

IVERIC  
BIO

DEVELOPING TRANSFORMATIVE  
THERAPIES  
FOR RETINAL DISEASES

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May 2022

NASDAQ: ISEE

# Forward looking statements

Any statements in this presentation about the Company's expectations, plans and prospects constitute forward-looking statements for purposes of the safe harbor provisions under the Private Securities Litigation Reform Act of 1995. Forward-looking statements include any statements about the Company's strategy, future operations and future expectations, plans and prospects, and any other statements containing the words "anticipate," "believe," "estimate," "expect," "intend", "goal," "may", "might," "plan," "predict," "project," "seek," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions.

In this presentation, the Company's forward looking statements include statements about its expectations regarding availability of top-line data from and patient retention in its second Phase 3 trial (GATHER2) of Zimura in geographic atrophy secondary to AMD, its ability to use its completed clinical trial of Zimura for the treatment of geographic atrophy secondary to AMD (GATHER1) as a Phase 3 trial for purposes of seeking regulatory approval, its development and regulatory strategy for Zimura and its other product candidates, including additional indications, such as intermediate AMD, that the Company may pursue for the development of Zimura and IC-500, its ability to obtain the first marketing approval for the treatment of geographic atrophy and its expectations regarding the market dynamics for the treatment of GA and other commercial matters, the Company's hypotheses regarding complement inhibition and HtrA1 inhibition as potential mechanisms of action for the treatment of retinal diseases, the implementation of its business and hiring plan, expectations regarding its cash and financial resources, the timing, progress and results of clinical trials and other research and development activities, including regulatory submissions, the clinical meaningfulness of clinical trial results, the potential utility of its product candidates, estimates regarding the number of patients affected by the diseases and indications the Company's product candidates are intended to treat and statements regarding the potential for the Company's business development strategy.

Such forward-looking statements involve substantial risks and uncertainties that could cause the Company's research and development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, those related to the progression and duration of the COVID-19 pandemic and responsive measures thereto and related effects on the Company's research and development programs, operations and financial position, expectations for regulatory matters, the initiation and the progress of research and development programs and clinical trials, including enrollment and retention in clinical trials, availability of data from these programs, reliance on contract development and manufacturing organizations, contract research organizations and other third parties, establishment of manufacturing capabilities, developments from the Company's competitors and the marketplace for the Company's products, human capital matters, need for additional financing and other factors discussed in the "Risk Factors" section contained in the quarterly and annual reports that the Company files with the Securities and Exchange Commission.

Any forward-looking statements represent the Company's views only as of the date of this presentation. The Company anticipates that subsequent events and developments may cause its views to change. While the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so except as required by law.

Positioned  
to be the  
leader in  
retina

## Therapeutics for Age-Related Retinal Diseases (Large Market)

- Zimura (C5 inhibitor):
  - Positive data for the first of two Phase 3 trials (GATHER1)
    - Statistically significant 27% reduction in GA growth over 12 months (primary endpoint achieved)
  - Completed patient enrollment for second Phase 3 trial (GATHER2) in July 2021; topline data expected in 3Q2022
  - Received Special Protocol Assessment (SPA) from FDA for GATHER2
  - Plan to file for NDA/MAA approvals following positive 12-month GATHER2 data
  - Commercial planning underway; potential for market leading position
  - Plan to initiate clinical development in intermediate AMD in 4Q2022 with additional lifecycle initiatives ongoing
- IC-500 (HtrA1 Inhibitor): Complementary MOA adding to development stage AMD franchise

### Cash Position

- Expected YE 2022 cash: \$215 million - \$225 million\*

\*Estimate as of 5/4/22

# STRONG SENIOR TEAM WITH SIGNIFICANT OPHTHALMOLOGY EXPERIENCE

<b>GLENN SBLENDORIO</b> Chief Executive Officer					
<b>PRAVIN DUGEL, MD</b> President					
<b>DAVID CARROLL</b> Chief Financial Officer					
<b>TONY GIBNEY</b> Chief Business & Strategy Officer					
<b>KEITH WESTBY</b> Chief Operating Officer					
<b>XIAO-PING DAI, PhD</b> Chief Technical Officer					
<b>CHRISTOPHER SIMMS</b> Chief Commercial Officer					
<b>EVELYN HARRISON</b> Chief Clinical Operations Officer					
<b>DHAVAL DESAI, PHARM D</b> Chief Development Officer					
<b>SNEHAL SHAH, PHARM D</b> Chief Regulatory and Pharmacovigilance Officer					

# Iveric Bio Pipeline

Preclinical

Phase 1

Phase 2

Phase 3

## THERAPEUTICS PIPELINE

## Status/Milestones

**Avacincaptad pegol (ZIMURA)**  
Geographic atrophy (GA)



GATHER1 (1<sup>st</sup> Phase 3): Positive 12 & 18 month data reported  
GATHER2 (2<sup>nd</sup> Phase 3): enrollment complete and SPA received; top-line data expected **3Q 2022**

**Avacincaptad pegol (ZIMURA)**  
Intermediate AMD



Plan to initiate in **4Q 2022** following regulatory interactions

**Avacincaptad pegol (ZIMURA)**  
Autosomal recessive Stargardt disease (STGD1)



Expanded enrollment (up to ~25 additional patients); trial on-going

**IC-500: HtrA1 inhibitor**  
GA



Plan to file IND in **mid-2023**

## AAV GENE THERAPY PIPELINE

**IC-100: RHO-adRP**  
Rhodopsin-mediated autosomal dominant RP



Evaluating development options  
Seeking collaborator

**IC-200: BEST1-Related IRDs**



Evaluating development options  
Seeking collaborator

**mini-CEP290: LCA10**  
Leber congenital amaurosis type 10



Evaluating development options

**mini-ABCA4: STGD1\***  
Autosomal recessive Stargardt disease (STGD1)



Additional research ongoing

**mini-USH2A\***  
Usher syndrome type 2A



Additional research ongoing

\*IVERIC bio has an option to exclusively in-license intellectual property resulting from these programs.



# AGE-RELATED MACULAR DEGENERATION (AMD)

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Disease Overview & Market Size



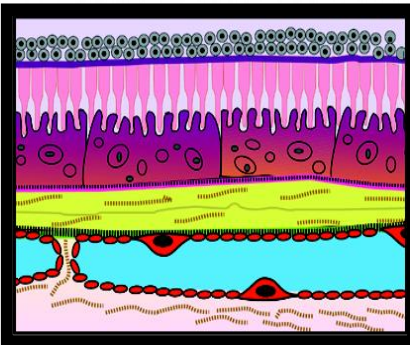
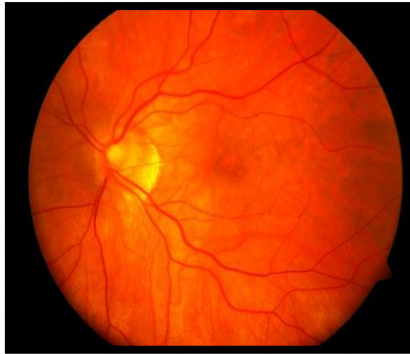
# AMD LEADS TO PROGRESSIVE VISION LOSS WITH END-STAGE ATROPHY

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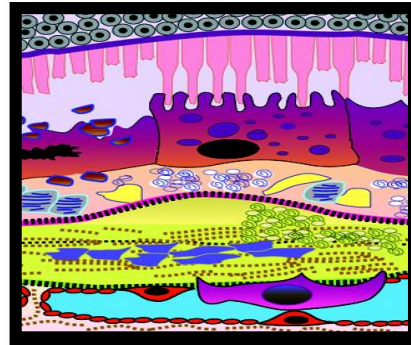


# COMMON PERCEPTION: ADVANCED AMD IS EITHER DRY (LEADING TO GA) OR WET

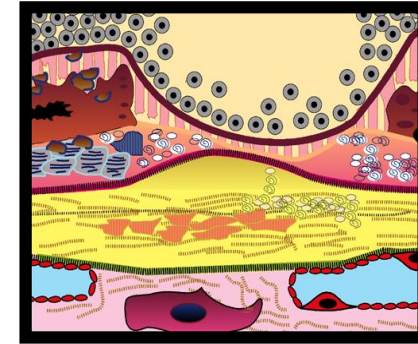
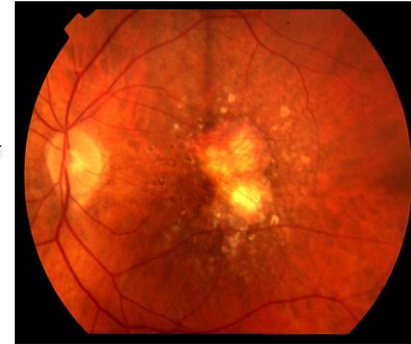
NORMAL



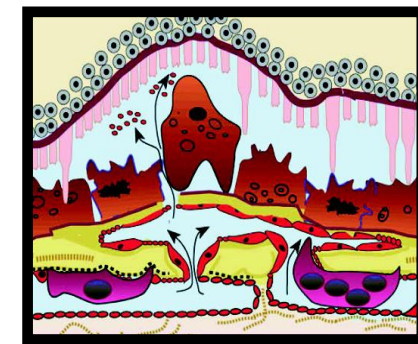
EARLY DRY AMD DEPOSITS



LATE DRY AMD "GEOGRAPHIC ATROPHY"

