



Investor Presentation

November 7, 2018

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Forward Looking Statements

This presentation contains forward-looking statements within the meaning of the “safe harbor” provisions of The Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical facts, contained in this presentation, including statements regarding the Company’s strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, and objectives of management, are forward-looking statements. 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 Company’s 2022 goals, achieving preclinical proof-of-concept for additional programs and establishing alliances. 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 preclinical studies and clinical trials and clinical development of the Company’s product candidates; 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; availability of funding sufficient for the Company’s foreseeable and unforeseeable operating expenses and capital expenditure requirements; and other factors discussed in the “Risk Factors” section of the Company’s most recent Quarterly Report on Form 10-Q, which is on file with the Securities and Exchange Commission, and in other filings that the Company may make with the Securities and Exchange Commission in the future.

In addition, the forward-looking statements included in this presentation represent the Company’s views as of the date of this presentation. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company’s views as of any date subsequent to the date of this presentation.



**Convergence of technologies
for advanced medicines**

**Gene editing expands and
accelerates the universe of
genomic medicines**

Editas Medicine 2022 Goals – EM22



Build on Our Current Success

At least one program from our Celgene collaboration

More than one program in ocular diseases

Establish New Areas & Leverage Our Platform

At least one engineered cell medicine program beyond engineered T cells in cancer

At least one program in an additional cell or tissue type or using an advanced editing modality

Broadest Access to Genomic Targets

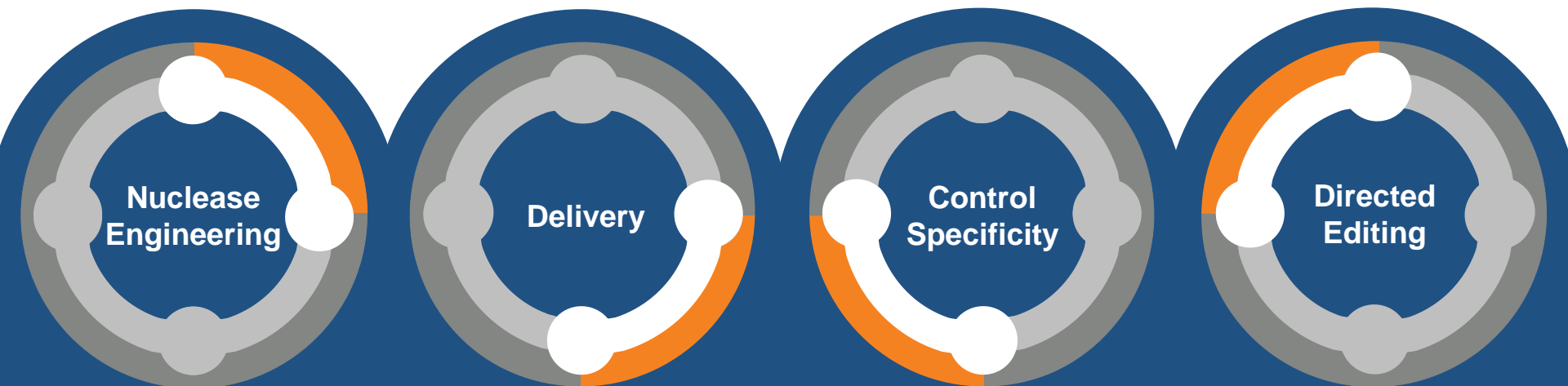
Proprietary portfolio of Cas9 and Cpf1 enzymes may directly edit ~95% of the human genome

