
CLINICAL TRIALS
at the
SUMMIT
CLINICAL TRIALS AT THE SUMMIT 2026
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OPUS GENETICS®

A Paradigm for Guiding Treatment Decisions in BEST1 AAV Gene Therapy

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Disclosures and Forward-Looking Statements

Certain statements contained in this presentation are not statements of historical fact and are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements give current expectations or forecasts of future events or our future financial or operating performance. Such statements include, but are not limited to, statements concerning our data from and future enrollment for our clinical trials, our pipeline of additional indications and anticipated regulatory milestones.

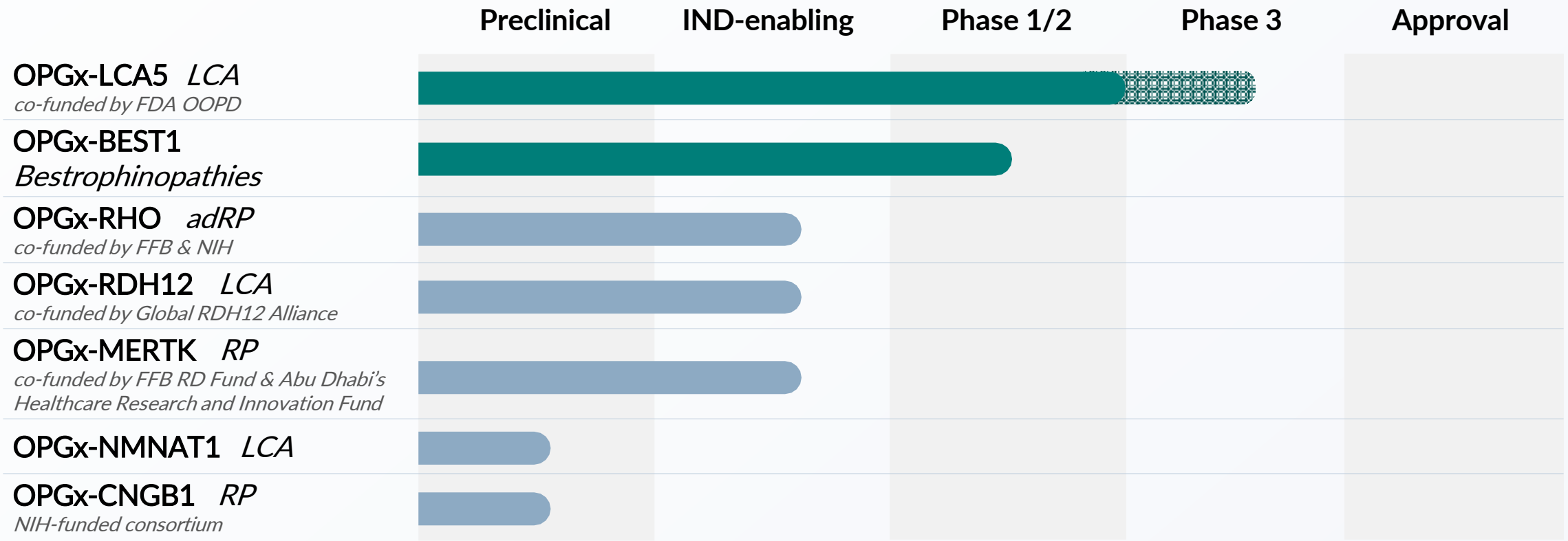
In some cases, you can identify forward-looking statements by the following words: “aim,” “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “ongoing,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” or the negative of those terms, and similar expressions that convey uncertainty of future events or outcomes to identify these forward-looking statements.

