Corporate Overview

3Q2022

OPUS GENETICS

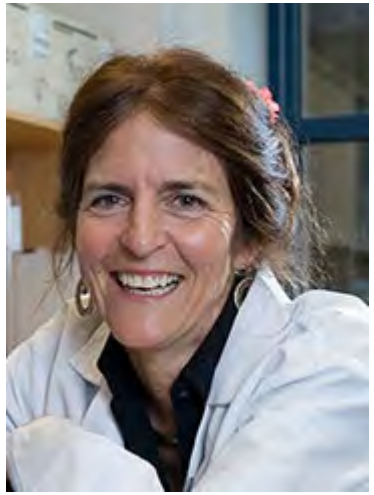
Overview of Opus Genetics

Unique gene therapy company focused on patients with rare inherited retinal diseases

Braydon (RDH12)

Advanced pipeline built by & for patients

The Opus Genetics Origin Story: A New Model is Needed



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

"A few years ago, [Dr. Bennett] found herself in a surprising place for a woman who invented the first gene therapy ever approved in the United States: No one, it seemed, wanted her work." (1)

Competitors (non-Opus) Approach	Implications
Seek diseases with large prevalence/market size	• High level of competition (eg: 10 programs in wet AMD, 9 in dry AMD, 8 in Stargardt, 5 in XLRP, etc.)(2) • Challenging clinical execution, commercial outlook
Invest heavily in next-generation technology and alternate delivery routes	• Compounds program risk (capsid, promoter, payload) • Unclear clinical differentiation vs. natural serotypes • Little to no manufacturing experience • High ocular doses, inflammation
Unproven biology and/or uncharacterized natural history	• Lower program probability of technical success

1. Endpoints article, 09/22/2021 “Luxturna inventor Jean Bennett starts a new gene therapy company to tackle rare diseases left behind by pharma, VCs”.
2. Evercore ISI Gene Therapy landscape (September 2021).

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, AKA not over engineered
  - Current AAV capsids delivered to the subretinal space is a tried and true method to get safe and effective gene transduction in the retina
- Manufacture using modern methods at a scale that makes sense
  - Low volume, high quality material

Pipeline of First-in-Class Gene Therapies Treating Severe IRDs

Genetic Target	Research/ Pre-Clin	IND Enabling	Phase 1/2	Phase 2/3	Delivery(1)	Common Name	Prevalence US, Est (2)	Key Milestones
LCA5					AAV8 PR	LCA5	~200	• IND 2nd half 2022
RDH12					AAV8 PR	LCA13	~1,100	• IND 2nd half 2023
NMNAT1					TBD	LCA9	~750	• IND early 2024

Multiple additional programs are in active discussion for in-licensing and/or internal development

(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*

Senior Management Team

Ben Yerxa, Ph.D.
CEO

Ash Jayagopal, Ph.D.
CSO

Joe Schachle
COO

Jennifer Hunt
CDO

Nikki Heron
CFO

FOUNDATION FIGHTING BLINDNESS

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Scientific Advisory Board

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Radha Ayyagari, Ph.D.

UC San Diego

Sanford Boye, M.S.

UF
UNIVERSITY of FLORIDA

- Decades of experience in the fields of gene therapy, ophthalmic genetics, and gene therapy vector engineering
- Early priorities will be to evaluate new candidate gene therapy targets for Opus portfolio and to evaluate external opportunities

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

- Pioneers in clinical development of gene therapies for IRDs, leadership and/or oversight of the most significant ophthalmic gene therapy clinical trials
- Decades of experience in clinical management of IRDs and development of novel endpoints
- Early focus on establishing the Opus paradigm for efficient clinical trials evaluating safety and efficacy and de-risking clinical development

Relationship with FFB Further Strengthens the Opus Strategy

Prevalence Estimates	• Proprietary data set from MyRetinaTracker registry enables decision-making across the company: indication selection, trial sizing, site selection, BD discussions
Natural History / Window of Intervention	• Deep investments in natural history elucidate appropriate time of intervention; creates the possibility for efficient regulatory path (e.g., synthetic or natural history control arm)
Efficient Clinical Trial Execution	• Strong relationship with leaders in the IRD field; all potential trial PI's and advisory board leads • Activated and engaged patient communities/groups, informed and willing to participate
Opus as BD Partner of Choice	• Funding from FFB and ongoing trusted relationships allow FFB / Opus a potential "first look" at promising scientific discoveries and programs • Capabilities and focus (corporate strategy) further strengthen competitive edge as licensor
Leverage Across Ecosystem	• Center of support for regulation, legislation, advocacy, community with strong relationships • Possible synergies with 12+ RD Fund portfolio companies across two funds (and counting)

Nationally-Recognized GMP-grade Manufacturing Partners

Opus relationship with key partners to establish high quality, boutique manufacturing:

