Narrative Review Article

Gene Therapy and Leber Congenital Amaurosis: A Review of Treatments and Clinical Trials

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ABSTRACT

Leber Congenital Amaurosis (LCA) is an early-onset genetic disease that causes severe vision loss beginning in childhood. This disease arises from biallelic mutations in genes that program photoreceptor function, the visual cycle, or phototransduction. Among more than 25 genes associated with LCA, *RPE65, CEP290,* and *GUCY2D* account for the largest number of LCA cases, which makes them more amenable to therapeutic development. To treat this disease, gene therapy treatments emerged as a promising solution because they target genetic mutations rather than just the symptoms, and currently include Luxturna as the only FDA-approved treatment. Beyond approved therapies, AAV and CRISPR-Cas9-based genomic editing strategies are being evaluated in clinical trials. This paper will analyze FDA-approved treatments such as Luxturna, as well as ongoing clinical trials aimed at achieving long-term efficacy, while highlighting that restorative potential might be limited by the amount of photoreceptors, genotype and age.

Keywords: Leber Congenital Amaurosis; gene therapy; AAV vector; *RPE65*; *CEP290*; *GUCY2D*; CRISPR-CAS9; Luxturna

INTRODUCTION

Leber Congenital Amaurosis affects approximately 2 to 3 per 100,000 newborns (1). LCA is considered a severe form of *Retinitis Pigmentosa*, which is a genetic condition that progressively damages the photoreceptor cells (rod and cone cells). Due to its autosomal recessive inheritance pattern, a child must inherit two faulty copies of the same gene from each parent (2). Although there are more than twenty-five identified gene mutations linked to LCA's development, *CEP290*, *GUCY2D*, and *CRB1* are the most common gene mutations associated with LCA (3). The *CEP290* gene supports protein transport within photoreceptor cells, *GUCY2D* helps reset these cells after light exposure, and *CRB1* maintains retinal structure and organization.

This review primarily focuses on gene therapy used to treat LCA, with a specific emphasis on RPE65, CEP290, and GUCY2D, as they are the most frequently affected genes and have the most advanced gene therapy pipeline. The objective is to identify current evidence on how mutations in these genes affect photoreceptor structure, the visual cycle, and how gene therapy treatments counteract these effects. This article reviews the clinical trials and current FDA-approved gene therapy treatments aimed at correcting these genetic defects and restoring photoreceptor function. The scope of this review includes molecular disease mechanisms, therapeutic strategies across viral and non-viral platforms, and clinical trial

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outcomes, while excluding non-gene-based treatments and genes without active clinical development.

PATHOPHYSIOLOGY AND ETIOLOGY

CEP290 Mechanisms and Impairments

Despite the discovery of more than 100 distinct *CEP290* mutations, no distinctive genotype-phenotype correlations have yet been identified (4). *CEP290* encodes a centrosomal protein that is essential for the formation and function of cilia. Normally, *CEP290* localizes the transition zone (TZ) and controls the movements in and out of the cilium. The deep intronic variant c.2991 + 1665A>G accounts for over half of *CEP290*-associated LCA cases and activates a cryptic exon, creating a premature stop codon that shortens *CEP290* (5). The mouse model *CEP290*^{rd16} closely replicated the human condition, with shorter cilia and abnormal photoreceptor morphology (6). Furthermore, research shows clinical variability, as some alleles permit residual exon skipping or modifier gene effects, resulting in milder or later-onset retinal dystrophies (7). Exon skipping bypasses specific exons during RNA splicing, creating a shortened but functional protein (8).

RPE65 Mechanisms and Impairments

Furthermore, one of the most well-studied pathways affected in LCA is the visual cycle. This molecular process regenerates 11-cis-retinal, the chromophore of rhodopsin (the protein for vision) and a crucial component of phototransduction. Mutations in the *RPE65* gene disrupt this cycle by eliminating or severely reducing the activity of the 65-kDa retinoid isomerase (RPE65), an enzyme essential for processing Vitamin A within the visual cycle. Without the RPE65 enzyme, the essential chromophore 11-cis-retinal cannot be regenerated, leaving photoreceptors unable to respond to light (9).