These forward-looking statements reflect our management’s beliefs and views with respect to future events, are based on estimates and assumptions as of the date of this presentation and are subject to risks and uncertainties, many of which are beyond our control, that could cause our actual results to differ materially from those in these forward-looking statements, including, without limitation: our gene therapy product candidates are based on a novel technology and manufactured by a third party, which may result in delays and difficulties in obtaining regulatory approval; our planned clinical trials may face substantial delays, result in failure, or provide inconclusive or adverse results that may not satisfy U.S. Food and Drug Administration (“FDA”) requirements to further develop our therapeutic products; delays or difficulties associated with patient enrollment in clinical trials may affect our ability to conduct and complete those clinical trials and obtain necessary regulatory approvals; changes in regulatory requirements could result in increased costs or delays in development timelines; we depend heavily on the success of our product pipeline; if we fail to find strategic partners or fail to adequately develop or commercialize our pipeline products, our business will be materially harmed; others may discover, develop, or commercialize products similar to those in our pipeline before or more successfully than we do or develop generic variants of our products even while our product patents remain active, thereby reducing our market share and potential revenue from product sales; we do not currently have any sales or marketing infrastructure in place and we have limited drug research and discovery capabilities; the future commercial success of our products could significantly depend upon several uncertain factors, including third-party reimbursement practices and the existence of competitors with similar products; product liability lawsuits against us or our suppliers or manufacturers could cause us to incur substantial liabilities and could limit commercialization of any product candidate that we may develop; failure to comply with health and safety laws and regulations could lead to material fines; we have not generated significant revenue from sales of any products and expect to incur losses for the foreseeable future; our future viability is difficult to assess due to our short operating history and our future need for substantial additional capital, access to which could be limited by any adverse developments that affect the financial markets; raising additional capital may cause our stockholders to be diluted, among other adverse effects; instability and operational disruptions at government agencies, such as the FDA, may adversely impact our development and commercialization plans by causing delays and requiring the use of additional, unforeseen resources to obtain regulatory approval for trials or products in our pipeline; we operate in a highly regulated industry and face many challenges adapting to sudden changes in legislative reform or the regulatory environment, including due to government shutdowns and disruptions at government agencies, which cause delays, requires the use of additional, unforeseen resources, affects our pipeline stability, and could impair our ability to compete in international markets; we may not receive regulatory approval to market our developed product candidates within or outside of the U.S.; with respect to any of our product candidates that receive marketing approval, we may be subject to substantial penalties if we fail to comply with applicable regulatory requirements; our potential relationships with healthcare providers and third-party payors will be subject to certain healthcare laws and regulations, which could expose us to extensive potential liabilities; we rely on third parties for material aspects of our business, such as conducting our nonclinical and clinical trials and supplying and manufacturing bulk drug substances, which exposes us to certain risks; we may be unsuccessful in entering into or maintaining licensing arrangements or establishing strategic alliances on favorable terms, which could harm our business; inadequate patent protection for our product candidates may result in our competitors developing similar or identical products or technology, which would adversely affect our ability to successfully commercialize; we may be unable to obtain full protection for our intellectual property rights under U.S. or foreign laws; we may become involved in lawsuits for a variety of reasons associated with our intellectual property rights, including alleged infringement suits initiated by third parties; we are dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy; as we grow, we may not be able to operate internationally or adequately develop and expand our sales, marketing, distribution, and other corporate functions, which could disrupt our operations; the market price of our common stock is expected to be volatile and if we fail to comply with the continued listing standards of Nasdaq, our common stock may be delisted; and factors out of our control related to our securities, such as securities litigation or actions of activist stockholders, could adversely affect our business and stock price and cause us to incur significant expenses.

We discuss many of these risks in greater detail under Part I, Item 1A “Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2025 and in subsequent reports filed with or furnished to the Securities and Exchange Commission. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

Any forward-looking statement in this presentation speaks only as of the date hereof or as of the date specified herein. We undertake no obligation to publicly update any forward-looking statement, whether as a result of new information, future developments or otherwise, except as may be required by applicable laws or regulations.

