PREDICT Therapy Selection for JAK, T-cell, or IL-6 Inhibitor Therapies Using a Molecular Signature Response Classifier (PREDICT)

Protocol Number: PREDICT-001
Version: 1.0

Date: 22-Feb-2024

Sponsor:
Scipher Medicine Corporation
500 Totten Pond Road, Floor 6
Waltham, MA 02451

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1. Key Personnel

Sponsor: Jennifer Dines, MD
Vice President, Regulatory and Medical Affairs
Scipher Medicine Corporation
500 Totten Pond Road, Floor 6
Waltham, MA 02451

April Cobb
Senior Director, Clinical Operations
Scipher Medicine Corporation
500 Totten Pond Road, Floor 6
Waltham, MA 02451

2. Protocol Signature Page

Protocol Title: PREDICT Therapy Selection for JAK, T-cell, or IL-6 Inhibitor Therapies Using a Molecular Signature Response Classifier (PREDICT)
Protocol Number: PREDICT-001
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Date: 02/22/2024
Sponsor Name: Scipher Medicine Corporation

Declaration of Principal Investigator
I confirm that I have read the above-mentioned protocol and its attachments and understand it. I agree toconduct the described study in compliance with all stipulations of the protocol, as well as all applicable research regulations and ICH E6 Guideline for Good Clinical Practice (GCP).

Principal Investigator Name: _____

Principal Investigator Signature: _____

Date: _____

3. Protocol Summary

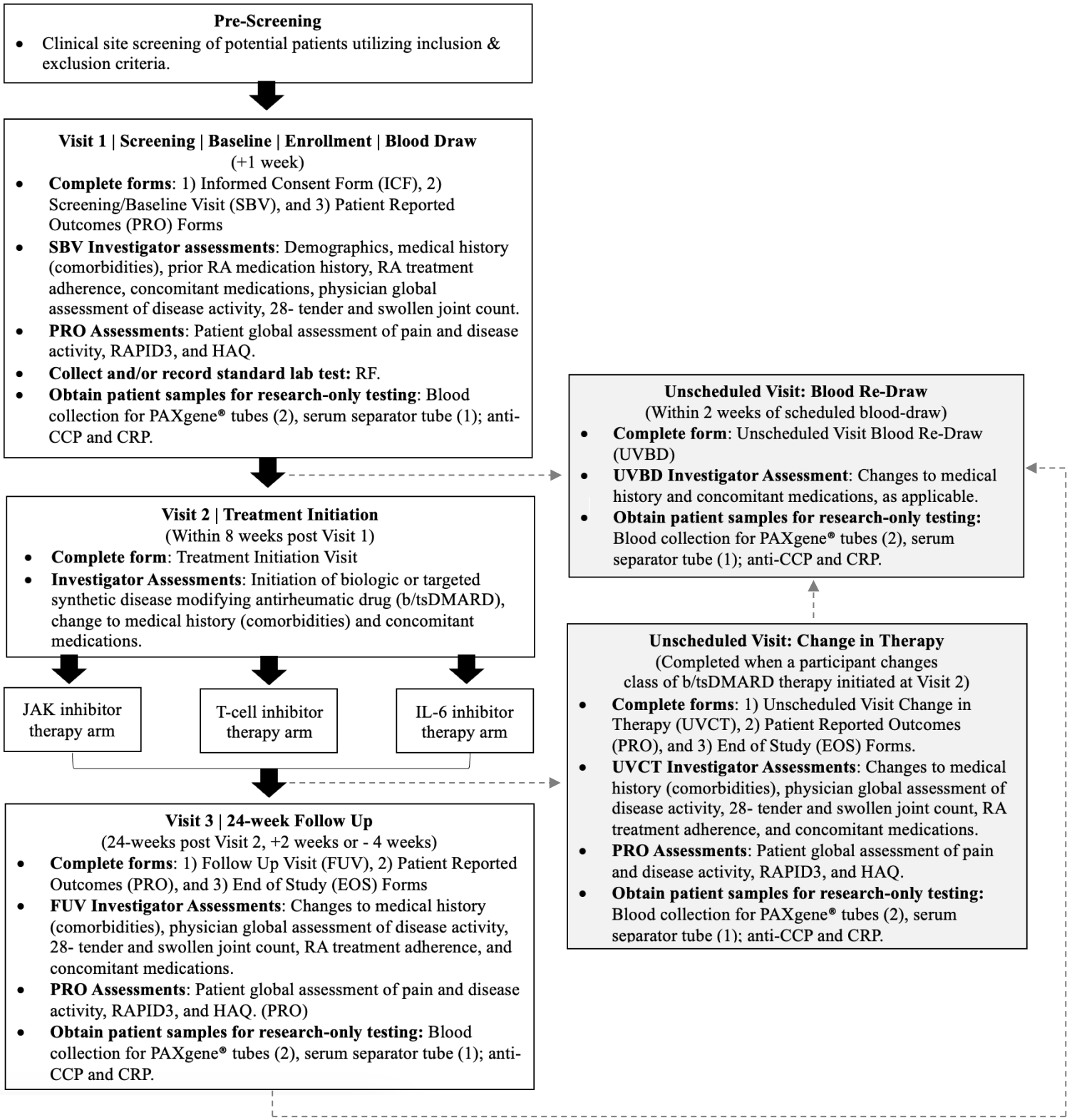
3.1. Synopsis

Protocol Title	PREDICT Therapy Selection for JAK, T-cell, or IL-6 Inhibitor Therapies Using a Molecular Signature Response Classifier (PREDICT)
Study Description	Prospective, multi-center-observational study conducted within the US, collecting patient samples for research and development to train, test, and validate precision medicine classifiers. These molecular signature response classifiers (MSRC) aim to predict response status to JAK, T-cell, and IL-6 inhibitor therapies in patients with rheumatoid arthritis (RA).
Study Population	RA patients with moderate or high disease activity and are eligible for treatment with a JAK, T-cell, or IL-6 inhibitor therapy who are either naïve to biologic and targeted synthetic DMARDs or TNFi-exposed.
Study Objectives	Collect patient blood samples, clinical, and laboratory data to develop, train, test, and validate precision medicine tests
Inclusion Criteria	1. Patient is eighteen years of age, or older (≥18) at time of consent. 2. Patient must meet the criteria for RA as defined by the 2010 ACR/EULAR classification atVisit 1 and documented by enrolling PI. 3. Patient has active RA, with moderate or high disease activity as confirmed by a CDAI score of >10 at Visit 1. 4. Patients must have a history of failure, contraindication, or intolerance to at least one csDMARD therapy. 5. Patient must be b/tsDMARD-naïve or TNFi-exposed prior to baseline visit only. 6. Patient must be initiating one of the following listed therapies (including biosimilars). a. JAK inhibitor therapy (only tofacitinib or upadacitinib) b. T-cell inhibitor therapy (abatacept) c. IL-6 inhibitor therapy (only tocilizumab) 7. Concomitant treatments are permitted per standard of care and are not limited to the following: a. csDMARD i. Methotrexate ii. Sulfasalazine iii. Leflunomide iv. Hydroxychloroquine b. Non-steroidal anti-inflammatory drugs c. Corticosteroids 8. Patient may participate in another observational study. 9. Patient is willing and able to complete the informed consent process and comply with all study procedures and visit schedule.
Exclusion Criteria	1. Patient has previously participated in a Scipher Medicine study (NETWORK-004, AIMs in RA, DRIVE, or INFORM). 2. Patients who have been treated with an altMOA (non-TNFi therapy) therapy for RA prior to baseline (Visit 1). 3. Women who are known to be pregnant or breast-feeding or plan to get pregnant during the study duration. 4. Concurrent treatment with an investigational product or use of an investigational product within 28 days of Visit 1. 5. The use of RA therapies outside of an FDA approved indication. 6. Patient is currently receiving systemic antimicrobial treatment for viral, bacterial, fungal, or parasitic infection at the time of baseline visit (Visit 1).

	7. Any known active, chronic, or recurrent invasive infection (e.g., listeriosis and histoplasmosis) and viral infection that, based on the Investigator's clinical assessment, makes the patient an unsuitable candidate for the study. This includes hepatitis B virus (HBV) or hepatitis C virus (HCV), recurrent or disseminated (even a single episode) herpes zoster, disseminated (even a single episode) herpes simplex, or human immunodeficiency virus (HIV). 8. Patient with any known active malignancy except non-melanoma skin cancer, localized prostate cancer treated with curative intent with no evidence of progression, low-risk or very low-risk (per standard guidelines) localized prostate cancer under surveillance/watchful waiting (without intent to treat), or carcinoma in situ of any type.
Study Duration	24-weeks (+2 weeks or -4 weeks)
Study Endpoints	**Primary**: Determine performance characteristics of the MSRC being developed, trained, and validated to predict a patient's response status to specific biologic or targeted therapies (specifically targeting JAK, T-cell, and IL-6 inhibitors) among rheumatoid arthritis patients with moderate or high disease activity using standard clinical outcome measures (i.e. CDAI and/or ACR50) as determined by the analysis plan. **Secondary**: The discovery of novel genomic predictors of response status for specific JAK, T-cell, and IL-6 inhibitor therapies. **Exploratory**: Including but not limited to - Clinical outcome response rate of patients with a molecular signature compared to the overall response rate of all patients given specific JAK, T-cell, and IL-6 inhibitor therapies. - Clinical response rate to specific JAK, T-cell, and IL-6 inhibitor therapies amongst patients with a molecular signature. - Adherence to assigned JAK, T-cell, and IL-6 inhibitor therapies. - Evaluation of patient reported outcomes (PROs) and response rate with a molecular signature compared to overall response rate of all patients given specific JAK, T-cell, and IL-6 inhibitor therapies. Additional exploratory research and development may be performed and may include unrelated and additional analyses to these study endpoints, including but not limited to patient samples may be used for MSRC research & development prior to finalized locked MSRC validation study.
Regulatory Status	The MSRC is a minimal risk device and is exempt from 21 CFR 812.2(c) IDE regulation. The MSRC is a Laboratory Developed Test being researched, developed, and validated in this study is properly labeled in accordance with 21 CFR 809.10(c); is noninvasive and does not require an invasive sampling procedure; and is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

3.2. Study Schema

FIGURE 1. PREDICT-001 Study Design



4. Introduction

4.1. Introduction

Rheumatoid arthritis (RA) is a complex, chronic, systemic autoimmune disease that leads to inappropriate inflammation and systemic tissue damage leading to joint destruction, loss of function, and permanent irreversible disability (1). As RA progresses, it negatively affects the ability of patients to work and perform activities of daily living, leading to decreased quality and length of life (2,3). The objective of treatment is to slow, stop, or reverse disease progression and improve the quality of life for RA patients.

Medication-based therapies comprise several classes of agents, including nonsteroidal anti-inflammatory drugs (NSAIDs), conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), and biologic disease-modifying antirheumatic drugs (bDMARDs). Biologic and non-biologic agents targeted at mediators of inflammation in RA are sometimes categorized collectively as targeted immune modulators (TIMs). TIMs represent a subcategory of DMARDs, including bDMARDs and targeted synthetic DMARDS (tsDMARDs), that have come into widespread use in the past decade. The clinical response to TIMs varies within phenotypically similar populations. Identifying those most likely to respond at a molecular level is an unmet need as earlier treatment with the right TIMs can slow disease progression (4,5). This study aims to develop, test, and validate precision medicine tests that identify which patients are more likely to respond to specific TIMs with a blood-based MSRC.

4.2. Background

The 2021 American College of Rheumatology (ACR) Guideline for the Treatment of Rheumatoid Arthritis defines Treat-to-Target (T2T) as a treatment strategy in which the clinician treats the patient aggressively to reach and maintain T2T goals, such as low disease activity or remission, with regular assessment of disease progress and prompt switching of the medication regimen if targets are not achieved in a timely manner (6,7). The ACR also recommends using low disease activity (LDA) or remission as the target for a T2T approach for all RA patients (7). However, given the heterogeneity of underlying RA disease biology that manifests in a phenotypically similar patient population, it is challenging to determine which targeted treatment will be most effective for an individual patient who has failed csDMARDs. Due to this reason, clinical guidelines do not recommend any specific targeted therapies after csDMARD failure as all b/tsDMARDs share similar efficacies and safety profiles (7-9).

These therapies span different biologic mechanisms of action (MOA) including tumor necrosis factor inhibitors (TNFi), IL-6, B-cell, T-cell, and JAK inhibitors (7,8). Patients with suboptimal responses often switch to alternative MOA through a trial-and-error process. There's a pressing need for a precision medicine test to help clinicians avoid prescribing ineffective therapies for RA. This approach would aim to achieve early, sustained low disease activity or remission by starting the patient on the right medicine sooner.