Widest Range of Tissues and Cells

Ability to use AAVs, RNPs, and LNPs to address diseases throughout the body

Diverse Spectrum of Therapeutic Edits

Disrupt, remove, replace, or insert DNA to precisely and durably treat illness



Ocular Medicines

Inherited Retinal Diseases

- LCA10 (EDIT-101)*  
- USH2A 
- Additional unnamed targets

Infectious Diseases

- Ocular HSV 

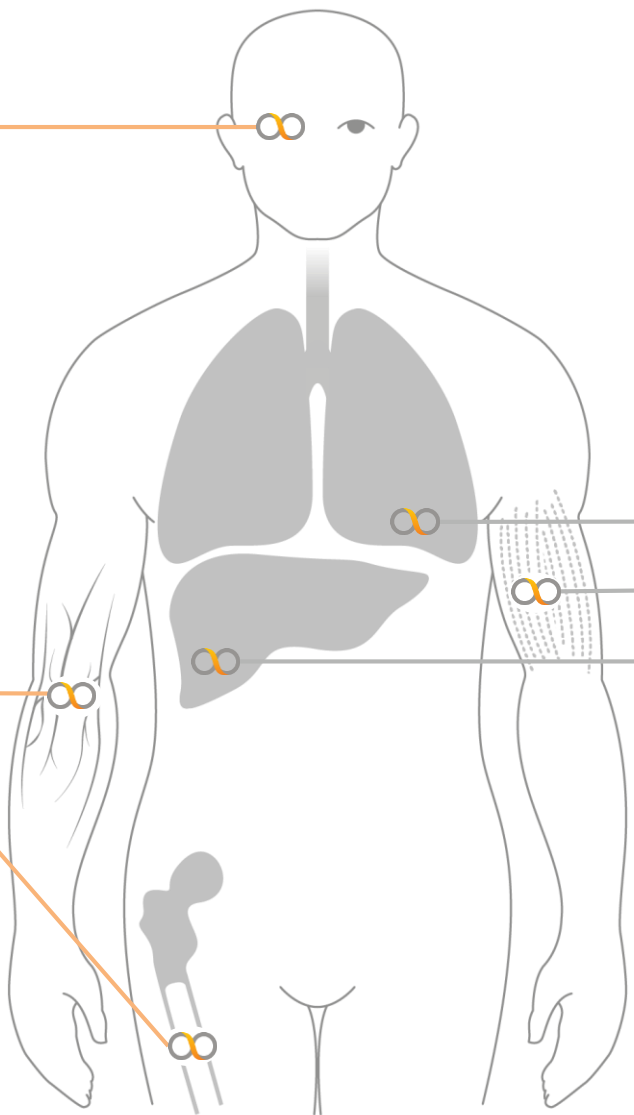
Engineered Cell Medicines

Immune Cells




- T Cells – Cancer** 
- T Cells – Autoimmune diseases

Stem Cells

- HSCs – Sickle Cell Disease  
- HSCs – Beta-thalassemia  



Early Discovery

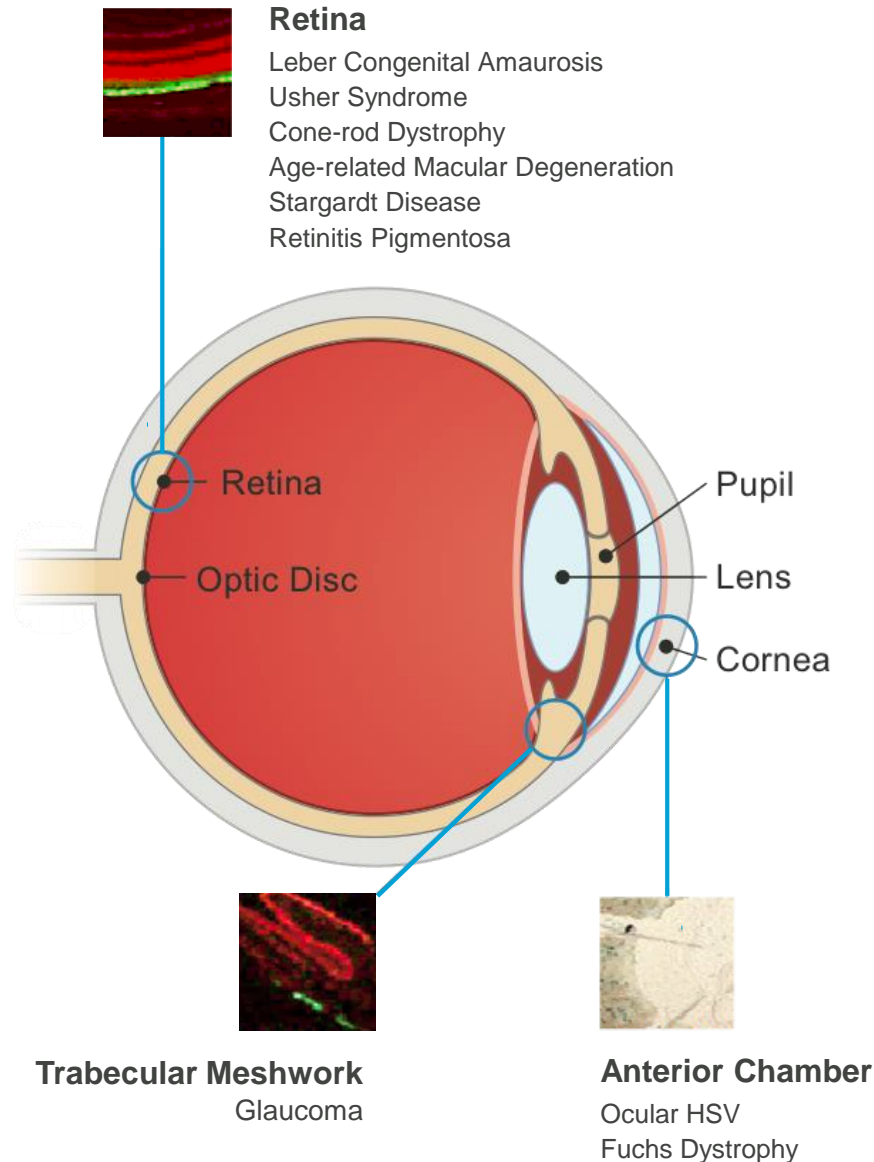
- Lung – CF
- Muscle – DMD 
- Liver – AATD  

 *in vitro* proof-of-concept

 *in vivo* proof-of-concept

*Partnered with Allergan – US 50/50 plus milestones and ex-US royalties; **Partnered with Celgene – global milestones and royalties; LCA10: Leber Congenital Amaurosis Type 10; USH2A: Usher Syndrome Type 2A; HSV: Herpes Simplex Virus; CF: Cystic Fibrosis; DMD: Duchenne Muscular Dystrophy; AATD: Alpha-1 Antitrypsin Deficiency; HSC: Hematopoietic Stem Cell

| Durable Medicines for Serious Eye Diseases

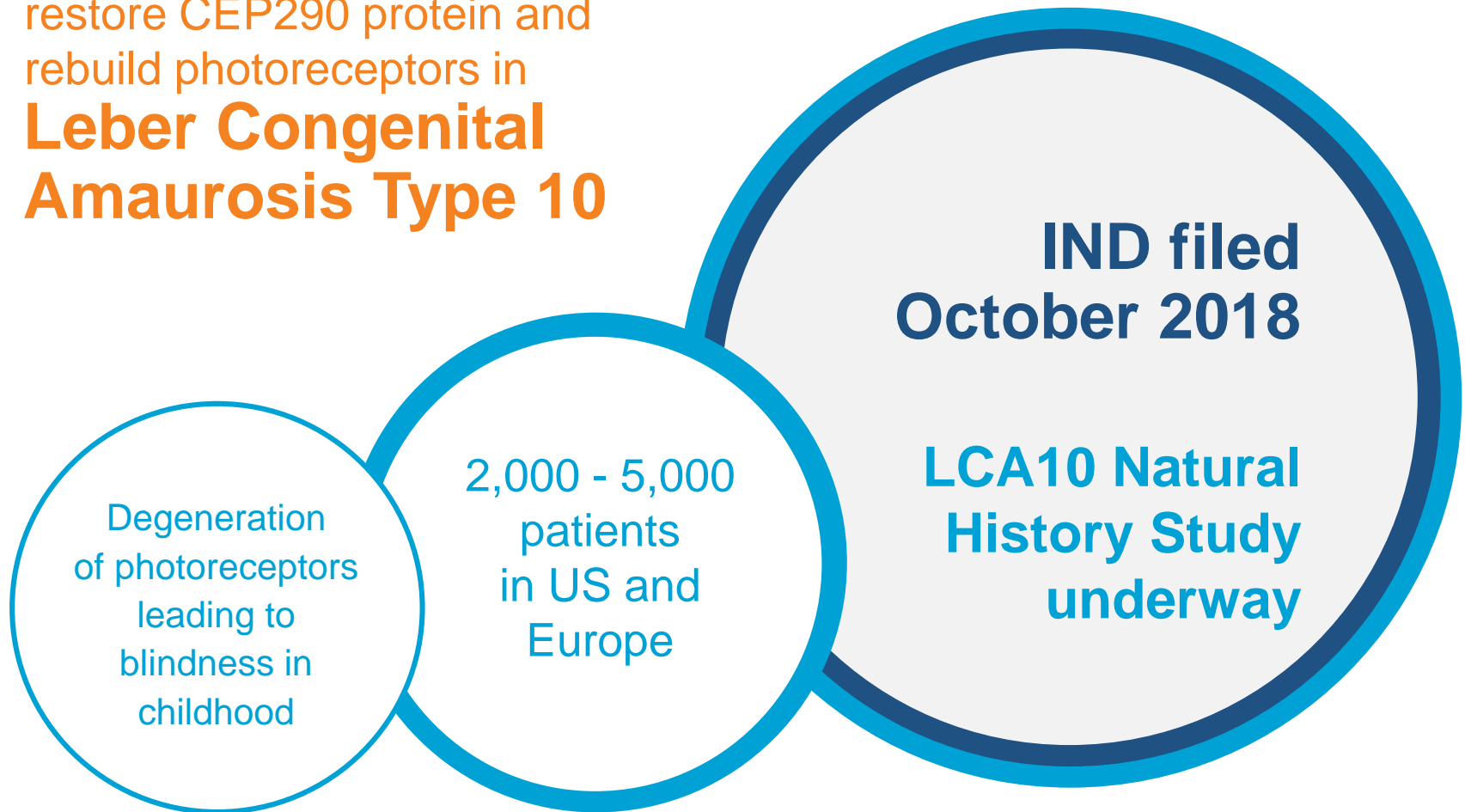


Hundreds of thousands of patients may benefit from durable CRISPR medicines addressing ocular diseases

Targeted local injection using proven viral vectors enables precise delivery to multiple compartments of the eye

Promising clinical and regulatory path with readily measurable endpoints and serious unmet need

