# Informed Consent Form

**Project title：** Study on the Intervention Effect of Denosumab on High-Risk Patients With Osteoporotic Fractures in Type 2 Diabetes

**Research center：** Peking Union Medical College Hospital

**Major investigator：** Prof. Weibo Xia

**Version Number ：** V3.1

**Version date：** 2025.12.05

**Subject`s name：** _____

**Subject enrollment number：** _____

You are invited to participate in the study titled “Study on the Intervention Effect of Denosumab on High-Risk Patients With Osteoporotic Fractures in Type 2 Diabetes.” This study will conduct a nationwide multicenter randomized controlled trial, combining clinical risk factors, bone density, and complications to investigate the effects of denosumab on bone density, bone turnover markers, and the risk of new fractures in patients with type 2 diabetes mellitus and high fracture risk. The study aims to provide evidence-based recommendations for the rational selection of anti-osteoporosis medications.

The study is led by Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, and will be jointly completed by multiple centers nationwide. Please read this informed consent form carefully and make a decision whether to participate in

this study. Participation in this study is entirely voluntary. As a participant, you must provide written consent before joining the clinical study. When your research doctor discusses the informed consent form with you, you may ask him/her to explain any parts that you do not understand. We encourage you to fully discuss with your family and friends before making a decision to participate in this study. You have the right to refuse to participate in this study, and you may withdraw from the study at any time without penalty or loss of any rights to which you are otherwise entitled. If you are participating in another study, please inform your research doctor. The background, purpose, study process, and other important information of this study are as follows：

## I、Background

With the changes in lifestyle and the intensification of population aging, type 2 diabetes has become a major public health issue worldwide. Osteoporosis and type 2 diabetes are both age-related diseases. Type 2 diabetes not only increases the risk of complications such as cardiovascular, cerebrovascular, and renal diseases but also significantly increases the risk of osteoporotic fractures. Osteoporotic fractures have high rates of disability and mortality, greatly exacerbating the health threats of type 2 diabetes. However, the impact of type 2 diabetes and its hypoglycemic drugs on osteoporosis and fractures still needs to be clarified, and the fracture early warning and prevention strategies for this special population are urgently in need of improvement. In our country, clinical research on type 2 diabetes and osteoporosis and fractures is still in its infancy, and there is a lack of data on the efficacy and safety of osteoporosis treatment drugs for diabetic patients.

To address the above key scientific issues, this study, titled "Study on the Intervention Effect of Denosumab on High-Risk Patients With Osteoporotic Fractures in Type 2 Diabetes," has been set up. This project will address some of the major issues in the prevention and control of type 2 diabetes combined with osteoporosis and fractures,

establish an early warning mechanism, precise diagnosis and treatment, and effective management plan that are in line with national conditions, and provide important clinical research evidence for comprehensively improving the level of prevention and control, effectively reducing the harm of the disease, and formulating national health policies.

## II、Purpose of study

Patients with type 2 diabetes mellitus (T2DM) have a significantly increased risk of fractures, but there are few studies on anti-osteoporosis drug interventions for T2DM. Receptor activator of nuclear factor-κB ligand (RANKL) plays a key regulatory role in the differentiation, maturation, and function of osteoclasts. Denosumab is a specific monoclonal antibody that inhibits the formation and function of osteoclasts, thereby reducing bone resorption, increasing bone density, and lowering the risk of fractures. Eldecalcitol is an active vitamin D analog that increases bone density and treats osteoporosis by promoting calcium absorption in the intestines, inhibiting bone resorption, and promoting bone formation. However, there is currently a lack of high-quality evidence on the effects of Denosumab and Eldecalcitol in patients with T2DM and high fracture risk. This study will conduct a randomized controlled trial in patients with T2DM and high fracture risk to evaluate the effects of Denosumab and Eldecalcitol on bone density, bone turnover markers, and the risk of new fractures, providing a scientific basis for clinical diagnosis and treatment.

## III、Study process

### 1. How many people will participate in this study?

This study is a multicenter randomized controlled trial, recruiting a total of 358 participants based on clinical risk factors, bone density, complications, and other factors.

### 2. Procedure of the study

If you agree to participate in this study, please sign this informed consent form. You

will be randomly assigned to either the Denosumab Control group or the Denosumab in combination with eldecalcitol treatment group for a 12-month intervention. We will conduct surveys, bone density tests, blood tests, muscle strength tests, X-ray imaging, and other examinations to collect clinical data. After 12 months of treatment, we will compare the changes in bone density, clarify the occurrence of osteoporotic fractures, and assess the changes in blood biochemical markers.

**3. How long will be last in this study？**

The study will last for one year. You may choose to withdraw from the study at any time. If you decide to withdraw from the study, we suggest that you discuss it with your doctor for the first time. If your research doctor believes that continuing to participate in the study is not in your best interest, he/she will decide to withdraw you from the study. Your withdrawal will not affect your medical treatment or rights.

**4. Collecting date and blood specimens during the study**

The types of samples collected in this study are as follows: blood and urine. The samples collected in the study will be tested and analyzed in our hospital. If there are any remaining samples, they will be stored at -80℃ in the Peking Union Medical College Hospital Biobank and may be used for future medical research after obtaining ethical approval. If you withdraw from the study in advance, we will no longer collect new samples, but we will retain the samples or data that have already been collected or analyzed.

## IV、Risks and Benefits

**1. What the risks of participating this study？**

**① Medication-related risks：**

**Denosumab:** As the intervention drug in this study, denosumab is a medication that inhibits bone resorption. It may cause the following adverse reactions: hypocalcemia, musculoskeletal pain, rash, and increased risk of infections (such as urinary tract

infections and upper respiratory infections). In very rare cases, osteonecrosis of the jaw or atypical femoral fractures may occur, but these conditions are relatively uncommon.

