VERTEX ACADEMIC MEDICAL CENTER

Institutional Review Board (IRB) Research Proposal Application

Submission Information

Submission Date: August 2, 2026 **Protocol Number:** IRB-2026-NEX-8902
Application Status: New Protocol Submission **Review Category:** Full Board Review

1 Administrative Details

Below is the summary of administrative details for the proposed clinical research study.

Project Title	A Phase II, Randomized, Double-Blind, Placebo-Controlled Study of Vertex-902 in Patients with Moderate-to-Severe Rheumatoid Arthritis
Principal Investigator **Affiliation** **Contact Info**	Dr. Elena Vance, MD, PhD Department of Rheumatology & Immunology, Vertex Academic Medical Center email: e.vance@vertexmed.org | phone: +1 (555) 019-8902
Co-Investigators	Dr. Marcus Sterling, MD (Department of Immunology) Dr. Xi Chen, PhD (Department of Biostatistics)
Sponsoring Entity **Proposed Duration** **Primary Study Site**	Synapse Biopharmaceuticals, Inc. (Research Grant Ref: SYN-2025-V902) 24 Months (Estimated Start: October 1, 2026) Vertex Clinical Trials Unit (Building C, Suite 400)

Table 1: Administrative and investigator details for protocol IRB-2026-NEX-8902.

1.1 Funding and Conflict of Interest

This study is funded via a research grant from **Synapse Biopharmaceuticals, Inc.** The investigational product (Vertex-902) and matching placebo will be provided free of charge by the sponsor.

Dr. Elena Vance discloses that she serves as a non-compensated scientific advisor for Synapse Biopharmaceuticals, Inc. Dr. Marcus Sterling and Dr. Xi Chen declare no conflicts of interest. A formal Conflict of Interest (COI) management plan has been reviewed and approved by the Vertex Academic Medical Center Compliance Office and is attached to this application.

2 Protocol Summary & Rationale

2.1 Study Abstract

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by persistent synovial inflammation, leading to joint destruction, pain, and systemic comorbidities. Despite the success of current biologics, a significant portion of patients do not achieve clinical remission or experience side effects. Vertex-902 is a novel, selective Janus Kinase 1 (JAK1) inhibitor developed by Synapse Biopharmaceuticals, Inc. Pre-clinical models have shown superior efficacy in reducing inflammatory cytokine production with a highly favorable safety profile [3]. This study is a randomized, double-blind, placebo-controlled Phase II trial designed to evaluate the safety, tolerability, and preliminary efficacy of two dosing regimens of Vertex-902 in patients with moderate-to-severe RA who have had an inadequate response to methotrexate.

2.2 Scientific Rationale

The JAK-STAT pathway plays a critical role in the pathogenesis of RA by mediating signal transduction for multiple inflammatory cytokines (e.g., IL-6, IFN-γ, IL-12, and IL-23). While pan-JAK inhibitors have demonstrated therapeutic efficacy, they are frequently associated with dose-limiting toxicities such as cytopenia and hyperlipidemia, primarily due to non-selective inhibition of JAK2 and JAK3. Vertex-902 is designed to exhibit a > 50-fold selectivity for JAK1 over other JAK isoforms. By sparing JAK2 (essential for erythropoietin signaling) and JAK3 (essential for lymphocyte homeostasis), Vertex-902 is hypothesized to achieve equivalent or superior anti-inflammatory activity with significantly reduced hematological side effects. Ethical review of this protocol is required to ensure appropriate safety monitoring and risk mitigation for human participants in this first-in-human adjacent clinical trial phase [1].

2.3 Study Objectives

Primary Objective: To evaluate the clinical efficacy of Vertex-902 (5 mg and 10 mg daily doses) compared to placebo in achieving an ACR20 response (American College of Rheumatology 20% improvement) at Week 12.

