OPUS GENETICS

Gene therapies focused on patients with rare inherited retinal diseases (IRDs)

Advanced pipeline built by & for patients

4Q2022

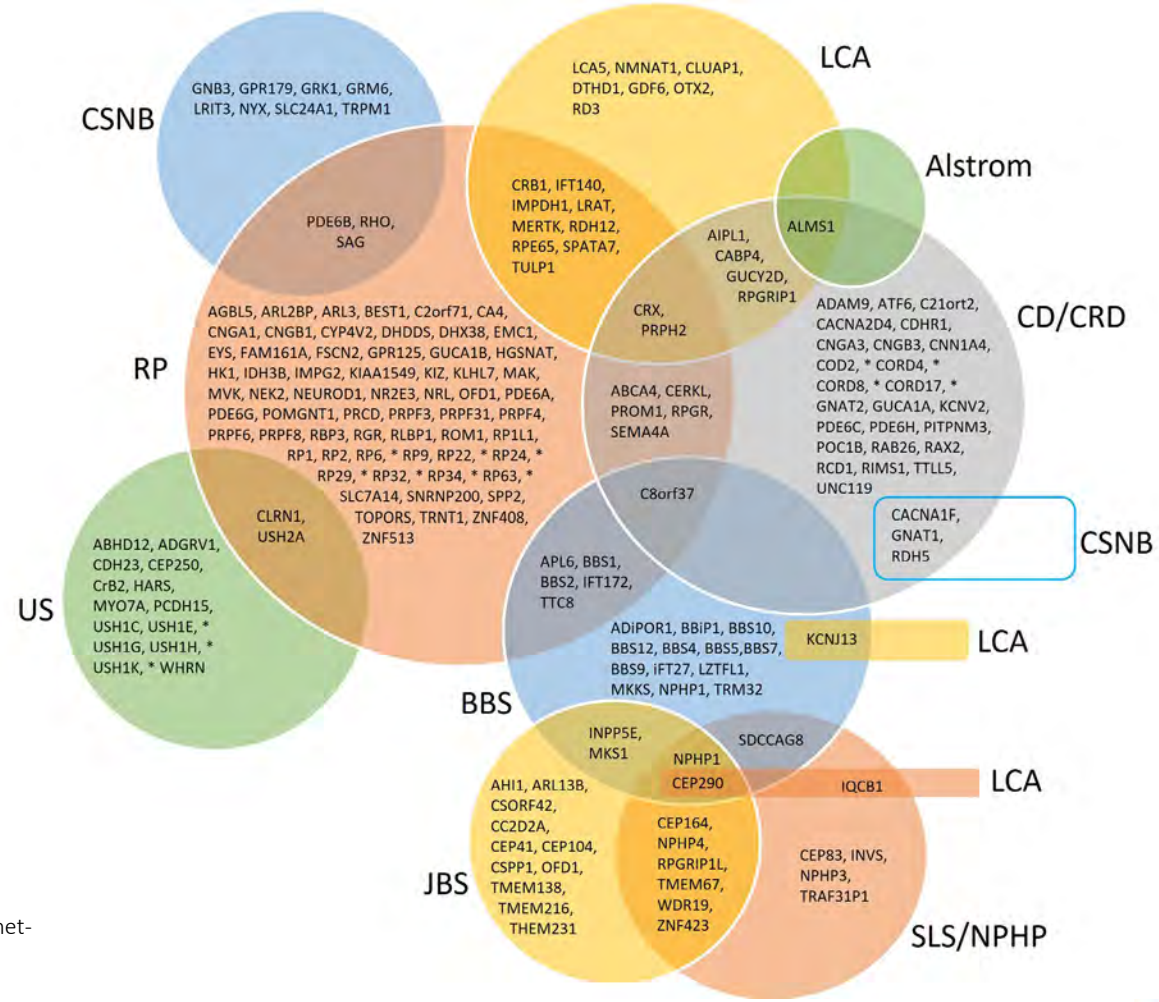
The Opus Approach: Fast and Efficient Retinal Gene Therapies

