



Courageous Innovation

*Dedicated to Bringing Game-Changing Gene & Cell Therapies  
and Vaccines to Market and Working Even Harder to Provide  
Access to Patients Globally*

OCGN  
August 2024



## Forward Looking Statements

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*This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995, which are subject to risks and uncertainties. We may, in some cases, use terms such as “predicts,” “believes,” “potential,” “proposed,” “continue,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “could,” “might,” “will,” “should,” or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Such statements include, but are not limited to, statements regarding our clinical development activities and related anticipated timelines. Such statements are subject to numerous important factors, risks, and uncertainties that may cause actual events or results to differ materially from our current expectations. These and other risks and uncertainties are more fully described in our periodic filings with the Securities and Exchange Commission (SEC), including the risk factors described in the section entitled “Risk Factors” in the quarterly and annual reports that we file with the SEC. Any forward-looking statements that we make in this presentation speak only as of the date of this presentation. Except as required by law, we assume no obligation to update forward-looking statements contained in this presentation whether as a result of new information, future events, or otherwise, after the date of this presentation.*



# Through Courageous Innovation, We are Leveraging Our First-in-Class Platforms to Address Serious Unmet Medical Needs



## Modifier Gene Therapy Platform

*First-in-Class*

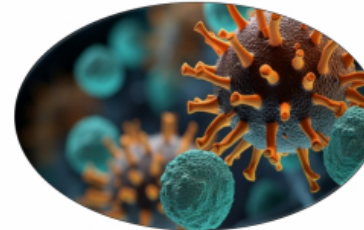
- Therapeutic Focus: Inherited retinal diseases & larger blindness diseases with unmet need
- Differentiator: Master gene regulator; gene-agnostic approach
- Pipeline:
  - OCU400 Phase 3 liMelighT clinical trial (retinitis pigmentosa)
  - OCU410 Phase 2 ArMaDa clinical trial (geographic atrophy)
  - OCU410ST Phase 1/2 GARDian clinical trial (Stargardt)



## Regenerative Cell Therapy Platform

*First-in-Class*

- Therapeutic Focus: Articular cartilage lesions
- Differentiator: 3D scaffold
- Pipeline:
  - NeoCart® (Ph3): articular cartilage defects in the knee



## Inhalation Vaccines Platform

*First-in-Class*

- Therapeutic Focus: Flu and COVID-19
- Differentiator: Inhalation for improved durability and transmission control
- Pipeline:
  - OCU500 (Pending Ph1): COVID-19 vaccine
  - OCU510 (Preclin): flu quadrivalent
  - OCU520 (Preclin): COVID-19 + flu combo



# Pipeline Overview

	Asset/Program	Indication	Current Status
Gene therapies	OCU400 * AAV-hNR2E3	<i>Retinitis pigmentosa (RP)—RHO Mutations</i>	<ul style="list-style-type: none"> <li>Actively dosing subjects in the OCU400 Phase 3 lIMeliGhT trial for the treatment of RP</li> <li>FDA granted RMAT** designation for RP indication associated with <i>NR2E3</i> and <i>RHO</i> mutations</li> <li>EMA provided acceptability of the U.S.-based trial for submission of a Marketing Authorization Application (MAA)</li> <li>FDA approved the OCU400 expanded access program (EAP) for the treatment of adult patients, aged 18 and older, with RP</li> </ul>
		<i>RP—gene-agnostic indication (other than RHO mutations)</i>	
	OCU410 AAV-hRORA	Dry Age-Related Macular Degeneration (Geographic Atrophy)	<ul style="list-style-type: none"> <li>Nine patients with GA have been dosed in the Phase 1/2 ArMaDa clinical trial (with low, medium, and high doses)</li> <li>Phase 2 of the clinical trial has been initiated</li> </ul>
	OCU410ST AAV-hRORA	Stargardt disease (orphan disease)	<ul style="list-style-type: none"> <li>Nearing completion of Phase 1 of the Phase 1/2 GARDian clinical trial</li> </ul>
Biologics	OCU200 Transferrin – Tumstatin	Diabetic Macular Edema	<ul style="list-style-type: none"> <li>Continue to work with FDA to address comments to lift clinical hold</li> </ul>
		Diabetic Retinopathy	<ul style="list-style-type: none"> <li>IND-ready</li> </ul>
		Wet Age-Related Macular Degeneration (Wet AMD)	<ul style="list-style-type: none"> <li>IND-ready</li> </ul>
Cell therapies (Regenerative Medicine)	NeoCart* (Autologous chondrocyte-derived neocartilage) RMAT	Treatment of Articular Cartilage Defects in the Knee	<ul style="list-style-type: none"> <li>Phase 3 clinical trial contingent on funding availability</li> <li>cGMP facility construction completed</li> </ul>
Vaccines	OCU500 Series		
	OCU500: COVID-19	For Prevention of Disease Caused by COVID-19	<ul style="list-style-type: none"> <li>NIAID plans to submit an IND to initiate the OCU500 (COVID-19) Phase 1 clinical trial this year</li> </ul>
	OCU510: Flu (Quadrivalent)	For Prevention of Disease Caused by Flu	
	OCU520: Flu + COVID-19	For Prevention of Diseases Caused by Flu and COVID-19	

