ulcerative colitis					Phase 3 to begin 2023
	Crohn's disease					Phase 3 to begin 2023
	SSc-ILD					Phase 2 results expected 1H 2024
PRA052* *CD30 ligand mAb*	Immune-mediated disease*					Phase 1 NHV results expected Q4 2023
PR1100 *cytokine receptor mAb*	Immune-mediated disease					IND expected Q4 2023
PR2100 *inflammatory cytokine mAb*	Immune-mediated disease					IND expected 2024
PR300 *GPCR small molecule*	Immune-mediated disease					

Additional undisclosed target candidates from our precision platform Prometheus360™ are under active investigation

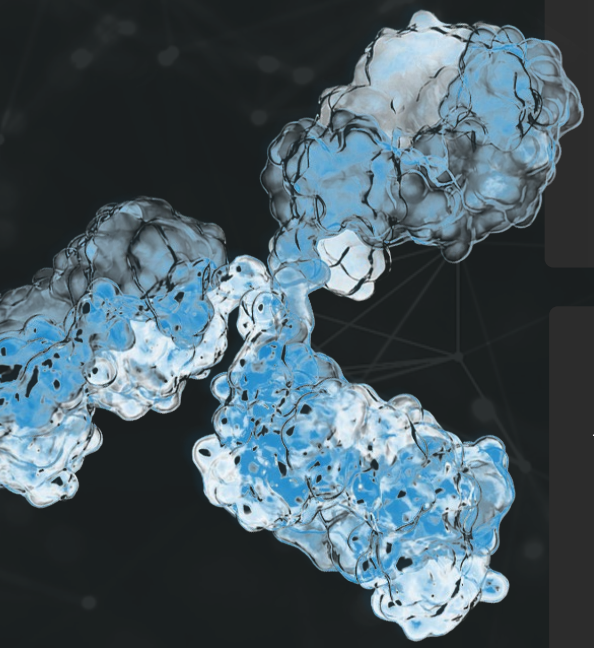
PRA052 partnered with Dr. Falk Pharma in Europe, Australia and New Zealand



Lead Product Candidate PRA023

Precision Targeting of TL1A to Address Inflammation & Fibrosis

PRA023: Potential Best-In-Class & First-in-Class TL1A Antibody



TL1A: A Compelling Novel IBD Target

TL1A discovered by Prometheus founder Dr. Stephan Targan; 300+ peer-reviewed publications linking TL1A to immune & fibrotic diseases; strong genetic association to IBD

Unique dual anti-inflammatory & anti-fibrotic mechanism creates pipeline-in-a-drug opportunity

Positive Phase 2 Studies in Both UC & CD

Anti-TL1A mAb PRA023 demonstrated category-leading safety and efficacy in Phase 2 studies in UC & CD

Phase 3 studies in ulcerative colitis and Crohn's disease expected to begin in 2023

Commercial Strategy Provides Optionality

Intended label for all-comer IBD population

Registrational studies to assess differential effect in Dx subgroups

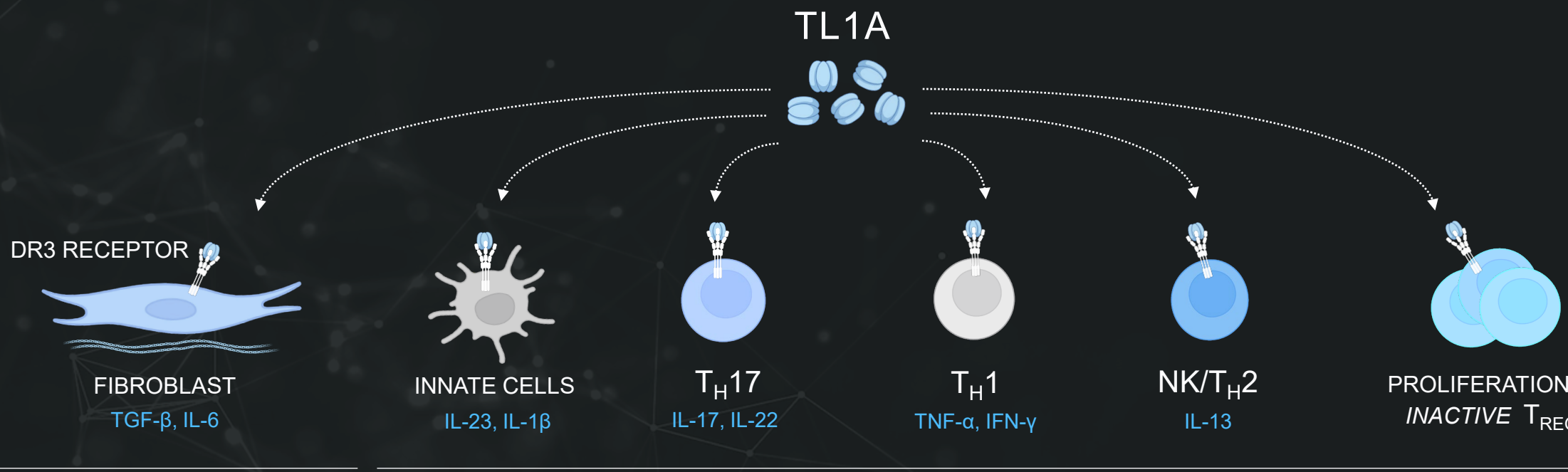
Differential efficacy could provide pathway to premium pricing

Broad PRA023 Patent Coverage into 2043+

3 issued US patents covering PRA023 mAb through 2041+ (including estimated patent term extension); 1 Issued US patent covering PRA023 Dx through 2040+

Several pending patent applications covering PRA023 formulation, dosing, Dx, and new indications into 2043+

TL1A Independently Mediates Both Inflammation and Fibrosis



FIBROSIS

TL1A directly activates fibroblasts

This leads to collagen disposition and fibrosis independent of inflammation

INFLAMMATION

TL1A has a broad pro-inflammatory effect

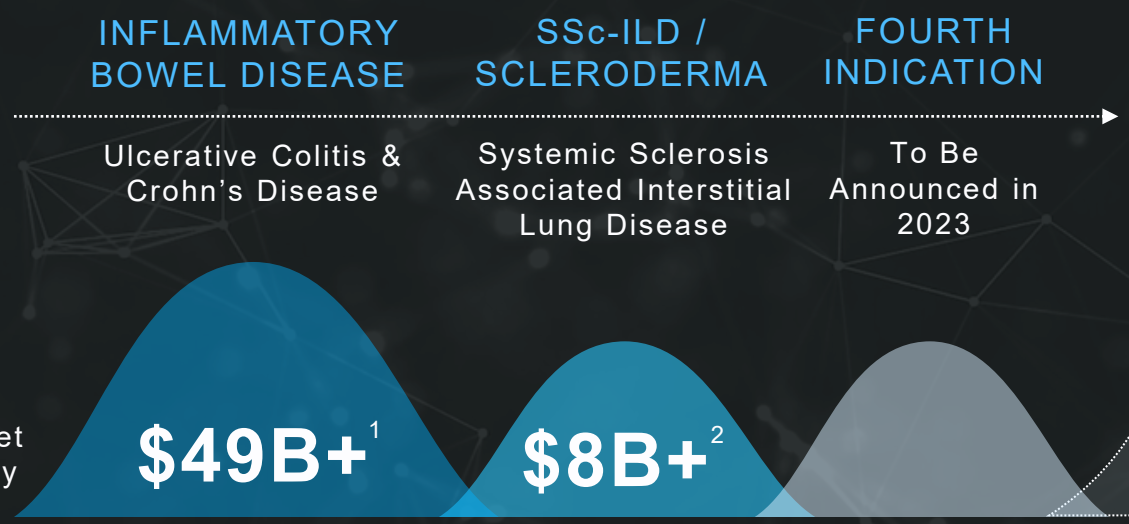
Early response cytokine setting the stage for inflammation

Stimulates both innate and adaptive immune responses

Inflammation also contributes to fibrosis

TL1A: Potential to Disrupt the $200B+ Immunology Category

Broadly applicable dual mechanism allows brisk indication expansion in immune-mediated diseases



Rheumatoid Arthritis	Pulmonary Sarcoidosis
Psoriatic Arthritis	Other ILDs e.g., IPF
Ankylosing Spondylitis	Liver Fibrosis
Psoriasis	Biliary Cirrhosis
Atopic Dermatitis	Systemic Lupus
Hidradenitis Suppurativa	ANCA Vasculitis
Inflammatory Asthma	Glomerulonephritis

$150B+ [3]

1. SVB Leerink. Prometheus Biosciences: Bringing Fire to IBD with a Precision Medicine Approach. April 6, 2021 | **2.** SSc-ILD market size estimates based on number of scleroderma patients with ILD[a,b,c] multiplied by the estimated net price of Ofev as an analog[d] | **a.** Clarivate, Evaluate Pharma diagnosed prevalence in 2030 | **b.** Hoffmann-Vold A-M, et al. Ann Rheum Dis 2021;80:219–227 | **c.** Walker et al. Ann Rheum Dis 2007;66:754–763 | **d.** Based on Ofev 2022 WAC of ~$140,000| **3.** Grandview Research: Immunotherapy Drugs Market Size, Share & Trends Analysis Report By Drug Type (Monoclonal Antibodies, Immunomodulators), By Indication (Infectious Diseases, Cancer), By Region, And Segment Forecasts, 2022 - 2030

PRA023: Path to Best-in-Class and First-in-Class TL1A Antibody

Ph 1 results indicate PRA023 is equivalent or differentiated vs. Pfizer/Roivant's RVT-3101 (formerly PF-06480605) in all meaningful metrics evaluated

ANTIBODY ATTRIBUTES

- Affinity and potency similar to RVT-3101
- Unique epitope binds both TL1A monomers and trimers
  - RVT-3101 binds only trimers
- SC formulation 200 mg/mL with >80% bioavailability - in GMP production with auto-injector planned for Ph 3 studies
  - RVT-3101 is 100 mg/mL with ~45% bioavailability

CLINICAL PERFORMANCE

- Favorable safety and tolerability
- >4-fold higher target engagement
- Superior immunogenicity profile
  - PRA023 ADA <20%[1] at clinically-relevant doses
  - RVT-3101 ADA >80% at similar doses
- Phase 2 dosing designed to reach steady state faster

COMMERCIAL POTENTIAL

- Broad clinical utility: UC, CD, SSc-ILD
- Precision approach could drive first-line reimbursement
  - First prospective use of Dx in immune-mediated disease study
- Rapid development; potential first to market
  - RVT-3101 not expected to reach market until at least 2028

1. PRA023 ADA was less than 20% in Phase 1; in Phase 2, ADA was 10.3% in UC and 14.5% in CD | US Pat. No. 9,683,998 | RXDX internal data on file | Danese S, et al. Anti-TL1A Antibody PF-06480605 Safety and Efficacy for Ulcerative Colitis: A Phase 2a Single-Arm Study. Clin Gastroenterol Hepatol. 2021 Nov;19(11):2324-2332.e6. | Banfield C, et al. First-in-human, randomized dose-escalation study of the safety, tolerability, pharmacokinetics, pharmacodynamics and immunogenicity of PF-06480605 in healthy subjects. Br J Clin Pharmacol. 2020;86(4):812-824. | Pfizer. Inflammation & Immunology Investor Day. Dec 13, 2021 | Results not based on head-to-head studies. See Disclaimer on page 2 for additional information.