- National Resilience: Unique partnership for dedicated GMP slots for 1st 3 programs (1 IND/year), with option to extend to other programs.
  - Leverages Resilience's proprietary Triple Transient Transfection Platform (s3T) at state-of-the art GMP facilities in Alachua, FL and Marlborough, MA
  - Opus has full license for Thermo CTS™ Viral Production Cells through commercialization of first three programs
  - If Opus decides to develop independent manufacturing, any Resilience-developed process is portable through a non-exclusive license to Opus
- Dark Horse Consulting, a leading cell and gene therapy consulting firm, advises on manufacturing strategy and choice of partners, audits facilities, and authors key regulatory documents in collaboration with Resilience

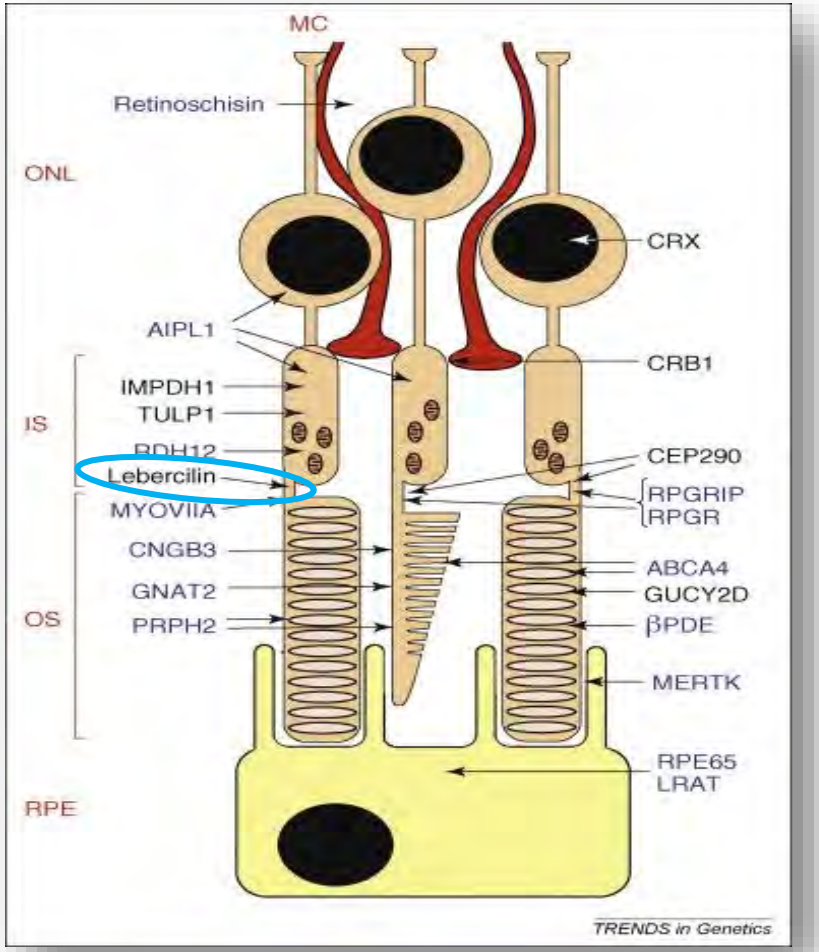
RESILIENCE

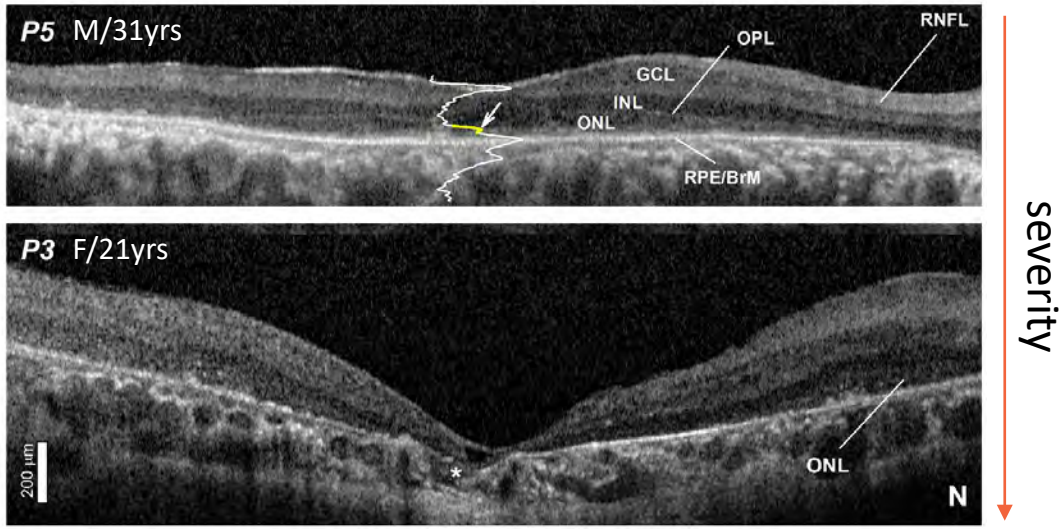
ThermoFisher SCIENTIFIC

DHC DARK HORSE CONSULTING


LCA5

