EDIT-101 Program: BRILLIANCE

Interim Data Analysis

November 17, 2022

SUSAN

Living with Leber Congenital Amaurosis 10

Forward Looking Statements

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Agenda and Speakers

- Introduction
- Review of EDIT 101 and Brilliance Study Results
- 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 for BRILLIANCE Study

- EDIT-101 was well tolerated with favorable safety profile
- BRILLIANCE study has demonstrated proof of concept of EDIT-101
- Three of the 14 (21%) treated participants are responders as defined by clinically meaningful BCVA improvement supported by 2 other positive clinical responses
- Two of 2 homozygous (100%) patients are responders
- Although a small population (1/12, 8%) of compound heterozygous patients may respond to EDIT-101 treatment, homozygous patients are the only population that can be predicted as responders based on current data

BCVA, Best-corrected visual acuity

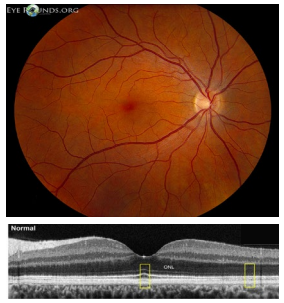
Leber Congenital Amaurosis 10 (LCA10): A Rare Retinal Dystrophy Characterized by Profound Vision Loss Starting in Early Childhood

No Current Treatment for LCA10

- LCA10 is an IRD caused by CEP290 mutations in photoreceptor cells
- Most prevalent mutation is IVS26 c.2991+1655A>G
- Approx. 1500 patients with the IVS26 mutation in US (~20% homozygous and ~80% compound heterozygous)[1]

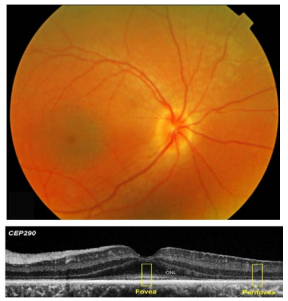
Early-onset Visual Impairment

NORMAL



LCA10

Impaired central vision retinal degeneration



Severely restricted visual field

EDIT-101 for CEP290 IVS26

- First CRISPR gene editing therapy under clinical development for treatment of IRDs
- EDIT-101 deletes the IVS26 mutation to restore expression of full length, functional CEP290

editas MEDICINE

1. Stone et al. *Ophthalmology*. 2017; OCT scans: Cideciyan and Jacobson. *IOVS*. 2019; Healthy retina fundus photo: Eyerounds.org, Retrieved from: https://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/normal-fundus.htm. Accessed Nov 10, 2022.; CEP290 fundus photo: Yzer et al. *Molecular Vision*. 2011. CEP290, Centrosomal protein 290; CRISPR; Clustered repeatable interspaced short palindromic repeats; IRD, Inherited retinal disease; LCA10, Leber congenital amaurosis 10; US, United states.

EDIT-101 Clinical Development
Natural History and BRILLIANCE Studies

Natural History Study
enLIGHTen

Completed

- Support EDIT-101 Phase 1/2 and future studies
- Characterize the clinical course of LCA10
  Evaluate variability, and reliability of efficacy and QoL endpoints
- 12-month prospective observation of 26 patients
  23 patients completed the study

