



# Corporate Presentation

October 7, 2019

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PIONEERING THE POSSIBLE

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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 clinical trial timeline for EDIT-101 (AGN-151587) and the Company’s 2022 goals. 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.*

## OUR MISSION

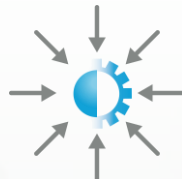
is to translate the promise of genome editing into a broad class of transformative genomic medicines to benefit the greatest number of patients





### **Clinical-stage company working to transform patient lives**

- First *in vivo* CRISPR clinical trial in history (EDIT-101 for LCA10)
- EDIT-101 patient screening initiated and dosing on track for 2H19
- Rapidly translating exciting science into revolutionary medicines



### **Leader across CRISPR *in vivo* and engineered cell medicines**

- Proven AAV delivery capability for *in vivo* CRISPR medicines
- Advancing engineered cell medicines to treat blood diseases and cancer
- Enabled by unparalleled platform of Cas9 and Cpf1 (Cas12a) enzymes



### **Strong progress towards EM22 goals**

- EDIT-101 IND accepted by FDA upon initial review
- Usher syndrome 2A (USH2A) *in vivo* proof of concept established
- EDIT-301 for sickle cell and beta-thalassemia IND-enabling activities initiated

## ACHIEVEMENTS

- ✓ Formed collaboration with BlueRock Therapeutics to advance universal allogeneic cell medicines for cancer
- ✓ Initiated IND-enabling activities for EDIT-301 for sickle cell and beta-thalassemia
- ✓ Established in vivo proof-of-concept for Usher syndrome 2A

## GOALS


- EDIT-101 first patient dosing in second half
- EDIT-301 pre-clinical data in second half
- Usher syndrome 2A ready for IND-enabling studies by year-end





# | Developing Best-in-Class CRISPR Medicines

## EDITING INSIDE THE BODY *IN VIVO CRISPR MEDICINES*

### OCULAR DISEASES

Leber congenital amaurosis 10\*  

Usher syndrome 2A  

Retinitis pigmentosa

Ocular HSV 

### EARLY DISCOVERY

Liver – AATD   

Muscle – DMD 

Lung – CF

## EDITING OUTSIDE THE BODY *ENGINEERED CELL MEDICINES*

### CANCER

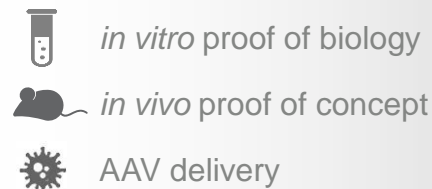
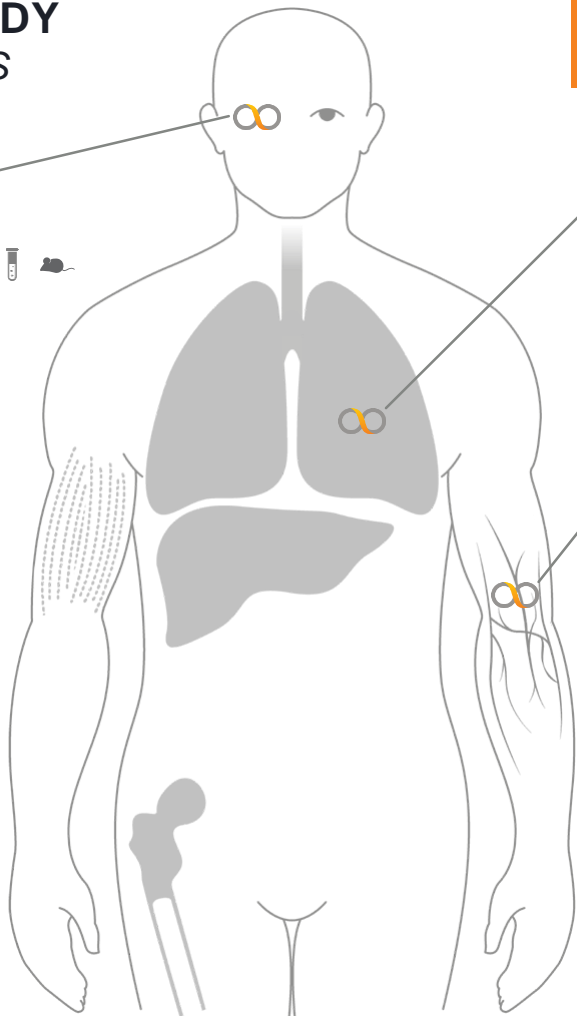
Autologous T cell medicines\*\* 

Allogeneic cell medicines

### BLOOD DISEASES

Sickle cell disease  

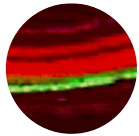
Beta-thalassemia  



\*EDIT-101 (AGN-151587) partnered with Allergan; \*\*Partnered with Celgene; LCA10: Leber congenital amaurosis 10; HSV: herpes simplex virus; CF: cystic fibrosis; DMD: Duchenne muscular dystrophy; AATD: alpha-1 antitrypsin deficiency; AAV: adeno-associated virus



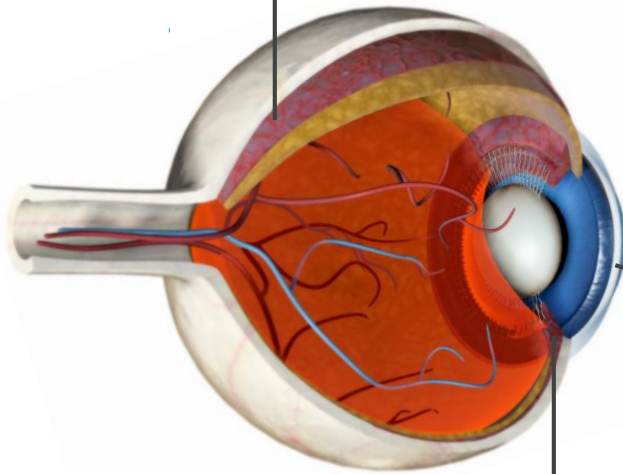
# | Durable Medicines for Serious Eye Diseases



## **Retina**

**LEBER CONGENITAL AMAUROSIS**  
**USHER SYNDROME**  
**RETINITIS PIGMENTOSA**

Cone-rod dystrophy  
Age-related macular degeneration  
Stargardt disease

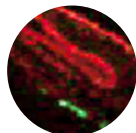


## **Anterior Chamber**

Ocular HSV  
Fuchs dystrophy

## **Trabecular Meshwork**

Genetic glaucoma



**Hundreds of thousands  
of patients**

**Targeted local injection  
with proven AAV vectors**

**Promising clinical and  
regulatory path**



# | Targeting Leading Genetic Form of Blindness

Remove genetic mutation to  
restore CEP290 protein and  
rebuild photoreceptors in  
**Leber congenital  
amaurosis 10**

First patient dosing  
expected in 2H19



and



**50/50 in US**

Degeneration  
of photoreceptors  
leading to  
blindness in  
childhood

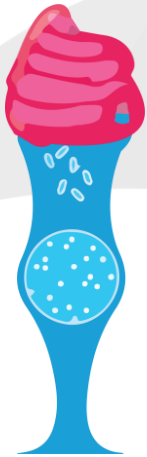
2,000 – 5,000  
patients  
in US and  
Europe