GUCY2D Mechanisms and Impairments

By generating cGMP (cyclic guanosine monophosphate) after light-inducing hydrolysis, *GUCY2D* produces retinal guanylate cyclase-1 (RetGC-1), an enzyme necessary for phototransduction recovery in rods and cones. Clinically, patients with *GUCY2D*-LCA have extinguished electroretinograms but largely intact retinal architecture, especially in rods, with anomalies in cone outer segments and foveal involvement (minor depression in the center of the retina), associated with visual impairments. In animal models of proof-of-principle gene therapy, RetGC-1 expression has been restored, cGMP levels have returned to normal, and photoreceptor function and survival have improved, leading to the initiation of further clinical trials (10).

Symptoms

Mutations in *RPE65*, *CEP290*, and *GUCY2D* are among the most common causes of LCA, and mutations in each gene are associated with distinct symptoms. *RPE65*, a less severe form of LCA, presents in infancy with severe nyctalopia (night blindness), nystagmus (involuntary, rapid eye movements), and reduced visual sharpness. In contrast, *CEP290* causes the most severe form of LCA symptoms, including little to no vision from birth, and non-detectable electroretinography (ERG) responses (7). *GUCY2D* also leads to infant blindness with reduced ERG response; however, patients often have well-preserved foveal function and may show mild light sensitivity rather than widespread retinal damage (11). All three genetic mutations result in visual impairment from infancy; nevertheless, the degree of retinal cell damage and symptoms vary depending on the affected gene.

GENE THERAPY TREATMENTS (Table 1)

CEP290 Gene Therapies

Laboratoires Théa QR-110 Trial

In 2017, Laboratoires Théa, in collaboration with Sepul Bio, began phase ½ of a study to determine how Sepofarsen (QR-110) could affect LCA in *CEP290* (12). QR-110 is an RNA antisense oligonucleotide administered by intravitreal injection to patients with LCA type 10 (LCA10). This type of LCA is caused by the deep-intronic *CEP290 c.2991 +1655A>G* mutation. Sepofarsen only worked on participants with the *CEP290 c.2991 +1655A>G* mutation, so it is entirely mutation-specific. All treated participants share the same deep-intronic IVS26 allele, but functional gains vary because the drug can only improve vision where enough photoreceptors remain capable of producing usable *CEP290* after splice correction (13).

Sepofarsen is injected directly into the vitreous humor of the eye. The injections were given at doses of 160 μg/80 μg or 320 μg/160 μg (loading/maintenance), typically at 3-month intervals over 12 months (13). Administration is performed in a clinical setting by an ophthalmologist, and patients are monitored closely for side effects such as cataracts and cystoid macular edema. 45% of patients gained at least 15 ETDRS letters, and

Table 1. Overview of Clinical Trials Investigating Gene Therapy Trials for LCA, specifically in CEP290, RPE65, and GUCY2D mutations.

Target Gene	Sponsor	Phase	Drug/Vector	Effects	Phase Status	Reference
CEP290	Laboratoires Théa	1/2	QR-110 (RNA-based oligonucleotides)	Some participants achieved clinically meaningful BCVA gains (≥15 ETDRS letters), but later-stage studies did not meet efficacy endpoints.	Completed	12, 13
	Editas Medicine Inc.	1/2	Edit-101 (CRISPR-Cas9)	At least 64% (9/14) showed improvement in ≥1 exploratory endpoint—BCVA, red-light FST sensitivity, mobility performance, or vision-related quality of life.	Paused	14, 15
RPE65	University College London	1/2	tgAAG76 (rAAV 2/2.hRPE65p. hRPE65)	Showed temporary retinal sensitivity gains peaking at 6-12 months, with a decline by year 3 and some mild inflammation and vision loss in a few patients.	Completed	16, 17, 18, 19, 20, 21
	Spark Therapeutics	1 1/2 3	Voretigene neparvovec-rzyl (AAV2-hRPE65v2)	After 1 year, 65% of treated patients (13 out of 20) in the study showed improvement on the Multi-Luminance Mobility test.	Completed	22, 23, 24
	Beacon Therapeutics	1/2	rAAV2-CBSB-hRPE65	At two years, 75% (9 of 12) of treated patients showed meaningful improvements in at least one vision measure.	Completed	25
	Nantes University Hospital	1/2	rAAV2/4.hRPE65	Published long-term safety/efficacy results of 9 patients; efficacy varied between patients.	Completed	26, 27
	MeiraGTx UK II Ltd	1/2	AAV2/5-OPTIRPE65	Showed meaningful and substantial vision improvements in all 11 treated children in clinical trials.	Completed	28
GUCY2D	Atsena Therapeutics Inc.	1/2	ATSN-101	The mean improvement was 20.3 dB, and 3 of 6 patients reached the maximum MLMT score, with no serious adverse effects.	Active, not recruiting	29, 30, 31, 32

