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INFORMED CONSENT
Protocol ID: SYN-1204-RA
Version: 3.2
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color MedNavy

Clinical Trial Informed Consent Form

Evaluation of the Efficacy, Safety, and Tolerability of SYN-1204 Immunotherapy in Patients with Moderate-to-Severe Active Rheumatoid Arthritis

The SUTURE-3 Trial

Investigational Product:	SYN-1204 (anti-TNF/IL-6 fusion protein)
Protocol Number:	SYN-1204-RA (Phase III)
Principal Investigator:	Dr. Sarah Jenkins, MD, PhD
Clinical Site:	Vertex Medical Center, Department of Rheumatology
Sponsor:	Synapse Biopharma Corp.
Participant ID:	_____ (To be completed by site coordinator)

1 Introduction and Study Background

You are being invited to participate in a clinical research study. Before you decide whether to participate, it is important that you understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with family, friends, or your personal physician if you wish.

1.1 Study Purpose

This clinical trial is designed to evaluate the safety, efficacy, and tolerability of an investigational drug named **SYN-1204**, developed by **Synapse Biopharma Corp**. SYN-1204 is a novel biological fusion protein targeting both tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) pathways. The study aims to determine if SYN-1204 is effective in reducing joint inflammation, pain, and progression of joint damage in patients diagnosed with moderate-to-severe active Rheumatoid Arthritis (RA) who have had an inadequate response to standard disease-modifying antirheumatic drugs (DMARDs) [1].

1.2 Why You Are Being Invited

You are being invited to participate because you have been diagnosed with moderate-to-severe active Rheumatoid Arthritis, have been on a stable dose of methotrexate for at least 12 weeks, and continue to experience active symptoms (such as swollen and tender joints). Approximately 450 participants at 35 clinical sites globally will participate in this trial, overseen by investigator **Dr. Sarah Jenkins, MD, PhD** at the **Vertex Medical Center**.

1.3 Voluntary Participation

Your participation in this study is entirely voluntary. You may choose not to participate, or you may withdraw your consent at any time without penalty or loss of benefits to which you are otherwise entitled. Your decision will not affect your current or future medical care at Vertex Medical Center.

2 Study Design and Procedures

This study is a randomized, double-blind, placebo-controlled Phase III clinical trial. "Randomized" means you will be assigned to a treatment group by chance (like flipping a coin). "Double-blind" means neither you nor the study doctors will know which treatment you are receiving during the study, although this information can be quickly accessed in an emergency. "Placebo-controlled" means some participants will receive an inactive substance (placebo) that looks identical to the investigational drug.

2.1 Patient Journey and Flow

The diagram below illustrates the pathway you will follow if you choose to participate in this study.

