

Executive Summary

STEM CELL IMMUNOTHERAPY TO CURE BLOOD AND AUTOIMMUNE DISORDERS



MISSION

The mission of Chimera Therapeutics is to develop and market curative immunotherapeutic treatments for hereditary blood and autoimmune disorders based on novel allogeneic hematopoietic cell transplantation technology.

OUR PROPRIETARY SOLUTION

Our scientists have developed a novel, patented technology based on hematopoietic stem cells (HSCs). With this technology, HSCs from haploidentical (half matched) donors can be engrafted into the bone marrow of the patient without eliminating the original patient hematopoietic system, such that the patient will have two systems – a mix of both donor- and patient-hematopoietic systems – called "mixed chimeras". Preclinical animal models as well as human patients with mixed chimeras appear to be healthy with no indication of graft versus host disease (GVHD), a severe and sometimes fatal side effect of bone marrow transplantation (BMT). Induction of mixed chimerism has cured Sickle Cell Disease (SCD) in human patients and has been demonstrated to cure multiple autoimmune diseases such as Systemic Lupus Erythematosus (SLE), Multiple Sclerosis (MS) and Juvenile or Type 1 Diabetes (T1D) in preclinical animal models, indicating the promise for treating these diseases in humans.

Unlike the current standard of care, our technology employs a less severe, reduced-intensity regimen that is radiationfree and non-myeloablative to treat the patient, which reduces, but not eliminate, the patient's bone marrow cells. This decreases the risk of cytopenia (a reduction of healthy blood cells), is less toxic, and facilitates the engraftment of donor cells to induce mixed chimerism. This process induces tolerance to both donor and host (patient) cell antigens, reducing the risk of GVHD in the patient. In addition, a haploidentical individual, as opposed to a complete HLA matched individual, can be the donor, significantly expanding the availability of allogeneic hematopoietic cell transplantation (allo-HCT) to patients, especially those belonging to certain minority groups.

CLINICAL OUTCOMES

In a Phase I clinical trial of SCD patients with severe disease, funded by the California Institute for Regenerative Medicine (CIRM), we have now treated three of six total SCD patients. The first patient clearly demonstrated that our treatment regimen was well tolerated with little toxicity, but unfortunately, did not develop measurable mixed chimerism. After modifying our regimen based on this outcome, we successfully induced mixed chimerism in the second patient. The modified regimen remained well tolerated and was able to induce mixed chimerism in a patient exhibiting RBC alloimmunization, a side effect of blood transfusion that increases with each subsequent blood transfusion. It is usually very difficult to engraft donor stem cells in these "pre-sensitized patients", but the mixed chimerism in this patient has been stable for more than 18 months, with complete cure of SCD and no signs of GVHD. In addition, other symptoms of SCD, especially recurrent pain crises, as well as chronic pain, have dissipated in the patient. Treatment of the third patient was completed and that patient had a faster development of mixed chimerism than the second patient.





KEY BENEFITS OF CHIMERA THERAPEUTICS TECHNOLOGY

For patients with hereditary blood disorders like SCD and Thalassemia major:

- Less expensive than current life-long blood transfusion and drug therapy that only treats the symptoms and not the disease with greatly improved quality of life
- Single treatment plan that provides persistent disease-free survival/life-long cure
 - Non-myeloablative, radiation-free treatment is less severe and toxic than standard allo-HCT, so patients
 recover faster with shorter hospitalization time
 - More successful than current BMT standard of care with no radiation-associated fatality
 - Minimal risk to patient because mixed chimerism reduces the risk of GVHD
 - No need for life-long immunosuppressive therapy to prevent GVHD, which weakens the patient's immune system making the patient more susceptible to infections and other side effects
- Significantly greater pool of potential donors since mixed chimerism requires only a haploidentical donor
- Superior, simpler, and less severe treatment alternative to gene therapy with no cell culturing and no immune system complications due to the use of viral vectors
- No risk of unintended "off-target" mutations from CRISPR-based genetic manipulation of patient genomic DNA

Potential curative therapy for autoimmune disease and organ transplant rejection:

- Induction of haploidentical mixed chimerism reverses firmly established autoimmune diseases such as T1D, SLE and MS in preclinical animal models and augments tissue regeneration of insulin-producing beta cells in T1D, glomerular membrane in SLE nephritis and myelin sheath in MS
- Induction of MHC-mismatched mixed chimerism provides immune tolerance to donor organs such as pancreatic islet, heart, and kidney and increases the potential for patient match

BUSINESS PLAN

Chimera Therapeutics' patented and proprietary mixed chimerism technologies provide the basis to pursue immunotherapeutic treatments for not only blood disorders like SCD and Thalassemia Major, but also for autoimmune disorders like SLE, MS and T1D. Chimera Therapeutics' initial goal is to raise the \$20-40 million to extend the CIRM-funded SCD clinical trial in adults with collaborators at the City of Hope, then extend the SCD clinical trial to pediatric patients. With an estimated 100,000 affected individuals in the US and an estimated lifetime cost of treatment at \$1.0 million per patient, the market opportunity for SCD alone is \$100 billion. The second goal is to begin parallel development of Thalassemia Major and aplastic anemia clinical trials, as well as design an autoimmune disease clinical trial.

