ILLUMINATING A POTENTIAL NEW THERAPY FOR SICKLE CELL DISEASE

Your guide to the **BEACON** Clinical Study and the informed consent process

Search **NCT05456880** on www.clinicaltrials.gov.

BEACON

THANK YOU FOR YOUR INTEREST IN THE BEACON CLINICAL STUDY

With help from potential study participants like you, new and improved treatments—and even a possible cure for sickle cell disease—may be available.

WHO WE ARE

We are Beam Therapeutics Inc., founded in 2017 to develop advanced genetic medicines. We are a mid-sized company with people working in Cambridge, Massachusetts, and Durham, North Carolina. Our vision is to provide lifelong cures for people suffering from serious diseases. To achieve our vision, we have built a strong, values-driven organization focused on people, advancing cutting-edge science, and developing a new class of precision genetic medicines.

New treatments are sorely needed for people who have sickle cell disease (SCD)—particularly for those who experience severe vaso-occlusive events despite therapy with disease-modifying agents. In addition, people who have complications from SCD, such as severe anemia and hemolysis or significant organ dysfunction, have an urgent medical need, even without vaso-occlusive events. They are at a higher risk of death than are people who have milder anemia and hemolysis.

We are committed to addressing these needs.

Beam THERAPEUTICS

The Beam Team is

- a community of fearless innovators
- rigorous and honest in research
- listening with open minds
- committed to each other

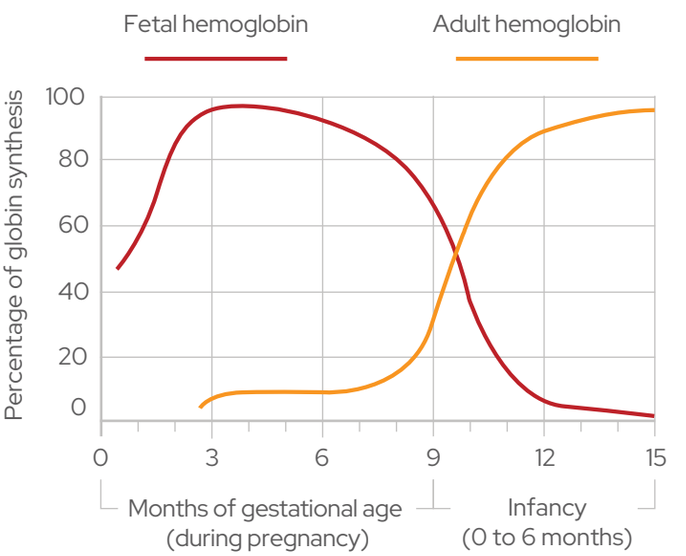
FACTS ABOUT SICKLE CELL DISEASE

What is SCD?

- Sickle cell disease is a group of inherited red blood cell (RBC) disorders
- People who have SCD have an abnormal type of blood protein called *hemoglobin S,* which alters the flexible shape of the RBC from a round disc to a rigid crescent moon shape. These sickled cells can stick to blood vessel walls, slowing or stopping blood flow and preventing oxygen from reaching tissues and organs
- People who have SCD can experience *vaso-occlusive events* that can cause sudden, often unpredictable pain that may require hospitalization. The effects of SCD vary from person to person and can change over time. The signs and symptoms often include severe pain, anemia, organ damage, and infection

Role of fetal hemoglobin

- All babies are born with fetal hemoglobin (hemoglobin F), which does not have the hemoglobin S abnormality
- As infants reach about 1 year of age, hemoglobin F production gradually **turns off** (declines) and adult hemoglobin production gradually **turns on.** Rarely, hemoglobin F production does not turn off. This condition is called hereditary persistence of fetal hemoglobin (HPFH)
- People who have SCD *and* HPFH usually have few or no complications of SCD. This is because fetal hemoglobin helps prevent the symptoms that occur when the bloodstream contains a high level of sickled hemoglobin