Secondary Objectives:

- To evaluate the safety and tolerability of Vertex-902 through adverse event monitoring, laboratory evaluations (hematology, lipid panels), and ECGs.
- To evaluate improvement in physical function and pain using the Health Assessment Questionnaire-Disability Index (HAQ-DI) at Week 12.
- To evaluate pharmacokinetics and pharmacodynamics (PK/PD) of Vertex-902 in the target patient cohort.

3 Study Design & Methodology

3.1 Overall Study Design

This is a Phase II, randomized, double-blind, placebo-controlled, parallel-group clinical trial. Eligible participants will be randomized in a 1:1 ratio to receive either Vertex-902 (5 mg orally once daily) or matching placebo for a total duration of 12 weeks. The trial incorporates a screening period of up to 4 weeks prior to baseline assessments, followed by a 12-week active treatment period and a follow-up safety visit at Week 14. The overview of the participant flow is illustrated in Figure 1.

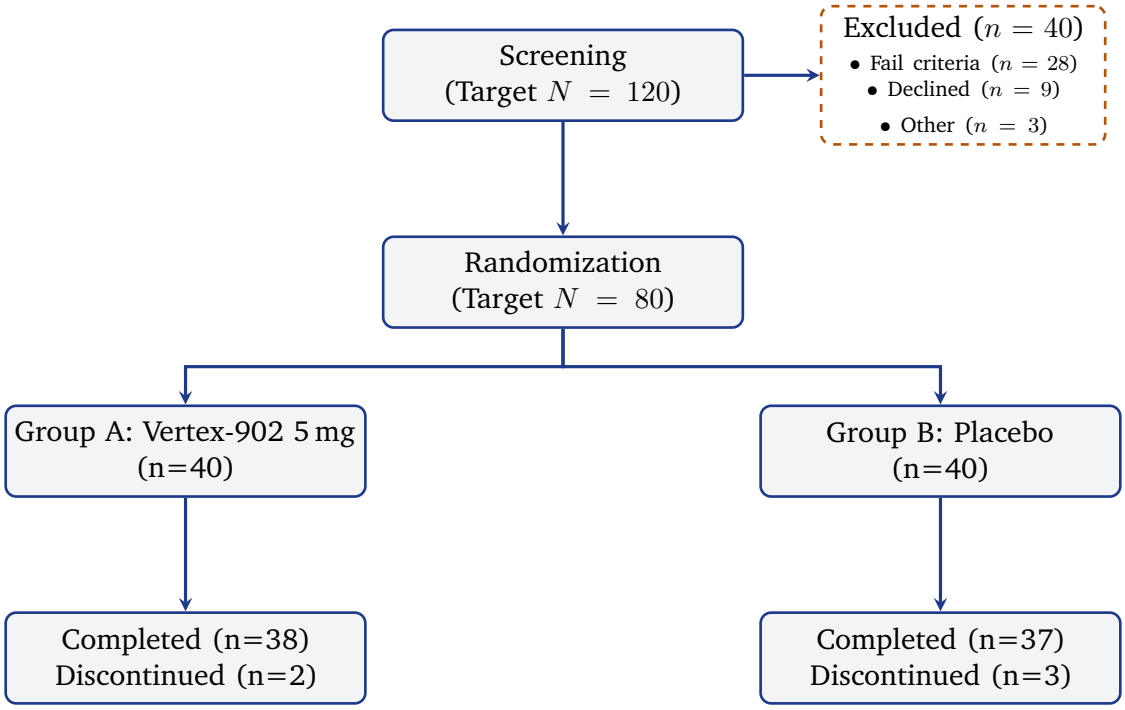

Figure 1: CONSORT-style study design and participant flow diagram.

3.2 Randomization and Blinding

Randomization will be performed electronically via an interactive web response system (IWRS) managed by an independent statistician not involved in the conduct of the trial. Block randomization will be used to ensure equal allocation.

To maintain double-blind conditions:

- Vertex-902 and placebo will be manufactured, packaged, and labeled identically.
- The investigators, study site personnel, clinical monitors, and patients will remain blinded to the treatment assignment.
- Unblinding will only be permitted in the case of a medical emergency where knowledge of the study drug is critical for patient management.