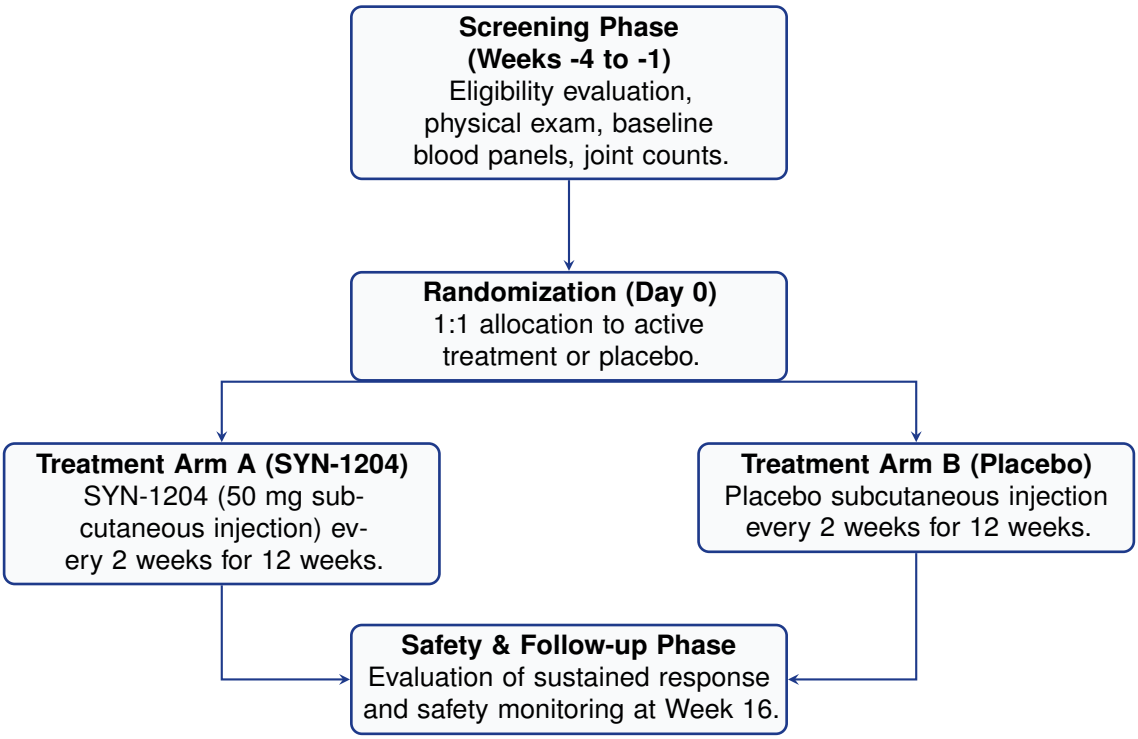

Figure 1: SYN-1204-RA Participant Flowchart

2.2 Schedule of Visits and Procedures

If you participate, you will need to visit the clinic a total of 7 times over a 16-week period. Table 1 details the specific assessments performed at each visit.

Table 1: Schedule of Assessments and Trial Procedures

Procedure / Assessment	Scr.	Base.	Wk 2	Wk 4	Wk 8	Wk 12	Wk 16
Informed Consent	X						
Eligibility Criteria	X	X					
Physical Examination	X	X		X		X	X
Vital Signs	X	X	X	X	X	X	X
Clinical Joint Count (DAS28)	X	X	X	X	X	X	X
Laboratory Blood Panels[a]	X	X	X	X	X	X	X
Investigational Drug Injection		X	X	X	X	X	
Adverse Event Monitoring		X	X	X	X	X	X

[a] Includes complete blood count (CBC), metabolic panel, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR).

3 Risks, Discomforts, and Benefits

As with any investigational drug, there are potential risks and side effects associated with SYN-1204. You should weigh these risks against the potential benefits before agreeing to participate in this study.

3.1 Potential Risks of SYN-1204

Since SYN-1204 is designed to suppress parts of your immune system to treat your rheumatoid arthritis, it may increase your risk of infections. The following side effects have been observed in early trials or are anticipated based on similar agents [2]:

- **Common Side Effects (occurring in 5% to 15% of participants):** Injection site reactions (such as redness, swelling, or itching at the injection site), mild upper respiratory tract infections, headache, and transient elevations in liver enzymes.
- **Less Common but Serious Side Effects (occurring in less than 2% of participants):** Serious infections (such as pneumonia or skin infections requiring hospitalization), reactivation of tuberculosis (TB) or viral hepatitis, and severe allergic reactions (anaphylaxis).

CRITICAL SAFETY NOTICE: Reproductive Risks

The effects of SYN-1204 on an unborn baby or nursing infant are currently unknown. Women who are pregnant, planning to become pregnant, or breastfeeding are strictly excluded from this study. Male and female participants of childbearing potential must agree to use highly effective double-barrier contraception (such as condoms combined with oral contraceptives or an intrauterine device) for the duration of the study and for at least 8 weeks following the last dose of the investigational product.

3.2 General Risks of Trial Procedures

- **Blood Draws:** Drawing blood may cause temporary pain, bruising, lightheadedness, or, rarely, an infection at the needle insertion site.
- **Placebo Group:** If you are randomized to the placebo group, your rheumatoid arthritis symptoms may not improve and could worsen during the 12-week treatment period. If your symptoms worsen significantly, rescue medication will be provided in accordance with clinical protocol.

3.3 Potential Benefits

There is no guarantee that you will receive any direct therapeutic benefit from participating in this study. However, if SYN-1204 is effective, you may experience a reduction in your joint pain, swelling, and morning stiffness, as well as an improvement in physical functioning. Furthermore, the information gained from this trial may help researchers develop better treatments for other patients with rheumatoid arthritis in the future.

4 Confidentiality and Data Protection

Your privacy is very important to us, and every effort will be made to protect your personal health information. Under the rules of the Health Insurance Portability and Accountability Act (HIPAA) and applicable regional data protection regulations (such as GDPR), your personal details will remain confidential.

