editas MEDICINE


# Renizgamglogene autogedtemcel (reni-cel) Program Update

*RUBY and EdiTHAL Trial Data Update*

December 11, 2023

# 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 potential market for EDIT-301, if approved. 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

- Welcome and 18-Month Check-in
- Key Takeaways of reni-cel (EDIT-301) Program
- Clinical Updates of reni-cel (EDIT-301): RUBY and EdiTHAL Trials
- Closing Remarks
- Q&A

## SPEAKERS

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

**Baisong Mei, MD, PhD**
CMO, Editas Medicine

# 18-Month Check-in

## Groundbreaking Science, New Management Team, Commercial Focus

- A world leading gene editing platform supported by foundational IP estate.
- Shareholder value driven team with a proven track record and strong domain expertise.
- Lead asset reni-cel (EDIT-301), a potentially differentiated treatment for sickle cell disease and beta thalassemia. Additional clinical data updates expected in mid-2024 and year-end 2024.
- Longer term focus on creating important medicines based on *in vivo* gene editing.
- Rigorous clinical, regulatory, and commercial criteria for investments in pipeline.
- Strong cash position.

# Desired Attributes of Reni-cel

- Clinical Outcomes:
  - Rapid correction of anemia to Normal Physiological Hemoglobin levels.
  - Fetal Hemoglobin levels ≥ 40%, well above anti-sickling threshold.
  - Safety profile consistent with myeloablative busulfan conditioning and autologous hematopoietic stem cell transplant.
  - SCD patients free of severe Vaso-occlusive events.
  - TDT patients achieving transfusion independence.

# Key Takeaways

**Reni-cel drives early, robust correction of anemia to normal physiological range of total Hb for SCD**

**Reni-cel drives robust sustained increases in HbF >40%**

**No VOEs seen to date in all dosed SCD patients**

**Reni-cel safety profile consistent with myeloablative busulfan conditioning and autologous HSCT**

**Initial Hb and HbF responses are consistent in SCD and TDT patients at the same follow-up time points**

Data cutoff for the RUBY study was November 22, 2023. Data cutoff for the EdiThal study was November 28, 2023.
Hb, hemoglobin; HbF, fetal hemoglobin; HSCT, hematopoietic stem cell transplantation; SCD, sickle cell disease; TDT, transfusion-dependent thalassemia; VOE, vaso-occlusive event.

# RUBY Participant: In His Own Words

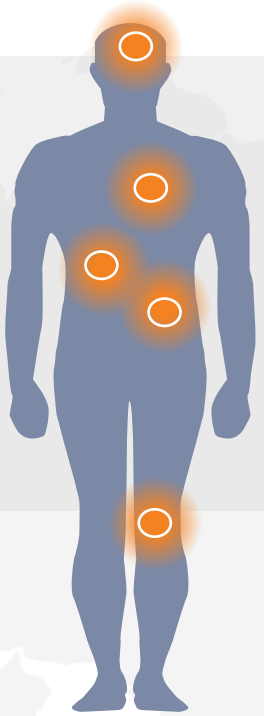
*Before the study, I was not able to complete many things that I should have been doing every day. I felt that I would be at the finish line of completing something, then I would have a pain crisis and then that episode would knock me down and sometimes take me even further from the starting line. I am able to complete things now; like school. I don't have to start things over again after a pain crisis interrupted me.*

*Before I had to work so hard at everything. I was a dreamer. I feel like myself now. I feel that I was not the person I am today because of sickle cell. I had an interview for med school already. During the interview, I talked about this study and how it has changed me. I am waiting to hear back from the school. I am so grateful for this opportunity.*

*26-year-old Male*
RUBY Trial Participant

# 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]

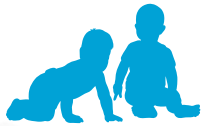
It is estimated that approximately **50%** of patients with HbSS **die before 45 years** of age[3]

## SCD AFFECTS[4,5,6]

**~6M**

PEOPLE GLOBALLY

**300K+**



BABIES BORN WITH SCD PER YEAR GLOBALLY

**~100K**

PEOPLE IN THE U.S.