\*Broad, gene-agnostic, ORPHAN DRUG DESIGNATIONS FOR RP/LCA FROM FDA AND EMA

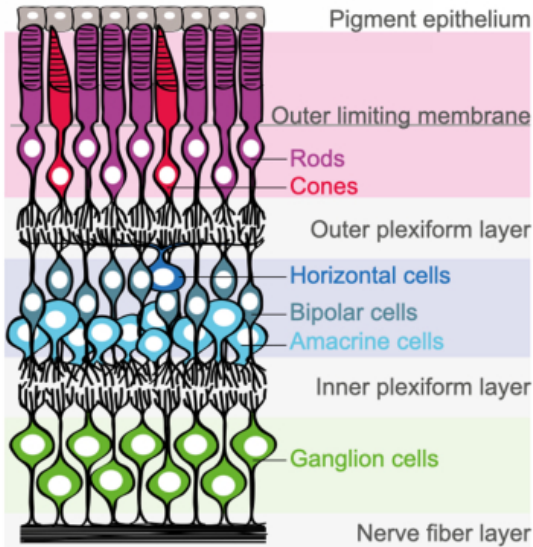
\*\*Regenerative Medicine Advanced Therapy Designation



# Modifier Gene Therapy Platform

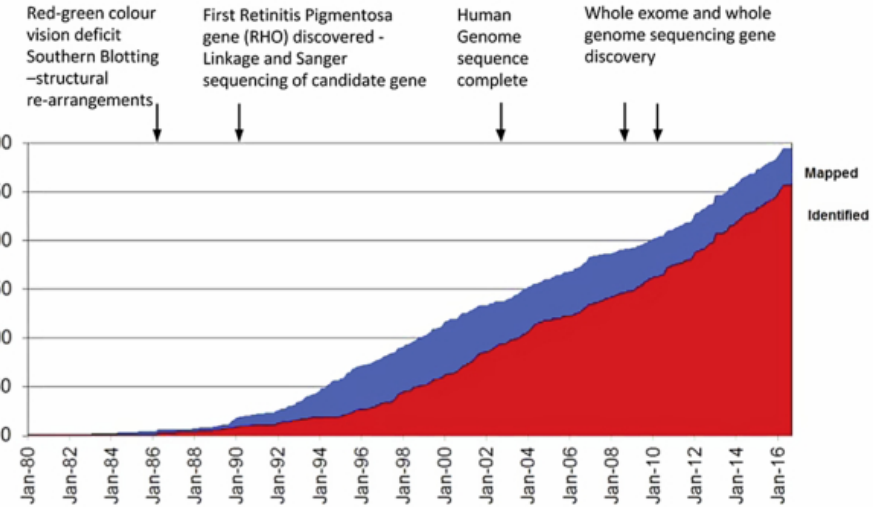
Breakthrough technology designed to address many rare diseases  
as well as complex diseases that affect millions

