GRAPHITE BIO

Realizing the full promise of gene editing to transform lives

Corporate Presentation

June 2022

Forward looking statements

Statements in this Presentation that are not statements of historical fact are forward-looking statements. Such forward-looking statements include, without limitation, statements regarding our research and clinical development plans, the clinical and therapeutic potential of our product candidates and platform technology, our expected manufacturing capabilities, strategy, regulatory matters, market size and opportunity, future financial position, forecasted expenses and cash runway, prospects, plans, objectives, and our ability to achieve certain milestones, and the timing thereof. Words such as “believe,” “anticipate,” “plan,” “expect,” “intend,” “will,” “may,” “goal,” “potential” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements necessarily contain these identifying words. These forward-looking statements are based on the beliefs of the management team at Graphite Bio, Inc. ("Graphite Bio") as well as assumptions made by and information currently available to us. Such statements reflect the current views of Graphite Bio with respect to future events and are subject to known and unknown risks, including business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about Graphite Bio, including, without limitation, risks inherent in developing therapeutic products, future results from our ongoing and planned clinical trials and preclinical research, our ability to obtain adequate financing to fund our planned clinical trials and other expenses, trends in the industry and competitive landscape, the legal and regulatory framework for our industry, our future expenditures and overall market conditions. In light of these risks and uncertainties, the events or circumstances referred to in the forward-looking statements may not occur. The actual results may vary from the anticipated results and the variations may be material. These forward-looking statements should not be taken as forecasts or promises nor should they be taken as implying any indication, assurance or guarantee that the assumptions on which such forward-looking statements have been made are correct or exhaustive or, in the case of the assumptions, fully stated in this presentation. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date this presentation is given. This presentation discusses product candidates that are or will be under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration (the “FDA”). No representation is made as to the safety or effectiveness of these product candidates for the therapeutic use for which such product candidates are being or will be studied.

This presentation contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other industry data. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Graphite Bio has not independently verified the data generated by independent parties and cannot guarantee their accuracy or completeness.

This presentation shall not constitute an offer to sell or the solicitation of an offer to buy any securities.

Graphite Bio: Realizing the full promise of gene editing

Powerful Next-Generation UltraHDR™ Gene Editing Platform

- Harnessing the power of **high-efficiency homology directed repair** to fulfill the original goal of CRISPR gene editing
- "Find & replace" genes anywhere in the genome – correct, replace, insert
- Preclinical validation across a wide range of cell types and diseases

Robust Pipeline of Potential One-Time Cures

- Initial focus on HSC-based cures for serious and life-threatening diseases
- **First-in-industry approach to directly correct** the sickle cell mutation
- R&D programs designed to validate broad platform capabilities

Poised to Deliver for Patients

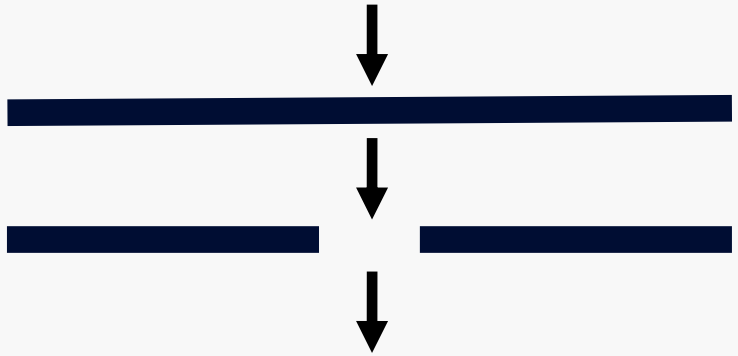
- Founded by Stanford University genetic medicine pioneers
- Experienced management team and board with track record of developing innovative therapies
- $352.1 million in cash, cash equivalents and investments in marketable securities (as of 3/31/2022); cash runway into 4Q 2024

HSC, hematopoietic stem cell; R&D, research and development.

Harnessing the power of homology directed repair to unleash the full potential of CRISPR gene editing

Cutting is easy

CRISPR Nuclease

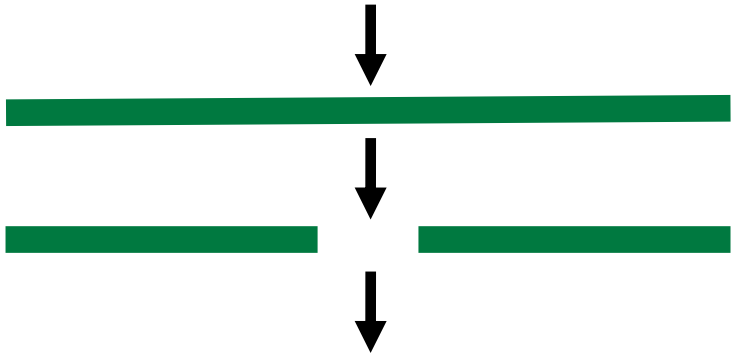


Non-homologous end joining
(Default error-prone repair)

Method to break and disrupt

Precision repair is hard

2nd gen CRISPR Nuclease



Homology directed repair
(Precision repair)

Donor DNA template

Method to find and replace

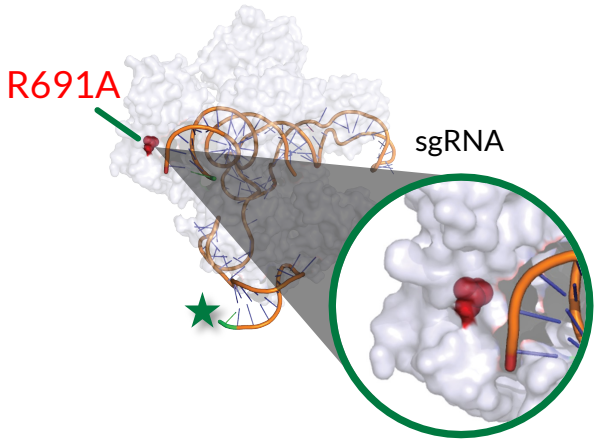
Homology directed repair

- The original goal of gene editing and CRISPR technology
- The most precise DNA editing system in nature
- Takes CRISPR beyond cutting and knock-outs – able to fix genetic lesions anywhere in the genome
- Has been historically difficult to achieve at high efficiencies until now

Our UltraHDR™ Platform: Building on CRISPR technology to ‘find & replace’ any gene

FIND:

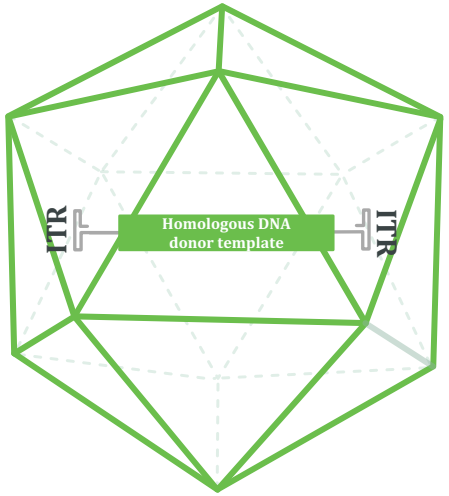
Proprietary HiFi Cas9 RNP / modified guide RNA finds gene and precisely cuts



- Retains high activity
- Reduced off-target edits by 30- to 100-fold
- Minimized cellular response

REPLACE:

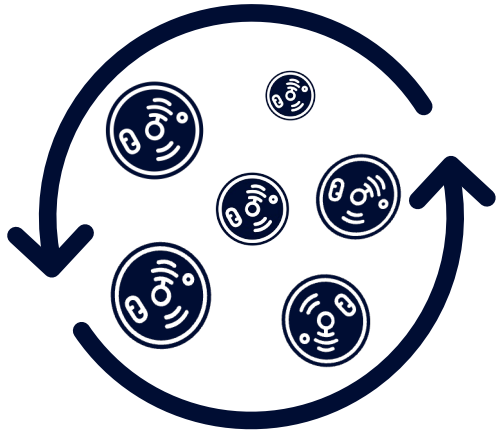
AAV6 delivers donor DNA template to drive high-efficiency HDR



- Non-integrating
- Up to 4kb template
- Enables high-efficiency HDR
- One lot may treat 1000s of patients

OPTIMIZE:

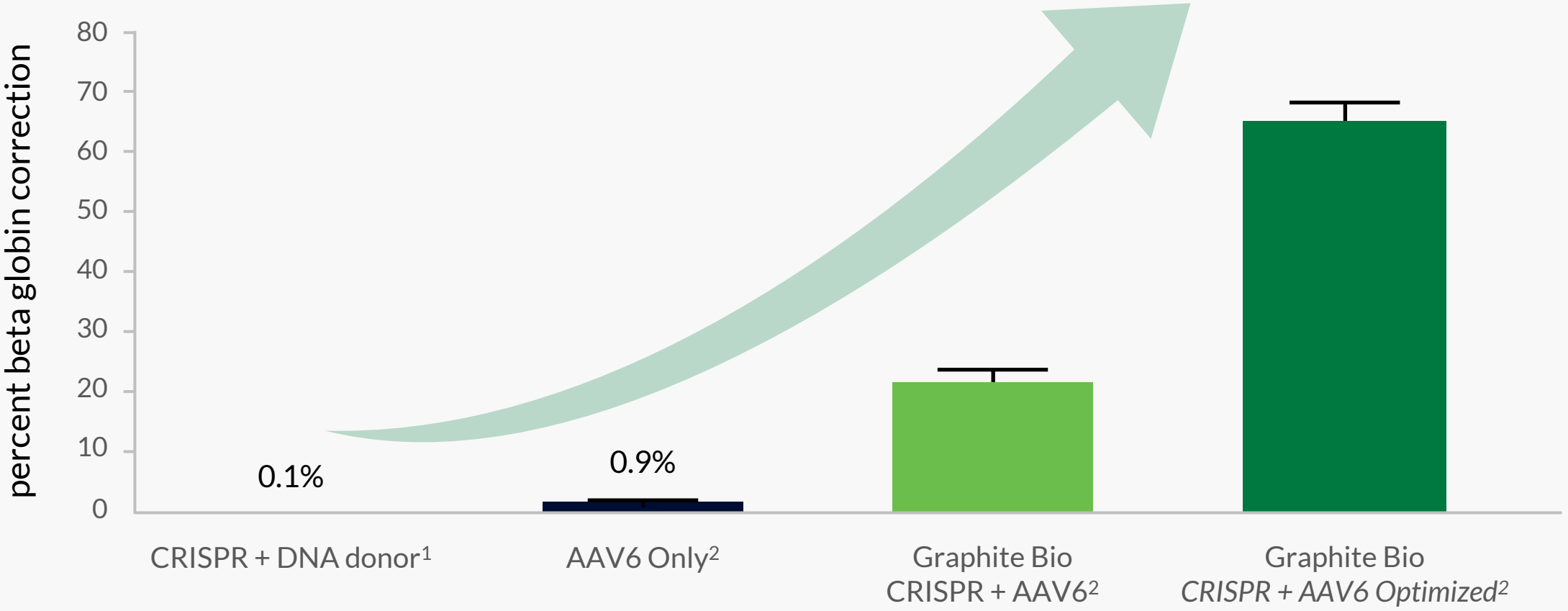
Stem cells prepared and optimized for HDR



- HSC biology expertise and culture optimization
- Unprecedented editing efficiencies as high as 70%
- Successful GMP manufacturing

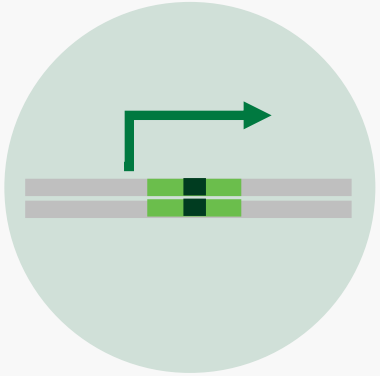
GMP, good manufacturing practices; HDR, homology directed repair; HiFi Cas9, high-fidelity Cas9; HSC, hematopoietic stem cell; RNP, ribonucleoprotein.