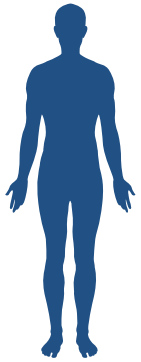
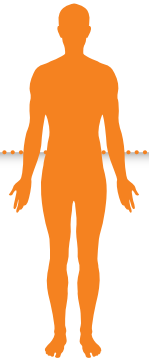
Although advances in supportive care and disease modifying therapies have improved outcomes for patients with SCD, **curative therapies** have been **limited to allogenic HCT**

*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.

# Increased Fetal Hemoglobin Correlates with Reduced SCD Symptoms

## Minimal or no symptoms when HbF >30% when SCD coinherited with Hereditary Persistence of Fetal Hemoglobin

| | 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 ↑>30%** |
| Vaso-occlusive Events | **Yes** | **No** |
| Organ Damage | **Yes** | **No** |
| Life Expectancy | **Reduced** | **Normal** |

- 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

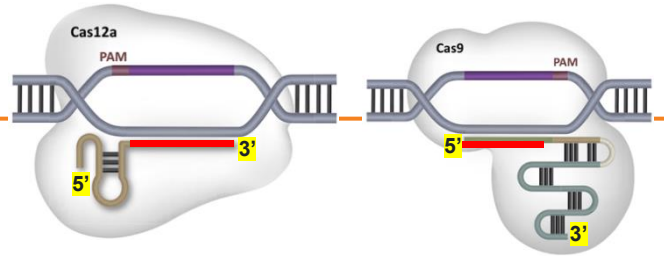
# Reni-cel's Rational Design: Target Choices AND CRISPR Enzyme Matter in Building a Medicine to Give Best Outcomes to Patients

## TARGET

| | *HBG1* and *HBG2* | *BCL11A* |
|---|---|---|
| RBC Production | Normal | Reduced |
| Proliferative capacity | Normal | Reduced |
| RBC Health | Normal | Reduced |
| Mimics Natural HPFH | Yes | No |

***HBG1* and *HBG2* promoters** are a **more appropriate genomic target** versus *BCL11A* for RBC production[1,2]

## ENZYME




| | AsCas12a | Cas9 |
|---|---|---|
| Specificity | Higher | Lower |
| Editing Efficiency | Higher | Lower |

Images from Moon *et al*. 2019.[3]

AsCas12a is a **differentiated** CRISPR nuclease with **higher specificity** and **efficiency** compared with Cas9[1,4]

*BCL11A*, B-cell lymphoma/leukemia 11A gene; Cas9, CRISPR-associated protein 9; AsCas12a, CRISPR-associated protein 12a; CRISPR, clustered regularly interspaced short palindromic repeats; *HBG*, γ-globin gene; HPFH, hereditary persistence of fetal hemoglobin; RBC, red blood cell.

1. Editas Medicine. Data on file. 2. Chang *et al.* Oral presentation at ASH 2018; San Diego, CA, USA, 2 December 2018. 3. Moon SB *et al*. *Trends in Biotechnology* 2019; 37 (8): 870-881. 4. Zhang L *et al. Nat Commun.* 2021; 12 (1): 3908.

# RUBY Study of Reni-cel in Patients with Severe SCD

## Design

- Phase 1/2
- International, multicenter
- 24 months follow-up post-reni-cel infusion

## Key Inclusion Criteria

- ~40 patients 18–50 years
- Diagnosis of severe SCD
- History of ≥2 severe VOEs per year in previous 2 years

## Key Endpoints

- Proportion of patients achieving complete resolution of severe VOEs
- Safety and tolerability of reni-cel

SCD, sickle cell disease; VOE, vaso-occlusive event.
ClinicalTrials.gov NCT04853576. Available at: https://clinicaltrials.gov/ct2/show/NCT04853576.

