editas MEDICINE

Dima, Tristan, & Stephanie
LIVING WITH SICKLE CELL DISEASE

EDIT-301 Program Update

RUBY and EdiTHAL Trial Data Update

June 12, 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

- Year-one Check-in
- Key Takeaways of EDIT-301 Program
- Clinical Updates of 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

Year-one Check-in

- Achieved two proof-of-concepts for *in vivo* and *ex vivo* editing platforms in 2022.
- Sharpened our focus on:
  - Execution of EDIT-301 development toward regulatory approval.
  - Discovery of *in vivo* edited therapeutics (including *in vivo HSC).*
- Decreased Cash Burn extending operational runway into 2025.
- Strengthened Leadership team.

Desired Attributes of EDIT-301

- 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 OR $CD34^+$ stem cell transplant.
  - Free of severe Vaso-occlusive events.

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Key Takeaways*

EDIT-301 drives early, robust correction of anemia to normal physiological range of total Hb in as early as 4 months

EDIT-301 drives robust sustained increases in HbF >40% beginning as early as 4 months

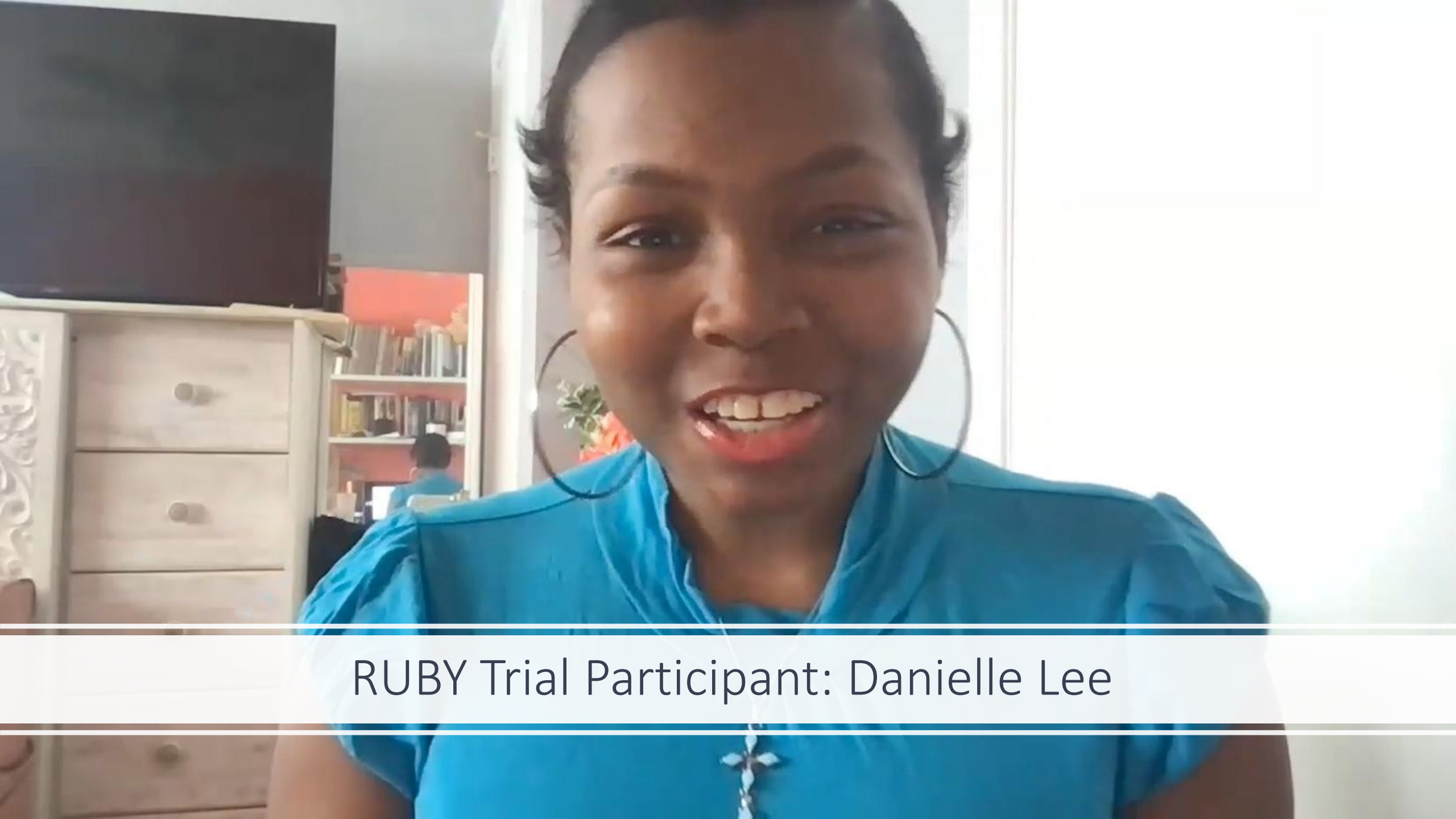
No VOEs seen to date in all dosed SCD patients

