Appendix 3

Informed Consent Form

Study Title: Efficacy and Safety of Tafolecimab with Different Dosing Intervals in Patients with Hyperlipidemia

Protocol Number: V2.0; Date: November 20, 2025

Informed Consent Form Version Number and Date: V2.0 /November 20, 2025

Dear Patient:

We invite you to voluntarily participate in the “Efficacy and Safety of Tafolecimab with Different Dosing Intervals in Patients with Hyperlipidemia”, approved for conduct by the First Affiliated Hospital of Shandong First Medical University (Shandong Qianfoshan Hospital). This study will be conducted at the First Affiliated Hospital of Shandong First Medical University (Shandong Qianfoshan Hospital), with an estimated 60 participants voluntarily enrolled. This study has been reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Shandong First Medical University (Shandong Qianfoshan Hospital).

Before you decide whether to participate in this study, please read this information sheet carefully. This sheet will help you understand the study’s purpose, process, and duration, how your information will be used, and the potential benefits and risks of participating. If you have any questions, please ask the researcher responsible for explaining the informed consent form to you to ensure that you fully understand the details of the study. Participation in this trial is voluntary. You may refuse to participate or withdraw at any time during the study without facing discrimination or retaliation; your medical care and rights will not be affected.

If you choose to participate in this study, please sign the participant declaration section of the informed consent form. Our research team will do its utmost to ensure your safety and protect your rights throughout the study!

I. Research Background

Cardiovascular disease is a leading cause of death and disability worldwide,

and its burden continues to increase in both urban and rural areas of China. Atherosclerosis is the common pathological basis for the vast majority of cardiovascular and cerebrovascular events, and hyperlipidemia — particularly elevated low-density lipoprotein cholesterol (LDL-C) levels—is a key risk factor driving the onset and progression of atherosclerosis.

A wealth of evidence-based medical data has clearly demonstrated that LDL-C levels exhibit a log-linear relationship with the risk of atherosclerotic cardiovascular disease (ASCVD), and that effectively lowering LDL-C yields significant cardiovascular benefits.Mendelian randomization studies have further confirmed that for every 1 mmol/L reduction in LDL-C, the risk of ASCVD decreases by approximately 50%. To more effectively manage residual cardiovascular risk, numerous authoritative guidelines both domestically and internationally have further strengthened lipid-lowering targets for high- and very high-risk populations.However, aside from LDL-C, more than 40% of patients still face significant residual cardiovascular risk. Lipoprotein(a) [Lp(a)] is a genetic risk factor independent of LDL-C; even when LDL-C levels are well-controlled (e.g., <70 mg/dL), high Lp(a) levels can still significantly increase the risk of coronary heart disease events.Currently, there are no effective means to lower Lp(a) levels. Statins not only fail to reduce Lp(a) but may even cause its levels to rise by approximately 11%, further exacerbating cardiovascular risk; moreover, there are currently no effective therapeutic agents available.The latest domestic and international consensus guidelines emphasize that for patients who remain non-compliant with treatment goals despite statin therapy, non-statin potent lipid-lowering drugs, such as PCSK9 (proprotein convertase subtilisin/kallikrein 9) inhibitors, should be added early in the treatment regimen.

Tafolecimab is a novel lipid-lowering injectable medication (a PCSK9 inhibitor) independently developed in China. It powerfully lowers lipid levels by enhancing the liver’s ability to clear LDL-C, while also effectively reducing Lp(a) levels. This drug has been demonstrated to have a long-acting effect. The current standard dosing regimen is one injection every two weeks.

Signature of the study participant:_____

Given its long-acting nature, we hypothesize that extending the dosing interval to once every three weeks may similarly maintain good lipid-lowering efficacy. If this regimen is validated, it will significantly reduce the number of annual injections for patients, offering you a more convenient treatment option that is expected to alleviate the treatment burden and improve long-term treatment adherence.