# | EDIT-101 Aims to Rescue Vision in LCA10

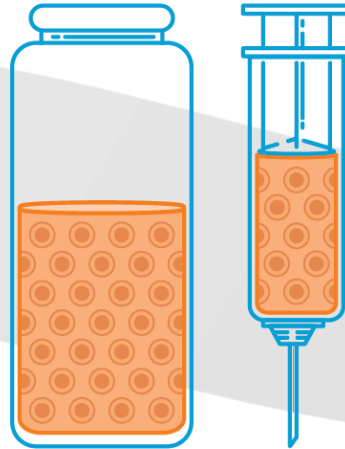
## LCA10 Photoreceptor

Outer Segment



Outer segment  
degenerates due to  
CEP290 deficiency

## EDIT-101



Editing removes  
disease-causing  
mutation

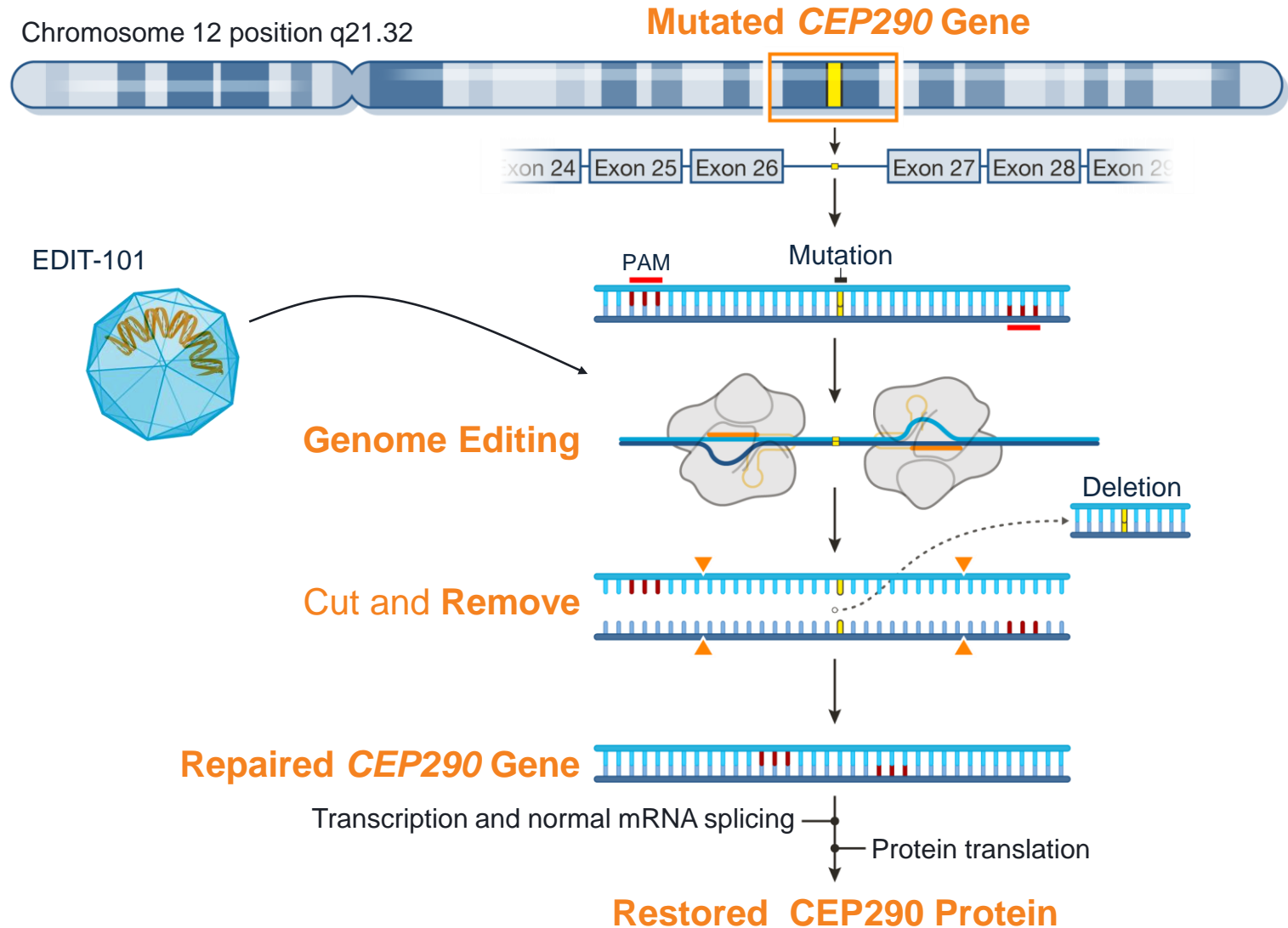
## Rescued Photoreceptor

Outer Segment



Outer segment  
regenerates with  
CEP290 protein

# EDIT-101 Aims to Rescue Vision in LCA10

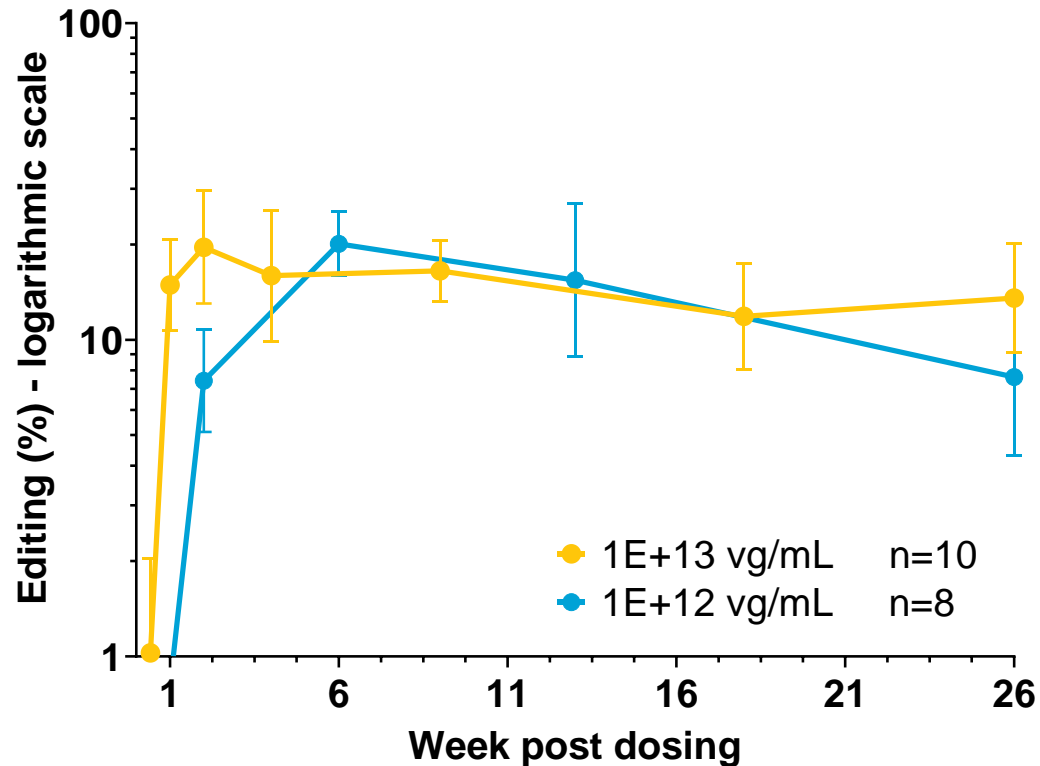




# EDIT-101 Demonstrates Rapid Editing

## CEP290 GENE EDITING

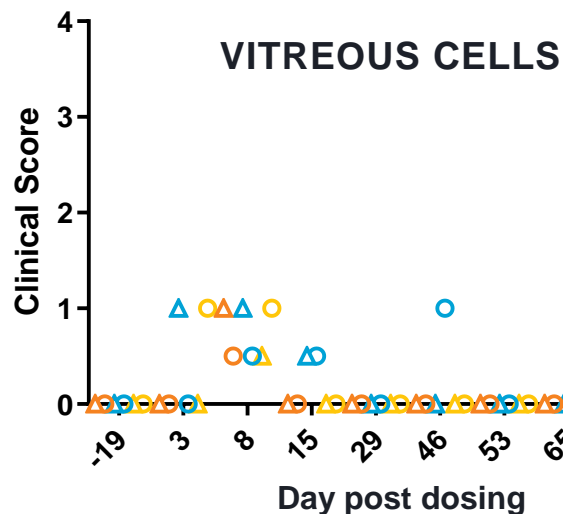
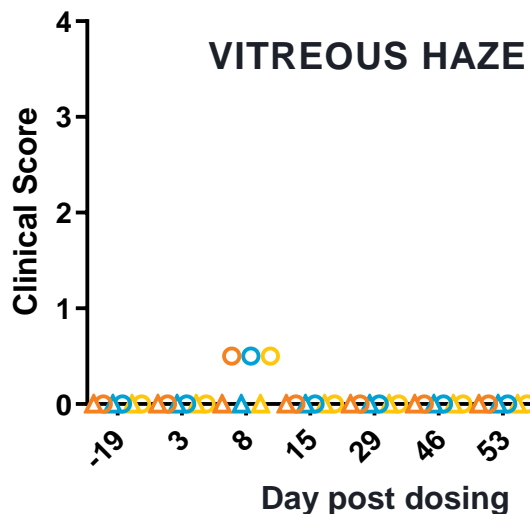
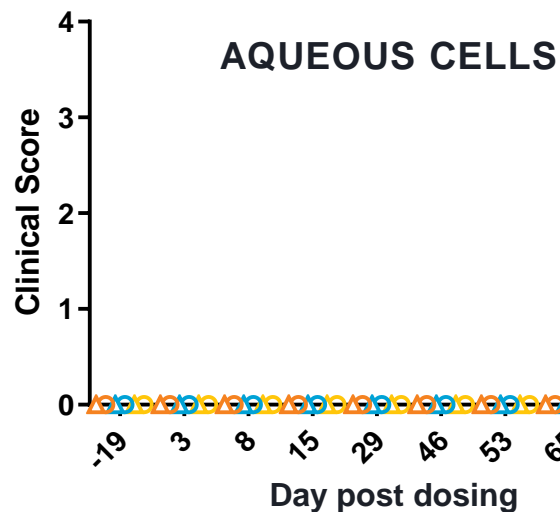
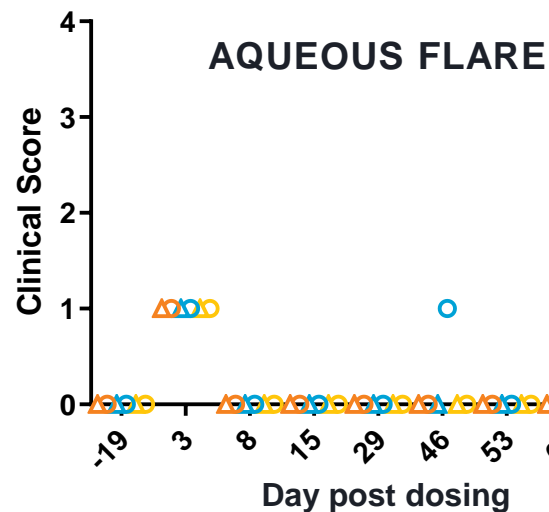
MOUSE FULL-THICKNESS RETINA



**Rapid onset of therapeutically relevant editing at AAV dose that has been safely administered to humans**



# EDIT-101 Well Tolerated in Non-Human Primates



## LEGEND

EDIT-101

Placebo

Animal 1

Animal 2

Animal 3

## CLINICAL SCORE

4.0 Severe

3.0 Marked

2.0 Moderate

1.0 Mild

0.5 Minimal

0 None

4 weeks of steroid prophylaxis;  $1E+12$  vg/mL x 100  $\mu$ L/eye