Initial clinical results are consistent with preclinical data

EDIT-301 safety profile consistent with busulfan myeloablative conditioning and autologous HSCT

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

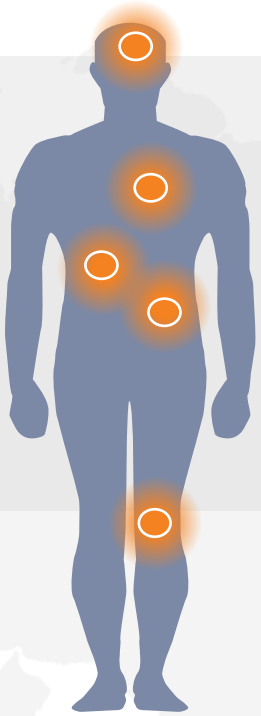
*Reflects data from four patients through data cutoff of May 3, 2023.
Hb, hemoglobin; HbF, fetal hemoglobin; HSCT, hematopoietic stem cell transplantation; SCD, sickle cell disease; TDT, transfusion-dependent thalassemia; VOE, vaso-occlusive event.



RUBY Trial Participant: Danielle Lee

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]

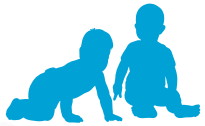
It is estimated that approximately **50%** of patients with HbSS **die before 45 years** of age[3]

SCD AFFECTS[4,5,6]

~6M

PEOPLE GLOBALLY

300K+



BABIES BORN WITH SCD PER YEAR GLOBALLY

~100K

PEOPLE IN THE U.S.

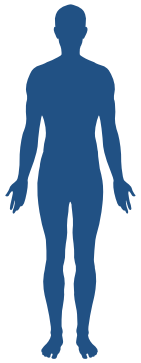
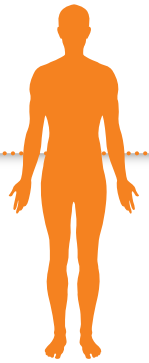
Although advances in supportive care and disease modifying therapies have improved outcomes for patients with SCD, **curative therapies** have been **limited to allogenic HCT**

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**

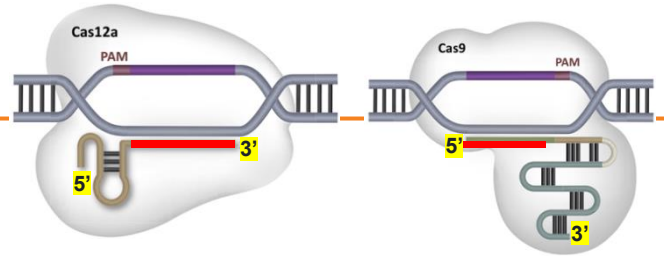
- Negative correlation between HbF and SCD events[3]
- Minimal or no symptoms when HbF >30% when SCD coinherited with HPFH[4]
- HbF concentration (mean corpuscular HbF) of 10 pg per red blood cell suppresses sickling[5]

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

CRISPR Enzyme AND Target Choices Matter in Building a Medicine to Give Best Outcomes to Patients

ENZYME



	AsCas12a	Cas9
Specificity	Higher	Lower
Editing Efficiency	Higher	Lower

Images from Moon *et al*. 2019.[1]

AsCas12a is a **differentiated** CRISPR nuclease with **higher specificity** and **efficiency** compared with Cas9[2,3]

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[3,4]

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. Moon SB *et al*. *Trends in Biotechnology* 2019; 37 (8): 870-881. 2. Zhang L *et al. Nat Commun* 2021; 12 (1): 4500. 3. Editas Medicine. Data on file. 4. Chang *et al.* Oral presentation at ASH 2018; San Diego, CA, USA, 2 December 2018.

RUBY Study of EDIT-301 in Patients with Severe SCD

Design

- Phase 1/2
- International, multicenter
- 24 months follow-up post-EDIT-301 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 EDIT-301

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

SCD, sickle cell disease; VOE, vaso-occlusive event.

ClinicalTrials.gov NCT04853576. Available at: https://clinicaltrials.gov/ct2/show/NCT04853576. Accessed May 2023.