# Traditional Gene Therapy is Highly Inefficient for Retinal Diseases

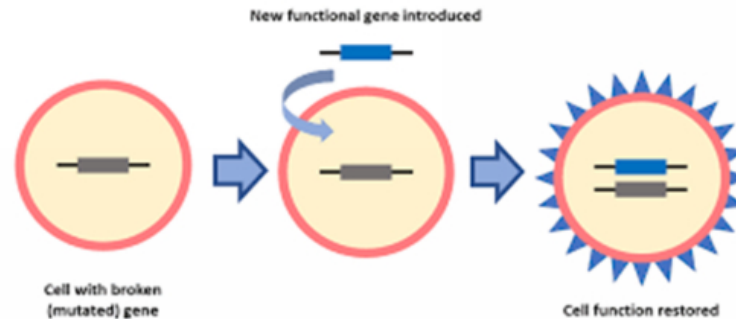


- **13,120 (65%)** of all human proteins expressed in retina
- **785** genes are highly specialized in the retina
- Nearly **300** mutations have been identified
- **100+** associated with RP
- **1** gene therapy for a single mutation is approved (2017)

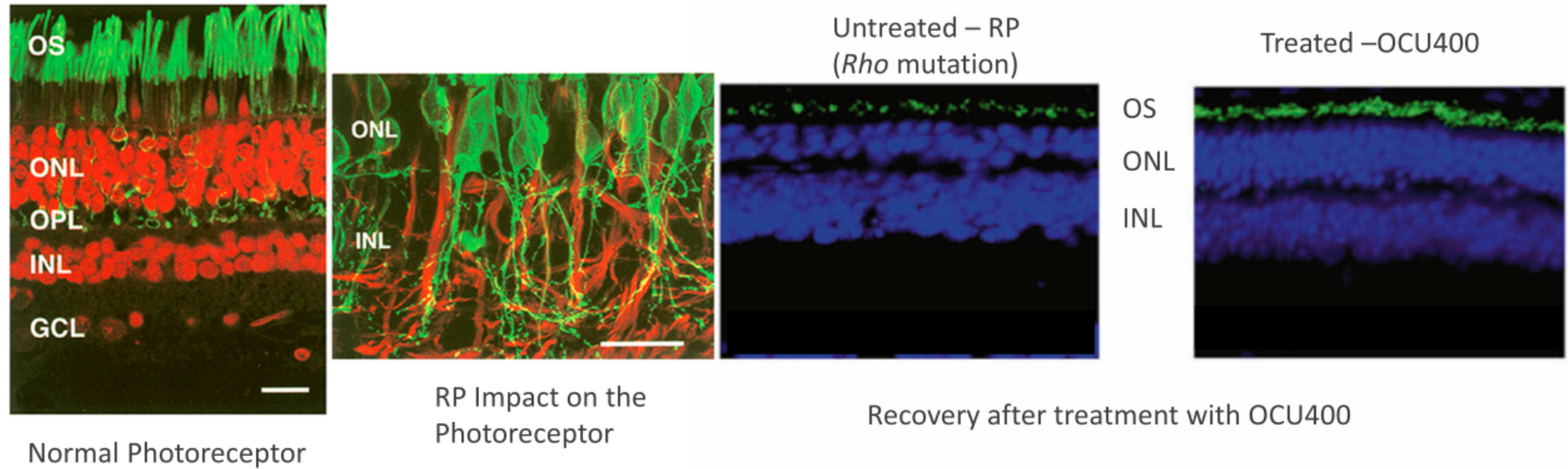
Traditional single therapy is not efficient for disease such as RP with multiple mutations



Mapped and Identified Retinal Disease Genes 1980 - 2017



# The Photoreceptor is Dependent on Cellular Homeostasis Regulated by Key Transcription Factors (TFs) such as *NR2E3* (OCU400)



- Immunolabeling of rod photoreceptors with anti-opsin (green) in normal human and in retinitis pigmentosa retinas<sup>1</sup>
- Rhodopsin (RHO) immunolabeling shows restored expression and homeostasis in photoreceptors of treated animals <sup>2</sup>

<sup>1</sup> Jones BW, Marc RE, Pfeiffer RL. Retinal Degeneration, Remodeling and Plasticity. 2016 Oct 28. In: Kolb H, Fernandez E, Nelson R, editors. Webvision: The Organization of the Retina and Visual System [Internet]. Salt Lake City (UT): University of Utah Health Sciences Center; 1995-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK482309/>

<sup>2</sup> <https://www.nature.com/articles/s41434-024-00440-6>

# Ocugen's Gene Therapy – Fundamentally Changing Gene Therapy

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## What is Modifier Gene Therapy?

