Fulcrum Therapeutics

Partnering with the community to build better treatment options in Sickle Cell Disease

An introduction to Fulcrum and overview of how new treatments are developed

Contents

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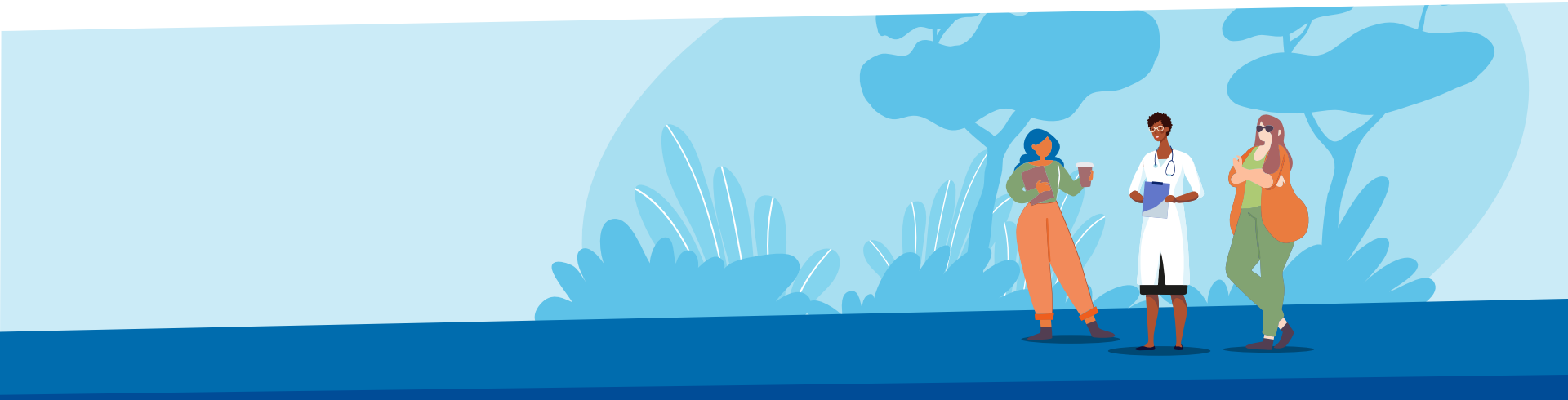
1. Introducing Fulcrum Therapeutics



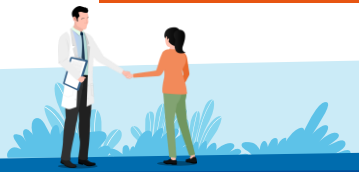
Who We Are

Fulcrum Therapeutics

Fulcrum Therapeutics was founded in 2015 in Cambridge, Massachusetts, US, with the aim of developing disease modifying treatments that result in meaningful outcomes for patients, caregivers, families, and medical teams

We are a group of committed and passionate professionals working in a culture of trust and transparency to enable our employees to do their best work

We take great pride in being purposeful patient partners who do this work not just for patients but with patients



Our Community Engagement Mission

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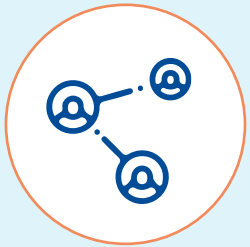
Cultivate relationships with the patient, caregiver, and advocacy community founded on trust and respect

Develop an active presence in patient communities and professional societies

Partner with the patient community to support disease state education, access, and advocacy activities



Incorporate the patient voice in Fulcrum's work and represent Fulcrum in the patient community