BRILLIANCE Phase 1/2 Study
brilliance

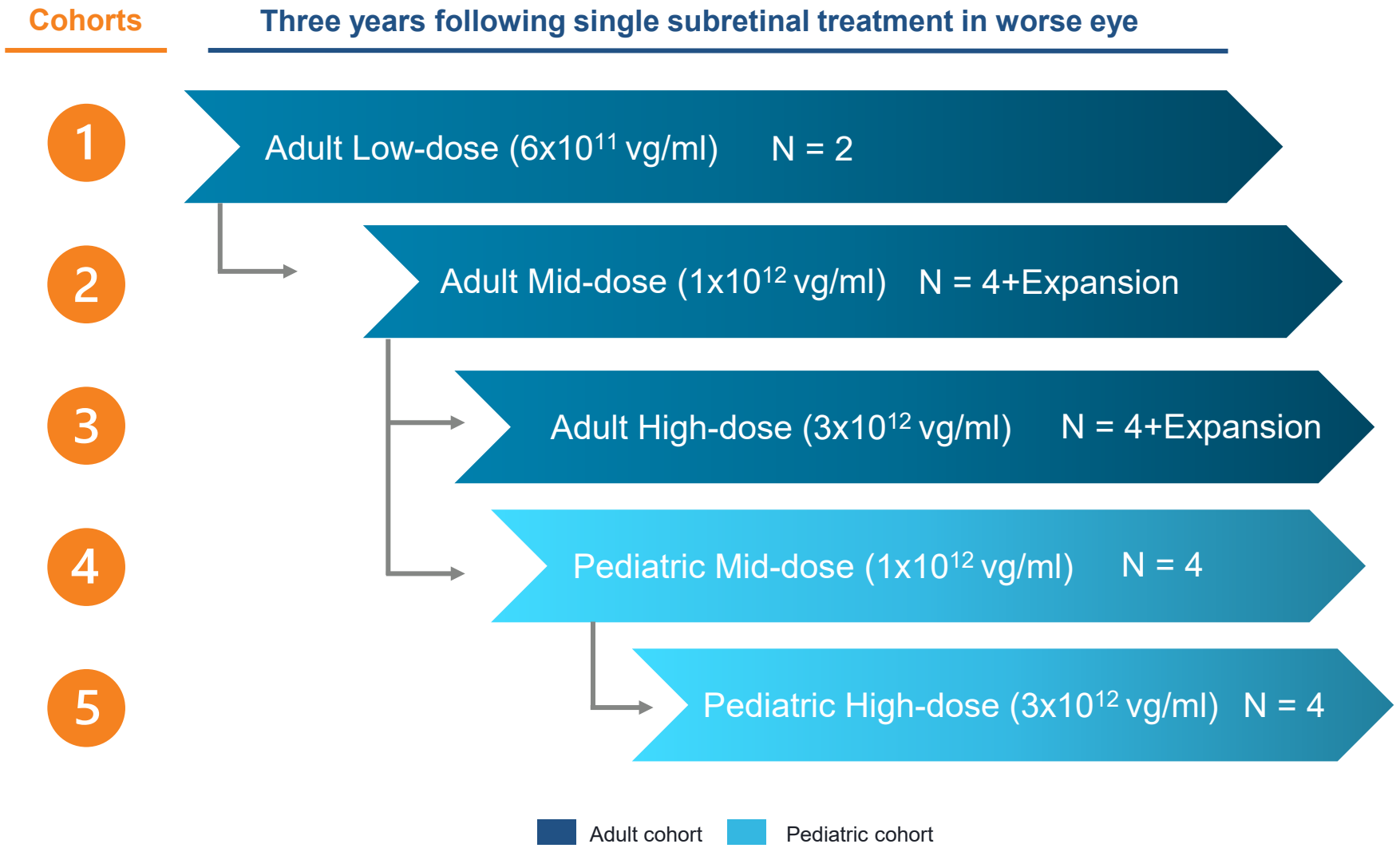
Ongoing

- Evaluate safety and tolerability of EDIT-101
- Evaluate dose, efficacy, QoL endpoints, and segmentation to support design of Phase 3 study
- 3-year study; 12 years of follow-up after Year 3
  14 enrolled patients

CEP290, Centrosomal protein 290; LCA10, Leber congenital amaurosis 10; QoL, Quality of life

BRILLIANCE Study Design

Phase 1/2, Open-label, Single Ascending Dose Study



Key Inclusion Criteria

- Homozygous or compound heterozygous IVS26 mutation
- ≥ 18 years old (cohorts 1-3)
  3-17 years old (cohorts 4-5)

Key Endpoints

- Safety and tolerability of a single sub-retinal dose of EDIT-101
- Changes in:
  - Best-corrected visual acuity
  - Full-field stimulus threshold
  - Visual function navigation
  - Vision-related quality of life

Patient Demographics and Baseline Characteristics

- 12 adult (18 – 63 years) and 2 pediatric patients (9 and 14 years)
- 2 homozygous and 12 compound heterozygous patients
- Broad range in baseline BCVA and FST with no correlation to age