ABOUT THE BEACON CLINICAL STUDY

Study purpose

- The Beacon Clinical Study will investigate a potential new therapy for SCD called **BEAM-101**
- People who have severe SCD may participate in the study and receive BEAM-101, which is both a *gene editing technology* and a *cell therapy.* Gene editing therapy alters genes to try to treat, stop, or prevent disease progression. Cell therapy is the transfer of living cells into a body to lessen or cure a disease. In the production of BEAM-101, **your own cells** are altered with the aim of reactivating your genes that produce hemoglobin F. The process of collecting your cells and giving them back to you is called an *autologous stem cell transplant*
    - Currently, hematopoietic stem cell transplantation (HSCT) is the only therapy option for SCD that is potentially curative. In HSCT, the transplanted stem cells come from a donor, usually a family member, who does not have SCD. Unfortunately, only about 1 in every 5 people who have SCD has a compatible donor and is eligible for HSCT

The purpose of this study is to learn whether BEAM-101 is a safe and effective therapy for people living with SCD.

What are the goals of the Beacon Clinical Study?

As a critical part of evaluating the safety and efficacy of BEAM-101, Beam Therapeutics and the study staff want to know

- how safe BEAM-101 is and whether, after therapy with BEAM-101, you experience fewer vaso-occlusive events and require less treatment
- how much hemoglobin F you are producing after receiving BEAM-101
- how your quality of life and ability to function may change after therapy with BEAM-101

BEAM-101: A BASE-EDITING TECHNOLOGY

Base editing is an emerging new class of **precision genetic medicines** designed to overcome the limitations of existing therapies.

DNA bases

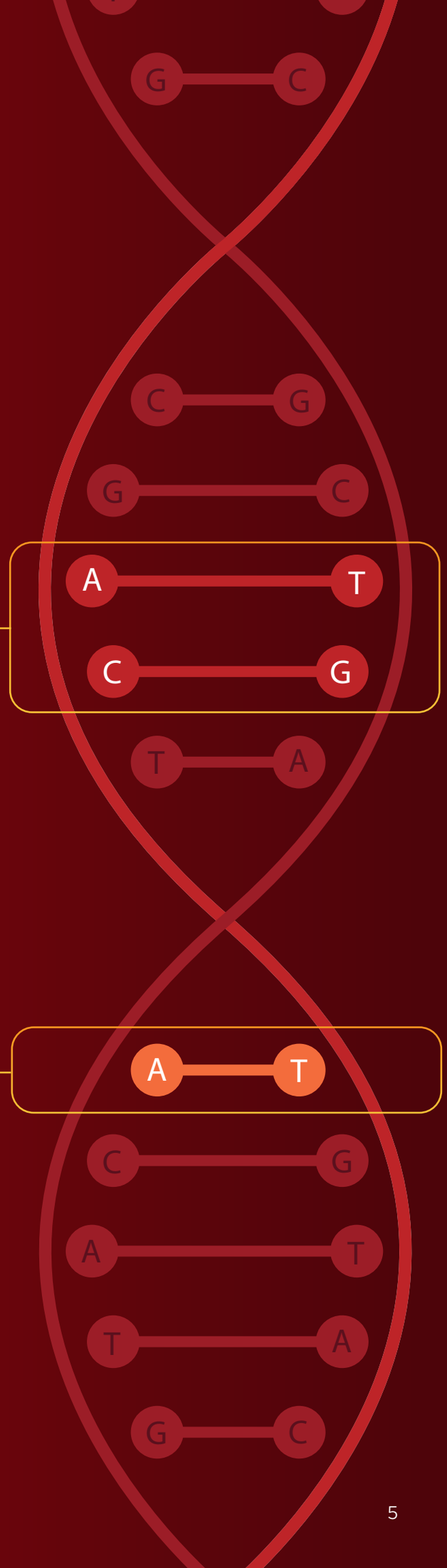
The foundational unit of your genetic information is a single DNA **base,** of which there are four, each defined by a letter: adenine (A), cytosine (C), guanine (G), and thymine (T). Together, these bases, or letters, form sequences that spell out the genetic information carried in your DNA.