treated eyes demonstrated a mean visual acuity of -0.55 logMAR (13). Performance on mobility courses and full-field stimulus testing also showed improvements. However, ten of 11 (90.9%) of treated eyes had mild to moderate side effects, the most common of which were cataracts, retinal degeneration, and cystoid macular edema (13).

Edit-101 Clinical Trial

In 2019, Editas Medicine began phase ½ of its research into how EDIT-101 could affect CEP290, a common cause of LCA (7, 14). It contains a smaller version of the Cas9 protein, called Staphylococcus aureus Cas9 (SaCas), which fits within the constrained space of the AAV type 5 viral vector used for delivery. Alongside SaCas9, two guide RNAs lead the enzyme to the exact spot in intron 26 of the CEP290 gene, where it produces a double-stranded DNA cut to remove the faulty sequence. This allows the DNA to be repaired by the cell's natural repair processes, restoring normal splicing and permitting the function of the CEP290 protein. Importantly, EDIT-101 is designed only for the

CEP290 intron 26 (IVS26) splicing defect and does not correct other types of mutations. EDIT-101 results appear to strongly correlate with retinal health, not mutation severity. 0 participants with relatively preserved baseline vision (≤ 1.4 logMAR) showed BCVA improvement, while 4/14 (29%) achieved a clinically meaningful ≥ 0.3 logMAR gain overall, indicating a ceiling effect in eyes with better starting vision (15).

EDIT-101 was administered to 2 participants in a low dose of 6×10^{11} vector genomes per mL, 5 participants in an intermediate dose of 1×10^{12} vg per mL, and 5 participants in a high dose of 3×10^{12} vg per mL. 11 out of 14 subjects (79%) showed improvements in at least one visual function metric, such as navigational skill or light sensitivity (15). Six of 12 (50%) patients who received intermediate or high doses showed improvements in 2 or more functional endpoints (15). EDIT-101 targets only the *CEP290* IVS26 splice defect, and clinical outcomes were not stratified by second-allele genotype. Nevertheless, mechanistically, a severe loss-of-function mutation on the non-edited allele could limit total *CEP290* protein restoration, potentially reducing therapeutic results (15).

RPE65 Gene Therapies

University College London and Moorfield Eye Hospital tgAAG76 Trial

In 2007, University College London collaborated with Moorfields Eye Hospital NHS Foundation Trust and Targeted Genetics Corporation to treat LCA using the AAV vector (16). The AAV vector is tgAAG76 (also called rAAV2/l2.hRPE65p.hRPE65). A functional copy of the human *RPE65* gene was delivered directly to the retinal pigment epithelial (RPE) cells via the recombinant AAV2 vector (rAAV2/2) tgAAG76. The human *RPE65* promoter (hRPE65p) in the vector ensures the gene is expressed only in appropriate target cells. It is delivered by subretinal injection to reach the gap between the retina and the RPE layer, and, as an AAV-based therapy, it is non-integrating, meaning it does not integrate into the host DNA. The disruption in the visual cycle that causes blindness in LCA2 (*RPE65-related*) was restored once tgAAG76 entered RPE cells, facilitating the synthesis of the *RPE65* enzyme (17).

The clinical response in early gene-replacement trials correlated more strongly with how much functional retina remained at the time of therapy rather than a specific mutation class. Patients with more preserved photoreceptors showed greater and longer-lasting improvements than those treated at more advanced stages (18). Patients with an Ellipsoid Zone (EZ) width of less than 637 μm showed little functional recovery, while those above 1,000 μm showed the strongest functional recovery with a mean sensitivity increase of 1.96 dB (19). At the one-year mark, 47.6% of the patient population with adequate baseline photoreceptor integrity showed functional recovery as measured by a sensitivity increase of at least 7 dB in five points in the retinal locus (20). The functional recovery was also strictly localized around the surgical bleb, with some patients showing a visual volume increase of up to 33.8% while those with more severe baseline photoreceptor damage showed no recovery (20).