3.3 Schedule of Assessments

The schedule of assessments and study procedures is detailed in Table 2.

Procedure	Screening	Baseline	Week 4	Week 8	Week 12 (EOS)
Informed Consent	X				
Eligibility Screening	X				
Randomization		X			
Study Drug Dispensing		X	X	X	
Clinical Joint Evaluation	X	X	X	X	X
Laboratory Evaluations	X	X	X	X	X
Adverse Event Monitoring		X	X	X	X
Pharmacokinetics (PK)			X		X

Table 2: Schedule of study procedures and visits (EOS: End of Study).

Note: Laboratory evaluations include complete blood count (CBC), liver function tests (LFTs), lipid panel, and serum creatinine.

4 Ethical Considerations & Human Subjects Protection

4.1 Basic Principles

This clinical trial will be conducted in strict compliance with the Declaration of Helsinki, the International Council for Harmonisation Good Clinical Practice (ICH GCP) guidelines, and all applicable national and local regulatory requirements. The study will not initiate recruitment until written approval has been obtained from the Institutional Review Board (IRB) of Vertex Academic Medical Center.

4.2 Subject Selection and Recruitment

Potential participants will be recruited from the outpatient rheumatology clinics at Vertex Academic Medical Center and affiliated network sites. Recruitment materials (posters, letters, and digital ads) will be submitted for IRB approval prior to use.

To ensure fair and ethical participant selection:

- Inclusion and exclusion criteria will be applied objectively without bias toward race, ethnicity, or socioeconomic status.
- Vulnerable populations (e.g., pregnant women, prisoners, cognitively impaired individuals, and employees of the investigators or sponsor) will be excluded from participation to protect them from coercion or undue influence [2].
- Pediatric patients will be excluded from this Phase II trial as the safety and efficacy profile has not yet been established in adult populations.

4.3 Privacy and Data Confidentiality

Patient privacy and confidentiality will be protected at all stages of the research. The following measures will be implemented:

- **De-identification:** All data collected will be pseudonymized. Participants will be assigned a unique multi-digit Study Identification Number at screening. Direct identifiers (name, date of birth, medical record numbers) will be removed from all electronic databases and analytical files.
- **Data Storage:** Electronic Case Report Forms (eCRFs) will be stored on a secure, encrypted database hosted on Vertex Academic Medical Center's secure private cloud. Access will be strictly controlled via role-based permissions and multi-factor authentication.
- **Physical Records:** Signed informed consent forms and physical medical history logs will be stored in locked filing cabinets within the Vertex Clinical Trials Unit. Only the Principal Investigator and designated study coordinator will have physical access to these keys.

5 Informed Consent Process

5.1 Consent Acquisition Protocol

No study-related procedures will be performed prior to obtaining written, signed, and dated informed consent from the participant. The consent process will follow a structured protocol designed to maximize patient comprehension and minimize any potential for coercion:

1. **Initial Discussion:** The Principal Investigator or a designated, trained sub-investigator will introduce the study to the patient, detailing the experimental nature of Vertex-902, study duration, scheduled visits, and procedures.
2. **Information Document:** The patient will be provided with a copy of the IRB-approved Informed Consent Form (ICF). The document will explain in plain language (8th-grade reading level or lower) the study's purpose, potential risks, benefits, alternatives to participation, and the voluntary nature of participation.
3. **Reflection Period:** Patients will be encouraged to read the form thoroughly, discuss the trial with family members, personal physicians, or advisors, and take up to 48 hours to make a decision.
4. **Question and Answer Session:** A follow-up face-to-face meeting will be scheduled where the investigator will address any questions the patient might have and test their understanding of the trial requirements.
5. **Signature:** Once the investigator is confident that the patient understands the study details and wishes to participate, both the patient and the investigator will sign and date two copies of the ICF. One original copy will be given to the patient, and the other will be retained in the investigator site file.