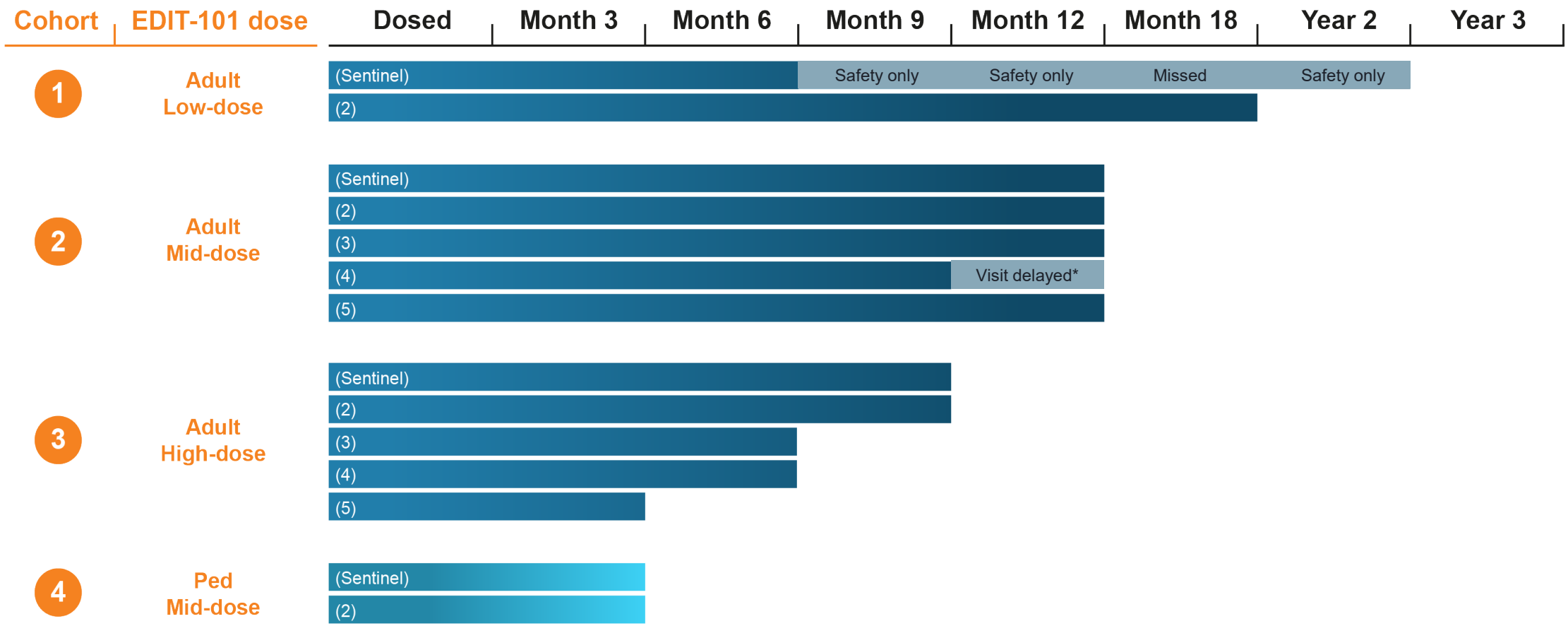
Patient	Gender	Age (years)	Zygosity	Baseline BCVA in Treated Eye (LogMAR)	Baseline Red FST in Treated Eye (Log cd/m^2)
Cohort 1 – Adult Low-dose					
Subject 1	F	50	CH	3.5	-2.00
Subject 2	M	42	CH	3.9	Insufficient data
Cohort 2 – Adult Mid-dose					
⬬ Subject 1	F	54	H	2.7	-1.66
Subject 2	M	20	CH	1.4	-2.14
Subject 3	F	19	CH	0.6	-3.22
Subject 4	F	63	CH	0.9	-3.94
Subject 5	F	17*	CH	3.9	-0.49
Cohort 3 – Adult High-dose					
Subject 1	F	28	CH	2.3	-1.46
Subject 2	F	38	CH	1.0	-3.69
Subject 3	F	36	CH	3.9	-0.62
Subject 4	M	35	CH	2.0	-1.60
Subject 5	F	59	CH	2.9	-1.28
Cohort 4 – Pediatric Mid-dose					
⬬ Subject 1	M	14	H	3.9	-1.31
Subject 2	M	9	CH	1.2	-2.56

⬬ Homozygous CEP290 IVS26 mutation.