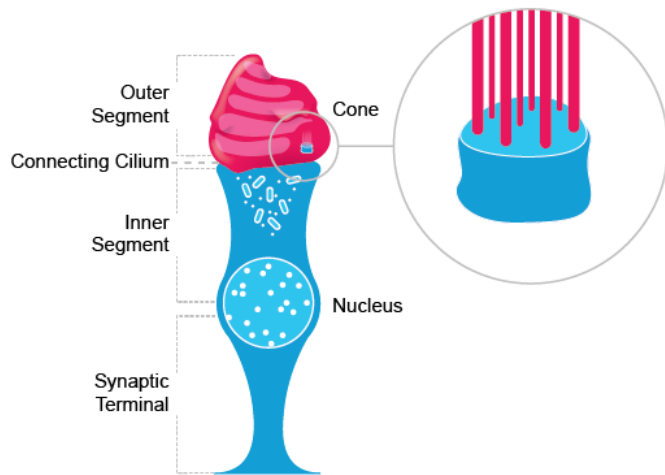
Remove genetic mutation to
restore CEP290 protein and
rebuild photoreceptors in
**Leber Congenital
Amaurosis Type 10**



| EDIT-101 Aims to Rescue Vision in LCA10

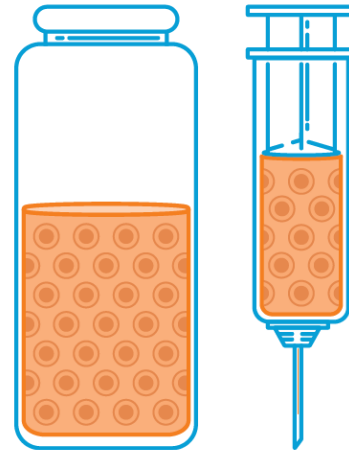
LCA10 Photoreceptor

Degenerates because CEP290 lacking



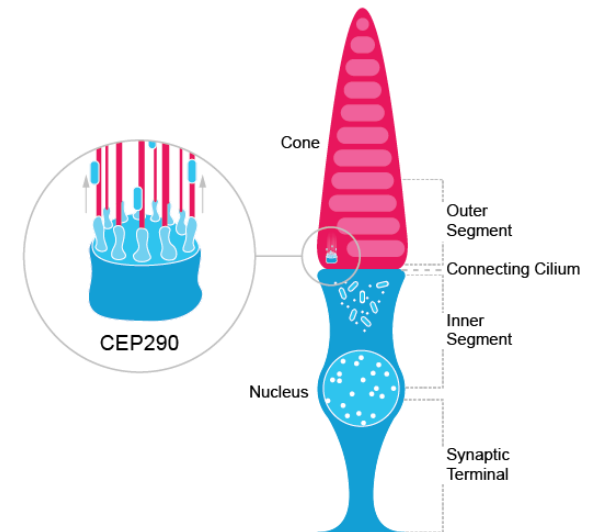
EDIT-101

Removes disease-causing mutation



Rescued Photoreceptor

By correcting CEP290 protein



Degeneration of outer segment but cell body remains intact

EDIT-101 subretinal injection to remove disease-causing mutation

Restoration of full-length protein and rebuilding of outer segment

**Critical Achievements
Advancing EDIT-101 to
Human Clinical Trials**

1 DOES EDITING RESTORE PROTEIN
EXPRESSION IN PATIENT CELLS?

2 CAN WE EDIT TARGET CELLS IN BEST
PRECLINICAL MODEL ANIMAL?

3 DOES PRODUCT CANDIDATE ACHIEVE
THERAPEUTIC EDITING IN HUMAN TISSUE?

4 DOES PRODUCT CANDIDATE HAVE
SPECIFICITY FOR HUMAN TESTING?

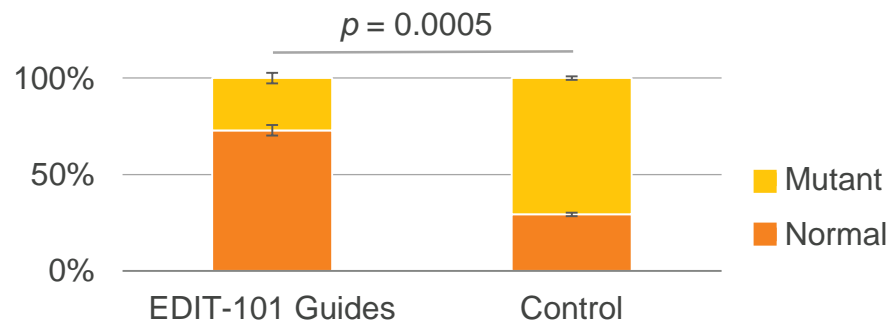
5 WHAT ARE BEST CLINICAL TRIALS
TO PROVE VALUE FOR PATIENTS?

1

EDITING APPROACH RESTORES FULL LENGTH CEP290 mRNA AND PROTEIN

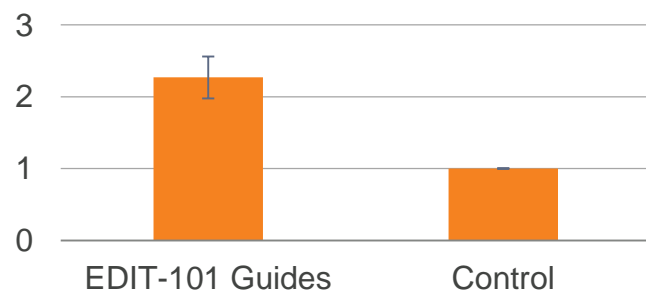
Demonstrated in cells from LCA10 patients

Relative Level of CEP290 mRNA



Deleting the disease-causing mutation **corrects full-length mRNA for CEP290**

CEP290 Protein Normalized to Control



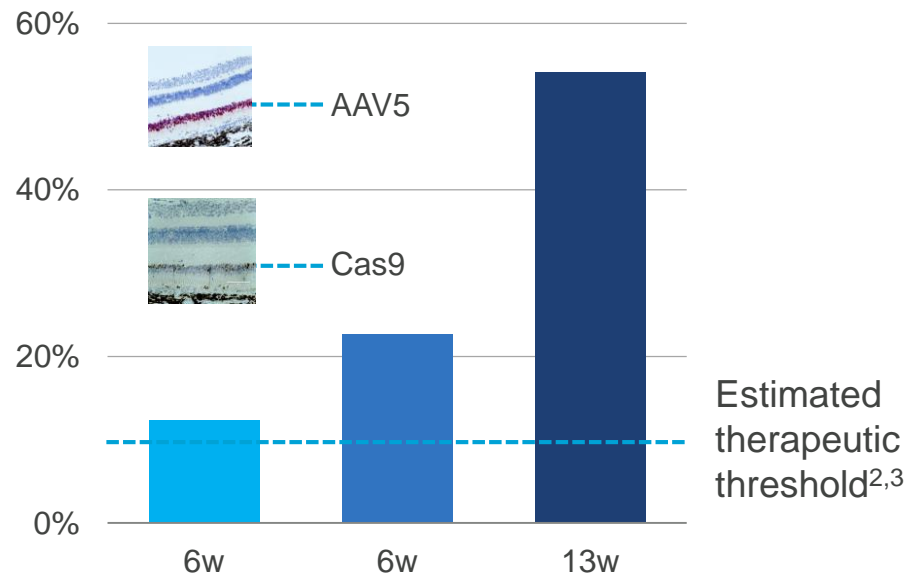
Deleting the disease-causing mutation **restores full-length CEP290 protein**

2 PREDICTED THERAPEUTIC EDITING ACHIEVED IN NON-HUMAN PRIMATES

Estimated productive editing in primate photoreceptors *in vivo*¹

Delivery vehicle specifically targets photoreceptors

Estimated Productive Editing Non-human Primate Photoreceptors



AAV5 vector and GRK1 promoter limit expression to photoreceptors, providing a **highly targeted therapy**

Productive editing with subretinal delivery in anatomically relevant animal model **well above therapeutic threshold**

1. Editing measured across entire retina multiplied by 3.5 based on photoreceptors estimated to represent 25-30% of retina; 2. Geller, Sieving, and Green, *J. Opt. Soc. Am.*, 1992; 3. Geller and Sieving, *Vision Res.*, 1993; Guide RNAs in NHP experiments specific to NHP genome; NHP: Non-human Primate; GRK1: G Protein-Coupled Receptor Kinase 1

