BRILLIANCE: A Phase 1/2 Single Ascending Dose Study of EDIT-101, an *in vivo* CRISPR Gene Editing Therapy in CEP290-Related Retinal Degeneration

editas MEDICINE

September 29, 2021

Forward Looking Statements

This presentation contains forward-looking statements and information within the meaning of The Private Securities Litigation Reform Act of 1995. 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. Forward-looking statements in this presentation include statements regarding the initiation, timing, progress and results of the Company’s preclinical and clinical studies and its research and development programs, including the safety and efficacy of EDIT-101 and the application of results achieved in the study to any future studies, the timing for the Company’s receipt and presentation of additional data from its clinical trials and preclinical studies, the timing or likelihood of regulatory filings and approvals, and the therapeutic value, development, and commercial potential of the Company’s gene editing technologies. 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 factors, including: uncertainties inherent in the initiation and completion of pre-clinical studies and clinical trials and clinical development of the Company’s product candidates; availability and timing of results from pre-clinical 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 represent Company’s views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, the Company explicitly disclaims any obligation to update any forward-looking statements.

Agenda

Introduction

Overview of LCA10 and CEP290-Related Retinal Degeneration

Overview of EDIT-101

Phase 1/2 Brilliance Trial

Safety Assessments

Efficacy Assessments

Summary

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Professor of Ophthalmology, Harvard Medical School
Principal Investigator, BRILLIANCE Clinical Trial

EDIT-101 Timeline

2014

Ocular Genomics Institute

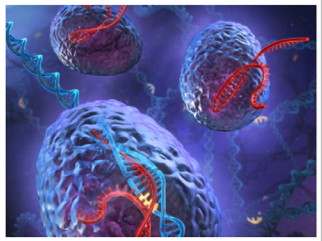
Editas Medicine Initiates Clinical Natural History Study to Evaluate Patients with Leber Congenital Amaurosis Type 10 (LCA10)

SEPTEMBER 21, 2017
Massachusetts Eye and Ear named as first site for the study

CAMBRIDGE, Mass., Sept. 12, 2017 (GLOBE NEWSWIRE) — Editas Medicine, Inc. (NASDAQ:EDIT), a leading genome editing company, today announced that the Company initiated a clinical natural history study of Leber Congenital Amaurosis type 10 (LCA10). LCA10 is caused by mutations in the *CEP290* gene. The study will prospectively evaluate patients to assess the course of the disease and to pilot potential clinical trial endpoints and designs. This knowledge will inform the interventional clinical trial design for EDIT-101, Editas Medicine's pre-clinical product candidate to treat LCA10.

Broad Institute awarded first patent for engineered CRISPR-Cas9 system

BROAD INSTITUTE



April 15th, 2014

The Broad Institute today announced that the United States Patent and Trademark Office has issued the first patent for an engineered CRISPR-Cas9 system that is enabling scientists to modify genes and better understand the biology of living cells and organisms. The institute applied for the patent in concert with the January 3, 2013 publication in *Science* (Cong, *et al.*) that described the use of the CRISPR enzyme, Cas9, for genome editing.

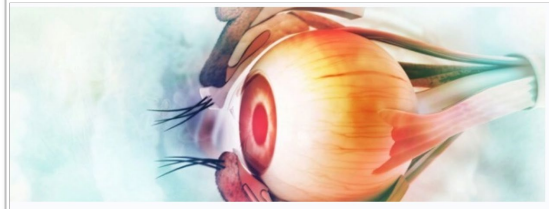
Originally discovered in bacteria, where several different CRISPR cascades function as innate immune systems and natural defense mechanisms, the engineered CRISPR-Cas9 system can be programmed to target specific stretches of genetic code and to make cuts at precise locations. Over the past few years, those capabilities have been harnessed and used as genome editing tools, enabling researchers to permanently modify genes in mammalian cells. In the future, these tools may make it possible to correct mutations at precise locations in the three billion-letter sequence of the human genome to treat genetic causes of disease in patients.

Editas Medicine to develop new class of genome editing therapeutics

Editas Medicine, a transformative genome editing company, today announced it has secured a $43 million Series A financing led by Flagship Ventures, Polaris Partners and Third Rock Ventures with participation from Partners Innovation Fund. Following an explosion of high profile publications on CRISPR/Cas9 and TALENs, genome editing has emerged as one of the most exciting new areas of scientific research. These recent advances have made it possible to modify, in a targeted way, almost any gene in the human body with the ability to directly turn on, turn off or edit disease-causing genes. Editas' mission is to translate its genome editing technology into a novel class of human therapeutics that enable precise and corrective molecular modification to treat the underlying cause of a broad range of diseases at the genetic level.

"Editas is exclusively positioned to leverage the very latest in genome editing to develop life-changing medicines for patients," said Kevin Bitterman, Ph.D., interim president, Editas Medicine and principal, Polaris Partners. "Our suite of foundational intellectual property, combined with the proprietary know-how of our founding team and our financial resources, will enable us to rapidly translate these groundbreaking discoveries into important medicines."

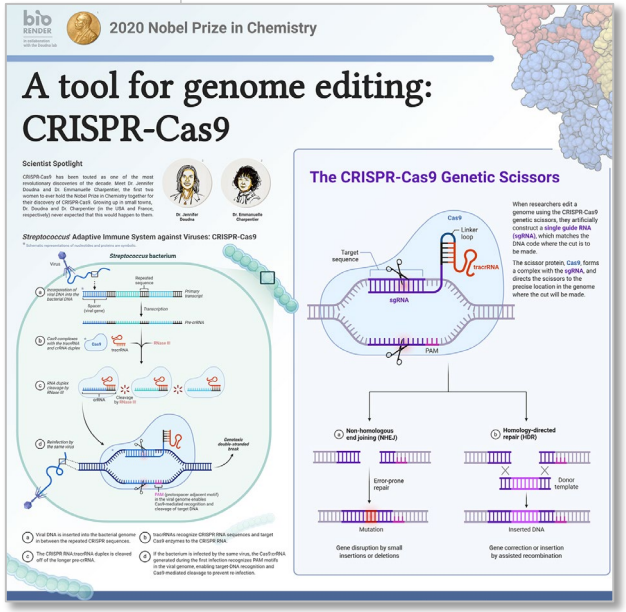
Editas & Allergan Dose First Patient in Phase I/II Historic Gene Editing Study – Accomplished via In Vivo Treatment



Editas Medicine, Inc. (EDIT) and Allegan plc (AGN) announced they have dosed the first patient in a Phase I/II study called BRILLIANCE to evaluate their CRISPR-based candidate, AGN-151587 (EDIT-101), in patients with Leber congenital amaurosis 10 (LCA10), an inherited form of blindness. A historical milestone as for the first time a patient's genes are actually modified within the body—in vivo treatment. Until now , gene editing operated on a ex vivo basis—targeted cells are taken from the patient, modified and thereafter returned. This pathbreaking study assesses EDIT-101 on 18 LCA patients.

2020 Nobel Prize in Chemistry

A tool for genome editing: CRISPR-Cas9



npr

Blind Patients Hope Landmark Gene-Editing Experiment Will Restore Their Vision

TODAY

September 29, 2021
Editas Medicine Presents Clinical Data on First *In Vivo* Gene Editing Treatment for LCA10

Key Findings & Acknowledgements

Initial Observations

EDIT-101 was associated with no serious adverse events (AE) or dose-limiting toxicities (DLT) to date.

Early efficacy signals in the mid-dose cohort suggest positive biological activity and potential early clinical benefits.

Thank You

Editas Medicine extends utmost gratitude to all trial participants and their families for their trust and support.

Thank you to all investigative sites for your partnership and ongoing collaboration.

Massachusetts Eye and Ear Infirmary*
Boston, Massachusetts

W.K. Kellogg Eye Center - University of Michigan
Ann Arbor, Michigan

Casey Eye Institute - OHSU*
Portland, Oregon

Bascom Palmer Eye Institute
Miami, Florida

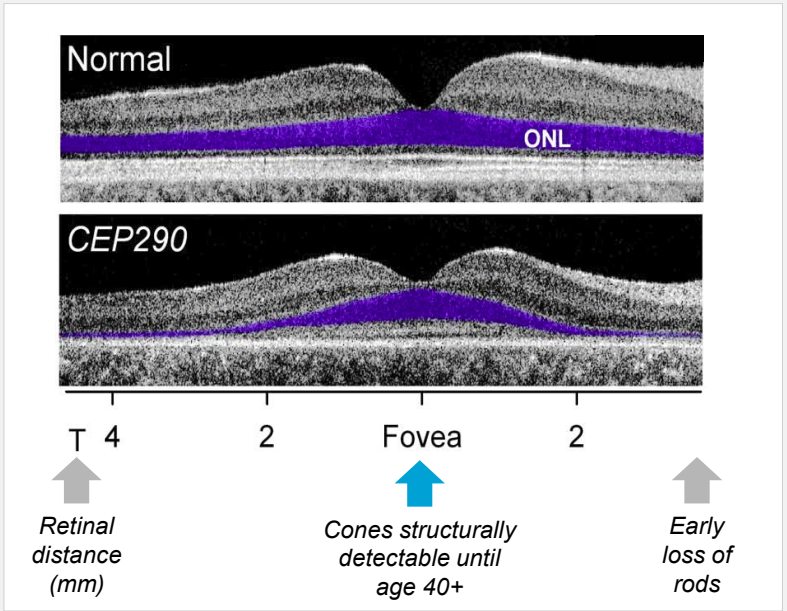
*Primary Surgical Sites

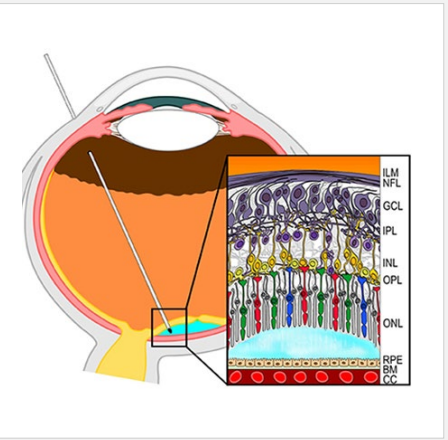
CEP290-Related Retinal Degeneration & EDIT-101

CEP290-Related Retinal Degeneration
A Rare Cause of Early Onset Loss of Vision

Currently No Approved Treatments for CEP290-related Retinal Degeneration

- CEP290-related retinal degeneration causes progressive vision loss/ blindness in children within the first decade of life[1,2]
- Autosomal recessive disease
- Disease characterized by early loss of photoreceptors in the eye
- Focal cone rich area of the retina in the area of the fovea however remains intact until adulthood, which provides the opportunity for gene correction





Cross-sectional OCT scans along the horizontal meridian through the fovea in a normal subject, a *CEP290*-LCA patient, ONL (outer nuclear layer) is highlighted in purple

1. Kumaran N, et al. Br J Opthalmol 2017
2. Weleber RG. LCA Gene Reviews 2013

Impact of CEP290-Related Degeneration on Patients

DISEASE SYMPTOMS

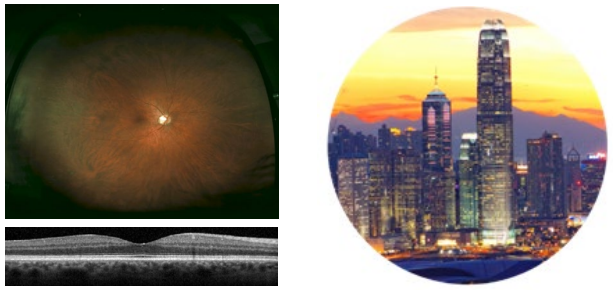
- Blindness usually diagnosed in infancy or early childhood
- Severely impaired visual acuity
- Loss of peripheral vision
- Night blindness
- Rapid, involuntary eye movements (nystagmus)

