

# CURE SICKLE CELL.

## CURRENT & ONGOING GENETIC THERAPY CLINICAL TRIALS IN SICKLE CELL DISEASE

*It's time to rewrite the story of sickle cell.*

Clinical trials are medical studies aimed at finding safe and effective ways to prevent, detect, or treat diseases. Some clinical trials are testing ways of treating disease by changing a patient's genetic material. These are called genetic therapies, and most often they work by adding a healthy copy of a defective gene into the patient's cells. In the future, these techniques may allow doctors to treat a disorder by inserting a gene into a patient's cells instead of using drugs or surgery. Researchers are testing other approaches in addition to replacing the mutated gene with a healthy copy. They are inactivating, or "knocking out," a mutated gene that is functioning improperly. They also are introducing a new gene into the body to help fight a disease. Although genetic therapy is a promising new treatment option for many rare diseases, the technique is still being studied to ensure that it is safe and effective.

How can you help rewrite the story of sickle cell disease? Clinical trial participation is one of the most important ways we can move towards a future without sickle cell disease. We encourage adults, as well as children, healthy volunteers, those living with sickle cell disease, and people from diverse ethnic and racial backgrounds to consider participating in clinical trials.

Researchers are currently studying a number of potential new treatment options and also working towards cures. This document includes genetic therapy trials only. For information on other sickle cell disease trials, please visit: <https://clinicaltrials.gov>.

*Have questions and want to learn more about clinical trials? Go to [www.nih.gov/health-information/nih-clinical-research-trials-you](http://www.nih.gov/health-information/nih-clinical-research-trials-you).*



► **Gene Transfer for Patients With Sickle Cell Disease: Phase 1 / 2**

RECRUITING

**Age Range** 18–45 Years  
**Trial Time Frame** 7/2014–6/2023  
**Ref. No.** NCT02186418

This study will assess the safety and efficacy of gene transfer using a gamma-globin lentiviral vector. Gene transfer will occur ex-vivo into human bone marrow or mobilized peripheral blood CD34+ hematopoietic stem cells of subjects with sickle cell disease.

<https://ClinicalTrials.gov/show/NCT02186418>

► **Pilot and Feasibility Study of Hematopoietic Stem Cell Gene Transfer for Sickle Cell Disease: Phase 1 \***

ACTIVE / NOT RECRUITING

**Age Range** 3–40 Years  
**Trial Time Frame** 2/2018–10/2022  
**Ref. No.** NCT03282656

This is an open-label, non-randomized, single center, pilot and feasibility, single-arm cohort study involving a single infusion of autologous bone marrow derived CD34+ HSC cells transduced with the lentiviral vector containing a short-hairpin RNA targeting BCL11a.

<https://ClinicalTrials.gov/show/NCT03282656>

► **Clinical Research Study of Autologous Stem Cell Transplantation for Sickle Cell Disease: Phase 1 / 2**

RECRUITING

**Age Range** 18 Years and Older  
**Trial Time Frame** 12/2014–10/2022  
**Ref. No.** NCT02247843

This Phase I clinical trial will assess the safety and efficacy of an autologous transplant of lentiviral vector modified peripheral blood for adults with severe sickle cell disease.

<https://ClinicalTrials.gov/show/NCT02247843>

► **Safety of Blood Stem Cell Mobilization With Plerixafor in Patients With Sickle Cell Disease: Phase 1**

RECRUITING

**Age Range** 18–40 Years  
**Trial Time Frame** 9/2018–12/2022  
**Ref. No.** NCT03664830

This study will investigate whether up to two injections of plerixafor represent a safe and effective strategy for mobilizing adequate numbers of CD34+ hematopoietic stem progenitor cells (HSPC) for autologous hematopoietic cell transplantation (HCT).