Our UltraHDR™ Platform has generated unprecedented gene editing efficiencies in therapeutic cells *in vitro*



1. Porteus lab (unpublished).
2. Lattanzi, Roncarolo, Dever, & Porteus. Development of β-globin gene correction in human hematopoietic stem cells as a potential durable treatment for sickle cell disease. Sci. Transl. Med. 13, eabf2444 (2021).

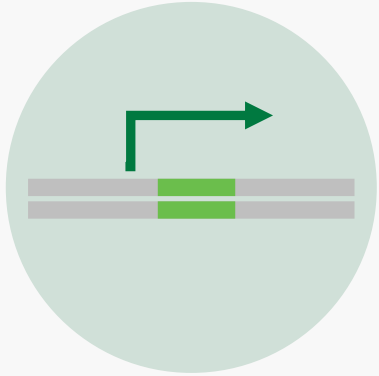
Our UltraHDR™ Platform is designed to enable a broad array of applications: Precisely correct, replace and insert genes



Gene Correction

Correct point mutations or short DNA stretches in endogenous locus

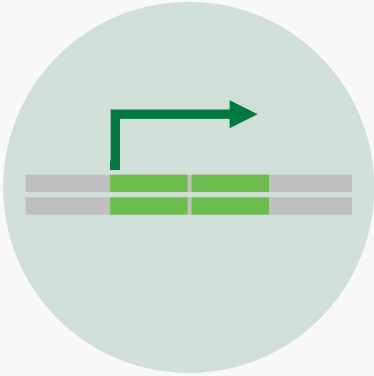
(*e.g., sickle cell disease*)



Gene Replacement

Replace gene driven by own promoter

(*e.g., beta-thalassemia, X-linked severe combined immunodeficiency syndrome (XSCID)*)

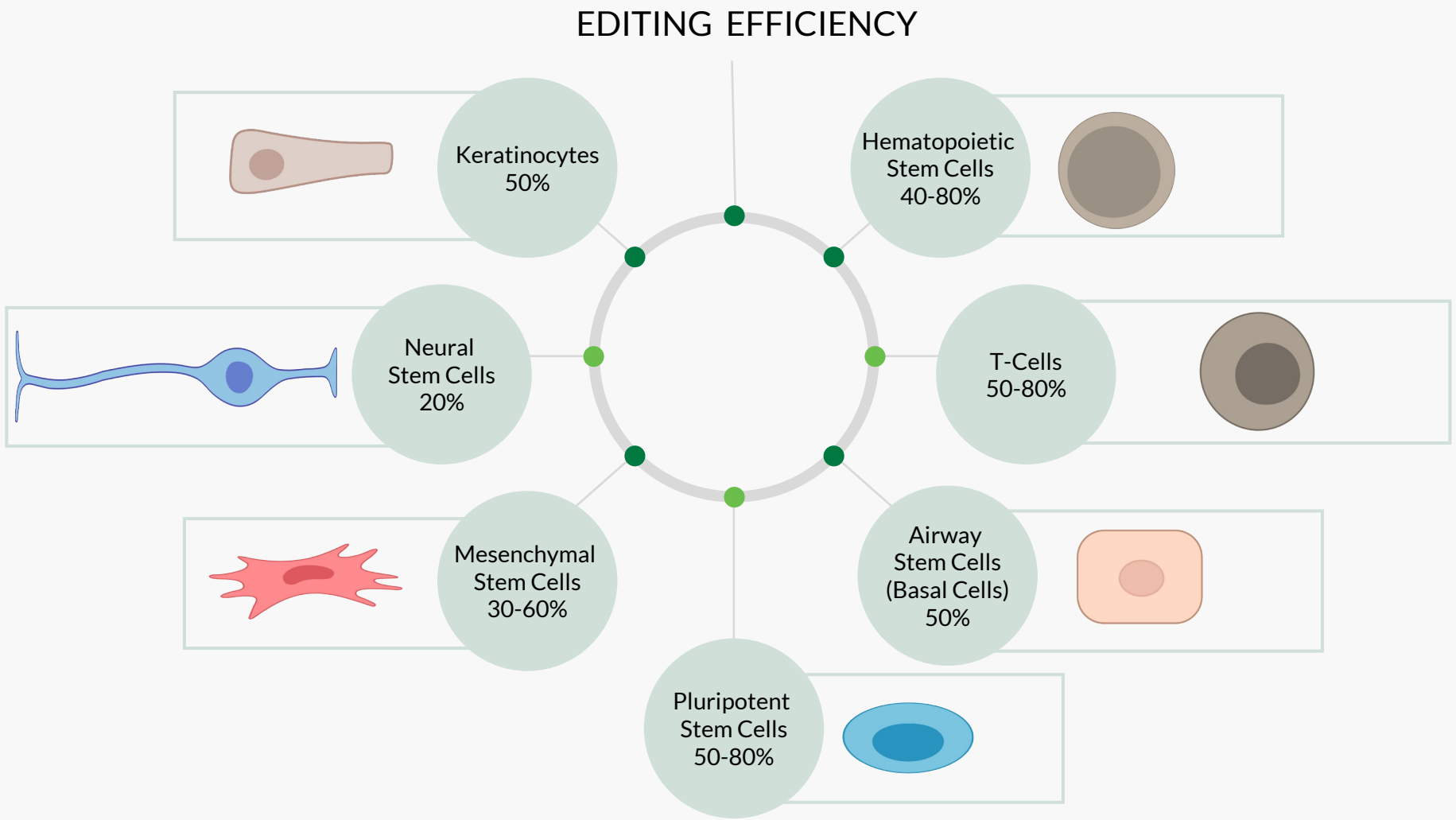


Targeted Gene Insertion

Knock-in promoter gene expression cassette into safe harbor location

(*e.g., alpha-1 antitrypsin deficiency, Gaucher disease*)

Our UltraHDR™ Platform is highly efficient across a wide range of cell types – yielding broad potential



Bonafont, Porteus et al. Homology-Directed Repair-based Ex Vivo Gene Editing for Recessive Dystrophic Epidermolysis Bullosa Correction in Somatic Stem Cells. Submitted to Molecular Therapy; Dever et. al. CRISPR/Cas9 β-globin gene targeting in human haematopoietic stem cells. Nature 539, 384–389(2016); Wiebking, Lahiri, Roncarolo, Porteus et. al. Genome editing of donor derived T-cells to generate allogenic chimeric antigen receptor modified T cells. Haemoatolgica 20210; 105; Vaidyanathan, Porteus et. al. High-efficiency, selection-free gene repair in airway stem cells from CF Patients rescues CFTR function in differentiated epithelia. Cancer Stem Cell 26; 1-11, January 2, 2019.; Martin, Porteus et. al. Highly Efficient and Marker-free Genome Editing of Human Pluripotent Stem Cells by CRISPR-Cas9 RNP and AAV6 Donor-Mediated Homologous Recombination. Cancer Stem Cell 24, 821-828. May 2, 2019; Srifa, Porteus et. al. Cas9-AAV6-engineered human mesenchymal stromal cells improved cutaneous wound healing in diabetic mice. Nature Communications 2020, 11:2470; Dever, Gomez-Ospina, Porteus et. al. CRISPR/Cas9 Genome Engineering in Engraftable Human Brain-Derived Neural Stem Cells. iScience 15, 524-535. May 31, 2019.

Our strategy

Demonstrate potential for definitive cure by targeting disease-causing gene

Severe SCD, beta-thalassemia

Leverage targeted gene insertion capabilities

Platform enhancements and optimizations

Targeted conditioning to expand eligible patients and addressable diseases

Alpha-1 antitrypsin deficiency, Gaucher

Leverage technology across a range of other cell types

Autoimmune, CNS, oncology, regenerative

Our goal

Deliver **one-time outpatient cures** across a range of genetic and other diseases

Transforming the paradigm for stem cell-based one-time cures

Differentiation

Clinical development and biomarkers to support best-in-disease profile

UltraHDR™ Platform

High-efficiency precision gene editing to correct, replace and insert genes

Non-genotoxic conditioning

Improve conditioning and engraftment

Mobilization and manufacturing

Process optimization to lead to greater scale

HDR, homology directed repair.

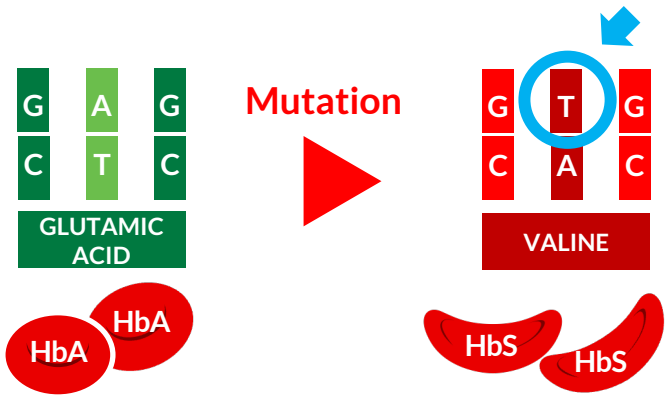
Developing therapies with curative potential for serious, genetic diseases

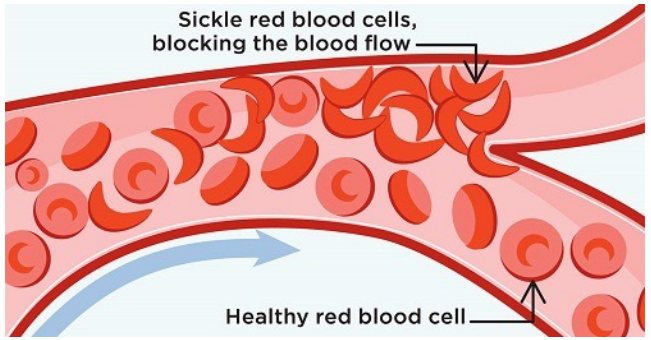
PROGRAM / INDICATION	APPLICATION	DISCOVERY/ VALIDATION	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	NEXT ANTICIPATED MILESTONE	COMMERCIAL RIGHTS
GPH101 Sickle cell disease (SCD)	Gene correction						Initial POC data (2023)	GRAPHITE BIO
GPH102 Beta-thalassemia	Gene replacement						IND submission (mid-2024)	GRAPHITE BIO
Therapeutic protein production (alpha-globin) Alpha-1 antitrypsin (AAT) deficiency	Targeted gene insertion						Program nomination	GRAPHITE BIO
Non-genotoxic conditioning (NGTC) Undisclosed targets	Engraftment						Program nomination	GRAPHITE BIO
GPH201 X-linked severe combined immunodeficiency syndrome (XSCID)	Gene replacement			Academic collaboration			IND submission	GRAPHITE BIO
GPH301 Gaucher disease – Type 1	Targeted gene insertion						Advance with NGTC	GRAPHITE BIO