PATIENT IMPACT

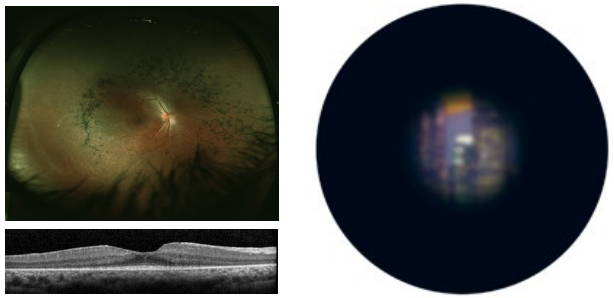
- Inability to adequately navigate enclosed spaces
- Risk of falls and injury
- Inability to be mobile or independently use public transportation
- Constrained social function
- Impaired academic performance
- Challenges with employment

PATIENT RETINA & VISION

NORMAL

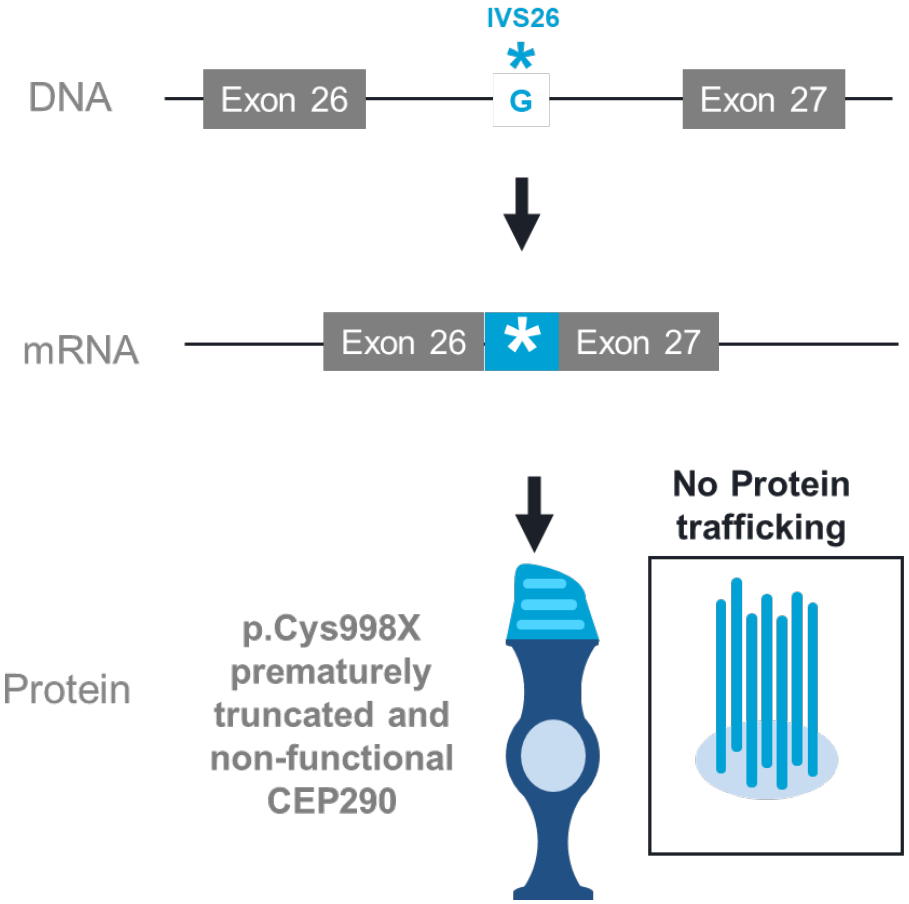


CEP290

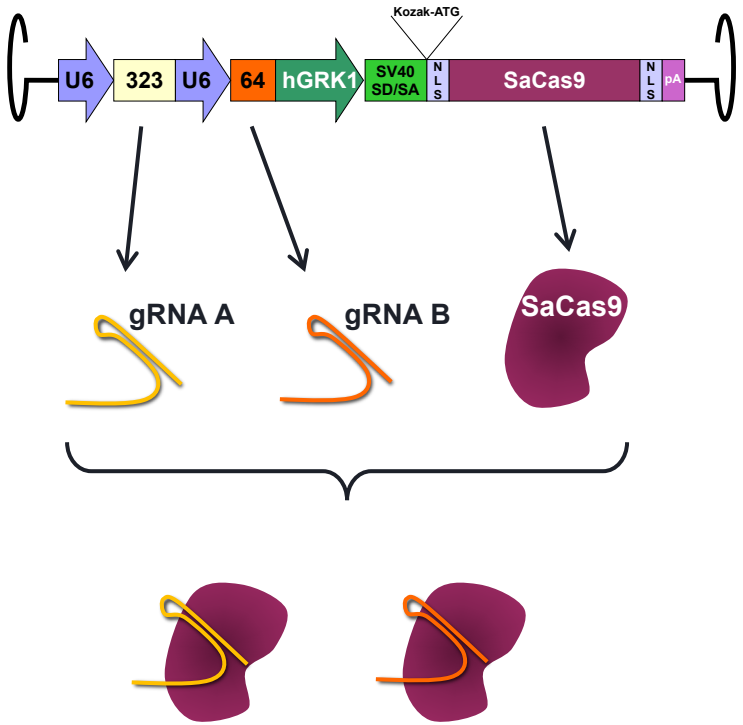


The IVS26 Mutation in CEP290 is a Clearly Defined Target for Gene Editing

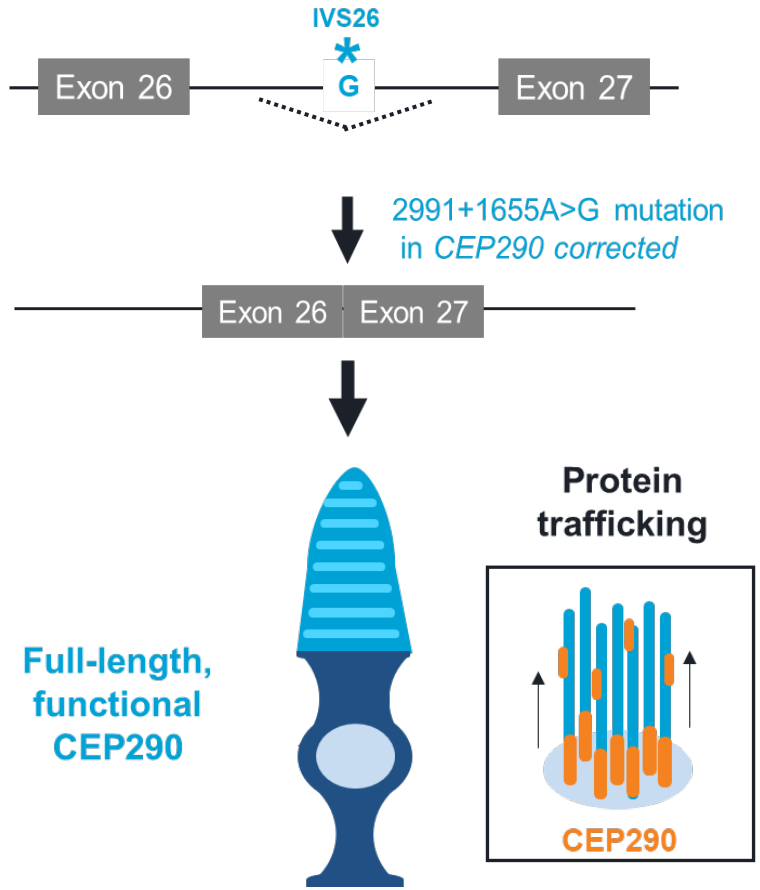
CEP290-Related Retinal Degeneration



EDIT-101



Gene Editing Therapeutic Concept

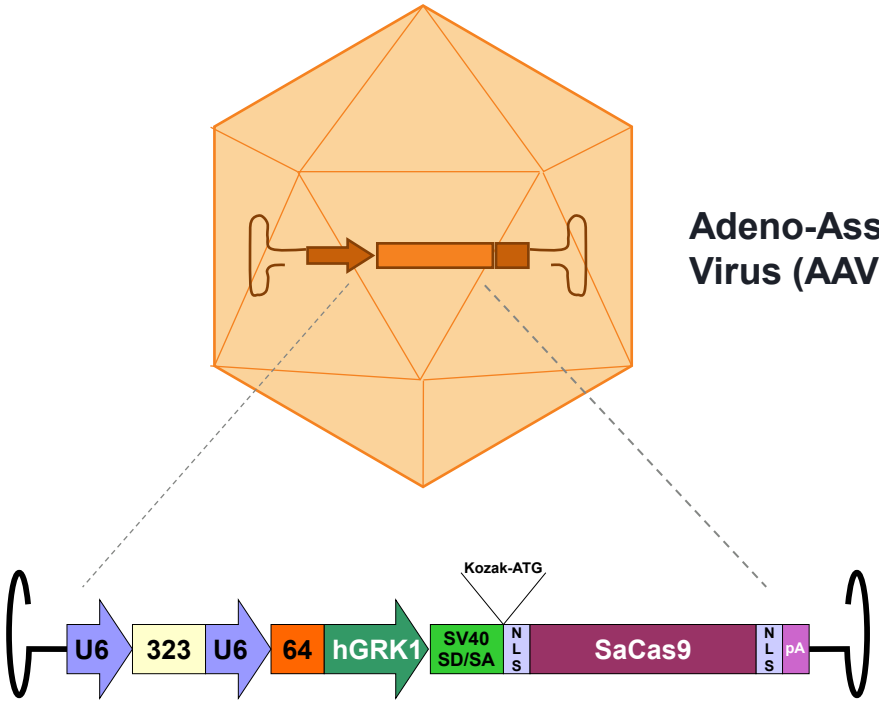


EDIT-101 Allows for Local Delivery of the Editing Complex to Specifically Target the Photoreceptors to be Corrected

AAV5 encoding two gRNAs and SaCas9 delivered subretinally as a single administration

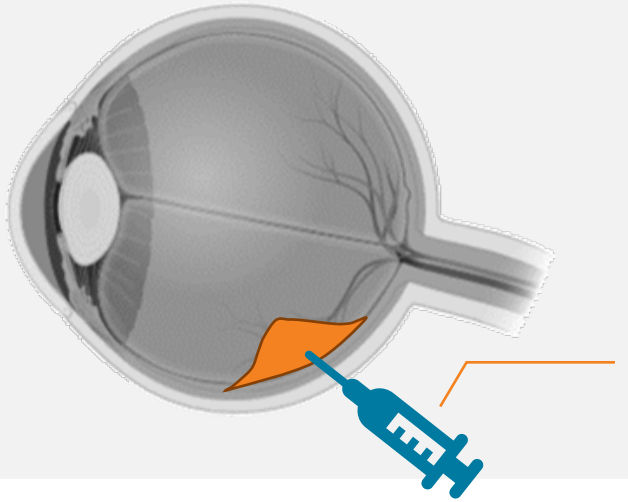
EDIT-101

CRISPR-Cas9 gene editing



EDIT-101 specifically targets the part of the retina where viable photoreceptors are found

- **Photoreceptor-tropic** AAV5 vector
- **Highly specific** Guide RNAs
- **Restricted** Cas9 expression in **Photoreceptor Cells**
- **Local delivery to subretinal space** limits the risk of biodistribution outside of the eye



Overview of Data Presentation

Data collection cutoff date: August 4, 2021

- Safety data include all subjects in the adult low and mid dose cohorts (N=6).
- Efficacy data include all treated subjects with at least 3 months of post treatment follow-up (N=5).
- Topline efficacy data are focused on reliable and confirmed efficacy measures* that are clinically relevant to CEP290-related retinal degeneration.
- Due to the limited number of subjects and differential follow-up, the efficacy findings are presented individually.