The first molecular signature response classifier (MSRC), PrismRA®, was developed to predict inadequate response to TNFi therapies in both biologic-naïve and TNFi-exposed patients with RA (10-12), and the classifier is being expanded to include prediction of response status to other biologic or targeted therapies. This predictive test can lead to the selection of appropriate targeted therapy for RA patients based on their individual disease biology characteristics, as opposed to the conventional trial-and-error process.

4.3. Study Purpose

One of the forementioned challenges in treating RA is the substantial variability in clinical outcomes among patients stemming from the disease's diverse pathophysiology, which affects how patients respond to individual biological or targeted treatments. Notably, those who do not respond well to their first trialed biological therapy will likely find less success with subsequent biological or targeted synthetic DMARD (b/tsDMARD) treatments (13,14). Given this challenge, there is a pressing need for precision medicine tests that can predict a patient's response to specific therapies independent of prior treatment exposure. Such a tool would enable more personalized treatment approaches, helping patients achieve low disease activity or remission more rapidly. This approach is crucial, especially considering the "window of opportunity" in RA treatment, where early and

effective intervention can significantly alter the disease's course. Avoiding the traditional “fail forward” method would not only save time but also spare patients from unnecessary delays in receiving the most effective treatment for their specific case.

Scipher Medicine Corporation is addressing this unmet need by developing a MSRC that accurately predicts, from a RA patient’s blood sample, the likelihood of achieving their treatment target on specific JAK, T-cell, and IL-6 inhibitor therapies. This study will collect patient blood samples, clinical, and laboratory results to develop, train, test, and validate precision medicine tests (MSRC).

4.4. Intended Use*

The MSRC is intended to be used by the treating clinician for patients with an established diagnosis of RA for whom current therapies (e.g., methotrexate) are not effectively managing symptoms, and who are considering starting a biologic or targeted therapy. The MSRC being developed, and validated aims to predict a patient’s likelihood of response or inadequate response to certain TNF, JAK, T-cell, and IL-6 inhibitor therapies so that resulting treatment selected is based on the patient’s unique disease biology. Consequently, a targeted therapy can be offered that has the best chance of success to treat moderate-to-severe RA.

*Final MSRC developed and validated may have a different intended use and will be based on development done prior to the validation of the precision medicine test.

5. Study Endpoints

5.1. Primary Endpoint

Determine performance characteristics of the MSRC being developed, trained, and validated to predict a patient’s response status to specific biologic or targeted therapies (specifically targeting JAK, T-cell, and IL-6 inhibitors) among rheumatoid arthritis patients with moderate or high disease activity using standard clinical outcome measures (i.e. CDAI and/or ACR50) as determined by the Clinical Validation Analysis Plan (CVAP) and associated Statistical Analysis Plan (SAP).

5.2. Secondary Endpoint

The discovery of novel genomic predictors of response status for specific JAK, T-cell, and IL-6 inhibitor therapies.

5.3. Exploratory Endpoints

Including but not limited to clinical outcome response rate of patients with a molecular signature compared to the overall response rate of all patients given specific JAK, T-cell, and IL-6 inhibitor therapies.

Clinical response rate to specific JAK, T-cell, and IL-6 inhibitor therapies amongst patients with a molecular signature.

Adherence to assigned JAK, T-cell, and IL-6 inhibitor therapies.

Evaluation of patient reported outcomes (PROs) to determine response rate of patients with a molecular signature compared to overall response rate of all patients given specific JAK, T-cell, and IL-6 inhibitor therapies.

Additional exploratory research and development may be performed and may include analyses unrelated to study endpoints; including but not limited to utilizing patient samples for R&D prior to finalized MSRC used in clinical validation.

6. Study Design

6.1. Study Type

This is a prospective, multi-center-observational study conducted within the US, evaluating the clinical performance of a molecular signature response classifier (MSRC) to predict response status to specific JAK, T-cell, and IL-6 inhibitor therapies in patients diagnosed with RA.

Whole blood and serum will be collected at Visit 1, Visit 3, and if applicable, an Unscheduled Visit: Change in Therapy and/ or an Unscheduled Visit: Blood Re-Draw in two PAXgene® tubes and one serum separator tube (SST). Samples will be labeled and shipped to Scipher's central laboratory for processing, testing, and generation of the molecular signature test results. Coded and de-identified data and/or specimens from the PAXgene® blood samples and/or SST may be used for future research or distributed to another third party for future use. CRP and anti-CCP values will be obtained by Scipher Medicine Laboratory for research purposes only and results will not be returned to the Investigator, patient nor enrolling sites.

6.2. Study Population

The study will enroll patients with a documented clinical diagnosis of RA with moderate-to-high disease activity (CDAI score >10) from the US across approximately 70 clinical and academic sites. Patients must have failed, had a contraindication, or intolerance to at least one non-biologic csDMARD therapy at the time of enrollment, are either b/tsDMARD-naïve or TNFi-exposed only, and are candidates for a specific JAK, T-cell, or IL-6 inhibitor therapy, as described in this protocol.

This study will screen approximately 1,500 patients across therapeutic modalities and at the discretion of the sponsor. Patients will be considered fully enrolled after they have initiated a biologic or targeted synthetic DMARD therapy during Visit 2 (index). The target for enrollment is approximately 1,100 patients. Final study enrollment numbers will be at the discretion of the sponsor and finalized in the CVAP and associated SAP.

6.3. Patient Selection Criteria

6.3.1. Inclusion Criteria

1. Patient is eighteen years of age, or older (≥18) at time of consent.
2. Patient must meet the criteria for RA as defined by the 2010 ACR/EULAR classification atVisit 1 and documented by enrolling PI.
3. Patient has active RA, with moderate or high disease activity as confirmed by a CDAI score of >10 at Visit 1.
4. Patients must have a history of failure, contraindication, or intolerance to at least one csDMARD therapy.
5. Patient must be b/tsDMARD-naïve or TNFi-exposed prior to baseline visit only.
6. Patient must be initiating one of the following listed therapies (including biosimilars):
    a. JAK inhibitor therapy (only tofacitnib or upadacitinib)
    b. T-cell inhibitor therapy (abatacept)
    c. IL-6 inhibitor therapy (only tocilizumab)
7. Concomitant treatments are permitted per standard of care and are not limited to thefollowing:
    a. csDMARD
        i. Methotrexate
        ii. Sulfasalazine
        iii. Leflunomide
        iv. Hydroxychloroquine
    b. Non-steroidal anti-inflammatory drugs
    c. Corticosteroids
8. Patient may participate in another observational study.
9. Patient is willing and able to complete the informed consent process, comply with all study procedures, and visit schedule.

6.3.2. Exclusion Criteria

1. Patient has previously participated in a Scipher Medicine study (NETWORK-004, AIMs in RA, DRIVE, or INFORM).
2. Patients who have been treated with an altMOA (non-TNFi therapy) therapy for RA prior to baseline (Visit 1).
3. Women who are known to be pregnant or breast-feeding or plan to get pregnant during the study duration.
4. Concurrent treatment with an investigational product or use of an investigational product within 28 days prior to Visit 1.
5. The use of RA therapies outside of the FDA approved indication.
6. Patient is currently receiving systemic antimicrobial treatment for viral, bacterial, fungal, or parasitic infection at the time of baseline visit (Visit 1).
7. Any known active, chronic, or recurrent invasive infection (e.g., listeriosis and histoplasmosis) and viral infection that, based on the Investigator's clinical assessment, makes the patient an unsuitable candidate for the study. This includes hepatitis B virus (HBV) or hepatitis C virus (HCV), recurrent or disseminated (even a single episode) herpes zoster, disseminated (even a single episode) herpes simplex, or human immunodeficiency virus (HIV).
8. Patient with any known active malignancy except non-melanoma skin cancer, localized prostate cancer treated with curative intent with no evidence of progression, low-risk or very low-risk (per standard guidelines) localized prostate cancer under surveillance/watchful waiting (without intent to treat), or carcinoma in situ of any type.

7. Study Procedures

7.1. Summary of Visits and Assessments

- **Visit 1: Screening/Baseline**
  - Time: +1 week*
  - Forms:
    - Informed Consent Form (ICF)
    - Screening/Baseline Visit (SBV)
    - Patient Reported Outcomes (PRO)
  - SBV Investigator Assessments: Medical history, comorbidities, demographics, physician global assessment of disease activity, 28- tender and swollen joint count, and concomitant medications
  - PRO Assessments: Patient global assessment of pain and disease activity,RAPID3, and Health Assessment Questionnaires (HAQ)
  - Standard Lab Tests: RF**
  - Obtain patient samples for research-only testing: Blood collection for PAXgene® tubes (2), serum separator tube (1); anti-CCP and CRP***

- **Visit 2: Treatment Initiation****
  - Time: Within 8 weeks post Visit 1
  - Form: Treatment Initiation Visit
  - Investigator Assessments: Initiation of biologic or targeted therapy, changes to medical history, comorbidities and concomitant medications

- **Visit 3: 24-week Follow-up*****
  - Time: 24-weeks post treatment initiation (+2 weeks or -4 weeks)
  - Forms:
    - Follow Up Visit (FUV)
    - Patient Reported Outcomes (PRO)
    - End of Study (EOS)
  - FUV Investigator Assessments: Changes to medical history, comorbidities, and

concomitant medications, physician global assessment of disease activity, 28- tender and swollen joint count, and RA treatment adherence
  - PRO Assessments: Patient global assessment of pain and disease activity, RAPID3, and Health Assessment Questionnaires (HAQ)
  - Obtain patient samples for research-only testing: Blood collection for PAXgene® tubes (2), serum separator tube (1); anti-CCP and CRP***

- **Unscheduled Visit: Blood Re-Draw***
  - Time: Within 2 weeks of scheduled blood-draw
  - Forms:
    - Unscheduled Visit Blood Re-Draw (UVBD)
  - UVBD Investigator Assessment: Changes to medical history, comorbidities and concomitant medications
  - PRO Assessments: None
  - Obtain patient samples for research-only testing: Blood collection for PAXgene® tubes (2), serum separator tube (1); anti-CCP and CRP***

- **Unscheduled Visit: Change in Therapy*****
  - Time: N/A [Visit to be completed when a participant changes class of b/tsDMARD therapy initiated at Visit 2]
  - Forms:
    - Unscheduled Visit Change in Therapy (UVCT)
    - Patient Reported Outcomes (PRO)
    - End of Study (EOS)
  - UVCT Investigator Assessments: Changes to medical history, comorbidities, and concomitant medications, physician global assessment of disease activity, 28- tender and swollen joint count, and RA treatment adherence
  - PRO Assessments: Patient global assessment of pain and disease activity,RAPID3, Health Assessment Questionnaires (HAQ)
  - Obtain patient samples for research-only testing: Blood collection for PAXgene® tubes (2), serum separator tube (1); anti-CCP and CRP***

*Clinical data and blood samples can be collected within 1 week of the initial screening/baseline visit. If the original MSRC blood sample fails at Visit 1, Visit 3, or Unscheduled Visit: Change in Therapy and a recollection is required, up to 2 weeks is allowed to complete an Unscheduled Visit: Blood Re-Draw.
**RF testing not necessary if previous results available via subject's medical record and are within 1 year of Visit 1.
*** Anti-CCP and CRP values will be obtained by Scipher Medicine Laboratory for research purposes only and will not be returned to the Investigator, patient nor enrolling sites. Patient samples must be shipped within 24 hours of the blood draw, but ideally the same day or next morning to avoid test failure. No samples should be shipped on Saturday.
****If according to standard of care at treatment center, sites will be permitted to conduct Visit 2 over the phone or virtual setting. Visit 2 may be conducted following Scipher Medicine Laboratory receiving and processing the subject's whole blood and serum collected at Visit 1, within 5 business days.
*****In-class therapy switch or adjustments to dose, route of administration, or frequency of b/tsDMARD therapy initiated at Visit 2 will be permitted and rationale for change will be recorded. If a therapy from a different class of b/tsDMARDs is initiated from Visit 2, the therapy, dose, route of administration, frequency and rationale for changing therapy will be collected and a major protocol deviation will be recorded. In addition, the patient will complete their Unscheduled Visit: Change in Therapy at that time.

The date of study treatment initiation (Visit 2) constitutes the index date for the beginning of the follow-up. The 0-8 weeks period following Visit 1 will be used to ascertain all baseline data is collected and the patient has initiated a treatment within this time frame. The 24-week follow-up (Visit 3) will be defined as the visit window at 24 weeks (+2 weeks or -4 weeks) from the index date.

Depending on final enrolled sample numbers and biostatistical power calculations and feasibility analyses, a data review may be conducted that may outline different follow-up (Visit 3) windows such as 24 (±6) weeks and 24 (±8) weeks. In these instances, a minor protocol deviation will be recorded for patients whose Visit 3 assessments were collected outside 24-week (+2 weeks or -4 weeks) window, and they may be included in the final analyses.