* Patient was 17 at time of original consent, turned 18 and was reconsented prior to dosing. BCVA, Best-corrected visual acuity; CEP290, Centrosomal protein 290; CH, Compound heterozygous; F, Female; FST, Full-field stimulus threshold; H, Homozygous; LogMAR, Log of the minimum angle of resolution; M, Male

Duration of Follow-up After EDIT-101 Dosing

- Safety and efficacy data for 14 patients (12 adult and 2 pediatric)
- 11/14 patients had at least 6 months of follow-up, including 7 patients with 12 or more months of follow-up
- 3/14 patients had 3 months of follow-up



* Visit delayed until after data cut date on 13AUG2022. No change in safety and efficacy profile.

EDIT-101 Demonstrates a Favorable Safety Profile

SAFETY & TOLERABILITY

- EDIT-101 was generally well tolerated
- No dose-limiting toxicities to date
- No drug-related SAEs to date
- No ocular SAEs to date

TEAE SUMMARY

- Majority of AEs were mild (77%) or moderate (22%)
- 50% of AEs were related to surgical procedure
- 7/14 patients (50%) reported no ocular AEs related to EDIT-101
- One patient (7%) reported a severe ocular AE at 6 months (non-serious visual impairment) which is improving. Patient was enrolled in the NHS, during which the same eye experienced similar vision fluctuation.

TEAE, Treatment-emergent adverse event; NHS, Natural history study; SAE, Severe adverse event

Efficacy Measures Based on the Natural History Study

Positive response defined as a clinically meaningful improvement in BCVA and improvement in 2 other endpoints

Endpoints	Direction of Improvement	Natural History Study Data	Threshold for Meaningful Change from Baseline
Best-corrected visual acuity (BCVA)[α]	↓	NHS data suggested good reproducibility	≥ 0.1 LogMAR - statistically meaningful ≥ 0.3 LogMAR - clinically meaningful*
Full-field stimulus threshold (FST)	↓	NHS data suggested variability	≥ 0.6 log cd/m2 - statistically meaningful
Visual function navigation (VFN)[‡]	↑	NHS data suggested variability	≥ 3-point increase in mobility score – statistically meaningful
PRO: Vision-related quality of life (QoL)[∞]	↑	Limited NHS data	≥ 4-point increase in composite score – clinically meaningful**

[α] BCVA assessed using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart and the Berkeley Rudimentary Visual Test (BRVT); [‡] VFN assessed using the Ora Visual Navigation Challenge; ∞ QoL assessed using the National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25) for cohorts 1-3 and the Children's Visual Function Questionnaire (CVFQ) for cohorts 4-5; * US Food and Drug Administration, "Human Gene Therapy for Retinal Disorders Guidance for Industry". Retrieved from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/human-gene-therapy-retinal-disorders. Accessed Nov 7, 2022. ** Validity and Minimal Clinically Important Differences of Outcome Measures. Retrieved from: https://www.ncbi.nlm.nih.gov/books/NBK349601/table/T40/#. Accessed Nov 8, 2022.

EDIT-101 Efficacy Summary for Patients with ≥ 3 Months of Follow-Up

- Multiple patients showed improvement in one or more endpoints

Patient	Gender	Age	Zygosity	Baseline BCVA in Study Eye	BCVA	FST (red)	VFN	PRO: VFQ/CVFQ‡
Cohort 1 – Adult Low-dose								
Subject 1	F	50	CH	3.5	-0.3	-0.01	-2	-13
Subject 2	M	42	CH	3.9	0	NA	+3	+13
Cohort 2 – Adult Mid-dose								
Subject 1	F	54	H	2.7	-1.3	-0.22	+2ᵒᵒᵃ	+10
Subject 2	M	20	CH	1.4	-0.2	-0.79	+7ᵃ	-4
Subject 3	F	19	CH	0.6	0	+0.07	0	+5
Subject 4	F	63	CH	0.9	0	+0.54	-1	+7
Subject 5	F	17*	CH	3.9	0	-0.60	-1	+15
Cohort 3 – Adult High-dose								
Subject 1	F	28	CH	2.3	+0.6	-0.25	-5	-23
Subject 2	F	38	CH	1.0	+0.2	+0.50	+2	-2
Subject 3	F	36	CH	3.9	0	-1.07	+3	+6
Subject 4	M	35	CH	2.0	0	+0.11	-3	-8
Subject 5	F	59	CH	2.9	-0.7	-1.01	-2	+13
Cohort 4 – Pediatric Mid-dose								
Subject 1	M	14	H	3.9	-1.0ᵃ	-1.09	+1	+3
Subject 2	M	9	CH	1.2	-0.2	-0.38	+2	0