*Oculomotor dysfunction in patients commonly affect quality and reliability of many common ophthalmologic evaluations

Natural History Study Assessments

Assessment	Endpoints	Category	Reliability	Stability 1 year Follow-Up
Optical coherence tomography (OCT)	Thickness of the outer nuclear layer (ONL) and integrity of the ellipsoid zone	Anatomic	?	?
Pupillometry	Pupil size, pupil constriction	Physiologic	✓	✓
Oculomotor control and instability (OCI)	Gaze tracking	Physiologic	?	?
Visual acuity	logMAR measurement of best-corrected visual acuity (BCVA)	Visual Function	✓	✓
Full field light sensitivity threshold (FST)	Dark adapted visual sensitivity to white, red, and blue light	Visual Function	✓	✓
Contrast sensitivity+	LogMAR measurement of contrast sensitivity	Visual Function	?	?
Microperimetry+	Macular sensitivity	Visual Function	⊗	⊗
Kinetic perimetry	Visual field	Visual Function	⊗	⊗
Color vision+	Farnsworth 15 score	Visual Function	?	?
Quality of Life (QoL)	QoL questionnaire (CVFQ; NEI VFQ-25) Global Impressions of Change Global Impressions of Severity	Patient Reported Outcomes	✓	✓
Visual Function Navigation (Ora-VNC™)	Visual Function Navigation course score	Functional Vision	? **	✓

** Natural history study is being conducted to assess and define reproducible results of visual navigation challenge (VNC) evaluation.

EDIT-101 Observations

EDIT-101 for the treatment of CEP290-related retinal degeneration is the **first clinically investigated in vivo CRISPR gene editing therapy**

To date, **no dose-limiting toxicities or serious adverse events** have been reported **in the six adult subjects** treated with the low and mid doses of EDIT-101

Early efficacy signals in the mid dose cohort suggest **positive biological activity and potential early clinical benefits**

High dose adult cohort is currently ongoing with **no DLTs or SAEs observed to date**

Pediatric mid dose cohort is **currently enrolling**

Brilliance Trial

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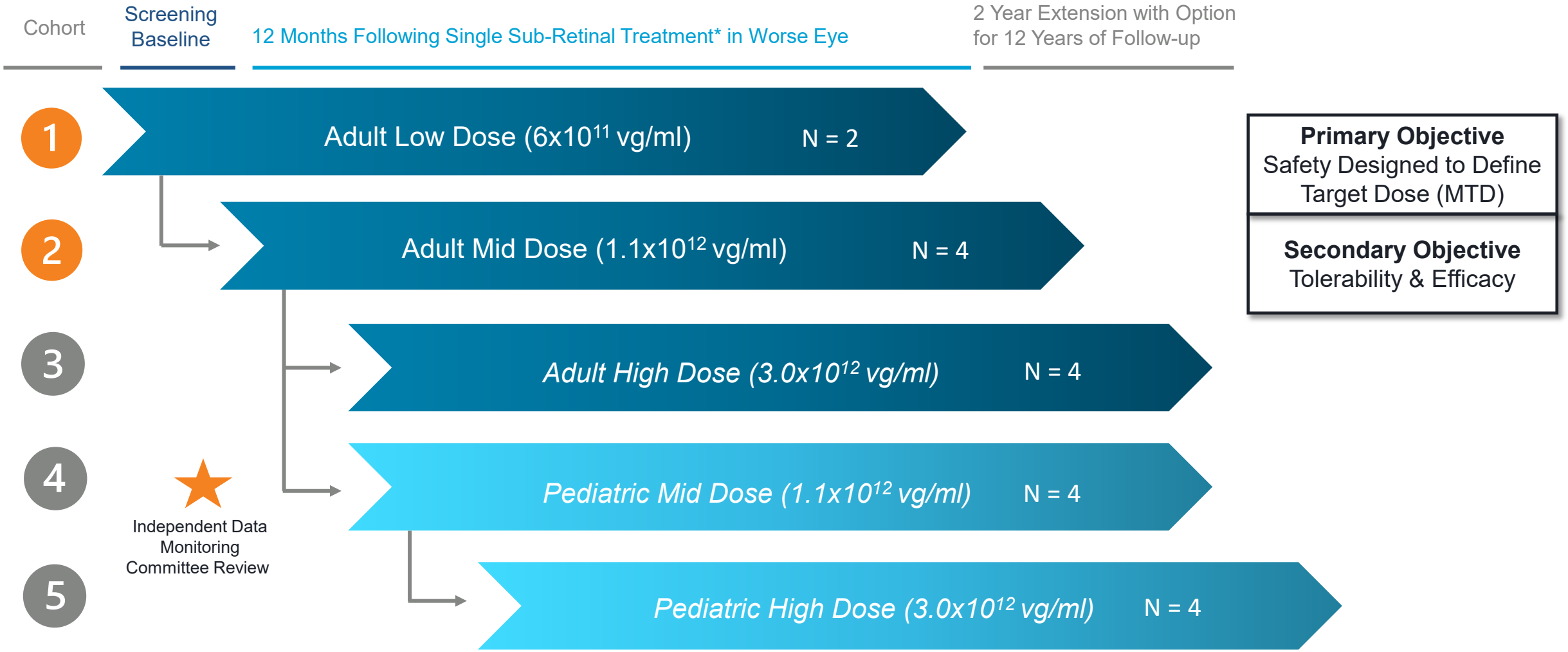
BRILLIANCE Phase 1/2, Open-label, Single Ascending Dose Study (NCT03872479)



Eligibility Criteria

Key Inclusion Criteria

- Adults aged 18 years or older in cohorts 1-3
- Pediatric and adolescent subjects aged 3 up to 17 years
- A clear genetic diagnosis of *CEP290*-associated retinal degeneration; being at least heterozygous for the c.2991+1655A>G mutation in *CEP290*

Cohort 1	Cohort 2-5	Cohort 2-5
	First Subject in Each Cohort	*Subsequent Subjects*
Light Perception, Black White Discrimination, or White Field Projection	Light Perception to 1.6 logMar (20/800 Snellen)	Light Perception to 0.4 logMar (20/50 Snellen)

Key Exclusion Criteria

- Other known disease-causing mutations detected in other retinal degeneration disease genes
- Able to pass the Visual Navigation Course at the highest level of difficulty
- Cataract surgery in the last 3 months
- Active ocular/intraocular infection or inflammation
- History of steroid-responsive intraocular pressure increase
- Inability or unwillingness to take oral prednisone
- Prior gene therapy or oligonucleotide treatment

Baseline Characteristics

	Cohort 1		Cohort 2			
	C1-P1*	C1-P2	C2-P1	C2-P2	C2-P3	C2-P4
Age	50	42	54	20	19	63
Sex	F	M	F	M	F	F
Race/Ethnicity	Caucasian	Caucasian	Caucasian	Hispanic	Caucasian	Caucasian
Genotype	Heterozygous	Heterozygous	Homozygous	Heterozygous	Heterozygous	Heterozygous
2nd Mutation	p.Leu482Ter: c.1445T>A	c.5587-1G>C	c.2991+1655A>G	p.Lys170Ter: c.508A>T	c.7344_7345delTT	p.Gly1890Ter: c.5668G>T
Trial Duration (months)	15	12	7	5	3	2
BCVA Study Eye (logMar)	3.5	3.9	2.7	1.4	0.6	0.9
BCVA CL Eye (logMar)	3.5	3.9	2.3	1.4	0.5	0.6

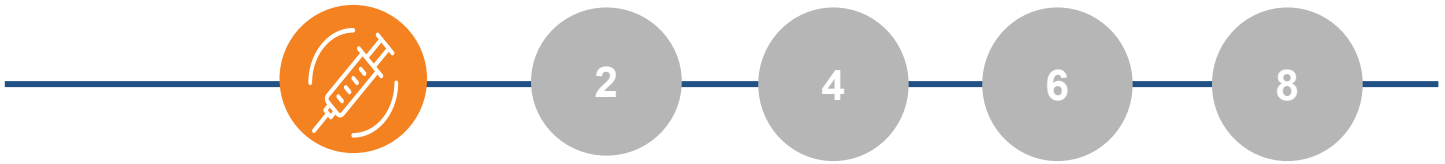
*Subject unable to return to study site for follow-up visits due to COVID.

Assessment of Safety in Brilliance

Evaluations of Safety

- Dose-limiting toxicities (DLTs) resulting in significant vision loss
- Non-ocular AEs
- Treatment-related AEs
- Procedure-related AEs

EDIT-101-related
(according to investigator)



Week

Definition

Vision-Threatening Toxicity
↓ BCVA by ≥0.6 logMAR

Loss of light perception (2 consecutive visits)
Corticosteroid-unresponsive inflammation (≥4 weeks)

Severe Non-Ocular AE

Safety Summary

- No DLTs or SAEs observed to date in first two cohorts.
- To date, no treatment-related cataracts, edema, or retinal thinning have been observed.
- Most frequently reported AE was eye pain in 4 subjects (1 low dose and 3 mid dose) related to the surgical procedure.
- Only mild cases of treatment-related inflammation have been reported.
- No Cas9-specific antibody detected.
- IDMC safety review allows enrollment of pediatric subjects into the mid dose cohort.

	Cohort 1 Adult Low Dose (n=2)	Cohort 2 Adult Mid Dose (n=4)
AEs	26 (22 Mild; 4 Moderate)	25 (23 Mild; 2 Moderate)
Ocular AEs	22 (18 Mild; 4 Moderate)	9 (9 Mild)
AEs Related to EDIT-101	8 (6 Mild; 2 Moderate)	3 (3 Mild)
Serious AEs	0	0
DLTs	0	0

Efficacy Assessment Overview

Reliable and Confirmed Efficacy Measures that are Clinically Relevant to CEP290 Retinal Degeneration

Assessment	Endpoints	Category
Visual acuity	logMAR measurement of best-corrected visual acuity (BCVA)	Visual Function
Full field light sensitivity threshold (FST)	Dark adapted visual sensitivity to white, red, and blue light	Visual Function
Visual Function Navigation (Ora-VNC™)	Visual Function Navigation course score	Functional Vision

Visual Acuity Test

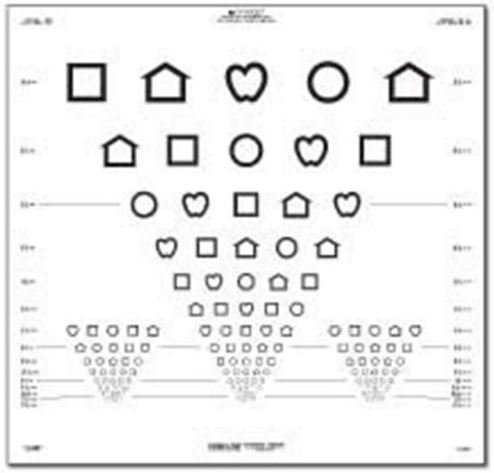
Best Corrected Visual Acuity (BCVA)

Able to read letters

Early Treatment Diabetic Retinopathy Study (ETDRS)/ logMAR Visual acuity

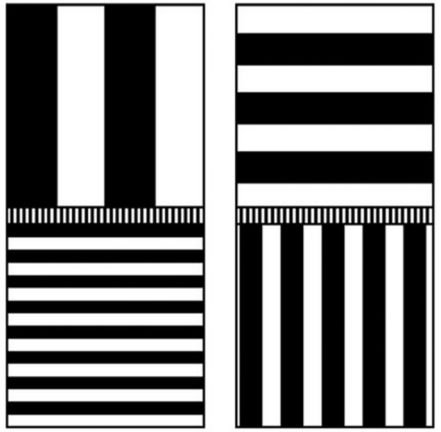
OR

Unable to read letters



Lea Symbols 15-line Pediatric Eye Chart

BCVA 20/800 or Worse
in at least one eye



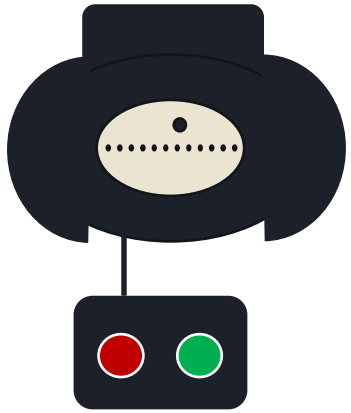
Berkeley Rudimentary Visual Test (BRVT)

Full Field Light Sensitivity Threshold Test (FST)