7.2. Participant Identification, Recruitment, Pre-Screening

Before Visit 1 (Pre-Screening), patient charts may be reviewed to determine eligibility for the study. Participants will be identified and recruited by, but not limited to, clinicians and other health care personnel at participating sites, online and printed marketing material, and radio and television advertisements. The identification and recruitment of participants will protect privacy and be free of undue influence. All patient-facing material will be submitted to the IRB for approval prior to use.

7.3. Screening

At Visit 1, potential study participants will be screened by study team members according to inclusion and exclusion criteria as outlined in the "Section 6.3 Patient Selection Criteria" above, and informed consent will be obtained.

7.4. Informed Consent Process

At Visit 1, a written informed consent form (ICF) will be used to document consent of the patient. This must be obtained prior to recording of any tests or assessments under this protocol.

The IRB approved informed consent form (ICF) will adhere to ICH GCP guidelines and comply with the United States Code of Federal Regulations as detailed in 21 CFR §50.25 and the Declaration of Helsinki.

7.5. Enrollment

1. At Visit 1, patients will complete the informed consent form (ICF) process prior to any study specific assessments being conducted. Each patient will be assigned a unique study identification number that will be used to track their de-identified data throughout their participation in the study.
2. At Visit 1, patient name, birth month and year and study identification number will be stored on a secure and HIPAA-compliant research database. The sponsor will have access to these data as applicable to appropriately conduct the study and adhere to consent and opt-in consent at time of enrollment.
3. At Visit 2, after the patient initiates one of the following targeted therapy options listed below, the patient will be considered enrolled into the study:
    - JAK inhibitor therapy (only tofacitinib or upadacitinib)
    - T-cell inhibitor therapy (abatacept)
    - IL-6 inhibitor therapy (only tocilizumab)

7.6. Schedule of Assessments

Procedure	Visit 1 (Screening/ Baseline)	Visit 2 (Treatment Initiation)	Visit 3 (24-Week Follow-up)[7]	Unscheduled Visit: Blood Re-Draw	Unscheduled Visit: Change in Therapy
Visit windows	+1 week[6]	Within 8 weeks of Screening/Baseline	+2 weeks or -4 weeks	Within 2 weeks of scheduled blood-draw	N/A
Informed consent	X				
Eligibility criteria	X				
Medical history[1]	X	X	X	X	X
Prior medication history for RA	X				
28-Joint count for tenderness	X		X		X
28-Joint count for swelling	X		X		X
Comorbidities	X		X		X
Smoking status	X	X	X	X	X
Height	X		X		X
Weight	X		X		X
RF[2]	X				
Anti-CCP[3]	X		X	X	X
2x PAXgene® tubes	X		X	X	X
1x Serum Separator tube	X		X	X	X
CRP[3]	X		X	X	X
Physician global assessment of disease activity	X		X		X
Patient global assessment of pain and disease activity	X		X		X
RAPID3 assessment[4]	X		X		X
Health Assessment Questionnaire	X		X		X
Initiation of biologic or targeted therapy[5]		X			
Rx Adherence Check			X		X
b/tsDMARD therapy[5]	X		X		X
Concomitant medications[1]	X	X	X	X	X

[1]Changes to medical history and concomitant medications will be collected at all visits in the case report form (CRF). Information collected will include any changes to medication list and medical history collected at Visit 1.
[2]Test result can be pulled from patient record if test results are within 1 year of Visit 1. If test result is not available, a new test is to beordered using standard local lab ordering practices.
[3]Anti-CCP and CRP values will be obtained by Scipher Medicine Laboratory for research purposes only and will not be returned to the Investigator, patient nor enrolling sites.
[4]Only 3 questions (Questions I and J, and PtGA) from the RAPID3 assessment will be collected on the patient assessment form and the score will be computed based on these answers and related questions from HAQ by sponsor.
[5]b/tsDMARD therapy the patient is on at time of Visit 1, if applicable, will be collected; Visit 2 will collect new

b/tsDMARD initiated; Between Visit 2 (index date) and Visit 3, in-class therapy switch or adjustments to dose, route of administration, or frequency of b/tsDMARD therapy initiated at Visit 2 will be permitted and rationale for change will be recorded. If a therapy from a different class of b/tsDMARDs is initiated following Visit 2, the therapy, dose, route of administration, frequency, and rationale for changing therapy will be collected and a major protocol deviation will be recorded. The patient will complete their Unscheduled Visit: Change in Therapy at that time.
[6]Clinical data and blood samples can be collected within 1 week of the initial screening/baseline visit. If the original MSRC blood sample fails at Visit 1, Visit 3, or Unscheduled Visit: Change in Therapy and a recollection is required, up to 2 weeks allotted to complete Unscheduled Visit: Blood Re-Draw.
[7]If there are no therapy class changes to the b/tsDMARD therapy initiated at Visit 2, patient will complete Visit 3 after 24-weeks (+2 weeks or -4 weeks) of Visit 2, index date.

7.7. Research Specimen Collection

Whole blood and serum will be collected at Visit 1, Visit 3, and if applicable, Unscheduled Visit: Change in Therapy or Unscheduled Visit: Blood Re-Draw. Blood will be collected in two 2.5 mL PAXgene® tubes and one 8-10 mL serum separator tube for a total 12 mL blood collection at Visit 1, Visit 3, and if applicable, Unscheduled Visit: Change in Therapy or Unscheduled Visit: Blood Re-Draw. Blood will be processed according to appropriate standard lab procedures.

Anticipated volume of blood to be drawn per patient over the scheduled study visits should not exceed 48 mL, unless standard of care tests are required. If the initial (Visit 1), follow-up (Visit 3), and/ or, if applicable, Unscheduled Visit: Change in Therapy MSRC analysis fails, a patient may have an Unscheduled Visit: Blood Re-Draw performed for an additional blood draw for the MSRC analysis.

Additional tests may be run on the participant's samples. This will be explicitly stated in the consent form.

7.8. Study Treatments

Patients are to initiate their targeted therapy per clinical guidance of the Investigator at Visit 2, index date. Patients can be b/tsDMARD-naïve or TNFi-exposed only at Visit 1, prior to enrollment.

7.8.1. Therapy, Dose, Modes of Administration

Dosage and selection of biologic or targeted therapy is at the Investigator's discretion, if within the FDA approved label.

Before Visit 3, in-class therapy switch or adjustments to dose, route of administration, or frequency of b/tsDMARD therapy initiated at Visit 2 will be permitted and rationale for change will be recorded. If a therapy from a different class of b/tsDMARDs is initiated from Visit 2, the therapy, dose, route of administration, frequency and rationale for changing therapy will be collected and a major protocol deviation will be recorded. The patient will complete their Unscheduled Visit: Change in Therapy at that time.

Information, including therapy, dose, route of administration, frequency, rational for change, and changes in medical history will be recorded for any change in b/tsDMARD therapy initiated at Visit 2 (index) in the study electronic data capture (EDC) system.

7.8.2. Stratification

Patients will be stratified based on the four potential biologic or targeted therapies in an approximate ratio of 225:225:225:225 for tofacitnib (JAKi): upadacitinib (JAKi): tocilizumab (IL-6i): and abatacept (T-cell inhibitor). These ratios are subject to change and at the discretion of study sponsor. Final cohort numbers will be outlined in the CVAP and associated SAP. If during the study, certain therapy arms are fully enrolled, the study sponsor may limit additional patients from enrolling and participating in the study within fully enrolled therapy arms.

7.8.3. Duration of Study and Treatment Selection

The study is 24 weeks (+2 weeks or - 4 weeks) in duration and is indexed after the patient's therapy is initiated at Visit 2 (index date) and associated clinical and laboratory data are collected.

7.8.4. Cost to Participants and Medication Expenses

This study is an observational study, and the Sponsor will not cover any medication costs or standard of care labs associated with this study. The Sponsor will pay for research procedures associated with the study and necessary for follow-up. Participants will not incur any costs, nor will insurance be billed for research procedures in this study which include venipuncture and medical record retrieval if applicable. Participants will not be compensated for any missed visits.

7.8.5. Concomitant Treatments

If the Investigator deems it medically necessary, a patient's concomitant treatment can be adjusted after Visit 1 and before Visit 3. Any changes to the dose, route of administration, frequency, and rational for change of concomitant medications during the course of the study will be collected at all study visits including Visit 2 (index), Visit 3 (24-week follow-up), and if applicable, Unscheduled Visit: Blood Re-Draw and/or Unscheduled Visit: Change in Therapy.

7.8.6. Participant Reimbursement

Patients will be reimbursed for their time participating in the study. Participants will qualify for visit compensation after the completion of the corresponding visit and all visit-related procedures. Participants will be compensated the following amounts for each respective visit completed: $100 for Visit 1, $50 for Visit 2, $100 for Visit 3 or an Unscheduled Visit: Change in Therapy, and $50 for an Unscheduled Visit: Blood Re-Draw.

7.8.7. Patient Withdrawal/ Completion

Patients may withdraw from the study at any time without prejudice to their care. The Investigator and/or the Sponsor or designee may withdraw patients at any time who violate the study protocol, to protect the patient for safety reasons, for administrative or other reasons at any time. It will be documented whether each patient completes the determined follow-up visits or not and rationale for withdrawal.

8. Data Collected and Statistical Methods

8.1. Metadata Summary

The following data will be collected from the study-eligible patients at Visit 1.

Domain	Variables
Demographics	• Age (calculated from birth month and year) • Sex at birth • Race (American Indian or Alaskan Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Other, Unknown) • Ethnicity (Hispanic, Non-Hispanic, Not reported, Unknown) • Geography (zip code and state of residence) • Height, Weight, BMI
Lifestyle	• Smoking (current, former, or never smoker)

RA related	• Date of RA diagnosis
	• Seropositivity (seropositive or seronegative)
	  ○ RF status (positive or negative)
	  ○ Anti-CCP status (positive or negative)
	• CRP
	• CDAI at baseline

	• Previous use of TNFi therapy • TJC and SJC at baseline • PGA at baseline • PtGA at baseline • RAPID3 at baseline • HAQ at baseline Concurrent RA medication dosage, route, frequency, and duration • csDMARDs • Folic Acid • NSAIDs • Glucocorticoids
Comorbidities (Medical History)	• Cardiovascular disease (including but not limited to Myocardial infarction, Cerebral Vascular Accident (CVA), Transient Ischemic Attack (TIA), Congestive Heart Failure (CHF)) • Hypertension • Anemia or other blood disease • Lung disease • Diabetes • Ulcer or stomach disease • Kidney disease • Liver disease • Cancer • Osteoarthritis, degenerative arthritis • Back Pain • Fractures spine, hip, or leg • Depression

Patient data will be collected from clinical assessments, medical records, laboratory results, and surveys at screening/ baseline (Visit 1), treatment initiation (Visit 2), 24-week follow-up visit (Visit 3), Unscheduled Visit: Blood Re-Draw, and Unscheduled Visit: Change in Therapy and entered in the study EDC.

If a completed medical records release form is on file, comprehensive demographic, medical, and health information (if available) may be directly collected from the patient's electronic medical records by the study sites or sponsor. Electronic Medical Records (EMR) data may be obtained indefinitely following a patient's enrolment unless the patient withdraws authorization.

CRP and anti-CCP data from the Visit 1, Visit 3, Unscheduled Visit: Blood Re-Draw, and Unscheduled Visit: Change in Therapy samples will be stored at Scipher Medicine's Clinical Laboratory Improvement Amendments (CLIA)-certified and College of American Pathologists (CAP)-accredited laboratory.

In order to reduce the loss of patients to follow-up, all patients will be asked for their personal contact information and an alternate person's contact information. Patients may be directly contacted by the Investigator or Sponsor/designee in order to support study follow-up. The designated alternate contact person may also be directly contacted in the event the patient cannot be reached.

For patients who are lost to follow-up, Investigator or Sponsor/designee will search available health status databases to determine vital status and cause of death in the case of mortality.

8.2. Statistical Methods

Additional information regarding the statistical methods and plan will supersede the following section (if applicable) and will be documented in the SAP for the Clinical Validation of MSRC. Samples to validate the classifier will be utilized from this study as well as retrospective samples collected in prior studies. This will be outlined in the CVAP and associated SAP.

8.2.1. Baseline Data

The primary and demographic variables will be examined with summary statistics, including means, medians, standard deviations (SD), minimum, and maximum values for continuous variables, and frequencies and proportions for categorical variables.

8.2.2. Analysis of Primary Outcome of Interest

MSRC performance characteristics will be determined by analyzing the samples collected in this study, with consideration of samples collected from other studies, and comparing the predicted response labels to the true clinical classifications.

