CURE SICKLE CELL.

NIH National Heart, Lung, and Blood Institute

The Cure Sickle Cell Initiative (CureSCi)

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

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National Heart, Lung, and Blood Institute

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Vision and Goals

NIH National Heart, Lung, and Blood Institute

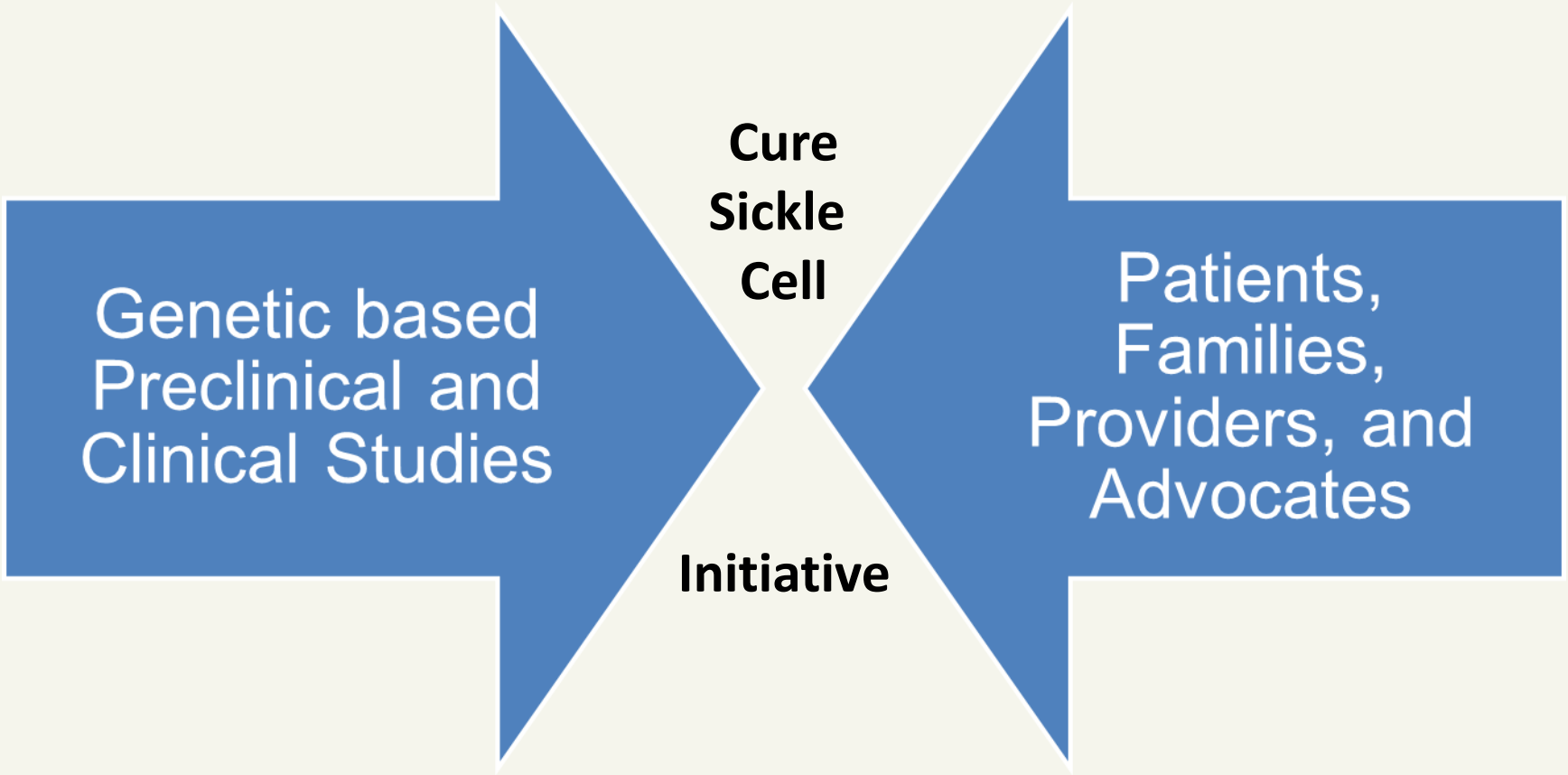
Funded by the National Heart, Lung, and Blood Institute (NHLBI) as an OTA and launched in September 2018.

Vision: To accelerate the development of treatments aimed at a genetic-based cure for sickle cell disease.

Goals:

- Create a collaborative, patient-focused research environment.
- Engage academic researchers, private sector researchers, advocates, patients, and caregivers to develop strategies for cures.
- Determine the safest, most effective, and most readily and widely adoptable genetic therapies.
- Move newly developed genetic therapies, including gene-editing approaches, into clinical trials within five to ten years.

Cure SCi Philosophy



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Key Leaders

NIH National Heart, Lung, and Blood Institute

Dr. Gary H. Gibbons

- Director, National Heart, Lung, and Blood Institute

Dr. Edward J. Benz, Jr.