ARTEMIS-UC Phase 2 Data

Topline Results in Ulcerative Colitis

Executive Summary: Positive Results from Phase 2 ARTEMIS-UC Study

Study population refractory with high disease severity:

- 47% were previously treated with at least 1 advanced therapy*
- 73% with baseline Mayo endoscopy subscore of 3

Primary and all ranked secondary endpoints for Cohort 1 were met

Clinical Remission Week 12	**Δ 25.0%**	**26.5% PRA023 vs. 1.5% placebo**	**p < 0.0001**
Endo Improvement Week 12	**Δ 30.8%**	**36.8% PRA023 vs. 6.0% placebo**	**p < 0.0001**

- Immunogenicity rate was low during induction therapy (11.8%) and did not impact efficacy
- Interim analysis indicated positive trend for enhanced treatment effects in Dx+ subjects
- PRA023 was well tolerated with no safety signal identified

* Advanced therapy: approved biologics and small molecules for UC (including ozanimod, tofacitinib, and upadacitinib) | P-values for testing the treatment difference are based on Cochran-Mantel-Haenszel test adjusted for prior biologic exposure status and Dx status. All endpoints are statistically significant according to multiplicity controlled 2-sided alpha of 0.05.

ARTEMIS-UC Placebo-Controlled Phase 2 Study Design

COHORT 1 TO EVALUATE EFFICACY OF PRA023

Key Inclusion Criteria

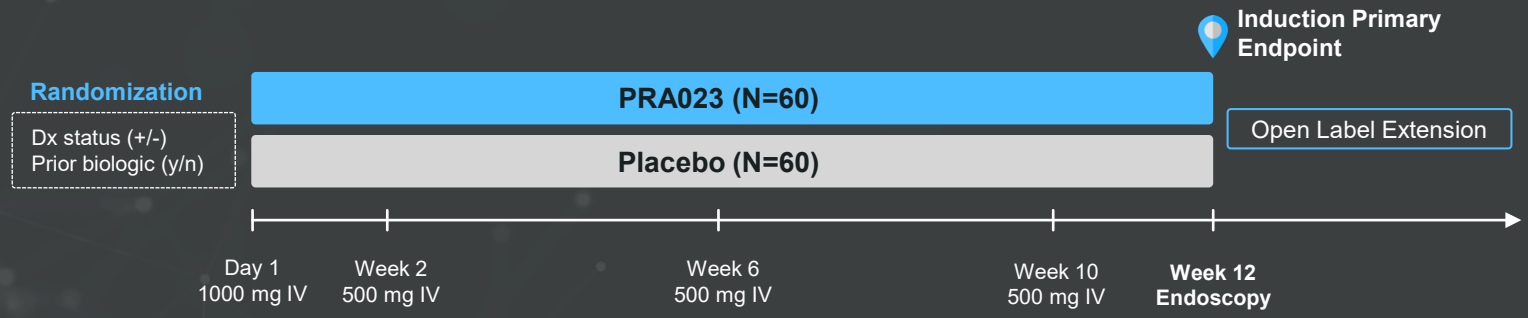
- Moderately to severely active UC
- No/insufficient response and/or intolerance to conventional or advanced therapy

Primary Endpoint

- Clinical remission at week 12 by 3 component Modified Mayo Score

Secondary Endpoints (α-controlled)

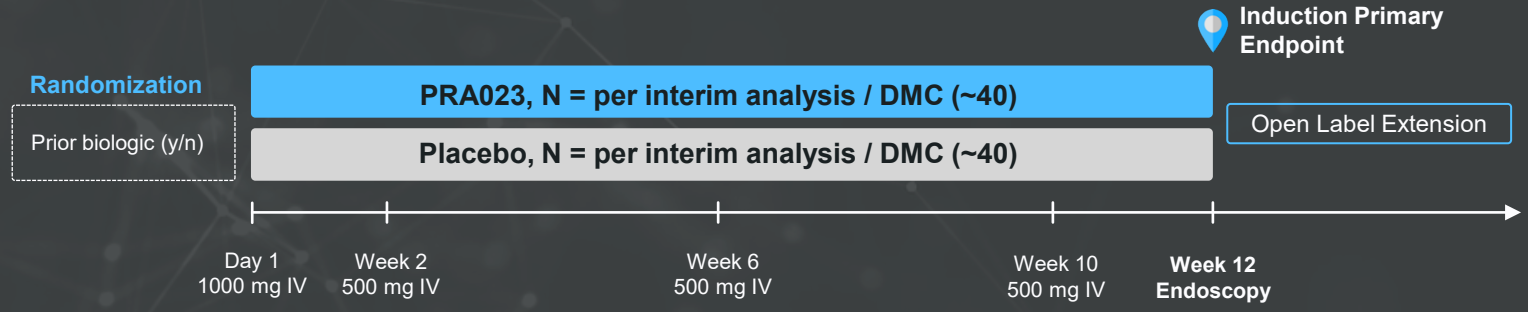
- Endoscopic improvement; clinical response; symptomatic remission; mucosal healing; histologic improvement; histologic-endoscopic mucosal improvement; IBDQ response



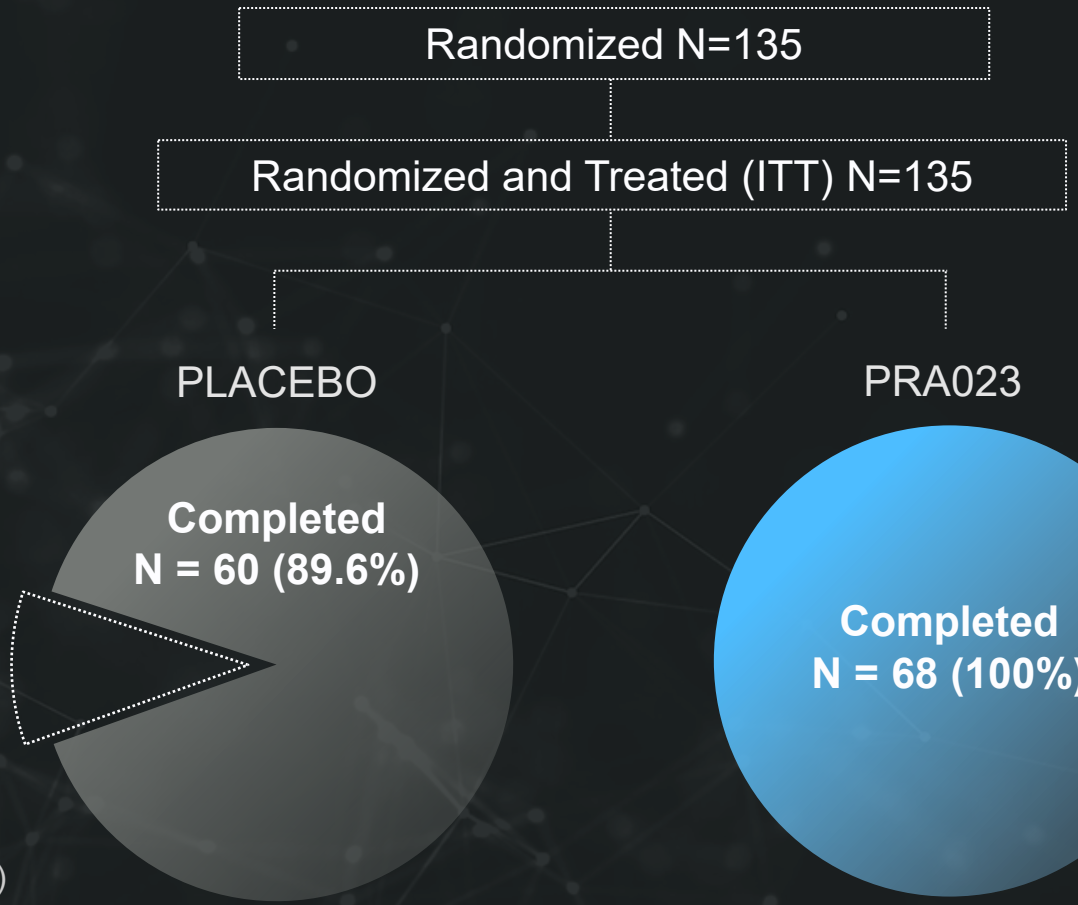
COHORT 2 TO ENRICH FOR Dx+ SUBJECTS (includes Dx+ from initial cohort)

Key Inclusion Criteria

- As in Cohort 1
- Must also be Dx+



Subject Disposition in the 12-Week Double-Blind Induction Period



Discontinued Treatment
N = 7 (10.4%)

Primary reason:

Adverse events, n=2 (3.0%)

Lack of efficacy, n=2 (3.0%)

Subject decision, n=2 (3.0%)

Prohibited medication, n=1 (1.5%)

Discontinued Treatment
N = 0 (0.0%)

Primary reason:

Adverse events, n=0 (0.0%)

Lack of efficacy, n=0 (0.0%)