# All Treated RUBY Patients Successfully Engrafted, Showed a Favorable Safety Profile

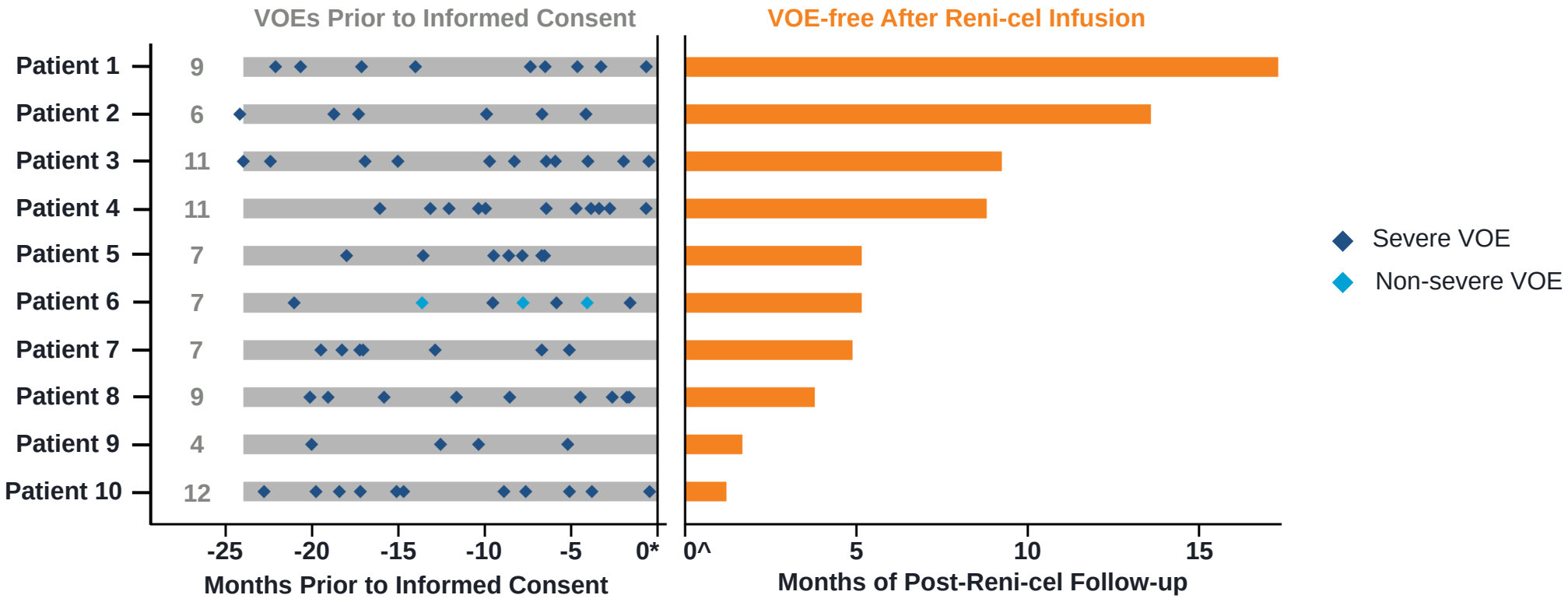
| DEMOGRAPHICS | (N=11) |
|---|---|
| Genotype, n(%) | |
| $\beta^S/\beta^S$ | 11 (100) |
| Sex, n (%) | |
| Female | 6 (54.5) |
| Age, years, mean (SD) | 27.6 (4.2) |
| Severe VOEs, pre-study annual rate*, mean (SD) | 3.9 (1.4) |

| INFUSION AND ENGRAFTMENT | (N=11†) |
|---|---|
| Total reni-cel dose administered, $\times 10^6$ $CD34^+$ cells/kg, mean (SD) | 5.2 (2.5) |
| Follow-up duration, months, mean (SD) | 6.5 (5.3) |
| Time to neutrophil engraftment†, ‡, days, mean (SD) | 23.7 (2.8) |
| Time to platelet engraftment†, §, days, mean (SD) | 26.1 (7.7) |

- Safety profile is consistent with myeloablative busulfan conditioning and autologous HSCT
- No serious adverse events (SAEs) related to reni-cel were reported after reni-cel infusion

Data cutoff November 22, 2023.
*The pre-study period is defined as the 2-year period prior to informed consent. †One patient had 23 days of follow-up after infusion as of the data cut; neutrophil engraftment and platelet engraftment were not achieved yet; engraftment values are therefore based on n=10. ‡ 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 platelet transfusion, and 10 days after thrombopoietin (TPO). No TPO was used for patients after reni-cel infusion.
HSCT, hematopoietic stem cell transplant; reni-cel, renizgamglogene autogedtemcel; SCD, sickle cell disease; SD, standard deviation; SAE, serious adverse event; VOE, vaso-occlusive event.
Hanna R *et al*. Poster presented at ASH 2023; San Diego, CA, USA, 9–12 December.