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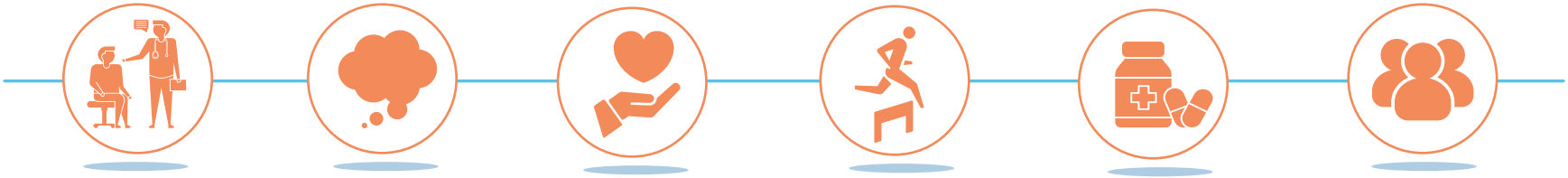
2. Our Goals

Collaborating with the Community

- We embrace a concept called co-creation
  - We listen to and learn from patients, parents, caregivers, and patient communities to develop programs, initiatives, and treatments
  - This collaboration ensures that treatments we develop best align with patient preferences and needs (e.g., oral treatments)
- We listen to and apply patient, caregiver, family and community insights at every step of their journey



Our Objectives

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Develop meaningful treatments

Our vision is to find novel ways to treat genetically defined diseases and our approach has helped us achieve this. We seek to develop medicines that can bring meaningful outcomes for as many people as possible

Our goals for a new SCD treatment

- Improves signs and symptoms of SCD
- Improves quality of life for people living with SCD

In addition to the science, we

- Build lasting partnerships
- Strive to understand the patient experience
- Develop impactful programs

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3. What is Sickle Cell Disease (SCD)?

What is SCD?

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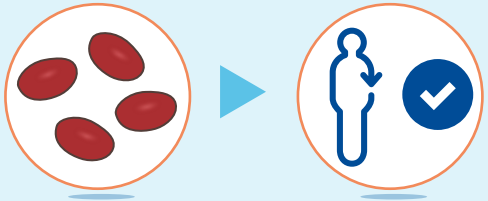
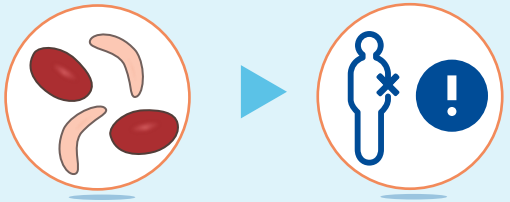
SCD is a genetic disorder that affects how red blood cells (RBC) work

- Red blood cells are usually round and flexible
- This means they can move easily through blood vessels and carry oxygen to all parts of the body



- In SCD, red blood cells become hard, sticky and crescent shaped (sickled). This can slow or block blood flow, reducing the amount of oxygen carried around the body
- People with SCD can experience pain events and related complications, such as stroke, eye problems and infections



Hemoglobin and Fetal Hemoglobin

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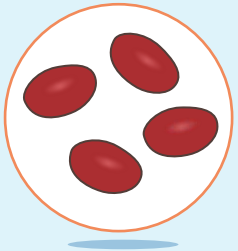
Hemoglobin is a protein found in red blood cells

There are many types of hemoglobin, such as hemoglobin A (HbA) and S (HbS)



One type is called fetal hemoglobin (HbF)

It carries more oxygen than HbA and HbS

People are born with high HbF levels that get lower over time

This can be different in people with SCD

The Role of Fetal Hemoglobin in SCD

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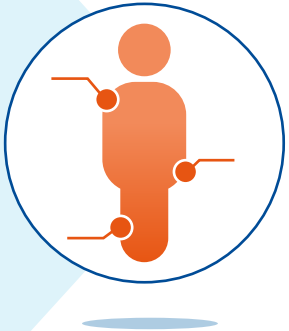
Some people with SCD may still have high levels of HbF as adults

HbF Level

People with SCD with high levels of HbF can have fewer clinical signs and complications compared to people with SCD
with lower levels of HbF