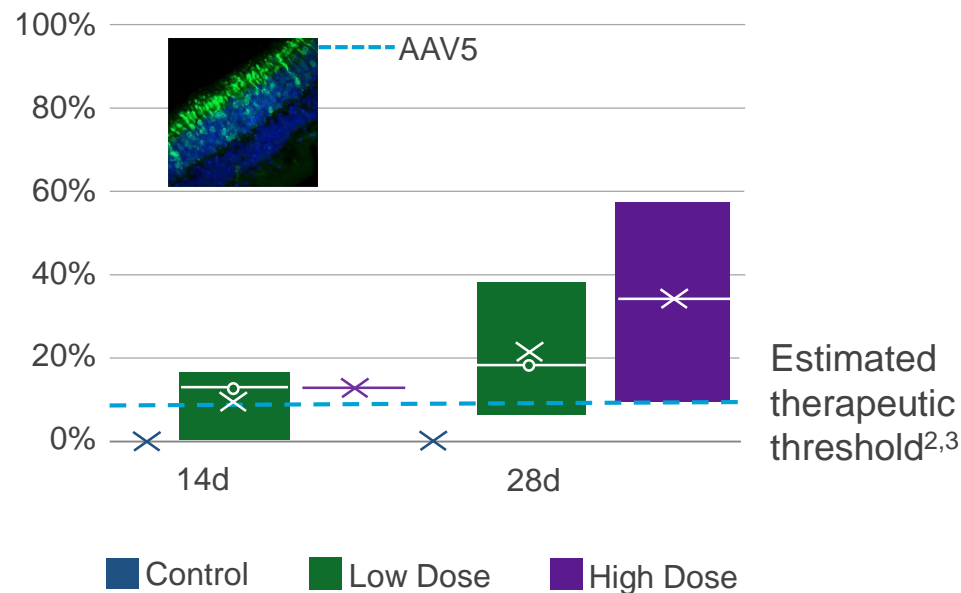
3

PREDICTED THERAPEUTIC EDITING ACHIEVED IN HUMAN RETINA

Productive editing in human retinal explant photoreceptors¹

Targeted transduction of photoreceptors

Estimated Productive Editing Human Retinal Explant Photoreceptors



AAV5 vector
selectively
targets human
photoreceptor cells

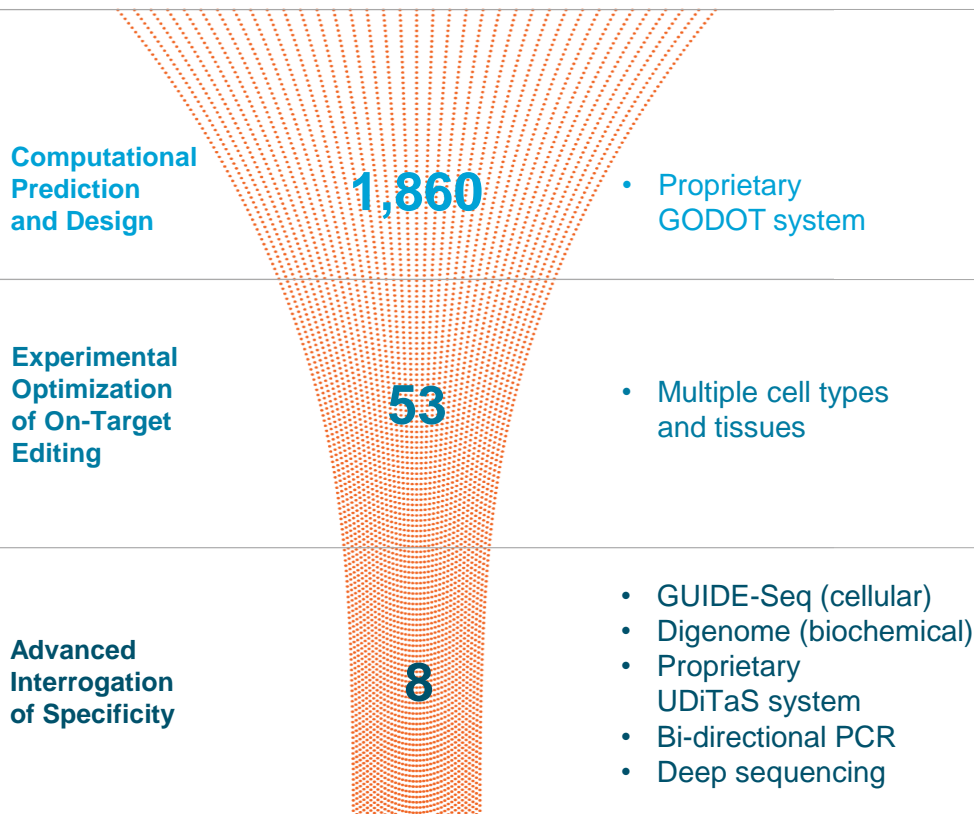
Product candidate
EDIT-101 achieves
predicted therapeutic
levels of editing in
human photoreceptors

1. Editing measured across entire retina multiplied by 3.5 based on photoreceptors estimated to represent 25-30% of retina; 2. Geller, Sieving, and Green, *J. Opt. Soc. Am.*, 1992; 3. Geller and Sieving, *Vision Res.*, 1993.

4

COMPREHENSIVE METHODS TO IDENTIFY EFFICIENT AND SPECIFIC GUIDE RNAs

Proprietary computational, biochemical, and cellular approaches



Systematic approach to guide RNA characterization

using a suite of comprehensive, empirical, and unbiased methods

Identified and selected product candidates with **no detected off-targets** verified in cells and tissues

EDIT-101

5

SETTING THE STAGE FOR
INTERVENTIONAL TRIALS

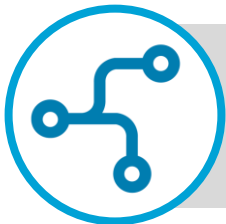
Ongoing Natural History Study

Patients



~40 patients, aged 3 and above

Objectives



Characterize patients, assessments, and rate of change and validate endpoints

Sites



6 to 8 sites in US and Europe

Follow-up



6 visits over 1 year

PHASE 1/2 TRIAL DESIGN IN DEVELOPMENT

Design



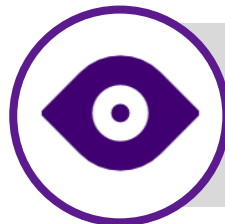
Open-label, dose escalation

Patients



~10 to 20 patients with IVS26 mutation

Comparator



Non-randomized comparison to natural history, contralateral eye, and patient baseline

Duration



1 year evaluation of efficacy and safety

Rescue vision by
restoring USH2A protein using
**similar product
construct and
delivery to
EDIT-101**

Progressive
vision loss
leading to
blindness due to
degeneration of
photoreceptors

4,000
patients with
target mutation

Additional 10,000
potentially
addressable

Collaboration
with Drs. Eric Pierce and Qin Liu
**to validate gene
editing approach**
in transgenic mouse model