8.2.3. Missing Data

Missing data will be minimized through rigorous conduct of data collection and monitoring as described in Section 8.1. No statistical methods will be employed to address missing data.

8.2.4. Sample Size

Approximately 1,500 participants will be enrolled in this study. Samples are to be collected prospectively for this study, with at least 300 patients enrolled the study for each standard of care therapy. The power analysis and sample size calculation details will be outlined in the CVAP and associated SAP.

9. Data Handling and Record Keeping

9.1. Study Database

Data will be collected in the study database through a secure, electronic database capture (EDC) system or an electronic data transfer via an encrypted secure sockets layer protocol as applicable.

Electronic case report forms will be maintained in the EDC, and all relevant observations and data related to the protocol-defined assessments will be recorded. This will include, at minimum, medical history, laboratory results, sample collection records, treatment information, and patient reported assessments.

Participants birth month and year will be recorded to determine satisfaction of inclusion criterion (age ≥18 at time of first study activity).

Prior to recording data in the eCRF, Investigators and site staff will be trained on how to use the EDC system. Investigators or the assigned trained and qualified site staff are responsible for ensuring timely and accurate data entry into the EDC system within 5 business days. Records of the patient visits will be filed as source documents for this study and used to input the data into the study database. If applicable, site specific assigned trained and qualified Sponsor or Sponsor designee may record timely and accurate data entry into the EDC system within 5 business days.

Investigators or assigned Sponsor or Sponsor designees are responsible for overseeing the eCRFs, including resolving data queries, reviewing and approving all changes to the patient data, and providing final approval of the data. The Investigator will provide final approval by electronically signing and dating each eCRF. Signed eCRFs will be retained in secure archives.

The study database will be password protected and access provided only to trained and authorized personnel. Data

collected into the study database may include protected health information (PHI). This PHI will not be shared beyond the Sponsor/designee or regulatory bodies as warranted and allowed based on patient's consent and optional opt-ins.

9.2. Inspection of Records

Sponsor or its designee will be allowed to conduct site visits either remotely or at the Investigator's clinical research facilities for the purpose of monitoring any aspect of the study. The Investigator agrees to allow the Sponsor or its designee to inspect the facilities, patient medical records, source documents, and any other records relevant to conduct the study. Data containing patient health information will be maintained in a confidential manner. If necessary, source documents containing PHI will be protected and may be transferred to the Sponsor or Sponsor designee via a secure, HIPAA compliant portal. Data containing patient health information will be maintained in a confidential manner.

9.3. Retention of Records

All primary data that are a result of the original observations and activities of the study and that are necessary for the reconstruction and evaluation of any study report will be retained in a secure archive at the study site for a period not less than 6 years after the last approval of a marketing application in an International Council for Harmonization (ICH) region, and until there are no pending or contemplated marketing applications in an ICH region, or until at least 6 years have lapsed since the formal discontinuation of the clinical development of the MSRC. All relevant country and region-specific requirements that may be more stringent than the 6 years included in ICH shall be followed.

The site will maintain an Investigator Site File (ISF), which will be maintained at the study site and in accordance with local and Federal regulations, as applicable. The site must keep this ISF current and available for review by the Sponsor, IRB, and/or regulatory bodies.

9.4. Optional Medical Record Retrieval, Linking to Electronic Health Records, and/or Tokenized Healthcare Data

As part of this study, protected health information, with the participant's consent, will be accessed to confirm medical information pertaining to the participant's medical history, symptoms, and diagnostic tests performed for rheumatoid arthritis and relevant comorbidities to collect all required study-related data.

Participants have the option to also authorize via a HIPAA-compliant authorization ("HIPAA form") additional access to medical records and claims data related to their rheumatoid arthritis condition or other autoimmune or immune-mediated conditions. The HIPAA form will authorize participants' physicians to give study personnel, including the study sponsor access to the participants' electronic health records and medical claims data. This may include but is not limited to authorizing the identifiable pairing of tokenized healthcare data with study data and residual blood samples on an ongoing basis. This will be explicitly stated in study consent form.

9.5. Confidentiality of Records

All study sites, laboratories, and parties supporting this study must comply with HIPAA, where applicable. All data and records generated throughout this study will be kept confidential in accordance with local and Federal policies.

At consent, personal identifying information, including subject name, zip code, birth month and year, and contact information will be collected and stored on a secure and HIPAA-compliant research database.

Following consent, each subject will be assigned a unique study identification number that will be used to track their de-identified data. Sample tubes collected and sent to Sponsor or delegates may include PHI. Upon receipt of samples, the unique study identification number will replace PHI during processing and prior to storage.

Records that may have patient identifying information will be kept confidential in accordance with applicable guidelines, regulations, and laws, as described in Section 12.2.

9.6. Review of Records

Sponsor and/or its designee will review source documents (i.e., medical records, laboratory results) and data collected throughout the study as applicable. In addition, an auditor, IRB, FDA, or national or local regulatory authorities may access and review applicable source documents, records, and data. All patients will be notified and provide consent to this possibility, during the consenting process.

10. Quality Control

10.1. Data Quality

Site and data monitoring will occur in accordance with the clinical monitoring plan. Data captured in the study database will be compared against the source data for completeness and accuracy. Discrepancies will be addressed and corrected, if required, by qualified site personnel and sponsor as applicable.

eCRF data will also be routinely reviewed for timeliness, errors, accuracy, and omissions. Data queries will be created and submitted to the sites for data requiring further clarification. Qualified site personnel will address queries and correct data in the study database.

10.2. Protocol Deviations

Study sites and database will be evaluated for protocol deviations which include but are not limited to:

- Minor protocol deviations:
  - Depending on final enrolled sample numbers and biostatistical power calculations and feasibility analyses, a data review may be conducted that may outline different follow-up (Visit 3) windows such as 24 ($\pm$6) weeks and 24 ($\pm$8) weeks. In these instances, a minor protocol deviation will be recorded for patients whose Visit 3 assessments were collected outside 24-week (+2 weeks or -4 weeks) window, and they may be included in the final analyses.
- Major protocol deviations:
  - If a therapy from a different class of b/tsDMARD is initiated after Visit 2's therapy, the new therapy, dose, route of administration, frequency and rationale for changing therapy will be collected and a major protocol deviation will be recorded. The patient will complete their Unscheduled Visit: Change in Therapy at that time.
  - If study assessments and procedures are conducted prior to obtaining a signed ICF, a major protocol deviation will be recorded, the patient will be excluded from completing the study, and the End of Study (EOS) form will be completed.
  - If a participant entered the study or initiated treatment at Visit 2 but did not satisfy the inclusion and exclusion criteria outlined in Section 6.3, a major protocol deviation will be recorded, the patient will be excluded from completing the study, and the End of Study (EOS) form will be completed.

A quarterly deviation meeting will be held by Sponsor to evaluate deviations identified during the study. Data integrity mitigation will be completed to ensure statistical power is not jeopardized and/or need for protocol amendments as applicable. The number and type of protocol deviations will be analyzed by the Sponsor to review the events by site to determine if the deviations could affect the integrity of the study data. The study biostatistician will report findings to the Sponsor. Sites with multiple deviations may be required to have remediation training as applicable.

10.3. Publications

If any results of the study are presented at scientific conferences or published, the subject's identity will remain confidential.

10.4. Future Use of Data or Specimens

De-identified data and samples collected and processed throughout the study may be used for future research and/or distributed to other investigators or third parties for future efforts at the discretion of the Sponsor. This includes but is not limited to Research & Development (R&D), Verification and Validation (V&V), or other commercial purposes.

MSRC samples processed at Scipher Medicine's CAP-accredited and CLIA-certified laboratory from study participants will also be de-identified and used for future research and/or distributed to partners, other third parties or investigators. Future research and other efforts include but is not limited to extracting and sequencing DNA/RNA or other analytical methodologies on the blood and serum samples. Future efforts may also include discovering novel biomarkers for disease diagnosis, monitoring, or progression as well as discovering new disease mechanisms, therapeutic targets, and therapies for autoimmune disorders.

De-identified data and specimen samples may be stored indefinitely or until the sample is exhausted following study completion. The de-identified data and specimens may be shared with research/institutions, third parties outside of Sponsor without additional informed consent from the participant or the legally authorized representative. This could include for-profit companies.

Participants may withdraw from the study at any time. Following a written request, if applicable, efforts will be made to remove their data and specimens.

11. Safety Assessments

11.1. Risk/Benefit Assessment and Anticipated and Unanticipated Adverse Device Effects

This is a minimal risk study and potential risks include standard risks associated with a venipuncture procedure, including:

Faintness, inflammation of the vein, bruising, temporary discomfort, and bleeding at the site of puncture. Though rare, infection may also occur. No unanticipated adverse device effects (UADE) will be reported for this study.

The blood draw and MSRC test is not expected to result in either anticipated or unanticipated adverse device effects (UADE) as it involves the analysis of ex-vivo blood samples from the participants and results will not be returned to the Investigator, patient nor enrolling sites during the study. The final MSRC being developed, trained, and validated will be determined by Scipher. In addition, all test results obtained for research-purposes only, including anti-CCP and CRP, will not be returned to Investigator, patients nor enrolling sites and will be conducted by the Scipher laboratory which is certified under the Clinical Laboratory Improvement Amendments (CLIA) and is College of American Pathologists (CAP)-accredited.

There are no investigational therapies being evaluated per the protocol. Patients will be treated for their RA in accordance with the standard of care by their treating physician. The Investigator is expected to follow all aspects of the FDA prescribing information when administering a pharmaceutical product in the course of treatment of patients included in this study.

Additional risks include a potential for loss of confidentiality by participating in this study.

No direct benefits from the study will be experienced by the patient.

11.2. Alternatives to Participation

Options include not participating or participating in other observational research studies. Not participating in this study will have no impact on the clinical care provided by clinician.

12. Regulatory, Ethical, and Study Oversight

12.1. Ethics Review

The protocol, ICF, and any advertisements must be approved or given a favorable opinion in writing by an IRB. The Investigator must submit written and dated verification of the IRB approval to Sponsor or designee before he or she can enroll any patients into the study.

The Sponsor/designee or Investigator will inform the IRB of any amendment to the protocol in accordance with local requirements. The protocol must be re-approved by the IRB upon receipt of amendments and annually, if required per local regulations.

Initial IRB approval, and all materials approved by the IRB for this study including the patient consent form and recruitment materials must be maintained by the Investigator and made available for inspection.

12.2. Compliance and Ethical Conduct of the Study

The Sponsor, Investigators, study staff, and designees will conduct the study in accordance with the protocol and with the following ethical principles that have their origin in the Declaration of Helsinki and are consistent with ICH, GCP, and other applicable local and federal laws, regulations, and guidelines. These include:

- Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines
- International Conference on Harmonisation Good Clinical Practice (ICH GCP) and United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812
- Applicable ICH E6 (R2) Good Clinical Practice (GCP) Guidelines and Human Subject Protection (HSP)
- Applicable ISO20916 (In vitro diagnostic medical devices – Clinical performance studies using specimens from human participants)
- Good study practice standards

The investigator will be responsible for the following:

- Providing written summaries of the status of the study to the IRB/IEC annually or more frequently in accordance with the requirements, policies, and procedures established by the IRB/IEC
- Providing oversight of the conduct of the study at the site and adherence to requirements of 21 CFR, ICH guidelines, the IRB/IEC, and all other applicable local regulations

In addition, the investigators and clinical study site staff who are responsible for the conduct, management, or oversight of this clinical trial must have completed Human Subjects Protection and ICH GCP Training.

12.3. Regulatory Status

The MSRC is a minimal risk device and is exempt from 21 CFR 812.2(c) IDE regulation. The test results of the Laboratory Developed Test being researched, developed, and validated in this study will not be returned to the Investigator, patient nor study sites. In addition, the device is:

- properly labeled in accordance with 21 CFR 809.10(c)
- noninvasive and does not require invasive sampling procedure in accordance with 21 CFR 812.3(k) as the test requires routine blood sampling that involves a simple venipuncture
- not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure

12.4. Financial Disclosure

Investigators and sub-investigators will provide the sponsor with sufficient, accurate financial information as requested to allow the sponsor to submit complete and accurate financial certification or disclosure statements to the appropriate regulatory authorities. Investigators are responsible for providing information on financial interests during the course of the study and for 1 year after completion of the study.