HbF Level

Typical Complications of SCD

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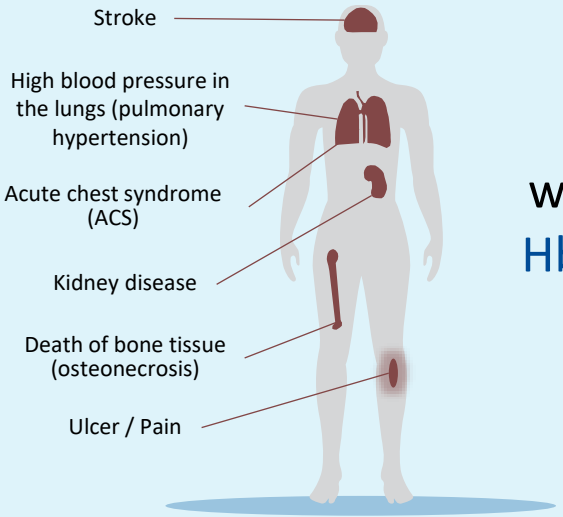
People with SCD have a higher risk of complications



People with SCD who have high levels of HbF have a lower risk of complications

4. How are New Treatments Developed?

How New Treatments are Developed

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Data must be gathered to prove it is safe and effective for its intended use before a drug can be approved for sale

After pre-clinical (laboratory) studies, there are three phases of clinical studies:

Laboratory studies

Study treatments are typically tested on animals before being given to people

This helps find a safe starting dose for Phase 1

Researchers assess potential safety concerns

Phase 1

Small numbers of people take part

Early information is gathered about the study treatment with focus on safety and unwanted effects

Participants can be healthy volunteers or have the condition being studied

Phase 2

More information is gathered about the study treatment in a larger study

How well it works

Unwanted effects it causes

The best amount (dose) to give

Phase 3

Focused on how well the treatment works and unwanted effects

Larger numbers of people take part

Phase 1 Studies: First Studies in People

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Phase 1

The aim of phase 1 is to find out

- How the treatment works in the body
- The side effects associated with different amounts of the treatment taken (doses)
- Early information about how effective the treatment may be

Phase 1a

Participants in the study receive a set dose of the treatment for a period of time

Phase 1b

The dose is carefully and slowly increased at certain points during the study

Phase 1 Studies: First Studies in People

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Phase 1

The aim of phase 1 is to find out:

- How the treatment works in the body
- The side effects associated with different am
- Early information about how effective the tr

Fulcrum is running a SCD phase 1b study called PIONEER

Phase 1a

Participants in the study receive a set dose of the treatment for a period of time

Phase 1b

The dose is carefully and slowly increased at certain points during the study

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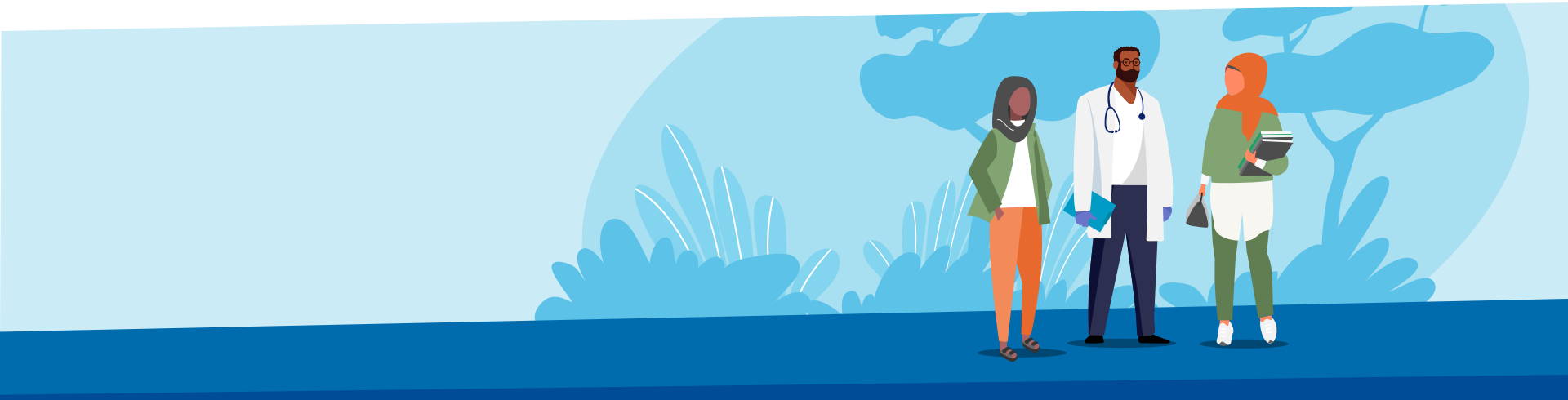
5. What is Pociredir?