LCA5 – An Early-Onset Retinal Degeneration Addressable by Gene Therapy

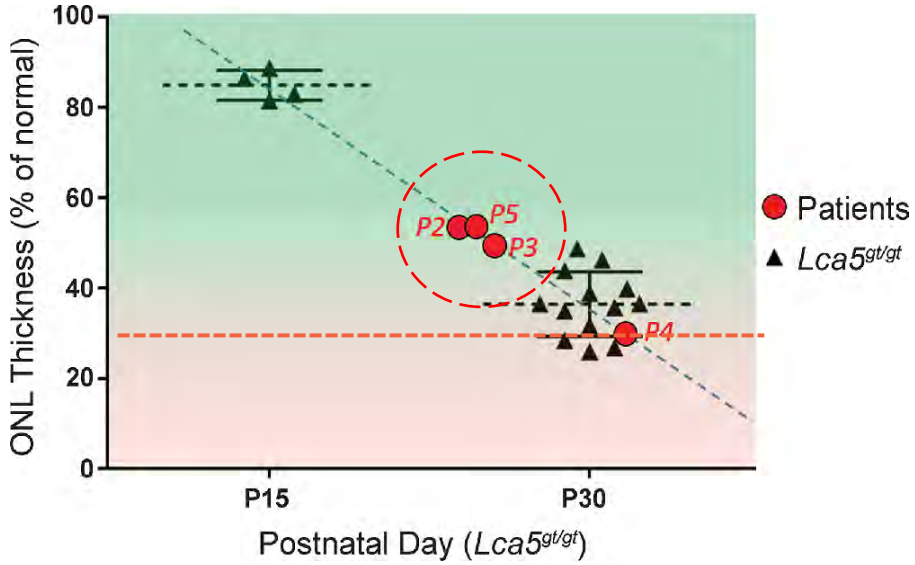




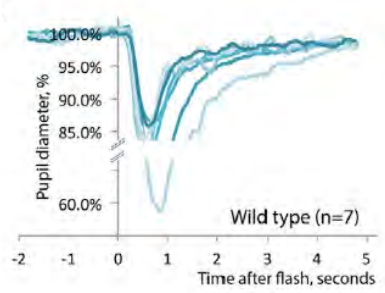
Evidence of structural-functional dissociation suggests therapeutic opportunity (e.g. patients can exhibit preserved photoreceptor/RPE into adulthood)

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

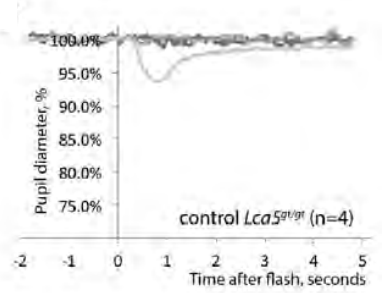
Demonstrated Functional Rescue in Faithful Animal Model



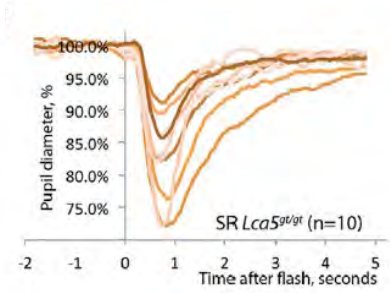
Pupillary light response



Wild type



Lca5 null



Treatment in Lca5 null

LCA5 null mice exhibit photoreceptor loss comparable to LCA5 moderate (P15) and severe (P30) disease, serving as a preclinical model for therapeutic interventions

AAV encoding functional LCA5 was shown to preserve visual function in mice when administered prior to peak disease severity (< 30% ONL thickness) suggesting broad therapeutic window in LCA5 patients