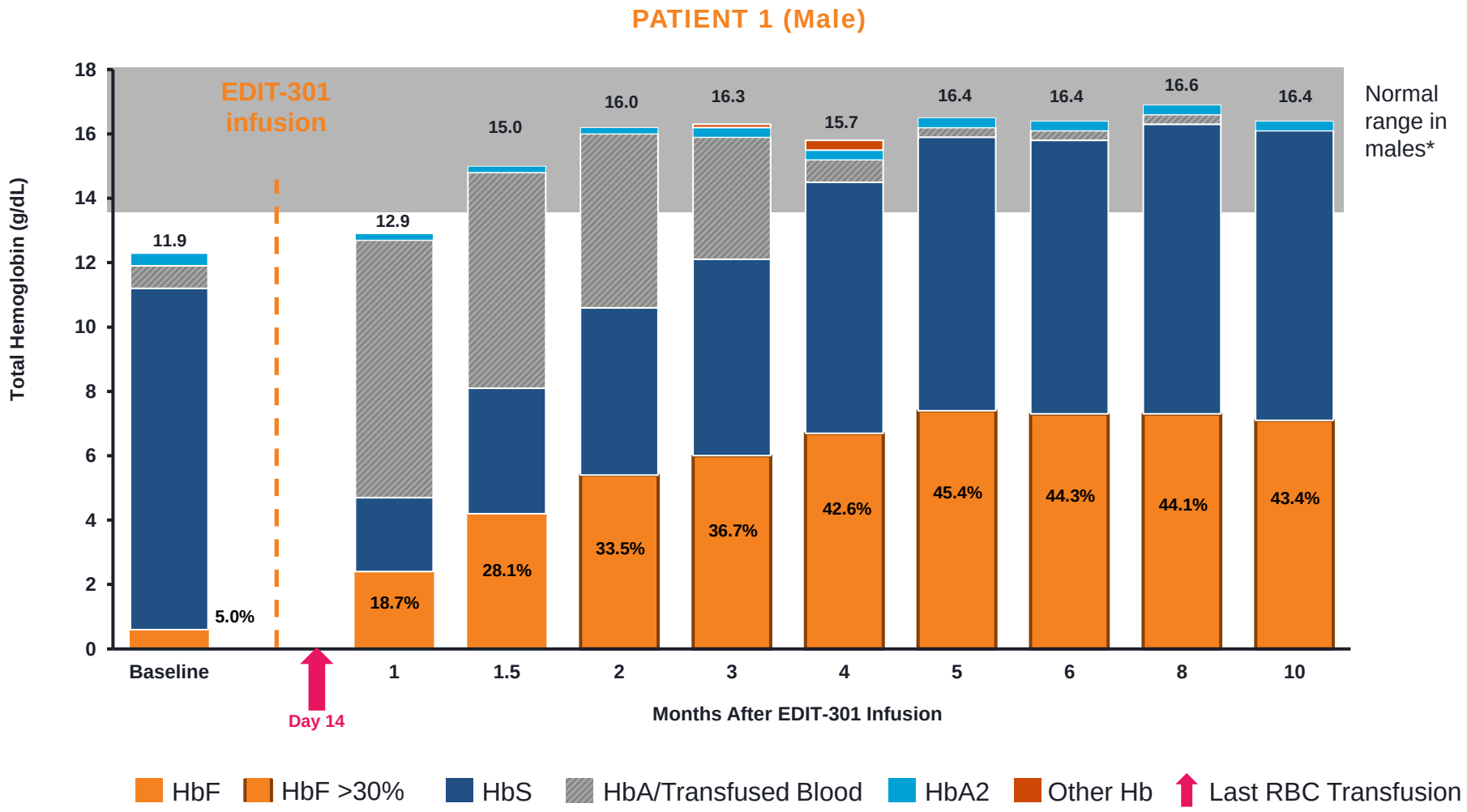
All Treated RUBY Patients Successfully Engrafted, Showed a Favorable Safety Profile, and are VOE-free Since Infusion

	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

- All 4 patients experienced early successful engraftment
- Safety profile is consistent with busulfan myeloablative conditioning and autologous HSCT
- No SAEs occurred after EDIT-301 infusion; No AEs were reported to be related to EDIT-301
- No patients experienced VOEs following EDIT-301 infusion

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 (TPO).
AE, adverse event; CD, cluster of differentiation; HSCT, hematopoietic stem cell transplantation; SAE, serious adverse event; VOE, vaso-occlusive event.
Editas Medicine. Data on file.