Sickle Cell Disease: Direct Correction of the Genetic Mutation To Restore Adult Hemoglobin Expression

Sickle cell disease is one of the most prevalent monogenic diseases

SCD is caused by a point mutation in the human beta-globin gene[1,2]





About SCD

- Affects ~100,000 people in the U.S. and millions worldwide
- Carrier state essentially normal; protects against malarial infection

Lifelong complications and early mortality

- Results in hemolytic anemia, chronic pain, VOC, ACS, progressive end-organ damage and, ultimately, shortened lifespan[1-8]
- 30-year reduced life expectancy in U.S.[6]

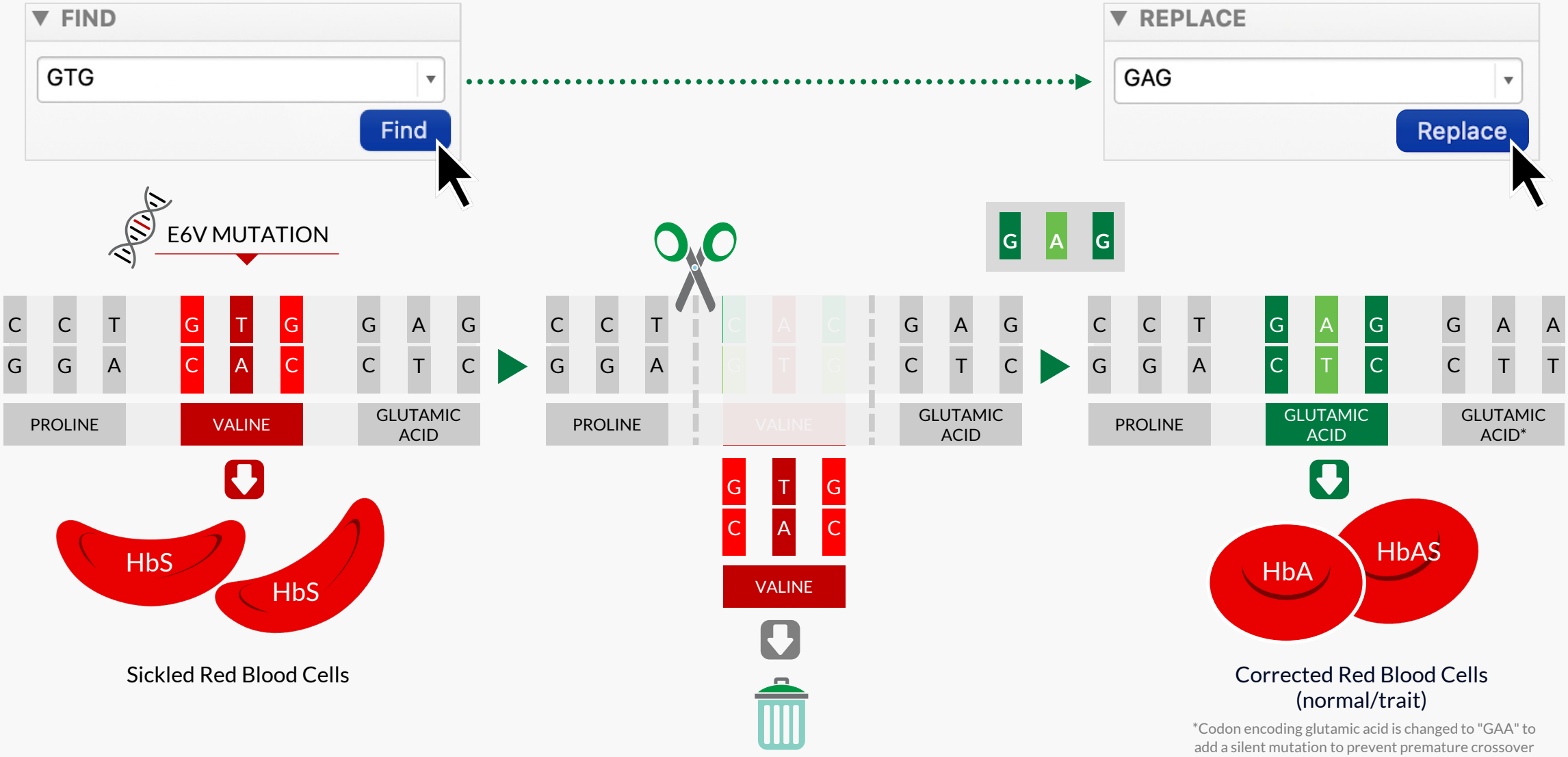
Limited treatment options

- The only available cure for SCD, allogeneic HSCT, carries significant risk and substantial burden[9-11]
  - Lack of well-matched donors
  - Need for immunosuppression
  - Risk of graft-versus-host disease and graft rejection
- Currently available non-curative therapies are palliative and do not impact irreversible chronic organ damage or prevent early mortality

ACS, acute chest syndrome; HbA, adult hemoglobin; HbS, hemoglobin sickle cell; HSCT, hematopoietic stem cell transplant; RBC, red blood cell; SCD, sickle cell disease; VOC, vaso-occlusive crisis.

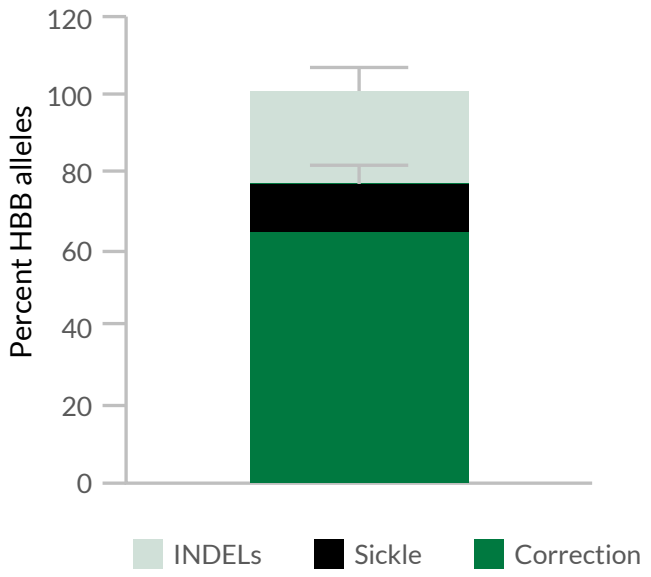
1. Kato GJ, et al. Nat Rev Dis Primers. 2018;4:18010; 2. National Organization for Rare Disorders. Sickle cell disease. Published June 25, 2020. Accessed March 24, 2021. https://rarediseases.org/rare-diseases/sickle-cell-disease; 3.Centers for Disease Control and Prevention. Data & statistics on sickle cell disease. Updated December 16, 2020. Accessed May 5, 2021. https://www.cdc.gov/ncbddd/sicklecell/data.html; 4. American Society of Hematology. Sickle cell trait. Published 2021. Accessed April 19, 2021. https://www.hematology.org/education/patients/anemia/sickle-cell-trait;
5. US Department of Health and Human Services. Evidence-based management of sickle cell disease. Expert panel report, 2014. Published 2014. Accessed April 1, 2021; 6. Piel et al. Sickle cell disease. N Engl J Med. 2017. 376(16):1561-1573.; 7. Kapoor S, et al. Mayo Clin Proc. 2018;93(12):1810-1824;
8. Telen MJ. Blood Adv. 2020;4(14):3457-3465; 9. Shenoy S. Hematology Am Soc Hematol Educ Program. 2011;2011(1):273-279; 10. Hulbert ML, Shenoy S. Pediatr Blood Cancer. 2018;65(9):e27263; 11. Magnani A, et al. Haematologica. 2020;105(5):1240-1247.

Our approach: Precisely correct the disease-causing mutation in the beta-globin gene to reduce HbS and restore HbA expression



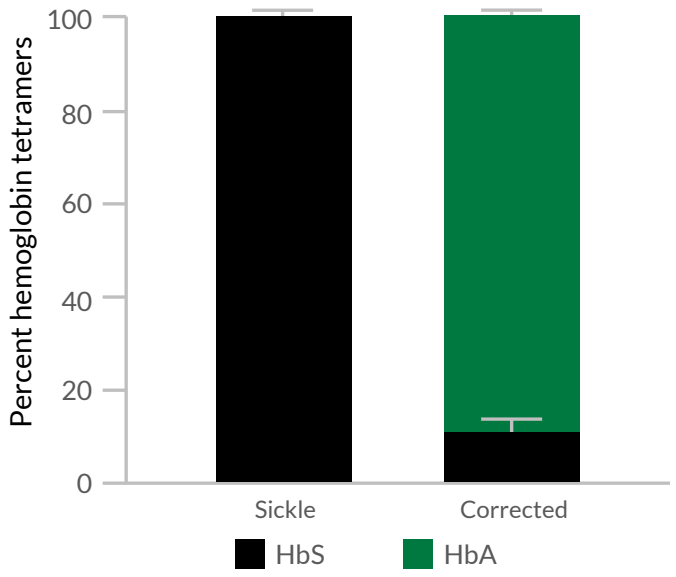
GPH101 preclinical data show potential to restore curative sickle trait biology

High-efficiency gene correction in SCD patient HSPCs[1]



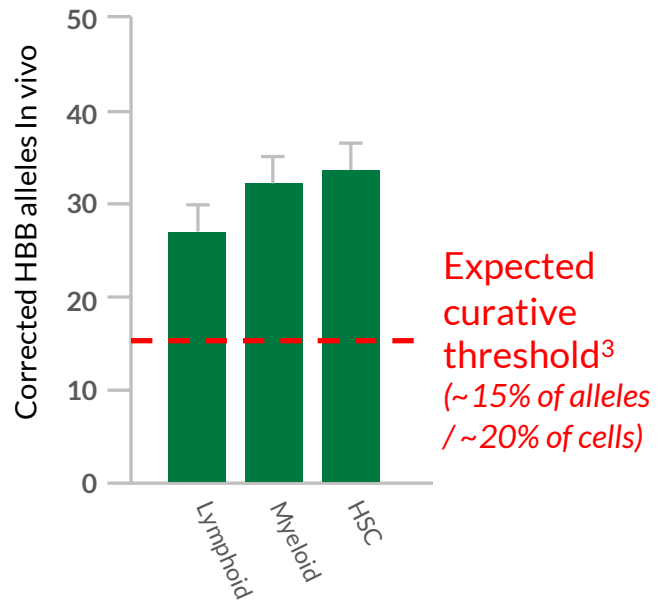
Gene correction efficiency in SCD patient derived HSPCs exceed expected curative threshold
(n=6 experiments, 2 patient donors)

Elimination of HbS and restoration of HbA



RBC differentiation *ex vivo*,
>90% normal hemoglobin4
(n=6 experiments, 2 patient donors)

