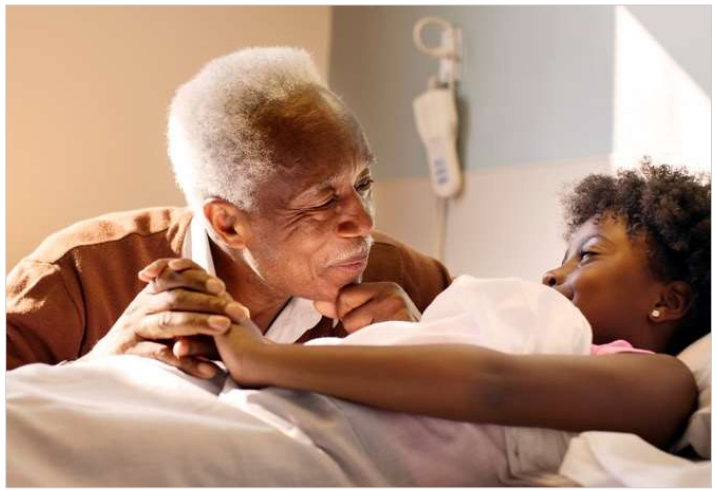
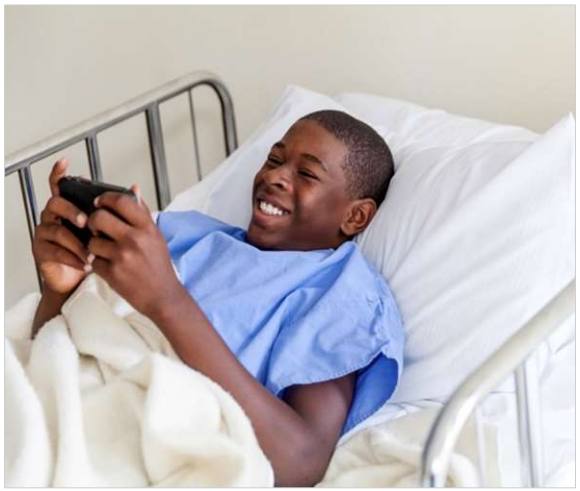




EDIT-301 Shows Promising Preliminary Safety and Efficacy Results in the Phase I/II Clinical Trial (RUBY) of Patients With Severe Sickle Cell Disease Using Highly Specific and Efficient AsCas12a Enzyme

Rabi Hanna, *Haydar Frangoul, Christopher McKinney, Luis Pineiro, Markus Mapara, Kai-Hsin Chang, Michael Jaskolka, Keunpyo Kim, Maha Rizk, Olubunmi Afonja, Adebayo Lawal, Mark Walters;* ***on behalf of Ruby study investigators***

EHA 2023 Hybrid Congress
Frankfurt, Germany
10 June 2023

editas MEDICINE

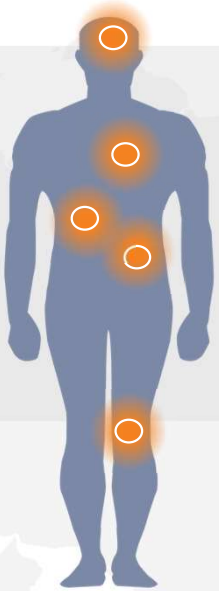
Disclosures

Dr. Rabi Hanna

- Consultant for Sanofi, AbbVie, and Cellularity
- Speaker bureau for Sobi

SCD Is an Inherited Life-Threatening Hematological Disorder Manifesting Shortly After Birth

SCD is a genetic blood disorder caused by mutations in the ***HBB* gene** that cause sickling of RBCs; this leads to **anemia, hemolysis, and VOEs**[1,2]



Lifelong complications, multi-organ damage, and comorbidities impact patient quality of life[1,2]

It is estimated that approximately **50%** of patients with HbSS **die before 45 years** of age[3]

SCD AFFECTS[4,5,6]

~6M

PEOPLE GLOBALLY

300K+

BABIES BORN WITH SCD PER YEAR GLOBALLY

~100K

PEOPLE IN THE U.S.