RUBY Patient 1 Maintained HbF >40% and is VOE-free Since Infusion; Total Hemoglobin Returned to the Normal Physiological Range by Month 5



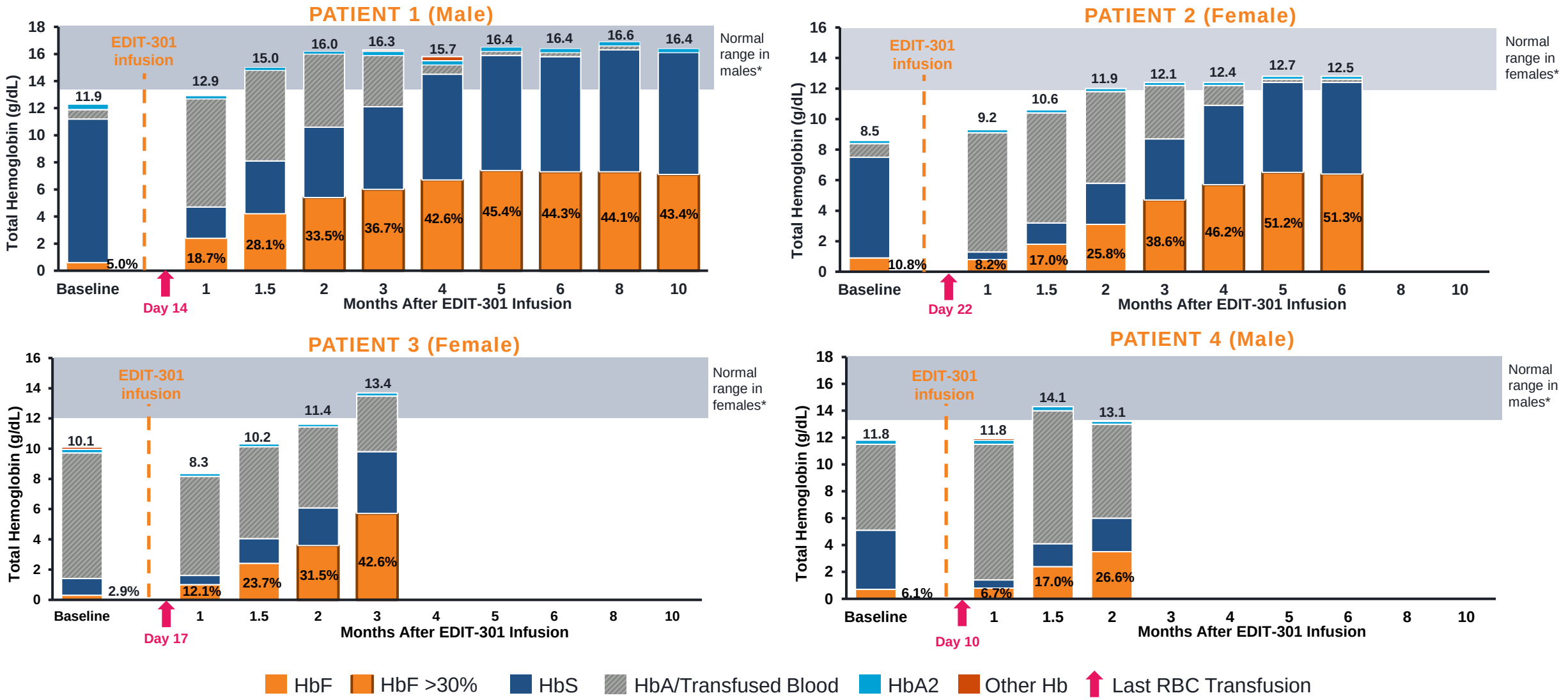
Bars show mean Hb (g/dL). Labels inside / to the right of the bars indicate mean proportion of HbF as a percentage of total Hb. Mean total Hb concentrations are shown directly above bars. Data cutoff May 3, 2023, for all timepoints except month 3 for patient 3, which was retrieved on May 12, 2023.

*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.

RUBY Patients Follow Same Total Hemoglobin and Fetal Hemoglobin Trajectory as Patient 1



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Editas Medicine. Data on file.

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

	PATIENT 1
EDIT-301 Total CD34+ (10^6/kg)	6.1
Neutrophil Engraftment (day)*	23
Platelet Engraftment (day)†	26
Follow-Up Duration (months)	1.5

- The first EdiThal patient experienced early successful engraftment
- Safety profile is consistent with busulfan myeloablative conditioning and autologous HSCT
- No SAEs occurred after EDIT-301 infusion; no AEs were reported to be related to EDIT-301