<https://ClinicalTrials.gov/show/NCT03664830>

► **Safety Trial of Escalation of Plerixafor for Mobilization of Cells and Evaluation of Gene Transfer: Phase 1**

RECRUITING

**Age Range** 18–65 Years  
**Trial Time Frame** 9/2014–7/2023  
**Ref. No.** NCT02193191

This study will look at the safety and efficacy of a drug called Plerixafor. Plerixafor is approved by the U.S. Food and Drug Administration (FDA) for use in increasing blood stem cell counts before collection in cancer patients.

<https://ClinicalTrials.gov/show/NCT02193191>

► **Evaluation of the Safety and Efficacy of the LentiGlobin BB305 Drug Product in Severe Sickle Cell Disease: Phase 1 / 2**

ACTIVE / NOT RECRUITING

**Age Range** 12–50 Years  
**Trial Time Frame** 8/2014–7/2023  
**Ref. No.** NCT02140554

This is a non-randomized, open-label, multi-site, single-dose study in approximately 50 adults and adolescents with severe SCD. The study will evaluate hematopoietic stem cell (HSC) transplantation (HSCT) using LentiGlobin BB305 Drug Product.

<https://ClinicalTrials.gov/show/NCT02140554>

► **A Safety and Efficacy Study Evaluating CTX001 in Subjects With Severe Sickle Cell Disease: Phase 1 / 2**

ACTIVE / NOT RECRUITING

**Age Range** 12–35 Years  
**Trial Time Frame** 11/2018–10/2024  
**Ref. No.** NCT03745287

This is a single-arm, open-label, multi-site, single-dose study to evaluate the safety and efficacy of autologous CRISPR-Cas9 Modified CD34+ Human Hematopoietic Stem and Progenitor Cells (hHSPCs) using CTX001.

<https://ClinicalTrials.gov/show/NCT03745287>

\* Funded by the Cure Sickle Cell Initiative

► **A Study Evaluating Gene Therapy With BB305 Lentiviral Vector in Sickle Cell Disease: Phase 3**

RECRUITING

**Age Range** 2–50 Years  
**Trial Time Frame** 2/2020–2/2025  
**Ref. No.** NCT04293185

This is a non-randomized, open-label, multi-site, single-dose study in approximately 35 adults and pediatric subjects with sickle cell disease. The study will evaluate hematopoietic stem cell (HSC) transplantation (HSCT) with LentiGlobin BB305 Drug Product for SCD.

<https://clinicaltrials.gov/ct2/show/NCT04293185>

► **Study of Safety and Efficacy of Genome-edited Hematopoietic Stem and Progenitor Cells in Sickle Cell Disease: Phase 1 / 2**

RECRUITING

**Age Range** 2–40 Years  
**Trial Time Frame** 8/2020–8/2025  
**Ref. No.** NCT04443907

This study will evaluate two genome-edited, autologous, hematopoietic stem and progenitor cell (HSPC) products - OTQ923 and HIX763 - each reducing the biologic activity of BCL11A, increasing fetal hemoglobin (HbF) and reducing complications of sickle cell disease.

<https://clinicaltrials.gov/ct2/show/NCT04443907>

► **Study to Evaluate the Safety and Efficacy of EDIT-301 for Autologous HSCT in Subjects With Severe Sickle Cell Disease: Phase 1 / 2**

RECRUITING

**Age Range** 18–50 Years  
**Trial Time Frame** 4/2021–8/2025  
**Ref. No.** NCT04853576

The purpose of this study is to evaluate the efficacy, safety and tolerability of treatment with EDIT-301 in adult subjects with severe sickle cell disease (SCD).

<https://clinicaltrials.gov/ct2/show/NCT04853576>

► **Gene Correction in Autologous CD34+ Hematopoietic Stem Cells (HbS to HbA) to Treat Severe Sickle Cell Disease (CEDAR): Phase 1 / 2**

RECRUITING

**Age Range** 12–40 Years  
**Trial Time Frame** 8/2021–5/2026  
**Ref. No.** NCT04819841

This study is a first-in-human, single-arm, open-label Phase I/II study of GPH101 in approximately 15 participants, diagnosed with severe Sickle Cell Disease. The primary objective is to evaluate safety of the treatment in this patient population, as well as preliminary efficacy and pharmacodynamic data.