Clinically or statistically meaningful improvement Homozygous CEP290 IVS26 mutation

* Patient 17 at time of consent, turned 18 and was reconsented prior to dosing; ᵒᵒ ≥ 3 change from baseline to Month 9; ᵃ Improvement also recorded in contralateral eye; ‡ Cohorts 1-3 - National Eye Institute Visual Function Questionnaire-25 composite score from: general vision, color vision, near vison, distance vision. (change of 4 considered clinically meaningful in this analysis) Cohort 4 - Children's Visual Function Questionnaire composite score from: general vision, competence; (change of 3 considered meaningful in this analysis) BCVA, Best-corrected visual acuity (LogMAR); CEP290, Centrosomal protein 290; CH, Compound heterozygous; F, Female; FST, Full-field stimulus threshold (Log cd/m^2); H, Homozygous; M, Male; VFN, Visual function navigation (mobility score)

EDIT-101 Efficacy Summary for Patients with ≥ 3 Months of Follow-Up

- Positive response defined as a clinically meaningful improvement in BCVA and improvement in 2 other endpoints
- Three (3) patients demonstrated clinically meaningful improvement in BCVA and consistent positive responses in 2 other endpoints

Patient	Gender	Age	Zygosity	Baseline BCVA in Study Eye	BCVA	FST (red)	VFN	PRO: VFQ/CVFQ‡
Cohort 1 – Adult Low-dose								
Subject 1	F	50	CH	3.5	-0.3	-0.01	-2	-13
Subject 2	M	42	CH	3.9	0	NA	+3	+13
Cohort 2 – Adult Mid-dose								
Subject 1	F	54	H	2.7	-1.3	-0.22	+2∞a	+10
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Subject 3	F	36	CH	3.9	0	-1.07	+3	+6
Subject 4	M	35	CH	2.0	0	+0.11	-3	-8
Subject 5	F	59	CH	2.9	-0.7	-1.01	-2	+13
Cohort 4 – Pediatric Mid-dose								
Subject 1	M	14	H	3.9	-1.0a	-1.09	+1	+3
Subject 2	M	9	CH	1.2	-0.2	-0.38	+2	0

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EDIT-101 Efficacy Summary for Patients with ≥ 3 Months of Follow-Up

- Two of 2 homozygous participants (2/2) are both responders
- One heterozygous participant (1/12) is also a responder

Patient	Gender	Age	Zygosity	Baseline BCVA in Study Eye	BCVA	FST (red)	VFN	PRO: VFQ/CVFQ‡
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Subject 1	F	50	CH	3.5	-0.3	-0.01	-2	-13
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Cohort 4 – Pediatric Mid-dose								
Subject 1	M	14	H	3.9	-1.0[a]	-1.09	+1	+3
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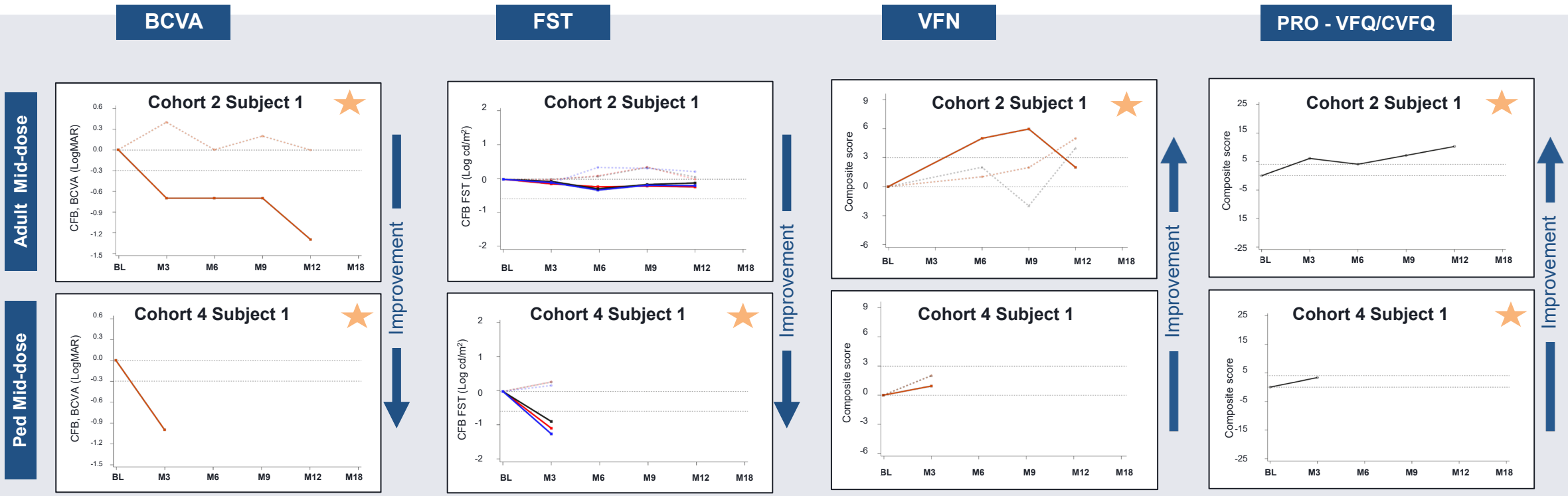
Homozygous Subjects (2/2) Were Responders, With Improvement in BCVA and at Least One Additional Endpoint