- Capitalize on key learnings from LUXTURNA
  - Dose, route of administration, immunosuppression protocols, timing of contralateral eye dose, functional vision endpoints, clinical designs
- Fit for use, not over engineered
  - Current AAV capsids delivered to the subretinal space is a tried and true method to get safe, effective, and durable gene transduction in the retina
- Manufacture using modern methods at a scale that makes sense
  - Low volume, high quality material

Jean Bennett, MD, PhD
F.M. Kirby Professor of Ophthalmology
University of Pennsylvania
Co-founder and Board Member, Opus Genetics

Business Model with Large Potential

- IRDs account for up to 20% of all blindness in individuals 16-64[(1)]
- 280+ genes to date have been associated with IRDs[(1)(2)]
- Estimates as high as 430,000 patients in the US alone[(3)]
- Estimated 5.5 million affected worldwide[(4)]



Source: EyeNet. https://www.aao.org/Assets/bebfbaef-a092-45b0-9883-c563331546ae/636649294795430000/july-2018-eyenet-supplement-pdf?inline=1.

(1) Shughoury et al, Intl Ophtha Clinics 2021 doi: 10.1097/IIO.0000000000000377
(2) RetNet; University of Texas Houston https://sph.uth.edu/retnet/
(3) Gong et al, Clin Ophth 2021
(4) Hanany et al, PNAS 2020 www.pnas.org/cgi/doi/10.1073/pnas.1913179117

Opus Genetics at a Glance: Today

Overview	• Team of 19 with plans to grow modestly upon reaching R&D milestones • Extensive network of experienced consultants • Offices and labs at Alexandria Launch Labs at 8 Davis Drive in Research Triangle Park
Major Collaborators	• Founders: Penn (Dr. Jean Bennett, Junwei Sun); Harvard (Dr. Eric Pierce) • Foundation Fighting Blindness • National Resilience, ThermoFisher, Dark Horse Consulting
Funding to Date	• $19 million seed financing • Led by RD Fund; participation from Manning Family Foundation and BIOS Partners • Seed funding through early 2023 gets first program in the clinic and builds company

Opus Initial Pipeline

Genetic Target	Research/ Pre-Clin	IND Enabling	Phase 1/2	Phase 2/3	Delivery(1)	Prevalence US, Est (2)	Key Milestones
LCA5	**OPGx-001**				AAV8 PR	~200	• IND late 2022
RDH12	**OPGx-002**				AAV8 PR	~1,100	• IND early 2024
NMNAT1	**OPGx-003**				AAV9 PR	~750	• IND late 2025