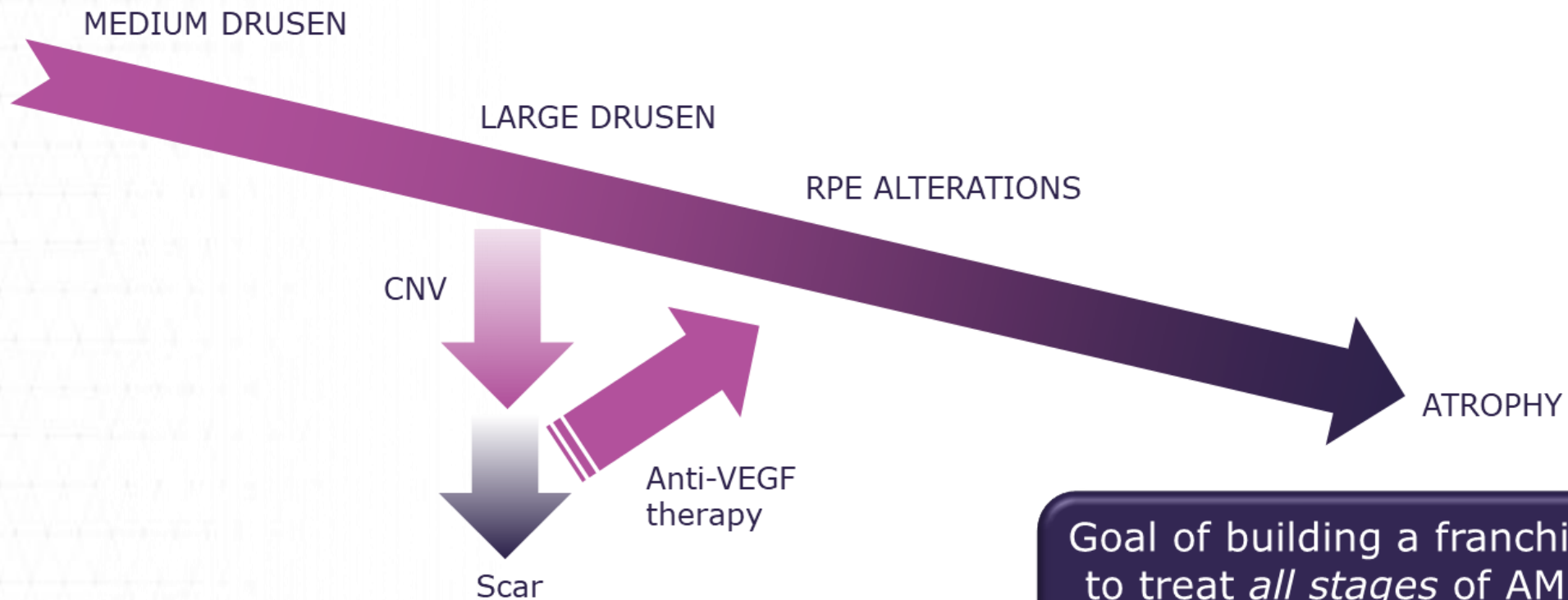


"NEOVASCULAR" AMD





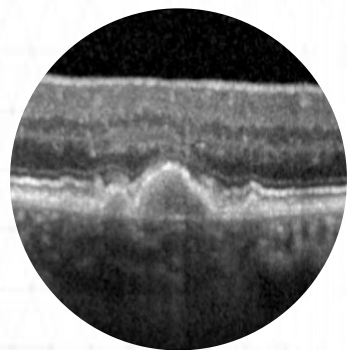
# Pathway of AMD disease progression



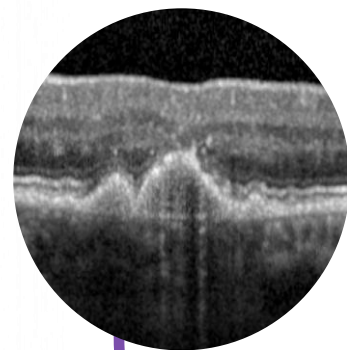
Goal of building a franchise to treat *all stages* of AMD with Zimura and IC-500 (HtrA1 inhibitor)

# Pathway of AMD disease progression

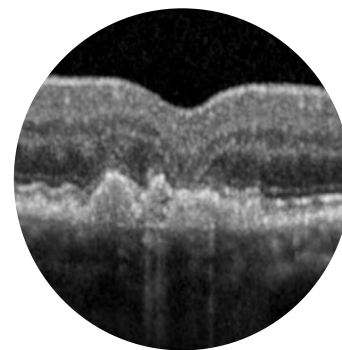
**Medium drusen**  
(Early AMD)



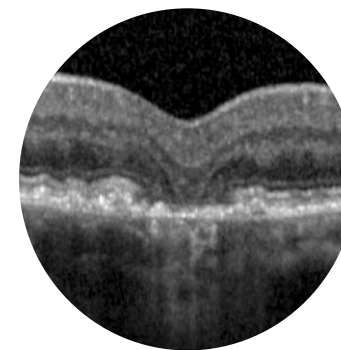
**Large drusen**  
(Intermediate AMD)



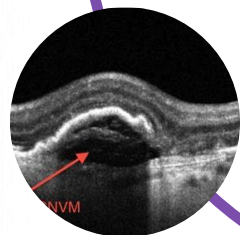
**RPE alterations**  
(iRORA)



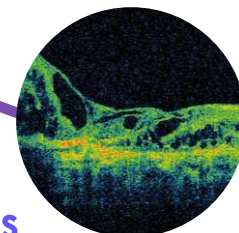
**Atrophy**  
(cRORA)



**CNV**  
(Wet AMD)



**Anti-VEGF**  
**therapy**

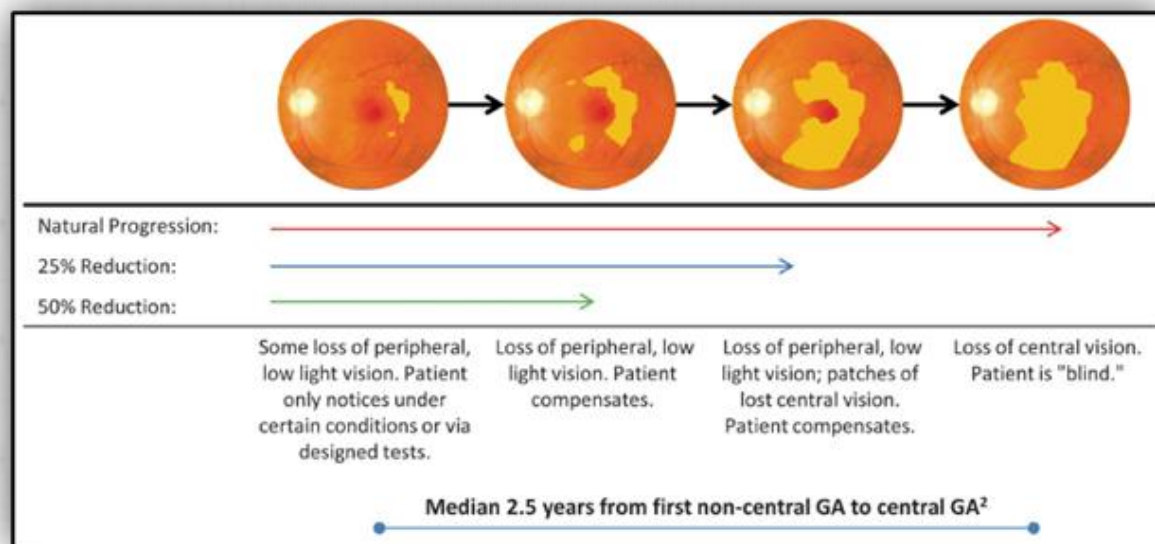


**Fibrosis**

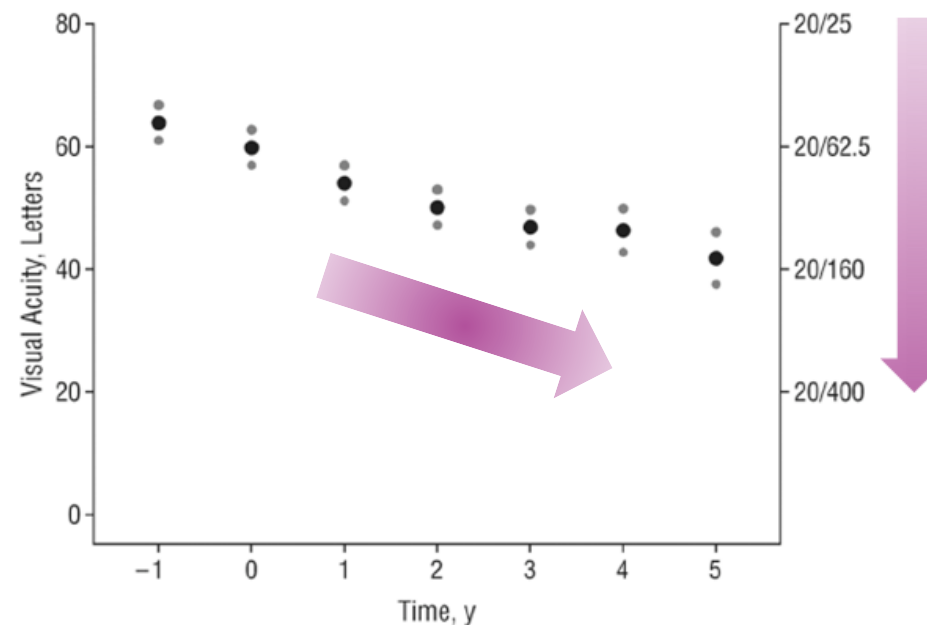
# Growth rate and loss of vision depend on GA location

## Geographic Atrophy: loss of photoreceptors over time

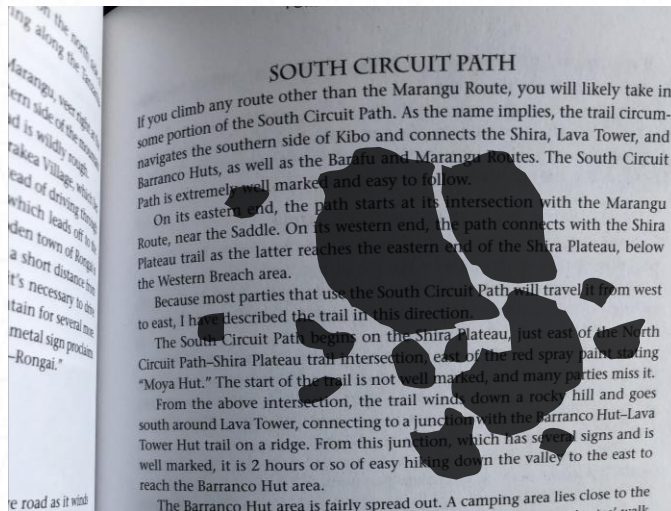
### Increase In Area of Degeneration Over Time