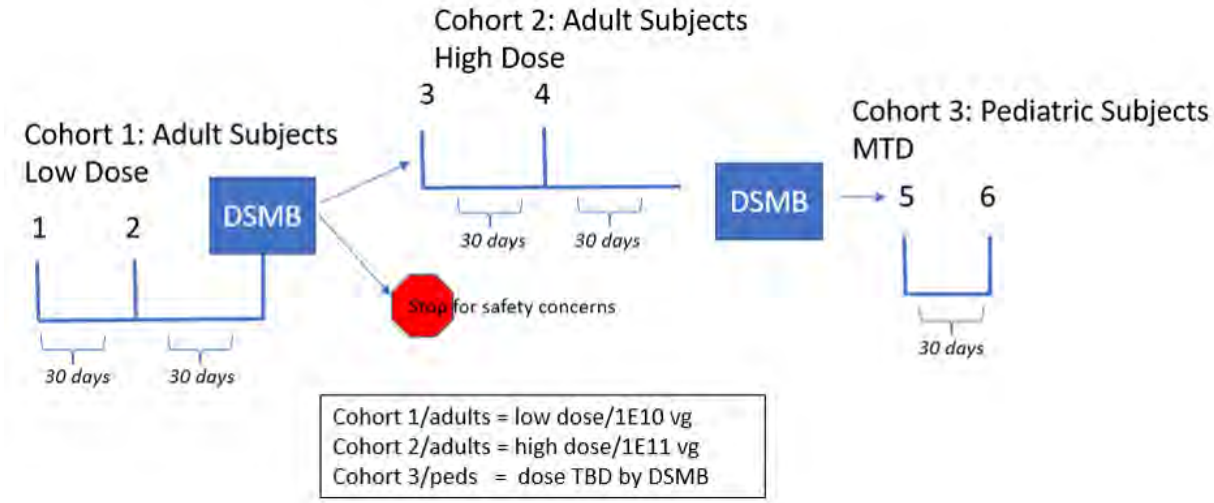
Uyhazi et al., IOVS 2020
Song et al., Mol. Ther. 2018

LCA5 – Development Progress

- Preclinical efficacy established in KO mouse and human iPSC models
- Manufactured cGMP clinical trial material at CAROT (U Penn)
- GLP toxicology in NHPs completed
- Orphan Drug Designation granted
- Pre-IND meeting with FDA completed
- Clinical protocol being developed in preparation for the IND filing targeted for 2H 2022

OPGx-001: Phase 1/2 Clinical Trial Design

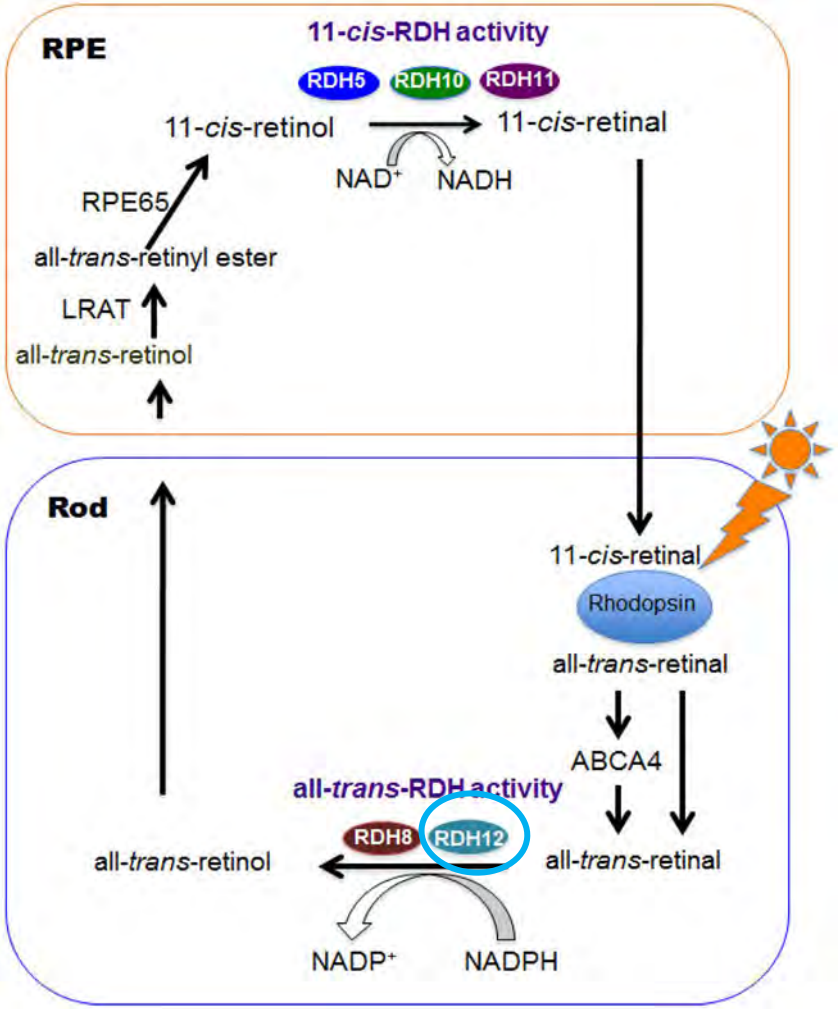
- Primary objective is safety, while monitoring key clinical endpoints for early efficacy (FST, pupillometry, ERG)
- Dose escalation study in adult and pediatric subjects
- Lean trial design based on over a decade of experience in gene therapy clinical trials at University of Pennsylvania / Children's Hospital of Pennsylvania