THE COMPANY

Chimera Therapeutics, (ChimeraTX; a California Limited Liability Corporation) has two of its physician-scientist founders on the faculty of the City of Hope in Duarte California, a non-profit medical research center and founding member of the National Comprehensive Cancer Network. With a combined 15 years' experience working together on induction of mixed chimerism research, this team has garnered over \$10 million in peer-reviewed grants from the National Institutes of Health (NIH), Juvenile Diabetes Research Foundation (JDRF) and the CIRM. They are inventors on 12 core technology patents filed by the City of Hope and Chimera Therapeutics holds an exclusive license to these proprietary technologies.





Chimera Therapeutics Company Founders, Board Members and Management Team:



Defu Zeng, MD: Scientific and Medical Advisor, Professor of Immunology and Hematopoietic Cell Transplantation at City of Hope. Dr. Zeng is a physician-scientist who developed much of the mixed chimerism methodology on which the ChimeraTX technology is based. He has vast expertise in the induction of mixed chimerism, dissecting immunological mechanisms of autoimmune disease pathogenesis, GVHD pathogenesis and transplantation immune tolerance.



Art Riggs, PhD: Scientific and Medical Advisor, Samuel Rahbar Chair in Diabetes & Drug Discovery; Director, Diabetes & Metabolism Research Institute at City of Hope. Dr. Riggs is a world-renowned expert in diabetes, best known for his role in the development of the first synthetic human insulin for patients, which led to the formation of Genentech and the biotechnology industry. He is a member of National Academy of Science, the founding scientist of modern epigenetics and a pioneer in the development of

recombinant antibodies, a precursor for the chimeric antigen receptor immunotherapies used as a treatment for cancer.



Wei Zhou, PhD, JD: Commercial and Funding Advisor, Chairman. Dr. Zhou is a biomedical scientist and patent attorney who has extensive commercial and legal experience in the biotech industry. Dr. Zhou served as VP of Intellectual Property at Affymetrix and was responsible for Affymetrix' China business. He was partner at the technology law firm Wilson Sonsini Goodrich & Rosati and is currently CEO of Centrillion Technologies, a genome services company founded in 2009.



Matthew Lorence, PhD, MBA: Chief Executive Officer. Dr. Lorence is a biomedical scientist and business professional with extensive commercial experience in the genomics and molecular diagnostic industries and has had extensive interactions with the FDA. He recently served as CEO of Edge BioSystems and CEO of Concise Separations, and has a track record of growing existing businesses, building new businesses, and developing strategies to enter new markets.

Chimera Therapeutics Scientific Advisory Board:



Stephen J. Forman, MD: Clinical Science Advisor. Dr. Forman is the Director of the T Cell Therapeutics Research Laboratory, Director of the Hematologic Malignancies Research Institute at the City of Hope and an international expert in leukemia, lymphoma, and bone marrow transplantation. In nearly 40 years at City of Hope, Dr. Forman has been instrumental in the advance survival rates for cancers of the blood and immune system with his current efforts focused on cancer immunotherapy utilizing CAR T cells.



Joseph Rosenthal, MD, JD: Clinical Science Advisor. Dr. Rosenthal is the Barron Hilton Professor and Chair in Pediatrics and Director, Pediatrics Hematology/Oncology at City of Hope. Dr. Rosenthal is a physician-scientist who is leading the \$5.74M CIRM-funded Phase I clinical trial treating SCD patients with the mixed chimerism methodology.



Ryotaro Nakamura, MD: Clinical Science Advisor. Dr. Nakamura is Professor, Department of Hematology/ HCT and Director, Transplant Center of the Hematologic Malignancies Research Institutes at City of Hope. Dr Nakamura is a physician-scientist whose research focuses on hemopoietic cell transplantation (HCT) as a treatment for blood cancers like AML and ALL, as well as post-transplantation immunotherapy.

For more information about Chimera Therapeutics and its mission to develop curative immunotherapeutic treatments for hematological and autoimmune disorders, please contact Matthew Lorence at **mclorence@chimeratx.com**.