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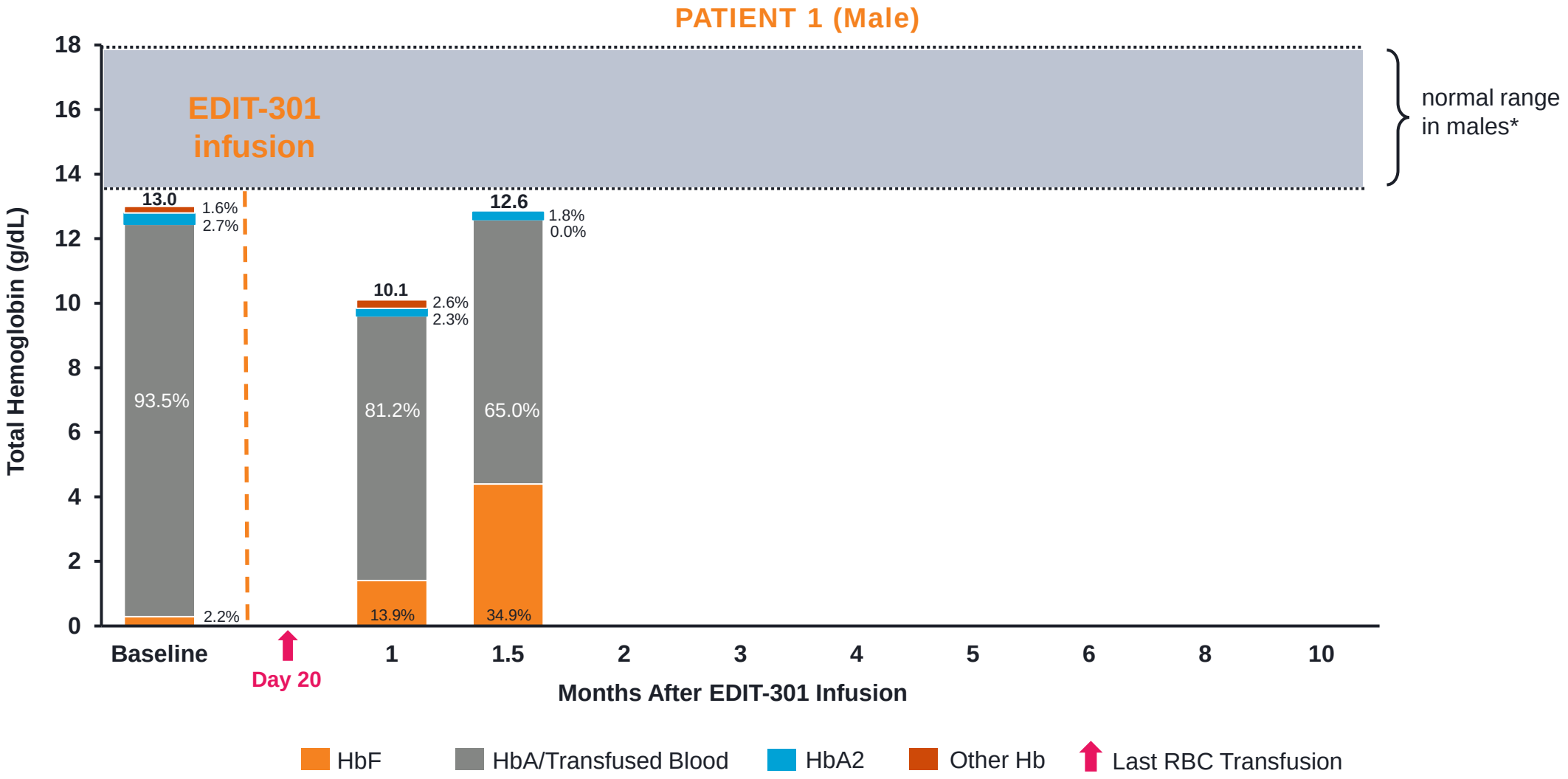
First Treated EdiTHAL Patient Followed Similar Trajectory Expressing >30% HbF (>4 g/dL) at 1.5 Months Post-infusion