Building a Differentiated Pipeline

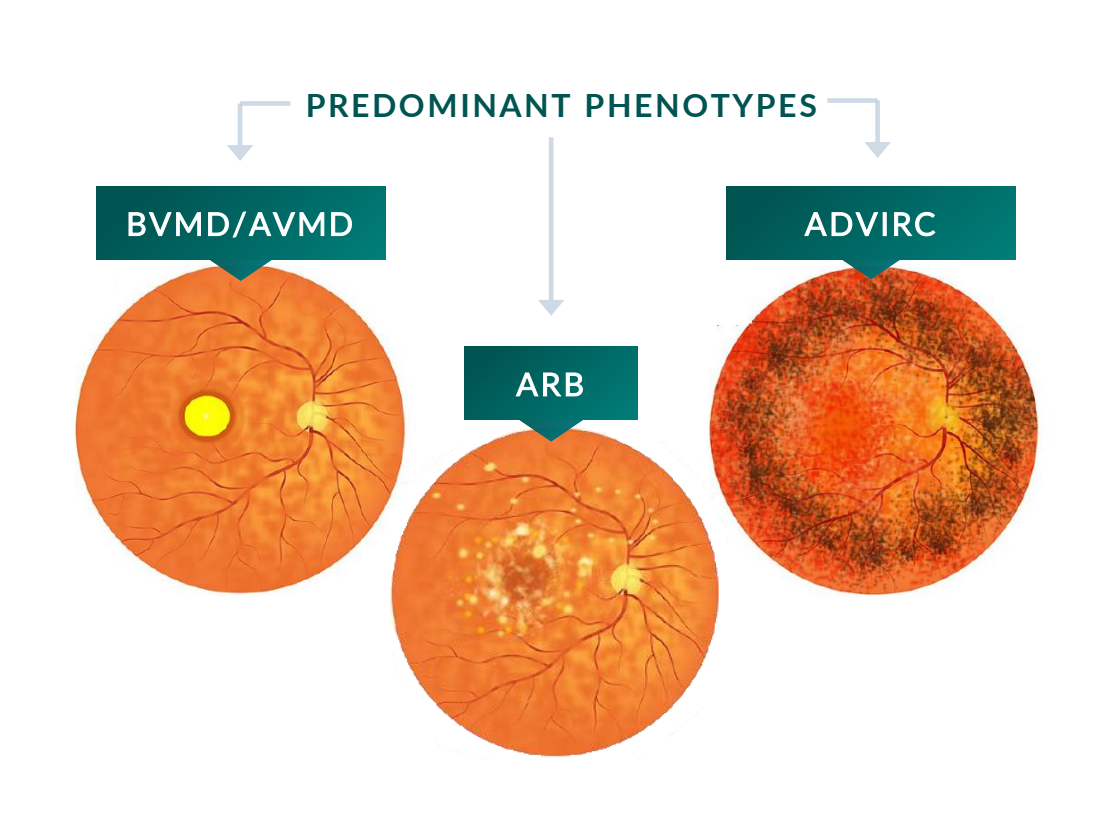


Opus Genetics owns worldwide rights to all gene therapy programs.

adRP, autosomal dominant retinitis pigmentosa; BEST1, bestrophin 1; CNGB1, cyclic nucleotide-gated channel β1; FDA OOPD, Food and Drug Administration Office of Orphan Products Development; FFB, Foundation Fighting Blindness; LCA5, Leber congenital amaurosis 5; NIH, National Institutes of Health; RD, retinal degeneration; RDH12, retinol dehydrogenase 12; RHO, rhodopsin; RP, retinitis pigmentosa; MERTK, MER proto-oncogene tyrosine kinase; NMNAT1, nicotinamide mononucleotide adenylyltransferase.

BEST1 IRDs (Bestrophinopathies): Phenotypic Diversity

- **Bestrophinopathies vary in inheritance pattern, clinical appearance, and molecular disease mechanisms**
  - Predominant phenotypes include autosomal dominant BVMD, AVMD, and ADVIRC, and autosomal recessive ARB
  - Clinical spectrum can include serous retinal detachment, macular vitelliform lesions, macular atrophy, CNV, and central vision loss
- **Two most common phenotypes**
  - **Autosomal dominant BVMD**: Prevalence = 1:5000 to 1:69,200; juvenile-onset macular dystrophy with characteristic ‘egg yolk’-like lesion
  - **Autosomal recessive ARB:** Prevalence = 1:1,000,000; more severe than BVMD, multifocal degeneration beginning in childhood