Point mutations

- A change to a single base (A, C, G, or T) can mean the difference between health and disease. This is called a **point mutation**
- Base editors, which are like molecular machines, can rewrite just a single letter. That very basic change can potentially treat a wide range of diseases

Learn more about BEAM-101 base editing on page 7.

BEAM-101 is not approved by any regulatory body, including the US Food and Drug Administration, for the therapy of any disease or condition, and it can be used only in a study like this one.



TAKING PART IN A CLINICAL STUDY

What is a clinical study?

A clinical study, also called a clinical trial, helps doctors and researchers

find new ways to prevent, diagnose, and treat illness

learn about the safety and effectiveness of an investigational drug

understand how an investigational drug may help treat certain conditions

explore ways to improve the quality of life of patients

TAKING PART IN THE BEACON CLINICAL STUDY

Do I qualify to participate?

Everyone's experience with SCD is different. Although you may qualify to participate in this study, someone else living with SCD may not. If you do not qualify for the study, it is possible that you will be able to participate in the future. The purpose of the inclusion and exclusion criteria listed below is to create a consistently similar group of study participants. This will help ensure the data gathered during the study will reflect more accurately the effect of the study treatment or drug.

You may be **eligible to participate** in this study if you

- are between 18 and 35 years of age
- have a confirmed diagnosis of SCD, including at least 4 severe vaso-occlusive events occurring over the past 2 years
- do not have suitable sibling-matched donor stem cells for HSCT

You may **not be eligible to participate** in this study if you

- have a hemoglobin F level greater than 20%
- previously received an HSCT or solid-organ transplantation
- have an available and willing matched sibling donor
- received a definitive diagnosis of moyamoya syndrome
- have an active bacterial, viral, or fungal infection necessitating IV antimicrobial or antiviral therapy

If you decide to participate in the Beacon study, then your study doctor will perform a detailed evaluation to confirm all trial eligibility requirements are met, including your ability to undergo the study therapy safely.

You can stop taking part in the study at any time.