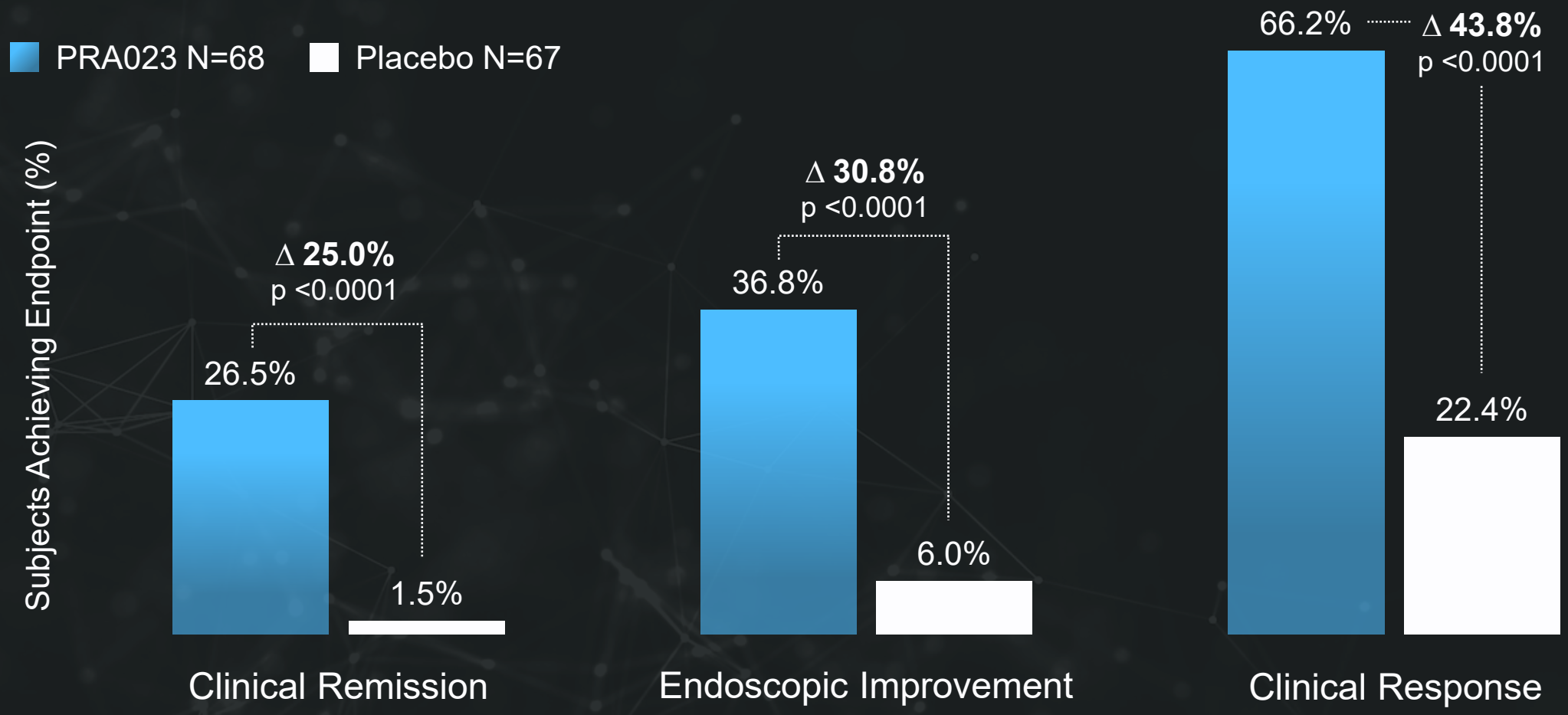
Subject decision, n=0 (0.0%)

Prohibited medication, n=0 (0.0%)

ARTEMIS-UC Baseline Characteristics and Demographics

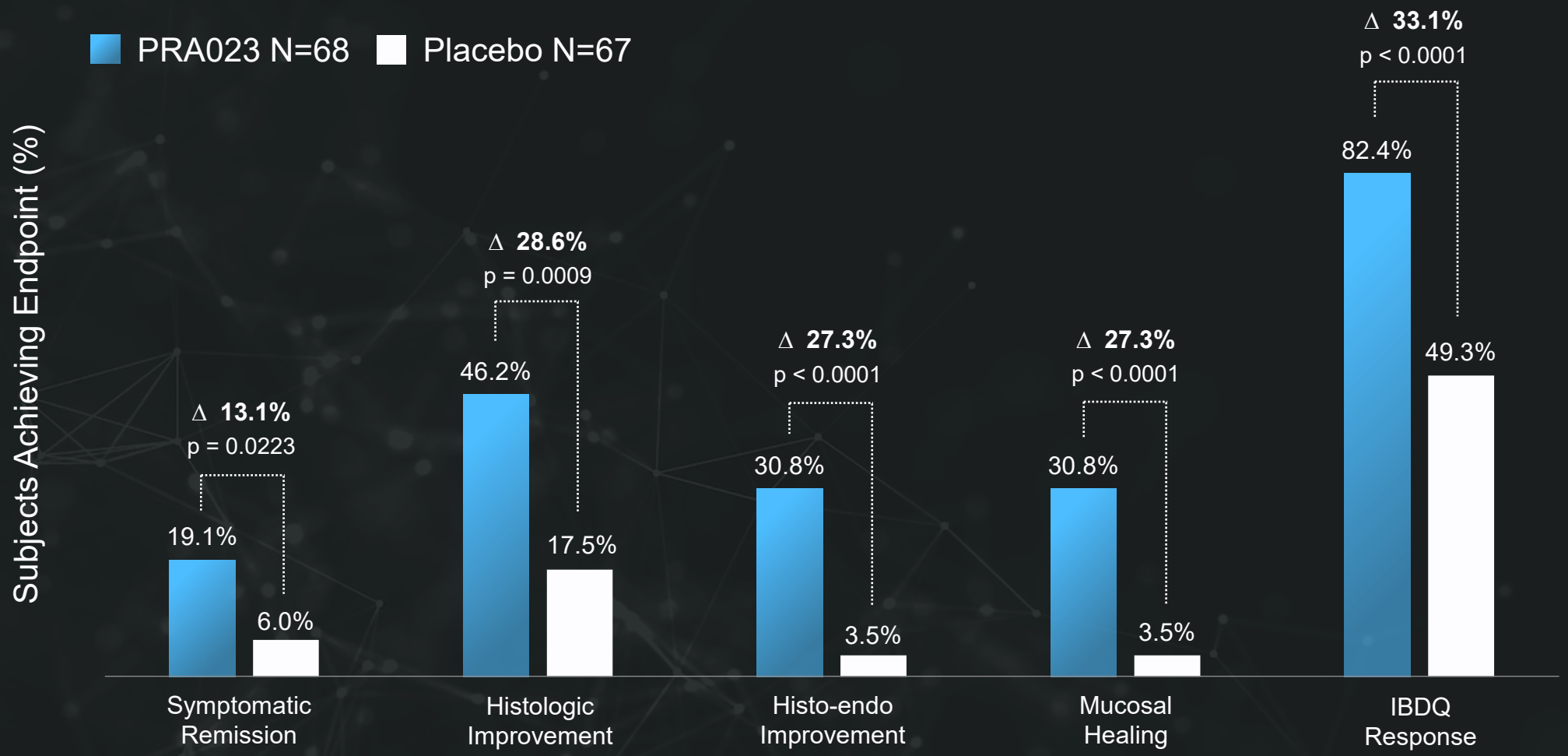
	Placebo (N = 67)	PRA023 (N = 68)	Overall (N = 135)
Age, years, mean (SD)	42.2 (16.3)	40.4 (14.4)	41.3 (15.3)
Female, n (%)	29 (43%)	34 (50%)	63 (47%)
Weight, kg, mean (SD)	77 (18.5)	74 (19.6)	75 (19)
Geographic region, n (%)			
Eastern Europe	39 (58%)	39 (57%)	78 (58%)
North America	17 (25%)	20 (29%)	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 (52%)	63 (47%)
Pancolitis	32 (48%)	31 (46%)	63 (47%)
3 Component Modified Mayo Score (mMS), mean (SD)	7.1 (1.1)	6.9 (1.2)	7.0 (1.2)
Mayo Endoscopy Score (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%)

UC Subjects Treated with PRA023 Achieved Significant Differences in Primary and Secondary Endpoints 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 Dx status. All endpoints are statistically significant according to multiplicity controlled 2-sided alpha of 0.05.

UC Subjects Treated with PRA023 Achieved Significant Differences in Primary and 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.