Well-established tool for testing **retinal sensitivity in low vision patients**

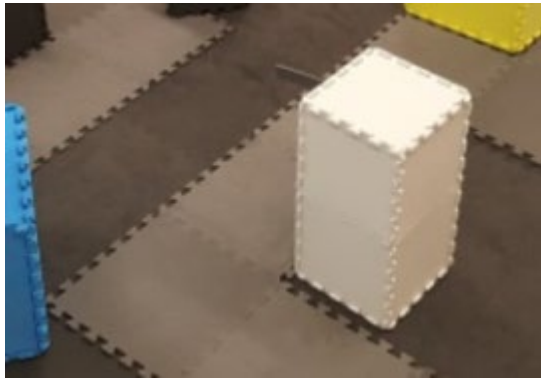
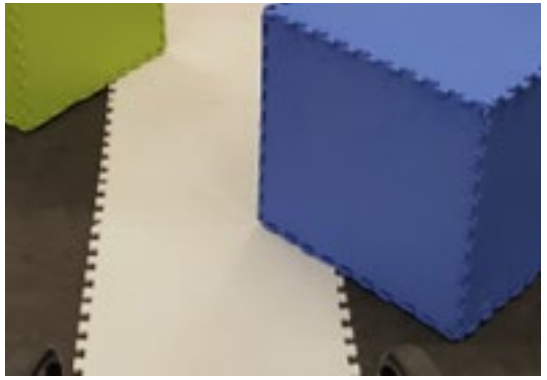
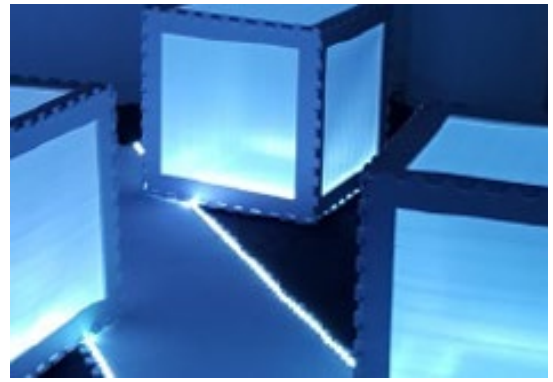
Measures the point of greatest sensitivity across the entire visual field by testing for lowest luminance flash which elicits visual sensation **(visual sensitivity)**

Blue, red, and white stimuli to assess **rod/cone/mixed sensitivity**



Visual Navigation Courses (VNC™)

brilliance

LOW CONTRAST VISUAL NAVIGATION CHALLENGE (LCVNC)	HIGH CONTRAST VISUAL NAVIGATIONS CHALLENGE (HCVNC)	HIGH CONTRAST ROOM EXIT (HCRE)	BACKLIT ROOM EXIT (BRE)
			
Low Contrast Path Multiple Turns Numerous Obstacles 8 Illumination Levels	High Contrast Path Wider Path with Turns High Contrast Obstacles 8 Illumination Levels	High Contrast Path No Turns High Contract Obstacles 3 Illumination Levels	Illuminated Path No Turns Illuminated Obstacles 2 Illumination Levels
VNC Level Score 14 to 21	**Score 6 to 13**	**Score 3 to 5**	**Score 1 to 2**

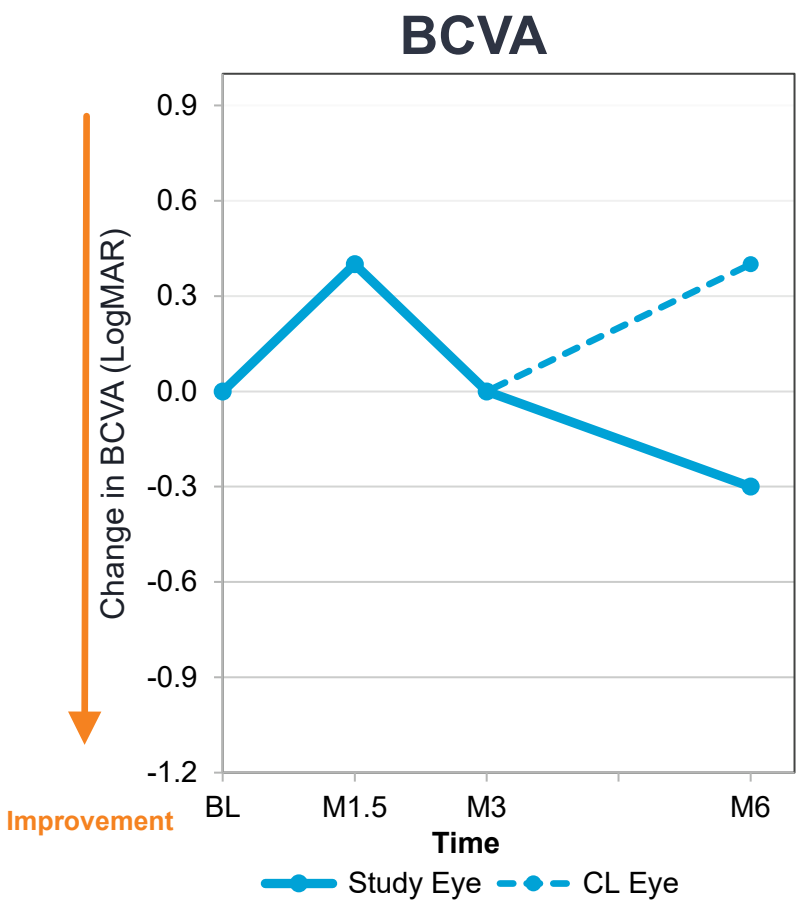
Four different courses with decreasing difficulty to assess relative levels of visual function

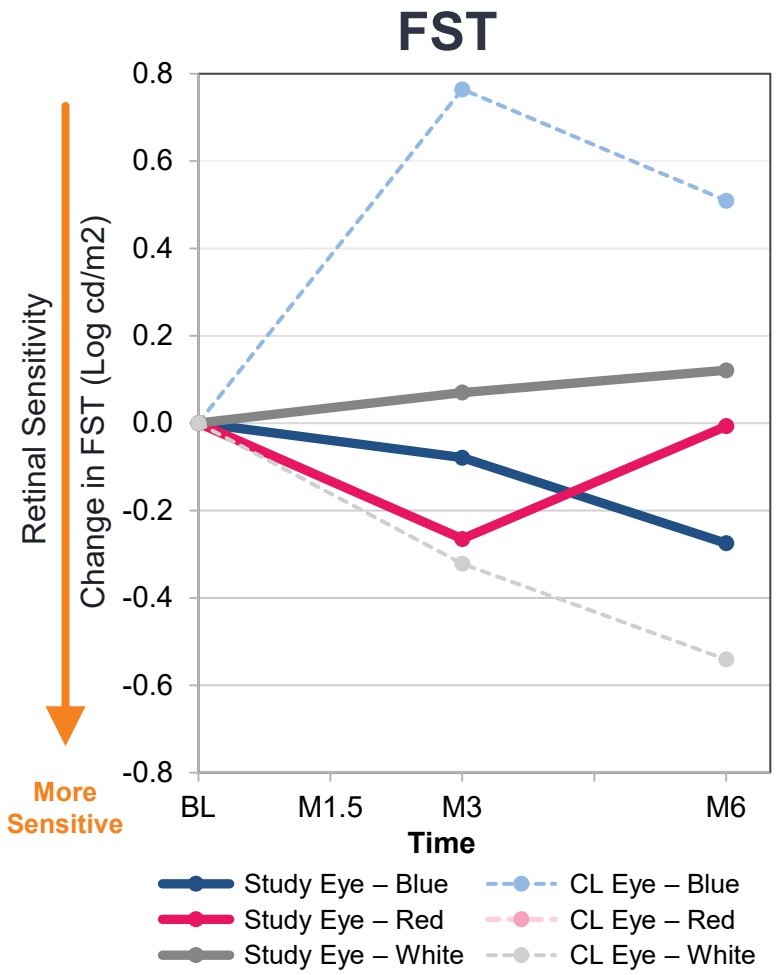
BETTER VISION **WORSE VISION**

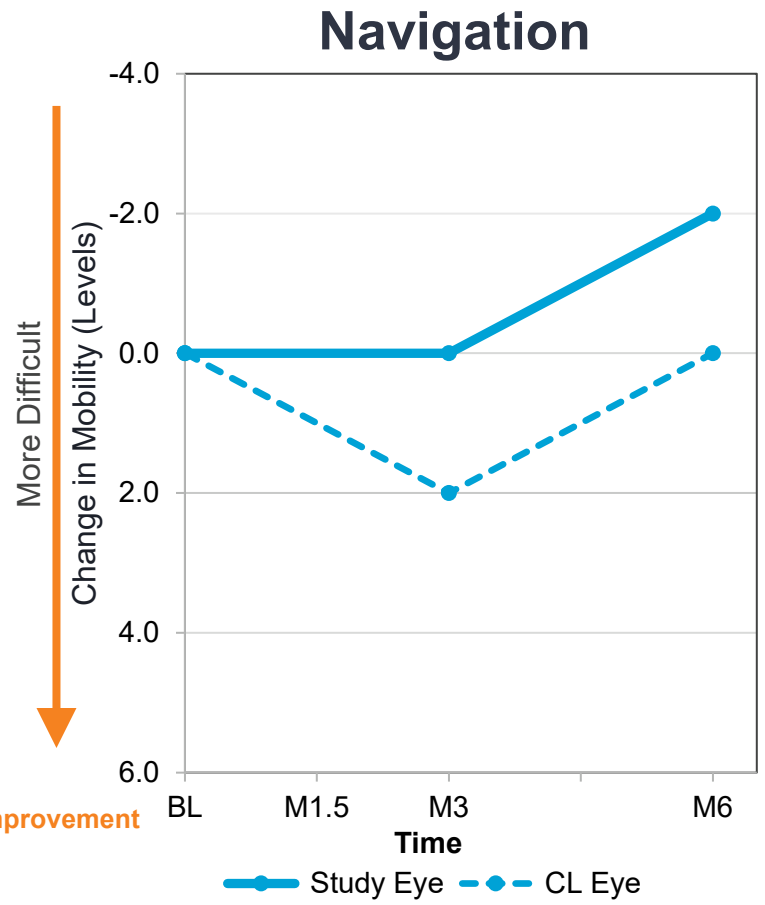
Cohort 1 (Low Dose) Subject 1

Indeterminant Changes in BCVA, FST or Visual Navigation

Efficacy data up to 6 months as patient unable to return for follow-up visits due to COVID