**Eldecalcitol：** As the drug in the control group, Eldecalcitol is an active vitamin D analog that may cause hypercalcemia, hypercalciuria, and gastrointestinal discomfort (such as nausea and vomiting).

**② Data Privacy Risks：**

This study will collect your personal information, clinical data, and biological samples (such as blood and urine). However, we will take strict measures to anonymize and encrypt your data to protect your privacy. There is no risk of data leakage.

**③ Biological Sample Collection Risks：**

During the collection of blood samples, there may be minor discomforts, such as brief pain, bruising, or local infection. These risks are generally low, and the collection process will be conducted by professional medical staff to ensure safety.

**④ Follow-up and Examination Risks：**

During the study period, you may need to undergo regular bone density tests and imaging examinations such as X-ray radiography. These examinations are generally non-invasive, but X-ray examinations involve exposure to a small amount of radiation, which is within the safe range.

**2. What the benefits of participating this study？**

**① Personalized Health Management：**

You will receive personalized health management recommendations based on the study data, which will help you better control type 2 diabetes and its complications and reduce the risk of fractures.

**② Contribution to Scientific Research：**

Your participation will provide valuable data support for the prevention and control research of osteoporotic fractures in patients with type 2 diabetes, helping more patients benefit in the future.

## V、Alternative Treatment Options

If you decide not to participate in this study, you can still receive conventional treatment for type 2 diabetes and osteoporosis. The conventional treatment options include:

① **Medication Therapy**: Such as other hypoglycemic drugs and anti-osteoporosis medications.

② **Lifestyle Interventions:** Such as dietary control, exercise therapy, smoking cessation, and alcohol restriction.

③ **Regular Follow-up：** You can have regular follow-ups within the conventional medical system to monitor blood glucose, bone density, and other indicators.

## VI、Use of Study Results and Confidentiality of Personal Information

With the understanding and assistance of you and other participants, the results of this study may be published in medical journals. However, we will keep your study records confidential as required by law. The personal information of study participants will be strictly protected, and your personal information will not be disclosed unless required by relevant laws. When necessary, government regulatory authorities, hospital ethics committees, and other relevant researchers may review your information in accordance with regulations.

## VII、Research cost and Related compensation

### 1. Cost of the medications/Devices and Related Tests in Study

The treatment medications used in this study, including Eldecalcitol and Denosumab, will be provided free of charge by the research team. All tests and treatments are conventional medical procedures, and you will need to bear the costs of the tests and examinations yourself.

### 2. Compensation of joining the study

Participation compensation: a total of CNY 500 will be provided in two instalments:

- CNY 200 after completion of the 6-month visit;
- CNY 300 after completion of the 12-month visit;

The full amount will be transferred to your bank account (or other designated method) once all follow-up visits are finished.

**3. Compensation/Remuneration for Injuries**

The tests and procedures involved in this study are all conventional medical practices with very low risks. If you experience any harm caused by the study or discomfort or injury related to the study medication, please inform your research doctor. The research doctor will provide you with appropriate treatment and guidance. Peking Union Medical College Hospital has purchased relevant insurance for this study, which will compensate you for any injuries caused by your participation in this study in accordance with the current laws and regulations of China.

## VIII、Rights and related precautions of participants

**1. Rights**

Your participation in the study is entirely voluntary. If you decide not to participate in this study, it will not affect any other treatments you are entitled to receive. If you decide to participate, you will be asked to sign this written informed consent form. You have the right to withdraw from the trial at any stage without discrimination or unfair treatment, and your medical treatment and rights will not be affected

**2. Precautions**

As a participant, you are required to provide truthful information about your medical history and current health status; inform the research doctor of any discomfort you experience during the study period; refrain from taking any restricted medications or foods that have been informed to you by the doctor; and inform the research doctor whether you have recently participated in other studies or are currently participating in

other studies.

**IX、Contact information for further information**

If there is any important new information during the study that may affect your willingness to continue participating, your doctor will notify you in a timely manner. If you have any questions about your research data, or if you wish to know the findings of the study after it ends, you may ask any questions about this study at any time and receive corresponding answers. Please contact [Name] at [Phone Number].

If you have any ethical concerns during the study, you may contact the Ethics Review Committee of Peking Union Medical College Hospital, Chinese Academy of Medical Sciences. The contact phone number is 010-69156874

**X、Signature Page**

**Participant：**

I confirm the following information:

I have been informed about the purpose, background, procedures, risks, and benefits of this study. I have had sufficient time and opportunity to ask questions, and I am satisfied with the answers provided.

I have also been informed about whom to contact if I have any questions, want to express difficulties or concerns, have suggestions for the study, want to obtain further information, or wish to provide assistance to the study.

I have read this informed consent form and agree to participate in this study.

I understand that I have the choice not to participate in this study, or to withdraw from the study at any time during the study period without any reason.

I am aware that if my condition worsens, or if I experience a serious adverse event, or if my study doctor believes that continuing to participate in the study is not in my best interest, he/she will decide to withdraw me from the study. Without my consent, the

sponsor or regulatory authority may also terminate the study during the study period. If this occurs, the doctor will notify me promptly, and the study doctor will discuss my other options with me.

I will receive a copy of this informed consent form, which includes the signatures of both myself and the study investigator.

Signature of Subject：_____ Date：_____

**(Note**: If the participant lacks legal capacity or has limited legal capacity, the signature and date of the legal representative are required.)

Signature of legal Representative：_____ Date：_____

Signature of Researcher：_____ Date：_____