**Massachusetts
Eye and Ear®**



HARVARD MEDICAL SCHOOL
AFFILIATE

**Knock out critical
viral genes**
to disable the
latent virus

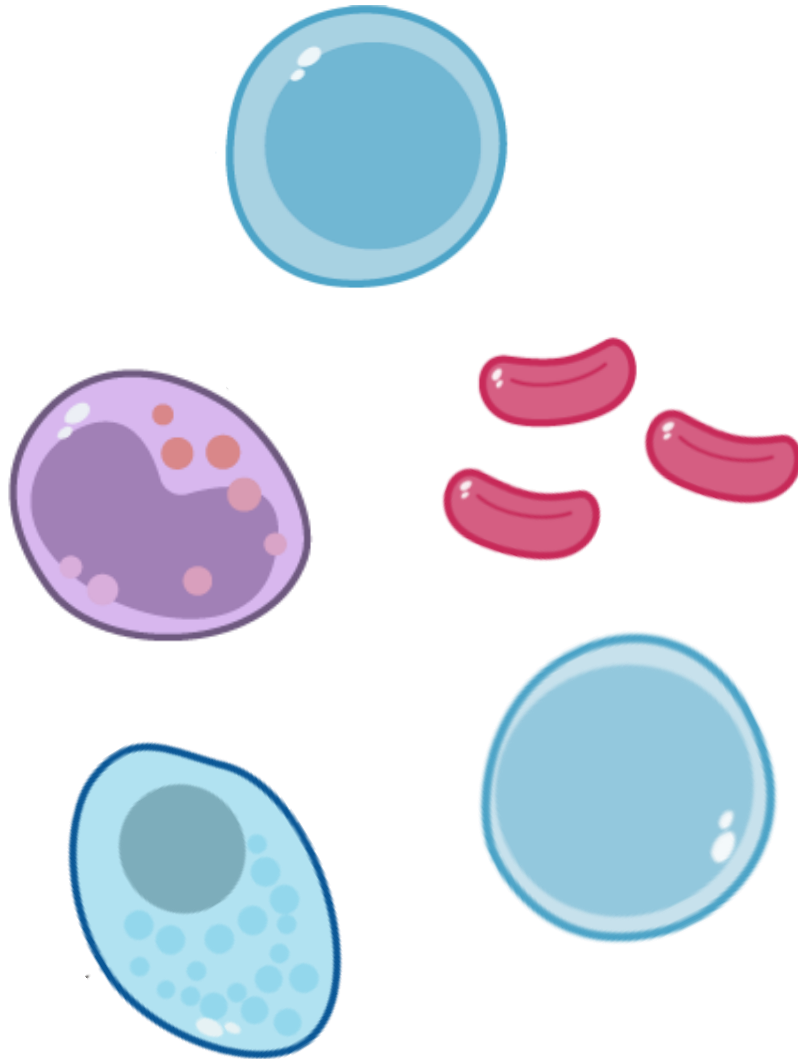
Recurrent
stromal ocular
herpes simplex
virus leading to
corneal scarring
and blindness

25,000 per year
in developed
economies

135,000
globally

in vivo
**proof-of-concept
in rabbit model**

presented at
ARVO 2018
Annual Meeting



Hematopoietic stem cells could yield **multiple medicines for blood diseases** including sickle cell disease and beta-thalassemia

T cells are therapeutic platform for **cancer, autoimmune, and infectious diseases**

Editas editing enables medicines across **many additional cell types**

Expand range of cancers that can be treated

with Editas engineered
CAR T and TCR
cell medicines

Achieved
highly efficient
editing of multiple
gene targets, both
individually and
in combination

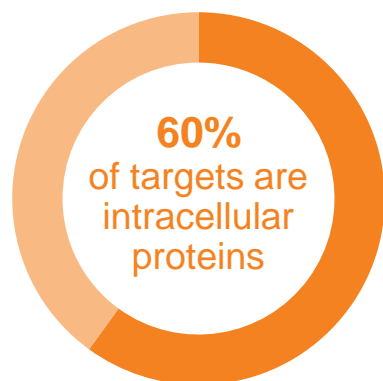
Celgene developing
**at-scale
gene editing
manufacturing**
process

**Multiple product
candidates** in alliance
advancing including
**an engineered
TCR candidate for
HPV-associated
solid tumors**



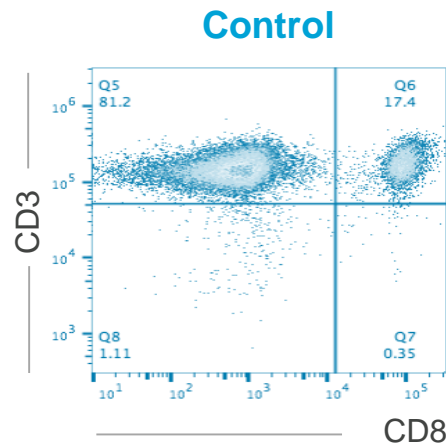
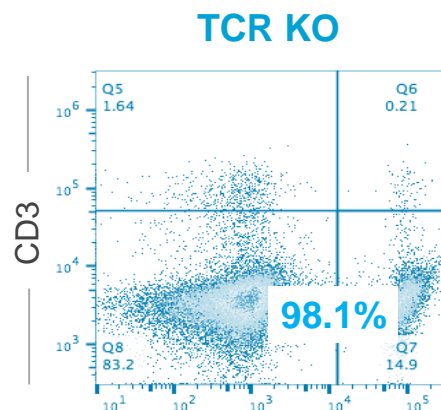


“Top 50” Cancer Antigen Targets¹



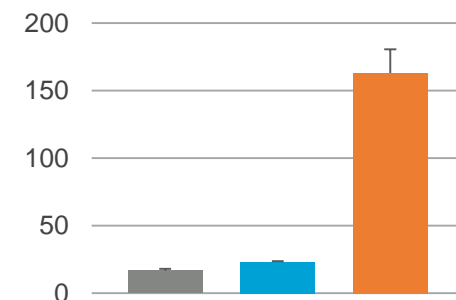
Rank	Antigen	Mechanism
1	WT1	Oncogenic
3	LMP2	Viral
4	HPV	Viral/Oncogenic
8	MAGE A3	Mixed
9	P53 WT	Oncogenic
10	NY-ESO-1	Prognosis
14	MelanA/MART1	Differentiation
15	Ras Mutant	Oncogenic
16	gp100	Differentiation
17	p53 Mutant	Oncogenic

Nearly Complete TCR Knockout



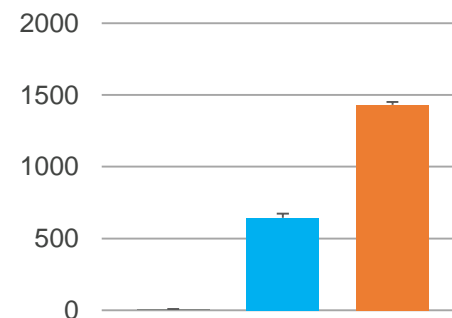
Increase in Functional Activity

CD4 IFN γ (pg/mL)



■ Mock ■ eTCR+ ■ eTCR+ KO

CD8 IFN γ (pg/mL)



Gene disruption to increase
fetal hemoglobin levels

Gene insertion to restore
adult hemoglobin expression

Candidates from two
distinct editing strategies
designed to deliver
best-in-class medicines