<https://clinicaltrials.gov/ct2/show/NCT04819841>

► **Transplantation of CRISPRCas9 Corrected Hematopoietic Stem Cells (CRISPR\_SCD001) in Patients With Severe Sickle Cell Disease: Phase 1 / 2**

NOT YET RECRUITING

**Age Range** 12–35 Years  
**Trial Time Frame** 12/2021–12/2024  
**Ref. No.** NCT04774536

This is an open label, non-randomized, 2-center, phase 1/2 trial of a single infusion of sickle allele modified cluster of differentiation (CD34+) hematopoietic stem progenitor cells (HSPCs) in subjects with in subjects  $\geq 12$  years old to 35 years old severe Sickle Cell Disease (SCD). The study will evaluate the hematopoietic stem cell transplantation (HSCT) using CRISPR/Cas9 edited red blood cells (known as CRISPR\_SCD001 Drug Product).

<https://clinicaltrials.gov/ct2/show/NCT04774536>

► **Evaluation of Safety and Efficacy of CTX001 in Pediatric Participants With Severe Sickle Cell Disease: Phase 3**

NOT YET RECRUITING

**Age Range** 2–11 Years  
**Trial Time Frame** 4/2022–5/2026  
**Ref. No.** NCT05329649

This is a single-dose, open-label study in pediatric participants with severe SCD and hydroxyurea (HU) failure or intolerance. The study will evaluate the safety and efficacy of autologous CRISPR-Cas9 modified CD34+ human hematopoietic stem and progenitor cells (hHSPCs) (CTX001).

<https://clinicaltrials.gov/ct2/show/NCT05329649>

**OBSERVATIONAL****▶ Longterm Follow-up of Subjects With Transfusion-Dependent  $\beta$ -Thalassemia Treated With Ex Vivo Gene Therapy**

RECRUITING BY INVITATION ONLY

**Age Range** Up to 50 Years  
**Trial Time Frame** 9/2013–3/2031  
**Ref. No.** NCT02633943

This is a multi-center, long-term safety and efficacy follow-up study for subjects with transfusion-dependent  $\beta$ -thalassemia (TDT) who have been treated with ex vivo gene therapy drug product in bluebird bio-sponsored clinical studies.

<https://ClinicalTrials.gov/show/NCT02633943>

**▶ Long-term Follow-up of Subjects With Sickle Cell Disease Treated With Ex Vivo Gene Therapy**

RECRUITING BY INVITATION ONLY

**Age Range** 2–53 Years  
**Trial Time Frame** 10/2020–5/2038  
**Ref. No.** NCT04628585

This is a multi-center, long-term safety and efficacy follow-up study for subjects who have been treated with ex vivo gene therapy drug product in bluebird bio-sponsored clinical studies. After completing the parent clinical study (approximately 2 years), eligible subjects will be followed for an additional 13 years for a total of 15 years post-drug product infusion.

<https://ClinicalTrials.gov/show/NCT04628585>

**▶ Long-term Follow-up Study in Subjects Who Received CTX001**

RECRUITING BY INVITATION ONLY

**Age Range** 18 Years and Older  
**Trial Time Frame** 1/2021–9/2039  
**Ref. No.** NCT04208529

This is a multi-site, observational study to evaluate the long-term safety and efficacy of CTX001 in subjects who received CTX001 in Study CTX001-111 (NCT03655678) or Study CTX001-121 (NCT03745287).

<https://ClinicalTrials.gov/show/NCT04208529>

*The Cure Sickle Cell Initiative is a collaborative research effort to identify and support the most promising genetic therapies for sickle cell disease. Created by the National Heart, Lung, and Blood Institute, the Initiative involves patients, advocates, caregivers, researchers, federal partners, and industry leaders. It builds on the legacy of research that has greatly improved clinical care of individuals living with sickle cell disease. To learn more, go to [www.curesickle.org](http://www.curesickle.org).*