Corrected stem cells engraft *in vivo* at >2x curative threshold



Edited HSCs show long-term persistence, multilineage production (16 weeks)
(n=7 mice)

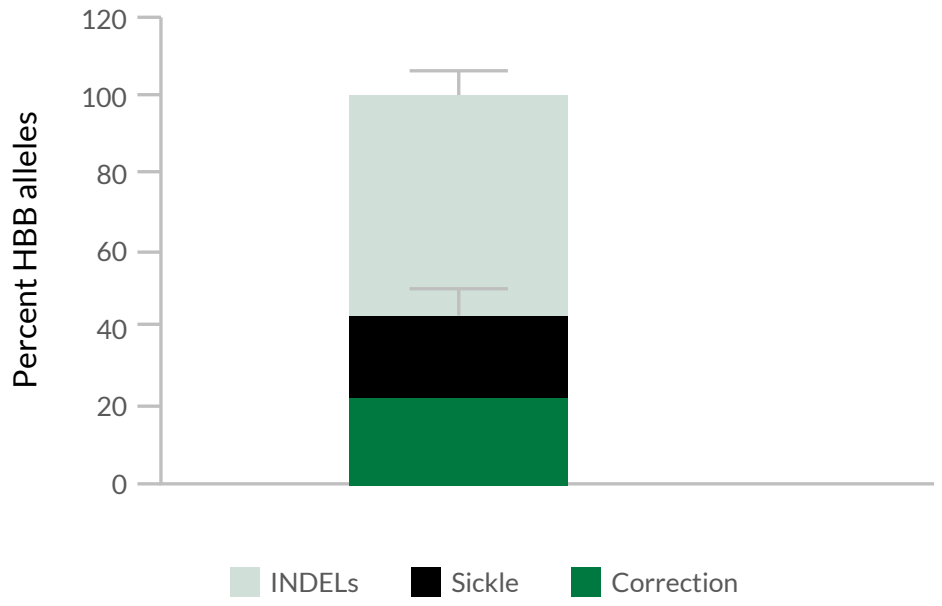
Source: Lattanzi, Roncarolo, Dever, & Porteus. Development of β-globin gene correction in human hematopoietic stem cells as a potential durable treatment for sickle cell disease. Sci. Transl. Med. 13, eabf2444 (2021).

1. HSPCs - CD34+ hematopoietic stem and progenitor cells.
2. HSC - hematopoietic stem cells capable of long-term engraftment and multilineage differentiation.
3. Magnani et al. Extensive multilineage analysis in patients with mixed chimerism after allogeneic transplantation for sickle cell disease: insight into hematopoiesis and engraftment thresholds for gene therapy. Haematologica, (2019). Fitzhugh et al. Blood 2017 Oct 26;130(17):1946-1948. curative threshold approximately 15% alleles / 20% cells.
4. Background HbF not included for ease of comparison. HbS is sickle hemoglobin protein. HbA is normal adult hemoglobin protein.

SCD mice achieving curative gene correction threshold show dramatic improvements in HbA expression

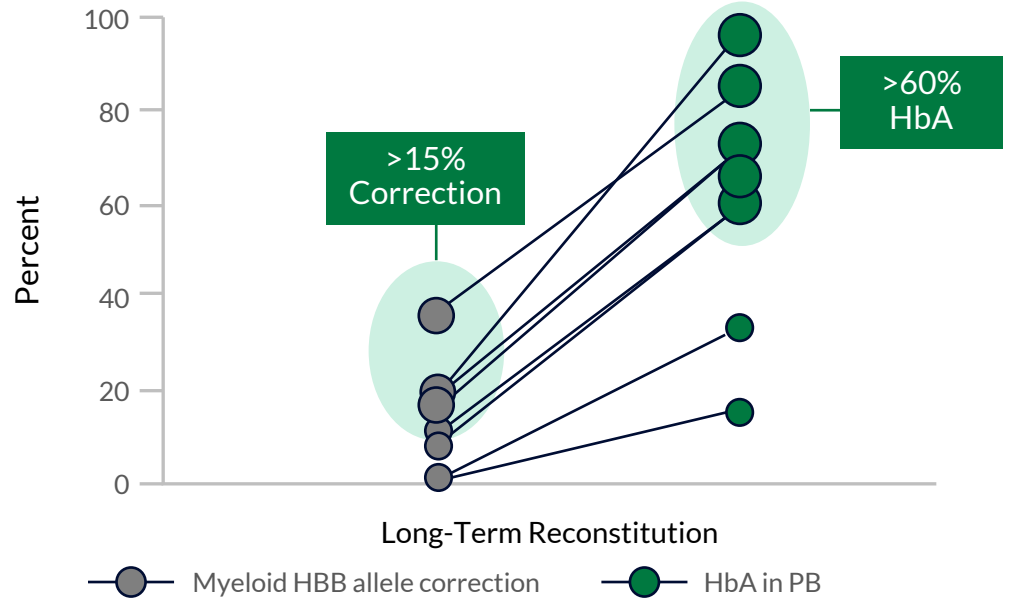
Townes Mouse
(high bar SCD model)

Correct mutation in sickle mouse HSCs



Less efficient than human (process not optimized for mouse cells) (n=8 experiments)

Measure HSC *in vivo* function



1. Gene corrected HSCs engraft (myeloid correction)
2. Survival bias for corrected RBCs leads to ↑HbA

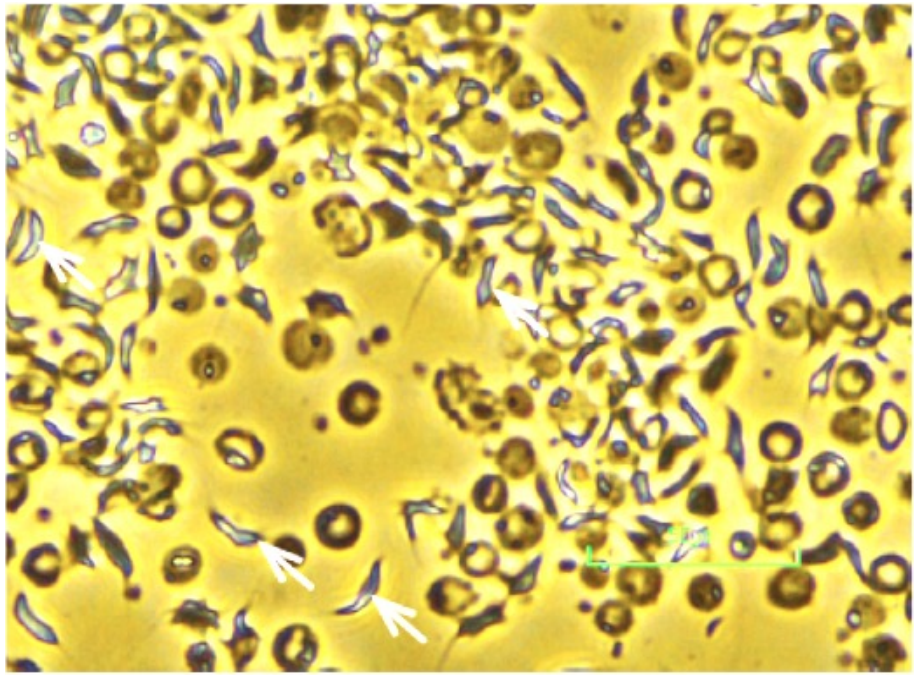
Wilkinson, Dever et al. Cas9-AAV6 gene correction of beta-globin in autologous HSCs improves sickle cell disease erythropoiesis in mice. Nature Communications 12, 686 (2021).

Gene correction eliminates red blood cell sickling

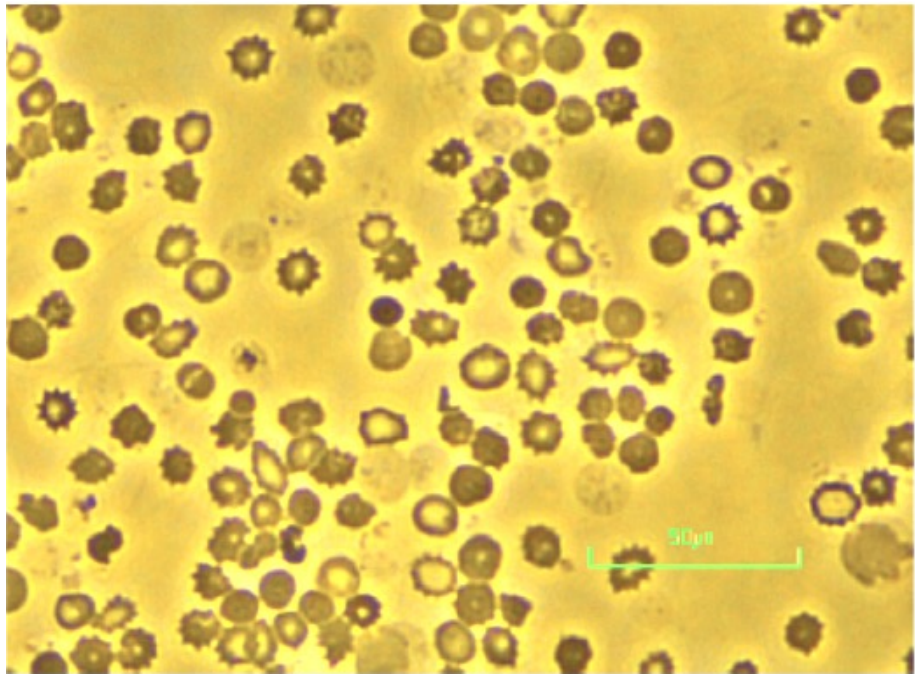
Townes Mouse
(high bar SCD model)

Metabisulphite assay

HBB-Sickle



Mouse A (HBB-corrected)



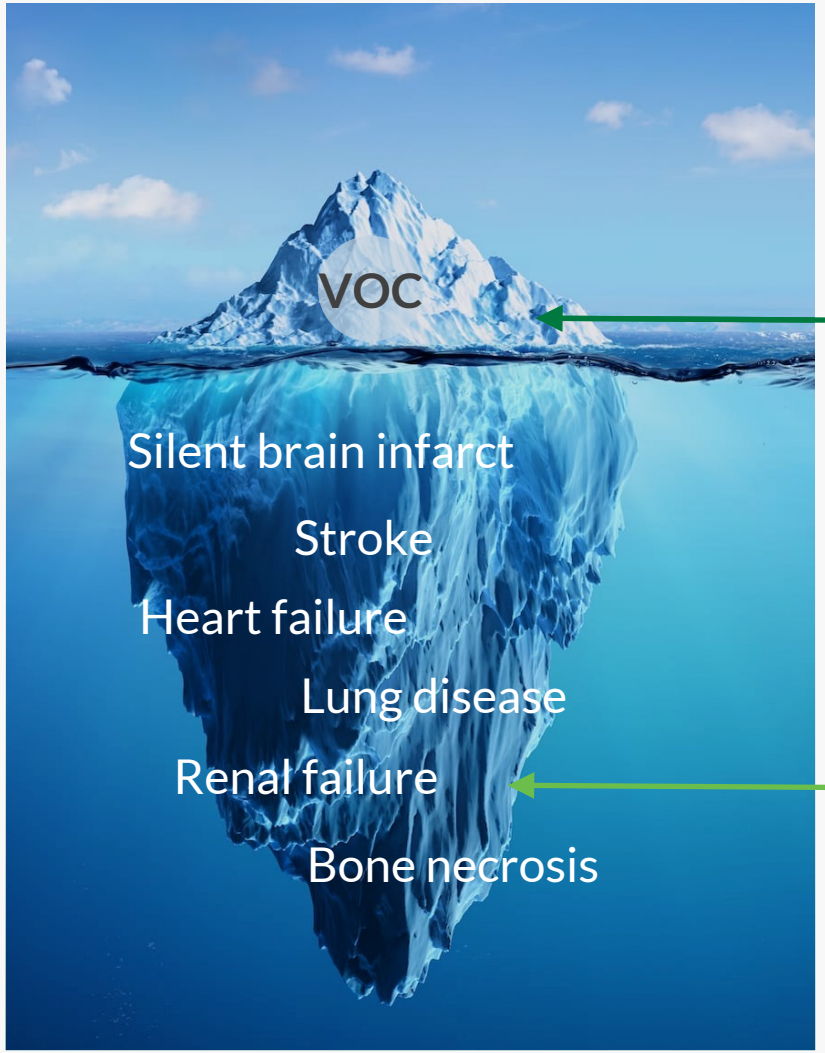
Eliminates sickling and restores normal RBC lifespan[1]

Source Wilkinson, Dever et al. Cas9-AAV6 gene correction of beta-globin in autologous HSCs improves sickle cell disease erythropoiesis in mice. Nature Communications 12, 686 (2021).