12 participants were studied over the course of 3 years, and 4 participants received a lower dose of the vector, while 8 received a higher dose of the vector (18). Six patients showed improvements in retinal sensitivity for up to 3 years, with the improvements peaking 6 to 12 months after therapy and subsequently decreasing (21). Using ERG, no improvement in retinal function was observed (19). Two subjects experienced a decline in visual acuity, while 3 participants experienced intraocular inflammation (inflammation in the eye) (21). Each subject exhibited a different reduction in central retinal thickness. A parallel study was also conducted in dogs to investigate visual function and ERG responses. In dogs, lower doses of the gene therapy using the same vector enhanced optically guided behavior, but only higher doses produced retinal function benefits measurable by ERG (21).

Luxturna Clinical Treatment

In December 2017, voretigene neparvovec-rzyl (Luxturna) was approved by the FDA, marking the first gene therapy approved for LCA. Luxturna is a gene therapy used to treat LCA caused by the *RPE65* gene. Using a safe AAV vector, the treatment introduces a functional copy of the *RPE65* gene directly into retinal cells. Luxturna is injected subretinally, targeting where photoreceptors are most affected. Once inside the RPE cells, the newly delivered RPE65 gene begins producing functional protein, allowing visual pigments to regenerate (22).

Luxturna should be administered to each eye on separate days, at least 6 days apart, with each dosage for each eye containing 1.5×10^{11} vector genomes and a total volume of 0.3 mL (22). After a year, 65% of patients treated (13 out of 20) in the Luxturna Phase 3 clinical study demonstrated an improvement of at least 2 light levels in the Multi-Luminance Mobility Test (MLMT)

(23). In comparison, just 10% (2 out of 9) of the control group did the same (23). Luxturna is indicated only for patients with confirmed biallelic *RPE65* mutations who retain viable retinal cells. Structural follow-up work supports that long-term benefit is most likely in retinal regions with relatively preserved structure, showing why disease stage is so crucial (24). Phase 2 and long-term follow-up data indicate that patients with better preserved retinal structure, with posterior pole thickness greater than 100 μm and higher photoreceptor density, demonstrate much larger, longer-lasting gains in vision (23). However, participants with more progressed photoreceptor loss typically exhibit little improvement or only slowed disease progression (23). Additionally, the most frequent adverse reactions of Luxturna occur in 5% or more of patients, including conjunctival redness, cataracts, increased pressure inside the eye, retinal tears, corneal thinning, macular holes, subretinal deposit, inflammation of the eye, eye irritation, eye pain, and maculopathy (wrinkling of the macula's surface) (24).

Beacon Therapeutics rAAV2-CB-hRPE65 Trial

In 2009, Beacon Therapeutics collaborated with Oregon Health and Science University and the University of Massachusetts, Worcester, using the rAAV2-CB-hRPE65 AAV gene vector. rAAV2-CB-hRPE65 uses a recombinant AAV2 vector to deliver a functional copy of the human *RPE65* gene to the RPE cells. Targeting the area between the retina and RPE, the therapy is delivered by subretinal injection, enabling the vector to convert the desired cells without integrating into the genome. 6 out of 12 subjects in the clinical trial had increased retinal sensitivity, with some gains lasting up to 3 years (25). Usually, these changes peaked between 6 to 12 months after therapy; however, there was variable improvement in visual acuity and no discernible increase in ERG responses (25). 3 patients experienced intraocular inflammation as a side effect, and 2 experienced clinically severe vision loss (25). Younger patients consistently showed better outcomes because they had higher photoreceptor density, with some pediatric participants gaining seven or more ETDRS letters and maintaining improved light sensitivity for up to five years (25). Overall, the results indicate that although the therapy corrects the underlying genetic defect in *RPE65*, it cannot restore visual function once photoreceptor cells have already been lost (25).