13. Protocol Revision History

Rev. #	Effective Date	Summary of Changes
1.0	22-Feb-2024	Initial Release

14. References

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15. Appendix

15.1. List of Abbreviations and Key Terms

Abbreviation or Specialist Term	Explanation
ACR	American College of Rheumatology
AE	Adverse event
AATT	Alternative approved targeted therapy
altMOA	Alternative mechanism of action (non-TNFi therapy)
bDMARD	Biologic disease modifying anti-rheumatic drug
CCP	Anti-cyclic citrullinated peptide antibodies
CD20	Cluster of differentiation 20
CDAI	Clinical disease activity index
CRF	Case report form
CRP	C-reactive protein
csDMARD	Conventional synthetic disease-modifying antirheumatic drug
CVAP	Clinical Validation Analysis Plan
DAS28	Disease activity score, 28-joint version
DMARD	Disease modifying anti-rheumatic drug
eCRF	Electronic case report form
EDC	Electronic Data Capture
EMR	Electronic Medical Records
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act of 1996
ICF	Informed consent form
ICH	International Council for Harmonization
IEC	Independent ethics committee
IL-6	Interleukin-6
IRB	Institutional Review Board
JAK	Janus kinase
MSRC	Molecular signature response classifier
NSAID	Non-steroidal anti-inflammatory drug
RA	Rheumatoid arthritis
RAPID3	Routine Assessment of Patient Index 3
RF	Rheumatoid factor
RNA	Ribonucleic acid
Rx	Treatment
SAE	Serious adverse event
SAP	Statistical analysis plan
TIM	Targeted immune modulators
TNFα	Tumor necrosis factor alpha

TNFi	Tumor necrosis factor inhibitor
tsDMARD	Targeted small molecule synthetic disease modifying anti-rheumatic drug
T2T	Treat to target
UADE	Unanticipated adverse device effect
US	United States

15.2. Definitions

Terms	**Definition of Terms**
Alternative Approved Targeted Therapy (AATT)	Alternative approved targeted therapy is a protocol-defined pharmacologically active agent approved in the territory or region in which the patient is being treated (e.g., for rheumatoid arthritis) other than a TNFi agent.
Baseline	Assessments of patients as they enter the study.
Endpoint	Variable that pertains to the efficacy or safety evaluations of a study.
Enrollment	The point at which the patient a biologic or targeted therapy at Visit 2.
Investigationalperiod	Period when major interests of protocol objectives are observed, when the intervention is given to a patient and that continues until the last assessment after the intervention.
b/tsDMARD-naïve	Patient has no history of initiating a biologic or targeted synthetic disease modifying antirheumatic drug (b/tsDMARD) at baseline (visit 1) including therapies from the following drug classes: TNFi (including TNFi biosimilars), JAKi, IL-1i, B-cell inhibitor, T-cell inhibitor, and IL-6i
csDMARD failure	Patient treated with a csDMARD $\geq$ 3 months and did not achieve an adequate response (low disease activity or remission)
csDMARD contraindication	Specific patient situations or factors that would make csDMARD therapy inadvisable to patient as it may be harmful (i.e., pregnancy, severe hypersensitivity, hepatotoxicity, etc.)
csDMARD intolerance	Inability for patient to tolerate adverse effects of csDMARD therapy (i.e., nausea, vomiting, abdominal pain, etc.)
Comorbidity Active	Patient has a condition (outlined in Section 8.1 Comorbidities) that is being treated and managed at the time of assessment visit.
Comorbidity Inactive	Patient has a history of a condition (outlined in Section 8.1 Comorbidities) that is not being treated or managed at the time of assessment visit.
Screening	A process of active consideration of potential patients for enrollment in a study.
Screen failure	Potential patient who did not meet 1 or more criteria required for participation in a study.
Screening period	Period before entering the investigational period, usually from the time when a patient signs the consent until just before assigned therapy is given to a patient.
Study period	Period from the first site initiation to the last site completing the study.
TNFi-exposed	Patient has a history of initiating a TNFi therapy, did not reach treat-to-target goals of low disease activity or remission by the time of baseline visit, has not initiated an altMOA therapy (non-TNFi therapy) prior to Visit 1, and is being considered for a change in b/tsDMARD therapy.

Treatment initiation	The point at which a biologic or targeted therapy to treat RA is initiated.
Variable	Any entity that varies; any attribute, phenomenon or event that can have different qualitative or quantitative values.

15.3. 2010 ACR/EULAR Classification Criteria for Rheumatoid Arthritis

The 2010 ACR/EULAR RA classification criteria below are intended to be applied to patients who present with definite swelling of at least one joint on clinical examination, for whom another diagnosis (e.g. SLE, PsA, gout) does not better account for the synovitis.[15]

The points from each of domains A through D are added and the sum is considered to be the total score. A total score of ≥6 is needed to classify a patient as having definite RA.[15]

Domain	**Category**	**Point Score**
A	Joint involvement (0-5 points)[a]	
	1 large joint	0
	2-10 large joints	1
	1-3 small joints (large joints not counted)	2
	4-10 small joints (large joints not counted)	3
	>10 joints including at least one small joint	5
B	Serology (at least one test needed for classification; 0-3 points)[b]	
	Negative RF and negative ACPA	0
	Low positive RF or low positive ACPA	2
	High positive RF or high positive ACPA	3
C	Acute-phase reactants (at least one test needed for classification; 0-1 point)[c]	
	Normal CRP and normal ESR	0
	Abnormal CRP or abnormal ESR	1
D	Duration of symptoms[d]	
	<6 weeks	0
	≥6 weeks	1

[a]Joint involvement refers to any swollen or tender joint on examination, which may be confirmed by imaging evidence of synovitis. DIP joints, first CMC joints and first MTP joints are excluded from assessment. Large joints refers to shoulders, elbows, hips, knees and ankles. Small joints refers to MCP joints, PIP joints, second through fifth MTP joints, thumb IP joints and wrists.
[b]Negative means less than or equal to the upper limit of normal (ULN); low positive means >ULN; high positive means >3× ULN.
[c]Normal and abnormal are determined by local laboratory standards.
[d]Duration of symptoms as per patient's self-report.

15.4. Informed Consent Form (ICF)

Informed Consent Form
and Authorization to Use and Disclose Protected Health Information

Sponsor / Study Title:	**PREDICT Therapy Selection for JAK, T-Cell, or IL-6 Inhibitor Therapies, Using a Molecular Signature Response Classifier (PREDICT)**
Protocol Number:	**PREDCIT-001**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

WHY IS THIS RESEARCH BEING DONE?
This research is being done to make new tests, called precision medicine tests, that can help your doctor choose the medicine that is right for you and based on your own biology. Data collected in this study will be used to research, develop, and test whether a new test can predict which therapies you are most likely to respond to that are specific to your rheumatoid arthritis (RA) (Janus Kinase (JAK), T-Cell, and IL-6 inhibitor therapies). This future test being researched will help doctors decide which therapy is likely to work or not work but will not inform your current medical care.

The information collected in this study will be taken from routine clinical assessments, your blood sample, medical records, and a few surveys the study staff will complete. Data collected from the study may be used for research, development, and testing that the lab test works.

This is a prospective, multi-center-observational study conducted in the United States. This study does not involve any experimental drugs or devices. The study plans to enroll approximately 1,100 patients.

Scipher Medicine is paying for this study. There is no cost to you to enroll and participate in this study.

You will also have the option to authorize access to your future medical records and claims data solely related to your rheumatoid arthritis condition or other medical conditions after the conclusion of the study to help inform future research efforts.

WHAT HAPPENS TO ME IF I AGREE TO TAKE PART IN THIS RESEARCH?
Once you have consented to participate in the study by written signature, you can immediately start "Visit 1" study steps. These steps include the review of your medical history, health assessment questionnaires, and a blood draw. The reason for the blood draw is to run C-Reactive Protein (CRP) and anti-cyclic citrullinated peptide antibodies (anti-CCP) tests that will be used in the research study but results will not be returned to you nor used in your medical care. This study will require new tests for each blood draw since these can change with time. In addition, your blood will be used to look at your biology. This will be done by sequencing ribonucleic acid (RNA). RNA is the information your body

uses as the instructions to make proteins in your body. RNA and data collected in the study helps us predict which therapies are right for you.

Your blood will be collected at Visit 1, Visit 3, and/or (if applicable) unscheduled visits: Change in Therapy and/or Blood Re-Draw. Unscheduled visits may occur if your blood sample collected was not able to run all of the tests on it. Approximately 12 mL (1 tablespoon = 15mL) of blood will be drawn at study Visit 1 and 3, and/ or, if applicable, Unscheduled Visit: Change in Therapy and/ or Blood Re-Draw, which is about 2.5% of what would be drawn if you were to donate your blood.

For Visit 2, you will return or discuss over the phone with your study doctor which new biologic or targeted therapy you will start. The clinical care study team will review your health and medication history with you to identify any changes since Visit 1. They will also reaffirm your eligibility to go ahead with the study. You are not being instructed to try any investigational therapy. The therapy you start at Visit 2 will be the same if you were not in this research study.

For Visit 3, this will occur approximately six months after starting your new biologic or targeted therapy. Every effort should be made so that Visit 3 occurs six months after starting treatment, but a date four weeks before or two weeks after the target six month visit will be accepted. After confirming you have been taking your medicine for the past six months, the same tests that were conducted on Visit 1 will be repeated. These include the same health assessment questionnaires, collection of approximately 12mL of blood for RNA testing, anti-CCP and CRP testing and a standard clinical evaluation (for example, swollen/tender joint counts). Your doctor may change your therapy during the study. If you switch to a therapy that is in the same category as what you started at Visit 2 you can remain in the study. If a new therapy from a different category is started before six months, you will complete the Unscheuled Visit: Change in Therapy and conclude the study.

HOW LONG WILL I BE IN THIS STUDY?
If you agree to participate in this study, you will complete 3 scheduled study-specified visits (Visit 1 = screening/baseline, Visit 2 = treatment initiation, and Visit 3 = 6 month follow-up or Unscheduled Therapy Change Visit) over the maximum span of 7 months, starting at the time that you complete Visit 2.

COULD BEING IN THIS STUDY HARM ME?
This study does not involve any investigational drugs or devices, or medical procedures outside of your standard rheumatoid arthritis healthcare. Standard blood draws using a venipuncture procedure will be needed. This procedure will not be different from a standard blood draw done at your doctor's office or laboratory. Though rare, you may experience slight bruising or discomfort at the site of the blood draw. Rarely, there may be an infection, or you may feel dizzy.

Though your information will be kept confidential and private, there is a risk of loss of privacy. There may be risks which are currently unknown.

WILL BEING IN THIS RESEARCH BENEFIT ME?
There is no direct benefit to you by participating in this study.

WILL IT COST ME MONEY TO TAKE PART IN THIS RESEARCH?
This research study is intended to observe standard care of patients with RA. The study will not cover the cost of your RA management including treatments, standard of care labs or radiology tests that are ordered by your doctor.

IS PARTICIPATION IN THIS STUDY REQUIRED?
Your participation in this study is completely voluntary. It is your choice whether to participate or not and you may change your mind and stop at any time. Choosing not to participate in the study or leaving the study after you join will not result in any penalty or loss of benefits to which you are otherwise entitled.

If you decide to leave this study, contact your study doctor's office as soon as possible so they can withdraw you from the study. Once you withdraw, no additional information will be collected from you.

WHAT HAPPENS TO THE INFORMATION COLLECTED FOR THIS RESEARCH?
All information that you provide will be kept strictly confidential. Other than your contact information and information needed to conduct the study, information collected about you throughout the study will not directly identify you once deidentified (meaning any personal information like name or address that can identify you will be removed) with unique study number. Information, such as your zip code will be collected and stored in a secure place and used only for research with the unique study number.

Some of your information and medical records will be shared with individuals and organizations that conduct or watch over this research, including:

- Sponsor
- People who work with the Sponsor
- Government agencies, such as the U.S. Food and Drug Administration (FDA)
- Institutional Review Board (IRB)

These people may look at your records to make sure the study has been done the right way. They also want to make sure that your health information has been collected the right way, or for other reasons that are allowed under the law. This means that absolute confidentiality cannot be guaranteed.

We may publish or present the results of this research. However, any information that can identify you will be removed so your identity is protected.

We protect your information from disclosure to others to the extent required by law. We cannot promise complete privacy as there is a risk of loss of confidentiality in registries, though the amount of private information shared will be the minimal amount needed to conduct the study.

Data and specimens collected in this study might be deidentified and used for future research and other efforts or distributed to other investigators or other third-parties without your knowledge. Future efforts may include conducting additional tests and discovering new markers that help diagnose, treat, or monitor diseases.

While the precision medicine test uses RNA isolated from your blood samples to predict whether or not you are likely to respond to specific therapies (i.e., JAK, T-Cell, or IL-6 inhibitor therapy), DNA and Ribonucleic acid (RNA) isolated from your blood samples may also be used. Your blood sample and deidentified data may be used for research or commercial efforts. Your deidentified data and blood sample will be stored indefinitely or until the sample is exhausted following study completion.

ALTERNATIVES TO PARTICIPATION
The only alternative is to not participate in this study.