Over
100,000
hospitalizations
annually
in US alone

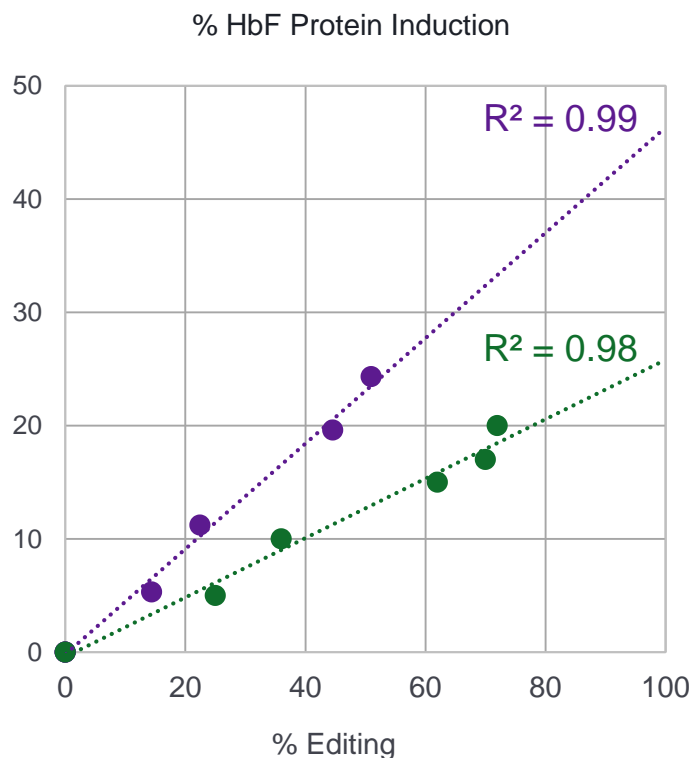
Sickle cell disease and beta-thalassemia
causing anemia, pain crises, organ failure, and even death

Gene Disruption

to increase fetal hemoglobin with
potentially more potent edit

Editas Novel Approach
to Editing β -globin Locus¹

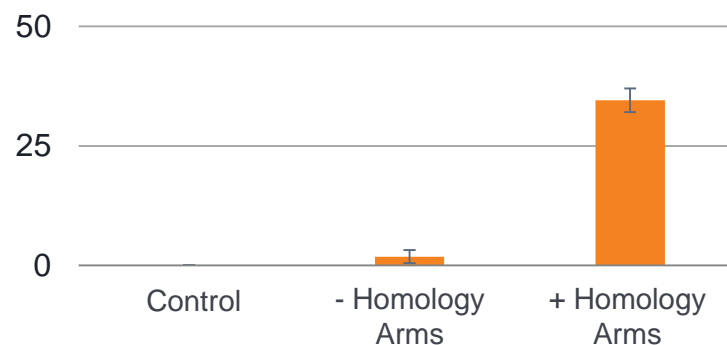
ZFN Published Approach
to Editing BCL11Ae²



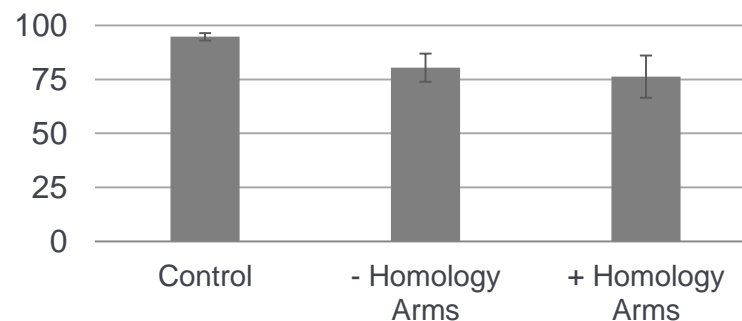
Gene Insertion

to restore hemoglobin expression
and eliminate mutation

% Homology Directed Repair at β -globin Locus



% Cells Viable at 48 hours



1. 0, 2.5, 3.75 μ M RNP tested, 2 different HSC donors; 2. Data estimated based on Chang et al., *Molecular Therapy*, 2016
HbF: Fetal Hemoglobin; RNP: Ribonucleoprotein

MEDICINES

TECHNOLOGY

OCULAR MEDICINES



Option to license up to
5 ocular programs

Partnership with innovator
in ophthalmology

\$90 million upfront plus
> \$1 billion contingent milestones
and tiered royalties; option for
50/50 profit split in US on 2 programs

ENGINEERED T CELL MEDICINES FOR CANCER



CAR T and TCR cell medicines
to treat cancer

Partnership with leader in
engineered T cells for cancer

\$30 million upfront and up to
\$22 million R&D funding plus
~ \$930 million milestones
and tiered royalties



MONITOR
BIOTECHNOLOGIES



| 2017 Sets Stage for Transformative 2018

2017 Accomplishments

-  Established Allergan strategic alliance in ocular medicines
-  Achieved preclinical proof-of-concept for multiple programs
-  Initiated LCA10 clinical natural history study
-  Expanded team to >110 Editors
-  Further advanced our intellectual property leadership position

2018 Goals

-  Submit IND for LCA10 program by mid-2018
-  Report preclinical proof-of-concept for additional programs
-  Advance manufacturing capabilities to enable additional IND(s) in 2019
-  Establish additional important strategic alliances
-  Continue to build a best-in-class organization and culture



Repairing broken genes
is just the beginning



Community



Resilience



Ingenuity



Science



Passion

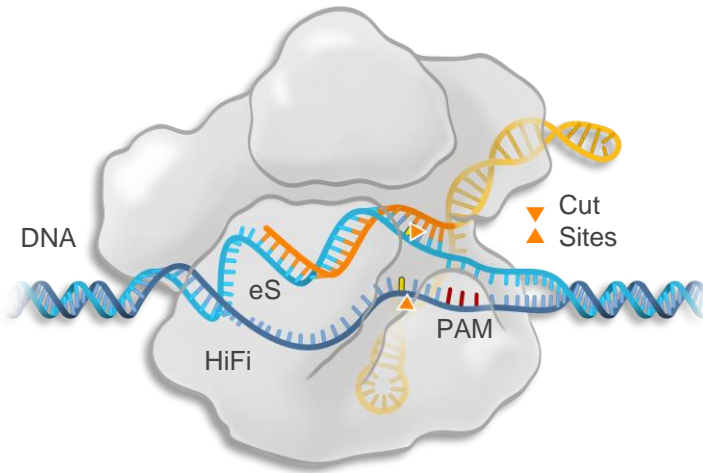


Revolution

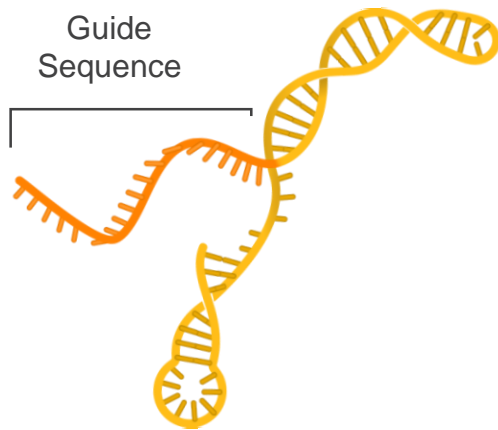
Appendix

| CRISPR Unlocks Genome Editing

Nuclease



Guide RNA



Complex of nuclease and guide RNA precisely locates and cuts genomic sites

Ability to target multiple sites simultaneously

Nuclease can be engineered to reach more sites and to modulate cutting



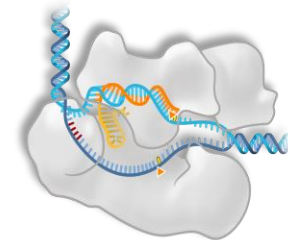
Broad Toolkit of CRISPR Nucleases

We are the **only**
company with
**multiple editing
systems**

Cas9



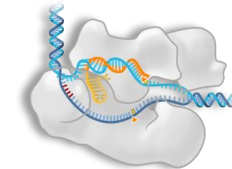
Cpf1



SpCas9



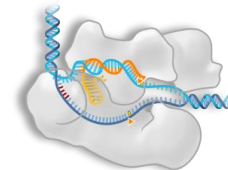
AsCpf1



SaCas9



LbCpf1



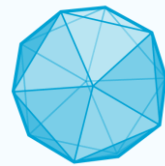
Cas9: CRISPR Associated Protein 9; Cpf1: CRISPR from *Prevotella* and *Francisella*; SpCas9: *Streptococcus pyogenes* Cas9; SaCas9: *Staphylococcus aureus* Cas9; AsCpf1: *Acidaminococcus* species Cpf1; LbCpf1: *Lachnospiraceae* bacterium Cpf1