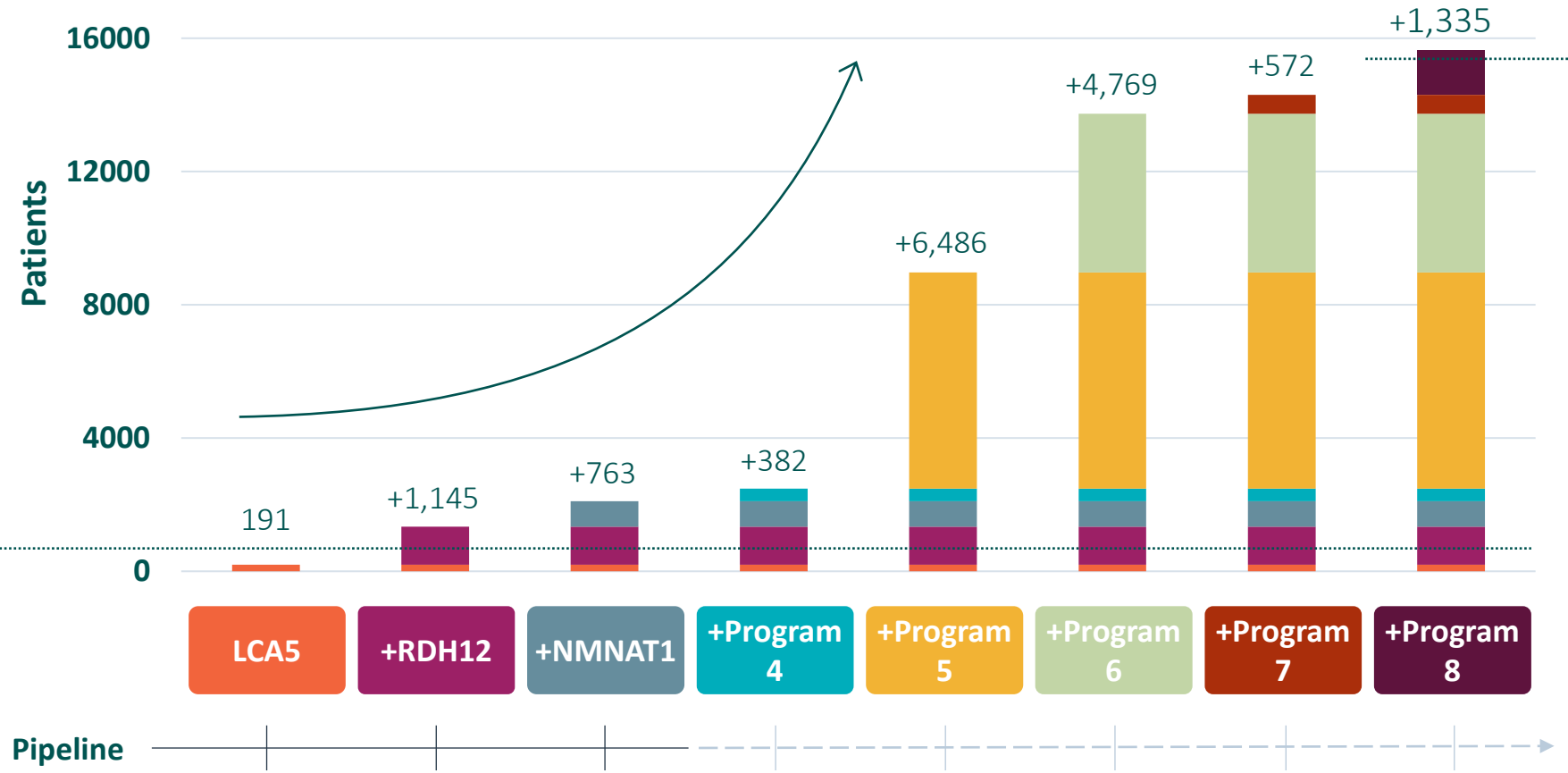
Multiple additional programs are in internal development and in active discussions for in-licensing

(1) All programs employ subretinal injection. PR = photoreceptor cell target.

(2) Based on current published estimates in literature. *PNAS, Hanany et al 2020 , Ophthalmology, Stone et al 2017*

A Pipeline Stack of IRD Treatments

Luxturna: marketed for **572 patients**



Over 15,500 patients in U.S. alone with first 8 proposed programs

Significant Ex-US prevalence

Note: Estimated US prevalence only; based on Stone et.al. 2017.

Executive Management Team

Ben Yerxa, Ph.D.
CEO

Ash Jayagopal, Ph.D.
CSO

Joe Schachle
COO

Jennifer Hunt
CDO

Nikki Heron
CFO

FOUNDATION FIGHTING BLINDNESS

RD FUND

INSPIRE

envisia THERAPEUTICS

VANDERBILT UNIVERSITY MEDICAL CENTER

Roche

KODIAK

gsk GlaxoSmithKline

INSPIRE

PARION SCIENCES

GRIFOLS

genzyme

QUINTILES

editas MEDICINE

Retrophin

stridebio

ATSENA THERAPEUTICS

PRECISION BIOSCIENCES

Scientific Advisory Board

Jean Bennett, M.D., Ph.D.

Penn
University of Pennsylvania

Eric Pierce, M.D., Ph.D.

Mass General Brigham
Mass Eye and Ear
HARVARD MEDICAL SCHOOL

Radha Ayyagari, Ph.D.

UC San Diego

Sanford Boye, M.S.

UF
UNIVERSITY of FLORIDA

Clinical Advisory Board

Daniel Chung, D.O.

SPARINGVISION

Elise Heon, M.D., FRCSC

SickKids

José-Alain Sahel, M.D.

UPMC
University of Pittsburgh Medical Center

Bart Leroy, M.D., Ph.D.