Currently, there is a lack of clinical studies systematically evaluating the actual efficacy and safety of the once-every-three-weeks dosing regimen. Therefore, we are conducting this study to compare the efficacy of Tafolecimab administered once every three weeks with the standard once-every-two-weeks regimen, with the aim of providing a better treatment option for you and future patients.

II. Study Objectives

This study aims to systematically evaluate the lipid-lowering efficacy and safety of Tafolecimab 150 mg administered every two weeks (Q2W) versus every three weeks (Q3W) for 12 weeks in patients with hyperlipidemia whose LDL-C levels have not reached the target values specified in the *Chinese Guidelines for Lipid Management (2023)* after 4 weeks of moderate-intensity statin therapy (which may be combined with a cholesterol absorption inhibitor). The primary efficacy endpoint was the percentage change in LDL-C from baseline at week 12 of the first treatment course.

III. Study Protocol

1. Number of Participants

This study plans to enroll a total of 60 patients.

2. Study Details

We will not change your current treatment regimen. Your treating physician has already developed a treatment plan that includes Tafolecimab based on your condition. The purpose of this study is simply to systematically and prospectively collect and compare the efficacy and safety of two different dosing schedules (every two weeks vs. every three weeks) in a real-world clinical setting.

Signature of the study participant:_____

3. Specific Study Procedures and Methods

This is an observational study, and we will not change your current treatment plan. You will continue to receive the standard treatment regimen recommended by your treating physician based on your condition and clinical guidelines, which involves the combination of Tafolecimab with statins.

This study aims to observe the actual effects of two dosing intervals that physicians may consider in clinical practice. Your doctor will determine the dosing interval most suitable for your current situation (every two weeks or every three weeks) after discussing it with you, taking into account your lipid levels, personal lifestyle preferences, and comfort level with different injection frequencies. This study fully respects and adopts the clinical decision made jointly by you and your doctor.

Based on this established treatment plan, you will be assigned to one of the following groups for follow-up observation:

Group A: Tafolecimab 150 mg, administered subcutaneously once every two weeks (14 ± 3 days)

Group B: Tafolecimab 150 mg, administered subcutaneously once every three weeks (21 ± 3 days)

Before the study begins, we will collect your basic information, medical history, and medication history, and perform blood tests to measure lipid levels, liver and kidney function, and other indicators as baseline data. Depending on your group assignment, you will visit the hospital for follow-up at different time points (Group A: Weeks 2, 6, and 12 after the first dose; Group B: Weeks 3, 9, and 12 after the first dose, with a ±3-day window for each visit).At each follow-up visit, we will measure your vital signs, ask about your health status, and draw blood to test lipid levels, liver and kidney function, and other indicators.

Please note that the three-week dosing regimen is an exploratory protocol proposed based on the long-acting pharmacological properties of Tafolecimab and is scientifically sound. If the study confirms that its efficacy is comparable to that

of the standard regimen, it will provide patients with a more convenient option. The purpose of this study is precisely to scientifically compare the performance of these two valid regimens in real-world settings. Your participation will help us answer this question, which is crucial for future patients.

4. Study Duration

Your total participation in this study will last approximately 12 weeks.

5. Information and Biological Samples Collected During the Study

We will collect your basic personal information, medical history, vital signs, laboratory test results, and records of any adverse reactions (adverse events). All your study information will be anonymized. The coding sheet linking this information to your identity will be strictly safeguarded by the principal investigator to ensure your privacy. This study does not collect biological specimens specifically for this purpose. We will use blood samples that have already been collected during your routine follow-up visits as part of your clinical care. These samples will be tested by our hospital's Department of Laboratory Medicine for lipid profiles, liver and kidney function, and other parameters required for this study. Any remaining samples will be uniformly disposed of as medical waste by the Department of Laboratory Medicine in accordance with the *Administrative Measures for Clinical Laboratories in Medical Institutions* and the hospital's internal procedures; they will not be retained or used for any other purpose.