- The insertion of a nuclear hormone receptor gene (transcription factor) to regulate the expression of multiple genes required for cell survival & maintenance

## Animal Proof of Concept – Gene Agnostic Mechanism

- OCU400 (*NR2E3*) demonstrated restoration of gene expression in 5 different animal models by regulating many functional genes resulting in retinal cellular function

## Human Proof of Concept – Gene Agnostic Mechanism

- A Phase 1/2 trial of OCU400 in patients with multiple mutations associated with RP demonstrated effectiveness and was generally well-tolerated in a validated mobility test

## How Does OCU400 compare to the only approved RP treatment (RPE65 single mutation)?

- Luxturna was FDA approved based on mobility test and has achieved the following responder rate in Phase 3 (greater than or equal to 2 Lux levels):
  - 52.4% responder rate
- Based on the intent-to-treat (ITT) analysis of Ph 1/2, the OCU400 Phase 3 outcome is projected to be greater – across multiple mutations
  - 62.5% responder rate





# OCU400: Modifier Gene Therapy Targeting RP—High Unmet Medical Need

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## Regulatory Achievements

- Received RMAT Designation from the FDA
- FDA/EMA granted expanded orphan drug designations for RP
- EMA provided acceptability of the U.S.-based trial for submission of MAA
- EAP for the treatment of adult patients, aged 18 and older, with RP

## Despite its prevalence, RP patients have very limited treatment options

- U.S. and EU: RP affects nearly 300,000
- Worldwide: conditions affect approximately 1.6M people

## Current approved and in-development gene therapies focus on individual genes

- More than 100 mutated genes associated with RP
- Developing a single therapy to treat each mutation is not feasible

## OCU400 addresses shortcomings of current gene therapy approaches

- Broad-spectrum, gene-agnostic approach to genetically diverse inherited retinal diseases
- Potential one-time therapy for life with a *single* sub-retinal injection using *NR2E3*

## Current Status

- Dosing patients in Phase 3 liMeliGhT clinical trial for RP
  - FDA granted RMAT designation for RP indication associated with *NR2E3* and *RHO* mutations
  - Luminance Dependent Navigation Assessment (LDNA)— that includes a wider range of light intensity—is the primary endpoint



## Human Proof of Concept: Phase 1/2 Safety and Efficacy Summary

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- OCU400 is observed to be generally well-tolerated and effective in subjects across different mutations and dose levels—18 patients
- Efficacy measurements suggest ***stabilization or improvement*** in the treated eye on validated mobility test course (score vs baseline) regardless of mutation
  - **78% (14/18)**
  - Post hoc analysis confirmed 2 patients were at ceiling effect (highest Lux) at enrollment and 2 non responders were due to surgical AE
- Treatment effect in *RHO* patients **supports the gene-agnostic mechanism of action of OCU400**
  - **80% (8/10)** of *RHO* mutation subjects had stabilization or improvement
  - **60% (3/5)** of ITT *RHO* subjects, who qualify for Phase 3, met FDA mobility test approval threshold of 2+ Lux levels



## Mobility Test (LDNA\*) is Primary Endpoint for Phase 3

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- **Primary endpoint (Efficacy):** Mobility test has been used for an approved product
- **Alignment with FDA to demonstrate clinical efficacy (Responder  $\geq 2$  Lux level improvement)**
  - Validated for RP patients
- **Phase 1/2 results:** More than 60% of the ITT patients from the Phase 1/2 clinical trial (*RHO* and *NR2E3*) meet the responder criteria