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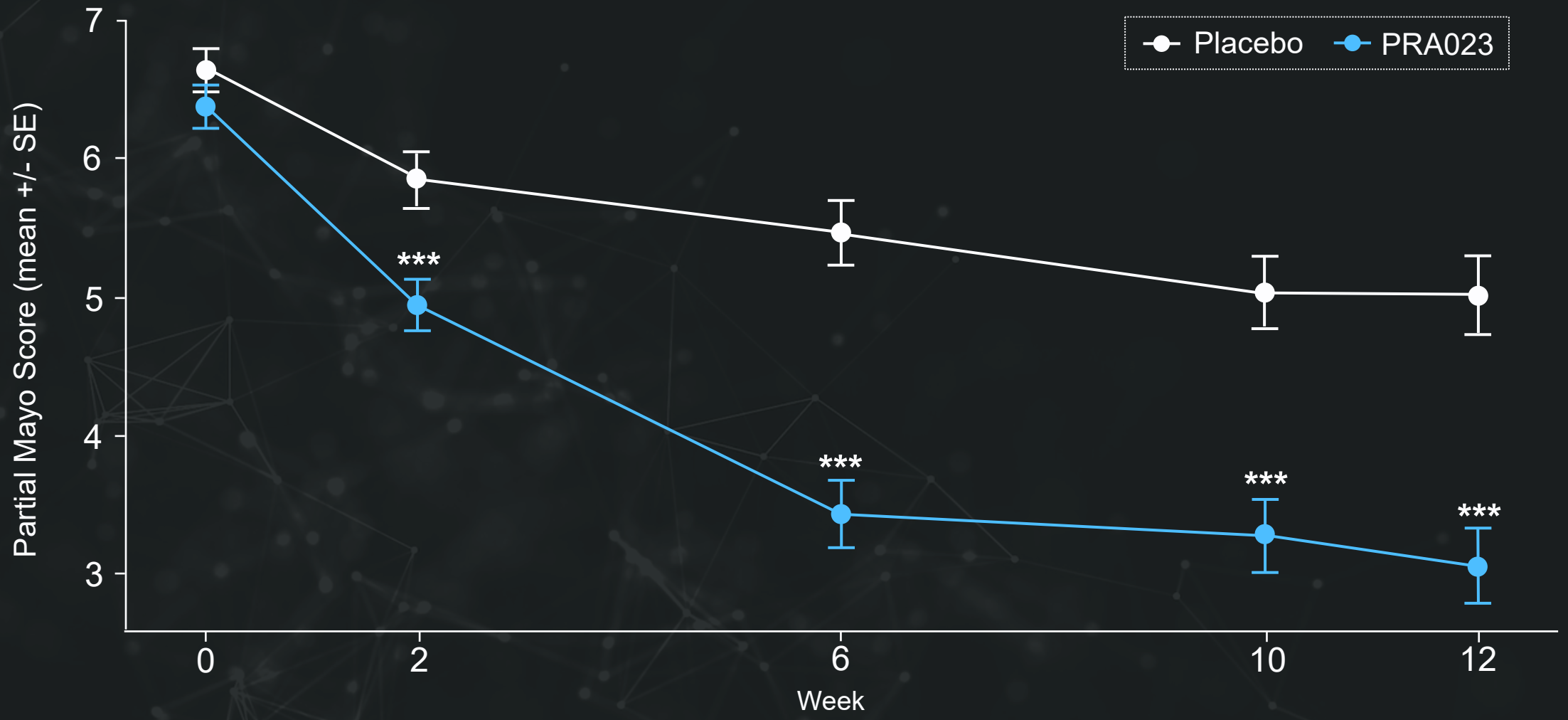
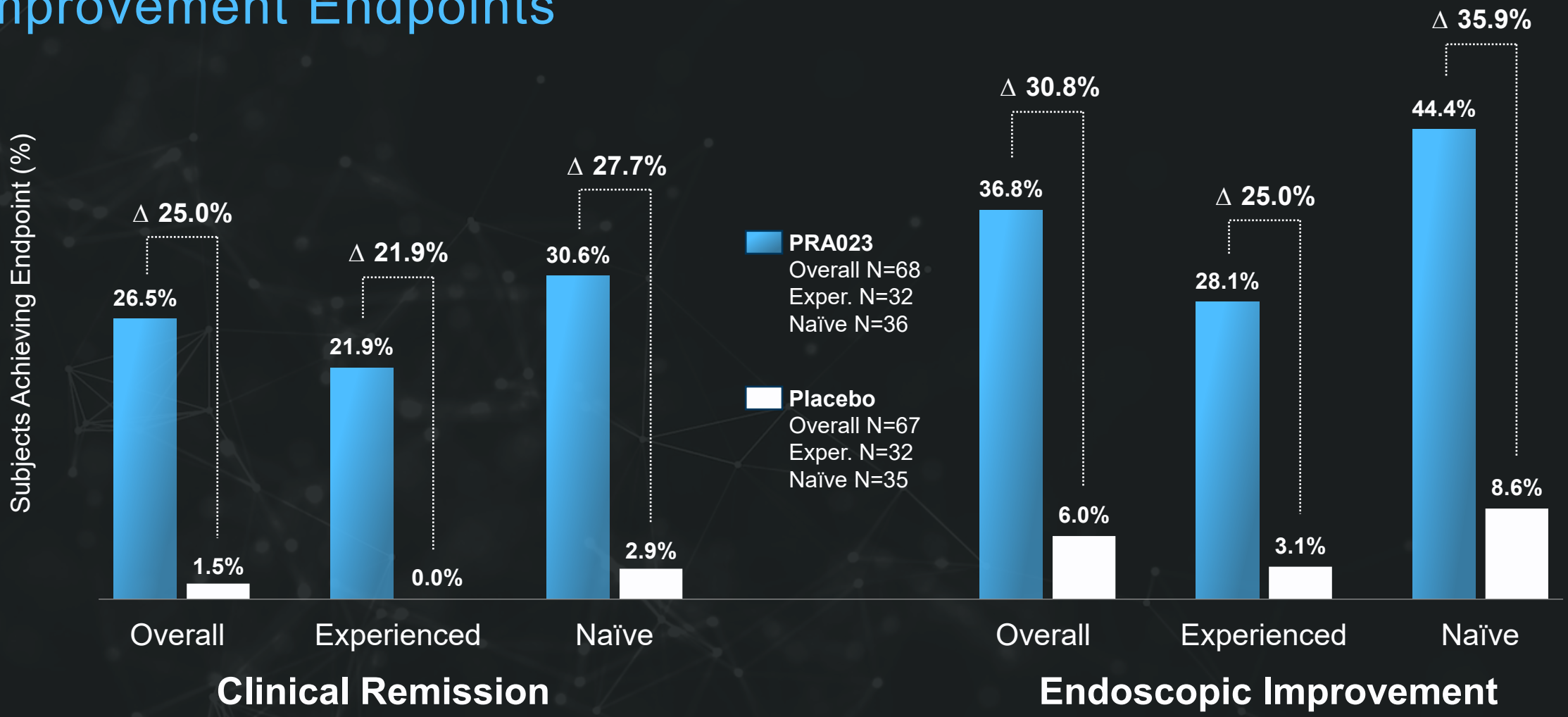
Treatment with PRA023 Led to Symptom Control as Early as Week 2



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

Experienced & Naïve Subjects Treated with PRA023 Achieved Significant Differences in Clinical Remission and Endoscopic Improvement Endpoints



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

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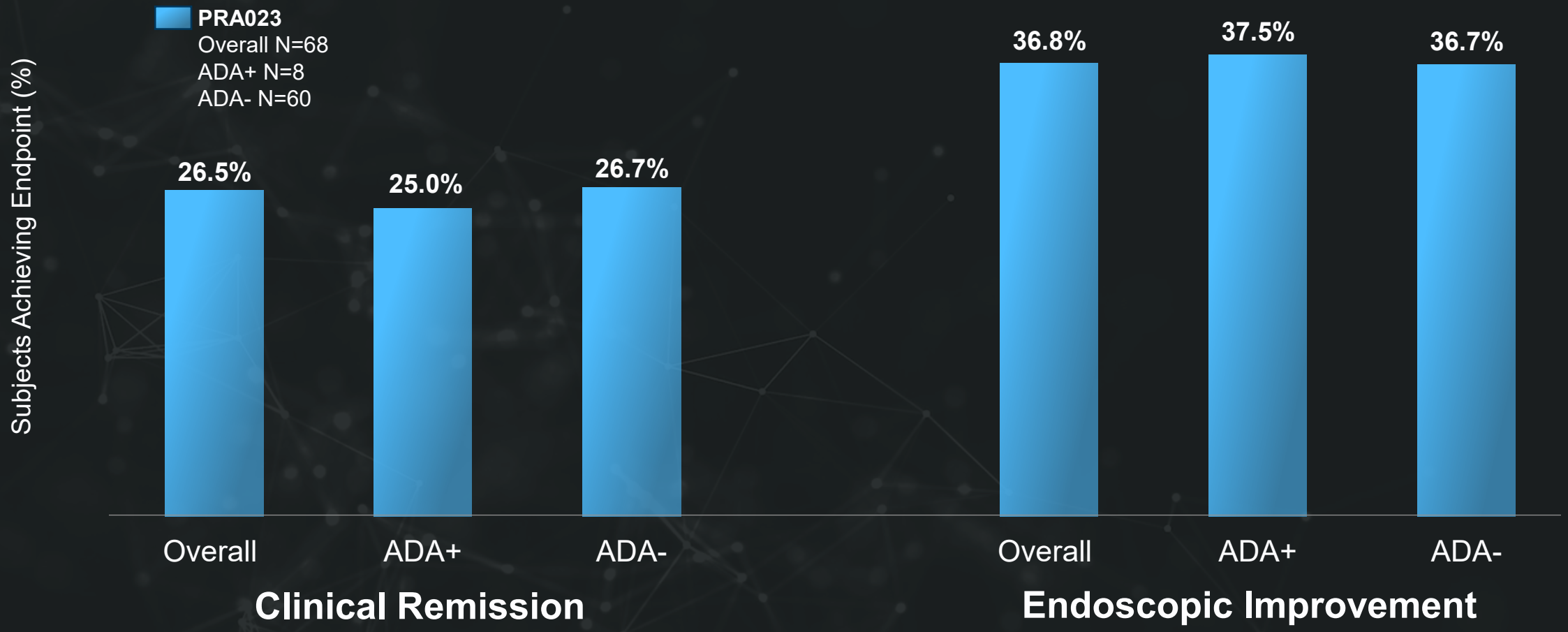
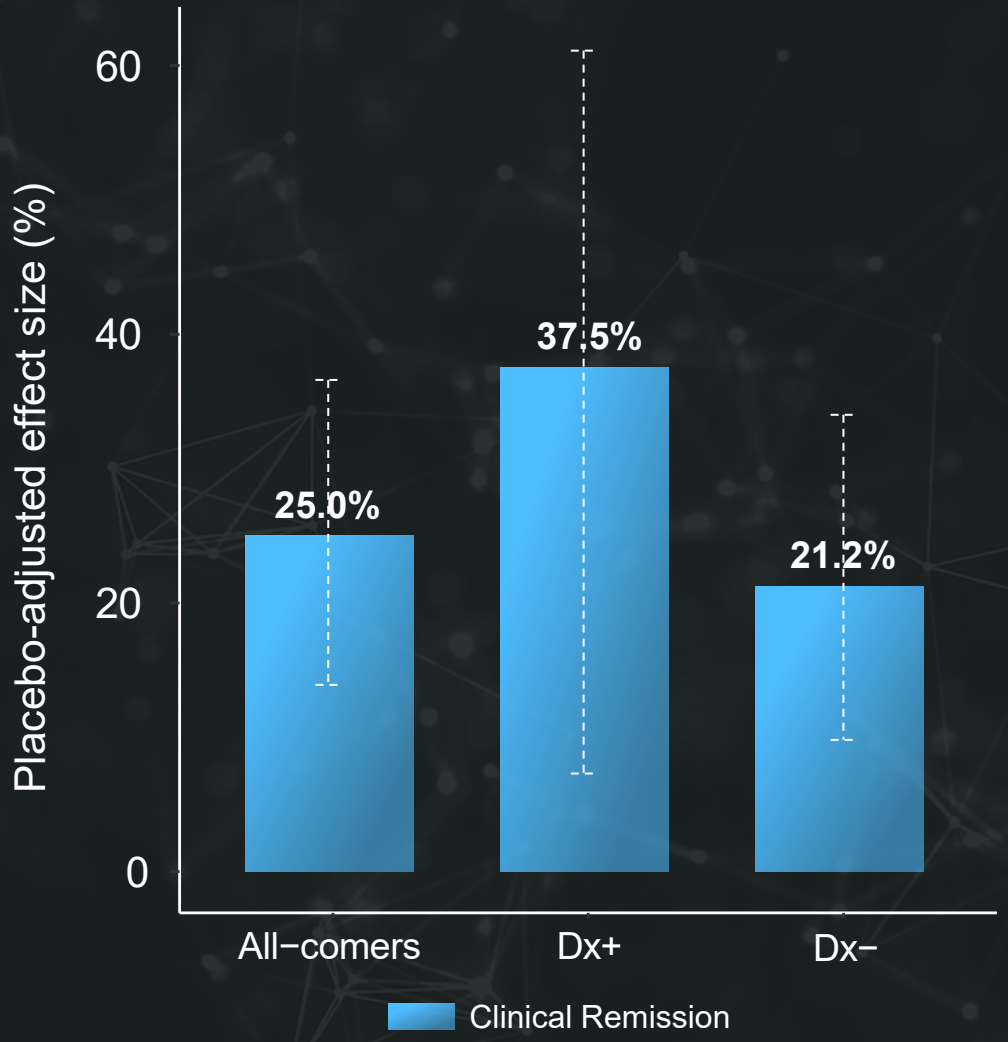
No Impact on Endoscopic Response and Clinical Remission Treatment Effects by Presence of Anti-Drug Antibody