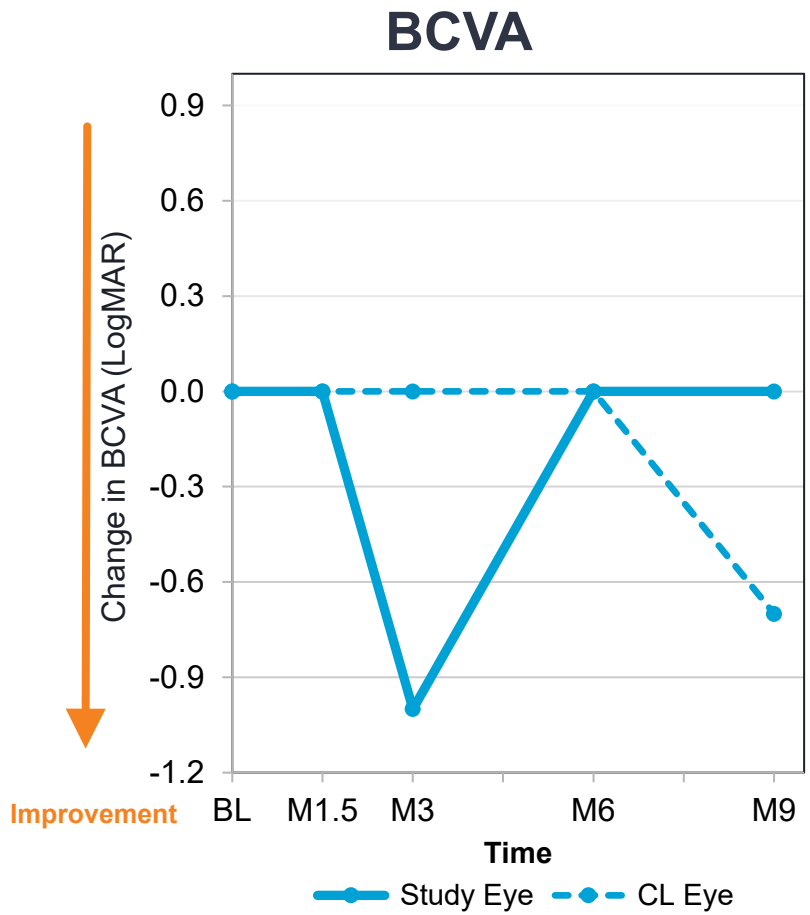


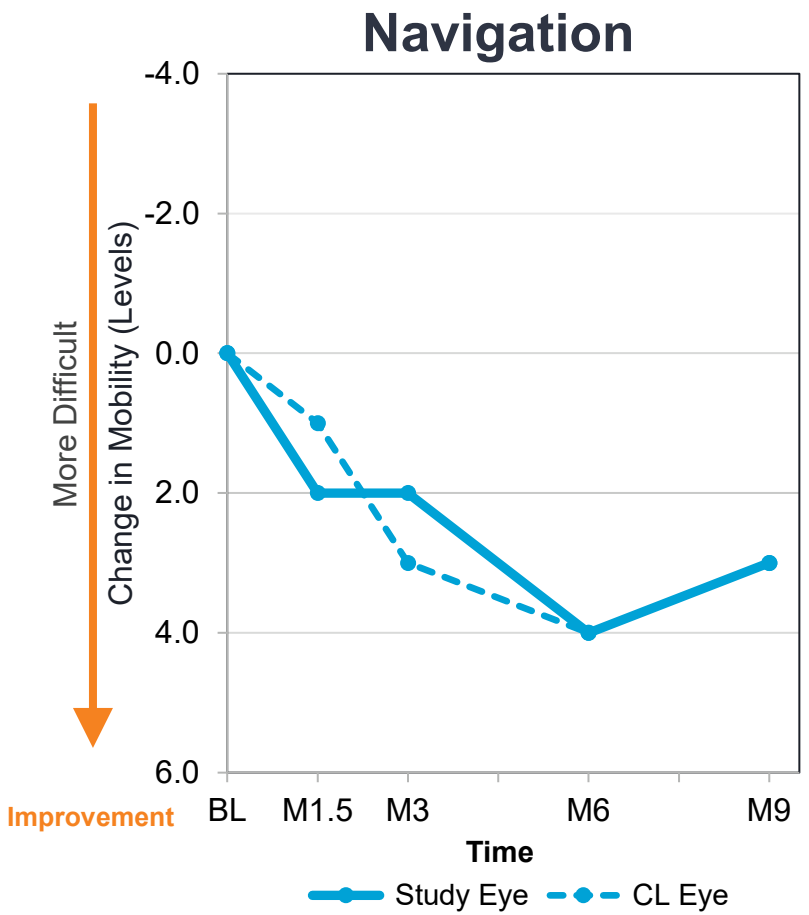
Change from baseline

Cohort 1 (Low Dose) Subject 2

Variable Data Outcomes for BCVA and Visual Navigation

Unable to detect FST thresholds





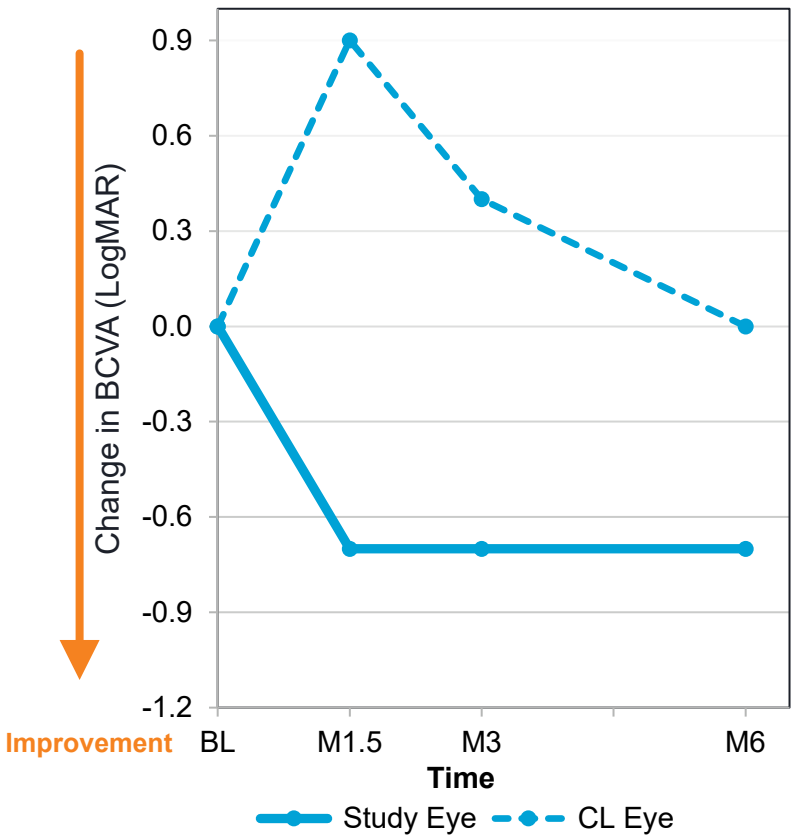
Change from baseline

Cohort 2 (Mid Dose) Subject 1

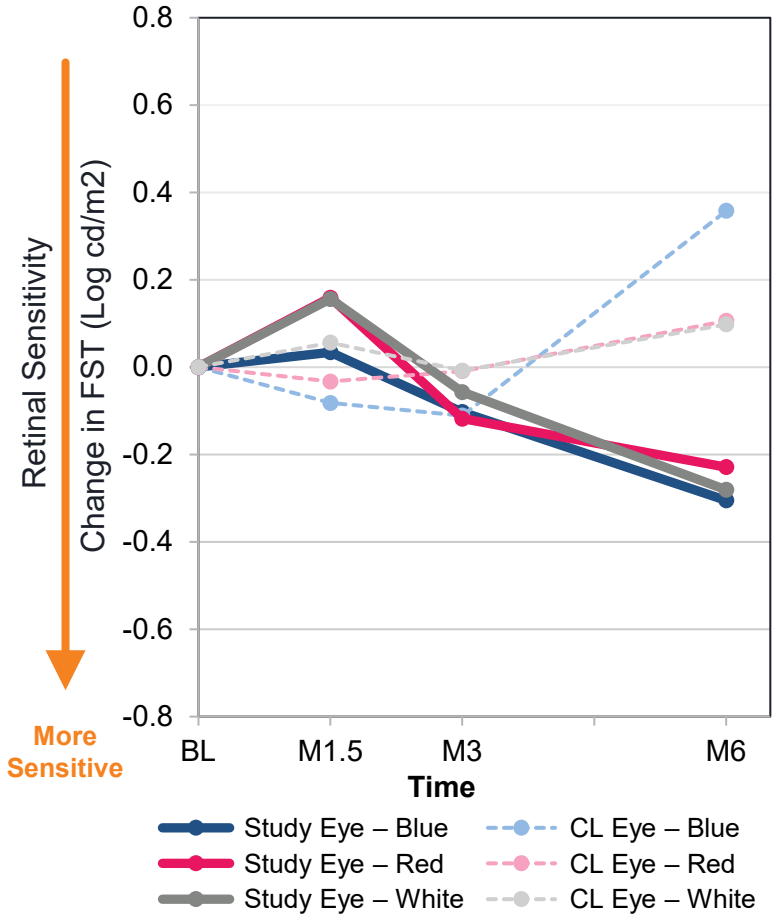
Early Signals of Productive Gene Editing and Clinical Efficacy

Early changes by month 3 with sustained or further improvements in BCVA, FST, and VNC by month 6

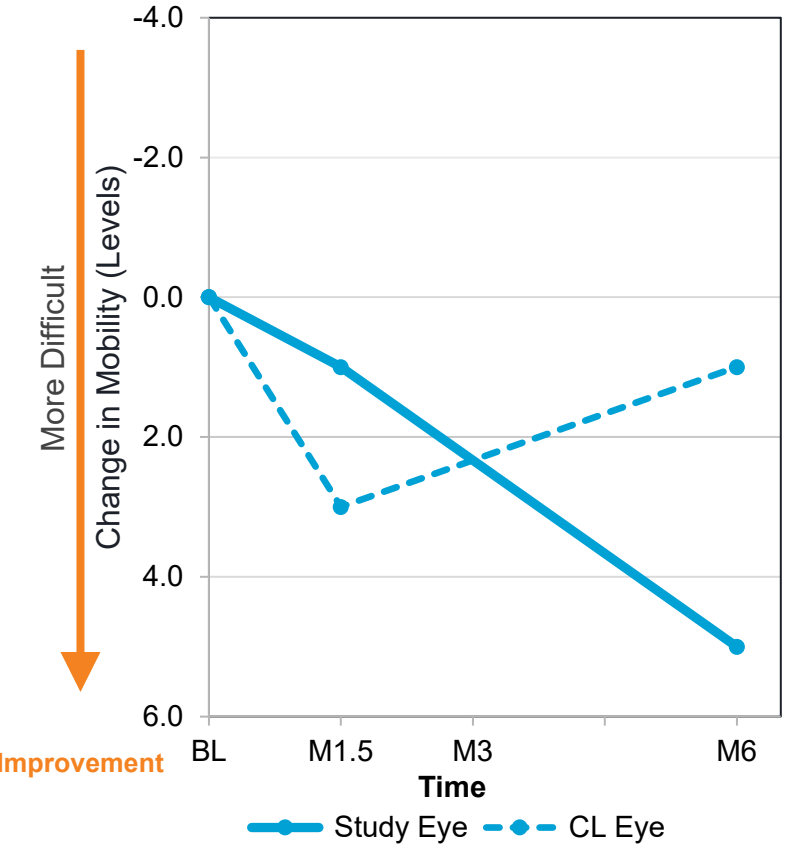
BCVA



FST



Navigation*



Cohort 2 (Mid Dose) Subject 1 in VNC

Improved ability to navigate visual navigation course over time in the study eye

brilliance

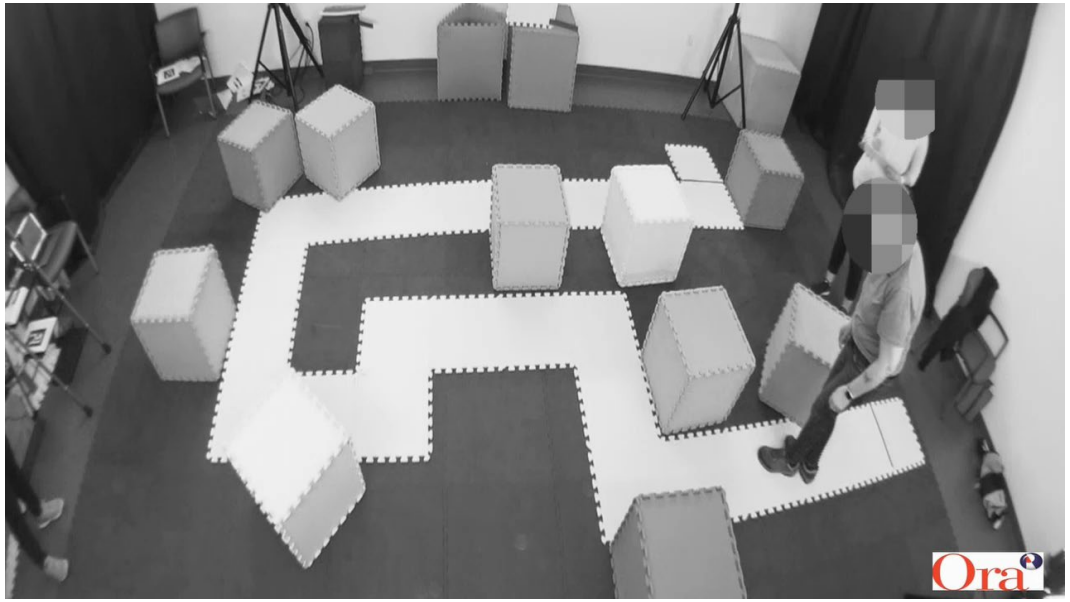
ILLUMINANCE (LUX) LEVELS

Low Light	Moderate Light	Commercial Light
50 lux	200 lux	500 lux
E.g., Dim Hallway	*E.g., Living Room*	*E.g., Office*