(poe sir’ e dir)



Fulcrum is Developing a Potential New SCD Treatment

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Continued commitment to the SCD community and SCD research

Education on treatment development and clinical studies

Fulcrum has a phase 1b study underway

Enrollment in phase 1b PIONEER Study of pociredir

Pioneer

Pociredir is an Investigational Treatment

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This investigational drug is not approved by the U.S. Food and Drug Administration (FDA) or any other regulatory agency.

It is not known if the investigational drug works or is safe.

Your health may get better, worse, or not change at all.

Please speak with your study doctor for more information about the potential risks and discomforts you may experience by participating in this study.

Pociredir is an Investigational Treatment

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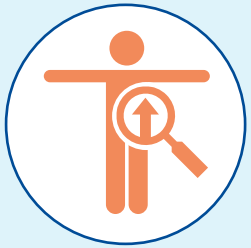
Pociredir aims to increase production of HbF in the body



High HbF can lead to reduced symptoms

Pociredir is planned to be a pill that is swallowed and taken once every day

Fulcrum Therapeutics is conducting a study to find out more about how pociredir works and the side effects it may cause

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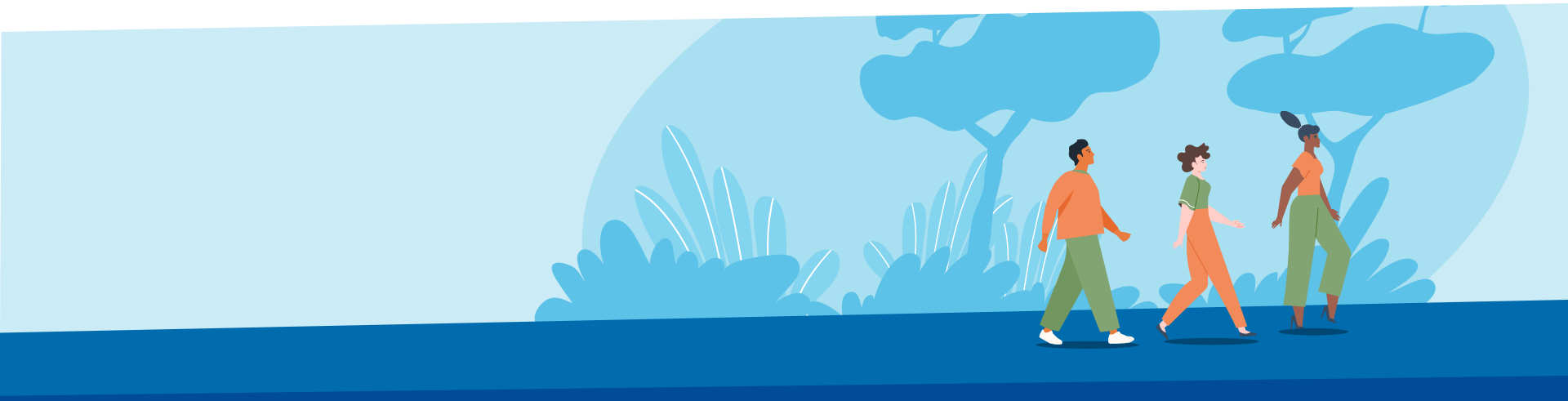
6. What is the PIONEER Study?