Jiang et al., *Evaluation of Tolerability and Immunogenicity of EDIT-101 Following Subretinal Injection in Non-human Primates*, American Society of Gene & Cell Therapy 21<sup>st</sup> Annual Meeting

## LCA10 NATURAL HISTORY STUDY



### PATIENTS



~40 patients, aged 3 and above

### OBJECTIVES



Characterize patients, assessments, rate of change and validate endpoints

### SITES



7 sites across US and Europe

### FOLLOW-UP



6 visits over 1 year; baseline data presented in April 2019



# Initiated LCA10 Phase 1/2 Clinical Trial



## LCA10 PHASE 1/2 TRIAL

### DESIGN



Open-label, dose escalation study  
to evaluate safety, tolerability, and efficacy

### PATIENTS



~18 patients with IVS26 mutation\*

### COMPARATOR



Patient's own baseline value  
for each efficacy measure

### FOLLOW-UP



Core measurements  
every 3 months for 1<sup>st</sup> year

\*Intervening sequence 26 in CEP290 gene containing the c.2991+1655A>G mutation



Rescue vision by restoring  
USH2A protein leveraging  
**same proprietary  
enzyme, vector,  
and promoter  
as EDIT-101**

Progressive  
vision loss leading  
to blindness due to  
degeneration of  
photoreceptors