Baseline

HCVNC Course at 500 lux

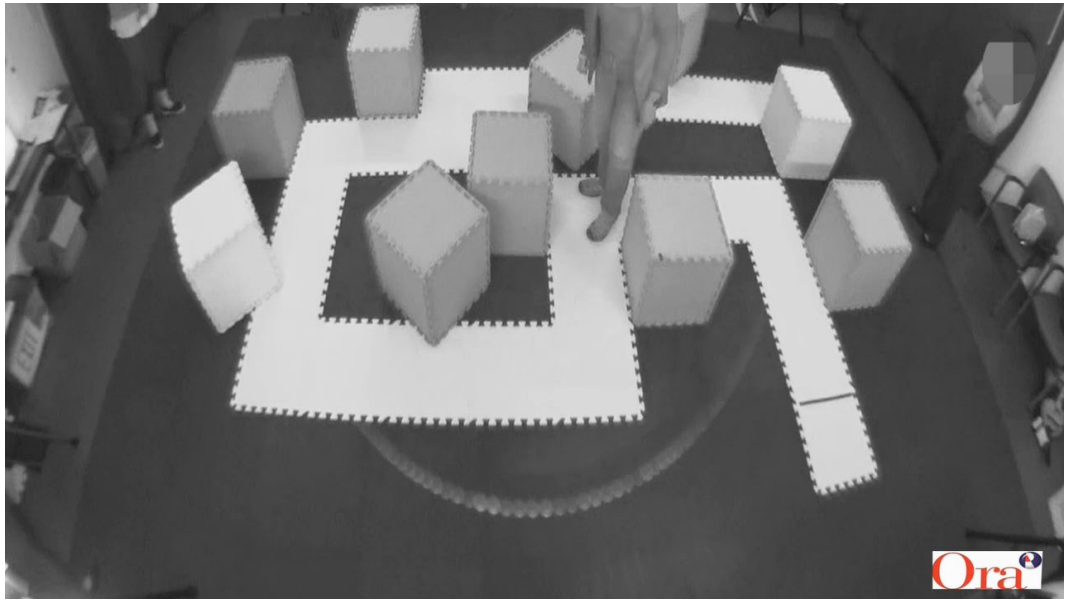
Fail



Month 6

HCVNC Course at 63 lux

Pass



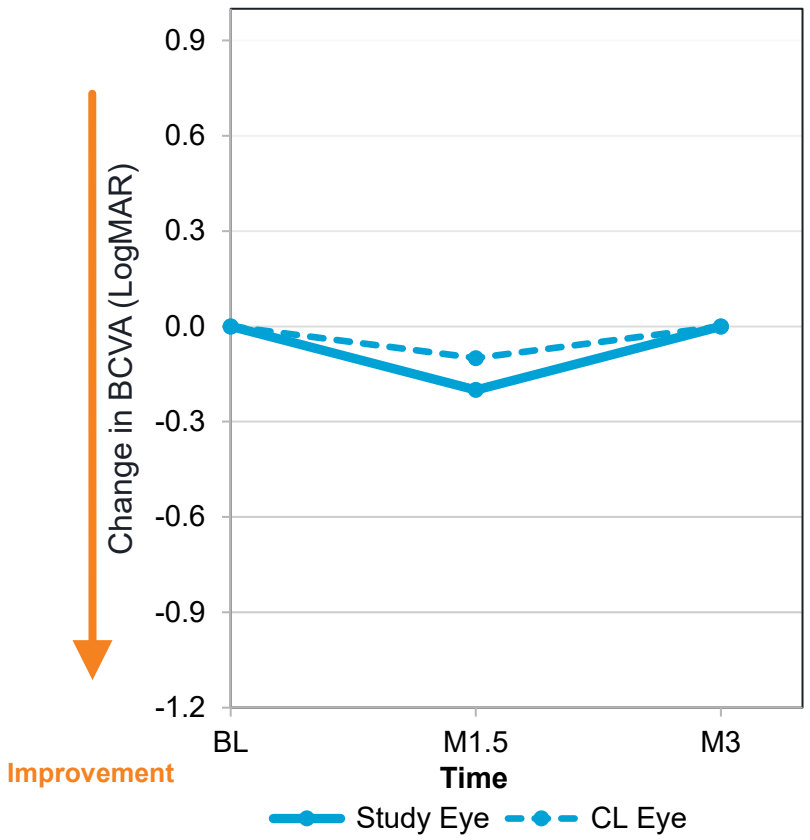
> "I can see lines more clearly now. I have been able to find things on the floor with my eyes sometimes. This is not all the time, but I have been able to notice objects on the floor more than before the treatment. I am also able to see doorways more easily at work."

Cohort 2 (Mid Dose) Subject 2

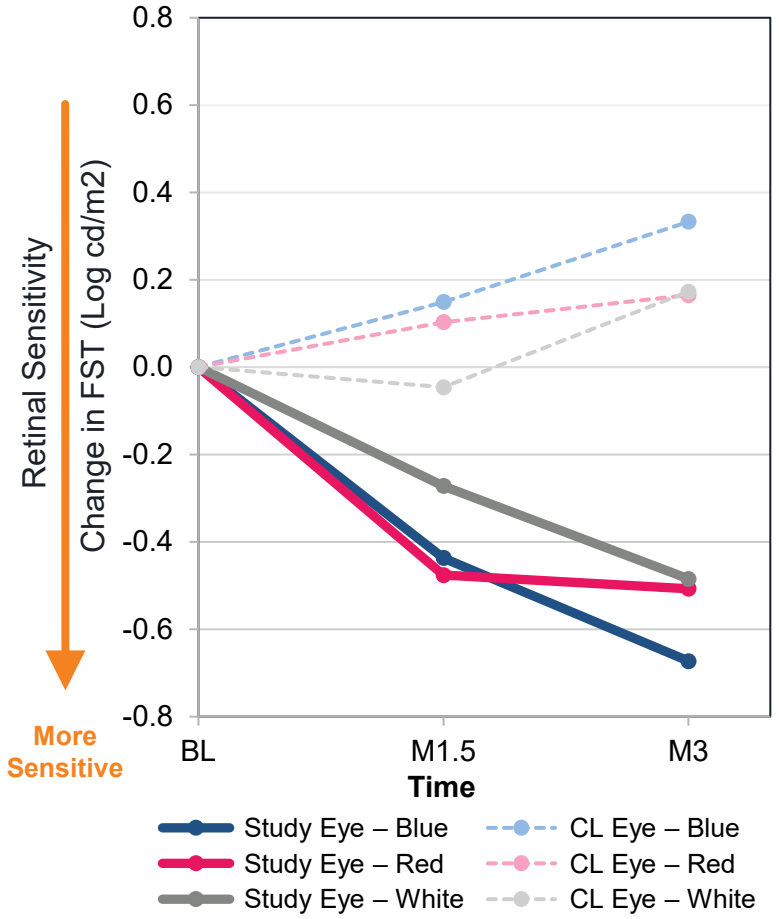
Early Signals of Efficacy Based on FST Assessment