More about the PIONEER Study

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What is the goal of the Phase 1b PIONEER study?

- The PIONEER study aims to determine if the study treatment (pociredir) understand the safety of pociredir when given to patients with SCD. The study also aims to determine if pociredir increases the level of HbF in the blood.

How long is the study?

- The total length of individual participation in the study will be 15 to 16 weeks

What will participants need to do?

- You will need to take the treatment once daily by mouth for 12 weeks with 3-4 weeks of follow-up visits
- At pre-specified times, you will be asked to come into the hospital or clinic for visits and lab tests

Participants will receive the study treatment, tests and procedures at no cost.
Daily compensation will be provided

Who Can Take Part in the Study

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Participants may be eligible to take part in this clinical research study if they

- Decide to participate and complete paperwork associated with the trial
- Are between the age of 18 and 65 years
- Have been diagnosed with these types of SCD:
  - Hemoglobin **SS** Disease
  - Hemoglobin **SB 0** (Beta Zero) Thalassemia
  - Hemoglobin **SB+** (Beta Plus) Thalassemia

Previous and Current Experience with SCD Therapies

- Have previously taken hydroxyurea (also known as hydroxycarbamide) but stopped because it was not effective or could not be continued

AND

- Have tried but stopped (or been unable to get access to) at least one other approved therapy for SCD

AND

- Are not currently taking hydroxyurea

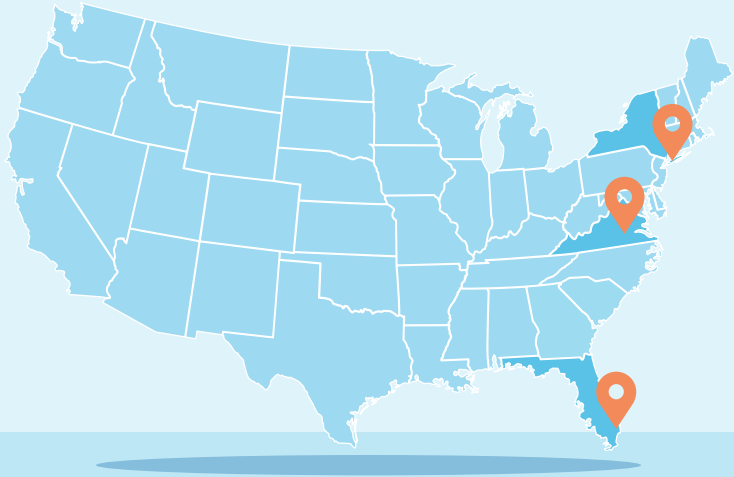
Other criteria also apply for this clinical study
Our research team will help determine if the study is right for you

Where PIONEER is Taking Place

The hospitals and clinics currently set up include

- University of Miami- Miami, FL
- Jacobi Medical Center- Bronx, NY
- University of North Carolina- Chapel Hill, NC

More locations are coming soon



What if I do not live in any of these cities but would like to join the study?
We may provide and support travel to study locations

Types of Support Available for Participants and Family Support

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Participants and caregivers may be eligible for support from Fulcrum

Support from Fulcrum may include

- Transportation
- Meals
- Wage Loss
- Gas
- Hotels
- Childcare

? Will you have patient assistance available?

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7. How do I Find Out More About the PIONEER Study?

Contact Us to Learn More

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Patient Liaison

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Website: https://www.pioneerscdstudy.com

Scan this QR code

ClinicalTrials.gov Identifier: NCT05169580

Contact Us to Learn More

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Patient Experience

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Scan this QR code

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Thank You