Assent to Participate in Research
(12 to 17 years of age)

[Insert site logo and/or address]

Study Title: **A Multi-Center, Phase 2 Gene Transfer Study Inducing Fetal Hemoglobin in Sickle Cell Disease**

Protocol: **BMT CTN 2001**

Principal Investigator: [Insert site PI]

Source of Support: This study is co-sponsored by the National Heart, Lung and Blood Institute, a part of the National Institutes of Health, and the California Institute of Regenerative Medicine.

A. Why am I here?

You're being asked to join our study because you have sickle cell disease (SCD). We are asking you to take part in a research study because we are trying to learn more about this disease.

B. Why are you doing this study?

In sickle cell disease, red blood cells don't work properly. Your red blood cells sometimes have a different shape, break more easily, and have trouble carrying the oxygen to other parts of your body, causing you to have problems like frequent sickle cell pain, difficulty breathing with or without pain (acute chest syndrome) and several other medical problems. To be included in this study you must have frequent sickle cell pain or acute chest syndrome. Red blood cells are made by "mother cells" that give rise to all your blood cells from your blood called "**stem cells**".

We want to see if a new treatment called **gene therapy** helps people like you with sickle cell disease.

C. What will happen to me?

If you agree to be in this study, we will do tests to make sure that you are eligible for the study. This can take 1 to 2 months of coming to different tests and appointments on different days. Below is a list of what you would do if you participate in this study:

- We will draw some blood from you for tests. The amount of blood that we take will not be harmful to your body.

- A specially trained doctor will place a small tube put through the skin into a vein while you are asleep. This tube is called a central IV line. This tube will be placed if you do not already have a central IV line or port. It will allow us to give you medicine, give you blood transfusions, and collect your stem cells more easily. The central IV line may be removed before you leave the hospital, unless we need to continue to give medicine or transfusions through the line.

- Collection of your stem cells: Your stem cells will be collected by a process called peripheral blood mobilization. This means that you will receive a subcutaneous injection (a shot) of a medicine called plerixafor which causes the stem cells to move from your bone marrow into the blood. Then, starting at least 2 hours after the plerixafor injection you will go through a procedure called apheresis to collect your stem cells. During the apheresis procedure, your doctors will connect your IV lines to a machine called a cell separator. First your blood and blood cells go into the machine through your IV line. Then the stem cells get collected into a sterile plastic bag. Lastly, most of the blood and other blood cells in the cell separator are returned to your body. During the apheresis procedure a nurse will be monitoring you closely, checking your vital signs (for example, heart rate and oxygen level) at least every 15 minutes. Usually a second dose of plerixafor will be given to you the next day, followed by a second apheresis procedure. If necessary, another apheresis procedure will be done at a later date too.

- Once we have the stem cells, we will mix them with the gene therapy medicine for a few days in a special laboratory. When the cells are ready, we will give the changed stem cells back to you through a drip like a blood transfusion. The new stem cells will then hopefully start to make good red blood cells that work better. This may take a few months. To help the new stem cells grow we first have to give you another medicine to get rid of the old bone marrow that wasn't working properly.

- You may have to stay in the hospital for up to 2 months but could stay longer if you are not feeling well. You will stay in the hospital to make sure that you don't get sick from the medicines or from the gene transfer.

- Lastly, you'll have more tests to see how your body is doing. You'll have these tests every few weeks or months for 2 years. We'll also ask you how you're feeling and how well you're able to do the things you normally do each day.

D. Will it hurt?

Sometimes things happen to kids in research studies that may make them feel bad. These are called "risks". You may have side effects during the study. Side effects can range from mild to severe to even life-threatening. Your health care team may give you medicine to help with certain side effects, like an upset stomach. In some cases, side effects can last a long time or may never go away.

The main consent form goes over these risks in more detail. They can be placed in several different categories, including some that are specific to the gene therapy experimental treatment, and some that are part of any stem cell transplant. Overall, this can include the risk of death or serious disability.

- Risks associated with gene therapy:
  - Blood cancer or other cancer.
  - Failure of the new cells to stay in you (failure to engraft).
  - Other cells (not blood cell producing cells) being affected.

- Risks associated with any stem cell transfer therapy:
  - Extreme anemia requiring blood transfusions
  - Lowering your white blood cell count and making it harder for you to fight off germs and infections. Some infections can make you very sick or even cause death.
  - Mouth ulcers
  - Bleeding
  - We will take some cells from your bone marrow which is the factory in your body that makes your blood cells. You may feel some discomfort from the needle that will be used to take the blood cells.
  - Side effects from the procedures and medications that are required to perform a stem cell transfer.
  - Staying in the hospital for a long time, having a lot of medical procedures, or dealing with side effects caused by treatments can be very hard, and this can cause some kids to have feelings of sadness, anger, stress, or depression.
  - Medication may make it difficult for both men or women to have children in the future.