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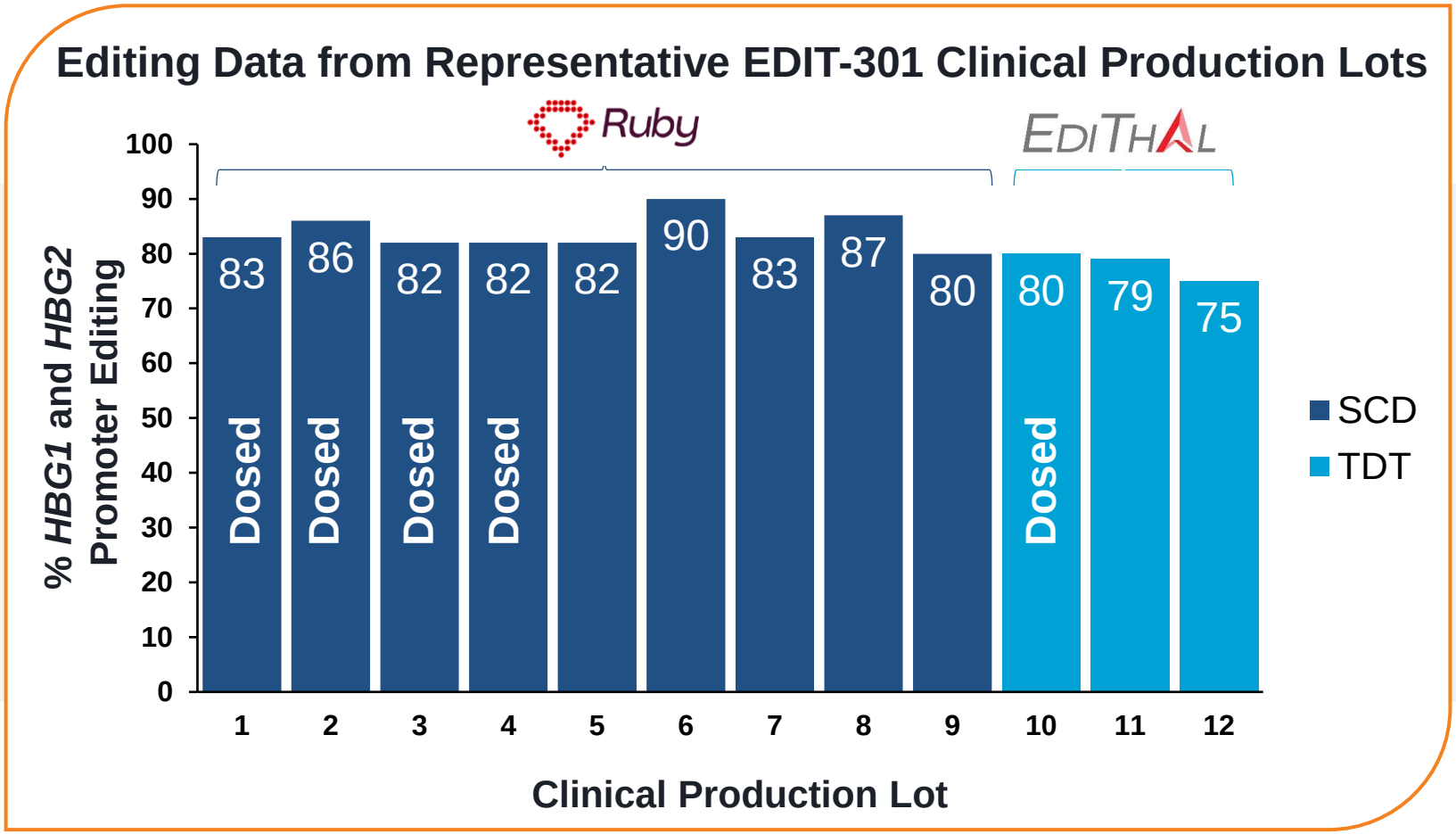
Hb, hemoglobin; HbF, fetal hemoglobin; HbS, sickle hemoglobin; RBC, red blood cell.
Editas Medicine. Data on file.

Consistent Levels of *ex vivo* Editing Correlated with Similar Clinical Responses in Dosed Patients

Similar editing levels achieved in cells from all patients, predicting similar and robust clinical responses; no detectable off target editing



Consistent production of EDIT-301 with:

- **≥80% editing in Ruby patients**
- **≥75% editing in EdiThal patients**

HBG, γ-globin gene; SCD, sickle cell disease; TDT, transfusion-dependent thalassemia. Editas Medicine. Data on file.

RUBY and EdiTHAL Study Site Activation and Patient Enrollment Remains On-track

22 RUBY sites activated

7 EdiTHAL sites activated

20 RUBY patients enrolled

5 EdiTHAL patients enrolled

Key Takeaways*

EDIT-301 drives early, robust correction of anemia to normal physiological range of total Hb in as early as 4 months

EDIT-301 drives robust sustained increases in HbF >40% beginning as early as 4 months

