Informed Consent Form

Project Name: BD111 Safety and Efficacy CRISPR/Cas9 mRNA Instantaneous Gene Editing Therapy to Treat Refractory Viral Keratitis

Dear Sir/Ms.,

We will invite you to participate in a clinical study. Before you participate in this study, please read this informed consent carefully and make a decision whether to participate in this study or not. You can consult your study physician or investigator about anything you don't understand and have him/her explain it to you until you fully understand. You can have a thorough discussion with your family and friends before you make the decision to participate in this study. If you are participating in another study, please inform your study physician or investigator. The main content of this study is as follows:

I, Study Background:

Viral keratitis is caused by the herpes virus. Once infected, the virus will remain dormant in the trigeminal ganglia and the cornea for life, causing keratitis symptoms when the body's immune system is weakened or subject to non-specific stimuli, and in severe cases, blindness. Existing drugs can only inhibit the replication of the virus, but not completely remove the virus's genome. Even after the replacement of the cornea patients are prone to relapse. As a new technology, the long-term safety of CRISPR gene editing for in vivo treatment is unknown, but the direct degradation of viral genome based on CRISPR gene editing technology has great advantages in efficacy. For this reason, we need you participate in this study and receive this surgical treatment, so as to explore its therapeutic effect and evaluate its safety and efficacy.

The study will comply with international principles such as the Declaration of Helsinki and relevant Chinese laws and regulations to protect the rights and interests of the subjects, and conform to medical ethics.

II, Research design and research process:

1. Six subjects will receive treatment in this study.

2. If you are willing to participate in this study, we will collect detailed medical history information, eye examination, auxiliary examination, give you standard drug treatment, and observe the therapeutic effect.

3, After we collect the samples, we will establish a case database, the database contents include "sample number", "name of participant pinyin initials", ensure the information accuracy in data analysis, sample personal identification information will be used in the collection process to identify, in order to protect the privacy of the participants; After patients and controls were enrolled, the unified project number was used. Personal data and case information were input and saved by the specially-assigned person in the sample management, and only the individual number was seen by the user, and the participant's name and other data were no longer contacted. Each follow-up, treatment, and adverse event will be recorded in the case data.

4. Confidentiality measures for personal privacy: Your medical records will be kept in the hospital for investigators' access only. If necessary, members of the government administration or ethics committee may have access to your personal data as required. The results of the study will be

statistically analyzed The data is published in a format that does not contain any identifiable subject information.

III, Possible risks and benefits:

1. Possible risks: This study is an intervention study, which may lead to adverse events and complications, such as injection site infection and bleeding. Before the trial, the investigator will conduct observation and analysis to assess the cause, and the study will be terminated, timely intervention treatment will be conducted, and the prognosis will be followed up. The whole process of the study is supervised by the hospital ethics committee. If you have any questions during the study, you can consult the investigator.

2. Possible benefits: You will not be paid to participate in this study, and study interventions may benefit your disease treatment. This study will be helpful for the effective treatment of refractory viral keratitis in the future and improve the cure rate. Here we would like to express our gratitude for your participation in scientific research and contribution to the development of medicine.

3, Treatment of severe adverse reactions and compensation: although this study is to ensure your safety, but still exist unable to forecast possible serious adverse reaction caused by complications, this study is to purchase insurance for the subjects after serious adverse reaction, the assessment, conducted by a third party to judge, and give corresponding compensation by insurance company.

IV. Voluntary Participation: Your participation in the study is entirely voluntary. You can drop out of the study at any time without a reason. In no way will it affect your relationship with the medical staff or your future treatment.

V Study fee: No surgical treatment fee will be charged for participating in this study, and no examination fee will be charged during the follow-up. At the same time, 100 RMB transportation subsidy will be provided for each patient. If all 3 postoperative visits are completed, 300 RMB transportation subsidy will be provided, and other expenses, including the cost of conventional drugs and registration fee, shall be borne by the patient.

VI Contact person and contact information: If you have any questions about this study, please contact your ophthalmologist directly

VII, The informed consent is in duplicate, properly kept by both parties and valid after being signed by both parties.

Informed consent Signing

I have read the above information and understood the purpose of the study and the potential benefits of participating in the study, and I have obtained satisfaction answers on all the questions I have asked about the procedure and content of the study. I voluntarily signed this informed consent form and volunteered to participate in this study.

Participant signature: date:

Contact number of participants:

We have read and interpreted this informed consent to the subject and answered all his/her questions. He/she has personally understood and agreed to participate in the scientific research.

Investigator signature: date:

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