- Executive Chair, Cure Sickle Cell Initiative
- CEO Emeritus, Dana-Farber Cancer Institute

Dr. Leslie Silberstein

- Scientific Director, Cure Sickle Cell Initiative
- Director, Joint Program in Transfusion Medicine (BWH)

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Partners and Collaborators

NIH National Heart, Lung, and Blood Institute

Leveraging Resources and Engaging a Community on the Path to a SCD Cure

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

AMERICAN SOCIETY OF HEMATOLOGY

SCDIC Sickle Cell Disease Implementation Consortium

PACT
Production Assistance for Cellular Therapies
National Heart Lung and Blood Program

NIMBL The National Institute for Innovation in Manufacturing Biopharmaceuticals

CMS CENTERS FOR MEDICARE & MEDICAID SERVICES

BLOOD AND MARROW TRANSPLANT CLINICAL TRIALS NETWORK

OMH U.S. Department of Health and Human Services Office of Minority Health

CIBMTR® CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

FDA

NIST National Institute of Standards and Technology U.S. Department of Commerce

CDC

U.S. Department of Health and Human Services HRSA Health Resources and Services Administration

Building a Comprehensive Approach to SCD

- **Filling gaps** that cannot be covered by traditional funding strategies.

- **Funding research** within academia and the private sector to identify the most promising cellular and genetic therapies.
  - NHLBI will continue to fund investigator-initiated applications focused on SCD.

- **Partnering** with federal agencies, academic institutions, pharmaceutical companies, professional societies, community advocacy organizations, patient representatives, and foundations.

- **Educating and engaging communities** to inform patients, providers, and stakeholders about our work, ensuring trust and collaboration, while also educating patients and caretakers to consider participating in clinical trials.

Priority Activities

- **Voices** – Patient Representatives/ Advocates serving on the Executive and Implementation Committees
- **Working with Federal Partners** led by HHS
- **Subcommittees** established to address:
  - Patient Outreach/Engagement
  - Communications/Social Media
  - Assay Development
  - Gene Editing/Gene Therapies
  - Clinical Trial Design

- **MOUs** with ASH and CIRM to:
  - Work together and coordinate resources and efforts to identify a curative therapy for individuals living with SCD
- **Data Consortium** established to enhance:
  - Recruitment and outreach
  - Data collection from a variety of sources
  - Common data elements/harmonization
  - Data management
  - Data analysis
  - Data sharing

Advisors

- In addition to subcommittees, the Initiative plans on establishing two external boards with the charge of looking at the overall program and giving recommendations
  - The first is a Patient Board to be comprised of patients and parents of children with sickle cell disease
  - The second is a Scientist Board to be comprised of physicians and scientists who are not funded by the Initiative or associated with any of the subcommittees

Workstream Organization

Patient Engagement & Communications	Biomanufacturing	Clinical Strategy	Patient Outcomes	Data & Bioinformatics
▪ Communications Plan ▪ Messaging strategy ▪ Communications artifacts ▪ Education materials ▪ Engagement models	▪ Cell sourcing ▪ SCD blood bank ▪ Assay standardization ▪ Safety & Quality Assurance ▪ GMP vector manufacturing ▪ PACT	▪ Clinical Trial design ▪ Endpoint strategy (e.g., surrogate markers) ▪ Gene therapies ▪ Biotherapeutic approach	▪ Clinical and economic analysis ▪ Health outcome models ▪ Implementation science	▪ Data strategy ▪ Federated data registry & repository compatible with Data STAGE platform ▪ Clinical data elements ▪ Patient registry

Initiative Infrastructure and Program Management

Guiding Initiative Messages

- Patient Engagement is Paramount to the Initiative's Success
- Concentrated Focus on Sickle Cell Disease is Warranted
- Scientific Advances Create Unprecedented Opportunities
- Building on the Legacy of NHLBI-supported Research
- Unique Opportunities Call for Unconventional Approaches
- Developing the Most Promising Next Generation Therapies to Find Cures

2018 Stakeholder Meeting Takeaways/Priorities

- Conduct ***economic analysis*** of the lifetime cost of SCD vs. the cost of a genetic cure to create incentive for insurance coverage (CMS) and determine anticipated cost requirements for long-term follow up.
- ***Involve patients and providers*** in advisory role for study designs.
- Develop ***patient-centric/meaningful clinical trial endpoints*** for SCD genetic therapy trials; develop common data elements to be collected.
- Establish a ***national data resource*** for SCD gene and cell therapy trials.