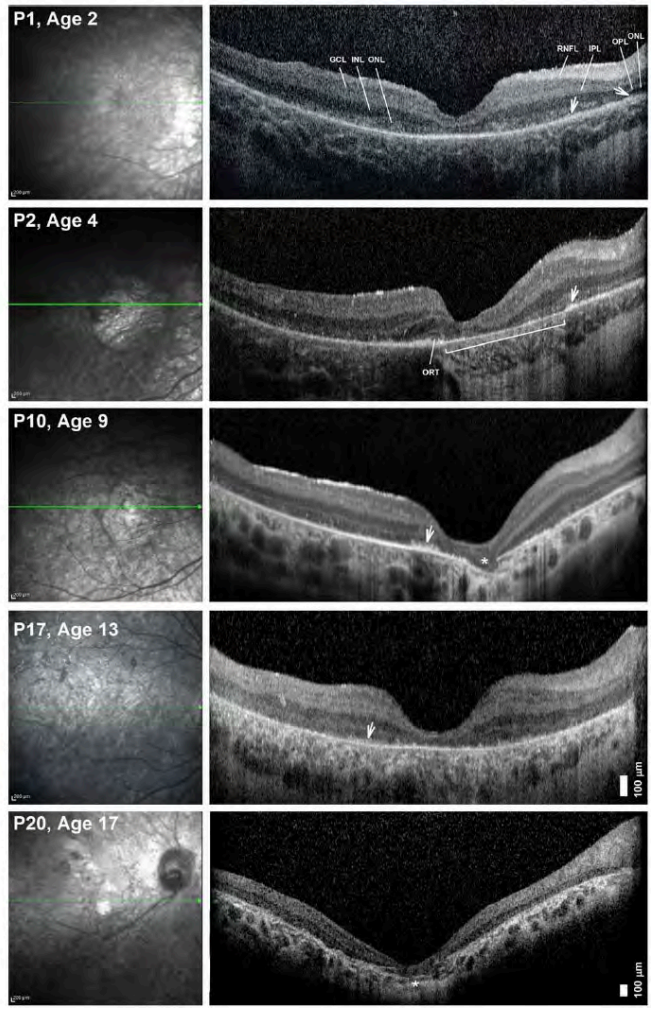



RDH12

RDH12

- Early visual acuity loss with retinal structural changes observed by 2 years of age
- RDH12 encodes for a key visual cycle enzyme in photoreceptor inner segments
- Longitudinal studies of RDH12 patients suggest relatively preserved visual acuity with steep decline in second decade of life

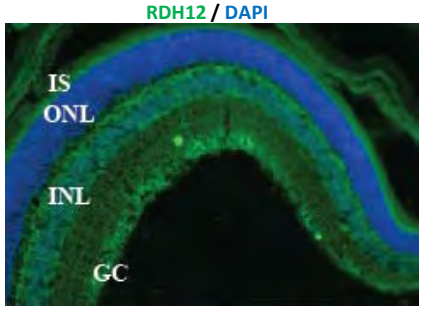




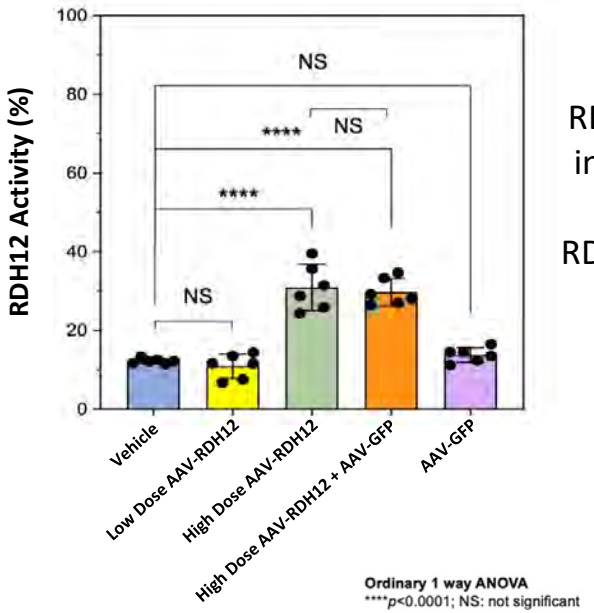
Aleman et al, IOVS 59:5225 (2018)

RDH12 – Development Progress

- Promoter and serotype-optimized for target tissue, expression and safety
- Robust, dose-dependent expression of hRDH12 using clinical candidate
  - *In vitro* potency assay
  - CD-1 and RDH12^{KO} mice
- Demonstration of functional improvement *in vivo*
  - Restoration of RDH12 activity in RDH12^{KO} mice approaching levels in wild type mice