1. Red blood cell (RBC) half-life sickle mouse 2.3 days, gene corrected mouse up to 19 days, wild type 25 days (normal from literature ~16 days). Belcher et al., ISRN Oxidative Medicine, 2013, 1-9. Nguyen et al. Phenotypic Characterization of Townes Sickle Mouse. Blood (2014) 124 (21): 4916.

Curing sickle cell requires more than reducing acute pain episodes

Gene correction has the potential to address all SCD morbidities



VOC

- The initial endpoint in clinical trials
- Experienced by some patients
- Reduction/elimination only addresses the tip of the iceberg of SCD morbidities

Organ Damage

- Leading indication for referral to transplant (stroke and silent infarct prevention)
- Leading cause of death among SCD complications
- No effective treatments

Outcomes from allo-HSCT
(with normal or sickle trait donor)

Reduction/
elimination of VOC

+

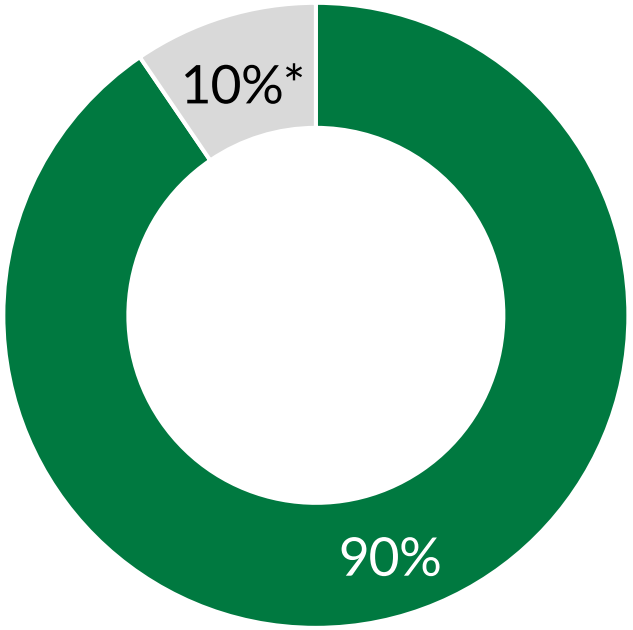
Prevention of progressive organ damage

=

CURE

allo-HSCT, allogeneic hematopoietic stem cell transplant; SCD, sickle cell disease; VOC, vaso-occlusive crisis.

Gene correction to restore HbA expression viewed as the ideal genetic outcome by KOLs and physicians



- Most preferred gene correction as it could **correct the underlying sickle cell mutation** by converting HbS production to HbA
- Gene correction seen as potentially more efficacious and durable

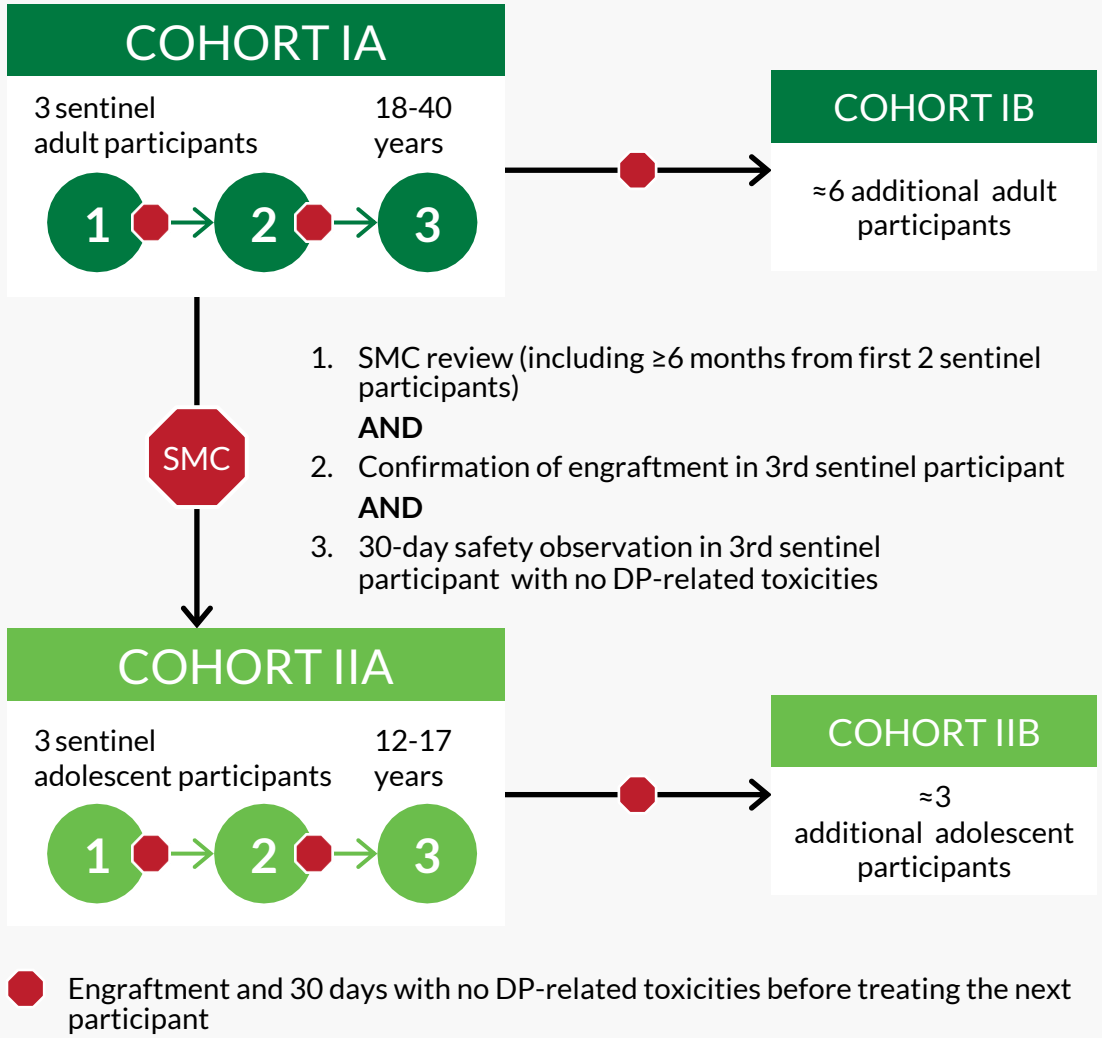
> Correction of the sickle cell mutation to normal hemoglobin A – this is the ideal genetic outcome.

– KOL at Graphite Bio's SCD Gene Correction Webinar

N = 21 (16 KOLs, 5 physicians) who treat SCD. KOLs and physicians were probed on the theoretical treatment strategy and were not shown efficacy or safety data. *Those who did not select gene correction expressed uncertainty around probability of technical success.
HbA, adult hemoglobin; HbS, sickle hemoglobin; KOL, key opinion leader; SCD, sickle cell disease.

GPH101 Phase 1/2 CEDAR clinical trial design

CEDAR



Primary Objective

Evaluate the safety of treatment with GPH101 in participants with severe SCD

Secondary Objectives

Evaluate the efficacy and pharmacodynamics of treatment with GPH101 in participants with severe SCD

- Levels of HbA, HbS, and total Hb
- Measurements of peripheral myeloid gene correction in cells
- Episodes of VOC and ACS following GPH101 infusion

Exploratory Objectives

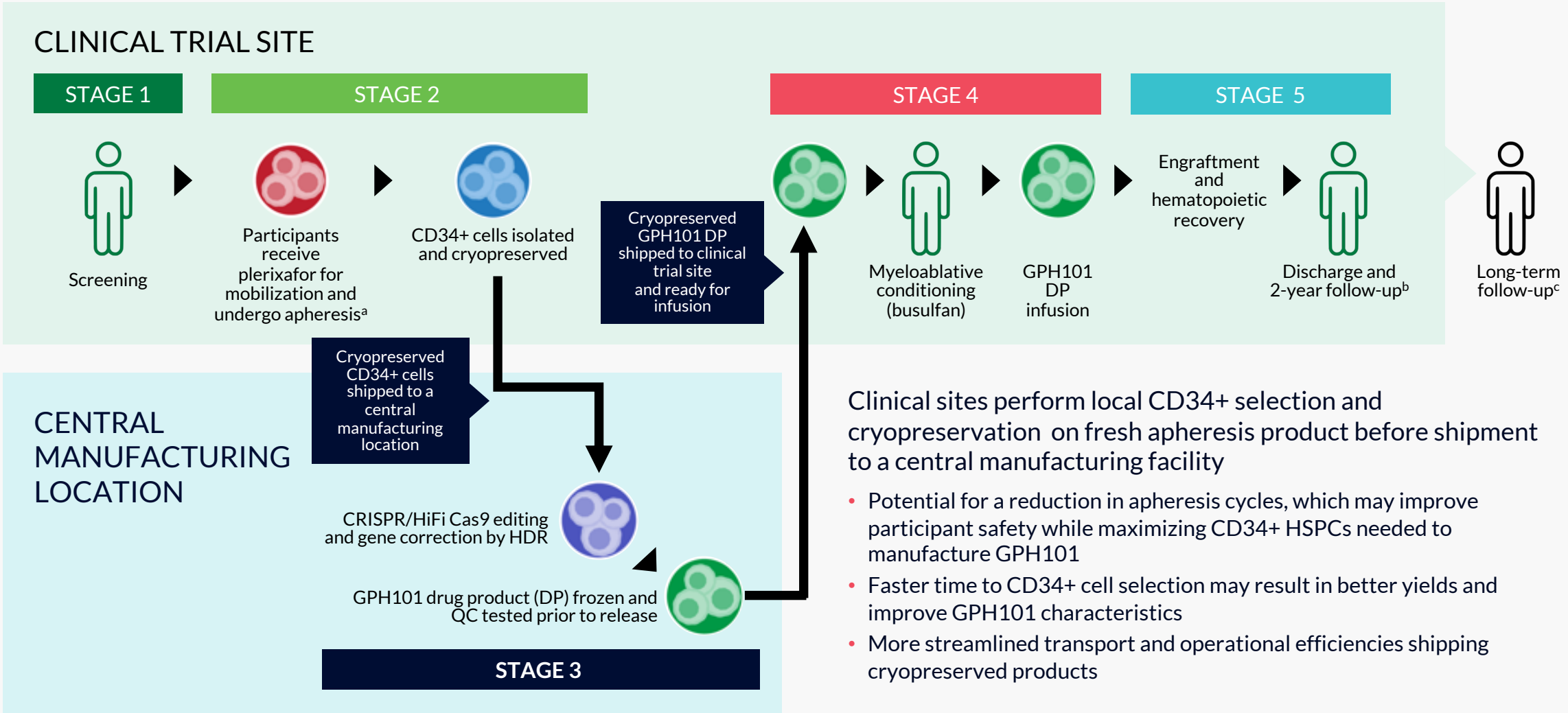
Evaluate PROs, erythrocyte function, characterization of gene correction rates, and change from baseline in select SCD characteristics and organ function