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 | ADA assay is validated drug-tolerant assay (up to Cmax)

Analysis of ARTEMIS-UC Cohort 1 for Dx Effect Reinforces Confidence in Precision Approach



- First prospective use of a co-diagnostic in IBD
- Payer/physician research suggests 10% absolute increase is a compelling improvement over all-comers
- Based on efficacy data and confidence in the precision approach, an interim analysis of the Dx was conducted to evaluate its performance in ulcerative colitis
- While only limited patient numbers are available, clinical remission of 37.5% in Dx+ patients was observed, compared with 25.0% for all-comers
- Initial trend expected to be confirmed with ARTEMIS-UC Cohort 2 data in 2Q 2023

PRA023 Was Well-Tolerated As Induction Therapy

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%)
Most common AEs (n, %)		
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%)

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 resolved as study drug continued

ARTEMIS-UC: Highly Differentiated Profile of Strong Efficacy with Favorable Tolerability

Strong Efficacy Results

12-Week Clinical Remission delta **25%**

12-Week Endo Improvement delta **30.8%**

No Safety Signal Identified

PRA023 was well-tolerated with no safety signal identified in Ph 2 UC & CD studies

Low Immunogenicity

Low ADA level of **11.8%** in ulcerative colitis

No apparent impact on efficacy or safety

Favorable Signal in Dx+

Interim analysis showed positive trend for enhanced treatment effect in Dx+ subjects

APOLLO-CD Phase 2a Data

Open Label Results in Crohn's Disease

Executive Summary: Positive Results from Phase 2a APOLLO-CD Study

Study population was highly refractory with **70.9%** biologic-experienced

Successful Proof of Concept for PRA023 for the induction of endoscopic response and clinical remission in CD

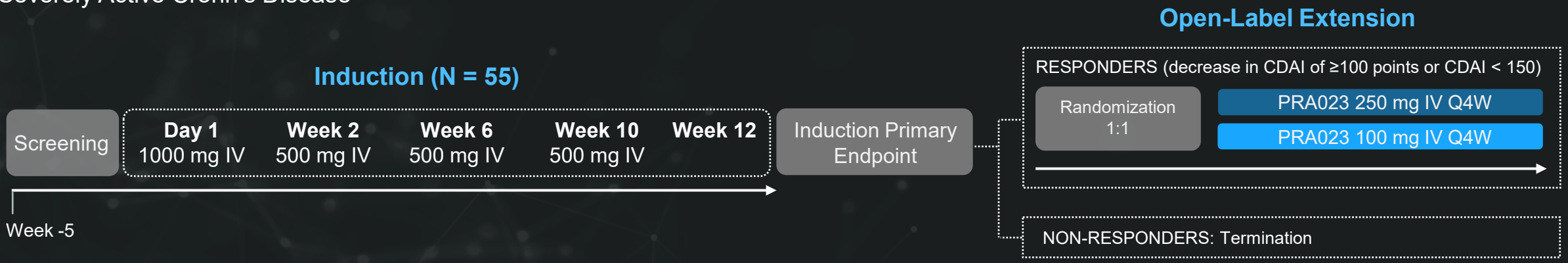
Endoscopic Response Week 12	**26.0%**	**vs. 12% historical placebo**	**p = 0.002**
Clinical Remission Week 12	**49.1%**	**vs. 16% historical placebo**	**p < 0.001**

- Endoscopic response and clinical remission were observed in subjects previously exposed to biologic therapy and with or without concomitant therapies
- Early onset of action as measured by symptoms and disease biomarker
- PRA023 was well tolerated in subjects with moderately to severely active Crohn's disease with no safety signal identified
- Rate of immunogenicity was low (14.5%) and did not impact efficacy or safety

* Advanced therapy: approved biologics and small molecules for UC (including ozanimod, tofacitinib, and upadacitinib) | P-values for testing the treatment difference are based on Cochran-Mantel-Haenszel test adjusted for prior biologic exposure status and Dx status. All endpoints are statistically significant according to multiplicity controlled 2-sided alpha of 0.05.

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



Key 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%)

Objectives

Primary

- Safety and tolerability
- Endoscopic response at Week 12

Secondary

- Clinical remission at Week 12
- Clinical response at Week 12
- Endoscopic 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

High Retention of Subjects in the 12-Week Induction Period

Treated, N = 55

Completed Induction
N = 53 (96.4%)

Discontinued Treatment
N = 2 (3.6%)

Primary reason:

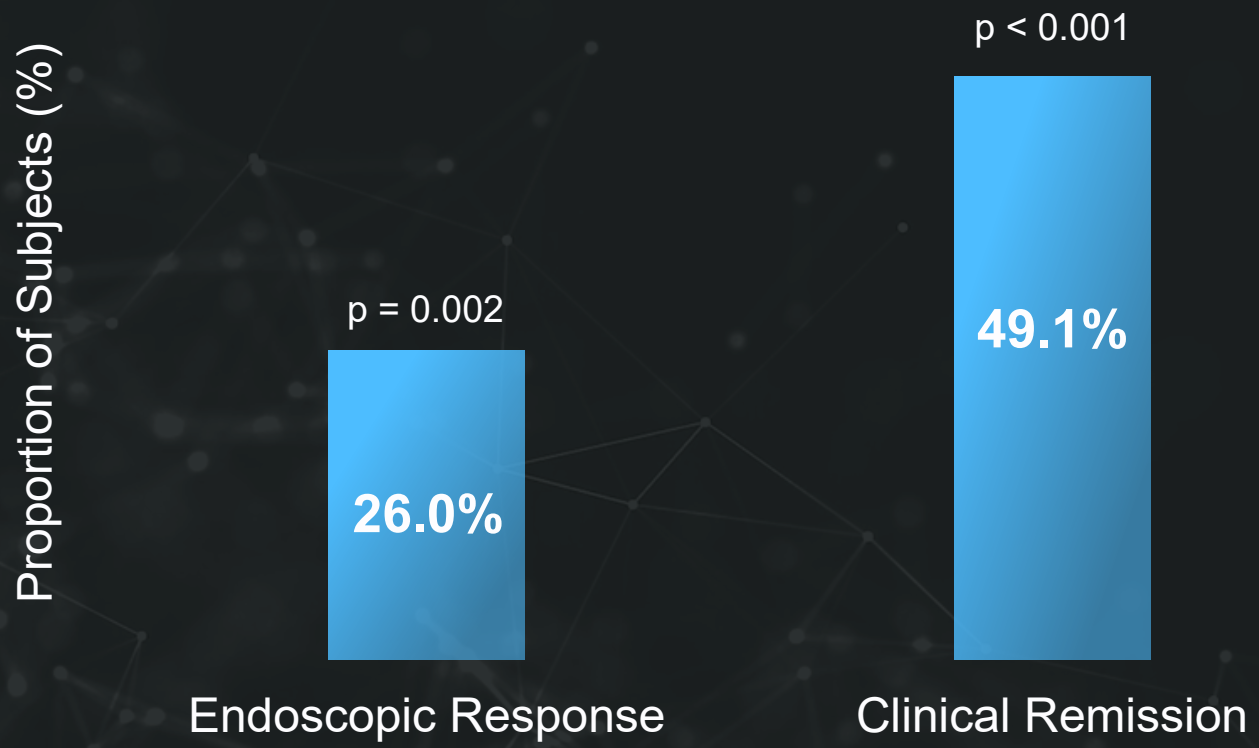
Adverse events, n = 1 (1.8%)

Lack of efficacy, n = 1 (1.8%)

APOLLO-CD 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	33 (60%)
Eastern Europe	13 (23.6%)
Western Europe	7 (12.7%)
Rest of world (Australia)	2 (3.6%)
Duration of disease, years, mean (SD)	10.29 (9.27)
Extent of disease, n (%)	
Ileal	8 (14.5%)
Colonic	15 (27.3%)
Ileocolonic	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	16 (29.1%)
1	10 (18.2%)
2	10 (18.2%)
≥3	19 (34.5%)

CD Subjects Treated with PRA023 Achieved Significant Differences in Primary and Secondary Endpoints at Week 12 Compared to Pre-specified Placebo



P-values 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).