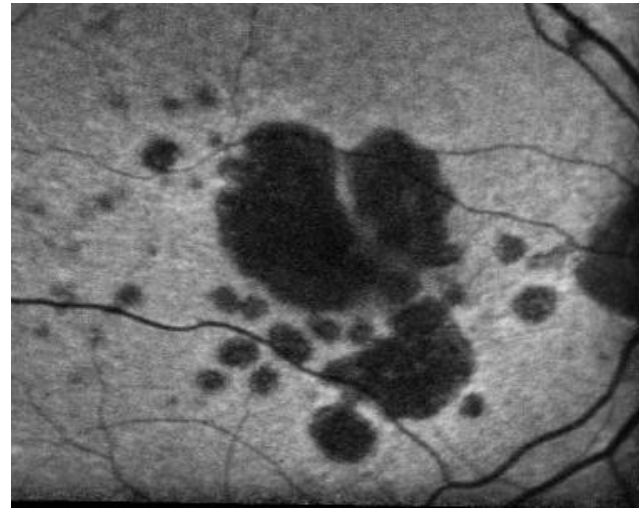
### Loss of Vision Over Time



# GEOGRAPHIC ATROPHY: IMPACT ON FUNCTIONAL VISION IN DAILY LIFE



**Areas of missing vision  
(scotoma)**

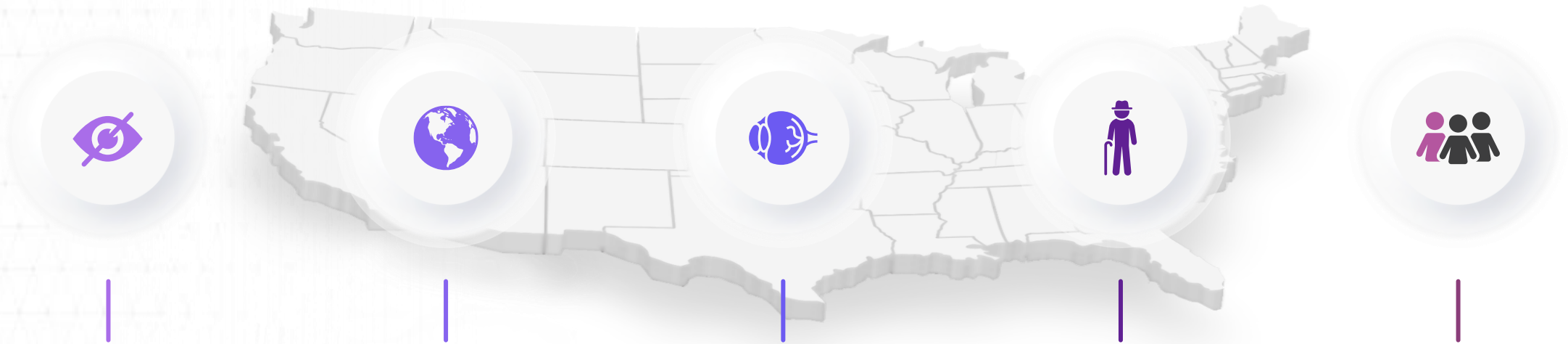


**Areas of geographic atrophy  
(Dead retinal cells)**



**Areas of missing vision  
(scotoma)**

# GA severely impacts vision in ~1.5 million patients in the US alone



Leading cause of central vision loss in individuals over 50 years old in developed countries<sup>1</sup>

Severely affects vision and often threatens complete vision loss in an estimated **1.5 million** individuals in the United States and **5 million** individuals worldwide<sup>2</sup>

Early signs of retinal changes are seen in individuals as young as **30–40 years old**<sup>3</sup>

Studies show **GA severity increases with age**<sup>1</sup>

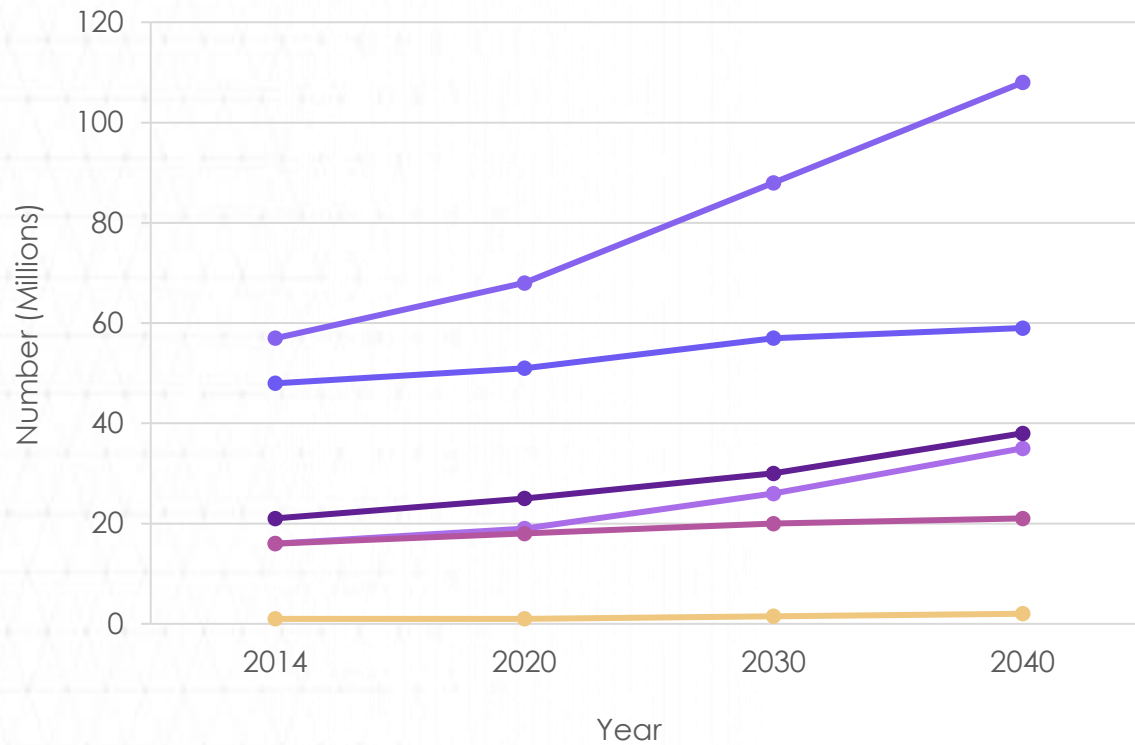
**One-third of the population is affected by GA** by the time individuals are 80 years old<sup>3</sup>



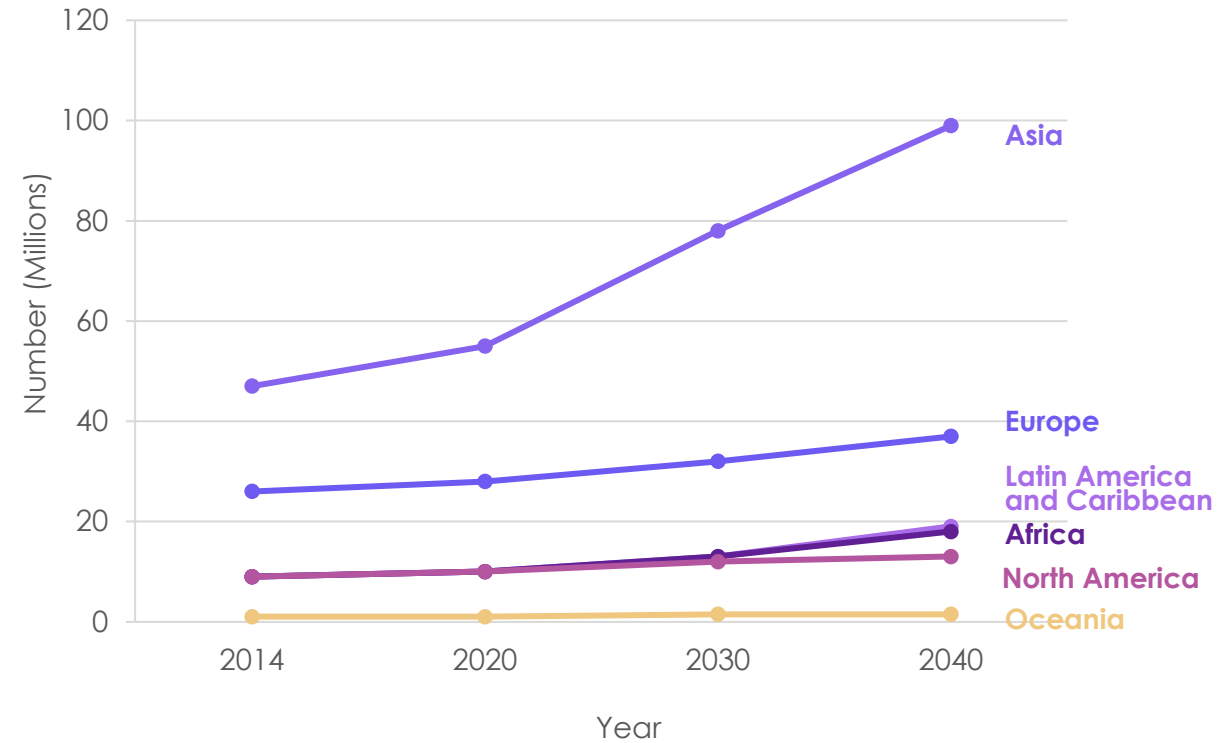
# AMD is projected to increase in global prevalence

Projected number of individuals with AMD by region<sup>1</sup>

## Early AMD



## Late AMD





# COMPLEMENT ACTIVATION IN GA

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What We Know About the Role of Complement in the Pathogenesis of GA

# Genetic link: Complement & AMD

## Complement Factor H Polymorphism in Age-Related Macular Degeneration

Robert J. Klein<sup>1</sup>, Caroline Zeiss<sup>2,\*</sup>, Emily Y. Chew<sup>3,\*</sup>, Jen-Yue Tsai<sup>4,\*</sup>, Richard S. Sackler<sup>1</sup>, Chad Haynes<sup>1</sup>, Alice K. Henning<sup>5</sup>, John Paul SanGiovanni<sup>3</sup>, Shrikant M. Mane<sup>6</sup>, Susan T. Mayne<sup>7</sup>, Michael B. Bracken<sup>7</sup>, Frederick L. Ferris<sup>3</sup>, Jurg Ott<sup>1</sup>, Colin Barnstable<sup>2</sup>, and Josephine Hoh.<sup>7,†</sup>

“In individuals homozygous for the risk allele, the likelihood of AMD is increased by a factor of 7.4” \*

## THE PATHOPHYSIOLOGY OF GEOGRAPHIC ATROPHY SECONDARY TO AGE-RELATED MACULAR DEGENERATION AND THE COMPLEMENT PATHWAY AS A THERAPEUTIC TARGET

DAVID S. BOYER, MD,\* URSULA SCHMIDT-ERFURTH, MD,† MENNO VAN LOOKEREN CAMPAGNE, PhD,‡ ERIN C. HENRY, PhD,‡ CHRISTOPHER BRITTAIN, MBBS§