Platform Enables Broad Product Pipeline

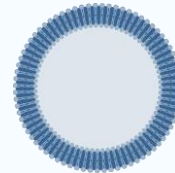

Broad
Range of
Sites




Wide
Delivery
Options



Viral Vector

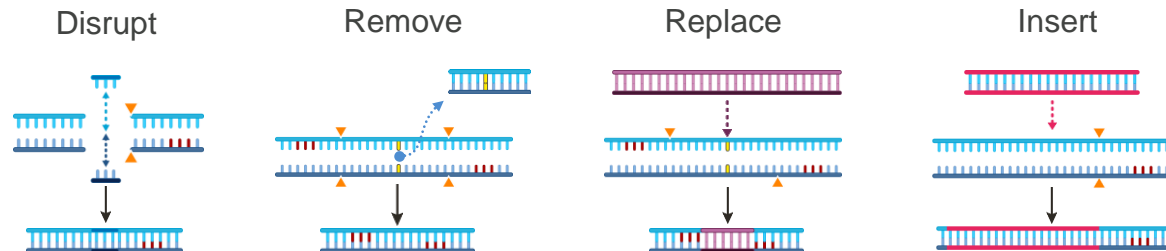


Lipid Nanoparticle



Electroporation

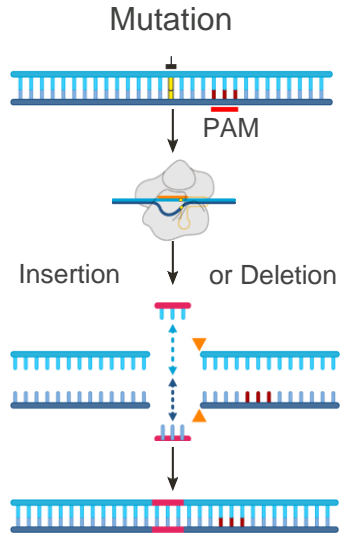

Diverse
Spectrum
of Edits





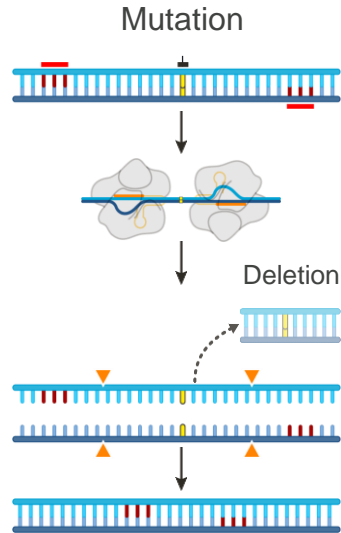
CRISPR Addresses Diverse Mutations

Cut and Disrupt



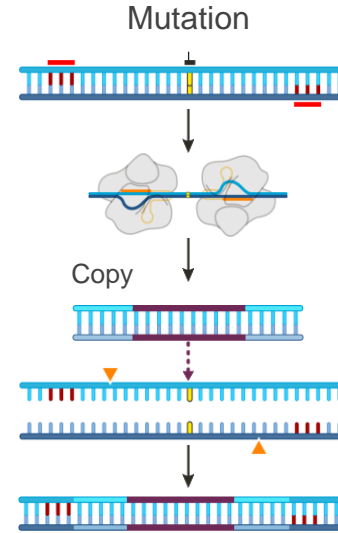
e.g., Engineered T cells

Cut and Remove



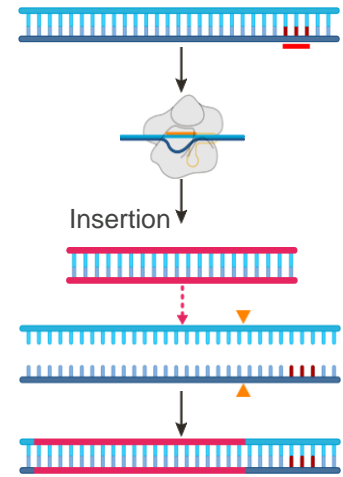
e.g., LCA10

Cut and Replace



e.g., Hemoglobin Beta

Cut and Insert



e.g., Safe harbor

Non-homologous end joining typically **disrupts a gene or eliminates a disease-causing mutation**

Homology-directed repair and targeted insertion aim to **promote expression of correct DNA sequences**

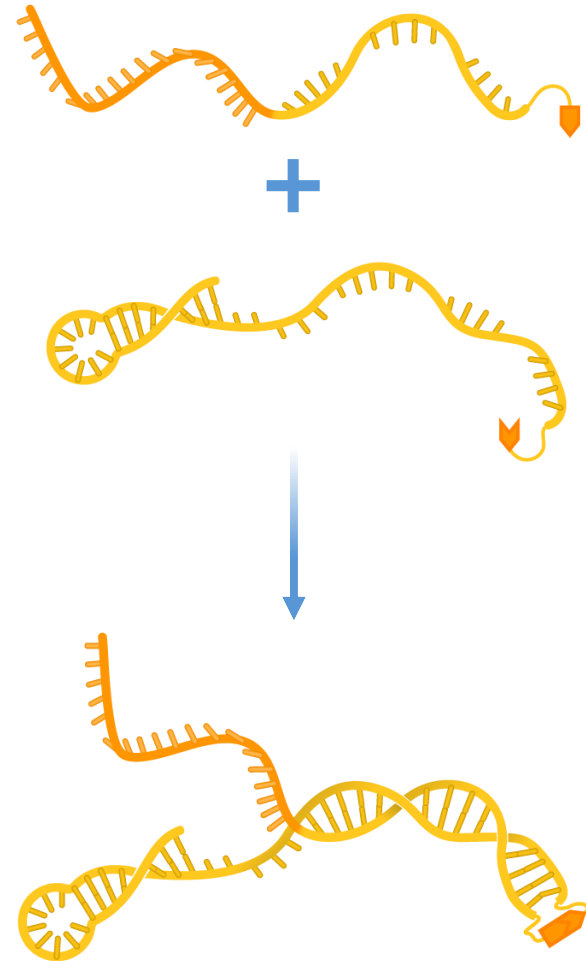
| Rigorous Approach to Specificity

	COMPUTATIONAL SCREEN	CELLULAR & BIOCHEMICAL ASSAYS	TARGETED SEQUENCING PANELS
# GUIDE RNA	1,000 – 2,000	50 – 100	5 – 10
TARGETED		Biased Library of Targets (BLT)	Uni-directional Targeted Sequencing (UDiTaS) Bi-directional PCR
COMPREHENSIVE	GODOT	GUIDE-Seq CIRCLE-Seq Digenome	