- Risks associated with plerixafor administration
  - Mild/temporary headache, redness and stinging at injection site
  - Numbness/tingling around the mouth, nausea and feeling fullness and tightness in stomach
  - Increase in your spleen size
  - Increase in your white blood cells that could cause problems like pain crises, acute chest syndrome, higher risk of brain injury caused by either bleeding or lack of oxygen (stroke), and other potential medical problems.

- Risks of central IV line:
  - Bruising or bleeding on your skin where the central IV line is placed. Your medical team will take care to prevent too much bleeding by putting pressure on the bleeding site.

- Infection which would require treatment with medicine called antibiotics.

- Blood clots in the vein or in the heart near your central IV line. If you do get a blood clot you would need to take a medicine called a blood thinner. If you get a clot, we many need to remove the central IV line and replace it with a new one to continue the treatment. Risks of blood transfusions:
  - We will give you several blood transfusions (at least every month) for at least three months before your cells are collected. Sometimes kids who receive blood transfusions can have certain problems. These include:
    - Infection, requiring antibiotics
    - Transfusion reactions such as allergic reactions
    - Fever
    - Hemolytic reactions (breakdown of red blood cells)
    - Local discomfort, loss of red blood cells, or air infusion into your central IV.

- Risks of Apheresis
  - Rare reactions, such as weakness, nausea or feeling like you might black out or faint during your needle insertions or if you have any blood loss.
  - Local discomfort at needle site or tenderness.

Your medical team will take many steps to try to avoid as many of these problems as possible.

If you are a male and you report a pregnancy of your partner, your study doctor will first need to obtain permission (consent) from your partner about sharing data before asking any questions about the pregnancy. If your partner consents to provide this information, your study doctor will follow up directly with your partner.

E. Will the study help me?

Possibly, but it is not guaranteed. You may have fewer symptoms of SCD after the gene therapy. What we learn from this study may help doctors learn more about a new treatment option for sickle cell patients in the future.

F. What if I have questions?

Your doctors and nurses will answer your questions. It's important that you get all of your questions answered.

If you forget to ask a question but think of it later, you can call your doctor at [phone number]. You can also ask your question the next time you see your doctor.

You can also call the study office at [insert office number].

If you want to talk with someone not directly involved in the study, or have any complaints or questions about your rights as a research participant or about potential risks and injuries, you may contact the NMDP IRB Administrator at:

1-800-526-7809

Be sure to get all of your questions answered.

G. Do I have to join this study?

You do **not** have to join this study. Tell your doctor and your parents or guardians if you don't want to be in the study. Your doctor won't be angry with you.

It's okay if you say yes now and then change your mind and say no later, even if you have already started some parts of the study.

You'll still need treatment for your sickness if you don't join this study, and your doctor can discuss other options with you.

Talk to your parents or guardians before you decide if you want to join this study. We'll also discuss the study with parents and ask your them if it's okay for you to join.

Long-term Follow-up Study:

We want to see how well the gene therapy treatment is working beyond 2 years. We will contact you to offer a long-term study for another 13 years, for a total of 15 years of follow-up. You can join the main study and say no to this extra study. Your doctor won't be angry with you if you don't want to join the extra study.

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Protocol: **BMT CTN #2001**

Writing your name on this page means that you agree to be in the study. If you decide to quit the study, all you have to do is tell the person in charge.

You and your parent or guardian will get a copy of this form after you sign it.

_____

Participant Name (To be written by child/adolescent)

_____

Printed Name of Parent/Legal Guardian

_____ _____

Parent/Legal Guardian Signature Date (MM/DD/YYYY)

_____

Printed Name of Parent/Legal Guardian #2 (*Optional*)

_____ _____

Parent/Legal Guardian #2 Signature (*Optional*) Date (MM/DD/YYYY)

Physician certification

I certify that I have provided a verbal explanation of the details of the research study, including the procedures and risks. I believe the participant has understood the information provided.

_____

Printed Name of Counseling Physician

_____ _____

Counseling Physician Signature Date (MM/DD/YYYY)

Interpreter certification (if needed)

I certify that I have provided an accurate interpretation of this consent form. I believe the participant has understood the information provided.

_____

Printed Name of Interpreter

_____ _____

Interpreter Signature Date (MM/DD/YYYY)