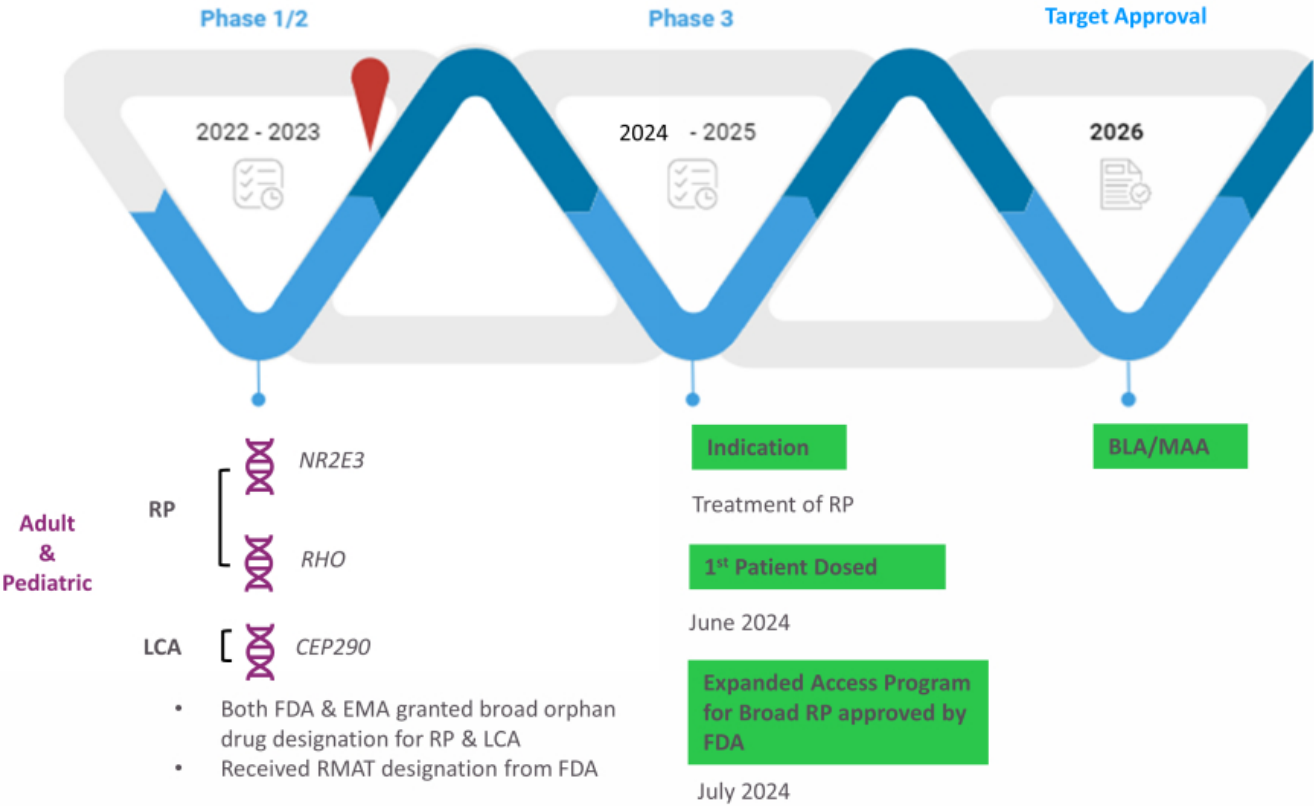
Dosing status	Approved Product Phase 3 <sup>1</sup>	OCU400 Phase 1/2
Treated	11/21 (52.4%)	5/8 (62.5%)

- **OCU400 Phase 3 provides > 95% power at 50% response rate (N = 150; 2:1 randomization)**



\* LDNA: Luminance Dependent Navigation Assessment is a sensitive and specific mobility test proprietary to Ocugen  
<sup>1</sup> <https://www.fda.gov/media/109906/download>

# OCU400: Expected Pathway to Clinical Development & Potential Approval



# OCU410 (RORA): A Single-Injection Approach to Addressing Unmet Needs in dAMD BEYOND the Complement System

- Phase 2 OCU410 ArMaDa study for GA currently underway
  - Limited options for dAMD, presenting significant unmet medical need
    - U.S. and EU: nearly 19M (GA: 2-3M)<sup>1</sup>
    - Worldwide: 266M<sup>2</sup>
  - Distinct 4-way MOA:  
Addresses multiple regulator pathways involved with the disease including:
    - Lipid Metabolism
    - Regulation of Inflammation
    - Oxidative Stress
    - Membrane Attack Complex (Complement)
  - Optimal delivery and durability:
    - A single subretinal injection designed to eliminate patient compliance concerns and the treatment burden associated with multiple injections
  - Improved retinal function:
    - Improved photoreceptor function in OCU410 treated eyes with all doses\*
- Advancement from recently approved therapies for GA: Potential to address limitations of recently approved therapies for GA focused only on the complement system, including:
    - Patient Compliance
      - Frequent intravitreal injections (~6-12 doses per year)
    - Observed Structural Impact
      - Limited effect of GA lesion growth rate
    - Safety Considerations
      - 12% of patients experienced nAMD when therapy is administered every month for two years (Syfovre\*)