World class RNA
chemistry expertise

Enables best-in-class
CRISPR medicines

Proprietary classes of
guide RNAs with distinct
intellectual property

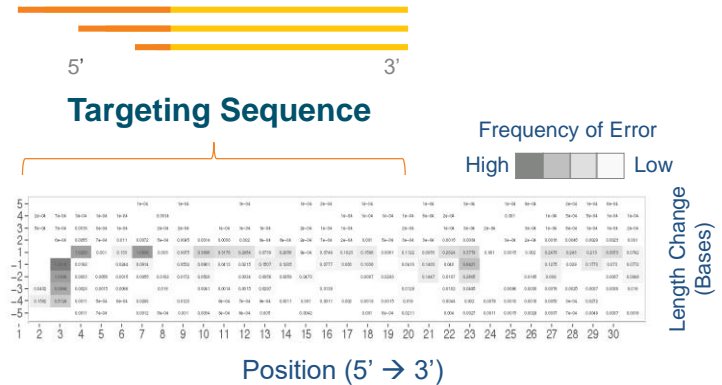


| Proprietary Guide RNA Engineering

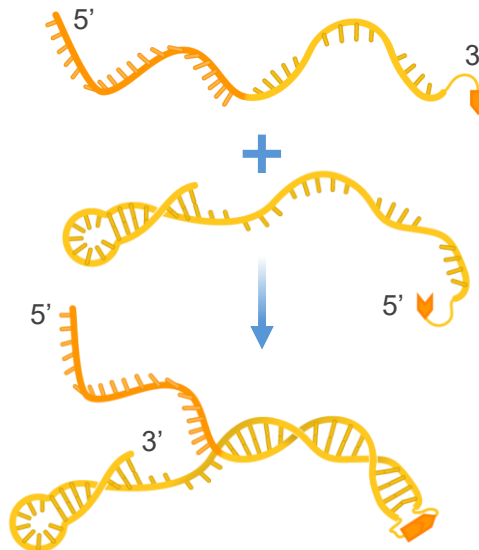
Single gRNA



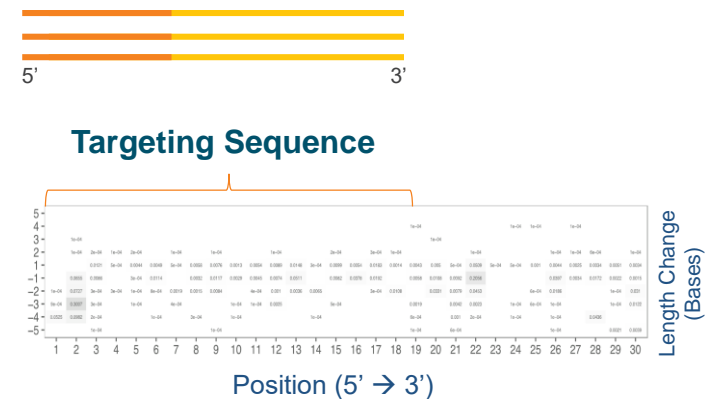
Heterogeneous product
(full-length, truncated, errors)



Covalently Coupled Dual gRNA



Well-defined product
(full-length only)



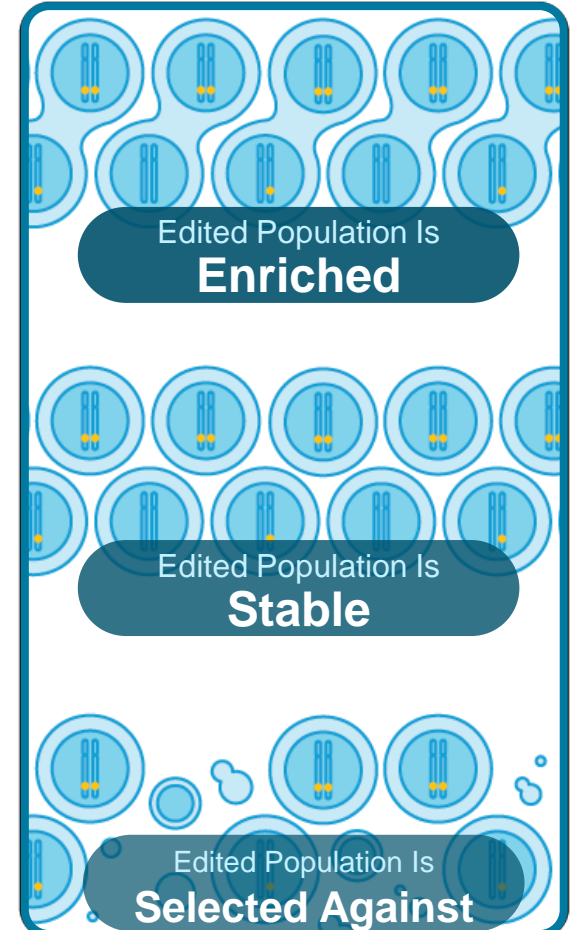
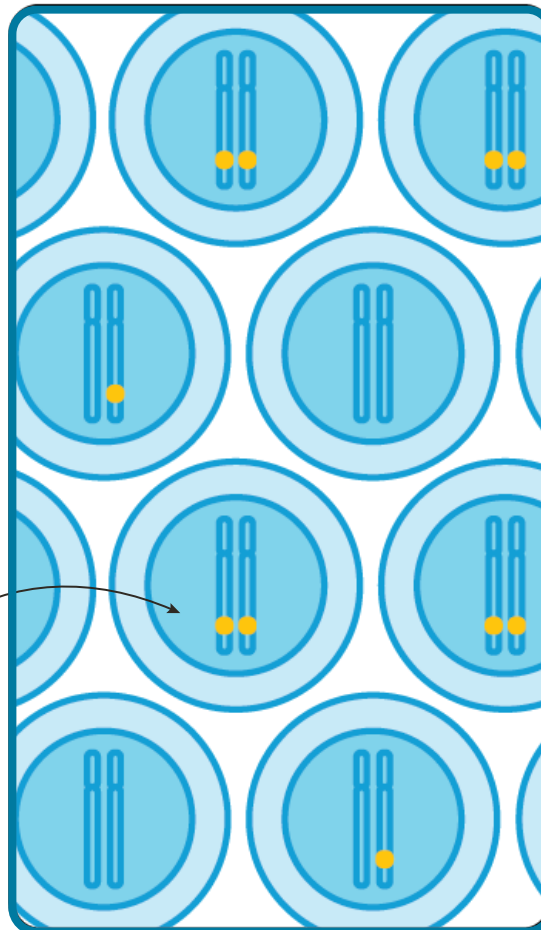
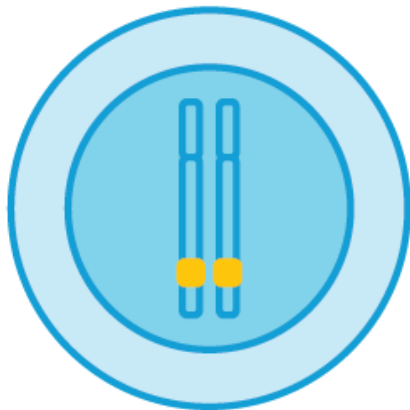
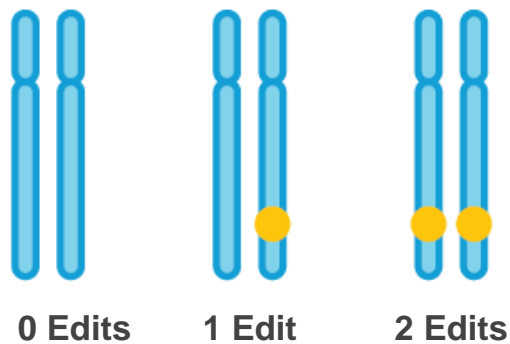


Fundamentals of Gene Editing Medicines

1 Editing Efficiency in Target Cell Type

2 Proportion of Target Cells Edited

3 Long-term Fate of Edited Cells



| Unmatched Patent Position in CRISPR Gene Editing

Exclusive access to Cas9 and Cpf1

patent portfolios, which are independent of each other

Exclusive access to advanced forms

including high specificity, PAM variants, others

Over 40 issued patents

worldwide, including in United States, Europe, and Australia

Over 500 pending patent applications

from Editas Medicine and academic institutions