5.2 Language and Comprehension Support

All consent materials will be written in English. For patients whose primary language is Spanish, an officially translated Spanish ICF approved by the IRB will be used. A certified translator or bi-lingual medical staff member not associated with the study will assist in the consent discussion to ensure accurate communication.

5.3 Modifications and Re-consent

If new safety information becomes available or if any significant modifications are made to the study protocol (such as changes in treatment duration or testing methods), the ICF will be updated. The revised ICF will be submitted for IRB approval. Once approved, all currently enrolled participants who are affected by the changes will undergo a re-consent process to continue their participation in the trial.

6 Risk-Benefit Analysis

6.1 Potential Risks of Vertex-902

As Vertex-902 is an immunomodulatory agent, it carries several potential risks based on its pharmacological class and pre-clinical observations:

Infection Risk: Suppression of the immune system may increase the susceptibility to upper respiratory tract infections, urinary tract infections, and opportunistic infections.

Laboratory Abnormalities: Potential for mild, transient elevations in liver transaminases (ALT/AST), serum cholesterol (LDL/HDL), and mild reductions in absolute neutrophil count (ANC) or hemoglobin.

Gastrointestinal Symptoms: Nausea, abdominal discomfort, or diarrhea may occur during the first few weeks of therapy.

Thromboembolic Events: Although Vertex-902 is highly selective for JAK1, thromboembolic events (e.g., deep vein thrombosis) are a known class-effect of JAK inhibitors and will be closely monitored.

6.2 Risk Mitigation Strategies

To minimize risk and ensure patient safety, the following measures are integrated into the protocol:

Safety Monitoring and Discontinuation Rules

Monitoring Frequency: Complete blood count (CBC) and liver function tests (LFTs) will be performed every 4 weeks. Lipid panels will be performed at baseline and Week 12.
Individual Discontinuation Criteria: The study drug will be permanently discontinued, and the patient will be put on standard clinical care if any of the following occur:

- Absolute Neutrophil Count (ANC) $< 1,000/\mu$L
- Hemoglobin < 8.0 g/dL
- ALT or AST $> 3\times$ the Upper Limit of Normal (ULN)
- Pregnancy (monitored via monthly urine pregnancy tests for female participants of childbearing potential)
- Any serious infection requiring intravenous antibiotics

An independent Data Safety Monitoring Board (DSMB) consisting of two rheumatologists and one biostatistician will review unblinded safety data after 20, 40, and 60 patients have completed their Week 4 evaluations. The DSMB has the authority to recommend halting the study for safety concerns.

6.3 Potential Benefits

There is no guarantee of direct therapeutic benefit to participants. However, based on pre-clinical data, participants receiving active treatment may experience a reduction in joint swelling, tenderness, stiffness, and pain. These physical improvements may lead to enhanced mobility and better overall quality of life. The data gathered from this study will also contribute to scientific understanding of JAK1 inhibitors and may benefit future patients with rheumatoid arthritis.

6.4 Risk-Benefit Ratio Justification

Given that moderate-to-severe rheumatoid arthritis is a debilitating disease, and the risks of Vertex-902 are mitigated by intensive laboratory monitoring, a DSMB, and strict discontinuation rules, the potential therapeutic benefits are considered to outweigh the risks. The clinical and ethical risk-benefit ratio is justified.

References

[1] Sarah Jones and Rohan Patel. Ethical challenges in institutional review board appraisals of novel biologics. *Medical Ethics Quarterly*, 18(2):45–56, 2024.

[2] Arthur Nimbus and Clara Walker. Informed consent in vulnerable populations: A comprehensive review of best practices. *Human Research Protection Review*, 29(4):201–215, 2023.

[3] Elena Vance, Marcus Sterling, and Xi Chen. Efficacy and safety of vertex-902 in pre-clinical models of chronic inflammation. *Journal of Clinical Therapeutics*, 42(3):115–128, 2025.