WHOM TO CONTACT ABOUT THIS STUDY
During the study, if you have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints about this research study, contact**:**

By mail	Study Subject Adviser Advarra IRB 6100 Merriweather Dr., Suite 600 Columbia, MD 21044
Or call **toll free**	877-992-4724
Or by **email**	adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: PREDICT-001.

WHAT IF I AM INJURED BECAUSE OF TAKING PART IN THIS STUDY?
If you are injured or get sick because of procedures in this research, call your study doctor immediately. Your study doctor will provide emergency medical treatment. Your insurance may be billed for this treatment. The Sponsor will pay any charges that are not covered by your insurance policy or the government if the injury was not due to your underlying illness or condition and was not caused by you or some other third party. No other payment is routinely available from the study doctor or Sponsor.

To pay medical expenses, the Sponsor may need to know information about you such as your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the Sponsor must check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

WHAT IF NEW INFORMATION BECOMES AVAILABLE?
We will tell you about any new information that may affect your health, welfare, or choice to stay in this research.

CAN I BE REMOVED FROM THIS RESEARCH WITHOUT MY APPROVAL?
The study doctor or the Sponsor of this research can remove you from this research without your approval. Possible reasons include:

- You knowingly provide false or misleading information
- The study is cancelled by the Sponsor

The Sponsor or the IRB may decide to stop the study at any time.

WILL I BE REIMBURSED FOR MY TIME TAKING PART IN THIS RESEARCH?
You will be reimbursed for your time taking part in this research. You will be compensated the following amounts for each visit completed: $100 for Visit 1 (screening/ baseline), $50 for Visit 2 (treatment initiation), $100 for Visit 3 (6 month follow-up) and/or, if applicable, $50 for each unscheduled visit.

WHAT IF SOMETHING IS DEVELOPED FROM THIS RESEARCH?
Your deidentified specimens and clinical data may be used for commercial profit. You will not receive a share in this commercial profit.

STATEMENT OF CONSENT:
I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing and dating this consent document. I will receive a copy of this signed and dated consent document.

Printed Name of Adult Subject Capable of Consent	Date
Signature of Adult Subject Capable of Consent	Date
Printed Name of Person Obtaining Consent	Date
Signature of Person Obtaining Consent	Date

OPTION TO BE CONTACTED IN THE FUTURE

The study staff and sponsor may want to contact you in the future. These are both optional.

Do you give your permission for the investigator or staff to contact you regarding your willingness to participate in future research studies?

☐ **Yes** ☐ **No** **Initials**_____

Do you give your permission for the study staff or sponsor to contact you to receive periodic email/ mail* with health-related articles, tips, and educational resources relevant to your disease?

*All relevant material will comply with relevant data privacy regulations such as HIPAA.

☐ **Yes** ☐ **No** **Initials**_____

If yes to either or both, email, mailing address, and/or phone to be used for future contact

Email: _____

Mailing Address:

(Street)_____

(City) _____(State) _____ (Zipcode)_____

Phone Number: _____

☐ **Yes** ☐ **No** **Initials**_____

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Federal privacy laws protect the use and release of your health information and related information that identifies you. We refer to this information as "health data." Health data may include:

- Your name
- Address (street, city, state, zip code)
- Phone number
- Date of birth
- Medical history
- Information from your study visits, including all test results.

If you enroll in the research study described in the informed consent form (above), the study doctor and study staff will use and share your health data with others as explained below. In addition, you hereby authorize your doctor to share your existing records with the study doctor and study staff. If you agree to the described uses and sharing of your health data, then after reading this entire document, please sign your name at the end on the line provided. If you have questions, you may ask the researcher who is reviewing the informed consent for the research with you or you can contact the researcher listed below.

In this study, we may collect health data about you from:

- Past, present, and future medical records
- Study records, including research office visits, tests, interviews, and questionnaires

Why will health data about you be used or shared with others?

Your health data will be used to conduct and oversee the study, including for instance:

- To complete this research.
- To evaluate the results of the study.
- To check that the study is being done properly.

Who may see, use, and share your health data and why they may need to do so:

For this study, the study staff may share health data about you with authorized users. Authorized users may include:

- Representatives of Scipher Medicine Corporation.
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- Governmental agencies of other countries.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this study, if applicable.
- A data safety monitoring board which oversees this study, if applicable.

Some people or groups who get your health data might not have to follow the same privacy rules that we follow and might use or share your health data without your permission in ways that are not described in this form. We share your health data only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. However, once your identifiable information is shared, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

The results of this research study may be published in a medical journal or used to teach others.

However, your name or other identifiable information **will not** be used for these purposes without your specific permission.

For how long will health data about me be used or shared with others?
Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health data. Your permission to use and share your health data does not expire.

Your Privacy Rights
You have the right not to sign this form that allows us to use and share your health data for research; however, if you don't sign it, you can't take part in this research study. Refusing to sign will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

You have the right to withdraw your permission for us to use or share your health data for this research study. If you want to withdraw your permission, you must notify the person at the following address:

Client Services Representative
500 Totten Pond Road, Floor 6
Waltham, MA 02451
(855) 724-7437 Opt. 2
client_services_team@scipher.com
Support@Scipher.com

Once permission is withdrawn, you cannot continue to take part in the study. If you withdraw your permission, no new health data that identifies you will be gathered after your written request is received. However, health data about you that as already been gathered may still be used and given to others as described in this form.

If you decide not to sign and date this form, you will not be able to take part in the study.

Optional Future Medical Record Release

□ By checking this box, you agree to allow your existing physician(s) to share and the sponsor, Scipher Medicine Corporation, to access, use and share your future medical records and claims' data related solely to your rheumatoid arthritis condition or other medical conditions after the conclusion of the study to help inform future research. This may include but is not limited to allowing access to your future medical records and associated claims data as well as authorizing the identifiable pairing of your healthcare data with study data and left-over blood samples on an ongoing basis. This permission can be withdrawn at any time by notifying the person at the following address:

Client Services Representative
500 Totten Pond Road, Floor 6
Waltham, MA 02451
(855) 724-7437 Opt. 2
client_services_team@scipher.com
Support@Scipher.com

If you withdraw your permission, no new health data that identifies you will be gathered after your written request is received. However, health data about you that as already been gathered may still be used and given to others as described in this form.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____

Printed Name of Subject

_____

Signature of Subject Date

15.5. CRF: Screening/ Baseline Visit (SBV)

PREDICT-001
Visit 1 – Screening/Baseline – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Enrollment

Date of Informed Consent: ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

ICF Version (**IRB Version Date**): ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Subject's Date of Birth: ☐☐☐ MMM ☐☐☐☐ YYYY

Subject's Sex at Birth: O Male O Female

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PREDICT-001
Visit 1 – Screening/Baseline – Investigator

Please complete this information on every page of the questionnaire

Subject ID | | | | | | | | Date of Visit | | | DD | | | MMM | | | | YYYY

Inclusion/Exclusion Questionnaire

Does the subject meet all eligibility criteria? O Yes O No

Inclusion Criteria

1. Is the patient eighteen years of age, or older (≥18) at time of consent? O Yes O No

2. Does the patient meet the criteria for RA as defined by the 2010 ACR/EULAR classification at Visit 1 and documented by enrolling PI? O Yes* O No
*(*please complete question below)*

When was the patient diagnosed with Rheumatoid Arthritis? | | | | MMM | | | | YYYY

3. Does the patient have active RA, with moderate or high disease activity as confirmed by having a CDAI score of > 10 at Visit 1? O Yes O No

4. Does the patient have a history of failure, contraindication, or intolerance to at least one csDMARD therapy? O Yes O No

5. Is the patient either b/tsDMARD-naïve or TNFi-exposed prior to baseline visit? O Yes O No

6. Will the patient be initiating one of the following listed therapies (including biosimilars)? O Yes O No
   a. JAK inhibitor therapy (only tofacitnib or upadacitinib)
   b. T-cell inhibitor therapy (abatacept)
   c. IL-6 inhibitor therapy (only tocilizumab)

7. Is the patient on any concomitant medications (they are permitted per standard of care, including but not limited to:) O Yes O No
   a. csDMARD
      i. Methotrexate
      ii. Sulfasalazine
      iii. Leflunomide
      iv. Hydroxychloroquine
   b. Non-steroidal anti-inflammatory drugs
   c. Corticosteroids

8. Is the patient participating in another observational study (patient may participate in another observational study)? O Yes O No

9. Is the patient willing and able to complete the informed consent process, comply with study procedures and visit schedule? O Yes O No

PREDICT-001
Visit 1 – Screening/Baseline – Investigator

Please complete this information on every page of the questionnaire

Subject ID | | | | | | | | Date of Visit | | | | | | | | | |
DD MMM YYYY

Exclusion Criteria

1. Has the patient previously participated in a Scipher Medicine study (NETWORK-004, AIMs in RA, DRIVE, or INFORM)? O Yes O No
2. Has the patient been treated with an altMOA (non-TNFi therapy) therapy for RA prior to Visit 1? O Yes O No
3. Is the patient pregnant or breast-feeding or planning to get pregnant during the study duration? O Yes O No
4. Is the patient on or has been on an investigational product within 28 days of Visit 1? O Yes O No
5. Is the patient on any RA therapies outside of an FDA approved indication? O Yes O No
6. Is the patient currently receiving systemic antimicrobial treatment for viral, bacterial, fungal, or parasitic infection at the time of Visit 1? O Yes O No
7. Does the patient have any known active, chronic, or recurrent invasive infection (e.g., listeriosis and histoplasmosis)and viral infection that, based on the Investigator's clinical assessment, makes the patient an unsuitable candidate for the study. This includes hepatitis B virus (HBV) or hepatitis C virus (HCV), recurrent or disseminated (even a single episode) herpes zoster, disseminated (even a single episode) herpes simplex, or human immunodeficiency virus (HIV)? O Yes O No
8. Does the patient have any known active malignancy except non-melanoma skin cancer, localized prostate cancer treated with curative intent with no evidence of progression, low-risk or very low-risk (per standard guidelines) localized prostate cancer under surveillance/watchful waiting (without intent to treat), or carcinoma in situ of any type (completely resected)? O Yes O No

PREDICT-001
Visit 1 – Screening/Baseline – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Demographics

Subject's Ethnicity (*Check all that apply*):

- ☐ Hispanic or Latino
- ☐ Not Hispanic or Latino
- ☐ Not Reported
- ☐ Unknown

Subject's Race (*Check all that apply*):

- ☐ American Indian or Alaskan Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ White
- ☐ Unknown
- ☐ Other (please specify): _____

Geography

Which state is the subject located in? _____

Which zip code is the subject located in? _____

PREDICT-001
Visit 1 – Screening/Baseline – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Medical History

Smoking History

Which of the following best describes the subject:

Current smoker? O Yes O No

Former smoker? O Yes O No

Subject has never smoked? O Yes O No

Does the subject have any history of the following conditions:

Please check yes/ active, yes/ inactive or no.

Condition	Patient's Comorbidity Status
Cardiovascular disease	O Yes/ active O Yes/ inactive O No history
Hypertension	O Yes/ active O Yes/ inactive O No history
Anemia or other blood disease	O Yes/ active O Yes/ inactive O No history
Lung disease	O Yes/ active O Yes/ inactive O No history
Diabetes	O Yes/ active O Yes/ inactive O No history
Ulcer or stomach disease	O Yes/ active O Yes/ inactive O No history
Kidney disease	O Yes/ active O Yes/ inactive O No history
Liver disease	O Yes/ active O Yes/ inactive O No history
Cancer	O Yes/ active O Yes/ inactive O No history
Osteoarthritis, degenerative arthritis	O Yes/ active O Yes/ inactive O No history
Back pain	O Yes/ active O Yes/ inactive O No history
Fractures spine, hip, or leg	O Yes/ active O Yes/ inactive O No history
Depression	O Yes/ active O Yes/ inactive O No history

PREDICT-001
Visit 1 – Screening/Baseline – Investigator

Please complete this information on every page of the questionnaire

Subject ID | | | | | | | | Date of Visit | | | DD | | | MMM | | | | YYYY

csDMARD History

Please complete the table below for all csDMARDs the subject has been ***prescribed (current or past) AND*** had a failure, contraindication, or intolerance to:

Medication	Had a failure, contraindication, or intolerance to the prescribed (current or past) csDMARD? Select all that apply
Methotrexate	O Yes O No
Hydroxychloroquine	O Yes O No
Leflunomide	O Yes O No
Azathrioprine	O Yes O No
Sulfazalazine	O Yes O No

Concomitant Medications

Please complete the table below for all RA medications the subject is ***currently prescribed:***

Please record only **csDMARDs**, **corticosteroids**, and **supplements (vitamin D and/or folic acid)**

Medication	Start Date	Dose (Units)	Frequency	Route
Methotrexate				
Leflunomide				
Hydroxychloroquine				
Azathioprine				
Prednisone				
Methylprednisolone				
Sulfasalazine				
Vitamin D				
Folic Acid				

PREDICT-001
Visit 1 – Screening/Baseline – Investigator

Please complete this information on every page of the questionnaire

Subject ID | | | | | | | Date of Visit | | | DD | | | MMM | | | | YYYY

Targeted Therapy History

Is the subject ***currently on*** or has been ***previously treated with*** a b/tsDMARD?: O Yes O No

If yes, please complete the table below for any b/tsDMARDs the subject is currently on or has been previously prescribed.