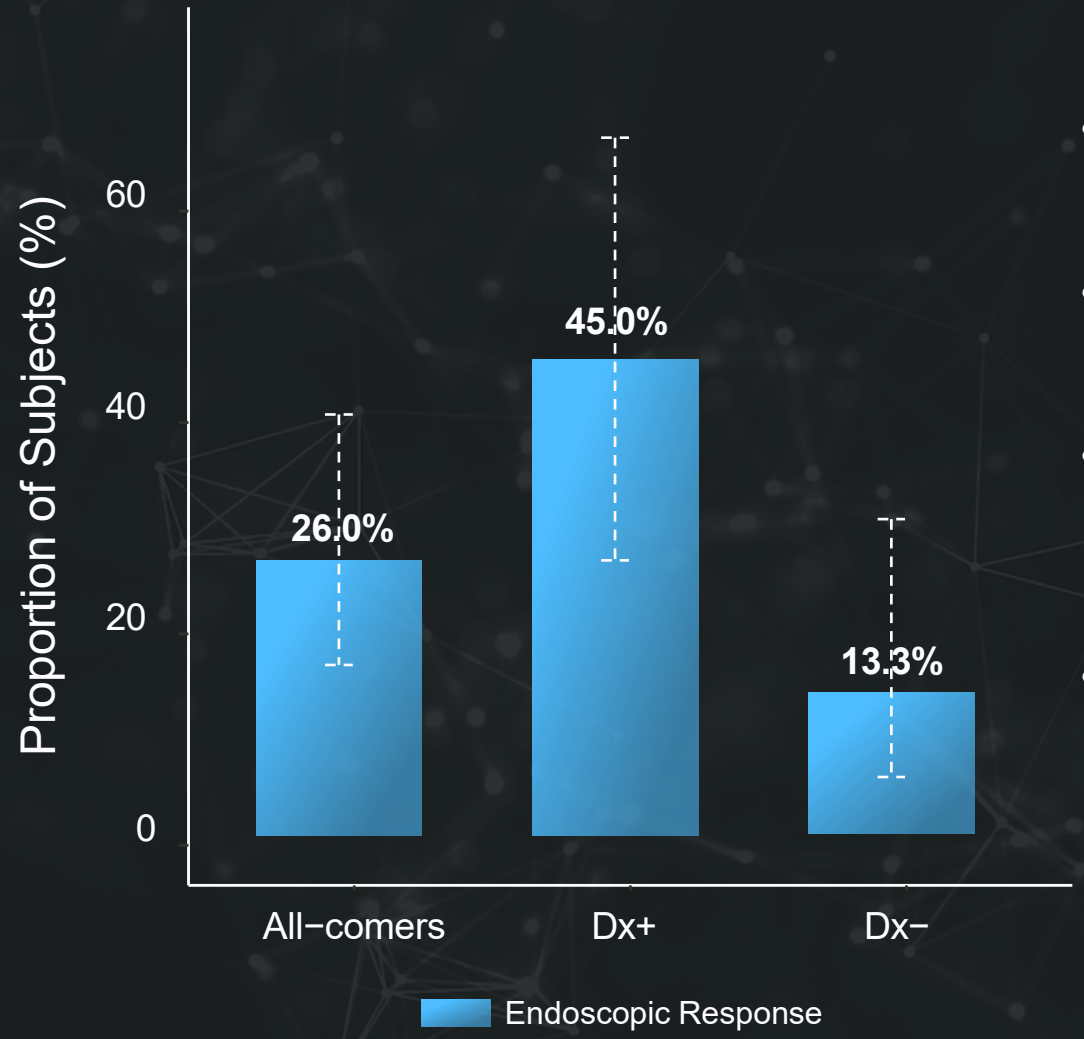
PRA023 Was Well-Tolerated As Induction Therapy

	All-causality TEAEs (N = 55)	Treatment-related TEAEs (N = 55)
Subjects with ≥ 1 AE(s)	**43 (78.2%)**	**4 (7.3%)**
Subjects with ≥ 1 Serious AEs (SAEs)	**8 (14.5%)**	**0 (0%)**
Subjects with ≥ 1 Severe (Grade ≥ 3) AE(s)	**3 (5.5%)**	**0 (0%)**
Subjects discontinued due to AEs	**2 (3.6%)**	**0 (0%)**
Death	**0 (0%)**	**0 (0%)**
Subjects with ≥ 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

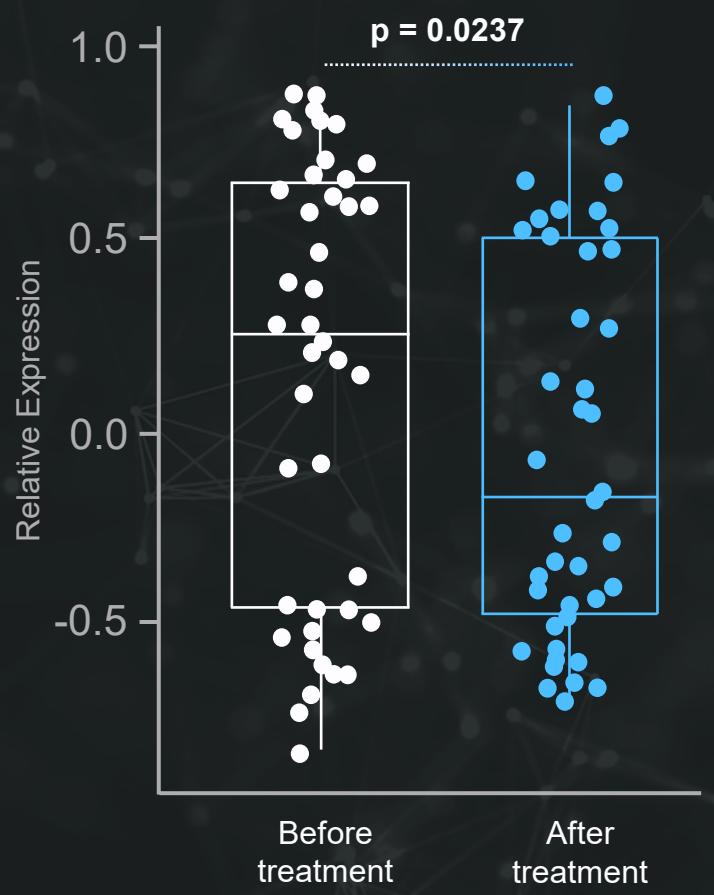
Analysis of APOLLO-CD Confirms Relevance of SNPs Used on Diagnostic Assay



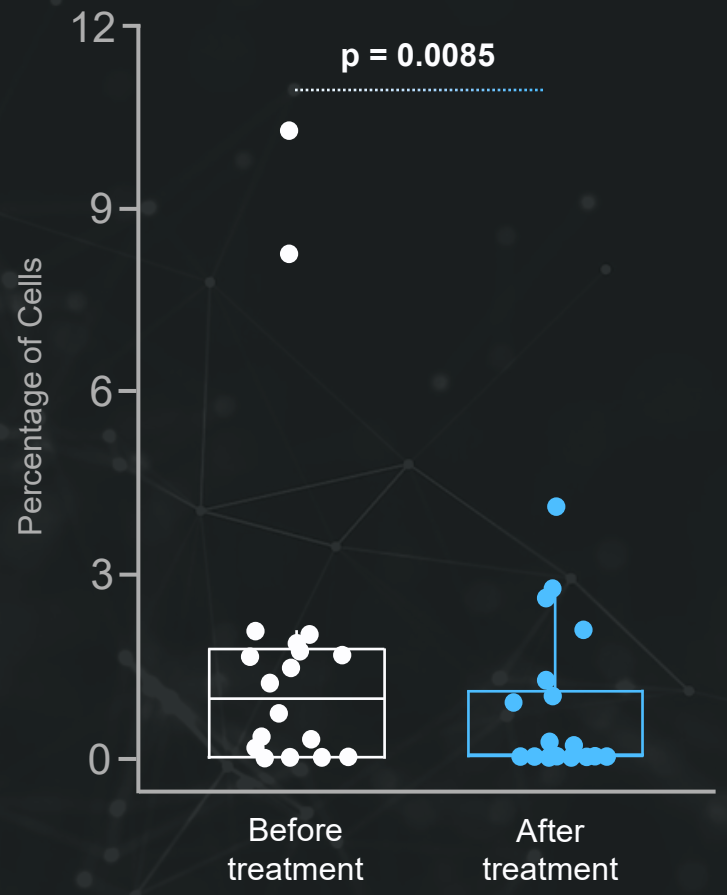
- Predictive power of the predefined SNPs was validated using an alternative Crohn's disease-specific algorithm
- Patient selection using the alternate algorithm resulted in 45.0% endoscopic response versus 26% in all-comers
- While the original algorithm provided limited benefit, the alternative algorithm provides enhanced performance across clinical and endoscopic outcomes
- The alternative Crohn's-specific algorithm will be carried forward into the phase 3 program

PRA023 Significantly Reduced Fibrosis Biomarkers

Fibrosis signature in disease tissue



% of activated fibroblasts in disease tissue



SIGNIFICANT REDUCTION IN FIBROSIS BIOMARKERS

PRA023 reduced:

- Expression of a composite signature of 24-genes associated with penetrating fibrosis[1]
- Level of expression in individual genes (MMP3, MMP9, COL1A1)
- Proportion of activated fibroblasts in disease tissue

1. Xiong, S. *et al.* Gut 71, 1289–1301 (2022) | Data shown are from APOLLO-CD Phase 2a study in Crohn's disease

APOLLO-CD: Strong Proof of Concept with Favorable Tolerability

Established Proof of Concept

12-Week Absolute Endoscopic Response **26.0%**

12-Week Absolute Clinical Remission **49.1%**

No Safety Signal Identified

PRA023 was well-tolerated with no safety signal identified in Ph 2 UC & CD studies

Low Immunogenicity

Low ADA level of **14.5%** in Crohn's disease

No apparent impact on efficacy or safety

Favorable Signal in Dx+

CD-specific algorithm showed 45% (9/20) endo response vs. 26% in all-comers (13/50)

PRA023: Expanding into SSc-ILD

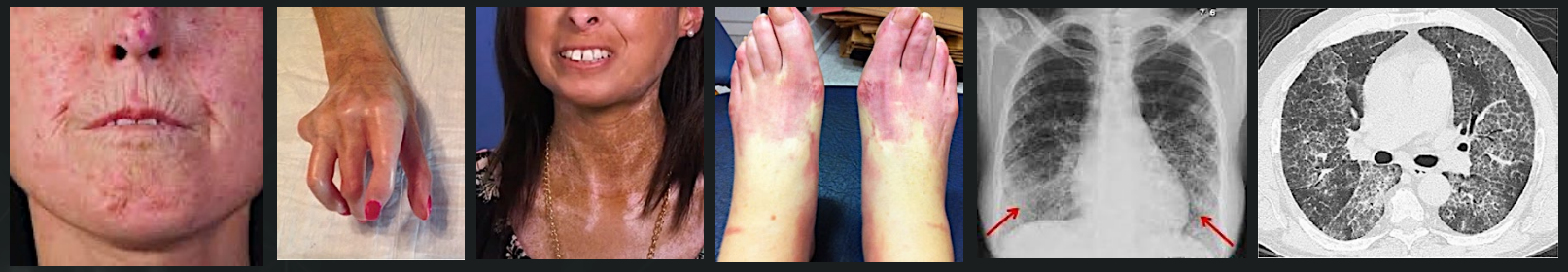
Systemic Sclerosis-Associated Interstitial Lung Disease

SSc-ILD: A Compelling Third Indication for PRA023

Systemic sclerosis-associated interstitial lung disease is an autoimmune condition with great unmet need and fibrotic & inflammatory etiology

FDA FAST TRACKED

- Highlights potential clinical utility
- Enhanced communication with FDA
- Expedited review of Phase 2 study



STRONG SCIENTIFIC RATIONALE

- PRA023's anti-inflammatory and anti-fibrotic mechanism of action is a compelling fit for this inflammatory and fibrotic disease
- TL1A and its receptor DR3 associated with lung fibrosis in mice and humans with SSc
- Animal models demonstrate reversal of SSc-ILD disease processes with TL1A blockade