RDH12 expression in AAV-RDH12 transduced RDH12^{KO} mouse retina



RDH12 Activity in AAV-RDH12 transduced RDH12^{KO} mouse retinas

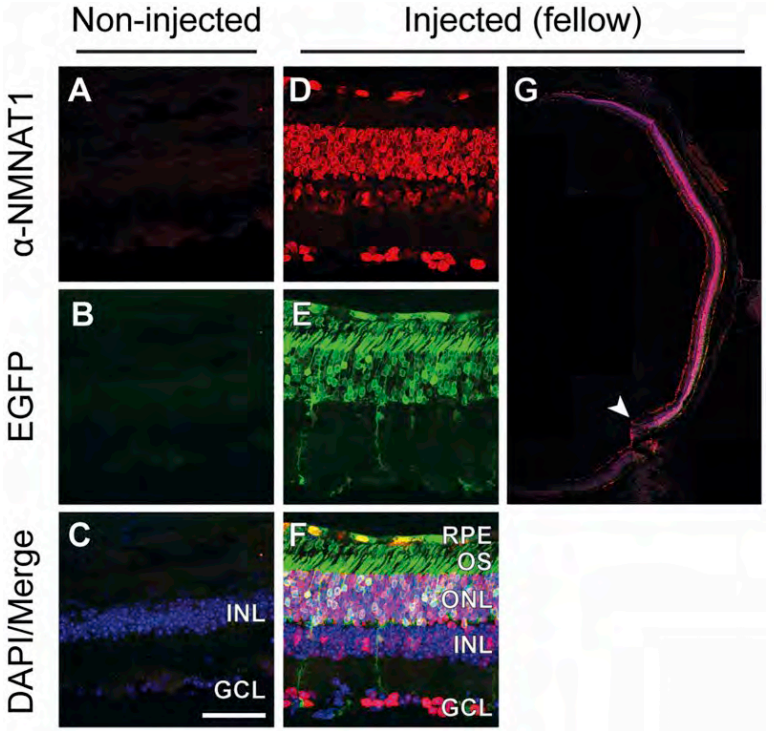
RDH12 – Development Plans

- Preclinical efficacy established in cellular and mouse models
- Pre-IND written responses received from FDA June 2022
- Manufacturing beginning now at Resilience
  - GLP toxicology material
  - cGMP clinical trial material
- GLP toxicology in NHPs Q4 2022
- Clinical protocol being developed in preparation for the IND filing targeted for 2H 2023


NMNAT1

Recent Progress in Pipeline Development – NMNAT1

- Latest addition to pipeline (Nov 2021)
- Based on the work of Opus co-founder Eric Pierce, M.D., Ph.D. (Massachusetts Eye and Ear, Harvard Medical School) investigating early-onset retinal neurodegeneration due to NMNAT1 mutations
- NMNAT1 is an enzyme essential for regeneration of NAD^+ retinal pools which govern essential cellular processes
- Photoreceptors are highly vulnerable to loss of NMNAT1 function
- Functional restoration of retinal structure and function demonstrated in mouse model exhibiting pathologic features of human LCA9
- Development and regulatory timelines in preparation