4,000  
patients with  
target mutation  
  
Additional 10,000  
potentially  
addressable

*in vivo*  
**proof of concept  
demonstrated**

in collaboration with  
Massachusetts Eye and Ear



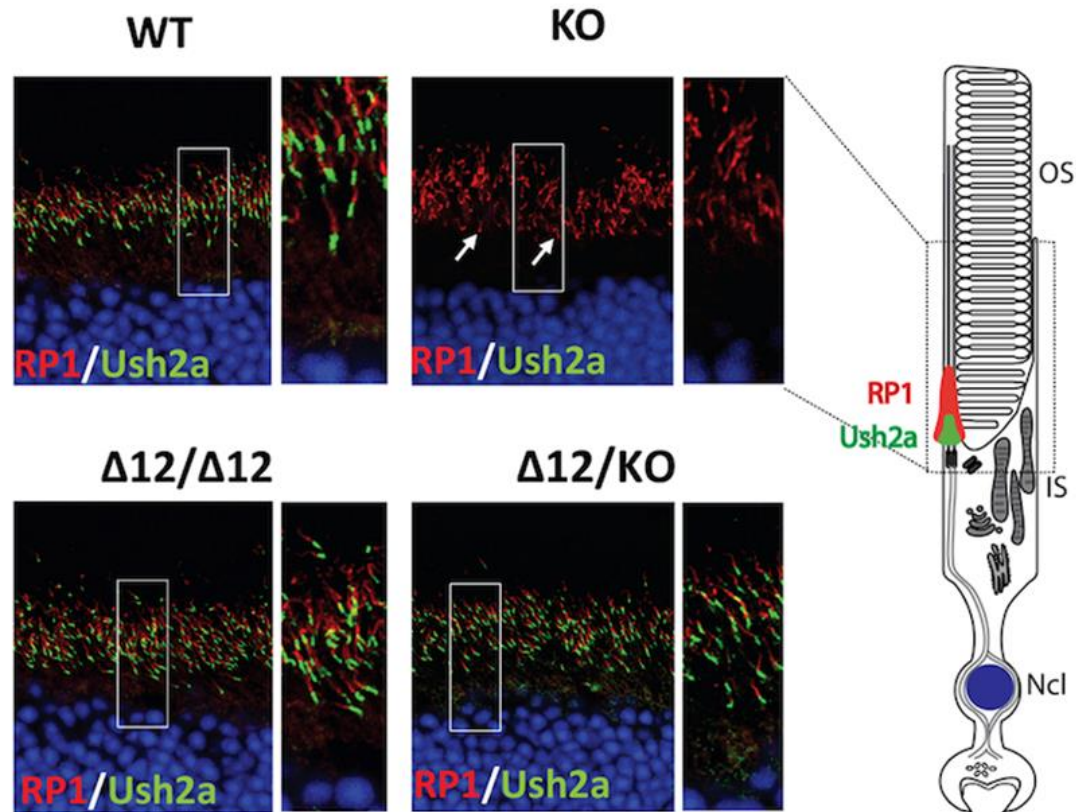
**Massachusetts  
Eye and Ear®**



**HARVARD MEDICAL SCHOOL  
AFFILIATE**



# | Editing *USH2A* Increases Cilia Length *in vivo*



Editing strategy results in desired phenotype

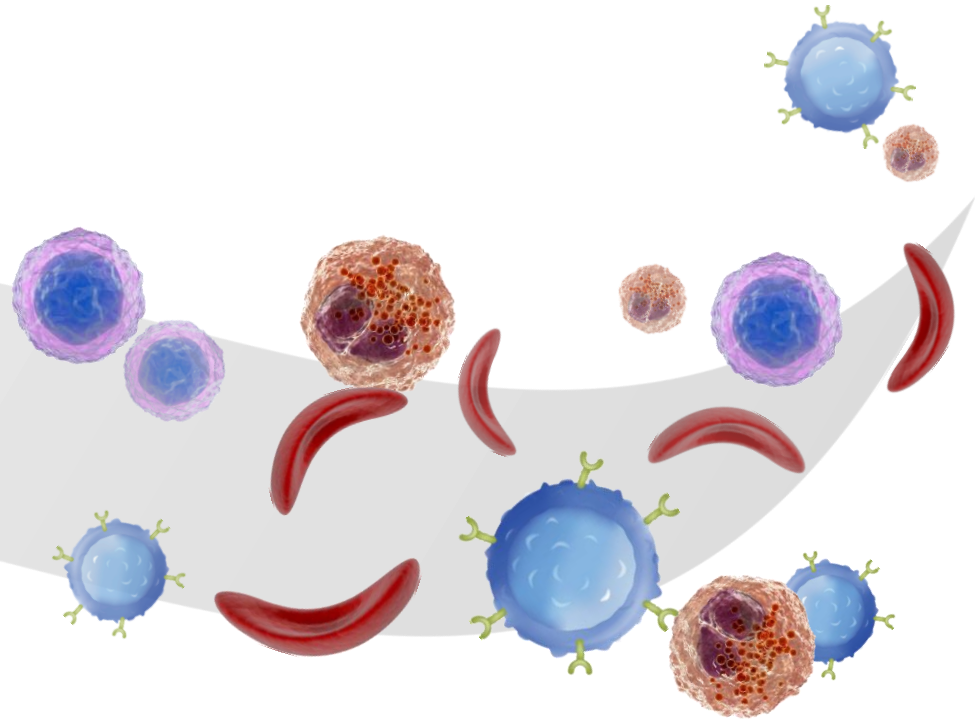


# Developing Transformative Engineered Cell Medicines

**Hematopoietic stem cells**  
could yield **medicines for multiple blood diseases**

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

**Editas Medicine editing**  
enables both **autologous and allogeneic cell medicines**



**Editing hematopoietic stem cells to increase fetal hemoglobin**  
and alleviate disease morbidity and mortality

**Sickle cell disease and beta-thalassemia**  
causing anemia, pain crises, organ failure, and mortality

Over **100,000** hospitalizations annually in US alone

**Differentiated editing strategy**  
designed to deliver **best-in-class medicines**