Although advances in supportive care and disease modifying therapies have improved outcomes for patients with SCD, **curative therapies** have been **limited to allogeneic HCT**

HBB, β-globin gene; HbSS, homozygous for the sickle cell mutation; HCT, hematopoietic cell transplantation; RBC, red blood cell; SCD, sickle cell disease; VOE, vaso-occlusive event.

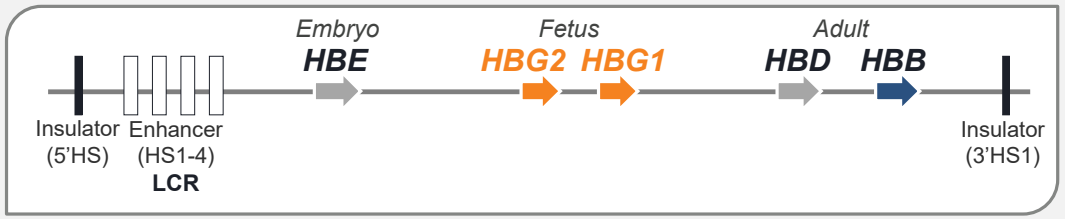
1. Kato GJ *et al. Nat Rev Dis Primers* 2018; 4: 18010. 2. Williams TN *et al. Annu Rev Genomics Hum Genet 2018; 19: 113–147.* 3. Platt OS *et al. NEJM* 1994;330:1639–44. 4. Sickle Cell Disorders. Available at: https://www.thelancet.com/pb-assets/Lancet/gbd/summaries/diseases/sickle-cell-disorders.pdf. Accessed June 2023. 5. Wastnedge E *et al. J Glob Health 2018; 8 (2): 021103.* 6. Sickle Cell Disease. Available at: https://www.nhlbi.nih.gov/health/sickle-cell-disease. Accessed June 2023.

EDIT-301 Employs AsCas12a to Edit *HBG1* and *HBG2* Promoters, Leading to HbF Induction

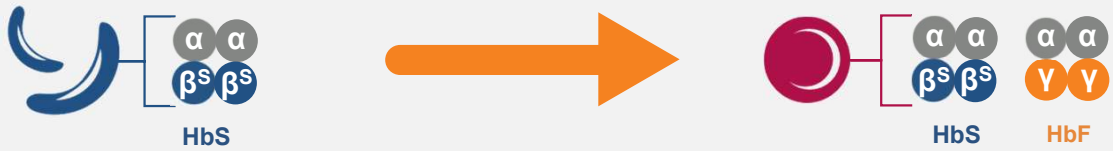
Utilizing proprietary **AsCas12a** to edit with high efficiency and minimize off-targets[1]

Targeting ***HBG1 and HBG2*** promoters to mimic naturally occurring mechanisms of HPFH[2]

β-globin locus



Adapted from Canver *et al*. 2016.



Higher percentages of HbF are associated with a reduction in SCD events[3]

Naturally occurring HbF-inducing mutations in HPFH predict the clinical relevance and safety of editing at the *HBG1* and *HBG2* promoters

AsCas12a, Acidaminococcus sp CRISPR-associated protein 12a; CRISPR, clustered regularly interspaced short palindromic repeats; *HBB*, β-globin gene; *HBD*, δ-globin gene; *HBE*, embryonic hemoglobin gene; HbF, fetal hemoglobin; *HBG*, γ-globin gene; HbS, sickle hemoglobin; HPFH, hereditary persistence of fetal hemoglobin; HS, hypersensitive site; LCR, locus control region; SCD, sickle cell disease.

1. Zhang L *et al. Nat Commun* 2021; 12 (1): 4500. 2. Canver MC *et al. Blood* 2016; 127 (21): 2536–2545. 3. Powars DR et al. Blood 1984; 63 (4): 921–928.

Ruby Study of EDIT-301 in Patients With Severe SCD

Design

- Phase 1/2
- International, multicenter
- Open-label, single-arm study
- 24 months of follow-up post-EDIT-301 infusion

Key Inclusion Criteria

- ~40 patients between 18–50 years of age
- Diagnosis of severe SCD (β^S/β^S, β^S/β^0, or β^S/β^+)
- History of ≥2 severe VOEs per year in previous 2 years

Key Exclusion Criteria

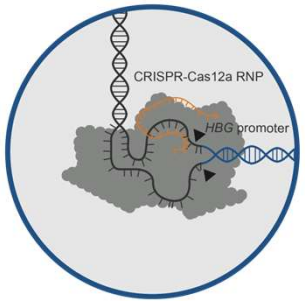
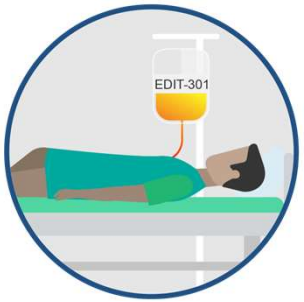
- Available genetically-matched (10/10 HLA) related donor
- Previous or current malignancy or immunodeficiency disorder
- Unable to tolerate stem cell therapy or receive RBC transfusion

Key Endpoints

- Proportion of patients achieving complete resolution of severe VOEs
- Safety and tolerability of EDIT-301

β, β-globin allele; HLA, human leukocyte antigen; RBC, red blood cell; SCD, sickle cell disease; VOE, vaso-occlusive event.
ClinicalTrials.gov NCT04853576. Available at: https://clinicaltrials.gov/ct2/show/NCT04853576. Accessed May 2023.

Patient Journey in the Ruby Study

SCREENING	MOBILIZATION & APHERESIS	DRUG PRODUCT MANUFACTURING	MYELOABLATION & EDIT-301 INFUSION	ENGRAFTMENT & 24 MONTH FOLLOW-UP
				
Obtain consent and screen patients	HSPC mobilization and apheresis	CD34⁺ cells edited at *HBG1* and *HBG2* promoters with CRISPR-AsCas12a	Busulfan myeloablation and EDIT-301 drug product infusion	24-month follow-up for primary endpoint

AsCas12a, Acidaminococcus sp CRISPR-associated protein 12a; CD, cluster of differentiation; CRISPR, clustered regularly interspaced short palindromic repeats; *HBG*, γ-globin gene; HSPC, hematopoietic stem and progenitor cells.
Editas Medicine. Data on file.

Demographics and Baseline Characteristics

DEMOGRAPHICS	EDIT-301 (N = 4)
Genotype, n	
β^S/β^S	4
Sex, n	
Male	2
Female	2
Age (years), median (min–max)	27.5 (25–31)
VOEs pre-study annual rate, median (min–max)	4.8 (3–6)
LIC (mg/g of liver), median (min–max)	4.2 (2.5–14.9)

Treated patients are homozygous for the HbS mutation and have a high pre-enrollment annual rate of VOEs

Data cutoff May 2023.
β, β-globin allele; HbS, sickle hemoglobin; LIC, liver iron concentration; VOE, vaso-occlusive event.
Editas Medicine. Data on file.

All Treated Patients Successfully Engrafted and Have No VOEs

	PATIENT 1	PATIENT 2	PATIENT 3	PATIENT 4
EDIT-301 Total CD34^{+} (10^6/kg)	10.0	4.0	4.1	3.7
Neutrophil Engraftment (day)*	23	29	23	24
Platelet Engraftment (day)†	19	37	23	28
Follow-up Duration (months)	10	6	3	2
VOEs Post-EDIT-301 Infusion	None	None	None	None

Data cutoff May 3, 2023.
*Three consecutive measurements with absolute neutrophil count (ANC) ≥0.5 × 10^9/L. †Three consecutive measurements with platelet count ≥50 × 10^9/L starting at least 7 days after the last platelet transfusion, and 10 days after thrombopoietin.
CD, cluster of differentiation; VOE, vaso-occlusive event.
Editas Medicine. Data on file.

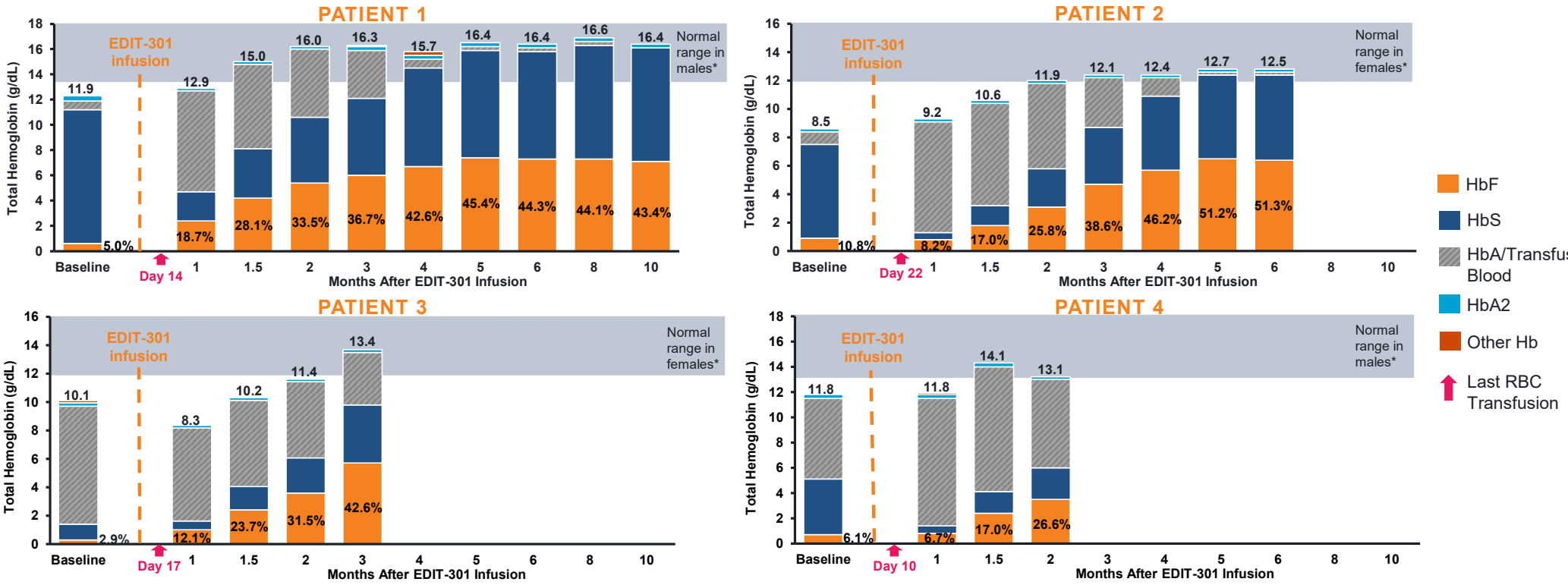
Safety Profile of EDIT-301 Is Consistent With That of HSCT and Myeloablative Conditioning With Busulfan

- Majority of TEAEs (E = 26) occurred within first 30 days after EDIT-301 infusion
- No TEAEs were reported as related to EDIT-301
- No TESAEs occurred after EDIT-301 infusion

TEAE CATEGORY	EDIT-301 (N = 4)	
	Number of patients	Number of events
Any TEAE	4	43
Any TESAE	0	0
Any TEAE related to EDIT-301	0	0
Any TEAE related to busulfan	4	19
Any EDIT-301-related TEAE leading to discontinuation of EDIT-301	0	0
Any EDIT-301-related TEAE leading to discontinuation of study	0	0
Any TEAE leading to death	0	0

Data cutoff May 2023.
Grade 3 TEAEs related to busulfan: n=2, Preferred Term "mucosal inflammation". Grade 3 TEAEs unrelated to busulfan or EDIT-301: n=1, Preferred Term "blood bilirubin unconjugated increased".
E, number of events; HSCT, hematopoietic stem cell transplantation; TEAE, treatment emergent adverse event; TESAE, treatment emergent serious adverse event.
Editas Medicine. Data on file.

Patients Show Clinically Meaningful Improvements in HbF Levels With Total Hb Returning to the Normal Range in as Early as 4 Months



Markers of hemolysis (reticulocyte count, indirect bilirubin, lactate dehydrogenase, and haptoglobin) displayed a trend of **improvement** or have **normalized** in treated patients

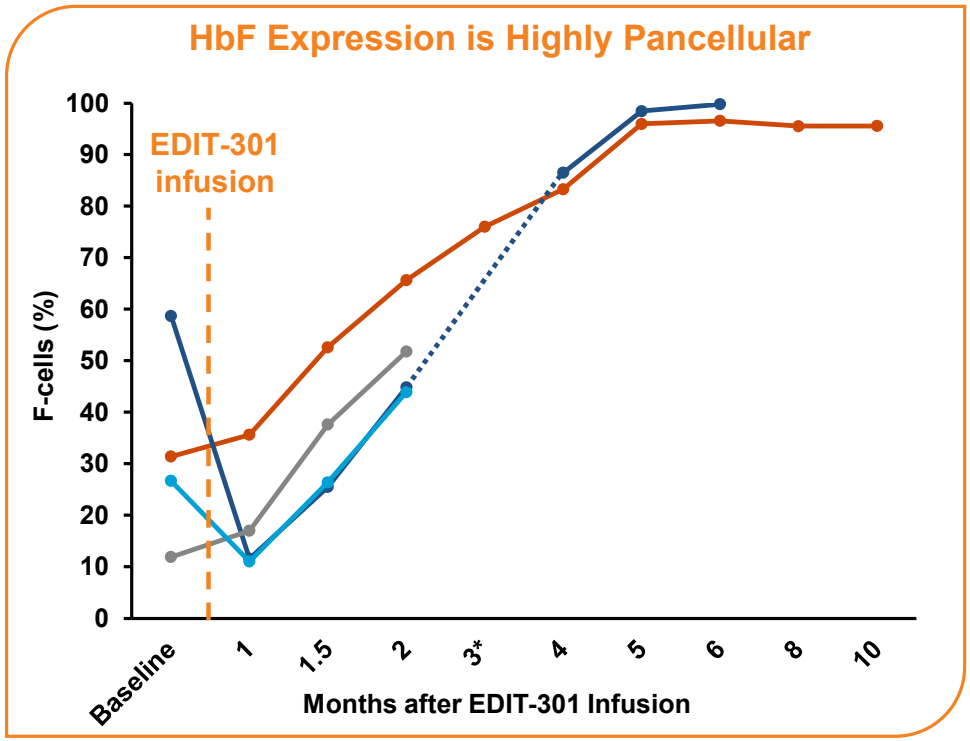
Bars show mean Hb (g/dL). Labels inside / to the right of the bars indicate mean proportion of HbF as a percentage of total Hb. Mean total Hb concentrations are shown directly above bars. Data cutoff May 3, 2023 for all timepoints except Month 3 for Patient 3, which was retrieved on May 12, 2023.

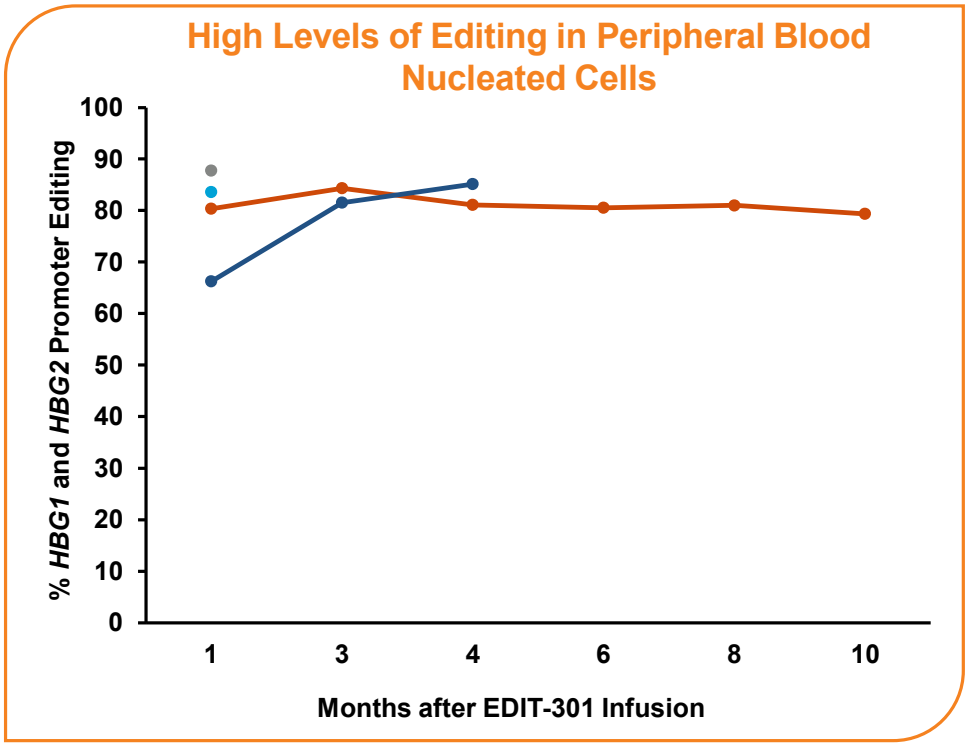
*Normal total hemoglobin range 13.6–18.0 g/dL for male patients and 12.0–16.0 g/dL for female patients. Central laboratory reference range. Data on file.

Hb, hemoglobin; HbF, fetal hemoglobin; HbS, sickle hemoglobin; HbA, adult hemoglobin; RBC, red blood cell.

Editas Medicine. Data on file.

Patients Show Pancellular Expression of HbF in RBCs and High Levels of Editing in Peripheral Blood Nucleated Cells Post-EDIT-301 Infusion





An increasing percentage of F-cells indicates that more RBCs are protected from sickling for potential clinical benefit

Persistent, high levels of editing in peripheral blood nucleated cells indicate robust editing of HSPCs, predicting durable clinical benefit

Patient 1 Patient 2 Patient 3 Patient 4

Data cutoff May 3, 2023.
*Data for Patient 2 at Month 3 post-EDIT-301 infusion are not available due to sample quality (hemolyzed sample).
HbF, fetal hemoglobin; HSPC, hematopoietic stem and progenitor cells; RBC, red blood cell.
Editas Medicine. Data on file.

Summary

EDIT-301 is a gene-edited autologous hematopoietic stem cell medicine with a **unique genomic modification** at the **γ-globin gene (*HBG1* and *HBG2*) promoters**, mimicking the natural mechanism of HPFH

EDIT-301 was **well-tolerated** by the first 4 patients treated

- Safety profile of EDIT-301 is consistent with that of myeloablative conditioning with busulfan and autologous HSCT
- No TEAEs were reported to be related to EDIT-301
- No TESAEs occurred after EDIT-301 treatment

Robust and **clinically meaningful improvements** were observed after treatment with EDIT-301

- All treated patients exhibited successful engraftment and have had no VOEs since treatment
- All treated patients exhibited increases in HbF; HbF was >40% starting at Month 4 post-EDIT-301 infusion in the first two patients treated
- Physiological normalization of hemoglobin in the non-anemic range started as early as Month 4
- Markers of hemolysis improved or normalized in treated patients

Initial clinical data from treated patients **confirm proof of concept**

HbF, fetal hemoglobin; *HBG*, γ-globin gene; HPFH, hereditary persistence of fetal hemoglobin; HSCT, hematopoietic stem cell transplantation; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event; VOE, vaso-occlusive event.

Acknowledgements

Thank you to participating patients, their families, clinical investigators, and study site teams for their support.