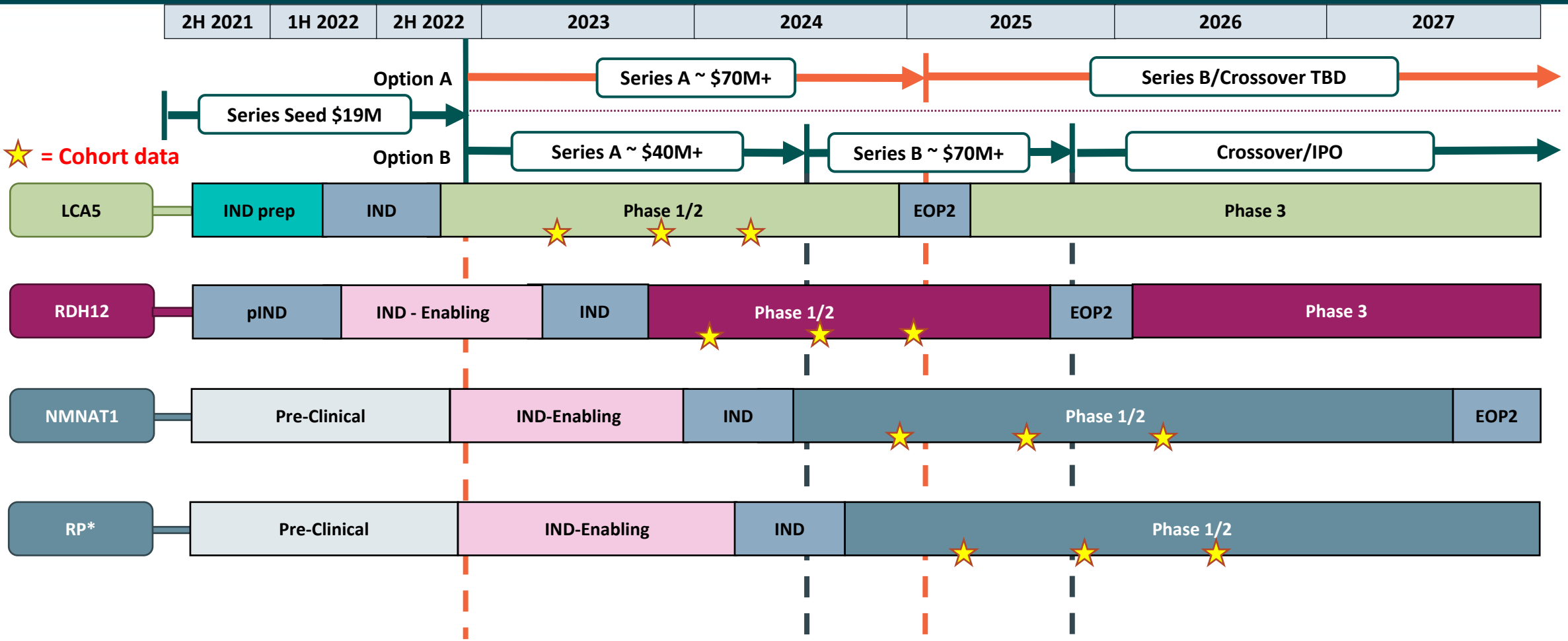


Structural rescue of the retinal tissue using NMNAT1 gene therapy in a mouse model of retinal degeneration (Nmnat1 $^{V9M/V9M}$)