Potential for a one-time therapy for life with a single sub-retinal injection to address the unmet needs and treatment burden in patients with dAMD



MOA: Mechanism of action | nAMD: Neovascular age-related macular degeneration

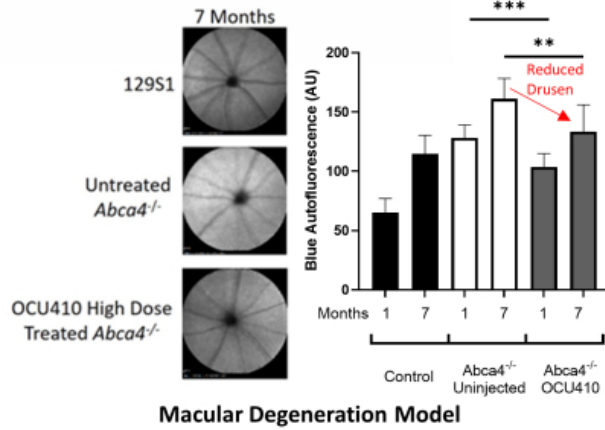
<sup>1</sup>DB Rein et al., *JAMA Ophthalmol*, 2022. doi: 10.1001/jamaophthalmol.2022.4401

<sup>2</sup>CJ Thomas et al., *Med Clin North Am*, 2021. doi: 10.1016/j.mcna.2021.01.003 (2021).

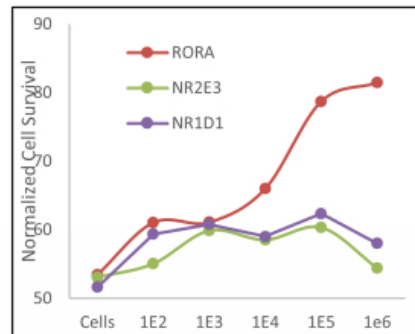
\*As demonstrated in peak scotopic B-wave amplitudes, N≥5 biological replicates

# OCU410 (RORA): A Potential Modifier Therapeutic for Dry-AMD and STGD

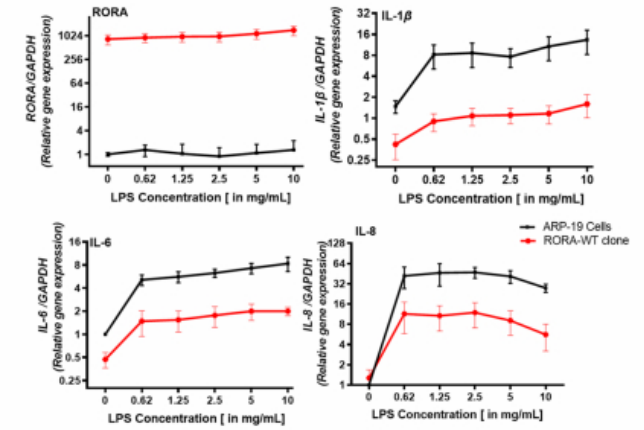
*Anti-drusen activity: Improves retinal function*



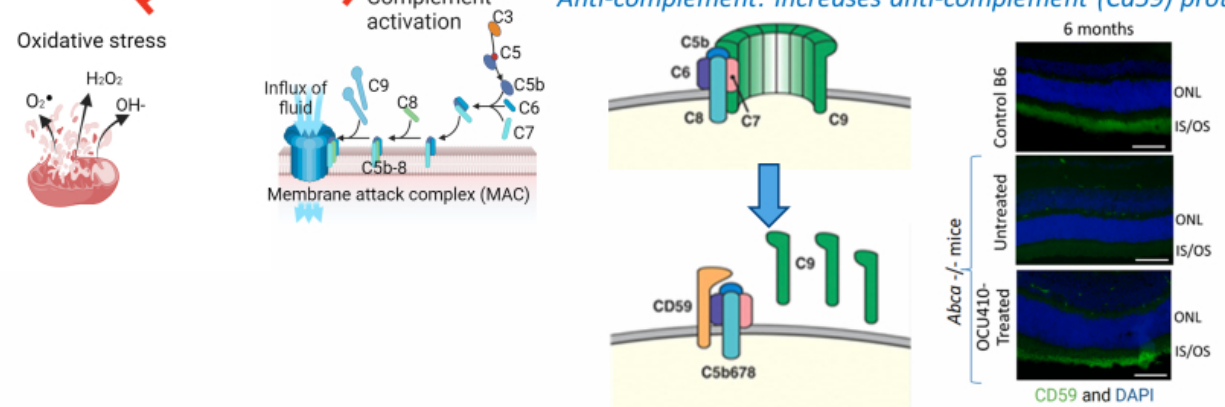
*Anti-oxidative: Improves ARPE19 cell survival*