- Cerebral hemodynamics and oxygen delivery (by MRA/MRI)
- Improvements in SCD-related events and changes in organ function (e.g., heart, brain, kidney, liver)
- Measurements of RBC health and function
- Characterization of gene correction rates

ACS, acute chest syndrome; Hb, hemoglobin; HbA, adult hemoglobin; HbS, sickle hemoglobin; MRA/MRI, magnetic resonance angiography/magnetic resonance imaging; PRO, patient-reported outcome; RBC, red blood cell; SCD, sickle cell disease; SMC, Safety Monitoring Committee; VOC, vaso-occlusive crisis.

Kanter J, et al. ASH 2021. Poster 1864.

GPH101 treatment process



Clinical sites perform local CD34+ selection and cryopreservation on fresh apheresis product before shipment to a central manufacturing facility

- Potential for a reduction in apheresis cycles, which may improve participant safety while maximizing CD34+ HSPCs needed to manufacture GPH101
- Faster time to CD34+ cell selection may result in better yields and improve GPH101 characteristics
- More streamlined transport and operational efficiencies shipping cryopreserved products

a Backup cells kept at site as a safety measure. b Patients will be followed for 24 months after GPH101 infusion with physical exams, laboratory and imaging assessments, and adverse event evaluations. c Patients who receive GPH101 will be followed for 13 years in a long-term follow-up study.
Cas9, CRISPR-associated protein 9; CD34, cluster of differentiation 34; CRISPR, clustered regularly interspaced short palindromic repeats; DP, drug product; HDR, homology directed repair; HiFi, high fidelity; HSPC, hematopoietic stem and progenitor cell; QC, quality control.

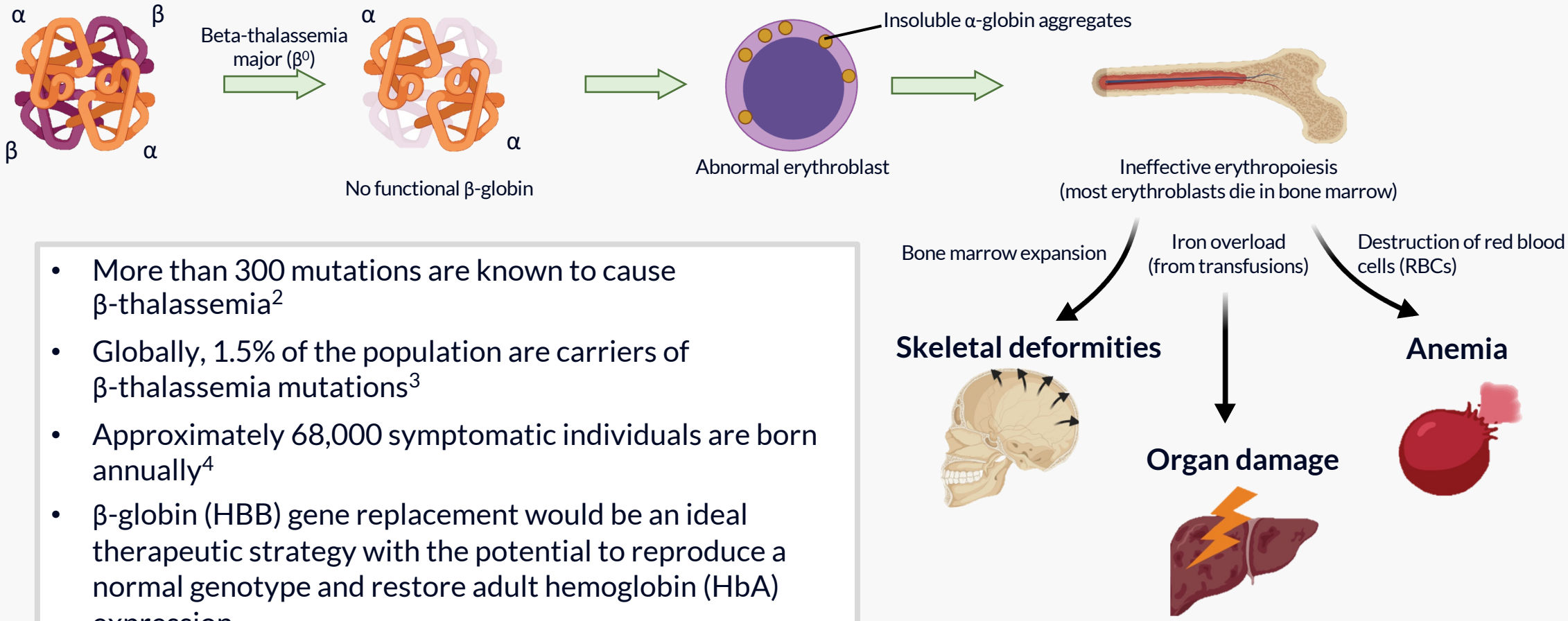
Gene correction is highly differentiated from indirect approaches and has high potential for cure

	Cure with allo-HSCT	Gene correction with GPH101	CRISPR HbF induction	Base editing conversion to variant
Directly corrects the SCD-causing genetic mutation	✓	✓	✗	✗
Restores normal HbA expression	✓	✓	✗	✗
Directly reduces HbS production	✓	✓	✗	✓
Reduce/eliminate VOCs	✓	*Initial POC data anticipated in 2023*	✓	Unknown
Normalize function in all RBCs	✓		Unknown	Unknown
Prevent progression of end organ damage	✓		Unknown	Unknown

allo-HSCT, allogeneic hematopoietic stem cell transplant; HbA, adult hemoglobin; HbF, fetal hemoglobin; HbS, sickle hemoglobin; POC, proof-of-concept; RBC, red blood cell; SCD, sickle cell disease; VOC, vaso-occlusive crisis.

Gene Replacement and Targeted Gene Insertion Programs

β-thalassemia is a genetic disorder with high unmet need characterized by reduced production of β-globin1



- More than 300 mutations are known to cause β-thalassemia[2]
- Globally, 1.5% of the population are carriers of β-thalassemia mutations[3]
- Approximately 68,000 symptomatic individuals are born annually[4]
- β-globin (HBB) gene replacement would be an ideal therapeutic strategy with the potential to reproduce a normal genotype and restore adult hemoglobin (HbA) expression

1. Beta thalassemia. National Organization for Rare Diseases (NORD). https://rarediseases.org/rare-diseases/thalassemia-major/; 2. Taher AT, et al. *N Engl J Med*. 2021;384(8):727-743; 3. Galanello R and Origa R. *Orphanet J Rare Dis*. 2010;5:11; 4. Origa R. *Genet Med*. 2017;19(6):609-619.
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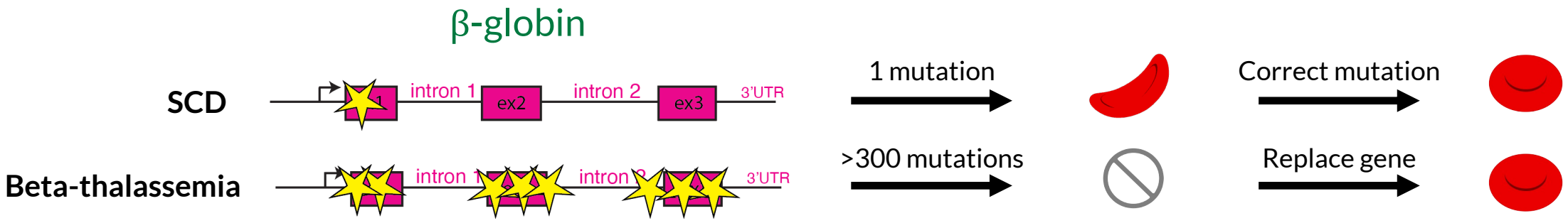
Beta-thalassemia gene replacement: Targeting the beta-globin gene to restore HbA expression

Harnessing synergies across our UltraHDR™ platform to uniquely restore gene function



About beta-thalassemia

- Inherited blood disorder characterized by reduced levels of functional hemoglobin[1]
- Caused by more than 300+ mutations in the beta-globin gene[2]
- ~68,000 people born with disease each year worldwide[3]
- Individuals with severe disease begin receiving medical attention between 6-24 months of age[3]
- 80-90 million people around the world reported to be carriers[3]

Urgent medical need

- Results in anemia requiring frequent red blood cell transfusions, with severe patients needing blood every 2-4 weeks[4]
- 70% of deaths are caused by cardiac complications due to iron overload, as a result of the chronic blood transfusions[4]

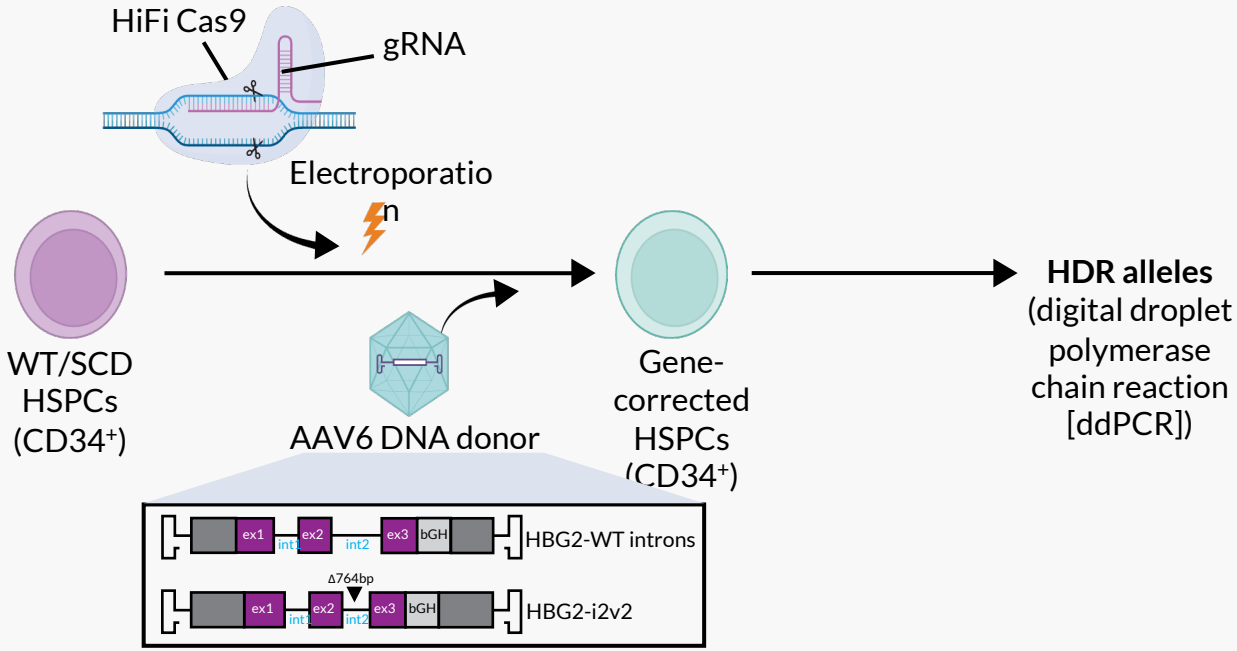
Synergistic with SCD gene correction program