GHENT UNIVERSITY

Children's Hospital of Philadelphia

Relationship with FFB Further Strengthens the Opus Strategy

FOUNDATION FIGHTING BLINDNESS

RD FUND

FOUNDATION FIGHTING BLINDNESS CONSORTIUM

FOUNDATION FIGHTING BLINDNESS My Retina Tracker® Registry

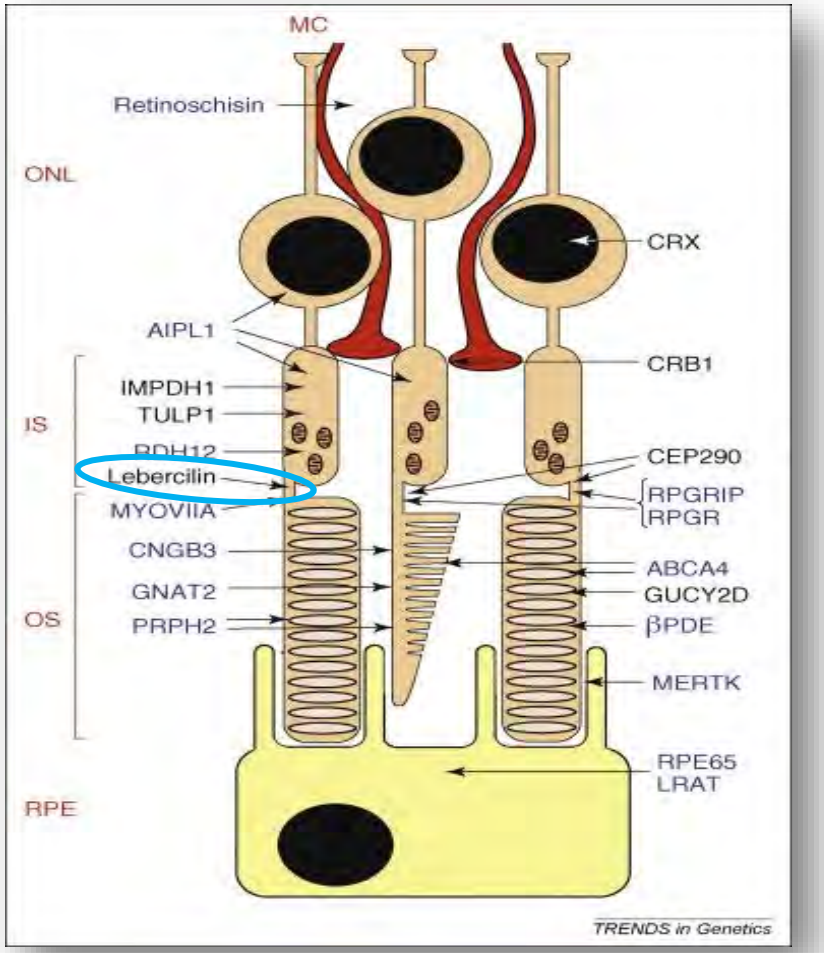
- Prevalence Estimates
- Natural History / Window of Intervention
- Efficient Clinical Trial Execution
- Opus as BD Partner of Choice
- Leverage Across Ecosystem

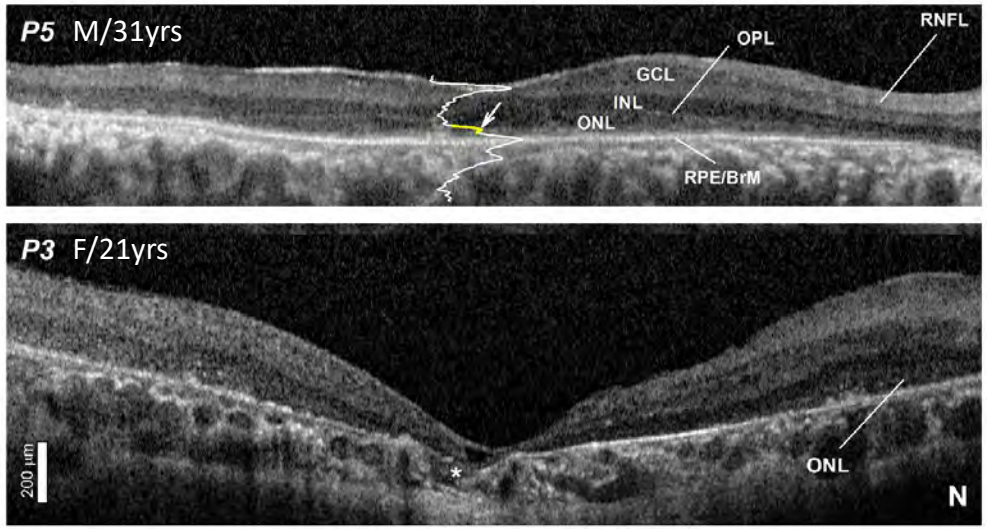
Opus Investment in Uni-Rare Natural History Study