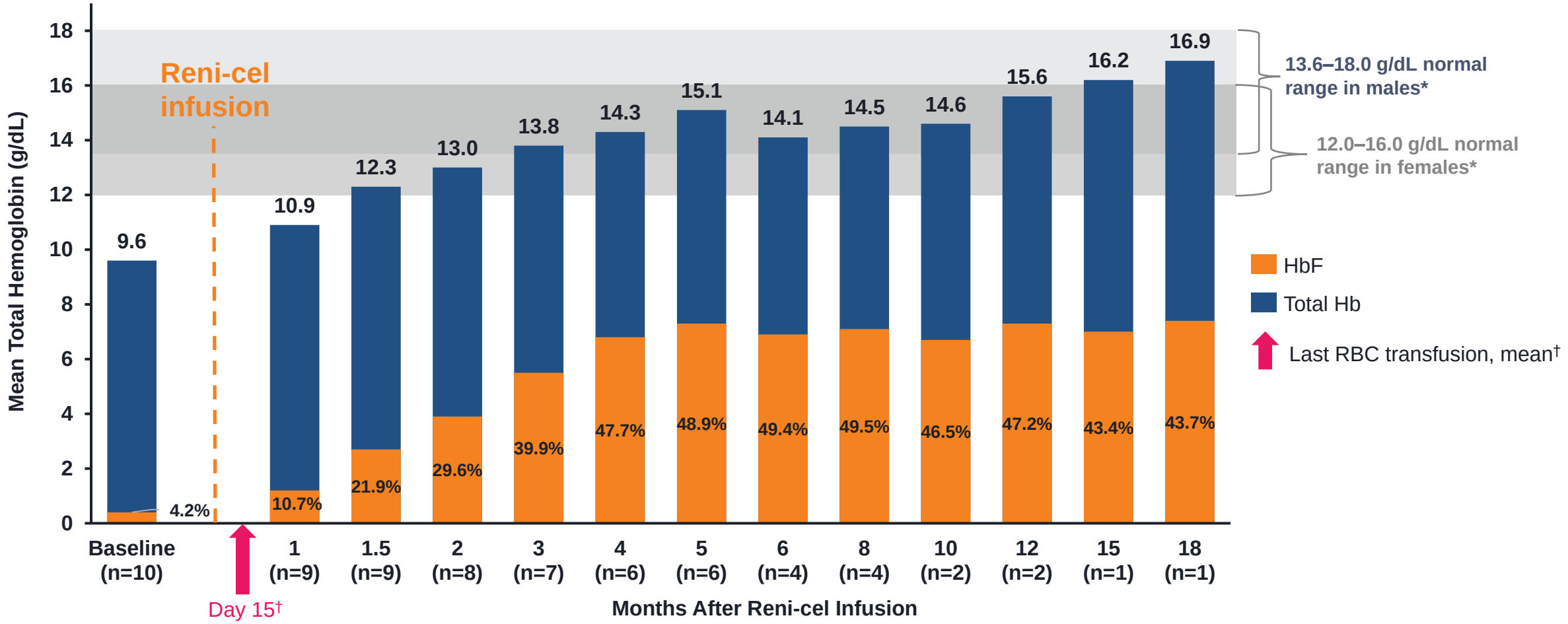
# All Treated RUBY Patients are VOE-free Since Reni-cel Infusion




**All 10 patients who reached the Month 1 visit have been VOE-free since reni-cel infusion**

Data cutoff November 22, 2023. Due to limited follow up period after dosing, Patient 11 was not included.
Left panel ends at informed consent date: *Day of informed consent. Right panel starts at infusion date: ^Day reni-cel was infused.
reni-cel, renizgamglogene autogedtemcel; VOE, vaso-occlusive event.
Hanna R *et al*. Poster presented at ASH 2023; San Diego, CA, USA, 9–12 December.