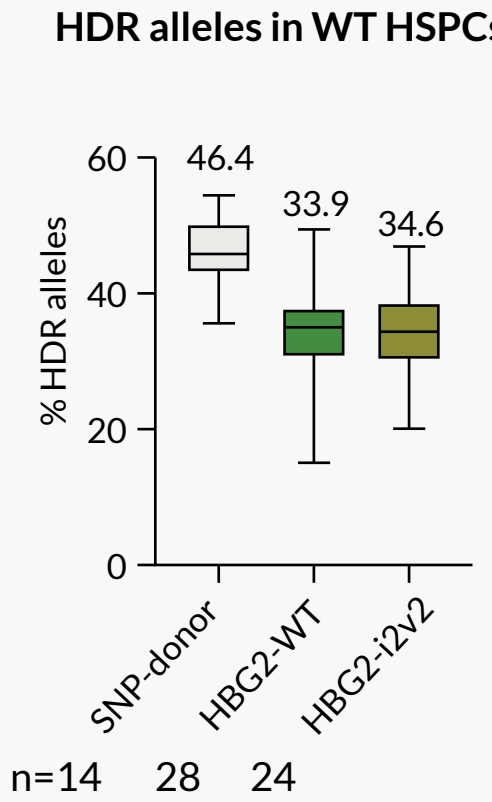
- Complementary benign hematology patient population
- Identical gRNA and HiFi Cas9 gene editing components

HbA, adult hemoglobin; SCD, sickle cell disease.

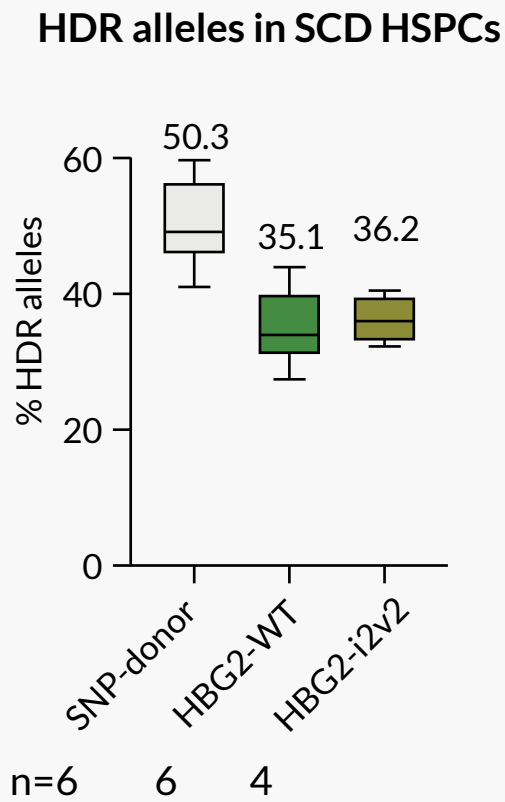
1. Beta thalassemia. National Organization for Rare Diseases (NORD). https://rarediseases.org/rare-diseases/thalassemia-major/. 2. Taher AT, Musallam KM, Cappellini MD. β-Thalassemias. N Engl J Med. 2021;384(8):727-743.
3. Origa R. β-Thalassemia. Genet Med. 2017;19(6):609-619. 4. Galanello, R., Origa, R. Beta-thalassemia. Orphanet J Rare Dis. 2010;5(11):1750-1172.

β-globin gene replacement is effective in both healthy and SCD patient HSPCs





WT HSPC donors: 10

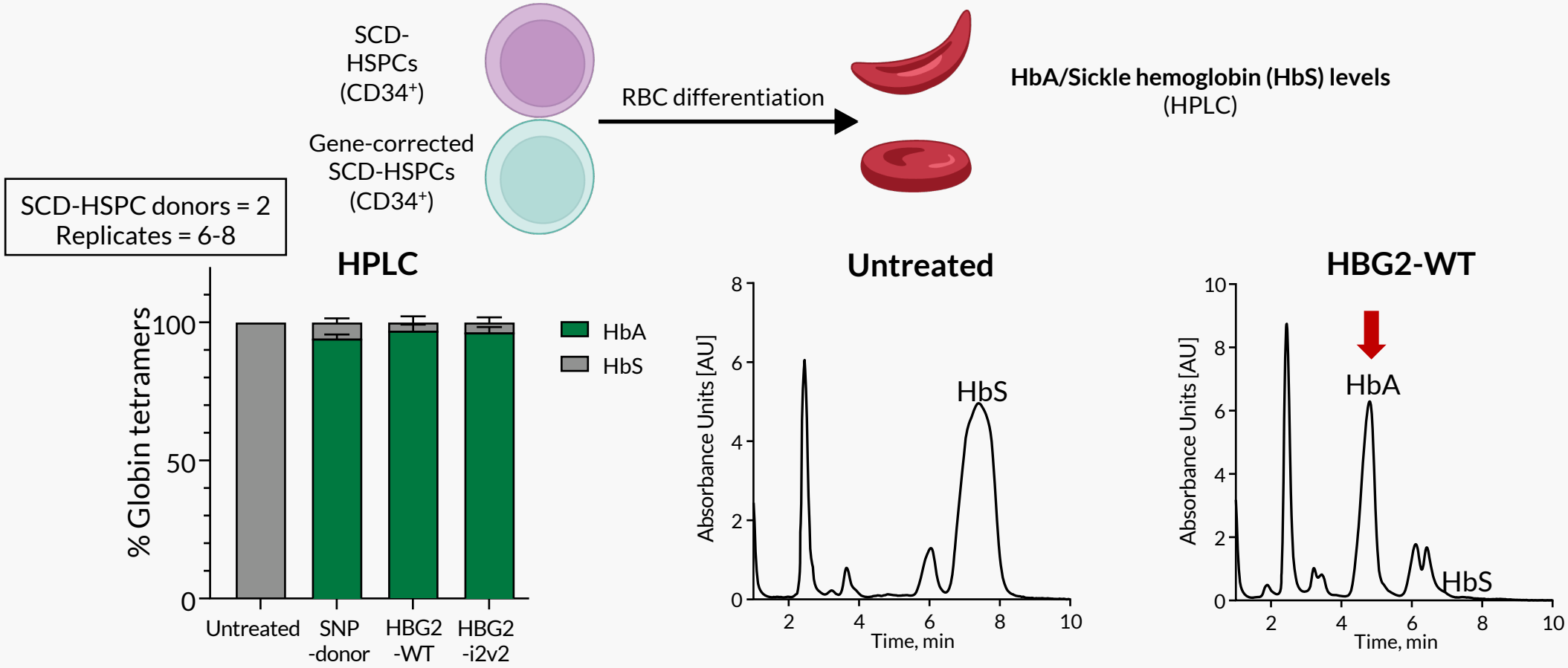


SCD HSPC donors: 2

HSPCs from sickle-cell patients serve as a surrogate for β-thalassemia patient HSPCs

Similar frequencies of HDR are achieved in HSPCs derived from healthy volunteers and from patients with sickle cell disease

β-globin gene replacement restores adult hemoglobin (HbA) expression in patient SCD-HSPCs

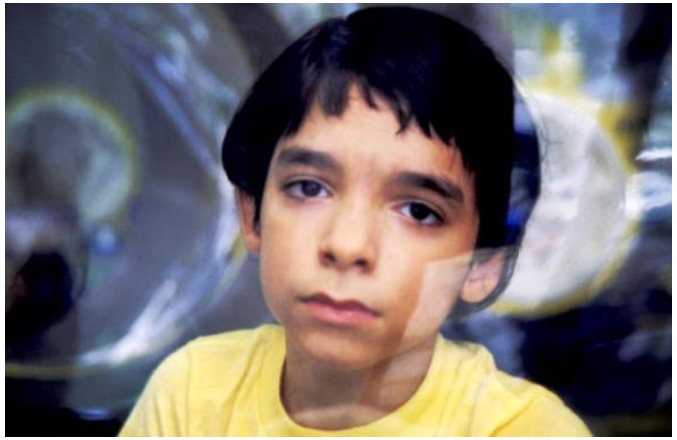


HBB gene replacement using the optimized DNA donors restored HbA expression to a level comparable to a SCD point mutation-correction strategy

XSCID gene replacement: Potential to address a serious rare disease and demonstrate broad utility of platform

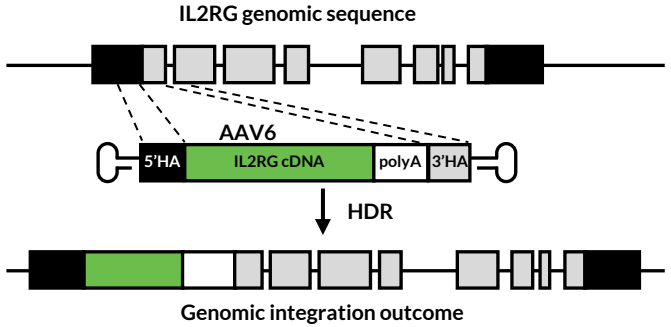
High unmet need

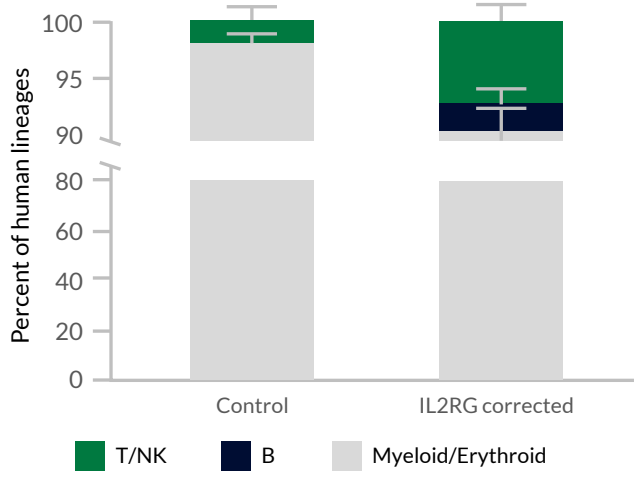
- IL-2 receptor common gamma (IL2RG) mutations severely impair T/B/NK cell function
- Severe unmet need: lifespan without treatment ~2 years[1]
- Allogeneic HSCT is only cure
- 45 births per year in major markets[2]