- Universal Rare Gene Study: A Registry and Natural History Study of Retinal Dystrophies Associated With Rare Disease-Causing Genetic Variants (Uni-Rare), ClinicalTrials.gov Identifier: NCT05589714
- 40 site, global study
  - registry open to all genes on RD Rare Gene list
  - natural history study open on by-gene basis
  - unifying goal of developing sensitive and reliable outcome measures
- Conducted by FFB's Clinical Consortium
- Coordinated by Jaeb Center for Health Research (JCHR)
- Opus funding will cover a portion of costs for patients with specific IRDs within our pipeline who are enrolled in the natural history study

LCA5

LCA5 – An Early-Onset Retinal Degeneration

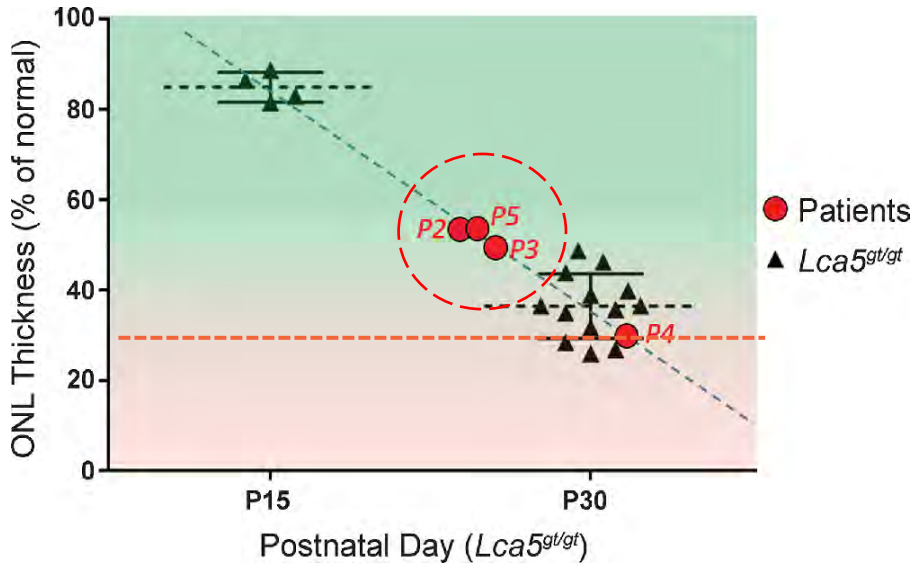




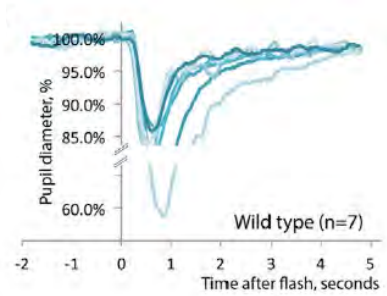
Structural-functional dissociation

Uyhazi et al., IOVS 2020
Boldt et al., JCI 2011

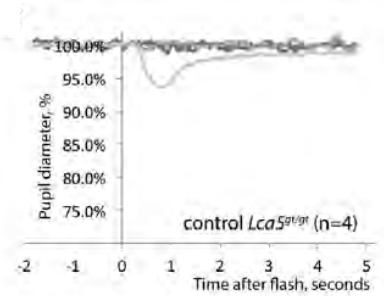
Demonstrated Functional Rescue in Faithful Animal Model