# RUBY Patients Show Total Hb Rapidly Returning to the Normal Range and Clinically Meaningful Improvements in HbF Levels of >40%




Data cutoff November 22, 2023. Number of male patients = 5; number of female patients = 5. Bars show mean Hb (g/dL). Labels inside / next to the bars indicate mean proportion of HbF as a percentage of total Hb. Mean total Hb concentrations are shown directly above bars.

*Central laboratory reference range. †The last RBC transfusion in patients occurred a mean (SD) of 15.4 (6.0) days after reni-cel infusion (n=10).

Hb, hemoglobin; HbF, fetal hemoglobin; RBC, red blood cell; reni-cel, renizgamglogene autogedtemcel; SCD, sickle cell disease.

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# EdiTHAL Patients Successfully Engrafted, Experienced Similar Engraftment and Similar Safety Profile to RUBY Patients

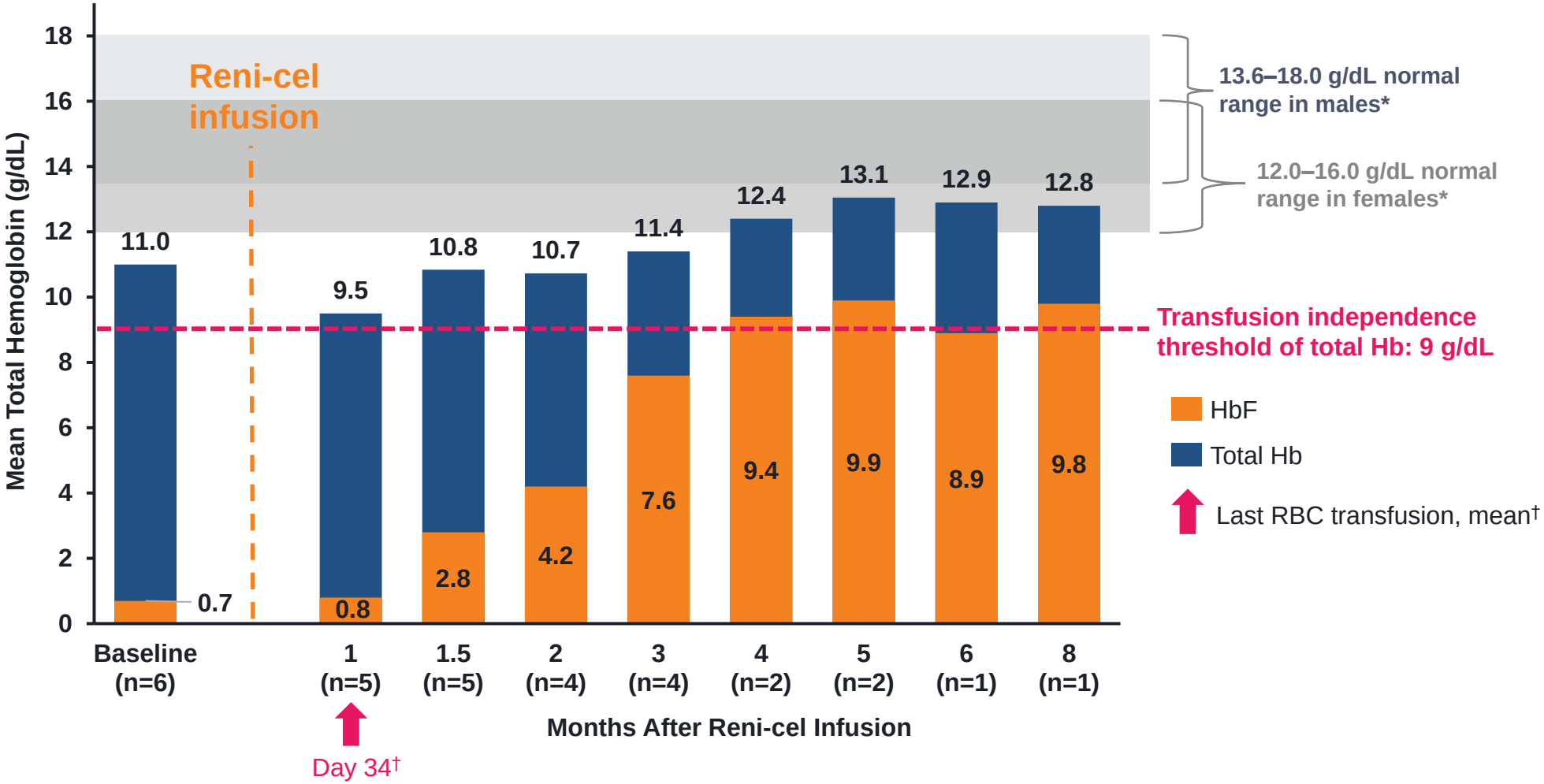
| DEMOGRAPHICS | (N=6) |
|---|---|
| Genotype, n(%) | |
| $\beta^0/\beta^0$ | 2 (33.3) |
| Non-$\beta^0/\beta^{0*}$ | 4 (66.7) |
| Sex, n (%) | |
| Female | 4 (66.7) |
| Age, years, mean (SD) | 18.8 (0.9) |
| RBC transfusion volume, pre-study annual rate†, mL/kg/year, mean (SD) | 162.3 (51.9) |