Nantes University Hospital rAAV2/4 Trial

In 2011, Nantes University Hospital created an rAAV2/4.The hRPE65 vector is intended to deliver a healthy copy of the human *RPE65* gene directly to RPE cells. The vector is delivered via a single subretinal injection following vitrectomy (removal of the vitreous gel from the middle of the eye). One eye was treated for nine individuals with *RPE65*-associated LCA, ages 6 to 50. The trial record indicates that there were no significant safety concerns and that the therapy was well tolerated (26). Using a distinct AAV4 serotype to target the retinal pigment epithelium specifically, the rAAV2/4-hRPE65 at Nantes University Hospital improved the patient's mean visual acuity by 5.8 ETDRS letters (27). Functional gains were only achievable in retinal regions that still had an Outer Nuclear Layer visible on OCT scans. All patients maintained good safety profiles over a 3.5-year period, but those with more preserved photoreceptor density at baseline showed the greatest stabilization of their visual fields and decreases in nystagmus, according to long-term results (27).

MeiraGTx AAV2/5-OPTIRPE65 Trial

In 2016, MeiraGTx UK 2 Ltd monitored patients who previously received AAV2/5-OPTIRPE65 gene therapy for *RPE65-LCA-associated* conditions. The trial's primary purpose was to examine the long-term safety with subsequent evaluations of visual function durability. No results or adverse effects have been reported, which could mean the trial has not yet been completed (28). In order to overcome the high *RPE65* protein demand in human eyes, MeiraGTx and researchers from University College London used a second-generation vector designed to be 300 times more potent than original versions (28). Clinical findings demonstrate that improvements in functional vision were solely dependent on the state of the retinal at baseline, with a visible Outer Nuclear Layer on SD-OCT scans being necessary for significant improvements in light sensitivity (28). The degree of success was largely dictated by the severity of the disease, with younger patients displaying the strongest and longest-lasting response profiles, even though the treatment safely supplied protein across a variety of *RPE65* mutations (28).

***GUCY2D* Gene Therapies**

In 2019, Atsena Therapeutics Inc. initiated phase 1 clinical trials of the AAV5 vector ATSN-101 for LCA caused by *GUCY2D* mutations (29). ATSN-101 is based on AAV5 and carries human *GUCY2D* cDNA, which is regulated by the human rhodopsin kinase (hGRK1) promoter. The treatment consisted of a normal three-

port pars plana (surgical procedure) vitrectomy followed by a subretinal injection of ATSN-101 into the macula of the eye (30). 91% of side effects relating to ATSN-101 were categorized as mild and 9% as moderate, but there were no significant adverse effects found (31). The high dose resulted in a 100-fold increase in retinal sensitivity measured by the dark-adapted full-field stimulus testing (FST), with two patients experiencing over 40 dB (decibel) enhancement (31). After 12 months of treatment, high-dose participants improved their visual acuity by around -0.16 logMAR. In the MLMT, 3 out of 6 high-dose participants obtained the maximum score of 6 by the 12th month (31). Although all participants carried *GUCY2D*-associated LCA, treatment response varied across individuals. The stronger improvements observed in the high-dose group suggest that retinal status and dose contribute to the extent of visual recovery (31). There is a "structural therapeutic window", where patients with advanced atrophy mainly experience disease stabilization, while those with higher baseline cell density, such as an EZ width exceeding 1,000 μm achieve robust vision restoration. Therefore, the presence of viable photoreceptor cells is crucial (32).

Comparing AAV Vectors and CRISPR for LCA

AAV Vector Approaches

AAV vectors and CRISPR-Cas9 are some of the most popular methods for gene therapy. Referencing Table 1, 6/8 (75%) of the vectors in the clinical trials were AAV, while 1 of the 8 (12.5%) was delivered by an AAV but was a CRISPR-Cas9 vector. AAV vectors deliver a functional copy of the defective gene to retinal cells without altering the patient's DNA. AAV vectors are particularly advantageous for gene therapy due to their non-pathogenic nature, low toxicity, high transduction efficiency, and ability to deliver genetic material to both dividing and non-dividing cells (33). Subretinal AAV delivery is technically mature and reliably targets photoreceptors and RPE cells with high transduction efficiency. The confined subretinal space allows controlled vector to spread, reducing off-target exposure and systemic leakage. Surgical delivery is well-tolerated, and modern microinjection systems minimize retinal trauma (34). AAV serotypes such as AAV2, AAV5, and AAV8 demonstrate strong tropism for retinal tissue, further enhancing delivery success. Overall, AAV deliverability in the retina is considered one of the most predictable and clinically feasible gene-delivery methods available.