Drug Class	Targeted Therapy (Generic name)	Brand/ Biosimilar name	Start Date	End Date	Dose (Units)	Frequency	Route
TNFi	Adalimumab	Humira ☐					
		Amjevita ☐					
		Hadlima ☐					
		Cyltezo ☐					
		Yusimry ☐					
		Hyrimoz ☐					
		Hulio ☐					
		Idacio ☐					
		Abrilada ☐					
		Yuflyma ☐					
TNFi	Etanercept	Enbrel ☐					
		Eticovo ☐					
TNFi	Infliximab	Remicade ☐					
		Inflectra ☐					
		Renflexis ☐					
		Avsola ☐					
		Ixifi ☐					
TNFi	Golimumab	Simponi ☐					
TNFi	Certolizumab Pegol	Cimzia ☐					

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PREDICT-001
Visit 1 – Screening/Baseline – Investigator

Please complete this information on every page of the questionnaire

Subject ID | | | | | | | | Date of Visit | | | DD | | | MMM | | | | YYYY

Clinical Assessment

What is the subject's current weight? _____ lbs or _____ kg

What is the subject's height? _____ft _____inches or _____ cm

Joint Assessment: Please indicate the presence of each by checking the corresponding box.

	Left Side		Right Side		
	Pain	**Swelling**	**Pain**	**Swelling**	**Not Present**
Shoulder	☐	☐	☐	☐	☐
Elbow	☐	☐	☐	☐	☐
Wrist	☐	☐	☐	☐	☐
Metacarpophalangeal I	☐	☐	☐	☐	☐
Metacarpophalangeal II	☐	☐	☐	☐	☐
Metacarpophalangeal III	☐	☐	☐	☐	☐
Metacarpophalangeal IV	☐	☐	☐	☐	☐
Metacarpophalangeal V	☐	☐	☐	☐	☐
Thumb Interphalangeal	☐	☐	☐	☐	☐
Proximal Interphalangeal II	☐	☐	☐	☐	☐
Proximal Interphalangeal III	☐	☐	☐	☐	☐
Proximal Interphalangeal IV	☐	☐	☐	☐	☐
Proximal Interphalangeal V	☐	☐	☐	☐	☐
Knee	☐	☐	☐	☐	☐

Joint Counts

Total number of tender/ painful joints: _____

Total number of swollen joints: _____

Physician Global Assessment of Disease Activity

Not Active ..... Very Active

0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100

Please enter a numerical assessment score (*0 = Not Active; 100 = Very Active*): _____

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PREDICT-001
Visit 1 – Screening/Baseline – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Laboratory

Lab reports included? (If yes, no need to complete below questions): O Yes O No

Rheumatoid Factor (RF)

Is an RF test result available in the subject's record? O Yes O No

If yes, what is the date of the most recent test? ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

RF Test Result: ☐ IU/mL *(include > or < sign if applicable)*

PAXgene™

Were two PAXgene™ and one SST tube lab samples collected? O Yes O No

If no, why were two PAXgene™ and one SST tube lab samples not collected? _____

PAXgene™ Date of Collection: ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

PAXgene™ Kit ID: ☐

15.6. CRF: Patient Reported Outcomes (PRO)

Patient Reported Outcomes

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Health Assessment Questionnaire

What visit was the Health Assessment Questionnaire completed at?

☐ Visit 1 ☐ Visit 3 ☐ Unscheduled Visit: Change in Therapy

Date of Completion: ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Please check the response which best describes your usual abilities **OVER THE PAST WEEK.**

	Without ANY difficulty	**With SOME difficulty**	**With MUCH difficulty**	**UNABLE to do**
Dressing and Grooming				
Are you able to…				
Dress yourself, including tying shoelaces and doing buttons?	O	O	O	O
Shampoo your hair?	O	O	O	O
Arising				
Are you able to….				
Stand up from a straight chair?	O	O	O	O
Get in and out of bed?	O	O	O	O
Eating				
Are you able to….				
Cut your own meat?	O	O	O	O
Lift a full cup or glass to your mouth?	O	O	O	O
Open a new milk carton?	O	O	O	O
Walking				
Are you able to…				
Walk outdoors on flat ground?	O	O	O	O
Climb up five steps?	O	O	O	O

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PREDICT-001
Patient Reported Outcomes

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Please check any AIDS OR DEVICES that you usually use for any of these activities:

- ☐ Devices used for dressing (button hook, zipper pull, long-handled shoe horn, etc.)
- ☐ Special or built up chair
- ☐ Built up or special utensils
- ☐ Cane
- ☐ Other (please specify):_____
- ☐ Walker
- ☐ Crutches
- ☐ Wheelchair

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

- ☐ Dressing and Grooming
- ☐ Eating
- ☐ Arising
- ☐ Walking

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PREDICT-001
Patient Reported Outcomes

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Select the option best describes your abilities OVER THE PAST WEEK.

	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do
Hygiene Are you able to….				
Wash and dry your body?	O	O	O	O
Take a tub bath?	O	O	O	O
Get on and off the toilet?	O	O	O	O
Reach Are you able to…				
Reach and get down a 5 pound object (such as a bag of sugar) from just above your head?	O	O	O	O
Bend down to pick up clothing from the floor?	O	O	O	O
Grip Are you able to…				
Open car doors?	O	O	O	O
Open jars which have been previously opened?	O	O	O	O
Turn faucets on and off?	O	O	O	O
Activities Are you able to…				
Run errands and shop?	O	O	O	O
Get in and out of a car?	O	O	O	O
Do chores such as vacuuming or yardwork?	O	O	O	O

Patient Reported Outcomes

Please complete this information on every page of the questionnaire

Subject ID | | | | | | | | Date of Visit | | | DD | | | MMM | | | | YYYY

Please check any **AIDS OR DEVICES** that you usually use for any of these daily activities:

- ☐ Raised toilet seat
- ☐ Bathtub seat
- ☐ Jar opener (for jars previously opened)
- ☐ Bathtub bar
- ☐ Long-handled appliances for reach
- ☐ Long-handled appliances in bathroom
- ☐ Other (please specify):_____

Please check any categories for which you usually need **HELP FROM ANOTHER PERSON**:

- ☐ Hygiene
- ☐ Reach
- ☐ Gripping and opening things
- ☐ Errands and chores

Pain Scale

On a scale of 0 to 100, where 0 represents “no pain” and 100 represents “severe pain,” how much pain have you had because of your illness in the past week?

No Pain .....Severe Pain

0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100

Please confirm the number you indicated above: _____

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Patient Reported Outcomes

Please complete this information on every page of the questionnaire

Subject ID | | | | | | | |

Date of Visit | | | DD | | | MMM | | | | YYYY

Routine Assessment of Patient Index Data (RAPID-3) Questionnaire

Please check the ONE best answer.

Over the last week, how well were you able to:	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do
Walk two miles or three kilometers, if you wish?	O	O	O	O
Participate in recreational activities and sports as you would like, if you wish?	O	O	O	O

Disease Activity

On a scale of 0 to 100, where 0 represents "very well' and 100 represents "very poorly," considering all the ways in which illness and health conditions may affect you at this time, please indicate below how you are doing:

Very Well.....Very Poorly

0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100

Please confirm the number you indicated above: _____

15.7. CRF: Treatment Initiation Visit (TI)

PREDICT-001
Visit 2 – Treatment Initiation – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Change in Medical History

Did the subject have a change in their medical history (comorbidities) since their last visit? O Yes O No

If yes, please update the table below to reflect the patient's current comorbidities at this visit:

Condition	Patient's Comorbidity Status
Cardiovascular disease	O Yes/active O Yes/inactive O No history
Hypertension	O Yes/active O Yes/inactive O No history
Anemia or other blood disease	O Yes/active O Yes/inactive O No history
Lung disease	O Yes/active O Yes/inactive O No history
Diabetes	O Yes/active O Yes/inactive O No history
Ulcer or stomach disease	O Yes/active O Yes/inactive O No history
Kidney disease	O Yes/active O Yes/inactive O No history
Liver disease	O Yes/active O Yes/inactive O No history
Cancer	O Yes/active O Yes/inactive O No history
Osteoarthritis, degenerative arthritis	O Yes/active O Yes/inactive O No history
Back pain	O Yes/active O Yes/inactive O No history
Fractures spine, hip, or leg	O Yes/active O Yes/inactive O No history
Depression	O Yes/active O Yes/inactive O No history

Did the subject have a Major Adverse Cardiovascular Event (MACE): Acute Myocardial Infarction (AMI), stroke, or cardiovascular mortality since their last visit? O Yes O No

If yes, check all the apply and specify:

☐ Related to prior medical history ☐ Related to non-RA medications subject was taking

☐ Related to current rheumatic disease/ activity

☐ Other (please specify)

(Required) Please specify the subject's Major Adverse Cardiovascular Event (MACE): _____

Smoking History

Did the subject have any changes to their smoking status since their last visit? O Yes O No

If yes, please complete below.

Which of the following best describes the subject:

Current smoker? O Yes O No

Former smoker? O Yes O No

Subject has never smoked? O Yes, never smoked O No

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PREDICT-001
Visit 2 – Treatment Initiation – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Treatment Initiation

What bDMARD or tsDMARD is the subject ***initiating***? Please complete the table below:

Drug Class	Targeted Therapy		Start Date	Dose (Units)	Frequency	Route
JAK inhibitor	Tofacitinib	Xeljanz ☐				
JAK inhibitor	Upadacitinib	Rinvoq ☐				
IL-6 inhibitor	Tocilizumab	Actemra ☐				
		Tofidence ☐				
T-cell inhibitor	Abatacept	Orencia ☐				

Concomitant Rheumatoid Arthritis Medication

Did the subject have any changes to their current RA concomitant medication since the last visit? O Yes O No

If yes, please complete the table below:

Type of Change	Medication Name	Dose (Units)	Frequency	Route	Start Date (DD/MMM/YYYY)	End Date (DD/MMM/YYYY)

15.8. CRF: 24-week Follow-Up Visit

PREDICT-001
Visit 3 – 24-week Follow-Up – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ ☐☐☐ ☐☐☐☐
DD MMM YYYY

Subject Status

Did the visit occur? O Yes O No*

**(if no, please complete End of Study Form)*

[Below only present on EDC if applicable – if not, sites will not see this within their EDC view]

Did the subject *re-consent* at this visit? *If applicable** O Yes O No

If **Yes**, ICF version **(IRB Version Date)**: ☐☐ ☐☐☐ ☐☐☐☐
*If applicable** DD MMM YYYY

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PREDICT-001
Visit 3 – 24-week Follow-Up – Investigator

Please complete this information on every page of the questionnaire

Subject ID | | | | | | | | Date of Visit | | | DD | | | MMM | | | | YYYY

Change in Medical History

Did the subject have a change in their medical history (comorbidities) since their last visit? O Yes O No

If yes, please update the table below to reflect the patient's current comorbidities at this visit:

Comorbidities

Condition	Patient's Comorbidity Status
Cardiovascular disease	O Yes/active O Yes/inactive O No history
Hypertension	O Yes/active O Yes/inactive O No history
Anemia or other blood disease	O Yes/active O Yes/inactive O No history
Lung disease	O Yes/active O Yes/inactive O No history
Diabetes	O Yes/active O Yes/inactive O No history
Ulcer or stomach disease	O Yes/active O Yes/inactive O No history
Kidney disease	O Yes/active O Yes/inactive O No history
Liver disease	O Yes/active O Yes/inactive O No history
Cancer	O Yes/active O Yes/inactive O No history
Osteoarthritis, degenerative arthritis	O Yes/active O Yes/inactive O No history
Back pain	O Yes/active O Yes/inactive O No history
Fractures spine, hip, or leg	O Yes/active O Yes/inactive O No history
Depression	O Yes/active O Yes/inactive O No history

Did the subject have a Major Adverse Cardiovascular Event (MACE): Acute Myocardial Infarction (AMI), stroke, or cardiovascular mortality since their last visit? O Yes O No

If yes, check all the apply and specify:

☐ Related to prior medical history ☐ Related to b/tsDMARD therapy initiated at Visit 2

☐ Related to non-RA medications subject was taking ☐ Related to current rheumatic disease/ activity

☐ Other (please specify)

(Required) Please specify the subject's Major Adverse Cardiovascular Event (MACE): _____

Smoking History

Did the subject have any changes to their smoking status since their last visit? O Yes O No

If yes, please complete below.