## Three Critical Product Candidate Criteria

1

**SUCCESSFUL  
EDITING**  
of long-term  
hematopoietic  
stem cells

2

**MAINTENANCE**  
of normal HSC  
function

3

**DURABLE**  
predicted therapeutic  
induction of fetal  
hemoglobin

**Differentiated editing strategy directly targets  
the genetic cause of the disease**

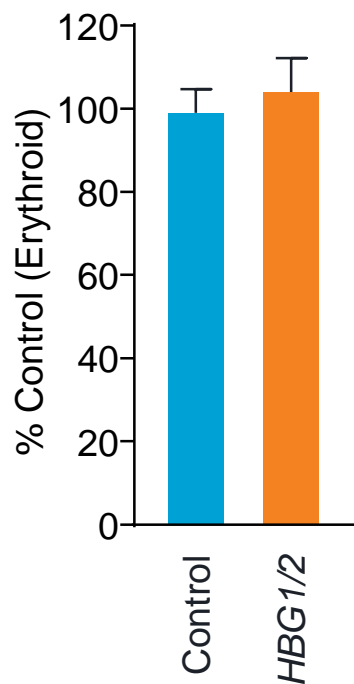


# Editing Strategy Maintains HSC Function

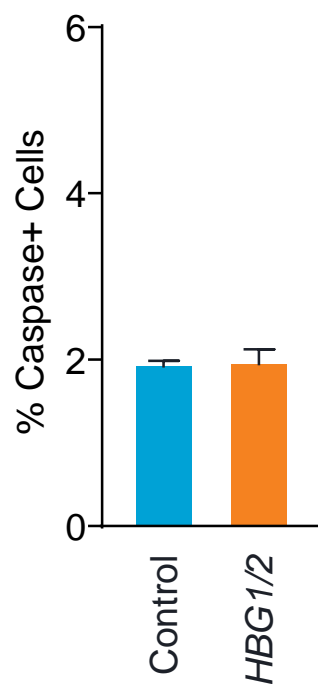
## GLOBALIN LOCUS EDITING

EDITAS MEDICINE APPROACH

SIMILAR LEVELS OF  
ERYTHROID OUTPUT



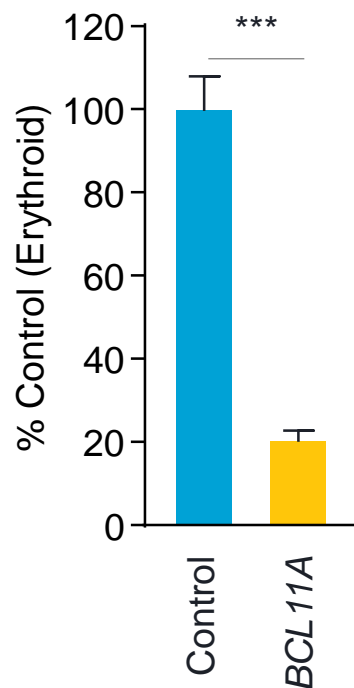
SIMILAR LEVELS  
OF CELL DEATH



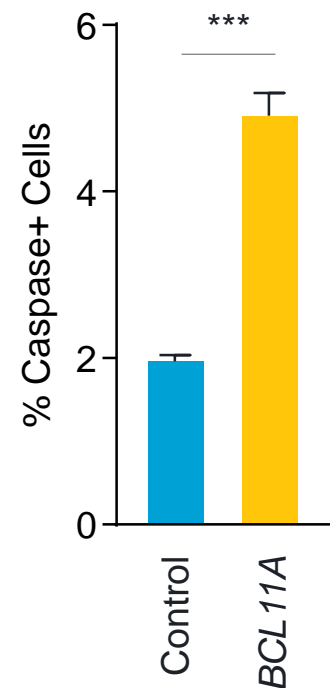
## BCL11Ae EDITING

COMPETING APPROACH

REDUCED  
ERYTHROID OUTPUT



INCREASED  
CELL DEATH



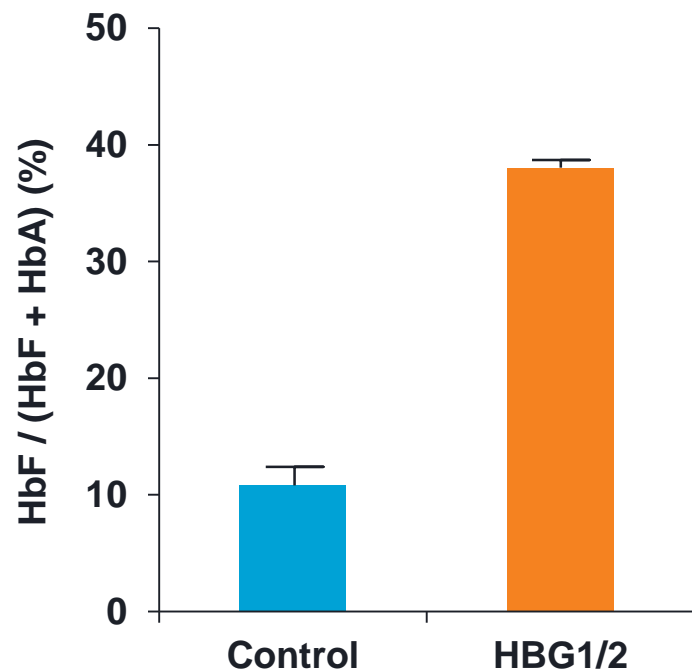
n = 5 healthy human donors; \*\*\*p<0.001

Chang et al., *Genome Editing of HBG1/2 Promoter Leads to Robust HbF Induction In Vivo While Editing of BCL11A Erythroid Enhancer Shows Erythroid Defect*, 60<sup>th</sup> ASH Annual Meeting & Exposition