Gene replacement approach[3]

Ideal strategy due to multiple mutations in IL2RG





Unlocks new and larger opportunities

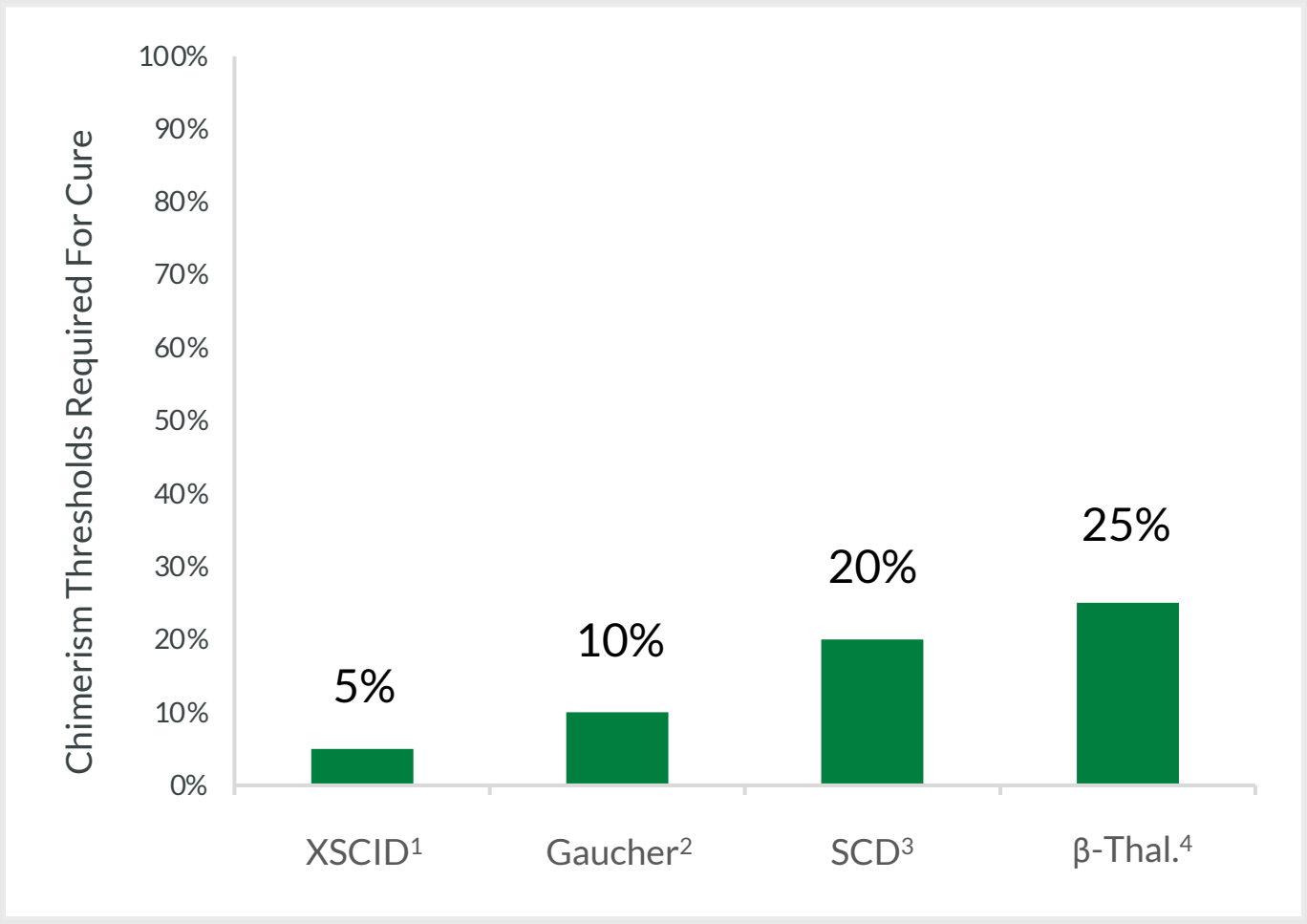
- Beta-thalassemia
- Auto-inflammatory syndromes
- Immunodeficiencies

Non-genotoxic HSC targeted antibody conditioning

Option to conduct XSCID clinical trial with JSP191 (AMG191), an anti-CD117 HSC-targeting mAb

1. Fischer, A et. al. Severe Combined Immunodeficiencies and Related Disorders. Nature Reviews Disease Primers 1, no. 1 (December 17, 2015): 15061.
2. Wall Street Analyst reports (JPMorgan, Cowen, Leerink, Morgan Stanley, HC Wainwright).
3. Dinu, Roncarolo, Porteus et. al. Gene correction for SCID-X1 in long-term hematopoietic stem cells. Nature Communications. (2019)10:1634.

Developing non-genotoxic conditioning (NGTC) regimens to enable more patients to benefit from potential one-time HSC-based cures



NGTC Conditioning: Strategic Considerations and Initial Plans

- Collaboration with Jasper on JSP191 in XSCID
- Ongoing assessment to identify additional partnering opportunities
- Building internal capabilities led by management team expertise in immunology and antibody development

HSC, hematopoietic stem cell.

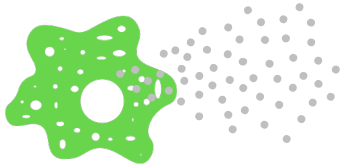
1. Dvorak, CC, et al. Low Exposure Busulfan Conditioning to Achieve Sufficient Multilineage Chimerism in Patients with Severe Combined Immunodeficiency. Biology of Blood and Marrow Transplantation 25, no. 7 (Jul 2019): 1355–62.
2. Chan et al. BMT in Gaucher's disease: effect of mixed chimeric state. Bone Marrow Transplant. 14, 327–330 (1994) and Ringden et al. 10 years' experience of BMT for Gaucher disease. Transplantation 59, 864–870 (1995).
3. Fitzhugh et al. At least 20% donor myeloid chimerism is necessary to reverse the sickle phenotype after allogeneic HSCT. Blood 2017 Oct 26;130(17):1946-1948.
4. Lisini, D., et al. Donor/Recipient Mixed Chimerism Does Not Predict Graft Failure in Children with β-Thalassemia given an Allogeneic Cord Blood Transplant from an HLA-Identical Sibling. Haematologica 93, no. 12: 1859–67.

Beyond genetic blood and immune disease: Targeted gene insertion to enable potentially permanent therapeutic protein production

CCR5 locus – Tissue specific protein production
(exogenous promoter)

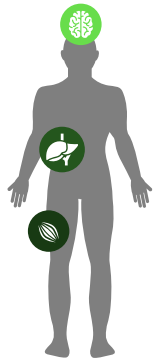
Targeted gene insertion

Lineage-specific expression



macrophage

Organ-specific expression



Lysosomal storage diseases

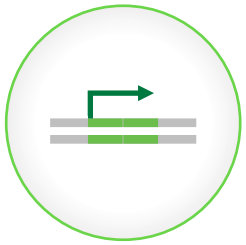
- **Gaucher***
- MPS*
- Krabbe*
- Pompe
- Fabry

CNS therapeutic protein delivery

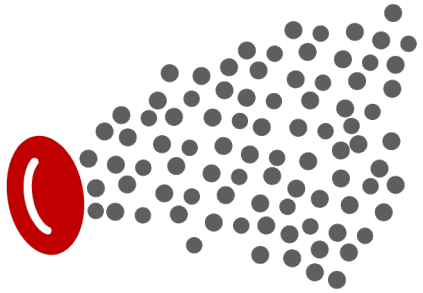
- GBA Parkinson's
- Progranulin
- Antibodies

α-globin locus – produce high plasma protein levels
(endogenous promoter)

Targeted gene insertion



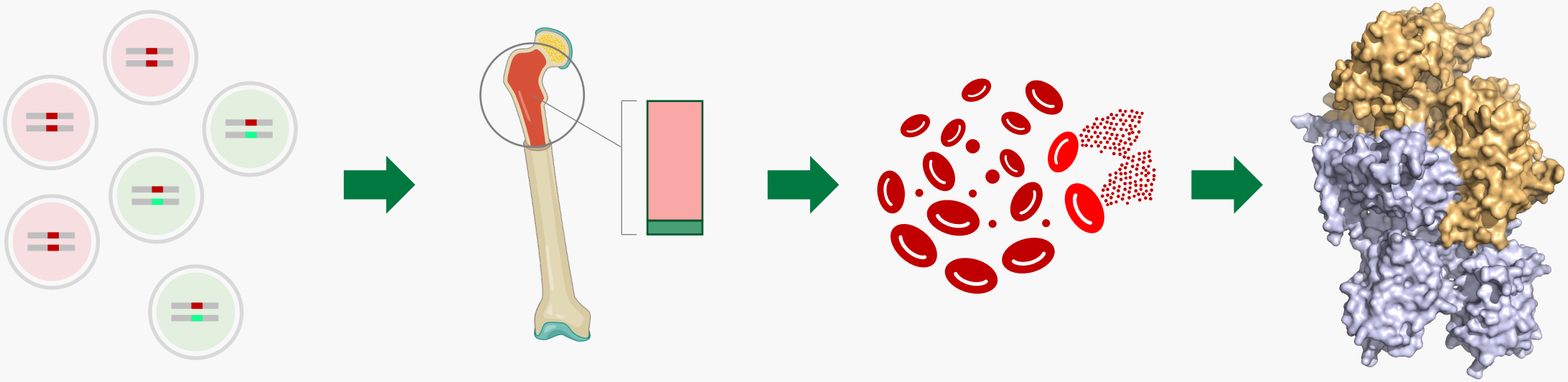
RBC-specific expression



- **Alpha-1 antitrypsin (AAT) deficiency**
- Hemophilia A/B
- Beta-thalassemia*
- PKU

*Published animal or in vitro data from Porteus lab

α-globin Locus: Designed for high integration efficiency, strong lineage-specific promoter



cDNA integration ▶ Engraftment ▶ RBC protein factories ▶ Protein production
> AAT, mAbs, FVIII, FIX, PKU

Graphite Bio: Realizing the full promise of gene editing

Powerful Next-Generation UltraHDR™ Gene Editing Platform

- Harnessing the power of **high-efficiency homology directed repair** to fulfill the original goal of CRISPR gene editing
- "Find & replace" genes anywhere in the genome – correct, replace, insert
- Preclinical validation across a wide range of cell types and diseases

Robust Pipeline of Potential One-Time Cures

- Initial focus on HSC-based cures for serious and life-threatening diseases
- **First-in-industry approach to directly correct** the sickle cell mutation
- R&D programs designed to validate broad platform capabilities

Poised to Deliver for Patients

- Founded by Stanford University genetic medicine pioneers
- Experienced management team and board with track record of developing innovative therapies
- $352.1 million in cash, cash equivalents and investments in marketable securities (as of 3/31/2022); cash runway into 4Q 2024

HSC, hematopoietic stem cell; R&D, research and development.

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