*Anti-inflammatory: Suppresses inflammation in HMC3 cells*



*Anti-complement: Increases anti-complement (Cd59) protein*



# OCU410ST: Received ODD for *ABCA4*-Associated Retinopathies: Stargardt, Retinitis Pigmentosa 19 & Cone-rod Dystrophy 3

## *ABCA4*-associated retinopathies—Genetic Rare Disease

- *ABCA4* gene produces an ATP-binding cassette (ABC) superfamily transmembrane protein involved in clearance of all-trans-retinal aldehyde, a byproduct of the retinoid cycle, from photoreceptor cells
- Mutation in *ABCA4* gene results in Stargardt disease. Different *ABCA4* alleles have been identified to cause other retinopathies such as cone-rod dystrophy type 3 (CORD 3), retinitis pigmentosa type 19 (RP 19)

## No treatment options exist

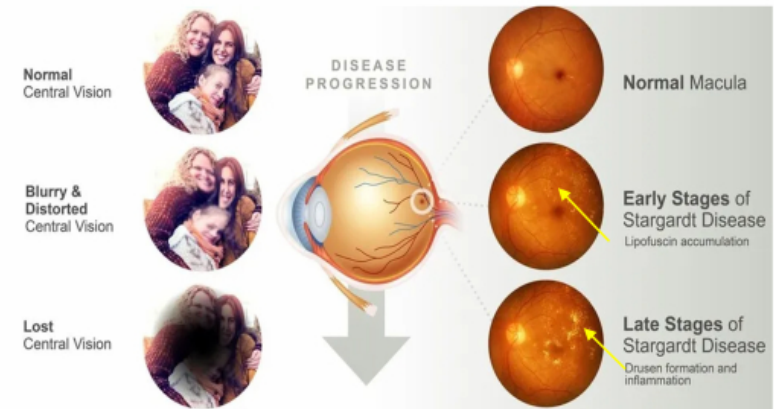
- U.S.: 44,000 patients\*

## Modifier gene therapy platform addresses shortcomings of current approaches

- AAV delivery platform delivers *RORA* (RAR Related Orphan Receptor A)
- Broad-spectrum, gene-agnostic approach
- Potential one-time, curative therapy with a single sub-retinal injection

## Currently dosing patients in Phase 1/2 GARDian clinical trial of OCU410ST

- Completed dosing of patients in cohort 2 (medium dose) and DSMB approved enrollment in cohort 3 in the dose-escalation phase of the study



\*P Kohli et al., StatPearls, 2024. <https://www.ncbi.nlm.nih.gov/books/NBK587351/>

# NeoCart<sup>®</sup>

Autologous chondrocyte-derived neocartilage



# NeoCart®: U.S. FDA Agreed to Proposed Control and Overall Design for Phase 3 Trial

## NeoCart is a regenerative cell therapy

- Received RMAT designation
- Combines bioengineering and cell processing to enhance autologous cartilage repair
- Potential to accelerate healing and reduce pain through reconstructing damaged knee cartilage

## High prevalence of knee cartilage damage, with progression to osteoarthritis (OA)

- Arthroscopic knee procedures: over 1M annually\*
- OA: 528M diagnosed worldwide
- Cell therapy global revenue forecast: \$45B+, with North America expected to hold largest share\*\*

## Current therapies to treat cartilage damage in the knee suboptimal

- Varying outcomes due to variable cellular responses
- Current standard of care suffers from one or more of the following: pain, reduced knee function, failure to address cartilage damage, donor tissue availability, open surgery