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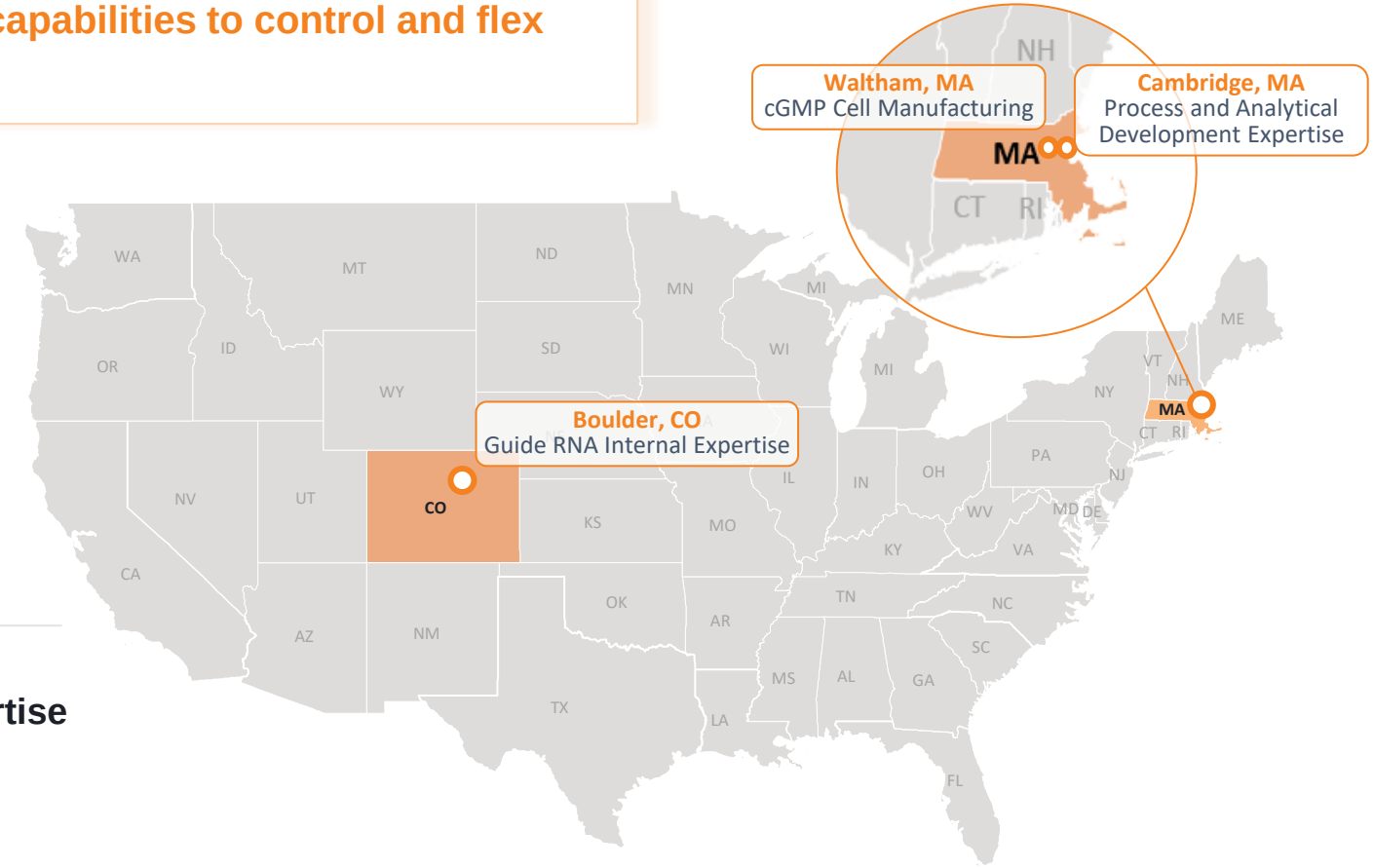
Editas' Gene Edited HSC Manufacturing Capabilities

- In-house manufacturing capabilities allow Editas to **expedite clinical development**
- Editas fully controls its manufacturing process with **capabilities to control and flex number of patients edited per month**

Guide RNA and protein production via CDMO and CROs

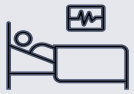
RNP formulation and cell editing developed and controlled in-house Waltham, MA

In-house quality analytics expertise Cambridge, MA



Majority of Patients will Still be Awaiting Therapy at Anticipated Time of EDIT-301 Launch

Prevalence of SCD in U.S.	Prevalence of Beta-Thal in U.S.
100K	1K



Patients will be hesitant, at first, to broadly embrace emerging gene edited therapies

Transplant center and cost logistics may further limit initial rollout of gene replacement / edited therapies

Payors are concerned about long-term durability and will look to outcomes-based reimbursement to offset risk

EDIT-301 Uses AsCas12a

- **EDIT-301 uses AsCas12a**
- **We have Exclusive Licenses to AsCas12a**
- **We do not require Cas9 cross-licenses to commercialize EDIT-301**