Top 6 Priority Activities for 2019

1. Biologic and Clinical Endpoints
2. Data Resources
3. Enhance Existing Bio Resources
4. Engage Patients through Outreach
5. Regulatory Interface
6. Enable/Accelerate Clinical Trials

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Areas of Planned Projects for the Initiative

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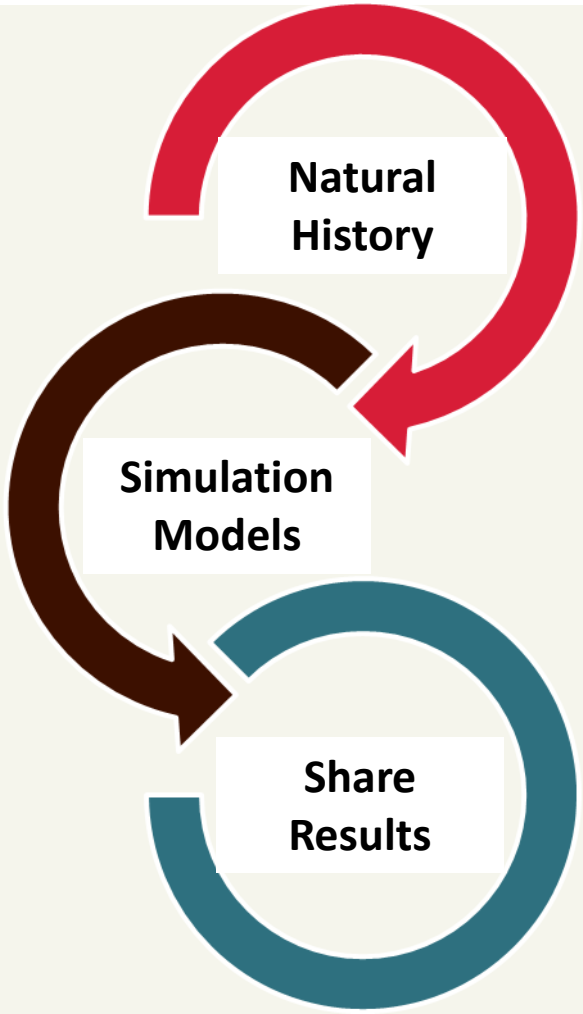
- **These are areas where the Initiative plans to partner with others, Initiative activities, or provide assistance through funding or technical support:**
  - Economic Analyses (burden of care versus cost of cure)
  - GMP manufacturing (vectors, cells, reagents for trials)
  - Natural history studies/contemporaneous controls
  - Assay development for gene therapy/gene editing and biological endpoints
  - IND-enabling preclinical studies
  - Regulatory support
  - Phase I and II clinical trials
- **To apply for regulatory services:** https://curesickle.org/researchers#pane-123

Goals of CureSCi CEIA Consortium



Landscape analysis to inform simulation models for SCD standard of care

- Valuable information for the research community

Clinical and cost effectiveness analysis that is most useful to insurers/payer community and considers societal perspective

- Publicly available web-based simulation modes

Dissemination of study results

- Peer-reviewed journals
- Professional society meetings and conferences

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Research Opportunity Announcement

NIH National Heart, Lung, and Blood Institute

Research Opportunities – OTA-19-005 for Cure Sickle Cell

Objectives

- The NHLBI is soliciting applications for preclinical and clinical projects focused on curative strategies for sickle cell disease in the areas of gene therapy (replacement) and gene editing.
- Proposed projects may also be focused on developing or refining activities that improve the safety or efficacy of the clinical protocol for gene therapy or gene edited autologous hematopoietic transplantation.

Eligibility

- Higher education institutions
- Nonprofits other than institutions of higher education
- For-Profit organizations

Full ROA available to view at https://curesickle.org/researchers under *Research Opportunities*

Addressing Concerns about Viral Vectors

- CureSCi is working to find cures for people living with sickle cell disease.
- We are studying many different approaches, including gene transfer, gene editing and small molecules.
- Researchers have found ways to use non-infectious parts of certain viruses to make the genetic therapies that would correct the incorrect DNA.
- Viruses are used because of their ability to easily transfer DNA into cells. One approach being studied is using a modified lentivirus to carry or deliver the healthy hemoglobin gene into the body. This is done by removing the parts of the virus that cause disease and replacing it with the corrected genetic material (healthy hemoglobin), which is then returned to the patient.
- HIV is one example of a group of viruses called lentiviruses that, when used in gene therapy, are called lentiviral vectors. Lentiviral vectors do not contain the infectious part of the virus and cannot give you HIV/AIDS. This technique has been used in research for many years to treat various diseases, including Severe Combined Immunodeficiency syndrome (SCID), thalassemia, Wiskott-Aldrich syndrome, as well as treating various cancers.

For more information, visit:
https://www.asgct.org/education/gene-therapy-basics
https://www.asgct.org/education/blood-disorders

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Keep Connected

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Visit curesickle.org to learn more about the Initiative and sign up for updates.

To subscribe to the NHLBI newsletter, visit:

https://www.nhlbi.nih.gov.health-topics/education-and-awareness/sickle-cell

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Questions?

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