BCVA, Best-corrected visual acuity; FST, Full-field stimulus threshold; VFN, Visual function navigation; PRO, Patient-reported outcome: Cohorts 1-3 - National Eye Institute Visual Function Questionnaire-25 composite score from: general vision, color vision, near vison, distance vision. Cohort 4 - Children's Visual Function Questionnaire composite score from: general vision, competence. Cohort 2 subject 1 had ≥ 3 change from baseline in VFN up to Month 9.

Key Takeaways for BRILLIANCE Study

- EDIT-101 was well tolerated with favorable safety profile
- BRILLIANCE study has demonstrated proof of concept of EDIT-101
- Three of the 14 (21%) treated participants are responders as defined by clinically meaningful BCVA improvement supported by 2 other positive clinical responses
- Two of 2 homozygous (100%) patients are responders
- Although a small population (1/12, 8%) of compound heterozygous patients may respond to EDIT-101 treatment, homozygous patients are the only population that can be predicted as responders based on current data

BCVA, Best-corrected visual acuity

Closing Remarks

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

Questions
& Discussion

Appendix

TEAEs Related to EDIT-101

System Organ Class Preferred Term	All Patients (N = 14) n (%)	Adult Low-dose Cohort 1 (N = 2) n (%)	Adult Mid-dose Cohort 2 (N = 5) n (%)	Adult High-dose Cohort 3 (N = 5) n (%)	Pediatric Mid-dose Cohort 4 (N = 2) n (%)
ANY TEAE RELATED TO EDIT-101	**7 (50%)**	**1 (50%)**	**3 (60%)**	**3 (60%)**	**-**
EYE DISORDERS (TOTAL)	7 (50%)	1 (50%)	3 (60%)	3 (60%)	-
Anterior chamber cell	1 (7.1%)	-	-	1 (20.0%)	-
Anterior chamber inflammation	2 (14.3%)	1 (50.0%)	1(20.0%)	-	-
Conjunctival edema	1 (7.1%)	1 (50.0%)	-	-	-
Conjunctival hyperemia	1 (7.1%)	1 (50.0%)	-	-	-
Photophobia	1 (7.1%)	-	1(20.0%)	-	-
Posterior segment of eye anomaly	1 (7.1%)	1 (50.0%)	-	-	-
Retinal cyst	1 (7.1%)	-	-	1 (20.0%)	-
Retinal degeneration	1 (7.1%)	-	-	1 (20.0%)	-
Retinal deposits	1 (7.1%)	-	-	1 (20.0%)	-
Retinal drusen	1 (7.1%)	-	1 (20.0%)	-	-
Retinal infiltrates	1 (7.1%)	1 (50.0%)	-	-	-
Retinal pigment epithelial tear	1 (7.1%)	1 (50.0%)	-	-	-
Retinal pigment epitheliopathy	1 (7.1%)	-	1 (20.0%)	-	-
Subretinal hyperreflective exudation	1 (7.1%)	-	1 (20.0%)	-	-
Visual impairment	2 (14.3%)	-	-	2 (40.0%)	-
Vitreal cells	2 (14.3%)	1 (50.0%)	-	1 (20.0%)	-

Number (n) and percentage (%) of patients experiencing TEAEs; TEAEs, Treatment-emergent adverse events