Greenwald et al., Mol Ther Method Clin Dev, 2020

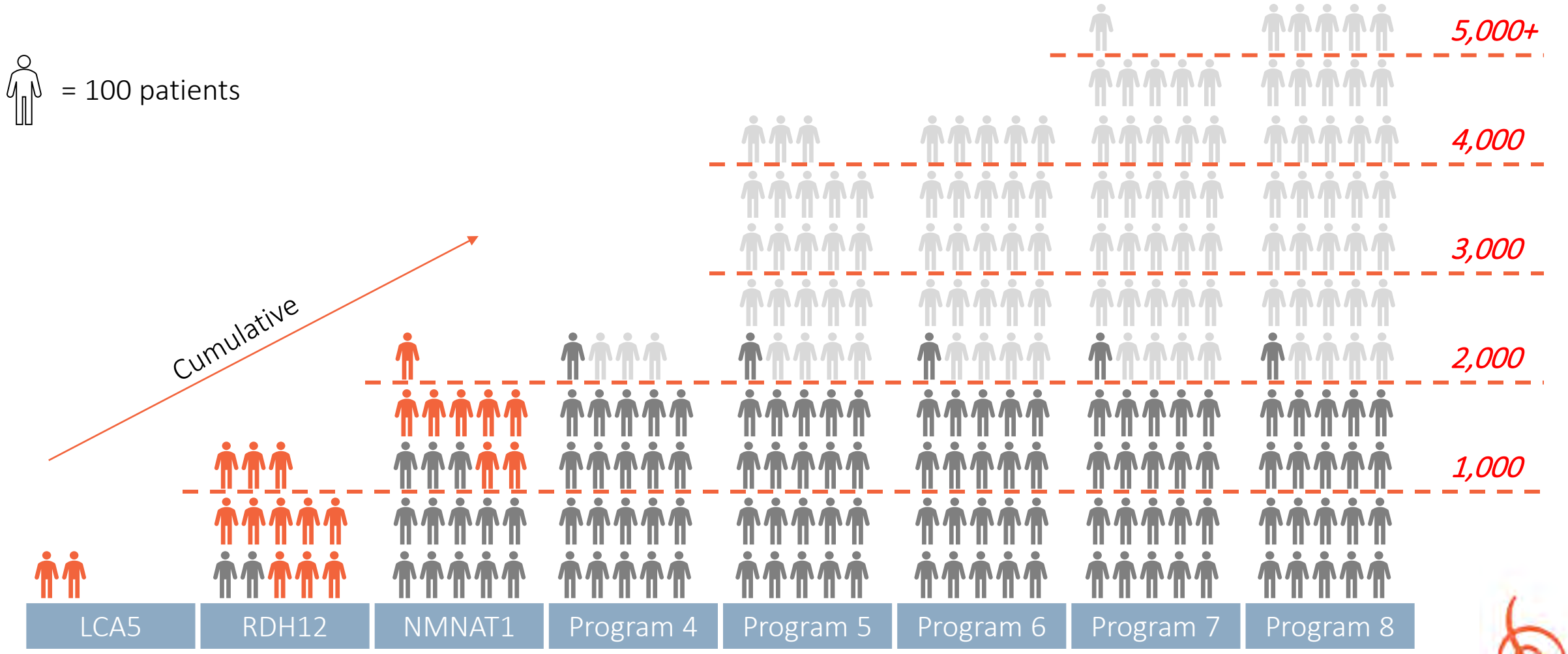
Opus Summary

Pipeline & Development Timelines



*License near completion

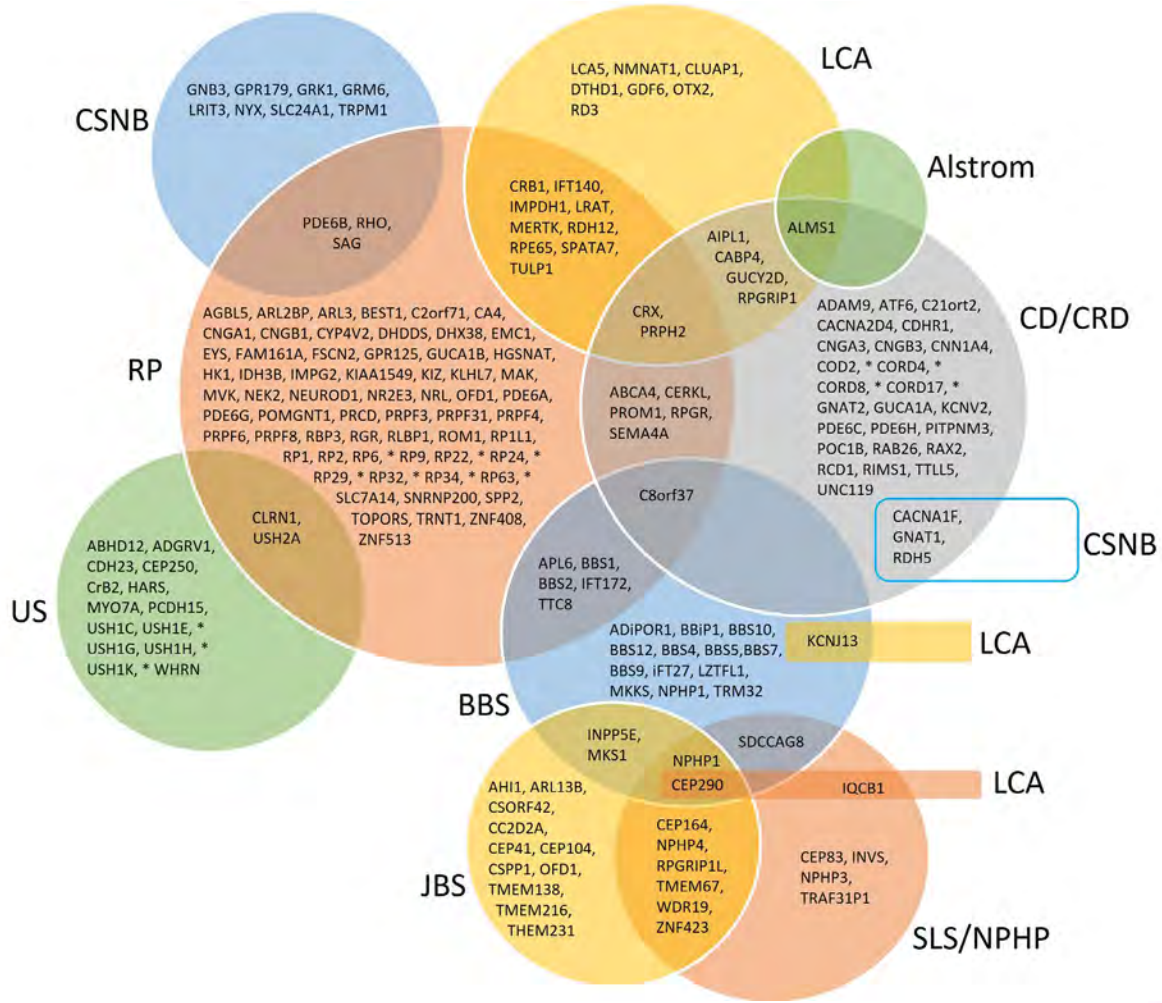
Existing Portfolio Alone Could Target Thousands of Patients



Note: Estimated US prevalence only; Stone 2017.

Opus: Unique Focus on Rare Inherited Retinal Diseases

- First-of-its-kind model supported by leading patient group
- Strong and growing portfolio of programs
- Expertise, insight, & commitment to deliver on strategy
- Significant long-term addressable market opportunities




Thank you!