Informed Consent Form

We sincerely invite you to participate in a clinical trial on the safety and efficacy of autologous CD34+ hematopoietic stem cells (HSC) transduced with a lentiviral vector encoding $\beta^{A\text{-}T87Q}$-Globin. Before you decide whether to participate in this study, please read the following as carefully as possible. It can help you understand the research and why you want to conduct the research, the research procedures and duration, the benefits, risks and discomforts that may be brought to you after participating in the research. If you want, you can also discuss with your relatives and friends, or ask a doctor to explain so that you can make a better decision.

I Background and Purpose of the Study

i. Disease or condition of β-Thalassemia

β-Thalassemia is an autosomal recessive disease. People with β-thalassemia fail to produce enough β-globin, resulting imbalance of α-globin / β-globin and an accumulation of excess uncomplexed α-globin chains in erythroblasts. The clinical implications are that patients lack sufficient red blood cells (RBCs) and hemoglobin (Hb) to effectively transport oxygen throughout the body, resulting in severe anemia. patients require regular RBCs transfusion throughout life for survival. Chronic blood transfusions lead to iron overload, so patients need take medication to remove excess iron. Even with the correct application of blood transfusions and chelation treatments, patients with β-thalassemia (TDT) have many complications. So far, the only radical treatment option is stem cell transplantation from a healthy donor. However, a human leukocyte antigen (HLA)-matched related HSC donor is difficult, and allogeneic donors for stem cell transplantation can cause serious side effects.

BD211 drug product is a gene therapy medicinal product designed to provide functional β-globin to patients with β-thalassemia (TDT), thus circumventing their need for chronic RBCs transfusions.

ii. Study purpose

Determine the safety, tolerability, and success of engraftment with autologous CD34+ hematopoietic stem cells transduced with BD211 lentiviral vector encoding the human $\beta^{A\text{-}T87Q}$-globin gene after myeloablative conditioning in subjects with β-Thalassemia (TDT).

Measure the effects of transplantation with BD211 Drug Product on the expression of disease-specific biological parameters and clinical events, including:

Hemoglobin levels in transfusion independence (TI) patients.

Duration of TI blood transfusions requirements (mL) reduction compared with the 2-year pre-treatment period.

The facility is in the department of hematology of 920th Hospital of Joint Logistics Support Force of People's Liberation Army of China. A total of 10 subjects with β-Thalassemia (TDT) are expected to participate in this study.

II The study content and procedure

The start date of the study was April 2021 and we will screen 10 eligibility candidates. The study includes 3 periods: screening phase (1 month), treatment (1 month) and following visits (2 years).

If you agree to participate in this study, the principal investigator will identify if you are meeting the study eligibility criteria.

In total, your participating duration will be approximately 27 months, including the following phases:

i. Day-97 prior to the transplant including screening phase, harvesting of autologous CD34+ hematopoietic stem cells for subjects, then is the waiting time, you will wait for Shanghai BDgene Co., Ltd. to manufacture gene therapy drug of autologous CD34+ hematopoietic stem cells transduced with the BD211 lentiviral vector encoding the human$\beta^{A\text{-}T87Q}$-globin gene.

ii. Conditioning

Chemical drug Busulfan IV is intended for IV administration.

iii. BD211 drug product treatment via IV infusion.

iv. Visiting and assessment phase through 24 months after treatment.

Scheduled visits will be performed in 2,3,4,5,6,9,12,15,18,21,24 months and subjects return to hospital after treatment.

v. The 13-year long-term follow-up study period.

III Regarding visiting

You will participate in the study for approximately 27 months. You must be back to the hospital as scheduled. During the visiting phase, the doctor may also learn about your status by telephone and other means. Your follow-up is very important, because the doctor will judge whether the cells infused are really working in the body and guide you in time.

IV Possible benefits of participating in the study

This study may contribute to the remission of your disease or may not be of any benefit to you. Although there is evidence that it may have a satisfactory effect, there is no guarantee that it

will work for you. If you believe that the treatment is not effective for your condition, you may choose to refuse to participate in this clinical trial.

The information obtained in this study may benefit future patients.

V Possible risks and corresponding measures of participating in the study

i. The manufacture of lentiviral-modified stem cells may be at risk of failure. If the transduction cells fail and cannot be used clinically, repeated mobilization and apheresis may be allowed, but it must be discriminated by the principal investigator. In this case, study will be repeated from Day-60, and if the product preparation process is delayed, the time window may be widened.

ii. Risk of pre-treatment conditioning

Conditioning is essentially a chemotherapy, and it has a great myeloablative effect. It provides a better implant for the transplanted cells. Conditioning is a necessary process for hematopoietic stem cell transplantation. All side effects of chemotherapy may appear during conditioning, including but not limited to blood cell reduction, bone marrow suppression, gastrointestinal reactions, mucositis, hair loss, fever, etc. Severe infections may also occur during bone marrow suppression. Conditioning will be performed in a laminar flow ward or a laminar flow hood. During the period of bone marrow suppression, blood components will be infused according to the condition to correct the low hemogram and use antibiotics to prevent infection to minimize the risk. You should fully understand that the risk of conditioning cannot be completely avoided, and you should fully evaluate your acceptance of the risk and decide whether to undertake the risk to participate in this study.

iii. Risk that BD211 drug product cannot be infused as planned due to freeze-thaw failure after conditioning is finished

BD211 drug product is a sort of cell product. Before infused into your body it will experience process of cell cryopreservation, logistics and transportation, clinical department receiving and storage, and cell recovery. If the conditioning is completed, problems in any of those procedures may cause you to face the risk of not being able to receive the cell infusion as planned, this study will strictly control each procedure to minimize the possibility of problems. But if this happens unfortunately, we will provide you infusion of autologous hematopoietic stem cells backed up in advance to restore your hematopoietic function.

iv. Risk of unsatisfactory treatment outcomes.