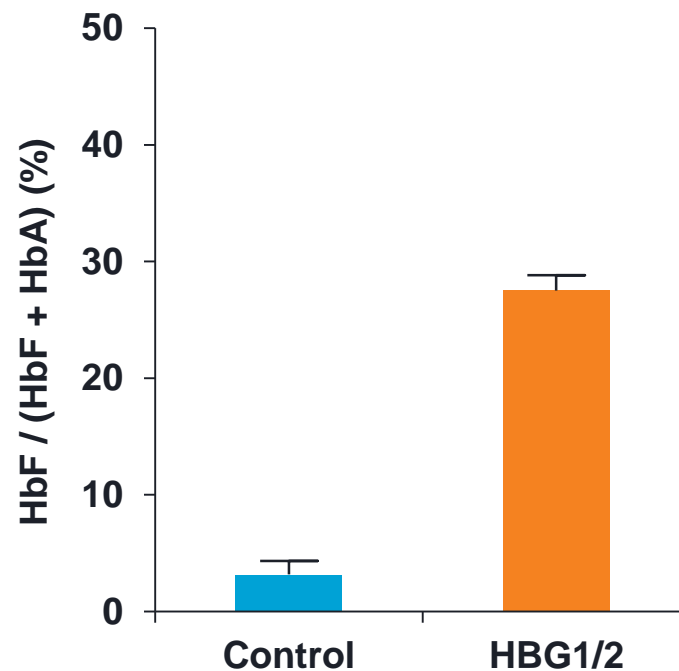


# Editing Strategy Induces Robust Fetal Hemoglobin

## HbF INDUCTION *ex vivo* CD34+ CELLS

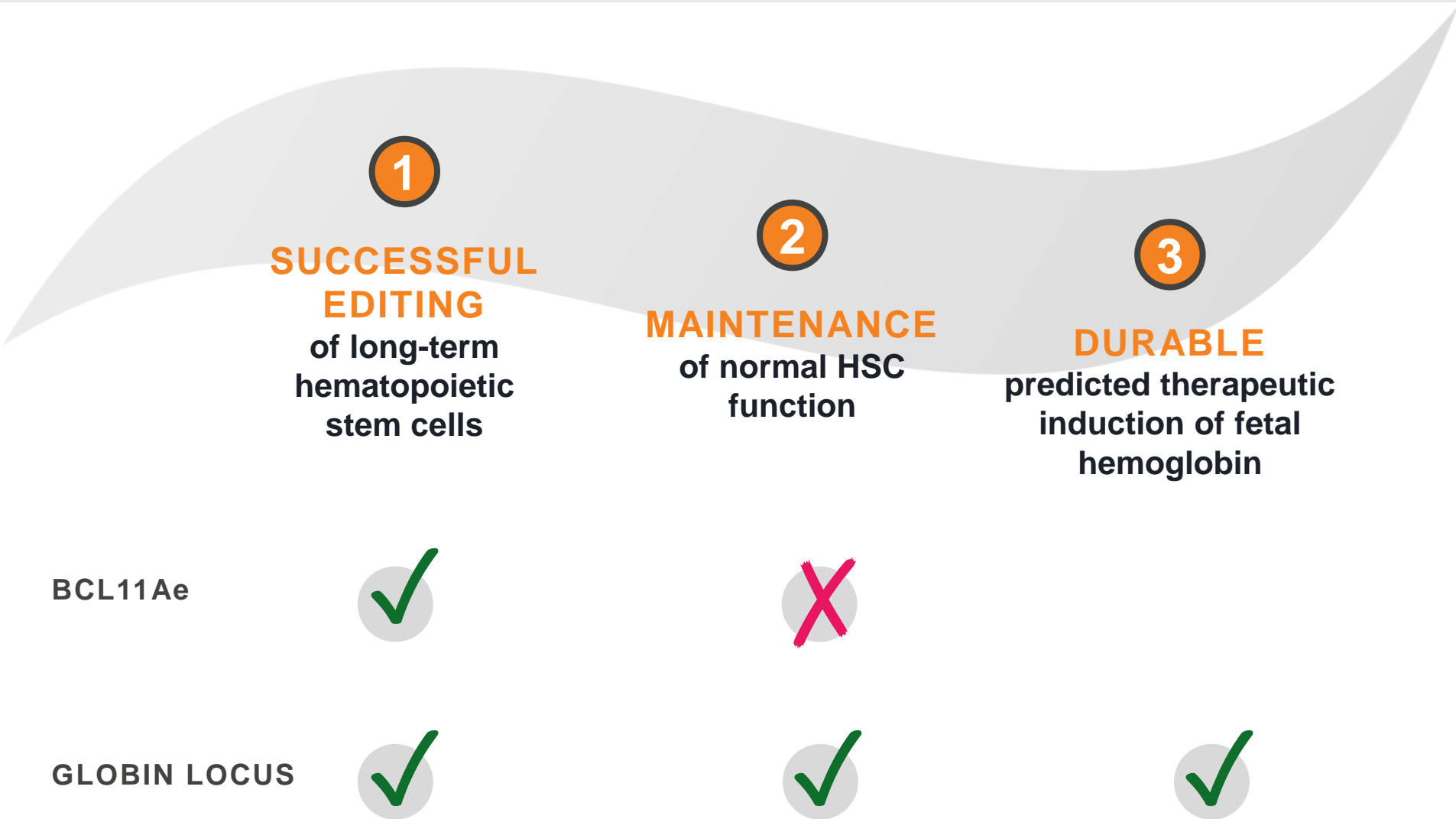


## HbF INDUCTION *in vivo* RED BLOOD CELL PRECURSORS

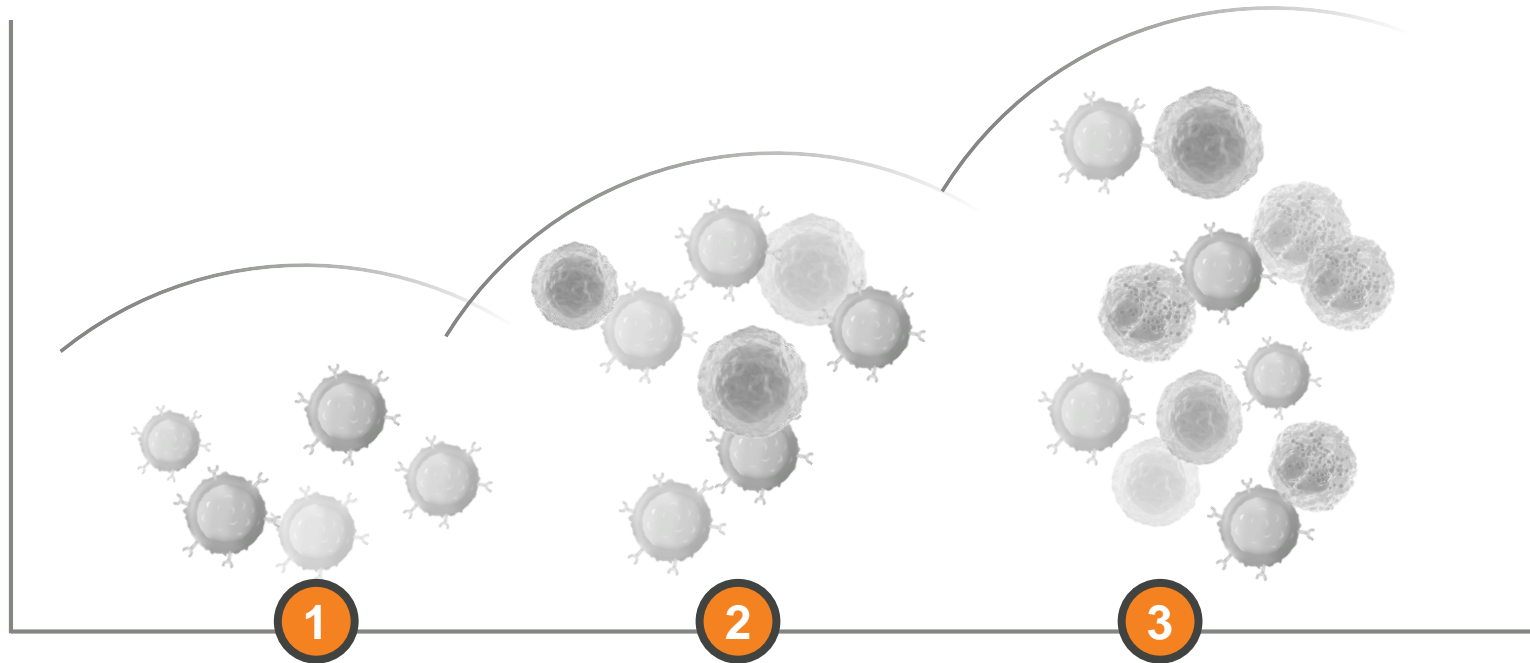


Potential to safely and effectively induce fetal hemoglobin *in vivo*





# | Rapid Innovation in Cell Medicines for Cancer



**CELL SOURCE**

Patient Donor

Healthy Donor

Universal (iPSC)

**CELL TYPE**

$\alpha\beta$  T cells

NK cells,  
 $\alpha\beta$  T cells,  $\gamma\delta$  T cells

NK cells,  
 $\alpha\beta$  T cells,  $\gamma\delta$  T cells

**MULTIPLEXING**

Modest

Modest

High



# Investing to Develop Best in Class Medicines

	PATIENT DONOR	HEALTHY DONOR	UNIVERSAL (iPSC)
 <b>T CELLS (<math>\alpha\beta</math> and <math>\gamma\delta</math>)</b>			
Milestones & royalties to			
 <b>NK CELLS</b>			 Milestones & royalties to  <b>BlueRock</b> Therapeutics