4.1 Data Anonymization

If you choose to participate, all of your medical records and samples collected during the trial will be labeled with a unique code (your Participant ID) rather than your name, social security number, or other identifying information. Only the study coordinators and Principal Investigator at Vertex Medical Center will hold the key that links this code to your identity. All biological samples and electronic clinical data will be stored securely on password-protected servers at Vertex Medical Center and Synapse Biopharma Corp.

4.2 Access to Research Records

By signing this consent form, you authorize the following groups to access your medical records for verification of study procedures and data analysis:

1. Representatives of the study sponsor, **Synapse Biopharma Corp.** and its designated clinical monitors.
2. Authorized inspectors from government regulatory agencies, including the Food and Drug Administration (FDA) and the European Medicines Agency (EMA).
3. The Institutional Review Board (IRB) overseeing the clinical safety and ethics of this study.

These entities are legally required to maintain your confidentiality. The results of this study may be published in scientific journals or presented at medical conferences; however, your individual identity will never be disclosed.

5 Right to Withdraw, Costs, and Alternatives

5.1 Right to Withdraw

You may change your mind and stop participating in this study at any time without giving a reason. Your decision will not lead to any penalty or loss of benefits. If you decide to withdraw, please inform Dr. Sarah Jenkins or the study staff immediately so that you can undergo a final safety check. Any data collected up to the point of your withdrawal will be kept as part of the study database to ensure scientific integrity, but no further data or samples will be collected.

5.2 Costs and Compensation

There are no costs to you or your insurance company for participating in this study. The investigational product (SYN-1204 or placebo), study-related doctor visits, laboratory tests, and clinical examinations will be provided at no charge.

You will receive a stipend of $50 per visit to cover travel expenses and parking. If you sustain a physical injury as a direct result of the study drug or study procedures, Synapse Biopharma Corp. will provide medical treatment at no cost to you, provided that you have followed the instructions of the study staff.

5.3 Alternatives to Participation

You do not have to participate in this study to receive treatment for your rheumatoid arthritis. Other treatments are available and include:

- Standard disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, or sulfasalazine.
- Approved biologic therapies (such as anti-TNF agents, IL-6 inhibitors, or JAK inhibitors).
- Non-steroidal anti-inflammatory drugs (NSAIDs) or corticosteroids to manage pain and inflammation.

Please discuss these alternatives with your personal doctor to determine the best course of treatment for your condition.

6 Participant Affirmation and Signatures

Affirmation of Informed Consent

By signing this form, I confirm that:

- I have read and understood the information in this document (Version 3.2, dated 12-May-2026).
- I have had the opportunity to ask questions, and all my questions have been answered to my satisfaction.
- I understand that my participation is voluntary and that I am free to withdraw at any time.
- I agree to participate in the SYN-1204-RA Phase III clinical trial and authorize the access of my medical records as described.

Participant Signature

Signature of Participant

Printed Name of Participant

Date (DD-Mmm-YYYY)

Person Obtaining Consent

Signature of Investigator / Staff

Printed Name of Investigator / Staff

Date (DD-Mmm-YYYY)

Witness (if applicable)

Signature of Witness

Printed Name of Witness

Date (DD-Mmm-YYYY)

Principal Investigator Approval

Signature of Principal Investigator

Printed Name: Dr. Sarah Jenkins

Date (DD-Mmm-YYYY)

References

[1] Josef S. Smolen, Ferdinand C. Breedveld, Gerd R. Burmester, Vivian P. Bykerk, Maxime Dougados, Paul Emery, Tore K. Kvien, Francisco Navarro-Sarabia, et al. Treating rheumatoid arthritis to target: 2018 update of the recommendations of an international task force. *Annals of the Rheumatic Diseases*, 79(6):685–698, 2020.

[2] Jane McIver, Sarah Jenkins, and Evelyn Vance. Safety and efficacy profile of novel fusion proteins in autoimmune diseases. *Journal of Immunology and Clinical Therapeutics*, 14(2):112–128, 2025.

[3] F. C. Arnett, S. M. Edworthy, D. A. Bloch, D. J. McShane, J. F. Fries, N. S. Cooper, L. A. Healey, S. R. Kaplan, M. H. Liang, H. S. Luthra, et al. The american rheumatism association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis & Rheumatology*, 31(3):315–324, 1988.