Early changes by month 3 with more pronounced improvements observed in FST

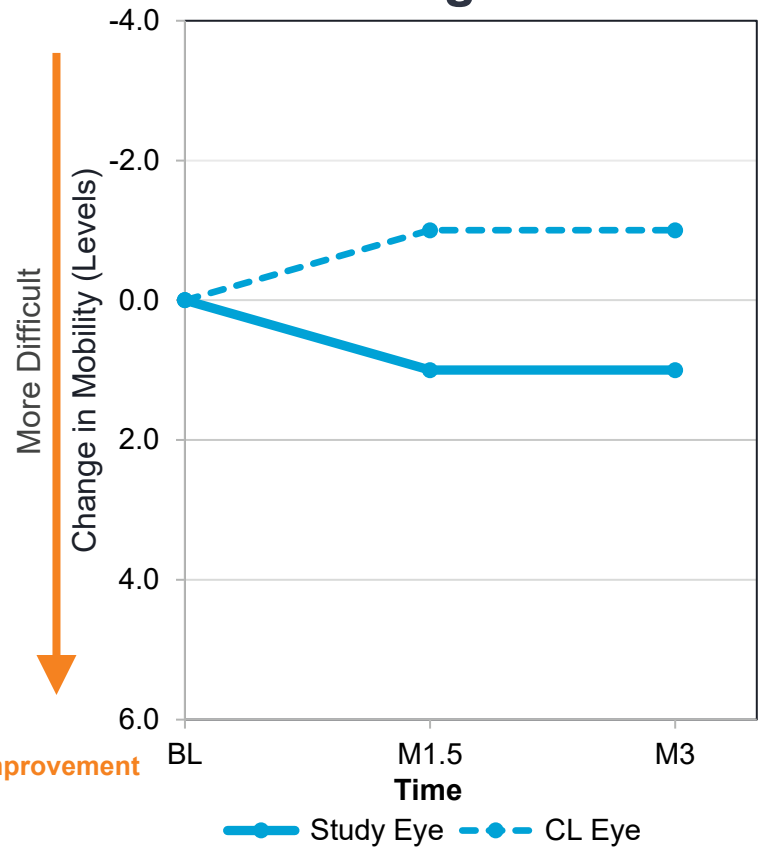
BCVA



FST



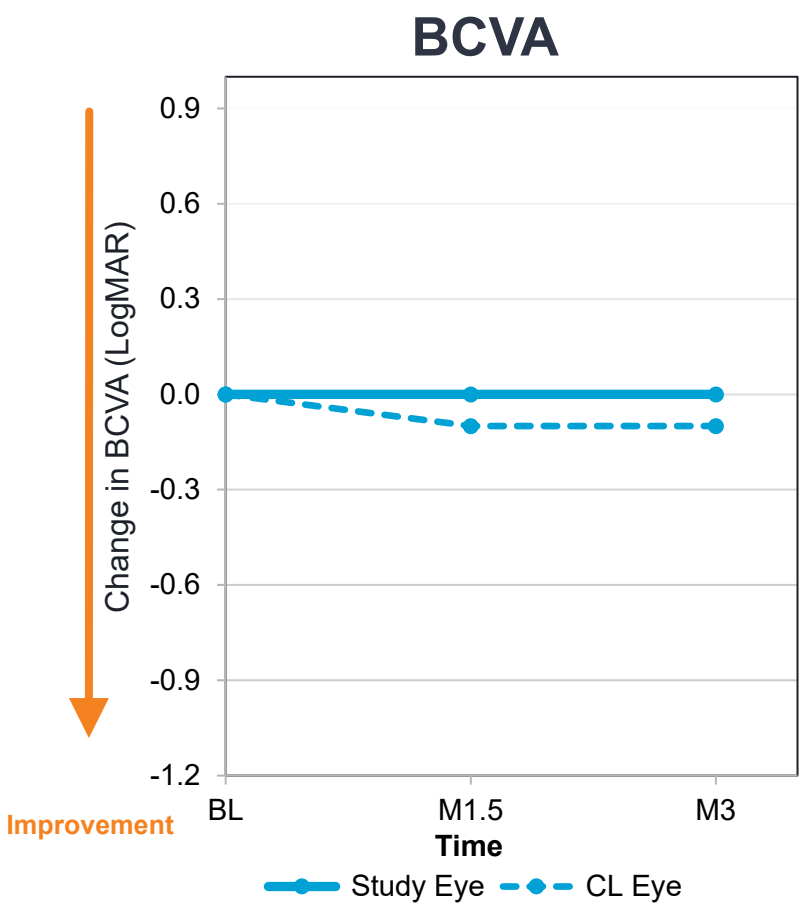
Navigation

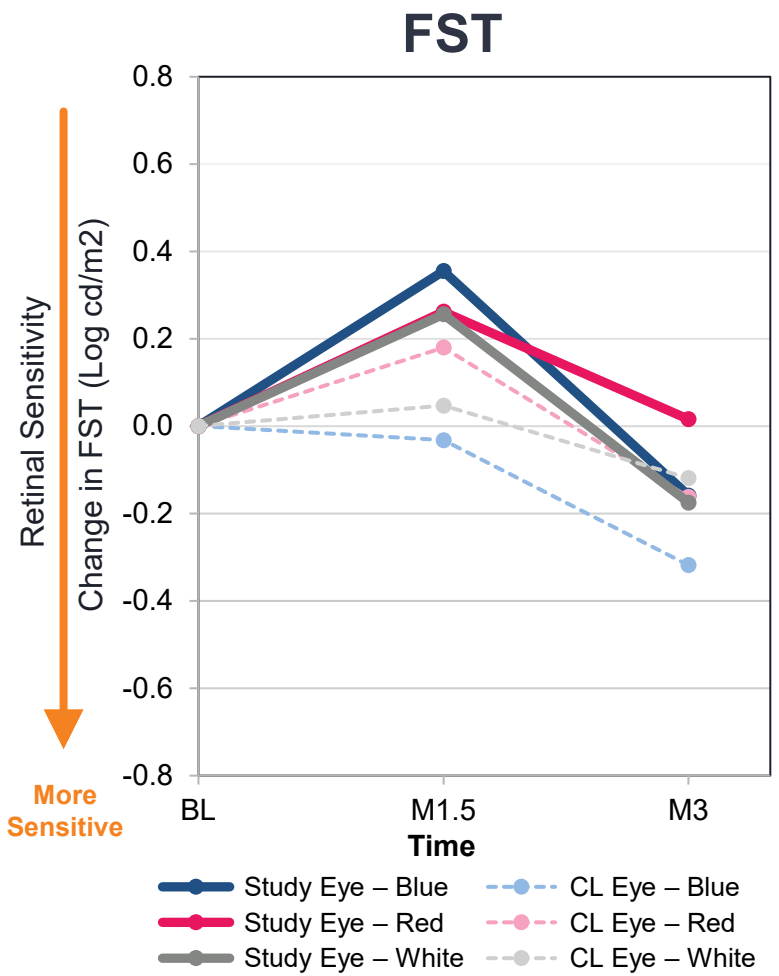


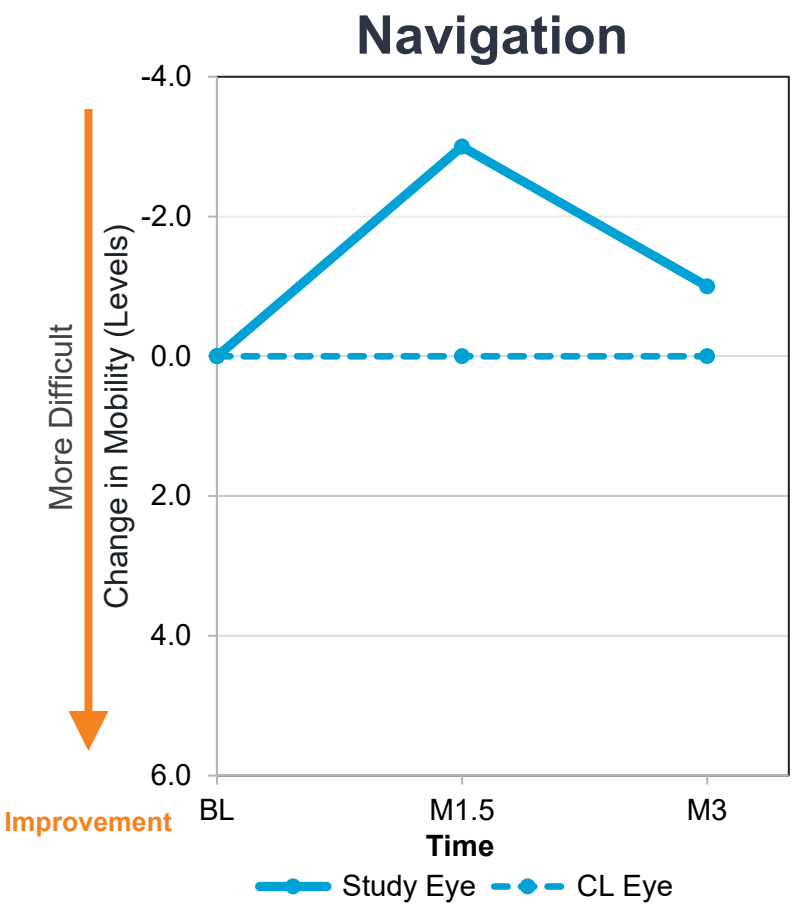
Change from baseline

Cohort 2 (Mid Dose) Subject 3

Indeterminant Clinical Improvements Up To 3 Months







Change from baseline

Efficacy Summary

Early analysis showed **2 of the 3 subjects** in the mid dose cohort followed for up to 6 months **showed efficacy signals**

Mid Dose Cohort Subject 1

Early changes by month 3 with sustained or further improvements in BCVA, FST, and VNC by month 6

Mid Dose Cohort Subject 2

Early changes by month 3 with more pronounced improvements observed in FST

Conclusion

EDIT-101 for the treatment of CEP290-related retinal degeneration is the **first clinically investigated *in vivo* CRISPR gene editing therapy**

SAFETY

To date, **no DLTs or serious AEs** have been reported in the first six adult subjects treated with the low or mid doses of EDIT-101

EFFICACY

Early efficacy signals in the mid dose cohort suggest positive biological activity and potential early clinical benefits

High dose adult cohort is currently ongoing with no DLTs or SAEs observed to date

Pediatric mid dose cohort is currently enrolling

Acknowledgements

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

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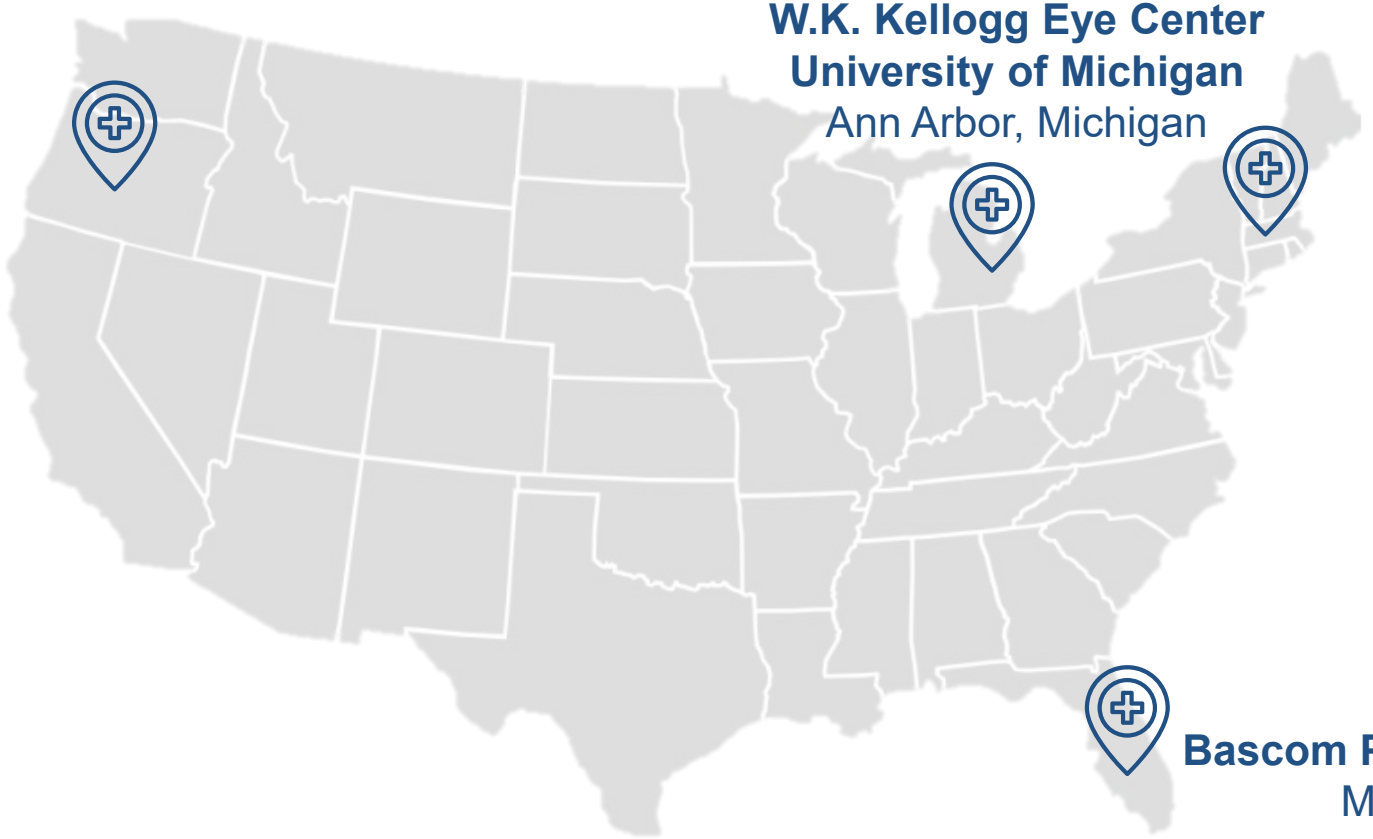
Boston, Massachusetts



Byron Lam
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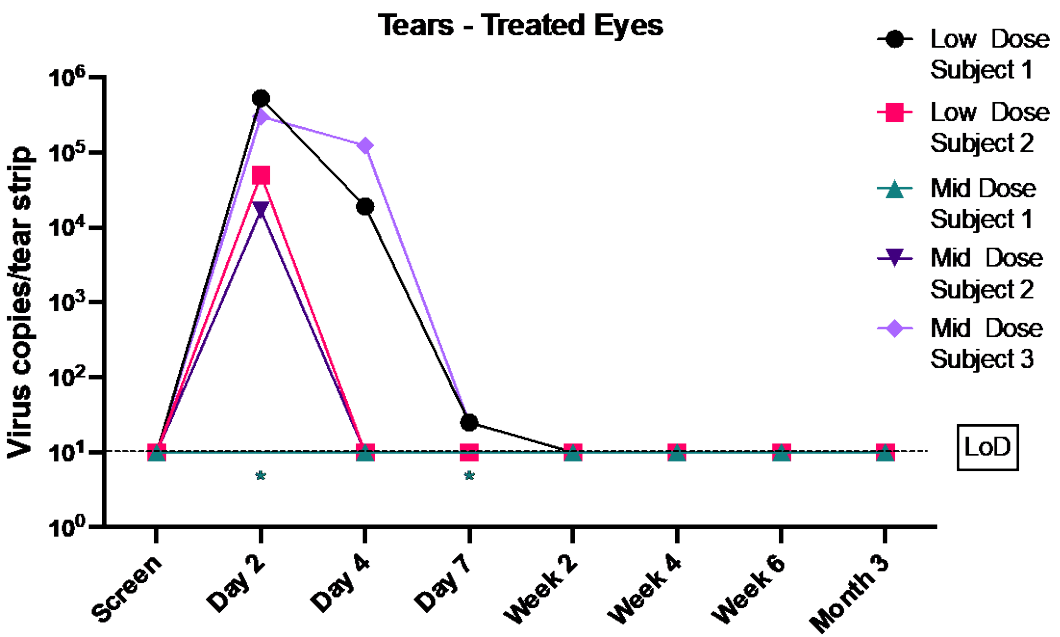
Thank You & Questions

editas MEDICINE

Appendix

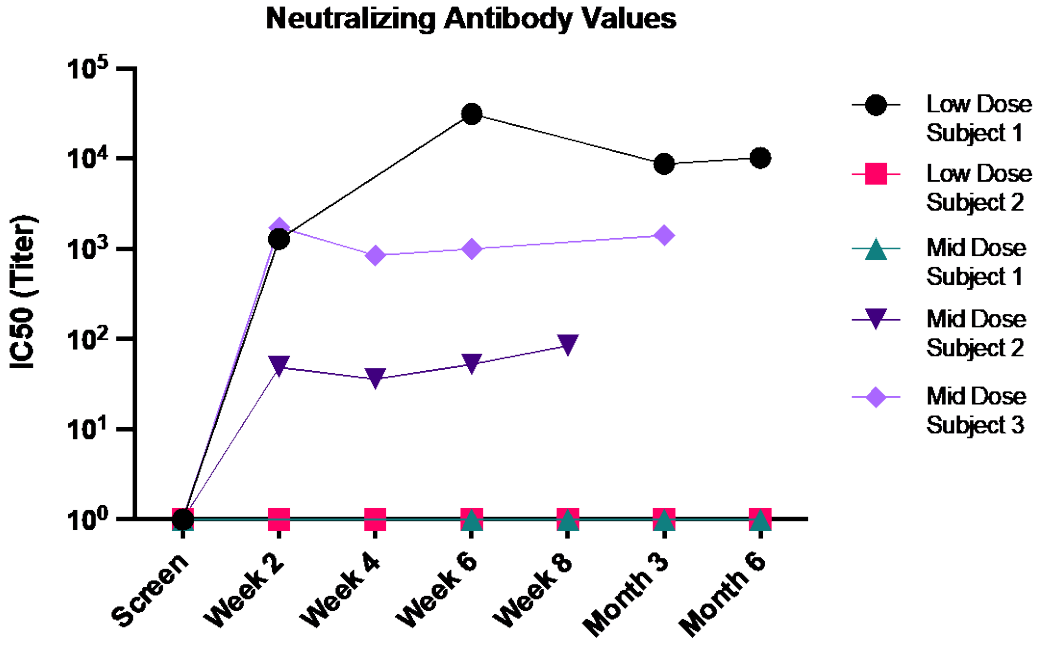
Viral Shedding and Neutralizing Antibodies