**Driving programs across both T cells and NK cells for best in class medicines to treat liquid and solid tumors**



# Powerful Engine for Genomic Medicines

## Broadest Access to Genomic Targets

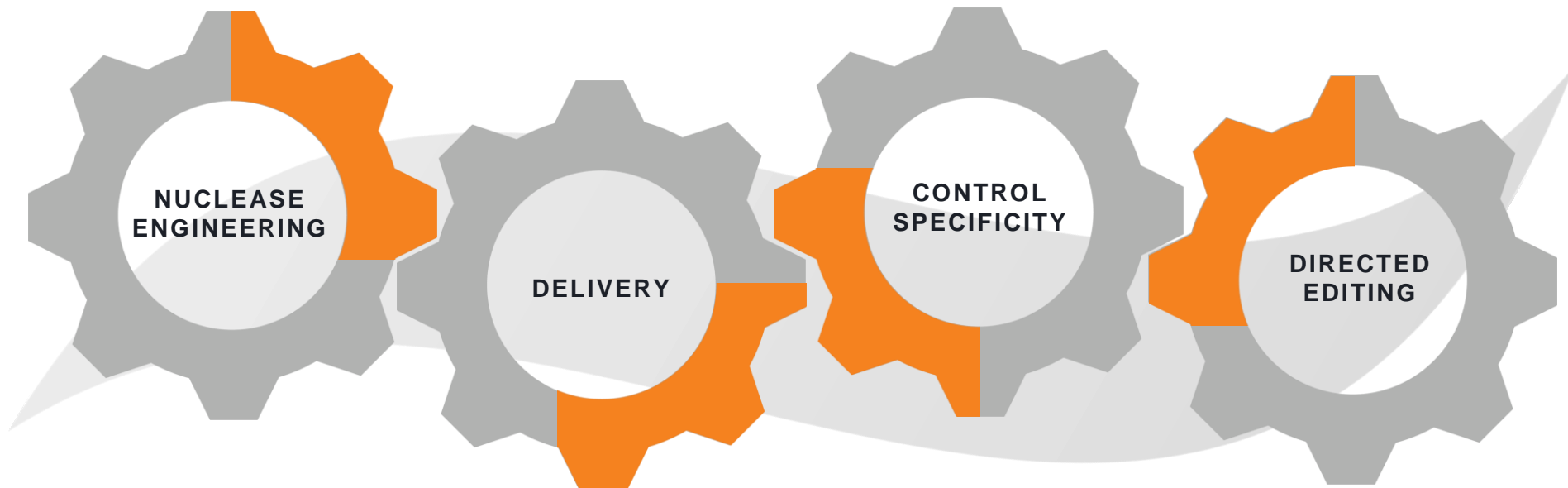
Proprietary portfolio of Cas9 and Cpf1 enzymes may directly edit ~95% of the human genome

## 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



# | Strong Foundation for Long-Term Leadership

## PARTNERS

### 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, including EDIT-101

### ENGINEERED T CELL MEDICINES FOR CANCER



CAR T and TCR cell medicines to  
treat cancer

Partnership with leader in oncology

\$30 million upfront and up to  
\$22 million in R&D funding;  
~\$930 million in contingent  
milestones plus tiered royalties;  
\$10 million in milestones achieved  
to date