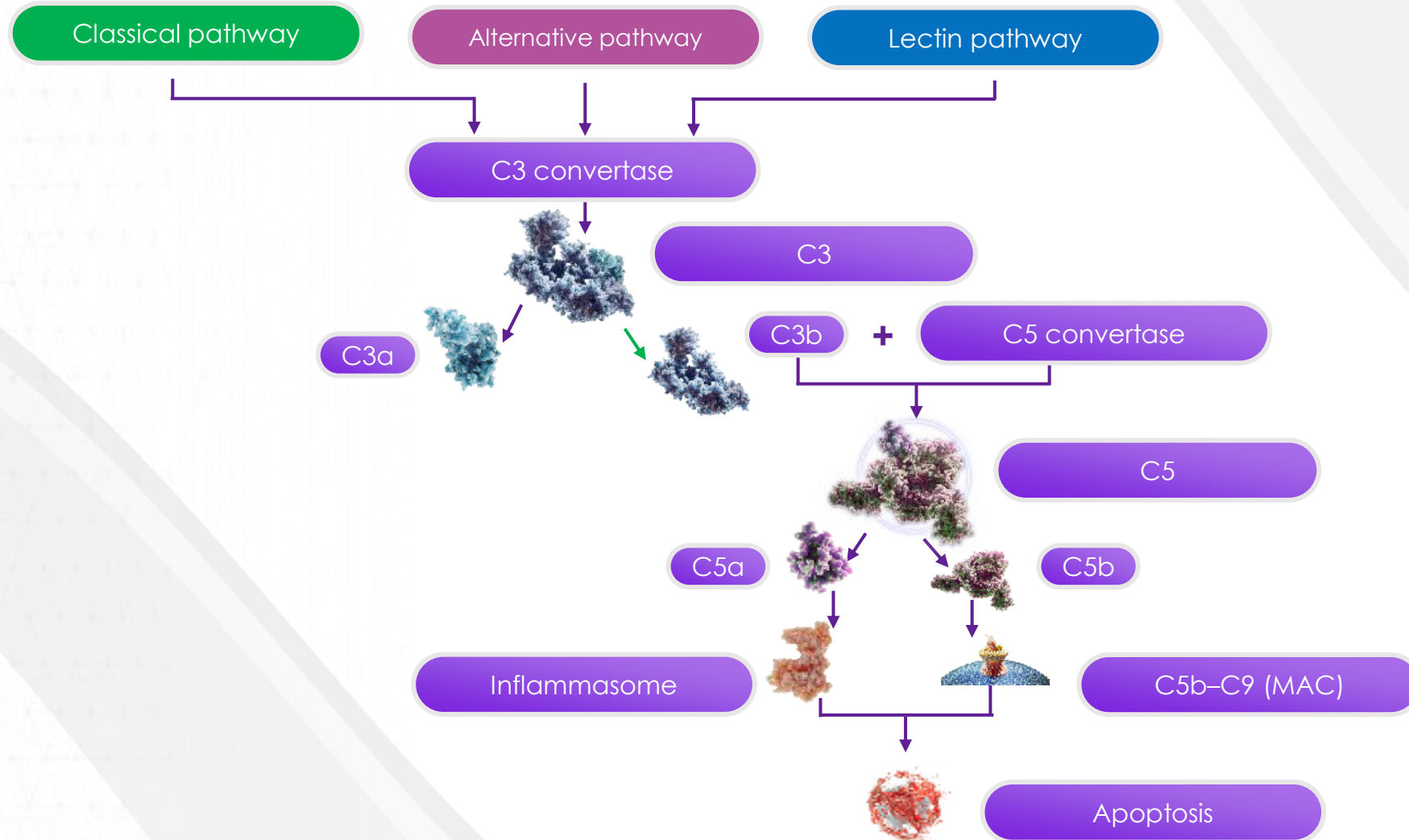
## Complement System in Pathogenesis of AMD: Dual Player in Degeneration and Protection of Retinal Tissue

Milosz P. Kawa,<sup>1</sup> Anna Machalinska,<sup>2,3</sup> Dorota Roginska,<sup>1</sup> and Boguslaw Machalinski<sup>1</sup>

## Complement Activation Levels Are Related to Disease Stage in AMD

Thomas J. Heesterbeek,<sup>1</sup> Yara T. E. Lechanteur,<sup>1</sup> Laura Lorés-Motta,<sup>1,2</sup> Tina Schick,<sup>3</sup> Mohamed R. Daha,<sup>4</sup> Lebriz Altay,<sup>3</sup> Sandra Liakopoulos,<sup>3</sup> Dzenita Smailhodzic,<sup>1</sup> Anneke I. den Hollander,<sup>1,2</sup> Carel B. Hoyng,<sup>1</sup> Eiko K. de Jong,<sup>1</sup> and B. Jeroen Klevering<sup>1</sup>

# Activated complement leads to inflammation and cell death



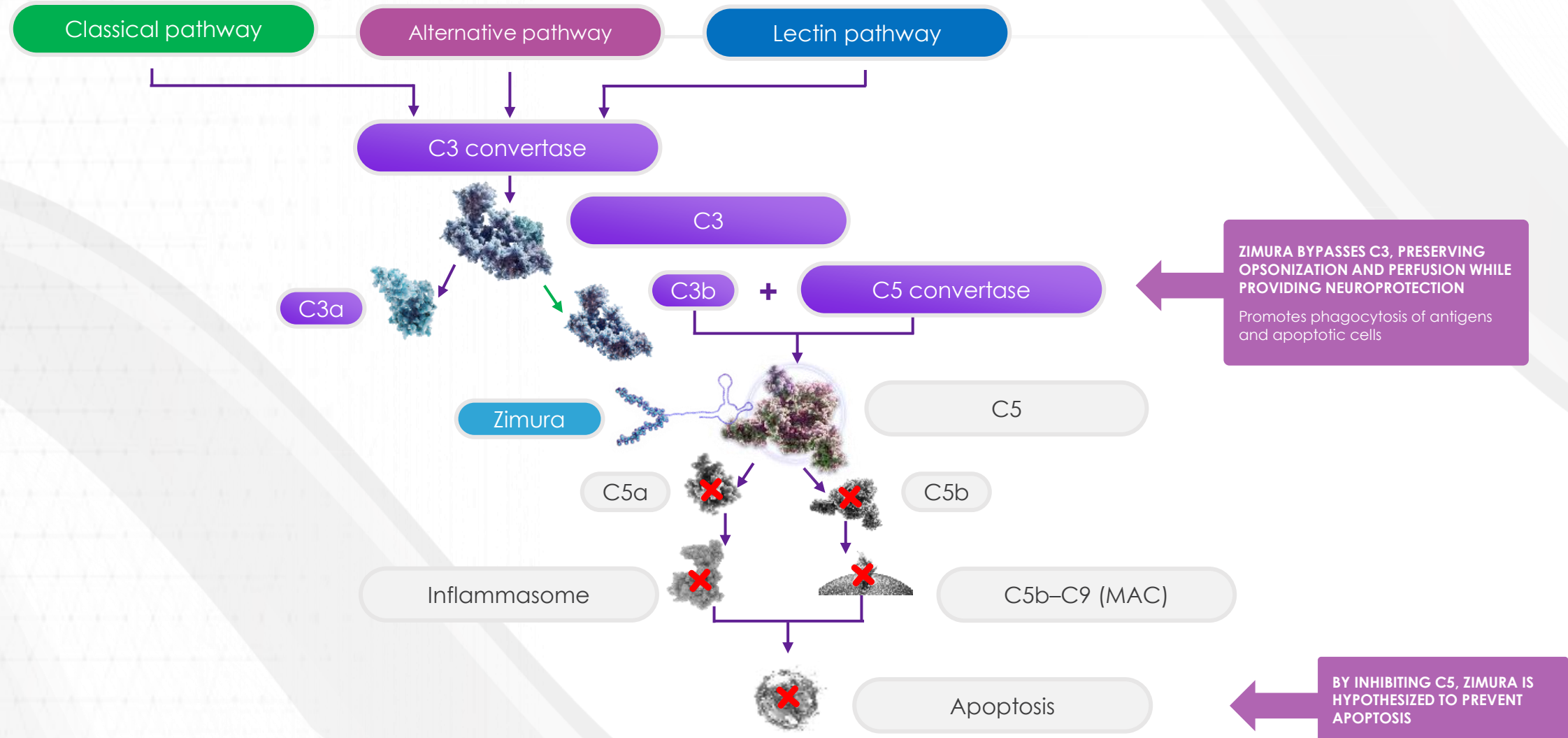
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WHY IS ZIMURA®  
IMPORTANT?

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# Zimura targets C5, inhibiting the 2 triggers of cell death, preserving the remainder of the pathway



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# ZIMURA® PHASE 3 PROGRAM IN GA SECONDARY TO AMD

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**GATHER 1** **GATHER 2**  
Geographic Atrophy Therapy Trial    Geographic Atrophy Therapy Trial

(Geographic Atrophy Therapy Trials)

# GATHER 1 Dosing Regimen

Geographic Atrophy Therapy Trial

Primary Endpoint at Month 12

## PART 1:

	D1	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18	
Zimura 2mg (n=25)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
Zimura 1mg (n=26)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
Sham (n=26)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	

■ Zimura 2mg      ■ Zimura 1mg      ■ Sham

Primary Endpoint at Month 12

## PART 2:

	D1	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18	
Zimura 2mg (n=42)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
Zimura 4mg (n=84)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
Sham (n=83)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	

■ Zimura 2mg +Sham      ■ Zimura 2mg + Zimura 2mg      ■ Sham + Sham

## GATHER1: Key Inclusion Criteria

- Non-foveal GA secondary to dry AMD
- Total GA area  $\geq 2.5$  and  $\leq 17.5$  mm<sup>2</sup> (1 and 7 disk areas [DA] respectively), determined by screening images of FAF
- If GA is multifocal, at least one focal lesion should measure  $\geq 1.25$  mm<sup>2</sup> (0.5 DA)
- GA in part within 1500 microns from the foveal center
- The atrophic lesion must be able to be photographed in its entirety
- Best corrected visual acuity in the SE between 20/25 – 20/320, inclusive

# GATHER1: Primary efficacy endpoint achieved

Mean Rate of Change in Geographic Atrophy (GA) Area from Baseline to Month 12 (MRM Analysis) (Square Root Transformation, ITT Population)

Cohort	Zimura 2mg (N=67)	Sham 2mg (N=110)	Difference	P-value	% Difference
Mean Change in GA <sup>(a)</sup>	0.292 <sup>(c)</sup>	0.402 <sup>(c)</sup>	0.110	0.0072 <sup>(b)</sup>	27.38%

Cohort	Zimura 4mg (N=83)	Sham 4mg (N=84)	Difference	P-value	% Difference
Mean Change in GA <sup>(a)</sup>	0.321	0.444	0.124	0.0051 <sup>(b)</sup>	27.81%



# GATHER 1 Dosing Regimen

Geographic Atrophy Therapy Trial

Primary Endpoint at Month 12

## PART 1:

	D1	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18	
<b>Zimura 2mg</b> (n=25)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
<b>Zimura 1mg</b> (n=26)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
<b>Sham</b> (n=26)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	

■ Zimura 2mg

■ Zimura 1mg

■ Sham

Primary Endpoint at Month 12

## PART 2:

	D1	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18	
<b>Zimura 2mg</b> (n=42)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
<b>Zimura 4mg</b> (n=84)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
<b>Sham</b> (n=83)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	