AAV5 Viral Copy Numbers by qPCR



* Early shedding data unable to be determined for Mid Dose Subject 1 as samples were not collected
Low Dose Subject 1 Day 7 readout BLOQ

Plasma AAV5 Neutralizing Ab Titer

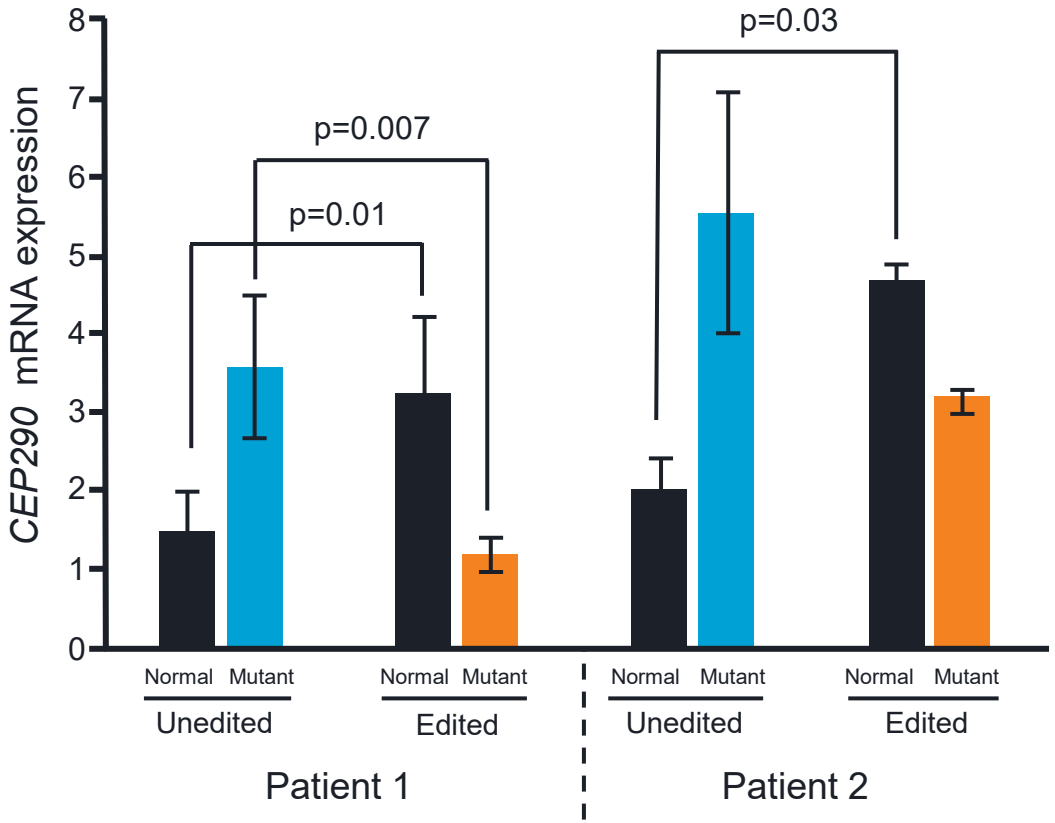


No week 4 or week 8 data for Low Dose Subject 1
No week 2 or week 4 data for Mid Dose Subject 1
No week 8 data for Mid Dose Subject 3

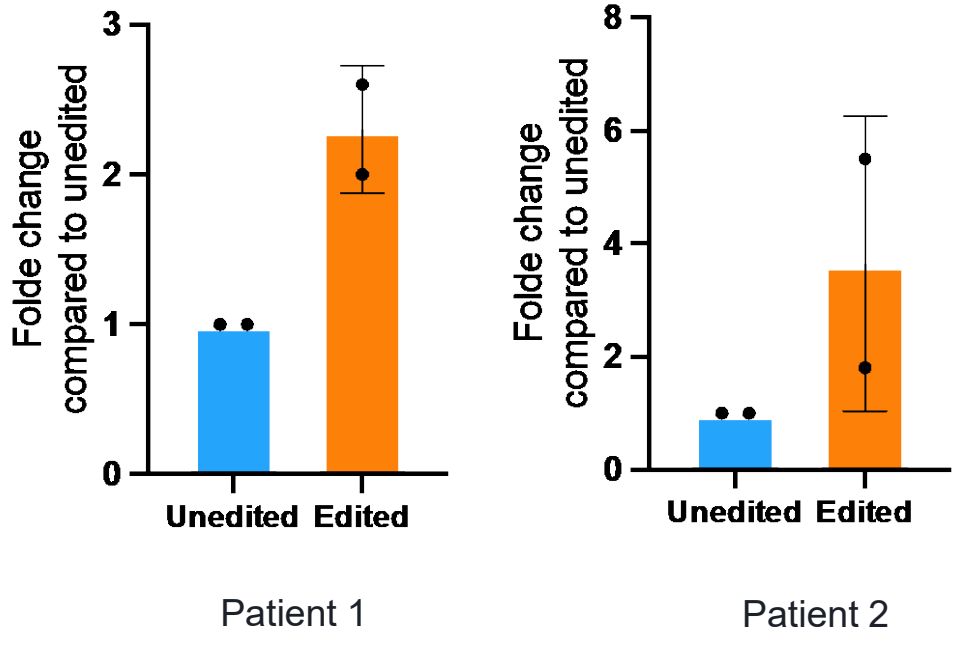
Transient viral shedding in blood and tears, approaching clearance around Day 7
No Cas9-specific antibody or T-cell response detected; AAV5-specific antibody detected in some subjects; No correlation with observed inflammation

Editing Corrects CEP290 Splicing, Restoring mRNA and Protein Expression in Fibroblasts of Patients with the 2991+1665A>G Mutation

CEP290 mRNA expression

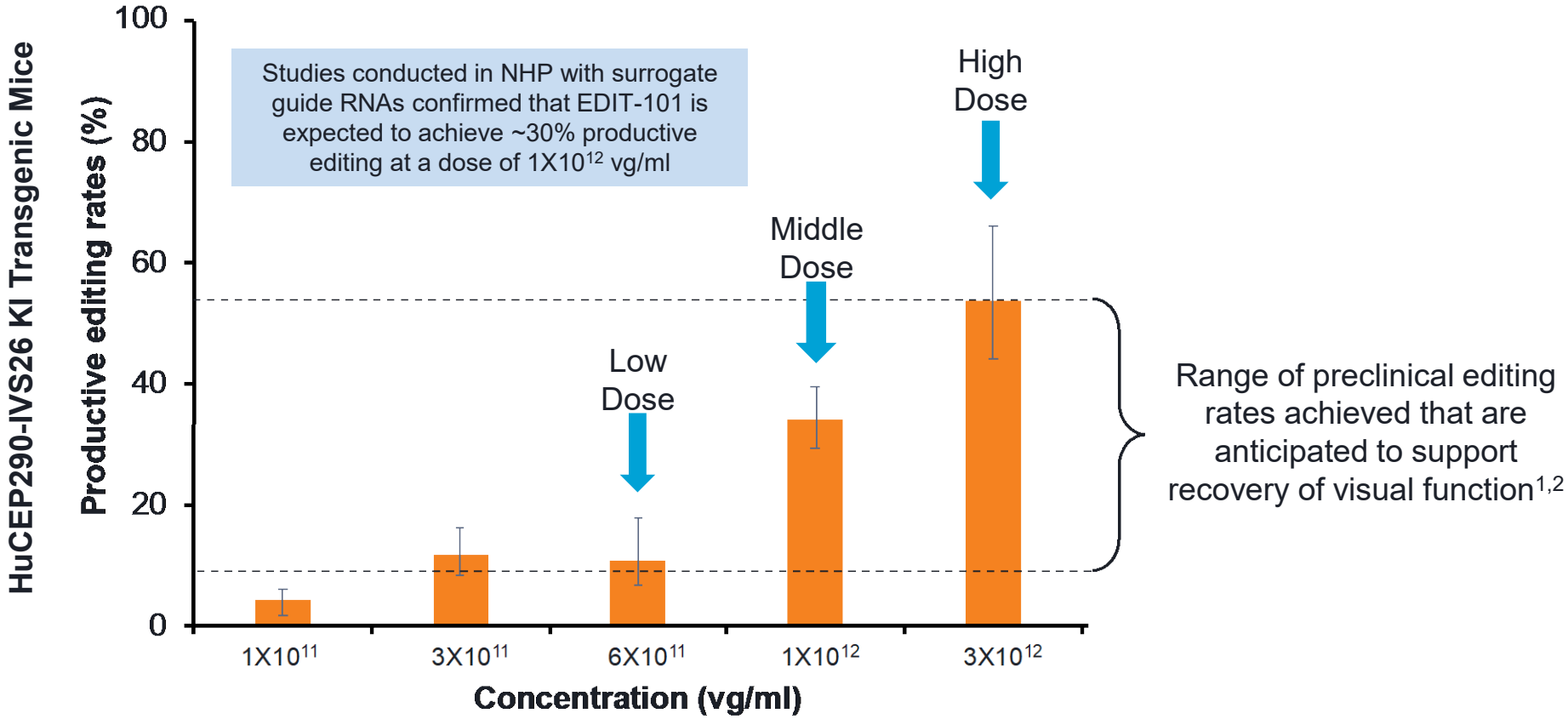


CEP290 protein expression



Clinical EDIT-101 Dose Selection

Based on Dose Response Studies in HuCEP290-IVS26 KI Transgenic Mice & Non-Human Primates



Comparable dose ranges in a clinical setting anticipated to have clinically meaningful and robust productive editing

[1] Geller AM, et al. *Vision Research,* 1993; [2] Geller AM, *J Opt Soc AM A*, 1992

Ocular Adverse Events

	Cohort 1 Adult Low Dose (N=2)	Cohort 2 Adult Mid Dose (N=4)
Eye Pain	1 (50%)	3 (75%)
Photophobia	1 (50%)	0
Conjunctival Hyperemia	1 (50%)	0
Conjunctival Edema	1 (50%)	0
Conjunctival Hemmorhage	1 (50%)	0
Eye Pruritus	1 (50%)	0
Retinal Tear	0	2 (50%)
Hypotony of Eye	1 (50%)	0
Retinal Hemorrhage	0	1 (25%)
Subretinal Fluid	1 (50%)	0
Lens Subluxation	1 (50%)	0
Anterior Chamber Inflammation	1 (50%)	1 (25%)
Anterior Chamber Cell	1 (50%)	0
Vitreal Cell	1 (50%)	0
Subretinal Infiltrates/RPE Disruption	1 (50%)	0

Most reported AEs were mild and related to the surgical procedures and subretinal injection associated with EDIT-101 administration

By Number of Subjects and Cohort