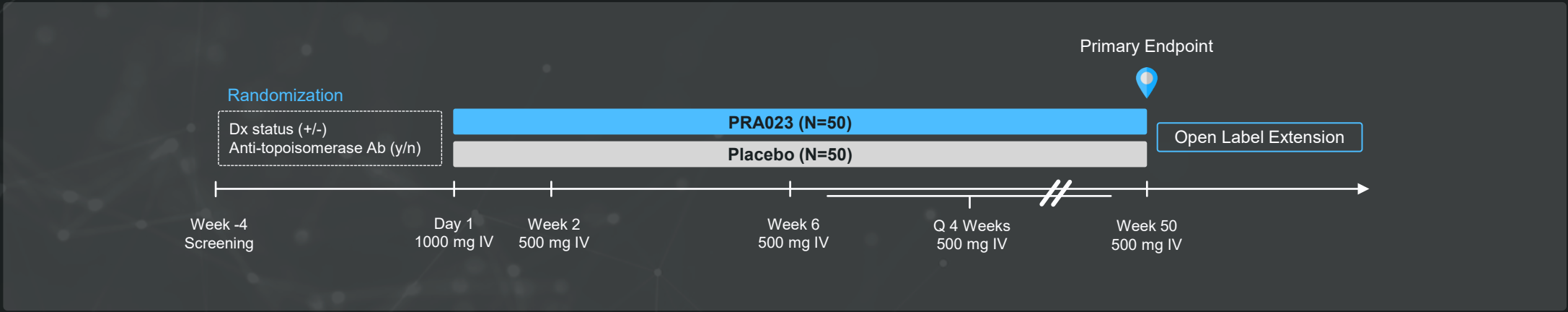
ALIGNED WITH OUR STRATEGY

- Efficacy in this disease area would further validate PRA023's anti-fibrotic capabilities
- Success could catalyze broad indication expansion into other fibrotic diseases
- Favorable trial feasibility and regulatory landscape: newly established clinical endpoints, clearer regulatory guidance

COMMERCIALLY ATTRACTIVE

- Severe chronic disease with morbidity and high unmet need for effective therapies
- Few treatment options: only two approved therapies, neither shown to modify disease or improve quality of life
- Potential for PRA023 market leadership, especially with disease-modifying efficacy

ATHENA-SSc Placebo-Controlled Phase 2 Study Design



Inclusion Criteria

- Adults with SSc with disease duration ≤5 years
- Diffuse cutaneous scleroderma subtype with modified Rodnan skin score (mRSS) 15-35 units, inclusive
- SSC-related ILD fibrotic disease in lung confirmed by HRCT as assessed by central reading
- Enrichment criteria for progressivity of SSc-ILD

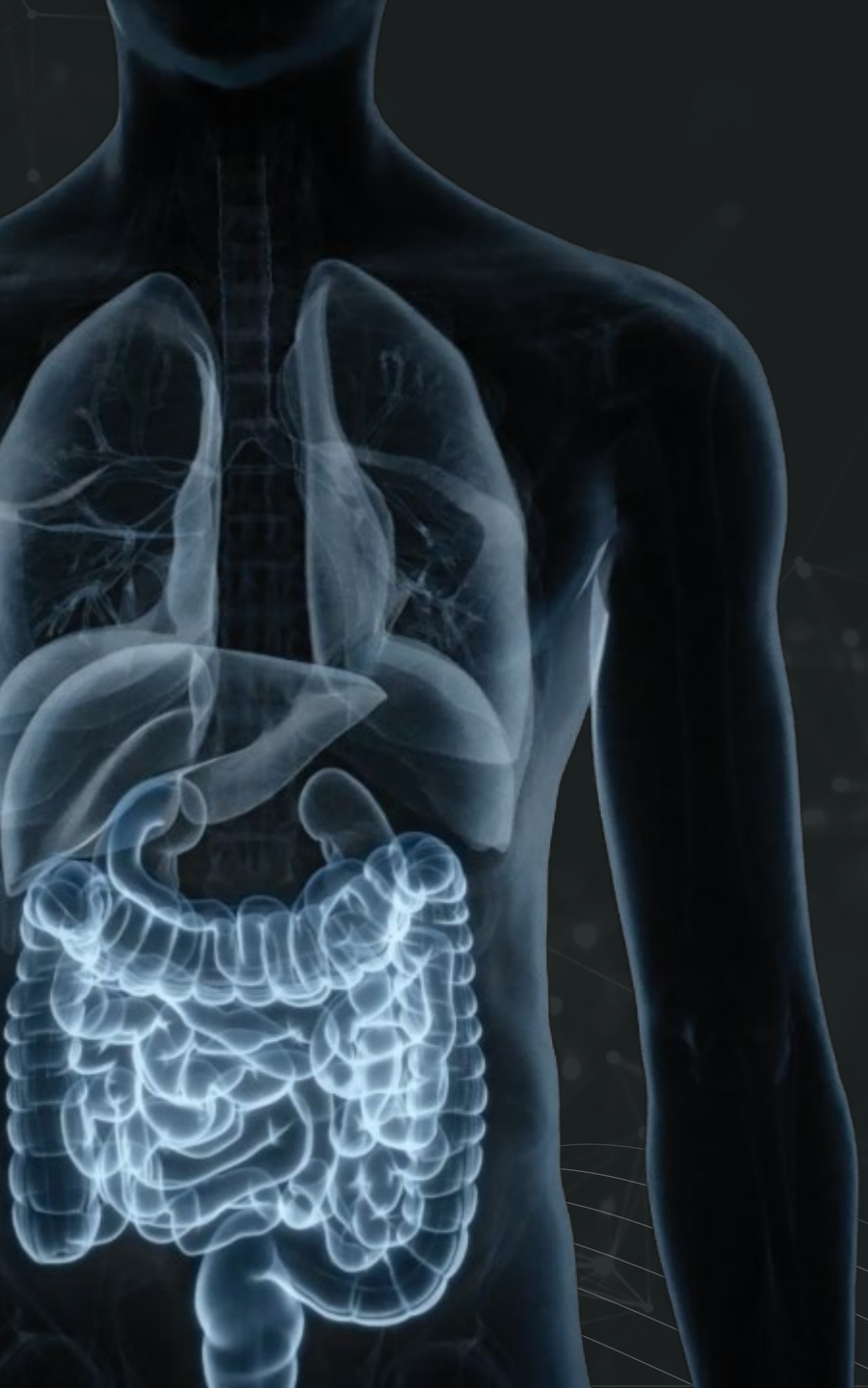
Primary Endpoint

- Annual rate of change in Forced Vital Capacity (FVC) over 50 weeks by centrally-read spirometry

Secondary Endpoints

- Change in quantitative interstitial lung disease by centrally-read HRCT
- Improvement in ACR Combined Response Index in SSc (ACR-CRISS) score

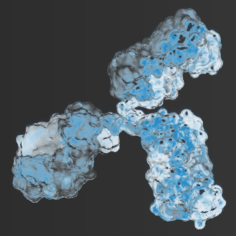
Phase 2 results expected 1H 2024



Second Product Candidate PRA052

Targeting CD30 Ligand with a Second Precision Rx Program

Expanding Impact in Immunology with a Second Precision Program

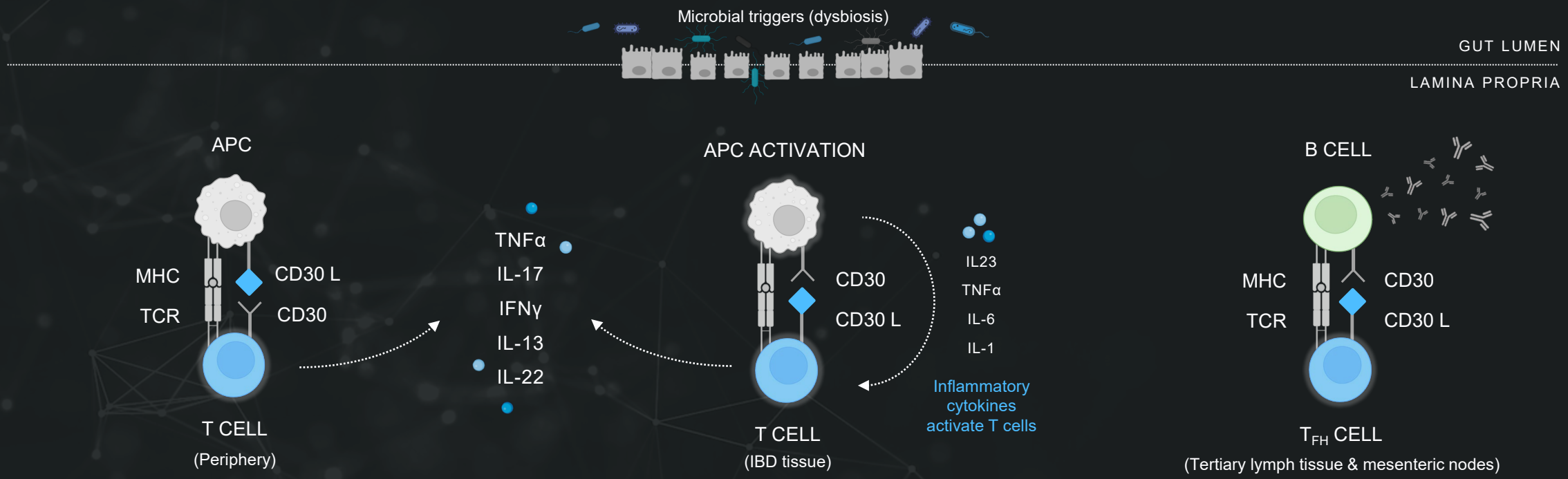


PRA052

anti-CD30L mAb

- CD30L-CD30 co-stimulatory pathway implicated in IBD by genetic, preclinical, and human translational data
- Pathway activates effector memory T cells, macrophages and B cells in chronic inflammatory diseases
- Accompanying Dx is designed to select patients who are more likely to respond to CD30L inhibition
- CD30L pathway has one of the strongest genetic links to inflammatory bowel disease
- PRA052 has a pleiotropic effect on both innate and adaptive immunity & targets a pathway distinct from TNF
- 6-week cyno GLP toxicology study completed with no drug-related clinical observations
- Phase 1 NHV study underway as the first clinical-stage CD30L antagonist with results expected 4Q 2023
- Inhibition of this pathway is thought to be broadly applicable across immune-mediated diseases

CD30L-CD30 Co-stimulation Drives Chronic Inflammation in IBD



T CELL ACTIVATION

Activation of inflammatory effector memory T cells by antigen-presenting cells

T CELL ACTIVATION

Stimulation of inflammatory monocytes and macrophages producing inflammatory cytokines