■ Zimura 2mg +Sham

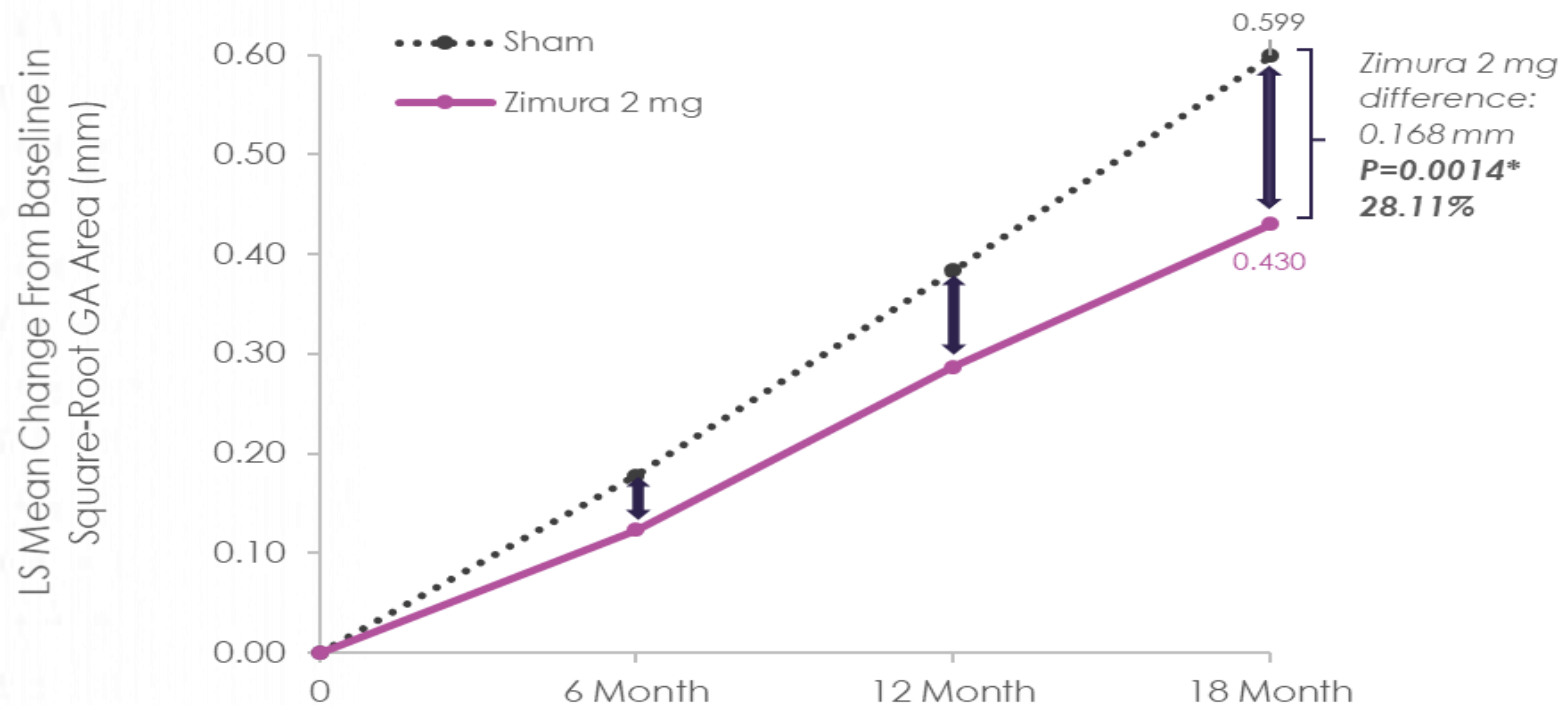
■ Zimura 2mg + Zimura 2mg

■ Sham + Sham

# GATHER1: Decrease in GA growth over 18 months Zimura 2 mg vs. Sham (square root transformation)

MEAN RATE OF GROWTH IN GA AREA AS MEASURED BY SQUARE ROOT TRANSFORMATION OVER 18 MONTHS

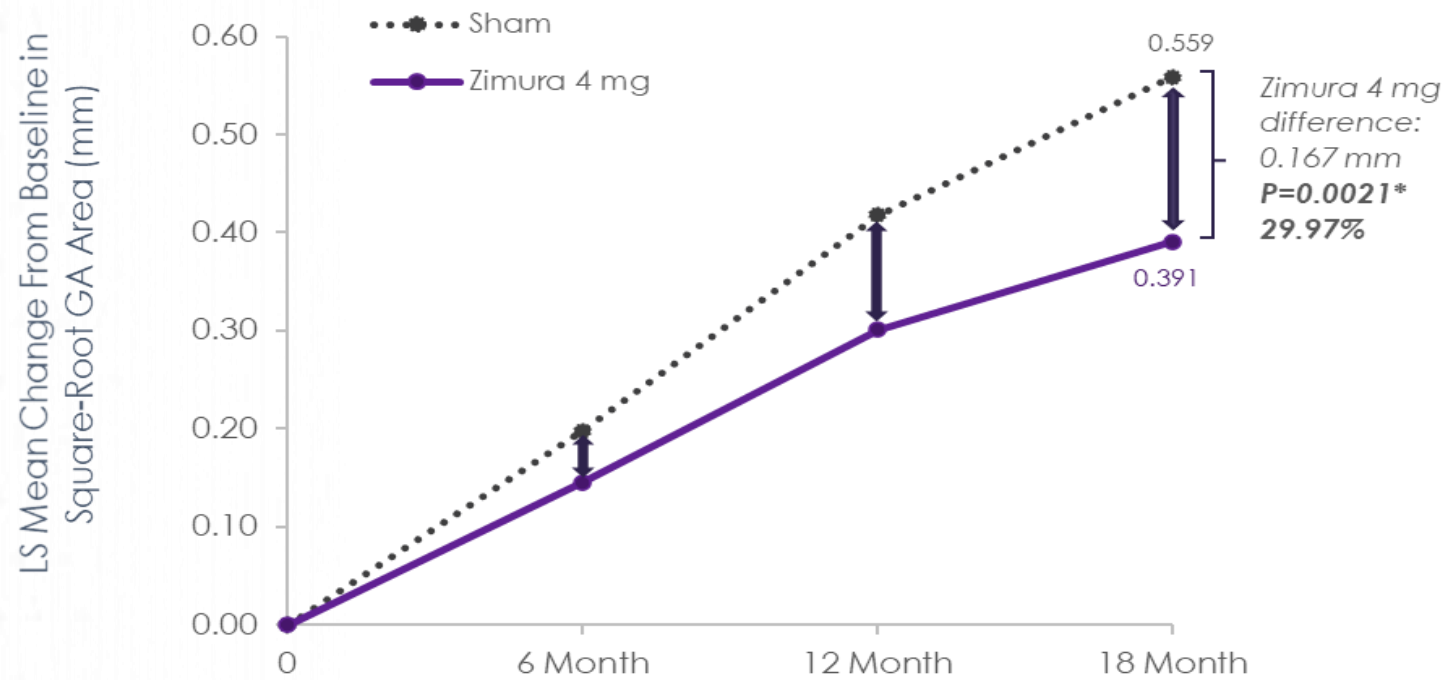
## Zimura 2 mg vs sham



# GATHER1: Decrease in GA growth over 18 months Zimura 4 mg vs. Sham (square root transformation)

MEAN RATE OF GROWTH IN GA AREA AS MEASURED BY SQUARE ROOT TRANSFORMATION OVER 18 MONTHS

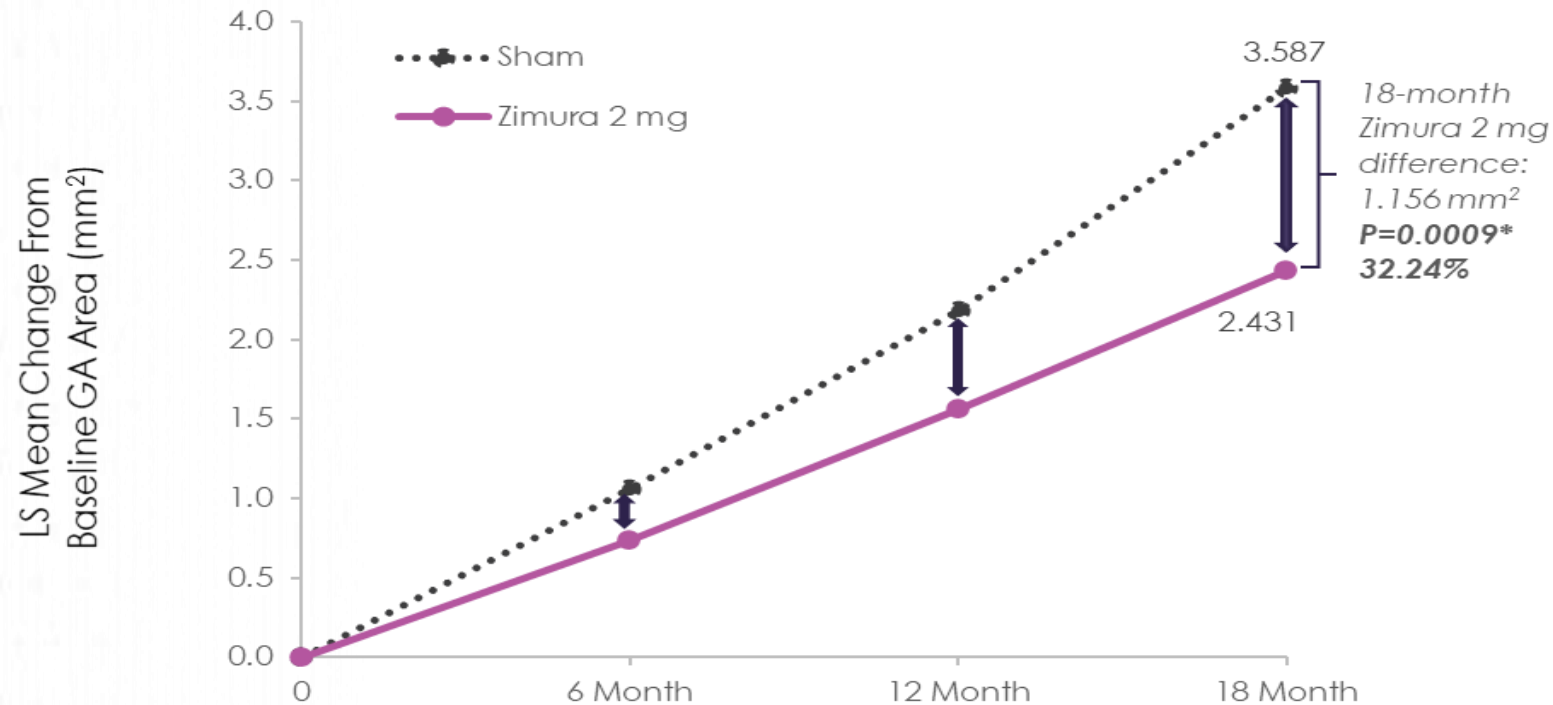
## Zimura 4 mg vs sham



# GATHER1: Decrease in GA growth over 18 months Zimura 2 mg vs. Sham (non-square root transformation)

MEAN RATE OF GROWTH IN GA AREA AS MEASURED BY NON-SQUARE-ROOT GA LESION AREA OVER 18 MONTHS

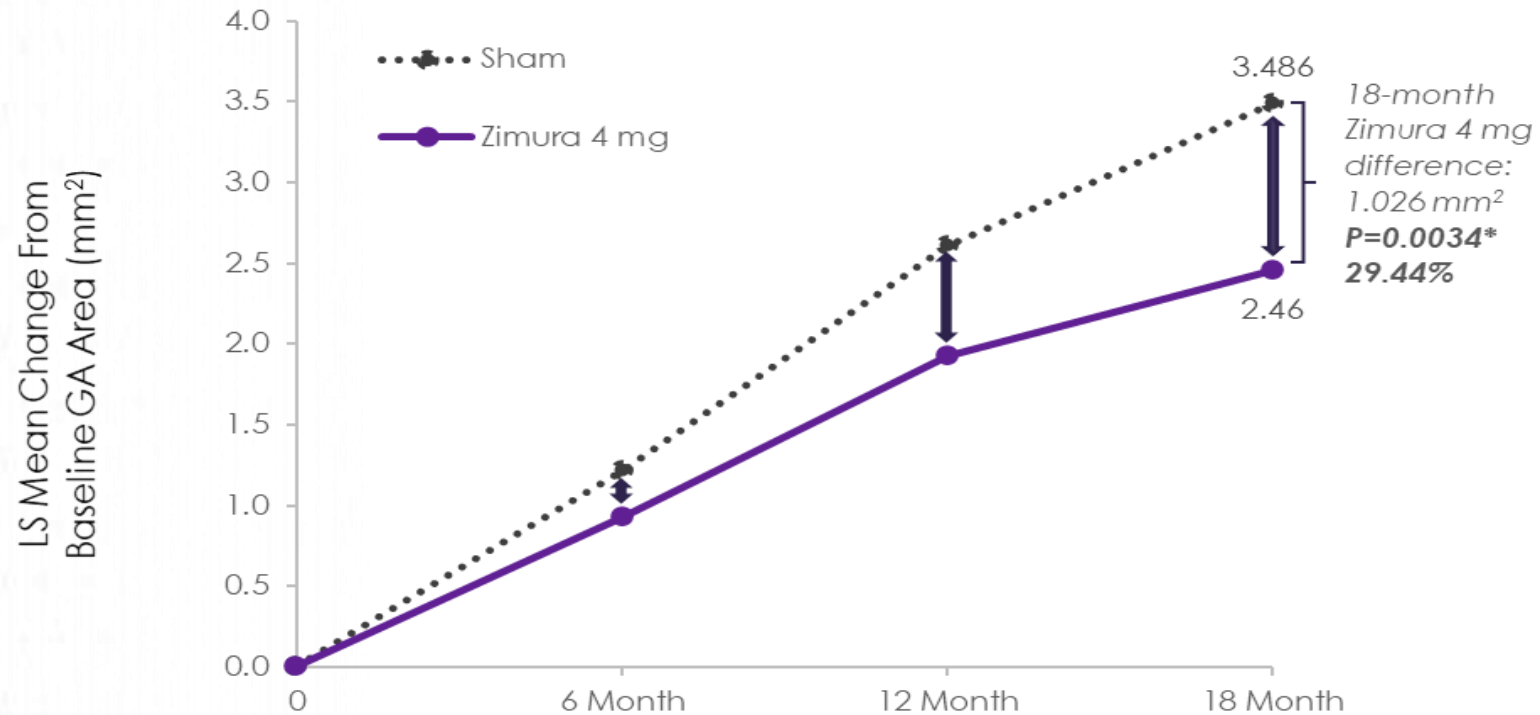