AsCas12a, CRISPR-associated protein 12a; Cas9, CRISPR-associated protein 9

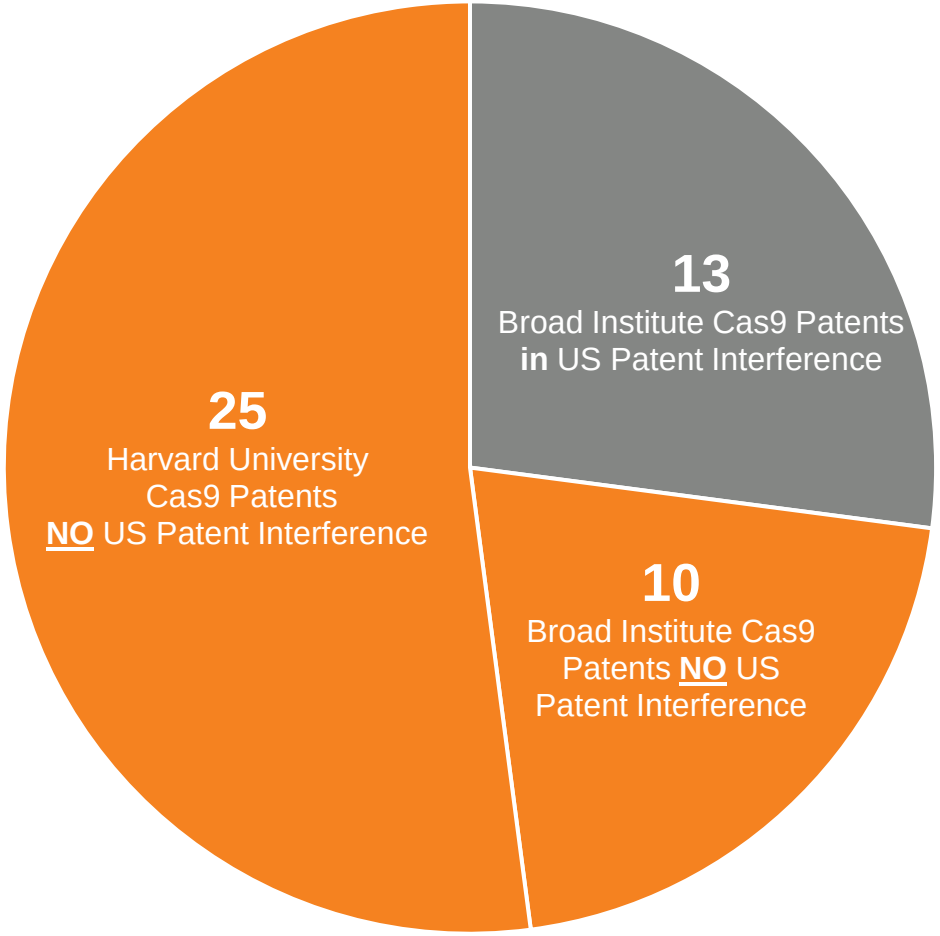
Editas Controls Valuable Foundational Cas9 IP from Broad Institute and Harvard University

Only a subset is subject to interference

Harvard University Cas9 patents (Church, N=25)

#	Patent No.
1	11,535,863
2	11,512,325
3	11,459,585
4	11,365,429
5	11,359,211
6	11,306,328
7	11,286,470
8	11,236,359
9	10,787,684
10	10,767,194
11	10,717,990
12	10,683,490
13	10,640,789
14	10,563,225
15	10,435,708
16	10,435,679
17	10,329,587
18	10,273,501
19	10,100,291
20	9,970,024
21	9,587,252
22	9,267,135
23	9,260,723
24	9,074,199
25	9,023,649

Cas9 Patent Status



Broad Institute Cas9 Patent Interference (N=13)

#	Patent No.
1	9,840,713
2	8,999,641
3	8,993,233
4	8,945,839
5	8,932,814
6	8,906,616
7	8,895,308
8	8,889,356
9	8,871,445
10	8,865,406
11	8,795,965
12	8,771,945
13	8,697,359

Broad Institute Cas9 patents (N=10)

#	Patent No.
1	11,332,719
2	11,041,173
3	11,008,588
4	10,946,108
5	10,930,367
6	10,781,444
7	10,711,285
8	10,577,630
9	9,822,372
10	8,889,418

Patent count numbers are as of 12/31/2022, reflects subset of patent count reported in the Company's 2022 10-K annual report.
Cas9, clustered regularly interspaced short palindromic repeats (CRISPR)-associated protein 9; IP, intellectual property; No., number.

Closing Remarks

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

Acknowledgements

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

Questions & Discussion

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