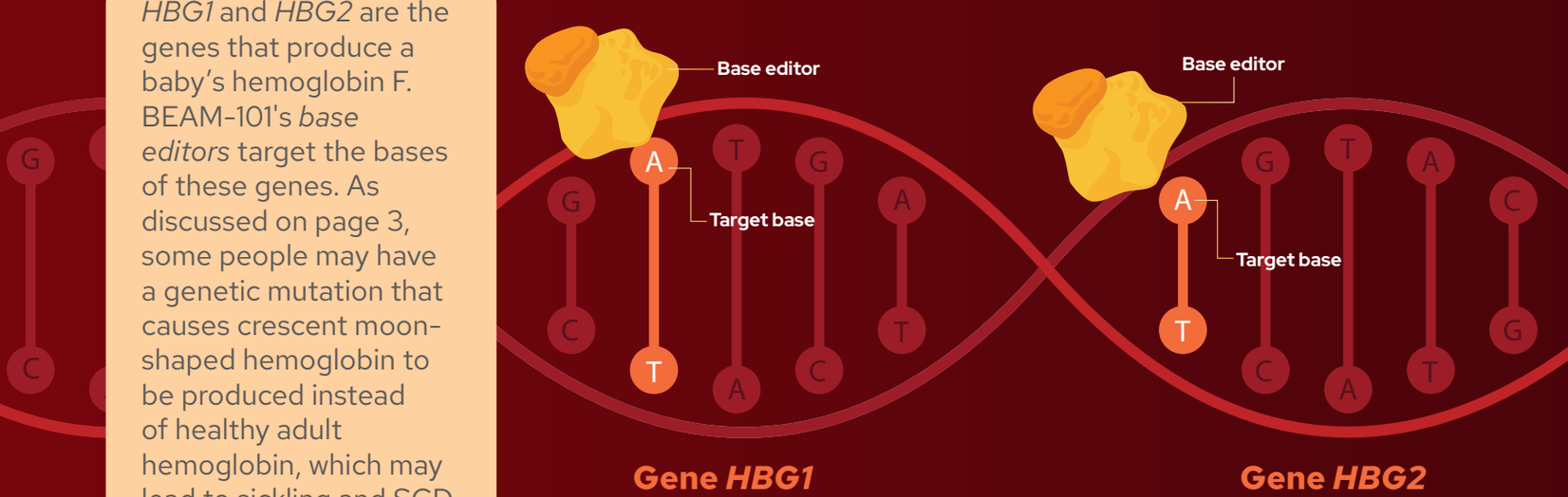
ABOUT THE BEACON CLINICAL STUDY THERAPY, BEAM-101

How does the study therapy, BEAM-101, work?

DNA is the genetic code that contains the instructions for life. These instructions are composed of chemical-compound bases, labeled A, C, G, or T. Genetic diseases like SCD are caused by gene changes, also called mutations, that may disrupt the structure of a protein or its function. Errors among the four bases that spell out the instructions carried in DNA are one type of mutation.

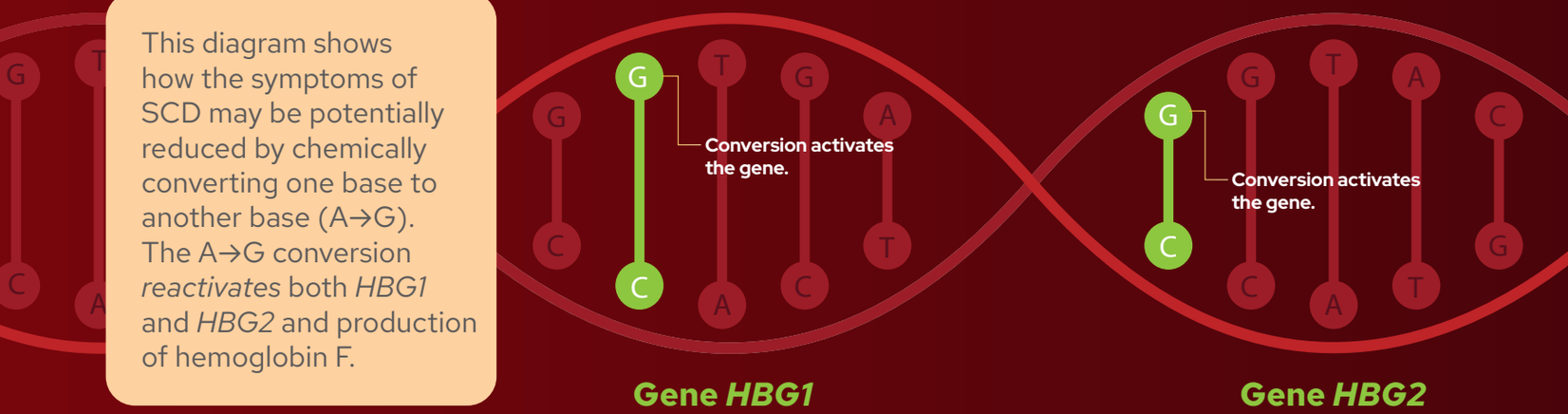
BEAM-101 uses a process called **base editing** to modify your DNA code and thereby activate the genes that make hemoglobin F. Adults typically have very small amounts of hemoglobin F, but BEAM-101 therapy aims to increase your hemoglobin F to block your red blood cells from sickling. In this way, the effects of SCD may be lessened or removed.

HBG1 and *HBG2* are the genes that produce a baby's hemoglobin F. BEAM-101's *base editors* target the bases of these genes. As discussed on page 3, some people may have a genetic mutation that causes crescent moon-shaped hemoglobin to be produced instead of healthy adult hemoglobin, which may lead to sickling and SCD symptoms.



A→G CONVERSION

This diagram shows how the symptoms of SCD may be potentially reduced by chemically converting one base to another base (A→G). The A→G conversion *reactivates* both *HBG1* and *HBG2* and production of hemoglobin F.



This study is sponsored by Beam Therapeutics.