## Zimura 2 mg vs sham



# GATHER1: Decrease in GA growth over 18 months Zimura 4 mg vs. Sham (non-square root transformation)

MEAN RATE OF GROWTH IN GA AREA AS MEASURED BY NON-SQUARE-ROOT GA LESION AREA OVER 18 MONTHS

## Zimura 4 mg vs sham





# Zimura was generally well tolerated over 18 months

✓ Zimura was generally well tolerated after 18 months of continuous administration

✓ No reported Zimura-related inflammation

✓ The most frequently reported ocular adverse events were related to the injection procedure

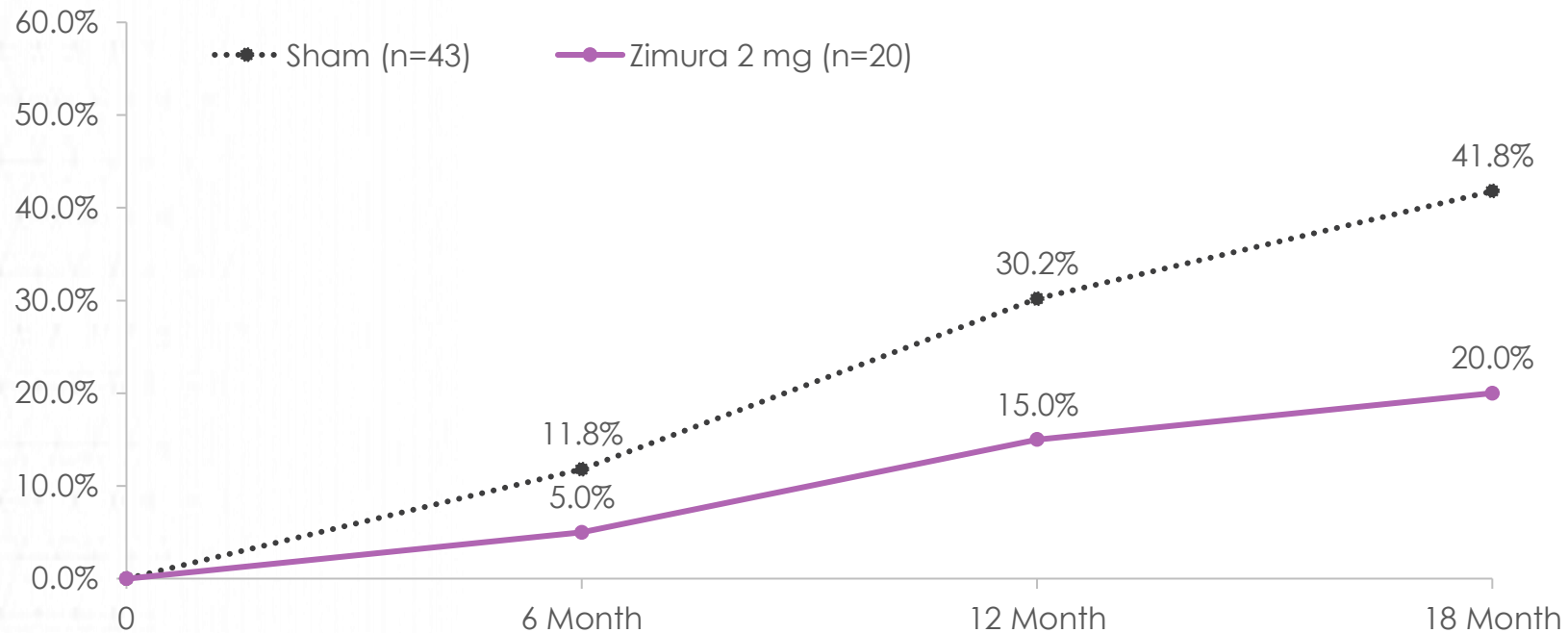
Incidence of study eye CNV:

n (%)	12 months	18 months
Sham	3 (2.7%)	3 (2.7%)
Zimura 1mg	1 (4.0%)	2 (7.7%)
<b>Zimura 2mg</b>	<b>6 (9.0%)</b>	<b>8 (11.9%)</b>
Zimura 4mg	8 (9.6%)	13 (15.7%)

# GATHER 1 Progression of iRORA to cRORA

Geographic Atrophy Therapy Trial

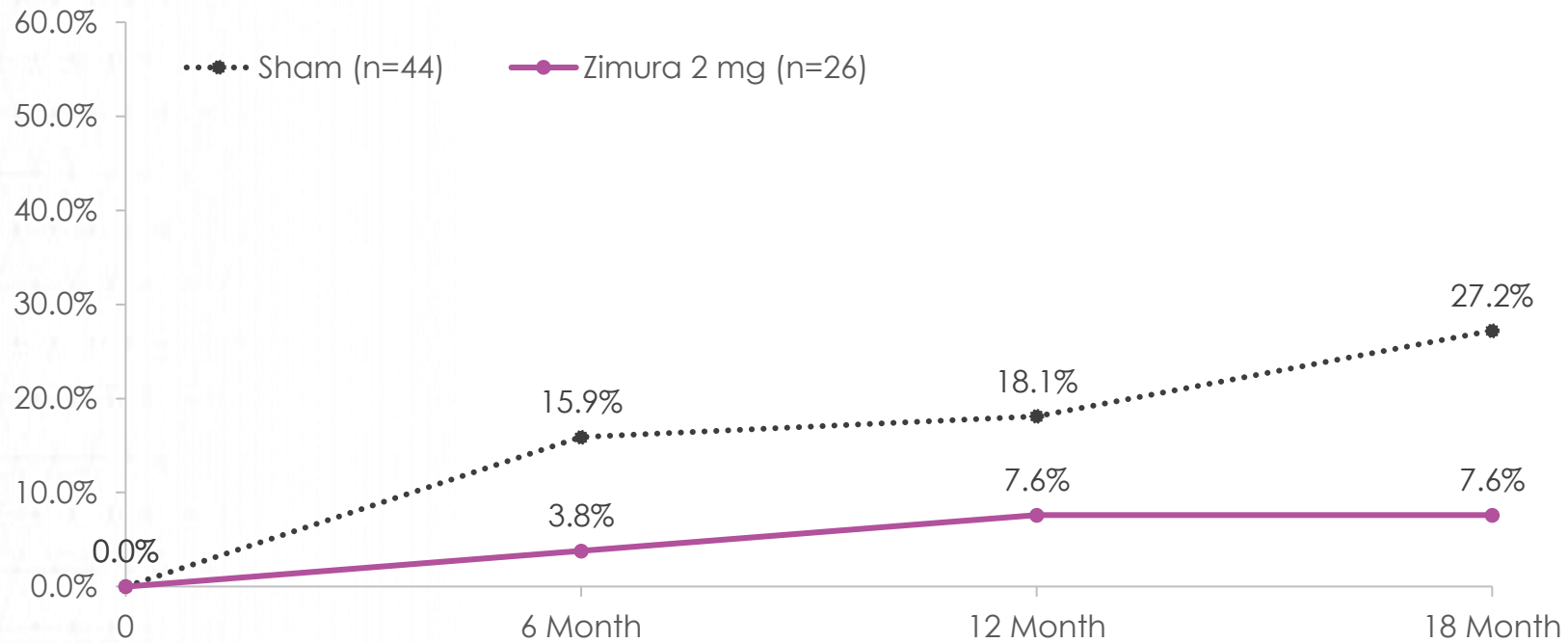
Proportion of patients that progress from iRORA to cRORA (Zimura 2 mg vs. Sham)  
(post-hoc analysis)