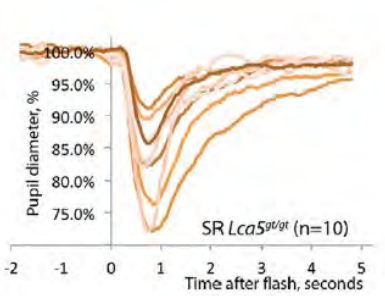
Pupillary light response



Wild type



Lca5 null



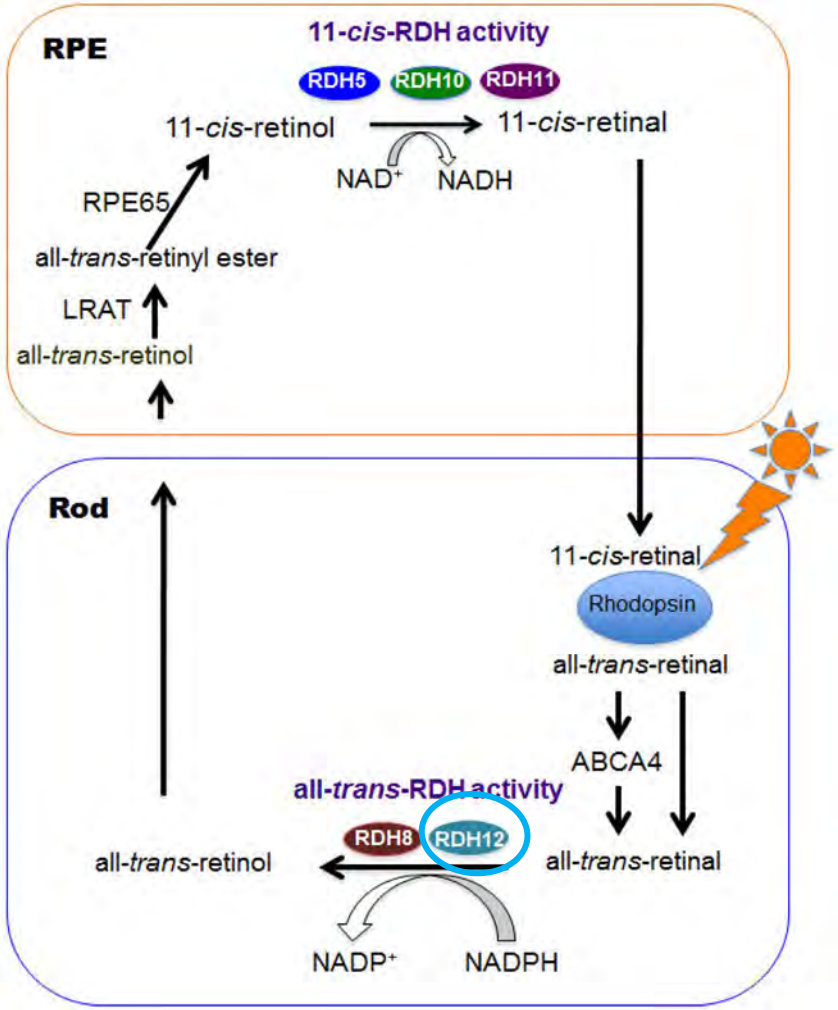
Treatment in Lca5 null

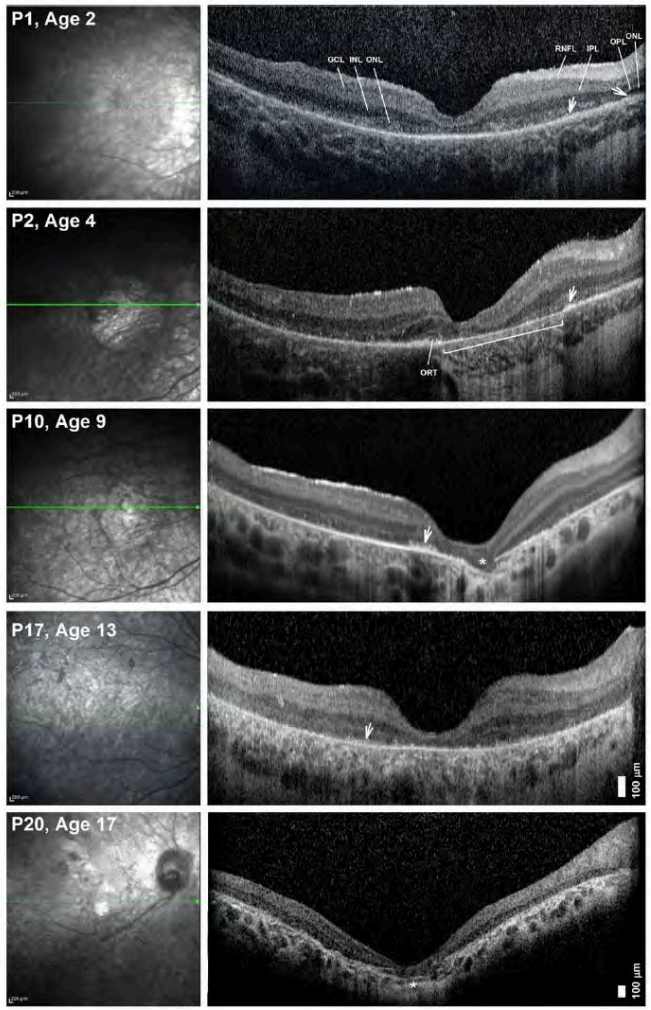
IND submission late 2022

Uyhazi et al., IOVS 2020