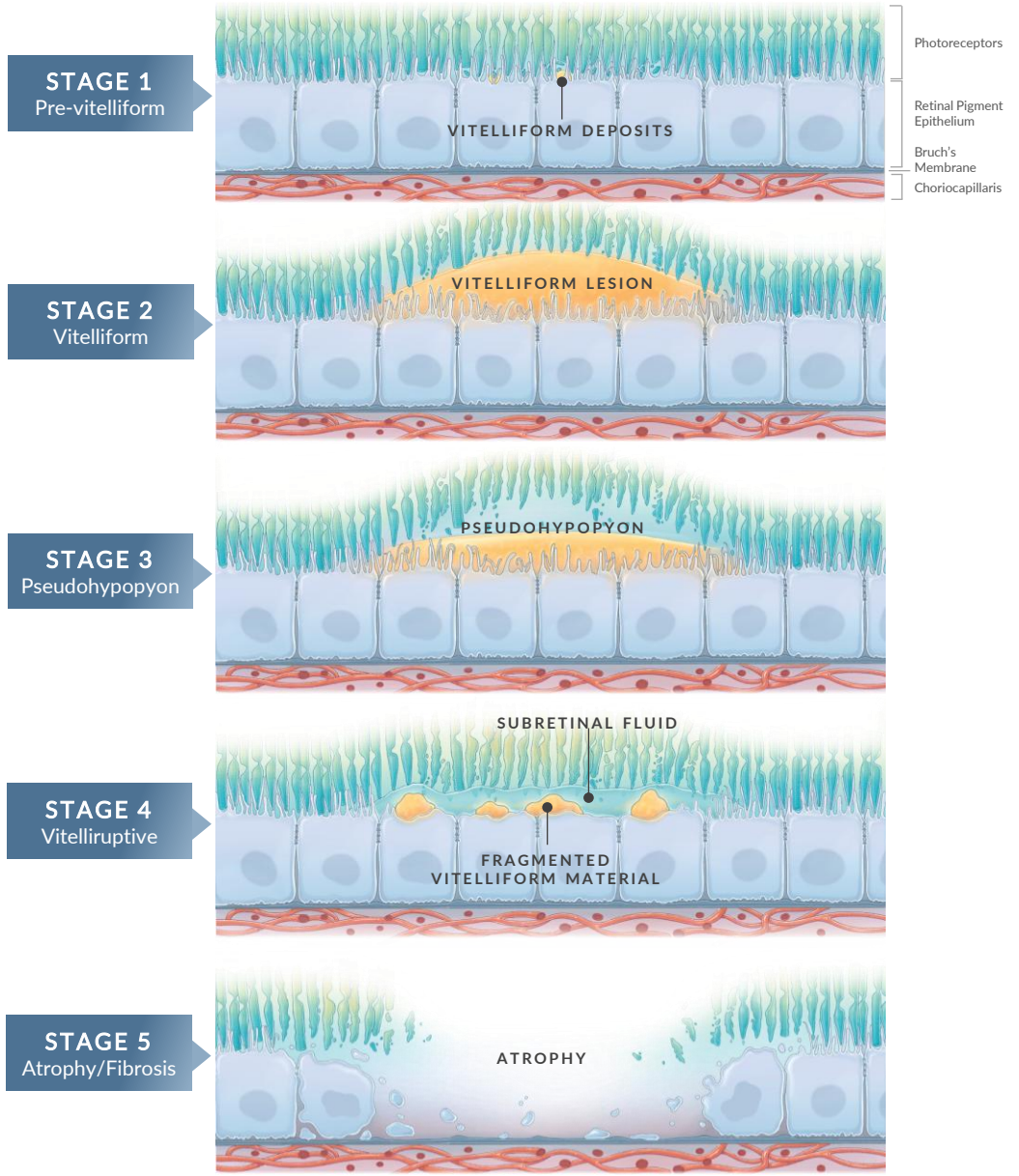


BEST1, bestrophin 1 gene; IRD, inherited retinal disease; BVMD, Best vitelliform macular dystrophy; AVMD, adult-onset vitelliform macular dystrophy; ADVIRC, autosomal dominant vitreoretinochoroidopathy; ARB, autosomal recessive bestrophinopathy; CNV, choroidal neovascularization; BCVA, best-corrected visual acuity

1. Grewal SS, et al. *Ther Adv Ophthalmol.* 2021;13:1-16. 2. MacDonald IM, et al. GeneReviews [Internet]. Updated 2020. University of Washington. 3. Laich Y, et al. *Ophthalmol Retina*. 2025;9(9):899-907.