# GATHER 1 Progression of Drusen to iRORA/cRORA

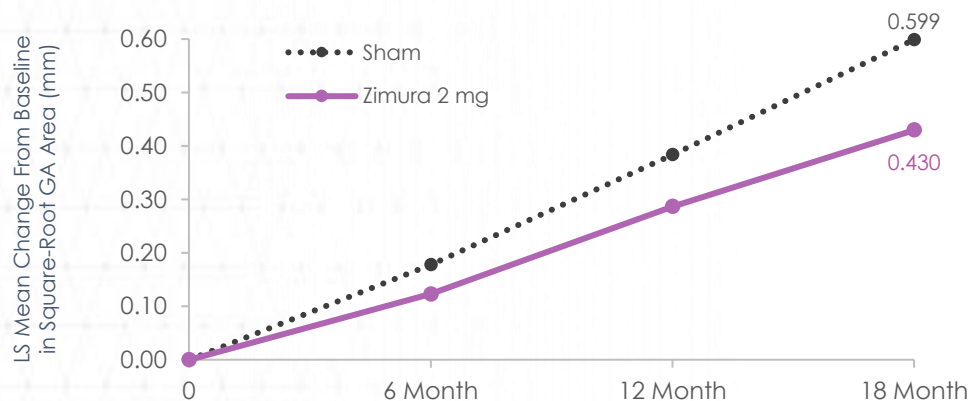
Geographic Atrophy Therapy Trial

Proportion of patients that progress from drusen to iRORA or cRORA (Zimura 2 mg vs. Sham)  
(post-hoc analysis)

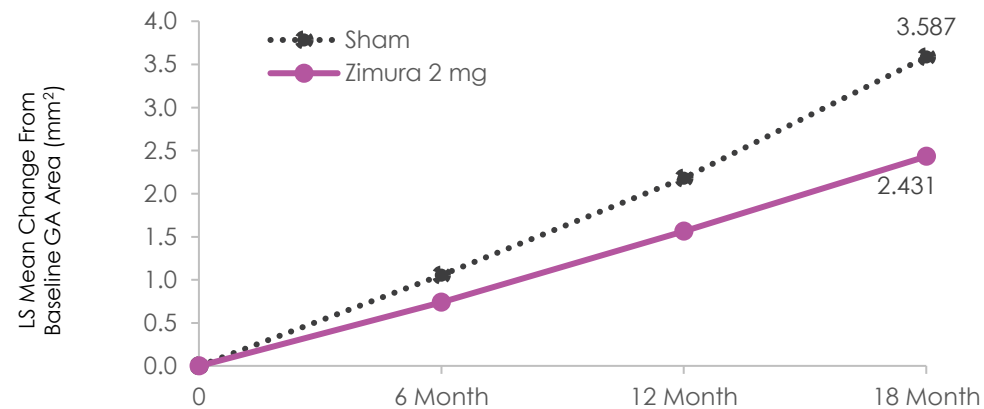


# Potential to alter natural history of disease

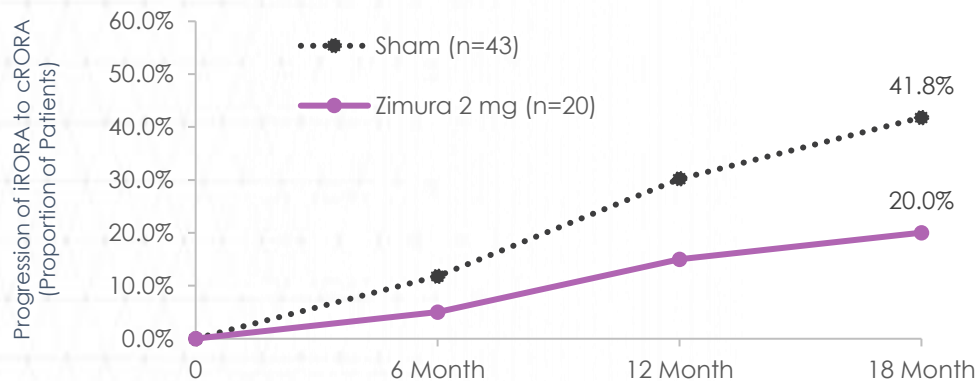
Zimura 2 mg vs sham (square root transformation)



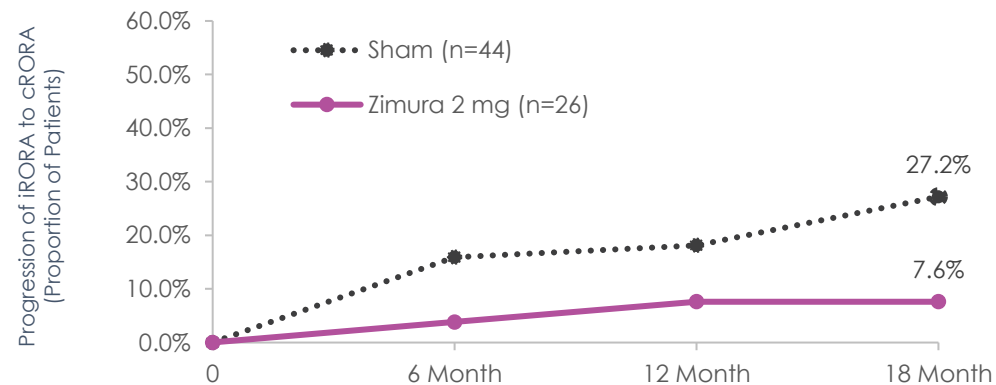
Zimura 2 mg vs sham (non-square root transformation)



Progression of iRORA to cRORA (post-hoc analysis)



Progression of drusen to iRORA/cRORA (post-hoc analysis)



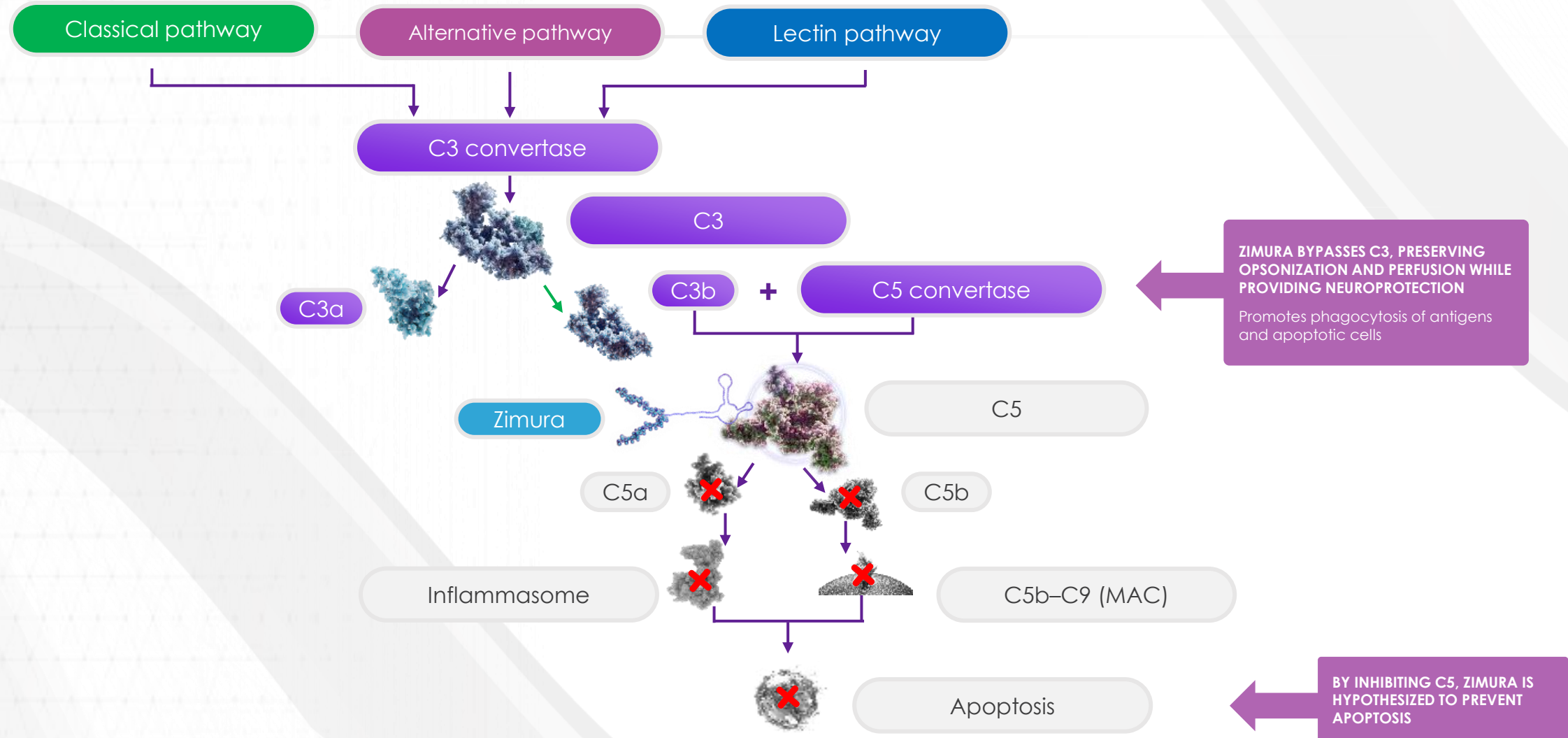


# INHIBITION OF C5

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What Are The Potential Advantages of Inhibiting the Complement System at C5?