## PATENTS

### BROADEST & DEEPEST PORTFOLIO OF CRISPR IP



Exclusive access to foundational  
Cas9 and Cpf1 patent estates

Exclusive access to multiple  
species and engineered forms of  
Cas9 and Cpf1

Over 70 issued patents and over  
600 patent applications pending

Issued patents covering EDIT-101



**C**ommunity



**R**esilience



**I**ngenuity



**S**cience



**P**assion



**R**evolution

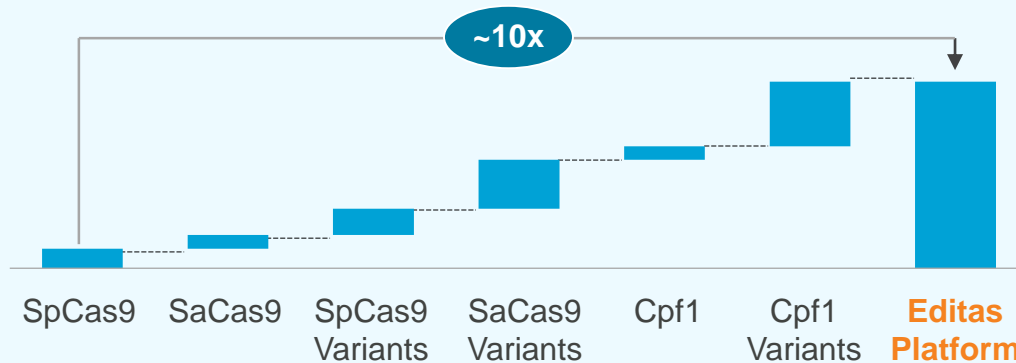
# Appendix



# Platform Enables Broad Product Pipeline



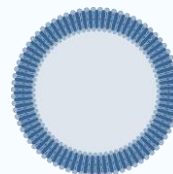
Broad  
Range of  
Sites



Wide  
Delivery  
Options



Viral Vector



Lipid Nanoparticle

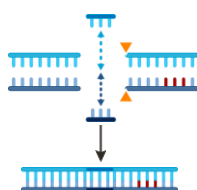


Electroporation

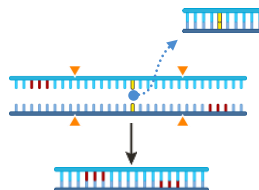


Diverse  
Spectrum  
of Edits

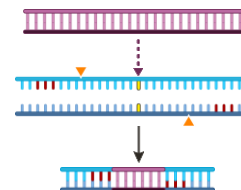
Disrupt



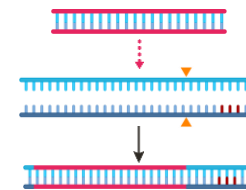
Remove



Replace



Insert





# | 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

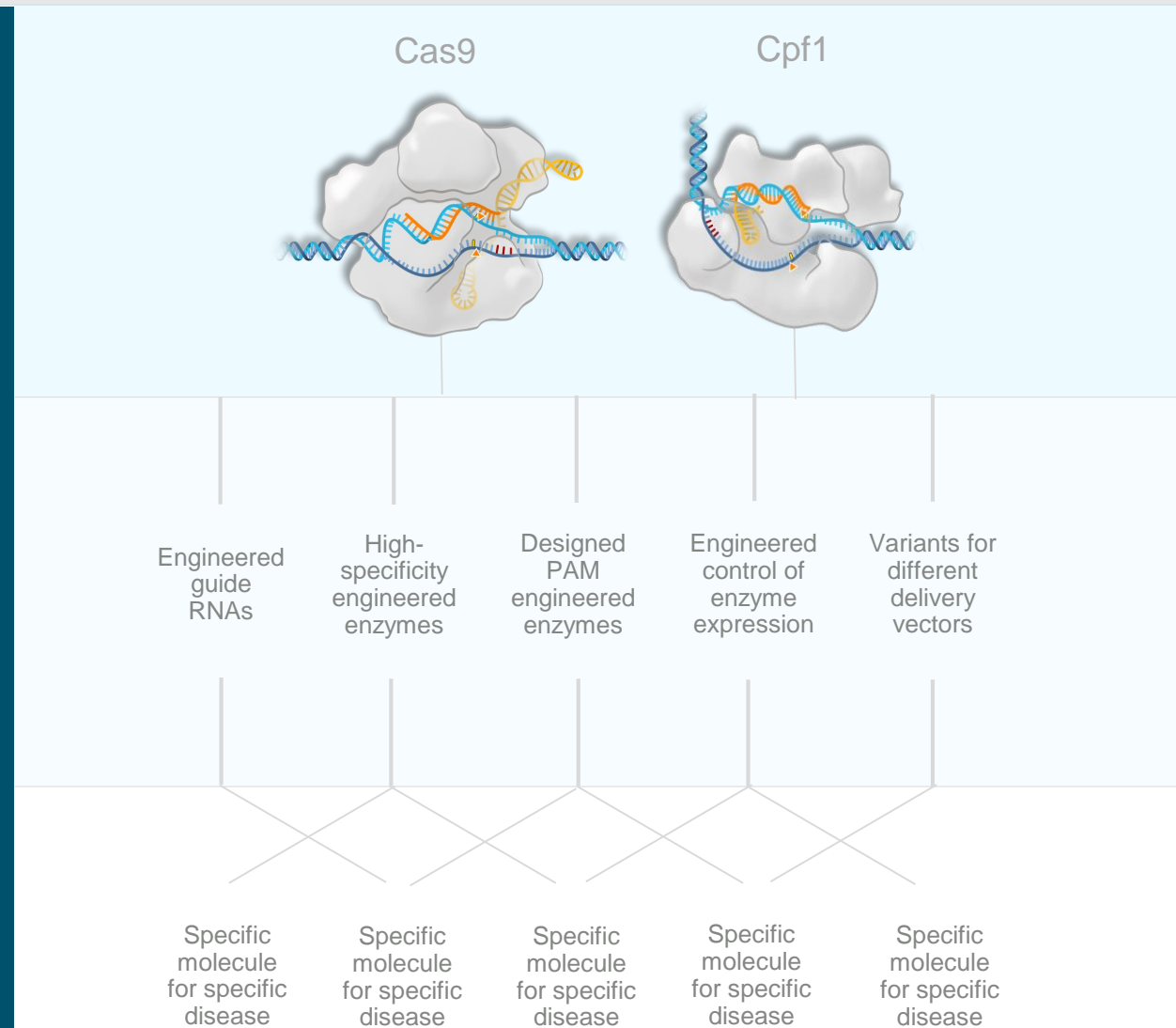
including high specificity, PAM variants, others

## Over 70 issued patents

worldwide, including in United States, Europe, and Australia

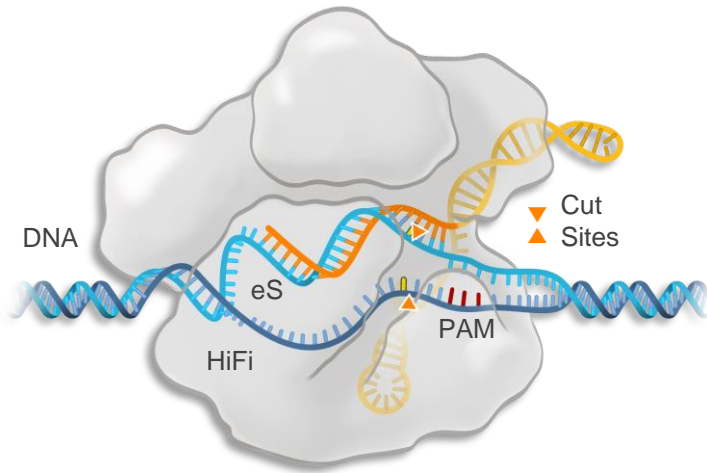
## Over 600 pending patent applications

from Editas Medicine and academic institutions

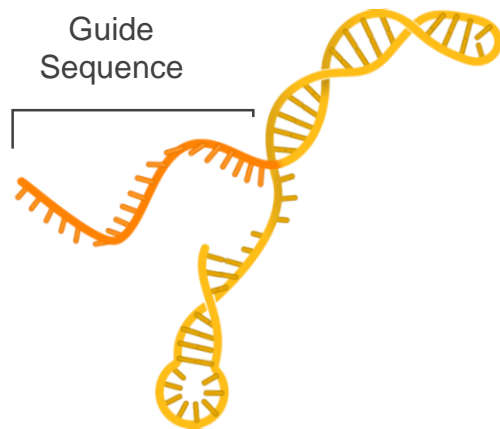


# | CRISPR Unlocks Genome Editing

## Nuclease



## Guide RNA



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

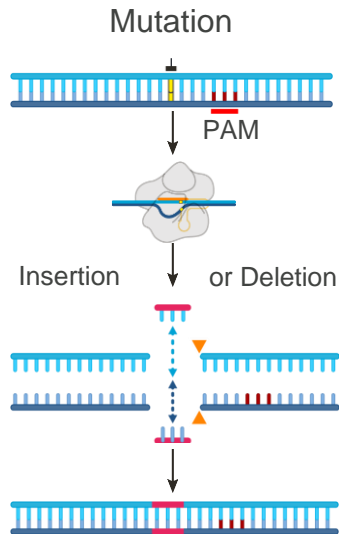
Ability to target multiple sites simultaneously

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

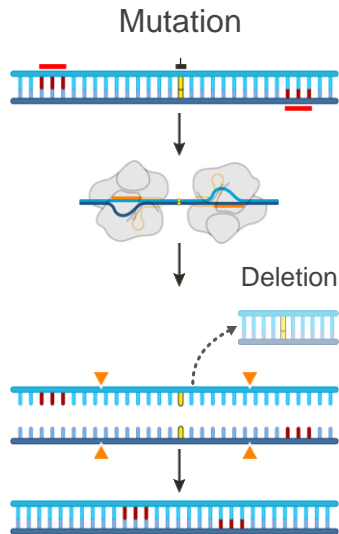


# CRISPR Addresses Diverse Mutations

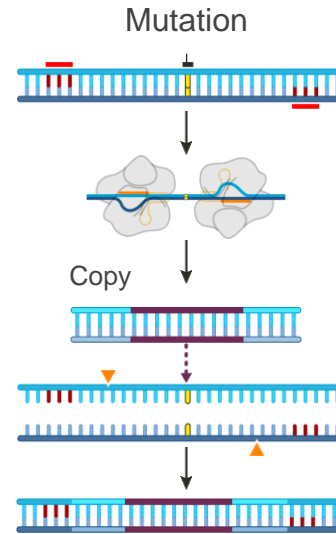
## Cut and Disrupt



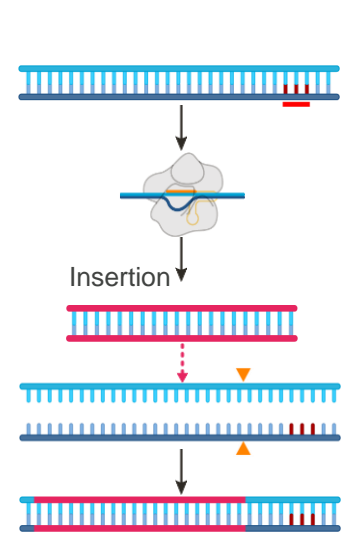
## Cut and Remove



## Cut and Replace



## Cut and Insert



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**