However, it is constrained by its ~4.7 kB (kilobase) cargo capacity, which is relatively smaller than many other types of vector cargo capacity (35). This limited cargo capacity can be problematic for LCA-associated genes such as *CEP290,* which exceed the natural AAV capacity and therefore cannot be delivered using a standard AAV construct. This limitation can be bypassed by oversized or dual AAV vectors. However, for oversized AAV vectors, their genome is often packed as truncated fragments that reassemble, resulting in a larger cargo capacity; however, transduction efficiency drops, and consistency is poor (36). Dual AAV vectors split one large expression into two halves, reassemble into a full-length gene in the same cell, but this gives lower expression efficiency and requires higher doses and more complex manufacturing (37).

Another drawback of AAV is that there exists a risk for an immune response (especially the development of neutralizing antibodies) that would decrease efficiency and possibly limit the ability to re-administer a treatment. Although the eye is partly immune-privileged, even low-level anti-AAV immunity can reduce photoreceptor transduction, and most patients cannot receive a second dose because capsid antibodies persist long-term. Additionally, AAV gene supplementation is not always permanent because episomal DNA will eventually degrade, raising long-term durability concerns in patients with chronic conditions such as Leber Congenital Amaurosis (LCA) (35). Although retinal cells are post-mitotic, AAV-mediated gene expression may decline over time due to progressive photoreceptor degeneration, immune-mediated clearance, or epigenetic silencing rather than episomal dilution (38).

CRISPR-Based Gene Editing

CRISPR-Cas9 typically requires a vector to deliver CRISPR into the cell for genomic editing. For the Editas Medicine clinical trial in Table 1, the SaCas enzyme had a cargo capacity of ~4.2 kB because it was specifically designed to fit within the AAV vector (39). Due to the fact that CRISPR-Cas9 requires another vector for gene editing, its cargo capacity can vary. CRISPR-based approaches target and repair mutations, offering potential permanent correction without size restrictions, and can address larger mutations such as *CEP290* because the size of their target gene does not restrict them (39). CRISPR can correct larger mutations but faces safety challenges, including off-target effects (40).

Additionally, Editas Medicine paused the development of the EDIT-101 clinical program due to efficacy shown

only in patients with LCA10 homozygous for the IVS26 mutation, which represents only a small proportion of LCA cases (41). Permanent correction is provided by CRISPR edits and therefore offers durable correction if successful; however, the main obstacle to delivering CRISPR is the difficulty in having Cas proteins and guide RNAs effectively delivered into retinal cells while minimizing or avoiding immune responses (42). Clinical feasibility of using CRISPR to treat LCA is still at an early stage when compared to AAV, and although it has the possibility of overcoming AAV's capacity constraints and providing a lasting cure, this represents a novel and innovative approach being actively researched (43).

The delivery of the Cas9 enzyme is hindered by pre-existing immunity in humans, which is derived from bacterial species such as *Streptococcus pyogenes* and *Staphylococcus aureus*, when using CRISPR. This means that some patients will have a strong inflammatory response against the nuclease, essentially ruining the therapy before the editing can be done effectively (44). The only CRISPR-based LCA clinical trial, the EDIT-101 trial, has been temporarily paused, so the long-term effects of CRISPR on LCA are vague (18). From a theoretical perspective, one of the main benefits of CRISPR is that it can circumvent the limitation of space in AAV vectors and potentially make permanent genome modifications, although these ideas remain unproven in practical applications (45).

CONCLUSION

Overall, the FDA-approved and clinical trial gene therapy treatments for LCA are a significant step forward for treating Leber Congenital Amaurosis. Clinical trial studies have established the effectiveness of AAV-mediated gene therapy in visual acuity, retinal sensitivity, and the MLMT test. CRISPR-based strategies, although newer, show potential for direct gene correction in humans and can bypass the limited cargo capacity of AAV vectors for larger genes such as *CEP290*. However, substantial gaps remain in current research. A large number of LCA-associated genes, such as *AIPL1*, *RDH12*, *CRX*, and *IMPDH1*, among others, lack advanced therapeutic programs, and the majority of existing trials focus narrowly on only a few genes.

As research advances, continued improvement of gene therapy strategies, editing precision, and long-term durability is expected to improve the clinical applicability of gene-based therapies for LCA. Collectively, the insights gained from the FDA-approved treatments and clinical trials are aimed at achieving more incremental and variable restoration for individuals with LCA.

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CONFLICT OF INTEREST

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