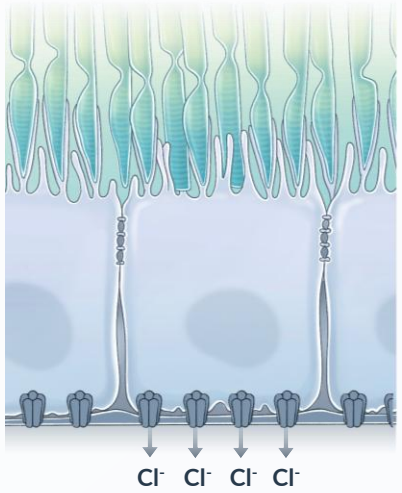
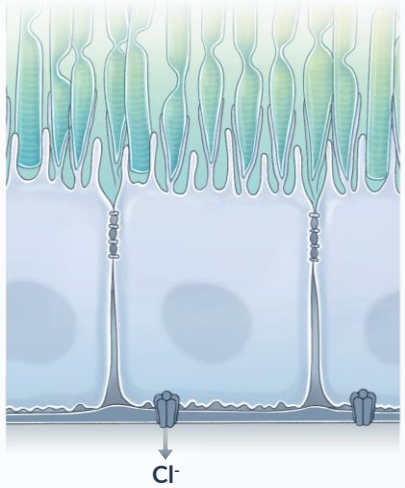
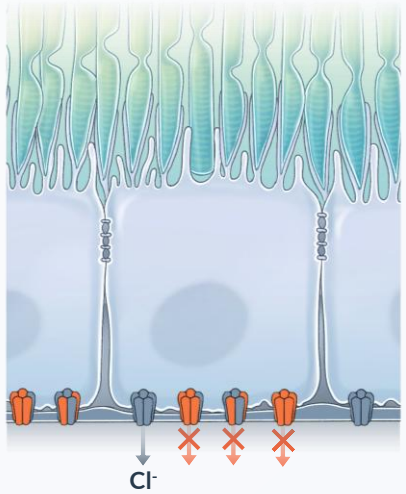
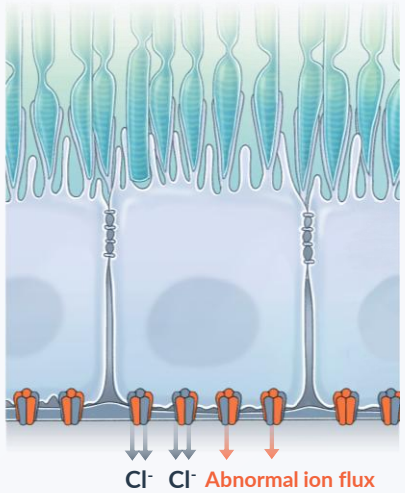
BEST1 Disease Biology

- **BEST1 gene encodes for bestrophin-1**, a homopentameric (i.e. 5 identical monomers) Ca^{2+}-activated chloride channel required for RPE maintenance and retinal physiology
- **BEST1 mutations disrupt cellular ion and fluid homeostasis** resulting in electrophysiological abnormalities, RPE dysfunction, and retinal degeneration via:
  - **Fluid accumulation** in subretinal space (detachment risk)
  - Defective **clearance of toxic waste** products (eg, lipid deposits)
  - **Impaired RPE-photoreceptor interactions** (eg, defective phagocytosis)



BEST1, bestrophin 1; RPE, retinal pigment epithelium
Guziewicz KE, et al. *Prog Retin Eye Res.* 2017;58:70-88.