6. Other: This study does not involve genetic testing.

IV. Inclusion and Exclusion Criteria

1. Inclusion Criteria

1) Age ≥18 years.

2) Diagnosed with hyperlipidemia and on a stable, regular dose of moderate-intensity statins for at least 4 weeks (specifically: Atorvastatin 10 mg/d, Rosuvastatin 5 mg/d, Fluvastatin 80 mg/d, Pitavastatin 2-4 mg/d, Pravastatin 40 mg/d, Simvastatin 20-40 mg/d, or Xuezhikang 1.2 g/d), with or without concurrent cholesterol absorption inhibitors.

3) Baseline LDL-C levels failing to reach the therapeutic target corresponding

to the patient's ASCVD risk categorization (defined as follows):ASCVD Primary Prevention (Low Risk): LDL-C ≥ 3.4 mmol/L; ASCVD Primary Prevention (Moderate/High Risk): LDL-C ≥ 2.6 mmol/L; ASCVD Secondary Prevention (Very High Risk): LDL-C ≥ 1.8 mmol/L OR reduction from baseline ≥ 50%;ASCVD Secondary Prevention (Ultra-High Risk): LDL-C ≥ 1.4 mmol/L OR reduction from baseline ≥ 50%

4) Meets the standard clinical criteria for PCSK9 inhibitor initiation, OR the treating physician estimates that continuing current moderate-intensity statins cholesterol absorption inhibitor therapy will not achieve the target LDL-C levels, thereby requiring combination therapy with a PCSK9 inhibitor.

5) First-time user of tafolecimab (PCSK9 inhibitor-naïve).

6) Voluntarily participates in the study, provides written informed consent, and meets all follow-up compliance requirements.

7) Candidates must meet ALL of the above criteria to be eligible for enrollment in the study.

2. Exclusion Criteria

All study participants who have signed the informed consent form and been screened as eligible for the study are considered dropouts if they withdraw from the clinical study at any time and for any reason, provided they have not completed the observation period specified in the protocol.After a study participant drops out, the investigator should make every effort to contact them to complete as many assessment items as possible and record the participant's last dose of medication to the best of their ability. The reason for the participant's dropout should be documented, and the study summary form should be completed. For participants who drop out due to an adverse event (AE), this should be recorded in the CRF.

V. Alternative Treatments

In addition to participating in this study, you may also discuss other lipid-lowering treatment options with your doctor, such as adjusting the type or dose of your statin, combining it with other types of oral lipid-lowering medications (such as ezetimibe), or choosing another PCSK9 inhibitor for treatment.

VI. Potential Risks and Discomforts

1. Injection of Tafolecimab may cause injection-site reactions, such as local redness, swelling, hardening, pain, or itching.

2. Systemic reactions may occur, such as flu-like symptoms, headache, and fatigue.

3. Blood draws may cause local pain or bruising; in very rare cases, infection or fainting may occur.

4. Although the likelihood is low, there is still a risk of other unknown adverse reactions.

VII. Expected Benefits

You will undergo regular lipid profile monitoring and professional medical follow-up, which will help you better manage your lipid levels. If longer dosing intervals are proven effective, you may benefit from a more convenient treatment regimen in the future, reducing the number of hospital visits and improving treatment convenience. The information gathered from your participation in this study will provide important insights for optimizing treatment strategies for patients with hyperlipidemia, benefiting more patients.

VIII. Compensation

This is an observational study that does not involve additional blood draws and does not provide compensation.

IX. Free Treatment

This study aims to observe the effectiveness of existing treatment regimens. Therefore, all visits, tests, and treatments conducted as part of the study are considered part of the routine management of your condition. The associated costs must be covered by you or your health insurance in accordance with standard policies; the research team does not provide any additional free tests or treatments.

X. Compensation

This study has not purchased any specific insurance for you related to this study. If your physical health is harmed and it is confirmed to be directly related to this study, the investigators will assist you in seeking compensation from the relevant liable parties in accordance with the provisions of China’s current laws

and regulations, including the Civil Code of the People's Republic of China.

