

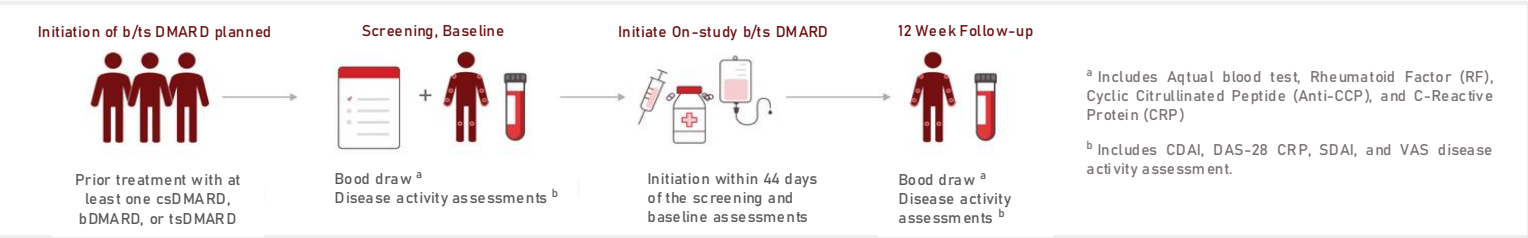
PRIMA-102 Clinical Study White Paper



Protocol title: PRIMA-102 (NCT05936970) Prospective, multi-center, observational, whole blood specimen collection study in participants with Rheumatoid Arthritis with inadequate response or intolerance to a DMARD starting a new bDMARD or tsDMARD treatment +/- csDMARD

Background: Targeted treatments for RA have significantly improved disease management by controlling symptoms and slowing progression. Despite these advances, a substantial proportion of patients exhibit suboptimal responses to specific biologic and targeted synthetic DMARDs (b/ts DMARDs), often cycling through multiple treatments before achieving disease control. This variability in therapeutic response underscores a critical gap in treatment selection and the pressing need for a precision medicine approach. A predictive test to identify responders to specific b/ts DMARDs would support more informed and effective treatment decisions, improving patient outcomes and cost-effectiveness. The PRIMA-102 study supports development and validation of a novel blood-based assay leveraging cell-free DNA derived from regulatory-active chromatin (cfDNA_{ac}) to predict response to bDMARDs and tsDMARDs.

Study design: Eligible participants are Rheumatoid Arthritis patients with inadequate response to prior therapy who are intending to switch to a new medication. Blood is collected at baseline and at follow-up. The primary analysis endpoint is clinical response to treatment measured as the change from baseline in CDAI at 12 weeks after initiating the on-study b/ts DMARD.



Clinical Disease Activity Index (CDAI) Assessments

Joint	Left		Right	
	Tender	Swollen	Tender	Swollen
Shoulder				
Elbow				
Wrist				
MCP 1				
MCP 2				
MCP 3				
MCP 4				
MCP 5				
PIP 1				
PIP 2				
PIP 3				
PIP 4				
PIP 5				
Knee				
Total	Tender:		Swollen:	



Patient Global Assessment of Disease Activity
Very Well (0) to Very Poor (10)

Provider Global Assessment of Disease Activity
Very Well (0) to Very Poor (10)

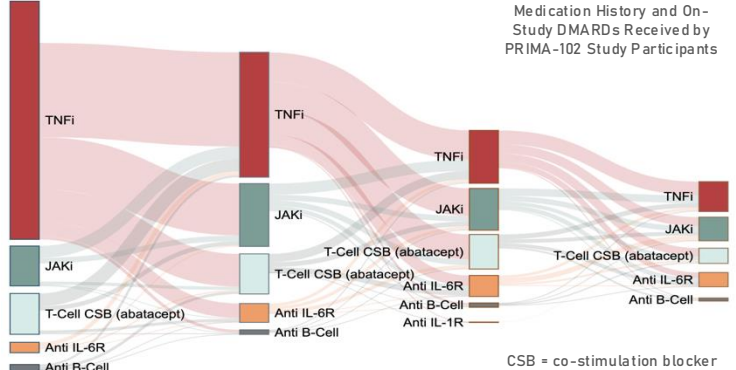
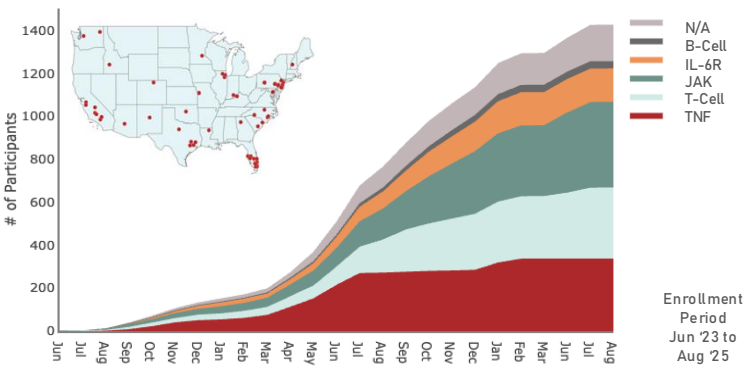
Response Criteria: Minimum Clinically Important Difference ^{1,2} in CDAI

Moderate CDAI score at baseline with a drop > 6 units, or a high CDAI at baseline with a drop of > 12 units

Variable	Range	CDAI Score Interpretation	
Tender joint score	(0-28)	0.0 – 2.8	Remission
Swollen joint score	(0-28)	2.9 – 10.0	Low Activity
Patient global score	(0-10)	10.1 – 22.0	Moderate Activity
Provider global score	(0-10)	22.1 – 76.0	High Activity

Formula: TJC + SJC + Patient Global + Provider Global

> 1,400 participants enrolled at 50+ sites across 22 states, including patients naïve to b/ts DMARDs and experienced with 1 or more lines of advanced therapy



Accumulation of data & samples supporting R&D and product launch

- > 400 evaluable participants and samples utilized for biomarker discovery and model training to support launch of test predicting the likelihood of response to 3 b/ts DMARD classes: TNFi, JAKi, T-Cell co-stimulation blocker (abatacept).
- > 350 evaluable participants and samples available for analytical and clinical validation, supporting review and approval by regulatory bodies including CLIA, CAP, and NYS CLEP.
- > 100 Anti IL-6R participant samples and data available for model training.

Clinical data and sample collection volume, sequencing progress

- ~ 1,500,000 clinical and sample data points captured
- > 71,600 ml of whole blood collected, and > 21,600 ml of plasma obtained
- > 850 evaluable patients with sample data supporting product development
- > 400 patients sequenced to date with cfDNA_{ac} profiles available

Compliance, quality, data integrity, and team experience

The study has been conducted in accordance with the protocol, the ICH Guideline for GCP, the World Medical Association Declaration of Helsinki, the provisions specified in Title 21 Parts 50, 54, 56, and 812 of the U.S. CFR, and any other applicable local regulations.

Clinical data are managed within the validated 21CFR11 compliant Medrio EDC system and sample data are managed in the validated Lockbox LIMS. Monitoring and source data verification performed throughout study conduct period. Study progress monitoring, data cleaning, and analysis supported by real time interactive clinical study dashboard visualizations.

Experienced clinical study management team with demonstrated success developing products involving blood collection, assay, sequencing, and machine-learning algorithms, supported by leading medical expert advisors in the field of rheumatology.

References: 1. Curtis et al., *Arthritis Care Res.* 2015; 2. Aletaha D, et al. *Arthritis Res Ther.* 2005