Pathogenic Mechanisms of BEST1 Variants

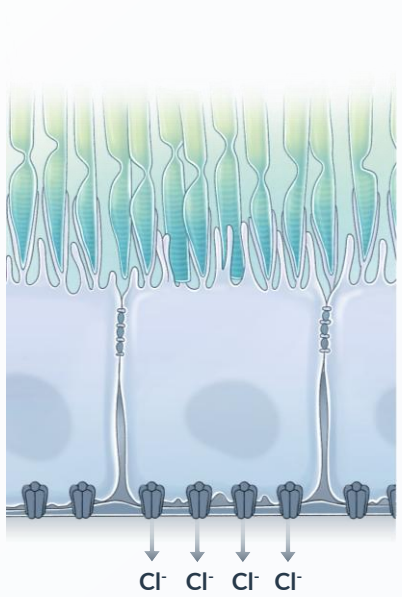
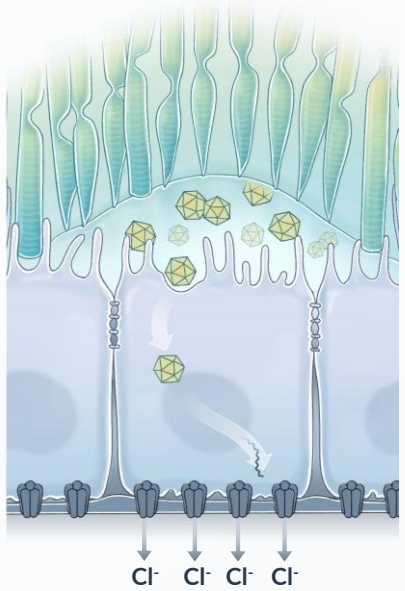
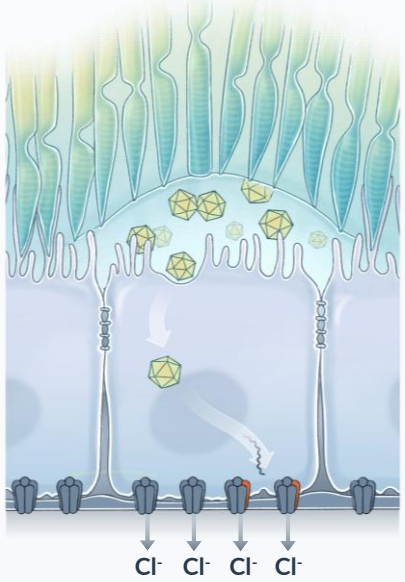
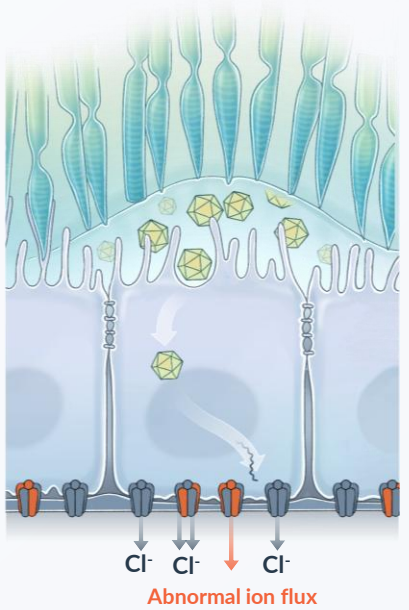
NORMAL	RECESSIVE	DOMINANT NEGATIVE	
	LOSS-OF-FUNCTION	LOSS-OF-FUNCTION	GAIN-OF-FUNCTION
			
Normal *BEST1*	**↓Reduced protein expression, trafficking, or channel activity** E.g., *BEST1* variants in ARB	**Mutant protein inhibits normal protein function** E.g., *BEST1* variants in BVMD	**Mutant protein increases protein activity or introduces new function** E.g., *BEST1* variants in ADVIRC (<2% of population, very rare)

Normal monomer

Mutant monomer

BEST1, bestrophin 1 gene; ARB, autosomal recessive bestrophinopathy; BVMD, Best vitelliform macular dystrophy; ADVIRC, autosomal dominant vitreoretinochoroidopathy.
Haldrup SB, et al. *Int J Mol Sci.* 2025;26(19).

Most BEST1 Variants May be Amenable to Gene Augmentation

NORMAL	RECESSIVE	DOMINANT NEGATIVE	
	LOSS-OF-FUNCTION	LOSS-OF-FUNCTION	GAIN-OF-FUNCTION
			
Normal *BEST1*	**Introduction of functional *BEST1* restores normal function** E.g., ARB	**Increasing functional *BEST1* expression *may* overcome mutant protein's dominant-negative effect** E.g., BVMD	Increasing functional *BEST1* does **not** overcome mutant protein function; **may require gene editing** E.g., ADVIRC

Normal monomer

Mutant monomer

BEST1, bestrophin 1 gene; ARB, autosomal recessive bestrophinopathy; BVMD, Best vitelliform macular dystrophy; ADVIRC, autosomal dominant vitreoretinochoroidopathy.

Haldrup SB, et al. *Int J Mol Sci.* 2025;26(19).