B CELL MATURATION

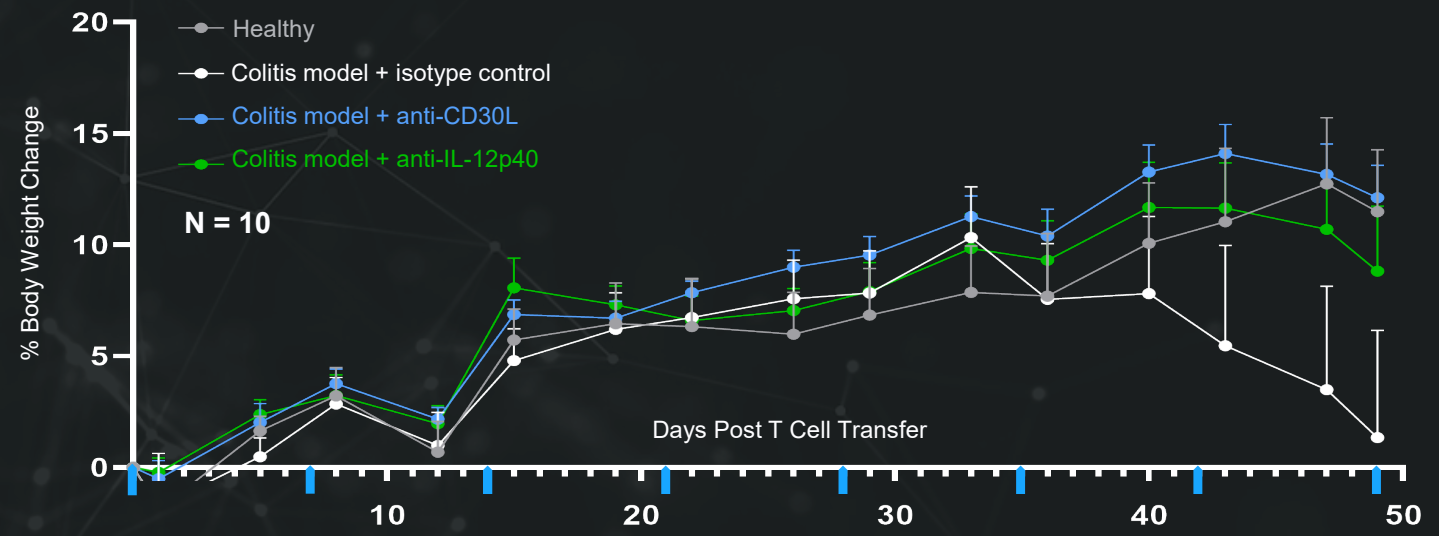
Helper T cells support B cell maturation and APC activation through antibody binding to Fc receptors

Smillie, C. S. et al. Intra- and Inter-cellular Rewiring of the Human Colon during Ulcerative Colitis. Cell 178, 714-730.e22 (2019) | Martin, J. C. et al. Single-Cell Analysis of Crohn's Disease Lesions Identifies a Pathogenic Cellular Module Associated with Resistance to Anti-TNF Therapy. Cell 178, 1493-1508.e20 (2019) | Kennedy, M. K., Willis, C. R. & Armitage, R. J. Deciphering CD30 ligand biology and its role in humoral immunity. Immunology 118, 143–52 (2006) In-house data / Sun, X. et al. CD30 ligand/CD30 plays a critical role in Th17 differentiation in mice. J Immunol 185, 2222–30 (2010) | Sun, X. et al. CD30 ligand is a target for a novel biological therapy against colitis associated with Th17 responses. J Immunol 185, 7671–80 (2010) | Somada, S. et al. CD30 Ligand/CD30 interaction is involved in Pathogenesis of Inflammatory Bowel Disease. Digest Dis Sci 57, 2031–2037 (2012) | Sun, X. et al. A critical role of CD30 ligand/CD30 in controlling inflammatory bowel diseases in mice. Gastroenterology 134, 447–58 (2008) | Croft M, So T, Duan W, and Soroosh P. (2009). The significance of OX40 and OX40L to T-cell biology and immune disease. Immunol. Rev., 229, 173–191.

CD30L Antagonism Reduces Colitis in T Cell Transfer Experiments

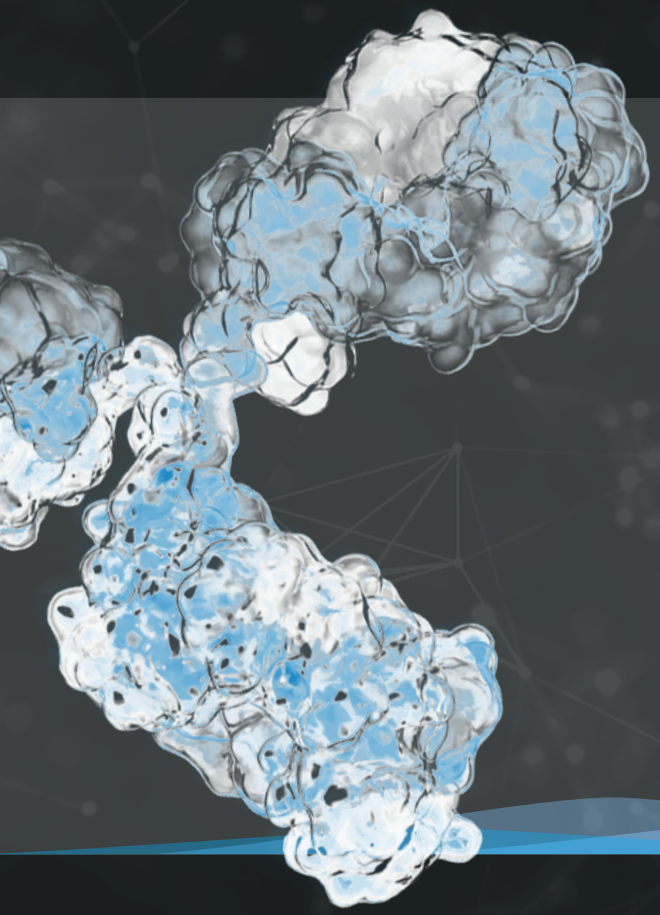
Anti-CD30L antibody ameliorates colitis in T cell transfer model

- Healthy mice gain weight as they grow
- T cell transfer causes weight loss as anti-host immune response results in colitis phenotype
- Blocking CD30L prevented colitis development including weight loss
- The anti-inflammatory effect of CD30L blockade was similar to that of anti-IL-12/23 treatment



In-house data

Momentum Continues with Significant Milestones Through 2024



2023

- ARTEMIS-UC Cohort 2 results (Q2)
- Initiation of two registrational studies of PRA023 in UC and CD
- R&D Day Presentation (2H)
- PRA052 Phase 1 NHV results (Q4)
- Additional IND for pipeline program (Q4)

2024

- Initiation of PRA052 Phase 2 study
- ATHENA-SSc-ILD Phase 2 results
- Initiate second registrational study in CD
- Additional IND for pipeline program

>$700 million cash[1] provides confidence to independently fund registrational studies and broad pipeline activities

1. End 4Q 2022 cash of $695.8 million and ~$50.1 million in additional net proceeds from full exercise of greenshoe in January 2023

Executive Team

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Chairman & CEO

Salix B+L Johnson & Johnson

Keith Marshall, PhD
Chief Financial Officer

J.P.Morgan Conatus Pharmaceuticals TORQUE

Mark Stenhouse
Chief Operating Officer

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Chief Medical Officer

abbvie Bristol Myers Squibb

Olivier Laurent, PhD
CSO & Head of R&D

SANOFI BAYER Genentech Pfizer

Chris Doughty
Chief Business Officer

McKinsey & Company STRATA oncology KaufmanHall Deloitte.

Nori Ebersole
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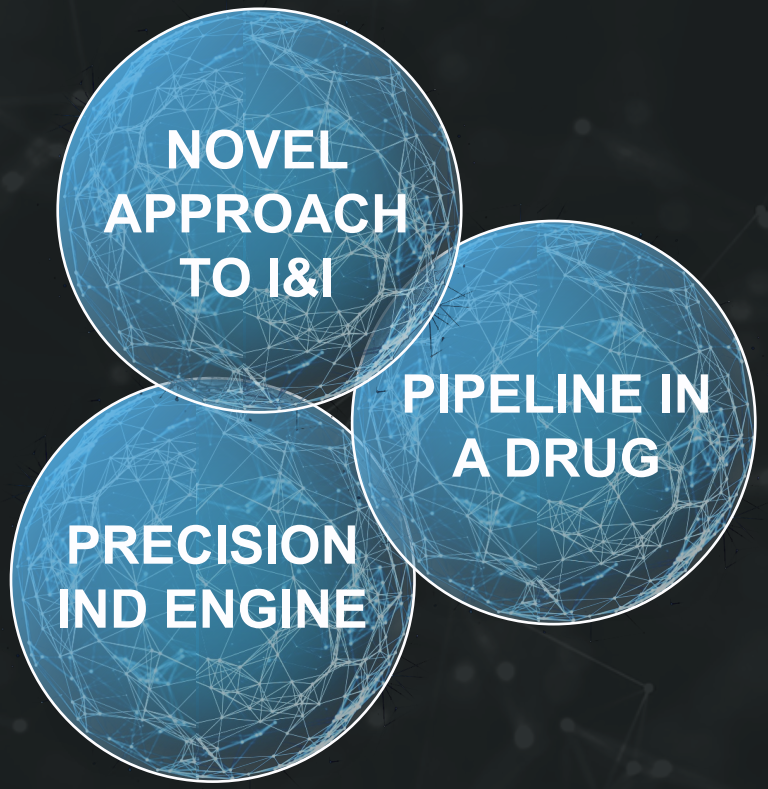
Martin Hendrix

Nestlé Health Science · Bayer

Pioneering Precision Medicine in Immunology, Beginning with IBD



Novel precision medicine approach to immune-mediated diseases, starting with IBD

Powered by Prometheus360™ Platform, one of world's largest precision GI biobanks

Lead Rx candidate PRA023 with unique dual anti-inflammatory & anti-fibrotic MOA

PRA023 showed class-leading Ph2 data in UC & CD; registrational studies begin 2023

Pipeline-in-a-drug potential via indication expansion; Ph2 SSc-ILD data expected 1H24

Second program PRA052 targeting CD30L in Phase 1; results expected 4Q23

Prometheus360™ IND engine equipped to produce a new IND every 12-18 months