## NeoCart potentially addresses shortcomings of current treatments

- Treat pain, improve function, and prevent progression to OA
- Potential for improved efficacy, long-term benefits

## Program advancing on several fronts

- Received FDA concurrence on confirmatory trial design of Phase 3 (plan to initiate contingent upon available funding)
- Construction of cGMP manufacturing facility complete

## Follow-up Arthroscopy Demonstrates NeoCart® Progression and Integration\*\*



Initial Lesion



Time Zero Implantation



8 Weeks



6 Months



\*Journal of Bone & Joint Surgery: June 1, 2011 - Volume 93 - Issue 11 - p 994-1000

\*\*<https://www.biospace.com/article/cell-therapy-market-size-cagr-trends-forecast-report-2022-2030/>

# OCU500 Series

OCU500: COVID-19 Mucosal Vaccine

OCU510: Flu

OCU520: COVID-19/Flu

# OCU500 Series: Next-Generation Vaccine Technology

## *Inhaled mucosal vaccine platform based on ChAd vector*

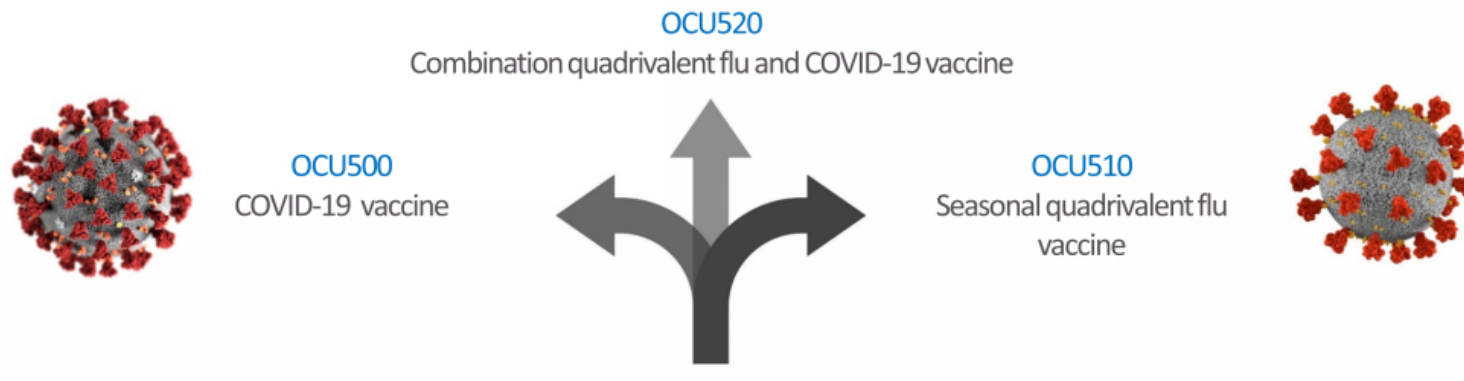
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### Inhalation technology as a differentiator

- Multiple preclinical studies using Ocugen's vector demonstrated vaccine-induced high neutralizing and effector responses
- Clinical studies using a similar vector administered via the inhalation platform showed mucosal antibodies, systemic antibodies, and durable immune response up to 1 year with 1/5 of the dose compared to the same vaccine given via intramuscular administration
- The inhaled method offers the potential for broad, durable protection from severe disease and reduction in transmission

### Alignment with American Pandemic Preparedness Plan to transform U.S. capabilities to rapidly and effectively respond to existing and emerging infectious diseases

- Legislative advocacy for next-generation mucosal vaccine development
- OCU500 was selected by the NIH/NIAID Project NextGen for inclusion in clinical trials. NIAID is planning to submit an IND and initiate the Phase 1 clinical trial this year.



## 2024 Near-Term Targeted Milestones

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- OCU400 Phase 3 dosing and recruitment updates – 2026 BLA/MAA approval targets on track
- Preliminary safety/efficacy updates – OCU410 Phase 1/2 clinical trial (GA)
- Preliminary safety/efficacy updates – OCU410ST Phase 1/2 clinical trial (Stargardt Disease)

# Ocugen™ Vision

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Fully integrated, patient-centric biotech company focused on vaccines in support of public health and gene and cell therapies targeting unmet medical needs through **Courageous Innovation**