The Opus Genetics Paradigm for Guiding Treatment Decisions

Clinical Diagnosis

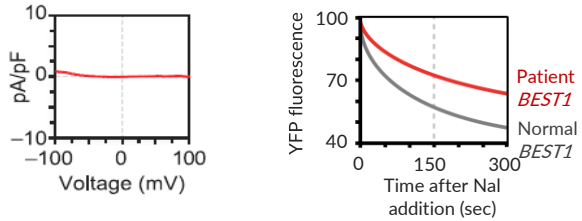
Genetic Testing to Identify *BEST1* Variant

‘Disease-in-a-dish’ Model

***In vitro* engineering of cell line with patient-specific *BEST1* mutation**

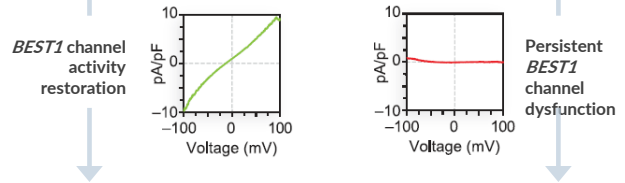
Functional Validation

Measure *BEST1* channel function via two assays



Treatment-Response Assessment*

Gene Augmentation



Clinician Recommendation

Potential responder	Potential non-responder
✓ Eligible for gene augmentation	✕ Not eligible for gene augmentation

*Treatment response assessment conducted on select mutations.
BEST1, bestrophin 1 gene; pA/pF, picoamperes per picofarad; YFP, yellow fluorescent protein; NaI, sodium iodide.
Sinha D, et al. *Am J Hum Genet.* 2020;107(2):278-292.

Functional Characterization of *BEST1* Disease-Associated Variants

Opus will map all *BEST1* mutations (prior to pivotal trial) to evaluate their amenability to gene augmentation

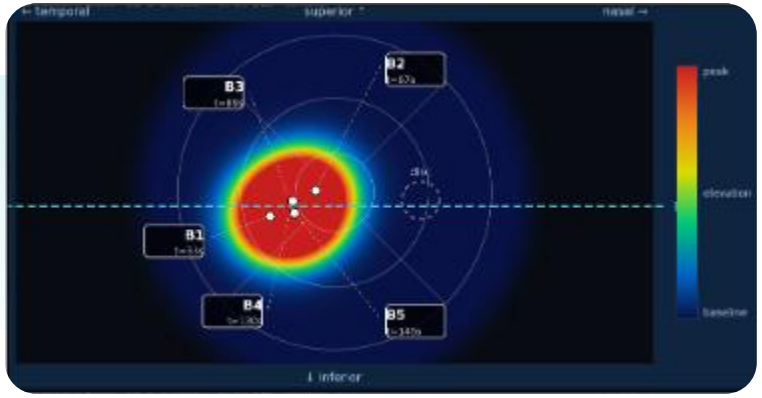
BEST1 VARIANT	BVMD/ARB	FUNCTIONAL EFFECT
Ala195Val	ARB	LOF
Glu300Asp	BVMD	LOF
Thr307Ile	BVMD	LOF
Ala243Val	BVMD	LOF
Arg92Cys	BVMD	LOF
Glu119Gln	BVMD	Similar to WT
Phe80Leu	BVMD	GOF
Leu140Val	BVMD	LOF
Arg141His	BVMD	LOF
Arg218His	BVMD	LOF
Leu37Pr0	BVMD	LOF
Arg130Ser	BVMD	LOF

BEST1, bestrophin 1 gene; BVMD, Best vitelliform macular dystrophy; ARB, autosomal recessive bestrophinopathy; LOF, loss-of-function mutation; GOF, gain-of-function mutation; WT, wild type.

Extending Our Partnership into the Surgical Suite

- **Proven subretinal delivery with established safety profile and clinical precedent**
- **How Opus Genetics partners with surgeons:**
  - **Where** to inject: En-face thickness map derived from productive blebs registered from operative video
  - **How much** to inject: Subretinal delivered volume = total injected volume – vitreous reflux*

SPATIAL AND TEMPORAL DELIVERY TOPOLOGY



VOLUMETRIC DOSING REPORT

*Total injected volume recorded at syringe and vitreous reflux quantified from optical signature in operative video.

Summary

BEST1 mutations challenging to treat due to poor genotype-phenotype correlation

- However, disease is slowly progressive, providing wide therapeutic window
- Most mutations are amenable to *BEST1* gene augmentation

Opus Genetics has a unique precision medicine platform using a cell screening approach

- Creating atlas of mutations to identify responders and non-responders
- Partnership into the surgical suite to guide where and how much to inject

Thank you!