| INFUSION AND ENGRAFTMENT | (N=6‡) |
|---|---|
| Total reni-cel dose administered, $\times 10^6$ $CD34^+$ cells/kg, mean (SD) | 7.7 (2.2) |
| Follow-up duration, months, mean (SD) | 4.1 (2.5) |
| Time to neutrophil engraftment§, days, mean (SD) | 25.5 (3.6) |
| Time to platelet engraftment‡,‖, days, mean (SD) | 36.6 (11.8) |

- Safety profile is consistent with myeloablative busulfan conditioning and autologous HSCT
- No serious adverse events (SAEs) related to reni-cel were reported after reni-cel infusion

Data cutoff November 28, 2023.
*Non-$\beta^0/\beta^0$ includes $\beta^0/\beta^+$ (n=3) and $\beta^E/\beta^0$ (n=1). †The pre-study period is defined as the 2-year period prior to informed consent. ‡One patient had 36 days of follow-up after infusion as of the data cut; neutrophil was engrafted, but platelet engraftment was not achieved yet; platelet engraftment values are therefore based on n=5. §Three consecutive measurements with absolute neutrophil count (ANC) ≥0.5 × $10^9$/L. ‖Three consecutive measurements with platelet count ≥20 × $10^9$/L starting at least 7 days after the platelet transfusion, and 10 days after thrombopoietin (TPO). No TPO was used for patients after reni-cel infusion. RBC, red blood cell; reni-cel, renizgamglogene autogedtemcel; SD, standard deviation; TDT, transfusion-dependent β-thalassemia; SAE, serious adverse event.
Hanna R *et al*. Poster presented at ASH 2023; San Diego, CA, USA, 9–12 December.

# EdiTHAL Patients Had Early and Robust Increase of Total Hb Above the Transfusion Independence Threshold




Data cutoff November 28, 2023. Number of male patients = 2; number of female patients = 4. Bars show mean Hb (g/dL). Labels inside / next to the bars indicate mean levels of HbF (g/dL). Mean total Hb concentrations are shown directly above bars.
*Central laboratory reference range. †The last RBC transfusion in patients occurred a mean (SD) of 34.4 (20.9) days after reni-cel infusion (n=5).
Hb, hemoglobin; HbF, fetal hemoglobin; reni-cel, renizgamglogene autogedtemcel; TDT, transfusion-dependent β-thalassemia.
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# Key Takeaways

**Reni-cel drives early, robust correction of anemia to normal physiological range of total Hb for SCD**

**Reni-cel drives robust sustained increases in HbF >40%**

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# Acknowledgements

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

# Closing Remarks

**Gilmore O’Neill, MB, MMSc**
President and CEO
Editas Medicine

# Questions & Discussion

**Gilmore O’Neill, MB, MMSc**
President and CEO

**Baisong Mei, MD, PhD**
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