XI. Precautions Before, During, and After the Study

During the study, please continue to take your current statin medication as prescribed. If you need to take any new medications, or if there are any changes in your health status, please be sure to inform your study doctor promptly. Please follow your study doctor's instructions and attend follow-up visits and take your medication on time.

XII. Use of Study Results and Confidentiality of Personal Information

Your study records will be kept strictly confidential and will appear in the study report using a code number rather than your name. Study findings may be presented at medical conferences or published in medical journals, but your personally identifiable information will never be disclosed. In accordance with legal provisions, the hospital ethics committee and relevant regulatory authorities have the right to access your study data for review, but they will also keep your information confidential.

XIII. Rights of Study Participants

Your participation in this study is entirely voluntary. You have the right to withdraw from the study at any time, without providing a reason, and this will not affect any future medical care you receive. If you decide to withdraw, please inform your study doctor.

XIV. As a participant in this study, please adhere to the following agreements:

1. Provide truthful and accurate information regarding your medical history and current health status;

2. Inform your study doctor whether you have participated in other studies in the past or are currently participating in any other studies, and provide detailed information regarding the duration and nature of such studies; this is important for ensuring your health and safety;

3. If there are any changes in your health, if you experience any symptoms, or if you feel any discomfort—regardless of whether you believe it is related to this study—you must promptly inform your study doctor;

4. Please make every effort to return to the hospital for follow-up visits on time as scheduled in the study protocol, and follow the study doctor’s instructions regarding the clinical study and the administration of the study medication;

5. Once you have enrolled in the study, you must inform your study doctor before taking any other medications, to prevent these medications from affecting your health;

XV. If you have any questions about this study, or if you experience any discomfort or injury during the study, please contact Dr. Li at 17658258600.

If your personal rights are affected during the study, you may contact the Research Ethics Subcommittee of the Medical Ethics Committee at the First Affiliated Hospital of Shandong First Medical University (Shandong Qianfoshan Hospital) at 0531-89269890.

Signature of the study participant:_____

Informed Consent Form - Signature Page

Clinical Study Title: A Study on the Clinical Efficacy and Safety of Toliximab Administered at Different Dosage Intervals in Patients with Hyperlipidemia

If you fully understand the content of this research project and agree to participate in this study, you will sign this Informed Consent Form. The Informed Consent Form must be signed by the research participant or their legal representative. It is prepared in duplicate, with one copy retained by the investigator and the other by the research participant or their authorized representative.

Statement of Consent:

1、 I confirm that I have read and understood the informed consent form for this study. Potential issues that may arise during the study and their solutions have been explained to me, and I have had the opportunity to ask questions.

2、 I clearly understand that participation in this study is voluntary, and that refusing to participate will not prejudice any of my rights or interests.

3、 I have been informed that the physician conducting this study, the person in charge of this project at the First Affiliated Hospital of Shandong First Medical University (Shandong Qianfoshan Hospital), and the Medical Ethics Committee of the First Affiliated Hospital of Shandong First Medical University (Shandong Qianfoshan Hospital) all have the right to review the study records and medical case files. I consent to these parties directly accessing my study records and understand that this information will be kept confidential.

4、 I agree to participate in this study.

Full Name of Study Participant:

Year Month Day Hour Minute

Full Name of the Research Participant’s Representative:

Year Month Day Hour Minute

Relationship to the study participant:_____ (If the representative is not a close relative, is there a letter of authorization from the study participant? Yes No)

To be completed by the physician conducting the informed consent process

Investigator’s Statement: I confirm that I have explained and discussed the nature, purpose, requirements, and potential risks of this study with the patient, explored alternative treatment options, and ensured that a copy of the study participant’s informed consent form has been provided to the study participant for their records.

Full Name of Investigator:

Year Month Day Hour Minute