Song et al., Mol. Ther. 2018

RDH12

RDH12: Early Blindness Due to Defect in Visual Cycle Enzyme

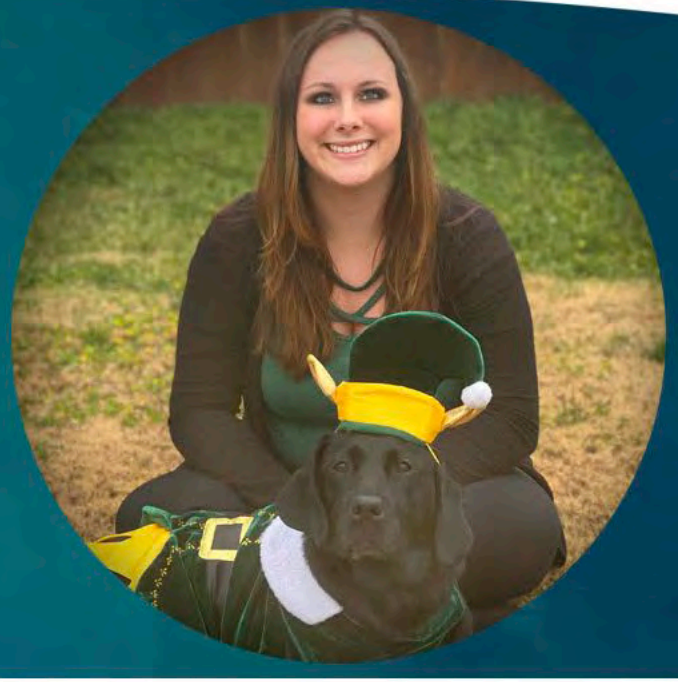




IND submission early 2024

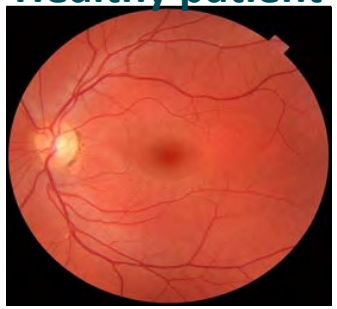
Aleman et al, IOVS 59:5225 (2018)