In theory, BD211 may reduce or even completely eliminate your blood transfusion dependence, but the actual efficacy is not yet known, and you still face the risk of unsatisfactory efficacy or

no effect at all. If the treatment is completely ineffective, compensation shall be made according to "VI Compensation ".

v. Risk of insertional oncogenesis

There are no reports of Lentiviral-mediated insertional mutagenesis resulting in oncogenesis. Nevertheless, there is a theoretical risk of leukemia or lymphoma after treatment with BD211, compensation shall be made according to "VI Compensation".

vi. Other unreported risks

vii. Effects on the ability to drive and use machinery

At present, there is no data on the effects of similar products on driving and using machines. However, as a precaution, subjects should avoid driving and using machines within six months of participating in this study.

viii. Influence on fertility

At present, there is no relevant research data on whether similar products affect fertility. However, to be on the safe side, the subjects of reproductive age participating in this study are required to strictly control contraception from the beginning to the end of the study.

If you experience any discomfort during the study, or any new changes, or any unexpected situation, whether related to the study or not, you should inform your doctor promptly, who will make a judgment and give appropriate medical attention.

VI. Compensation

The design of this study strictly follows the Declaration of Helsinki and protects the interests of the subjects to the greatest extent. In principle, there will be no additional expenses for you to participate in this study. The cell collection fee, freeze storage fee, sample logistics fee, lentiviral manufacture fee, insurance fee, pre-treatment conditioning drug fee, rescue fee directly related to BD211 and implantation test fee during your participation in the study will be afforded by the cooperative unit of this study.

The sponsor will insure every patient participating in this study. There is no compensation for subjects who significantly benefit from this study. The patients who has achieved blood transfusion independence within 2 years or the transfusion requirements (mL) has reduced by 50% ", will obtain a compensation of RMB 50,000 per person. If occur irreversible damage, death or insertional oncogenesis which is directly related to BD211 within 3 years after treatment due to participating in this study, the insurance company will pay the compensation. The maximum amount of compensation shall be RMB 300,000 / person.

VII Is personal information confidential?

Your medical records will be kept intact at the hospital. The doctor will record the results of the laboratory tests on your medical record. The investigators, the ethics committee, and the hospital superintendent committee will be granted access to your medical records. Any public report on the results of this study will not disclose your personal identity. We will protect the privacy of your personal medical data to the extent permitted by law.

VIII How can you get more information?

You may ask any question about this study at any time and receive an answer. If there is any significant new information during the study that may affect your willingness to continue to participate in the study, your physician will inform you promptly. If you have any questions about the procedure of this study, please contact Dr. Wang by phone (86-13187424131).If you have any questions about your rights to participate in this study, you can contact the Ethics Committee by phone(86-871- 64774287).

IX Withdrawal

You may refuse to participate or withdraw at any time during the study, without any loss of your medical or other benefits. At any time during the study, the physician or principal investigator may discontinue your participation in consideration of your best benefit.

If you withdraw from the study for any reason, you may be inquired about your status in the study. If your investigator deems it necessary, you may also be required to undergo laboratory tests and medical examinations to ensure your safety.

We will ask you to withdraw from the study if:

i. Some examination results indicate that you are unsuitable to continue the study;

ii. You cannot cooperate with treatment or timely visit hospital;

iii. During the study, you occurred new health problems;

iv. Become pregnant or decide to become pregnant;

v. For the sake of your health and interests, the principal investigator believe it should be stopped.

X Alternative therapy

In addition to participating in this clinical study, you may choose the following alternative treatment for your condition according to current medical guidelines:

i. Regular blood transfusion combined with iron chelation

ii. Hematopoietic stem cell transplantation therapy

iii. Traditional Chinese medicine treatment

XI What to do now?

It's up to you (and your family) to decide whether or not to participate in the study.

Ask your doctor as many questions as possible before you make the decision to participate in the study.

Thank you for reading the above. If you decide to participate in the study, please let your physician know, he/she will make all the arrangements for you. Please keep this information

Declaration

I have read the above introduction regarding the study and have had the opportunity to discuss and ask questions about the study with physicians.All my questions were answered satisfactorily.

I am aware of the possible risks and benefits of participating in this study.I am aware that my participation in the study is voluntary and I confirm that I have had sufficient time to consider.

- ✧ I can at any time ask the physicians for more information.
- ✧ I can withdraw from the study at any time without discrimination or retaliation, and my medical treatment rights and interests will not be affected.

I also know that if I withdraw from the study, it would be beneficial for me to inform my physician of the change in my status and complete the corresponding physical and chemical examination.

If I need to take any other treatment due to a change in my condition, I will consult my physician in advance, or I will tell my physician afterwards.

I consent to the hospital supervisory and administrative department, the ethics committee or the researcher to have access to my research materials.

I will obtain a signed and dated copy of the Informed Consent (including the Informed Notice page and the Consent Signed page).

In the end, I decided to agree to participate in the study and promised to try to follow the investigator's advice.

Sign by subject (or legal representative):

Date: (hr) (min) Contact phone:

I confirm that the patient has been explained the details of this trial, including their rights and the possible benefits and risks

Sign by the principal investigator:

Date: (hr) (min) Contact phone: