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Dima, Tristan, & Stephanie
LIVING WITH SICKLE CELL DISEASE

EDIT-301 Phase 1/2 Study in Patients with Severe Sickle Cell Disease

Ruby Study Data Update

December 6, 2022

Forward Looking Statements

This presentation contains forward-looking statements and information within the meaning of The Private Securities Litigation Reform Act of 1995, including statements regarding the Company's expectation for data from additional patients in mid-2023. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "target," "should," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The Company may not actually achieve the plans, intentions, or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various important factors, including: uncertainties inherent in the initiation and completion of preclinical studies and clinical trials, including the RUBY trial, and clinical development of the Company's product candidates, including EDIT-301; availability and timing of results from preclinical studies and clinical trials; whether interim results from a clinical trial will be predictive of the final results of the trial or the results of future trials; expectations for regulatory approvals to conduct trials or to market products and availability of funding sufficient for the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements. These and other risks are described in greater detail under the caption "Risk Factors" included in the Company's most recent Annual Report on Form 10-K, which is on file with the Securities and Exchange Commission, as updated by the Company's subsequent filings with the Securities and Exchange Commission, and in other filings that the Company may make with the Securities and Exchange Commission in the future. Any forward-looking statements contained in this presentation speak only as of the date hereof, and the Company expressly disclaims any obligation to update any forward-looking statements, whether because of new information, future events or otherwise.

Agenda and Speakers

- Introduction
- Review of EDIT-301 and Ruby Study Data
- Closing Remarks
- Q&A

SPEAKERS

Gilmore O'Neill, MB, MMSc
President and CEO, Editas Medicine

Baisong Mei, MD, PhD
Chief Medical Officer, Editas Medicine

Key Takeaways of Ruby Study Data Update

- EDIT-301 is safe and well-tolerated by the first two patients
  - No Serious Adverse Events (SAEs) occurred after EDIT-301 treatment
  - No Adverse Events (AEs) were reported as related to EDIT-301
- Both dosed participants showed successful engraftment and have no vaso-occlusive events (VOEs) since EDIT-301 treatment (5 months and 1.5 months follow up, respectively)
- Fetal hemoglobin (HbF) reached 45.4% at month 5 for the first patient dosed
  - Total hemoglobin[1] reached 16.4 g/dL
  - F-cell pancellularity was 96%
  - Mean corpuscular HbF rose to 13.8 pg/RBC, exceeding the 10 pg/RBC threshold to suppress RBC sickling
- The initial preliminary data suggest proof of concept

[1] Normal total hemoglobin range 13.6 – 18.0 g/dL for male patients. Central laboratory reference range. Data on file.
RBC: red blood cell

Sickle Cell Disease is an Inherited Life-Threatening Hematological Disorder Manifesting Shortly After Birth

Ruby

SCD AFFECTS

~6M

PEOPLE GLOBALLY

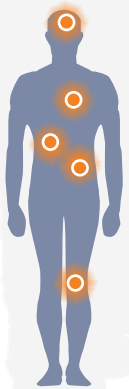
300K+

BABIES BORN WITH SCD PER YEAR GLOBALLY

~100K

PEOPLE IN THE U.S.

SICKLE CELL DISEASE is a genetic blood disorder caused by a single mutation in the **HBB gene** that causes sickling of red blood cells, leading to **anemia, hemolysis, and VOEs**[1,2]



Lifelong complications, multi-organ damages and comorbidities impact a patient's quality of life, ultimately leading to a **shortened lifespan**[1,2,4,5]

Limited treatment options currently **available**

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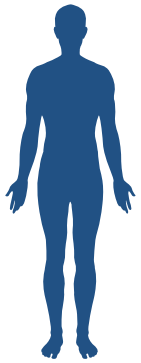
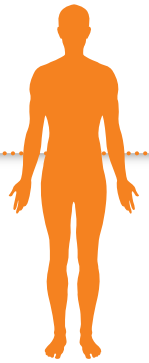
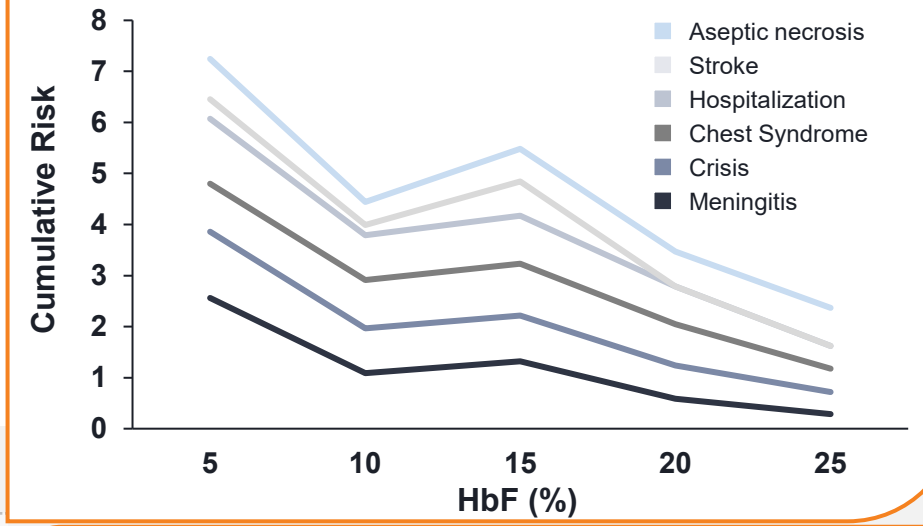
HBB, β-globin gene; SCD: sickle cell disease; VOE, vaso-occlusive event. 1. Kato GJ et al. Nat Rev Dis Primers 2018;4:18010 2. Pasricha SR et al. N Engl J Med. 2018; 3. Saraf S et al. Paediatr Respir Rev. 2014; 4. Dampier C et al. Am J Hematol 2011 5. Jonassaint CR et al. Br J Haematol. 2016; 174 (1): 136-147.

Increased Fetal Hemoglobin Correlates to Reduced SCD Symptoms

	Patient with Sickle Cell Disease (SCD)[1]	Patient with SCD and Hereditary Persistence of Fetal Hemoglobin (HPFH)[2, 4]
		
Sickle cell disease	**Yes**	**Yes**
Hemoglobin Production	**HbS**	**HbF ↑**
Vaso-occlusive Events	**Yes**	**No**
Organ Damage	**Yes**	**No**
Life Expectancy	**Reduced**	**Normal**

Higher Percentages of HbF are Associated with Reduction in SCD Events[3]



- Negative correlation between HbF and SCD events[3]
- Minimal or no symptoms when HbF >30% when SCD coinherited with HPFH[4]
- HbF concentration (mean corpuscular HbF) of 10 pg per red blood cell suppresses sickling[5]

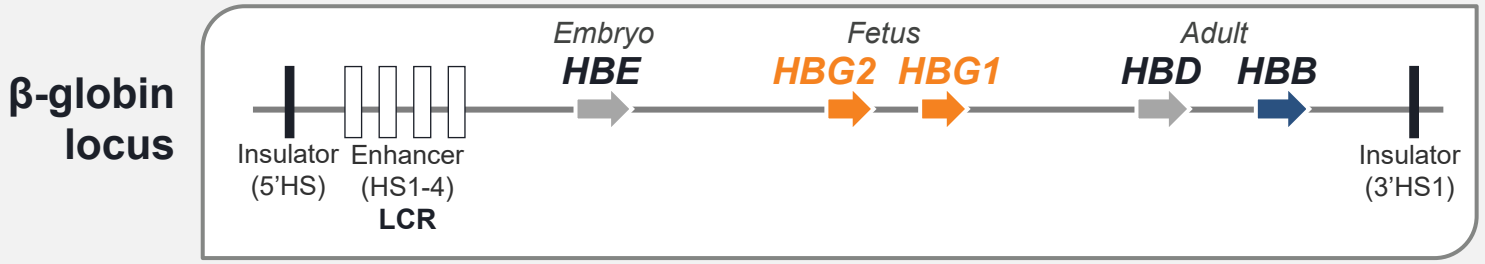
HbF, fetal hemoglobin; HPFH, hereditary persistence of fetal hemoglobin; SCD, sickle cell disease.

1. Kato GJ et al. Nat Rev Dis Primers 2018; 4: 18010. 2. Akinsheye I et al. Blood 2011; 118 (1): 19–27. 3. Powars DR et al. Blood 1984; 63 (4): 921-928.
4. Steinberg MH. Blood 2020; 136: 2392-400. 5. Steinberg et al, Blood. 2014;123(4):481-485

EDIT-301 Employs AsCas12a to Edit *HBG1* and *HBG2* Promoter Regions and Induces Higher HbF Expression

Utilizing proprietary
AsCas12a
to edit with
high efficiency and
high fidelity

Targeting
HBG1 and HBG2
promoter regions mimic
naturally occurring
mechanisms of HPFH



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

HS: hypersensitive site; LCR: locus control region; TSS: transcriptional start site. Hereditary Persistence of Fetal Hemoglobin (HPFH). Adapted from Higgs, Engel and Stamatoyannopoulos. Lancet 2012

Ruby Phase 1/2 Study of EDIT-301 in Patients with Severe SCD

Design

Phase 1/2, international, multicenter, open-label, single-arm study

Key Inclusion Criteria

40 patients 18-50 years old with severe SCD and a history of ≥ 2 severe vaso-occlusive events per year in previous 2 years

Key Endpoints

- Rate of severe vaso-occlusive events (VOEs) requiring medical attention
- Safety and tolerability of EDIT-301

Demographics & Baseline Characteristics

Both patients experienced 3 – 4 vaso-occlusive events annually from their severe sickle cell disease prior to enrollment in the RUBY trial

DEMOGRAPHICS	PATIENT 1	PATIENT 2
Genotype	β^S/β^S	β^S/β^S
Gender	Male	Female
Age, years	25	31
VOEs Pre-Study (average/year)	4	3

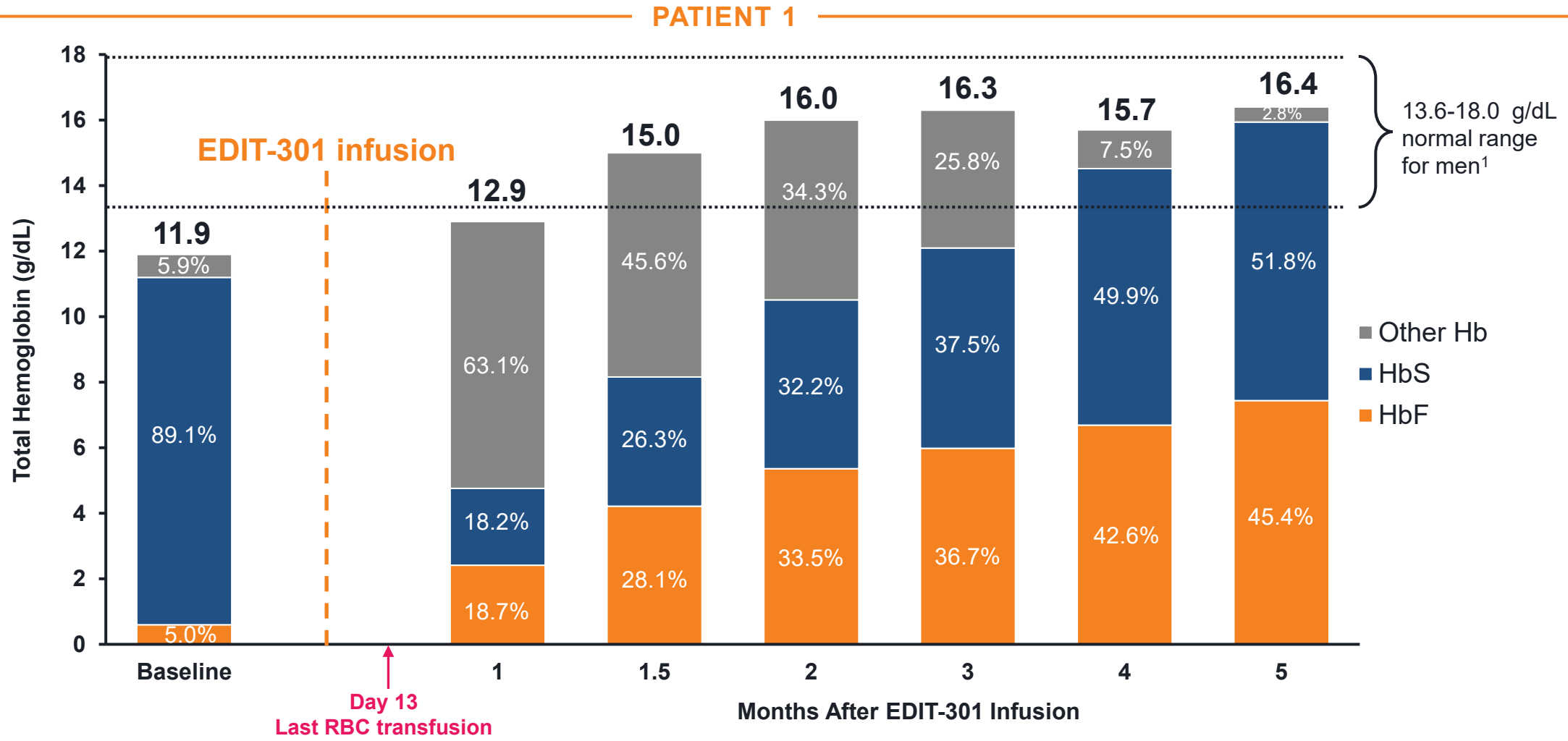
Both Patients Successfully Engrafted, Showed Favorable Safety Profile

- Successful engraftment
- Initial safety profile consistent with myeloablative conditioning with busulfan and autologous HSCT
- No SAEs occurred after EDIT-301 infusion; no AEs were reported as related to EDIT-301
- No VOEs following EDIT-301 infusion

TREATMENT	PATIENT 1	PATIENT 2
Neutrophil engraftment (day)*	23	29
Platelet engraftment (day)**	19	37
Follow-up Duration (months)	5	1.5
VOEs Post-EDIT-301 Infusion	None	None

* 3 consecutive measurements with absolute neutrophil count (ANC) ≥ 0.5 x 10^9/L
** 3 consecutive measurements with platelet count ≥ 50 x 10^9/L starting at least 7 days after the last platelet transfusion, and 10 days after TPO
CD, cluster of differentiation; TPO, thrombopoietin

Fetal Hemoglobin (HbF) Over 45% and Total Hemoglobin Returning to Normal Range

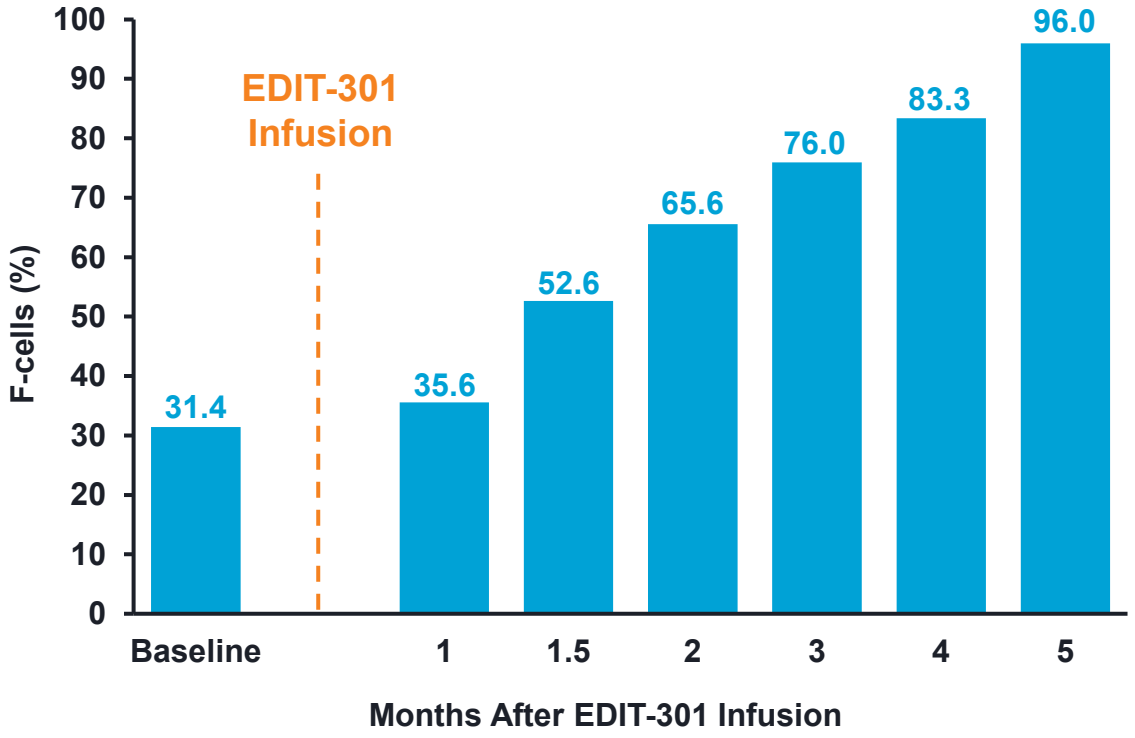


[1] Central laboratory reference range. Data on file.
Hb, hemoglobin; HbF, fetal hemoglobin; HbS, sickle hemoglobin; RBC, red blood cell. Bars show mean Hb (g/dL). Labels indicate mean proportion of HbS and HbF as a percentage of total Hb. Mean total Hb concentrations are shown directly above bars.

Fetal Hemoglobin Expressed in >95% of Red Blood Cells with Concentration Above Sickling Threshold (10 pg/RBC)

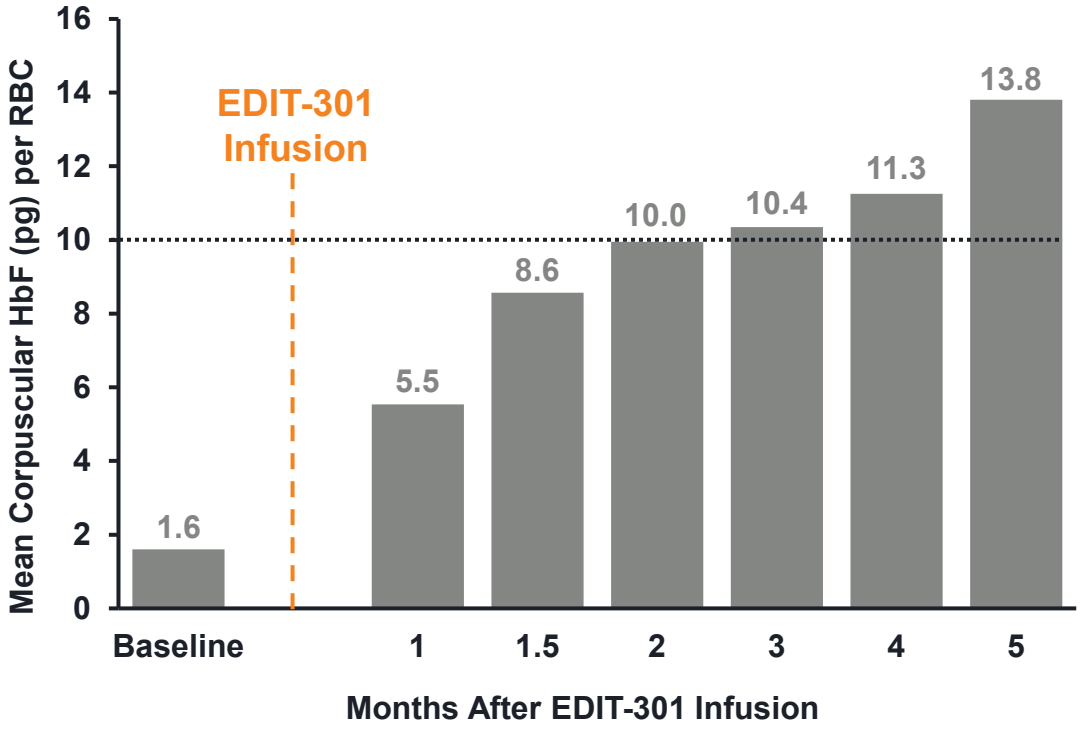
PATIENT 1

HbF Highly Pancellular (F-cells >95%)



Higher pancellularity indicates more red blood cells express HbF for potential clinical benefit

Mean Corpuscular HbF Clinically Meaningful



..... 10 pg/RBC threshold for protection from sickling[1]

1. Steinberg et al, Blood. 2014;123(4):481-485

HbF, fetal hemoglobin; RBC, red blood cell. Percentage of F-cells and mean corpuscular HbF (pg) concentrations are shown directly above bars. Mean Corpuscular HbF: (MCH (pg)*HbF(%))/100%= HbF(pg) per RBC.

Key Takeaways & Next Steps

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- Data from additional patients are expected in mid-2023

[1] Normal total hemoglobin range 13.6 – 18.0 g/dL for male patients. Central laboratory reference range. Data on file
RBC: red blood cell

Closing Remarks

Gilmore O’Neill, MB, MMSc
President and Chief Executive Officer
Editas Medicine

Acknowledgements

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

Questions & Discussion

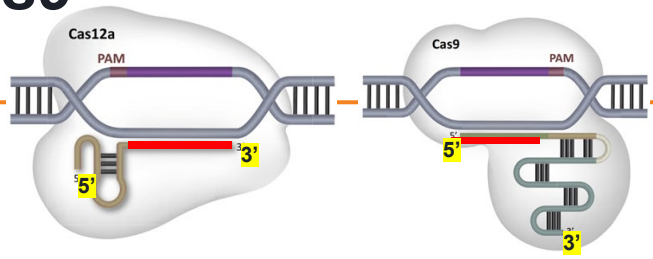
Gilmore O’Neill, MB, MMSc
President and CEO

Baisong Mei, MD, PhD
Chief Medical Officer

Mark Shearman, PhD
Chief Scientific Officer

Appendix

AsCas12a is a Differentiated CRISPR Nuclease With Higher Specificity and Efficiency Compared to Cas9

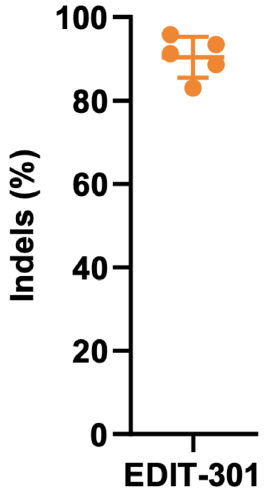


		Cas12a	Cas9
Enzyme	Specificity	Higher	Lower
	Editing efficiency	Higher	Lower
gRNA	Size	41mer	100mer
	Manufacture	Easier	Harder
	Yield & purity	Higher	Lower
	Target sequence location*	5' terminus	3' terminus
	Synthesis fidelity	Higher	Lower

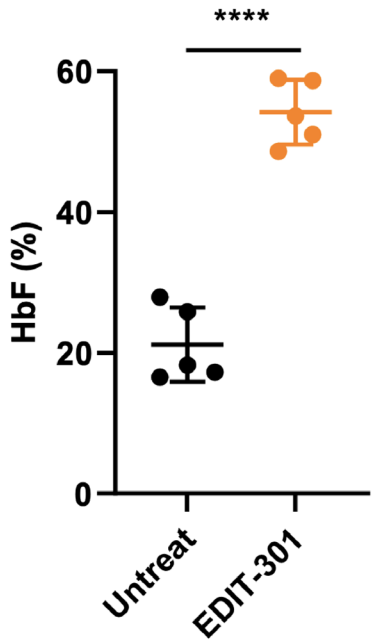
*Solid-phase RNA synthesis is carried out in a 3' to 5' direction. Fidelity decays toward 5' terminus. Cas, CRISPR-associated protein; gRNA, guide ribonucleic acid.
Images from Moon SB et al. Trends in Biotechnology 2019; 37 (8): 870-881.

EDIT-301 Edited Human CD34+ Cells: High Editing Efficiency, Highly Increased HbF, Reduced Sickling, and Close to Normal RBC Rheological Behaviors

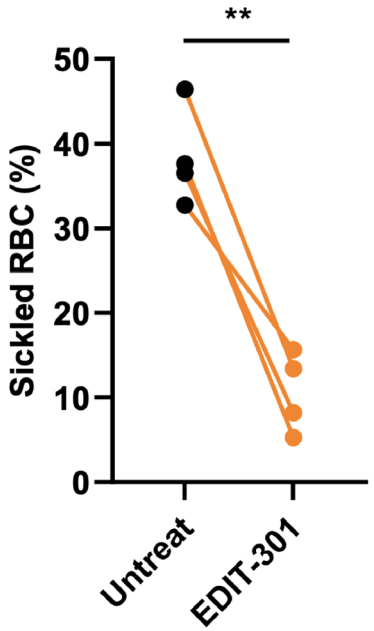
Efficient Editing



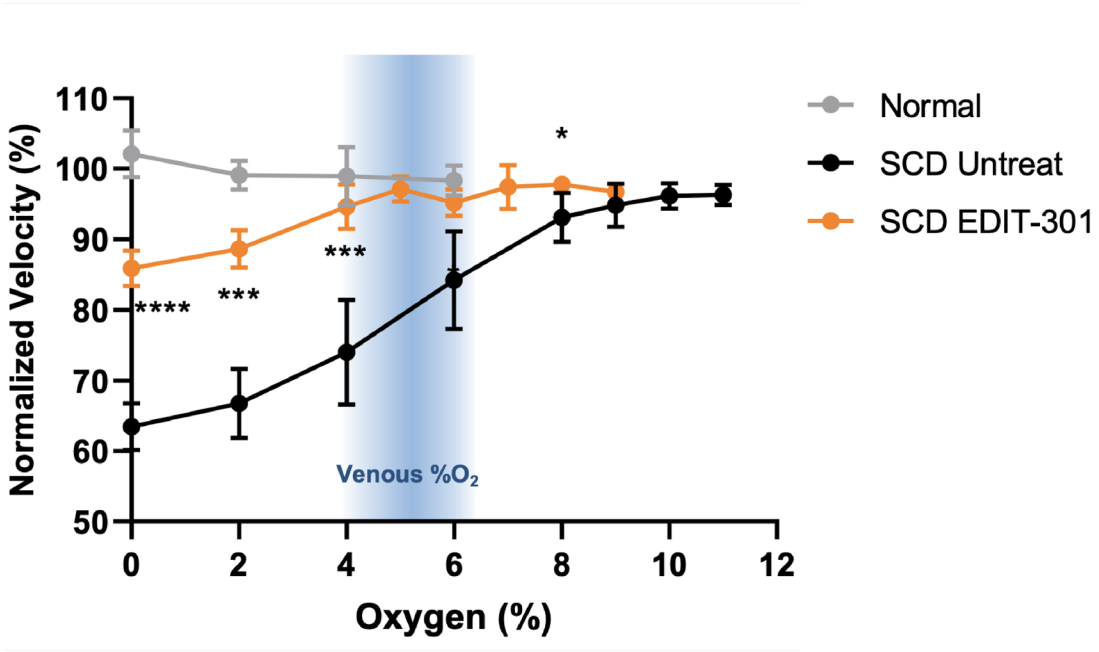
Robust HbF Induction



Reduced Sickling



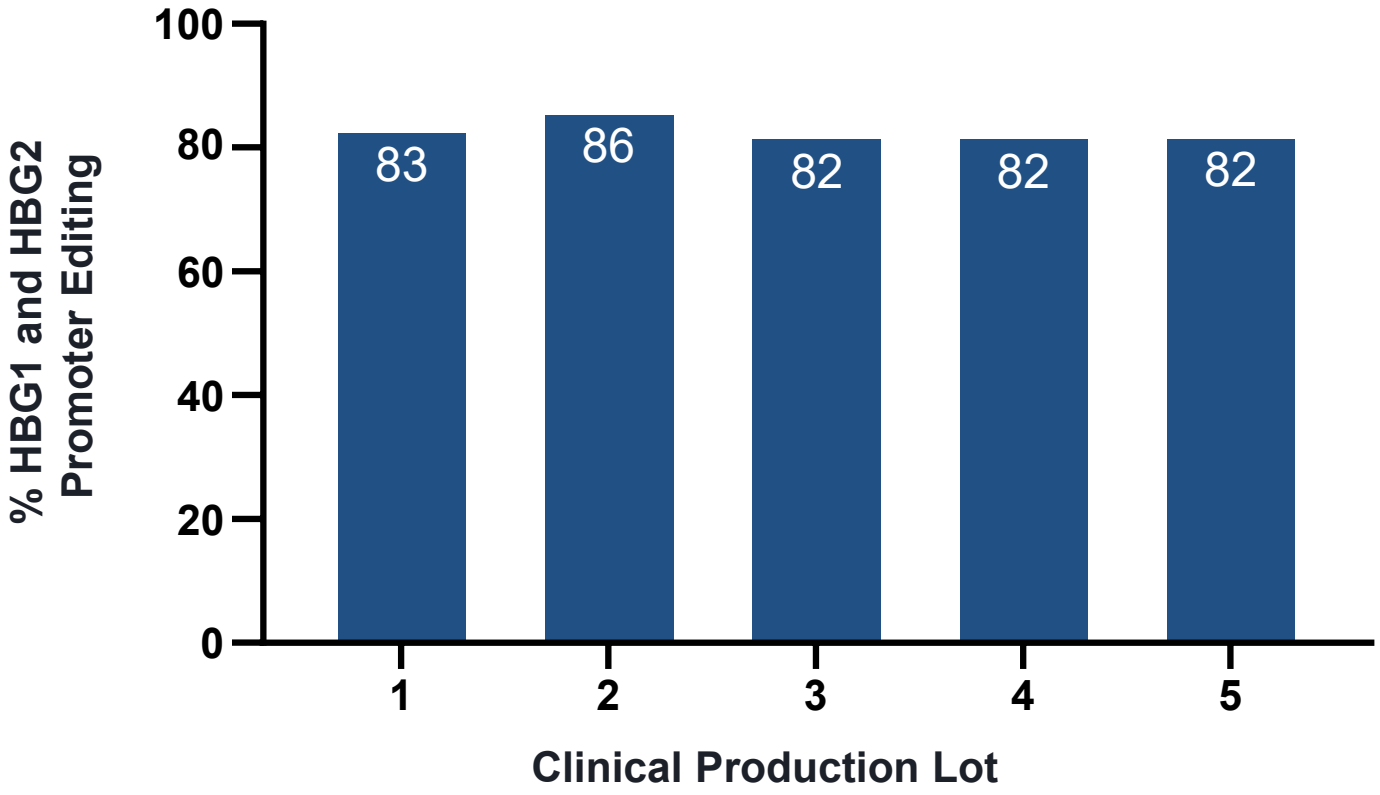
Improved Rheological Behavior



*p<0.05; **p<0.01; ****p<0.0001

CD, cluster of differentiation; HbF, fetal hemoglobin; RBC, red blood cell; SCD, sickle cell disease. De Dreuzy E et al. Poster 1540 presented at the American Society of Hematology Congress; 5–8 December 2020.

High Efficiency Allele Editing of CD34+ Cells from Ruby Study Patients in Clinical Production



>80% of consistent EDIT-301 editing clinical drug products already manufactured for Ruby study patients

CD, cluster of differentiation; HBG, γ-globin gene. Editas Medicine. Data on file.