NMNAT1

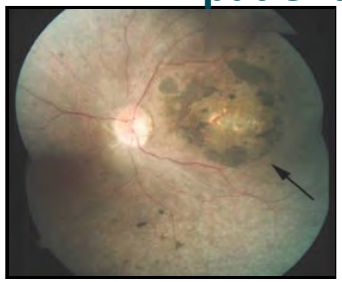


NMNAT1: IRD Caused by Nuclear NAD⁺ Dysregulation

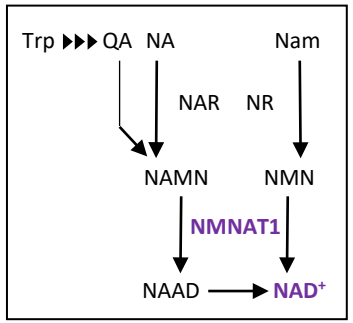
Healthy patient

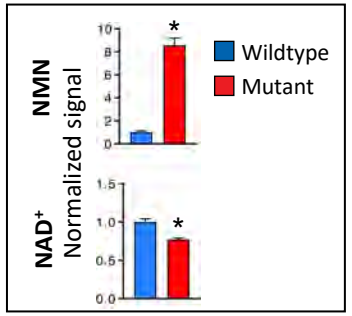


***NMNAT1* patient**

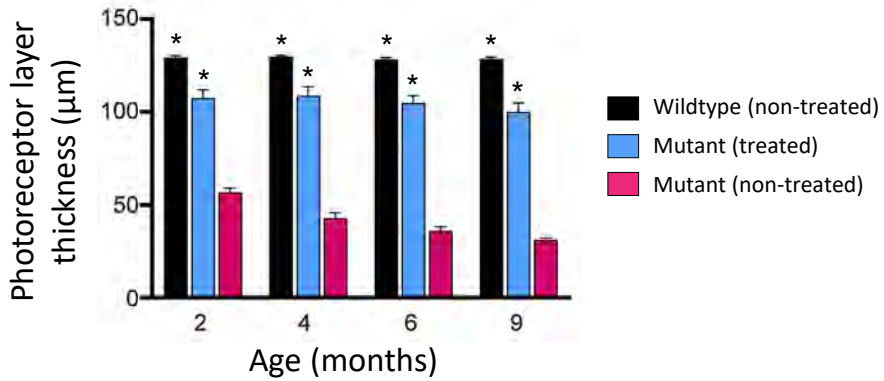


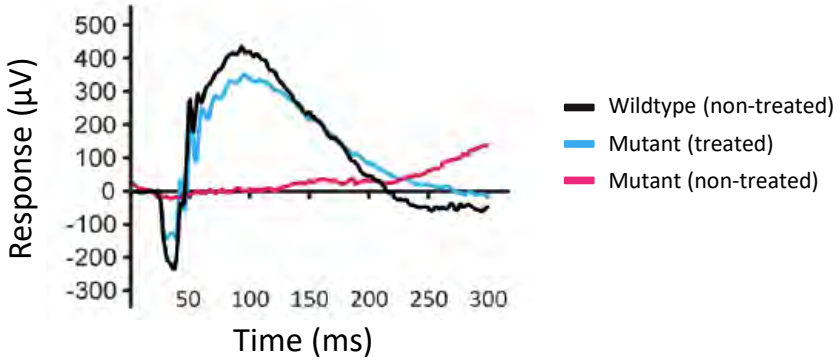
NMNAT1 is required for nuclear NAD⁺ production and homeostasis





Gene augmentation therapy rescues retinal structure and function in *NMNAT1* disease mouse model





Falk et al, Nature Genetics (2012)
Greenwald et al., Molecular Therapy – Methods & Clinical Development (2020)
Greenwald et al, Human Molecular Genetics (2021)

IND submission late 2025

Opus Summary

Opus Investment Thesis: Fast and Efficient Retinal Gene Therapies

Unmet Medical Need	De-risked Pipeline	Experienced Opus & Partner Teams	Significant Commercial Opportunities	Small Scale Manufacturing
280+ genes that cause vision loss with no existing treatments	Proven AAV delivery of gene therapies and efficient clinical development	Gene therapy, rare disease, ophthalmology, retinal therapeutics	Growing pipeline of 8+ focused and aligned IRD assets	High quality small batch sizes

Currently Raising $35M A Round:

- Funding through mid-2024
- Early clinical readouts for 2 programs
- On pace for at least 1+ IND per year
- Complete business development deals

OPUS GENETICS

Thank you!

Braydon RDH12

Bella RDH12

Abigail RDH12

Maci NMNAT1 with Mom Jenna

Alan LCA5

Kendall RDH12 with Maya