Which of the following best describes the subject:

Current smoker? O Yes O No

Former smoker? O Yes O No

Subject has never smoked? O Yes, never smoked O No

PREDICT-001
Visit 3 – 24-week Follow-Up – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Concomitant Rheumatoid Arthritis Medication

Did the subject have any changes to their current RA concomitant medication since the last visit? O Yes O No

If yes, please complete the table below:

Type of Change	Medication Name	Dose (Units)	Frequency	Route	Start Date (DD/MMM/YYYY)	End Date (DD/MMM/YYYY)

PREDICT-001
Visit 3 – 24-week Follow-Up – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

RX Adherence Questionnaire

Did the subject have an in-class b/tsDMARD therapy change (switch to different therapy in same class, adjustments to dose, route of administration, or frequency) since their last study visit (index date)? O Yes O No

If **yes**, prior b/tsDMARD **End Date**: ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

If **yes**, please indicate why the subject changed their prior targeted therapy (*please select all that apply)*

☐ Insurance prescription restrictions ☐ Loss of effectiveness after initial relief ☐ Patient preference
☐ Change in medical history ☐ Intolerance (please specify) ☐ Cost too high
☐ Inadequate improvement in symptoms ☐ Frequency, dose, or route of administration ☐ Disease flare
☐ Other (please specify)

Please specify any adherence discrepancy reasons: _____

If **yes**, new in-class b/tsDMARD change **Start Date**: ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

If **yes**, please complete the table below for the new in-class b/tsDMARD change.

Drug Class	Targeted Therapy	Brand/Biosimilar Name	Dose (Units)	Frequency	Route

PREDICT-001
Visit 3 – 24-week Follow-Up – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Clinical Assessment

What is the subject's current weight? _____ lbs or _____ kg

What is the subject's height? _____ft _____inches or _____ cm

Joint Assessment: Please indicate the presence of each by checking the corresponding box.

	Left Side		Right Side		
	Pain	**Swelling**	**Pain**	**Swelling**	**Not Present**
Shoulder	☐	☐	☐	☐	☐
Elbow	☐	☐	☐	☐	☐
Wrist	☐	☐	☐	☐	☐
Metacarpophalangeal I	☐	☐	☐	☐	☐
Metacarpophalangeal II	☐	☐	☐	☐	☐
Metacarpophalangeal III	☐	☐	☐	☐	☐
Metacarpophalangeal IV	☐	☐	☐	☐	☐
Metacarpophalangeal V	☐	☐	☐	☐	☐
Thumb Interphalangeal	☐	☐	☐	☐	☐
Proximal Interphalangeal II	☐	☐	☐	☐	☐
Proximal Interphalangeal III	☐	☐	☐	☐	☐
Proximal Interphalangeal IV	☐	☐	☐	☐	☐
Proximal Interphalangeal V	☐	☐	☐	☐	☐
Knee	☐	☐	☐	☐	☐

Joint Counts

Total number of tender/ painful joints: _____

Total number of swollen joints: _____

Physician Global Assessment of Disease Activity

Not Active ..... Very Active

0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100

Please enter a numerical assessment score (*0 = Not Active; 100 = Very Active*): _____

15.9. CRF: End of Study (EOS)

End of Study

PREDICT-001
End of Study Form – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

End of Study

Did the subject complete the study*?
**(completed Visit 3 and remained in same class of b/tsDMARD initiated at Visit 2)*

☐ Yes ☐ No

Date of study completion or discontinuation
☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

If the subject **did not** complete the study, please indicate the reason for discontinuation:

☐ Screen Failure ☐ Withdrawal by Subject ☐ Withdrawal of Consent
☐ Lost to Follow-up ☐ Stopped/Changed b/tsDMARD class ☐ Study Terminated by Sponsor
☐ Physician Decision ☐ Adverse Event ☐ Protocol Non-Compliance

If **adverse event, physician decision, or other** please specify: _____

If the subject **did not** complete the study, please indicate the date of last visit for the study:

☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

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15.10. CRF: Unscheduled Visit: Change in Therapy (UVCT)

PREDICT-001
Unscheduled Visit: Change in Therapy – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Change in Therapy

Has the subject changed b/tsDMARD drug class since their last study visit (Visit 2)? O Yes* O No

**(if yes, please complete below and the End of Study Form)*

Prior b/tsDMARD therapy **End Date**: ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

RX Adherence Questionnaire

Please indicate why the subject stopped their prior b/tsDMARD therapy (*please select all that apply)*

☐ Insurance prescription restrictions ☐ Loss of effectiveness after initial relief ☐ Patient preference
☐ Change in medical history ☐ Intolerance (please specify) ☐ Cost too high
☐ Inadequate improvement in symptoms. ☐ Frequency, dose, or route of administration ☐ Disease flare
☐ Other (please specify)

Please specify any adherence discrepancy reasons: _____

If **yes**, new class of b/tsDMARD therapy **Start Date**: ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

If **yes**, please complete the table below for the new class of b/tsDMARD therapy.

Drug Class	Targeted Therapy	Brand/Biosimilar Name	Dose (Units)	Frequency	Route

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PREDICT-001
Unscheduled Visit: Change in Therapy – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Change in Medical History

Did the subject have a change in their medical history since their last visit? O Yes O No

If yes, please update the table below to reflect the patient's current comorbidities at this visit:

Comorbidities

Condition	Patient's Comorbidity Status
Cardiovascular disease	O Yes/active O Yes/inactive O No history
Hypertension	O Yes/active O Yes/inactive O No history
Anemia or other blood disease	O Yes/active O Yes/inactive O No history
Lung disease	O Yes/active O Yes/inactive O No history
Diabetes	O Yes/active O Yes/inactive O No history
Ulcer or stomach disease	O Yes/active O Yes/inactive O No history
Kidney disease	O Yes/active O Yes/inactive O No history
Liver disease	O Yes/active O Yes/inactive O No history
Cancer	O Yes/active O Yes/inactive O No history
Osteoarthritis, degenerative arthritis	O Yes/active O Yes/inactive O No history
Back pain	O Yes/active O Yes/inactive O No history
Fractures spine, hip, or leg	O Yes/active O Yes/inactive O No history
Depression	O Yes/active O Yes/inactive O No history

Did the subject have a Major Adverse Cardiovascular Event (MACE): Acute Myocardial Infarction (AMI), stroke, or cardiovascular mortality since their last visit? O Yes O No

If yes, check all the apply and specify:

☐ Related to prior medical history ☐ Related to b/tsDMARD therapy initiated at Visit 2

☐ Related to non-RA medications subject was taking ☐ Related to current rheumatic disease/activity

☐ Other (please specify)

(Required) Please specify the subject's Major Adverse Cardiovascular Event (MACE): _____

Smoking History

Did the subject have any changes to their smoking status since their last visit? O Yes O No

If yes, please complete below.

Which of the following best describes the subject:

Current smoker? O Yes O No

Former smoker? O Yes O No

Subject has never smoked? O Yes O No

PREDICT-001
Unscheduled Visit: Change in Therapy – Investigator

Please complete this information on every page of the questionnaire

Subject ID | | | | | | | | Date of Visit | | | DD | | | MMM | | | | YYYY

Concomitant Rheumatoid Arthritis Medication

Did the subject have any changes to their current RA concomitant medication since the last visit? O Yes O No

If yes, please complete the table below:

Type of Change	Medication Name	Dose (Units)	Frequency	Route	Start Date (DD/MMM/YYYY)	End Date (DD/MMM/YYYY)

PREDICT-001
Unscheduled Visit: Change in Therapy – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ DD ☐☐☐ MMM ☐☐☐☐ YYYY

Clinical Assessment

What is the subject's current weight? _____ lbs or _____ kg

What is the subject's height? _____ft _____inches or _____ cm

Joint Assessment: Please indicate the presence of each by checking the corresponding box.

	Left Side		Right Side		
	Pain	**Swelling**	**Pain**	**Swelling**	**Not Present**
Shoulder	☐	☐	☐	☐	☐
Elbow	☐	☐	☐	☐	☐
Wrist	☐	☐	☐	☐	☐
Metacarpophalangeal I	☐	☐	☐	☐	☐
Metacarpophalangeal II	☐	☐	☐	☐	☐
Metacarpophalangeal III	☐	☐	☐	☐	☐
Metacarpophalangeal IV	☐	☐	☐	☐	☐
Metacarpophalangeal V	☐	☐	☐	☐	☐
Thumb Interphalangeal	☐	☐	☐	☐	☐
Proximal Interphalangeal II	☐	☐	☐	☐	☐
Proximal Interphalangeal III	☐	☐	☐	☐	☐
Proximal Interphalangeal IV	☐	☐	☐	☐	☐
Proximal Interphalangeal V	☐	☐	☐	☐	☐
Knee	☐	☐	☐	☐	☐

Joint Counts

Total number of tender/ painful joints: _____

Total number of swollen joints: _____

Physician Global Assessment of Disease Activity

Not Active ..... Very Active

0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100

Please enter a numerical assessment score (*0 = Not Active; 100 = Very Active*): _____

PREDICT-001
Unscheduled Visit: Change in Therapy – Investigator

Please complete this information on every page of the questionnaire

Subject ID | | | | | | | Date of Visit | | | DD | | | MMM | | | | YYYY

Laboratory

PAXgene™

Were two PAXgene™ and one SST tube lab samples collected? O Yes O No

If no, why were two PAXgene™ and one SST tube lab samples not collected? _____

PAXgene™ Date of Collection: | | DD | | | MMM | | | | YYYY

PAXgene™ Kit ID:

15.11. CRF: Unscheduled Visit: Blood Re-Draw

PREDICT-001
Unscheduled Visit: Blood Re-Draw – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ ☐☐☐ ☐☐☐☐
DD MMM YYYY

Change in Medical History

Did the subject have a change in their medical history (comorbidities) since their last visit? O Yes O No

If yes, please update the table below to reflect the patient's current comorbidities at this visit:

Condition	Patient's Comorbidity Status
Cardiovascular disease	O Yes/active O Yes/inactive O No history
Hypertension	O Yes/active O Yes/inactive O No history
Anemia or other blood disease	O Yes/active O Yes/inactive O No history
Lung disease	O Yes/active O Yes/inactive O No history
Diabetes	O Yes/active O Yes/inactive O No history
Ulcer or stomach disease	O Yes/active O Yes/inactive O No history
Kidney disease	O Yes/active O Yes/inactive O No history
Liver disease	O Yes/active O Yes/inactive O No history
Cancer	O Yes/active O Yes/inactive O No history
Osteoarthritis, degenerative arthritis	O Yes/active O Yes/inactive O No history
Back pain	O Yes/active O Yes/inactive O No history
Fractures spine, hip, or leg	O Yes/active O Yes/inactive O No history
Depression	O Yes/active O Yes/inactive O No history

Did the subject have a Major Adverse Cardiovascular Event (MACE): Acute Myocardial Infarction (AMI), stroke, or cardiovascular mortality since their last visit? O Yes O No

If yes, check all the apply and specify:

☐ Related to prior medical history ☐ Related to b/tsDMARD therapy initiated at Visit 2

☐ Related to non-RA medications subject was taking ☐ Related to current rheumatic disease/ activity

☐ Other (please specify)

(Required) Please specify the subject's Major Adverse Cardiovascular Event (MACE): _____

Smoking History

Did the subject have any changes to their smoking status since their last visit? O Yes O No

If yes, please complete below.

Which of the following best describes the subject:

Current smoker? O Yes O No

Former smoker? O Yes O No

Subject has never smoked? O Yes, never smoked O No

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PREDICT-001
Unscheduled Visit: Blood Re-Draw – Investigator

Please complete this information on every page of the questionnaire

Subject ID ☐☐☐ ☐☐☐☐ Date of Visit ☐☐ ☐☐☐ ☐☐☐☐
DD MMM YYYY

Concomitant Rheumatoid Arthritis Medication

Did the subject have any changes to their current RA concomitant medication since the last visit? O Yes O No

If yes, please complete the table below:

Type of Change	Medication Name	Dose (Units)	Frequency	Route	Start Date (DD/MMM/YYYY)	End Date (DD/MMM/YYYY)

PAXgene™ and SST Redraw

PAXgene™

Did the subject return and have two PAXgene™ and one SST tube lab samples collected? O Yes O No

PAXgene™ Date of Collection: ☐☐ ☐☐☐ ☐☐☐☐
DD MMM YYYY

PAXgene™ Kit ID: ☐☐☐☐☐☐☐☐☐☐

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