# Zimura targets C5, inhibiting the 2 triggers of cell death, preserving the remainder of the pathway





## Inhibition at C5: Potential safety advantages

- ✓ Complement C3a receptors play roles in endotoxemia, ischemia-reperfusion, neurotrauma and ALS models
- ✓ C3aR is protective in these models (knockout worsens disease)
- ✓ C3-CR3 is also protective in a retinal degeneration model
- ✓ Global blockade of C3, as opposed to C5, may prevent the beneficial activities of C3a, while also increasing infection risk

# Inhibition at C5: Potential safety advantages

**“Deficiency of C3 or CR3 decreased microglial phagocytosis of apoptotic photoreceptors and increased microglial neurotoxicity to photoreceptors,...”**

## **C3- and CR3-dependent microglial clearance protects photoreceptors in retinitis pigmentosa**



Sean M. Silverman, Wenxin Ma<sup>✉</sup>, Xu Wang, Lian Zhao<sup>✉</sup>, and Wai T. Wong<sup>✉</sup>

Complement activation has been implicated as contributing to neurodegeneration in retinal and brain pathologies, but its role in retinitis pigmentosa (RP), an inherited and largely incurable photoreceptor degenerative disease, is unclear. We found that multiple complement components were markedly up-regulated in retinas with human RP and the rd10 mouse model, coinciding spatiotemporally with photoreceptor degeneration, with increased C3 expression and activation localizing to activated retinal microglia. Genetic ablation of C3 accelerated structural and functional photoreceptor degeneration and altered retinal inflammatory gene expression. These phenotypes were recapitulated by genetic deletion of CR3, a microglia-expressed receptor for the C3 activation product iC3b, implicating C3-CR3 signaling as a regulator of microglia-photoreceptor interactions. Deficiency of C3 or CR3 decreased microglial phagocytosis of apoptotic photoreceptors and increased microglial neurotoxicity to photoreceptors, demonstrating a novel adaptive role for complement-mediated microglial clearance of apoptotic photoreceptors in RP. These homeostatic neuroinflammatory mechanisms are relevant to the design and interpretation of immunomodulatory therapeutic approaches to retinal degenerative disease.

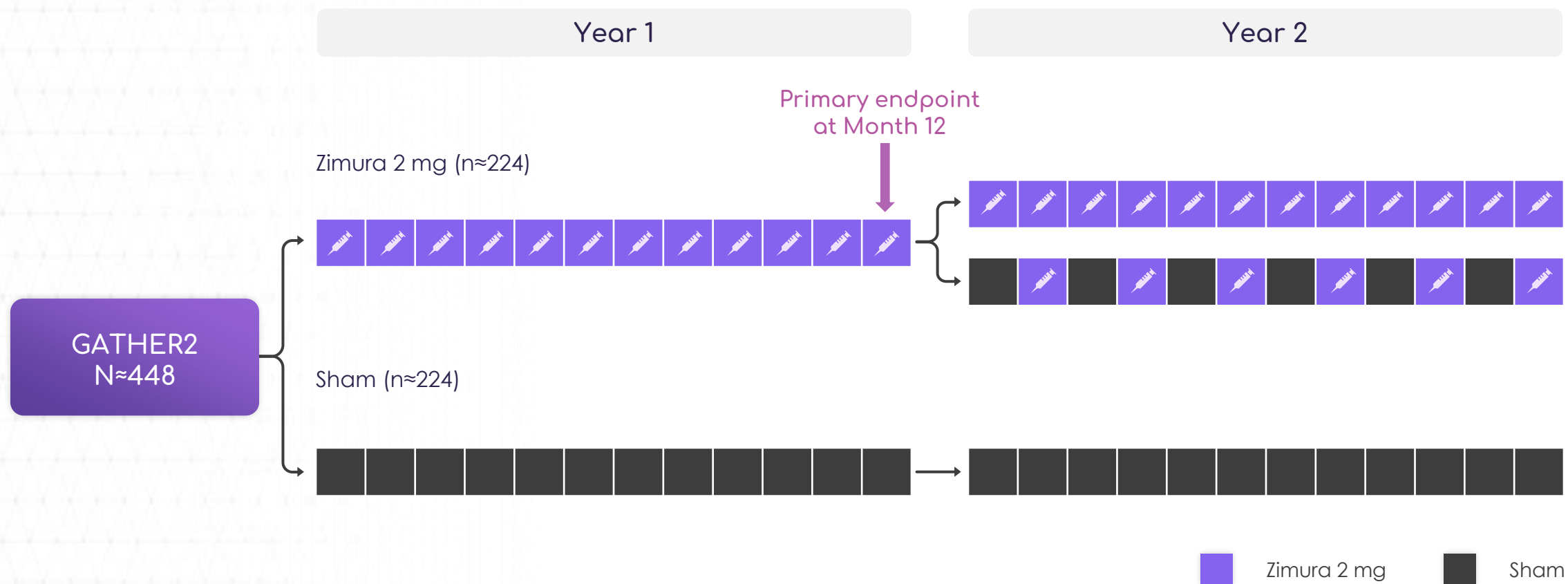
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**GATHER 2**  
Geographic Atrophy Therapy Trial

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Second Pivotal Clinical Trial of Zimura in GA

# GATHER2 Primary endpoint at Month 12



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EXECUTION AND  
REGULATORY CLARITY

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# GATHER2 Enrollment remained strong throughout the pandemic

Time to Complete Enrollment was Four Months Ahead of Original Timeline

## Press Release

Iveric Bio Completes Patient Enrollment of GATHER2 Pivotal Clinical Trial of Zimura® Ahead of Schedule

07.26.2021

*- Topline Data Expected in 2H 2022; if Positive, New Drug Application Expected -*



# Injection fidelity is the most meaningful marker of patient retention

## GATHER 1

12-Month Injection Fidelity Rate

87%

## GATHER 2

Target 12- Month Injection Fidelity Rate

> 90%

**Injection Fidelity Calculation:**  
Total Number of Injections or Sham Administered  
÷  
Total Number of expected injections or Sham

# GATHER2 Regulatory path

First Known Special Protocol Assessment in GA

## Press Release

Iveric Bio Receives FDA Agreement Under Special Protocol Assessment (SPA) for GATHER2 Phase 3 Clinical Trial of Zimura® in Geographic Atrophy Secondary to Age-Related Macular Degeneration

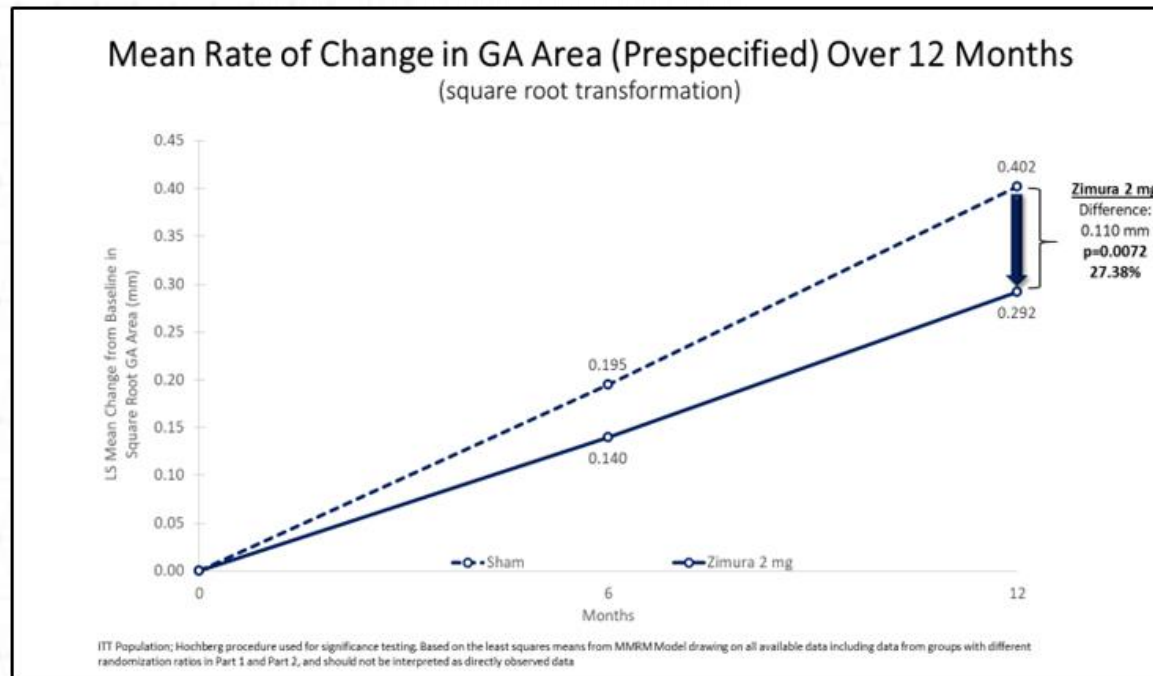
07.06.2021

*- GATHER2 Enrollment and Retention Continue to Exceed Expectations; Completion of Enrollment Expected Late July of this Year and Topline Data Expected Second Half of 2022 -*

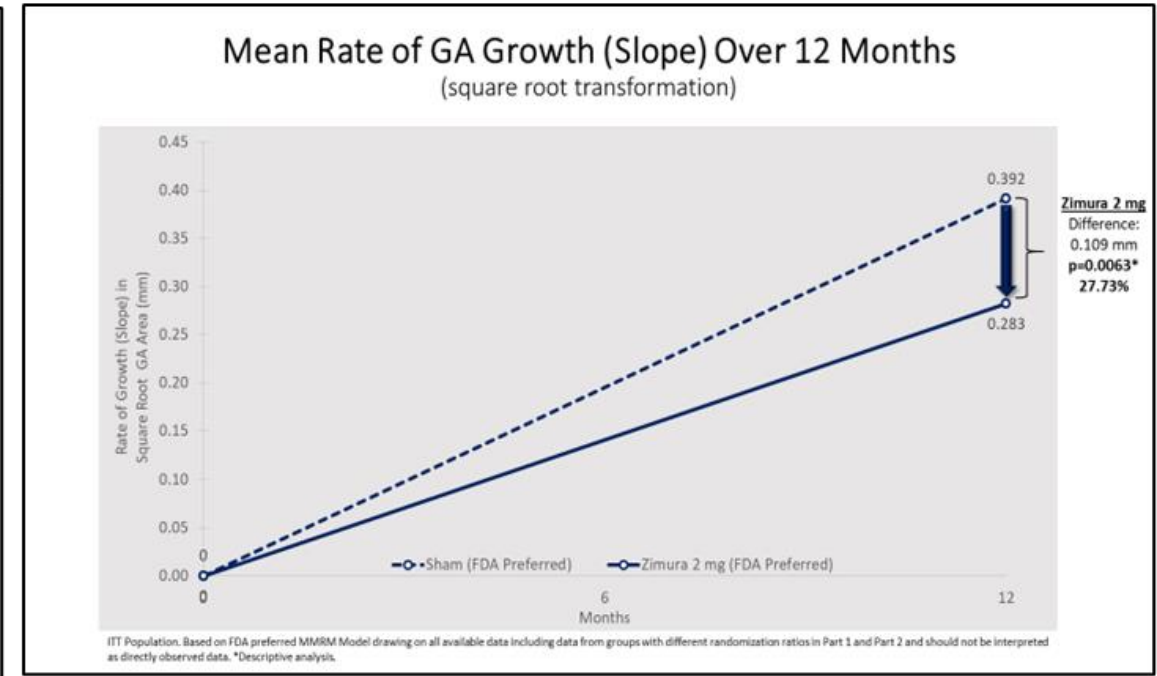
# GATHER1: 2mg vs. sham mean rate of change in GA area (pre-specified) and mean rate of GA growth (slope) (post-hoc)

## FDA Preferred Analysis Supports Prespecified Analysis

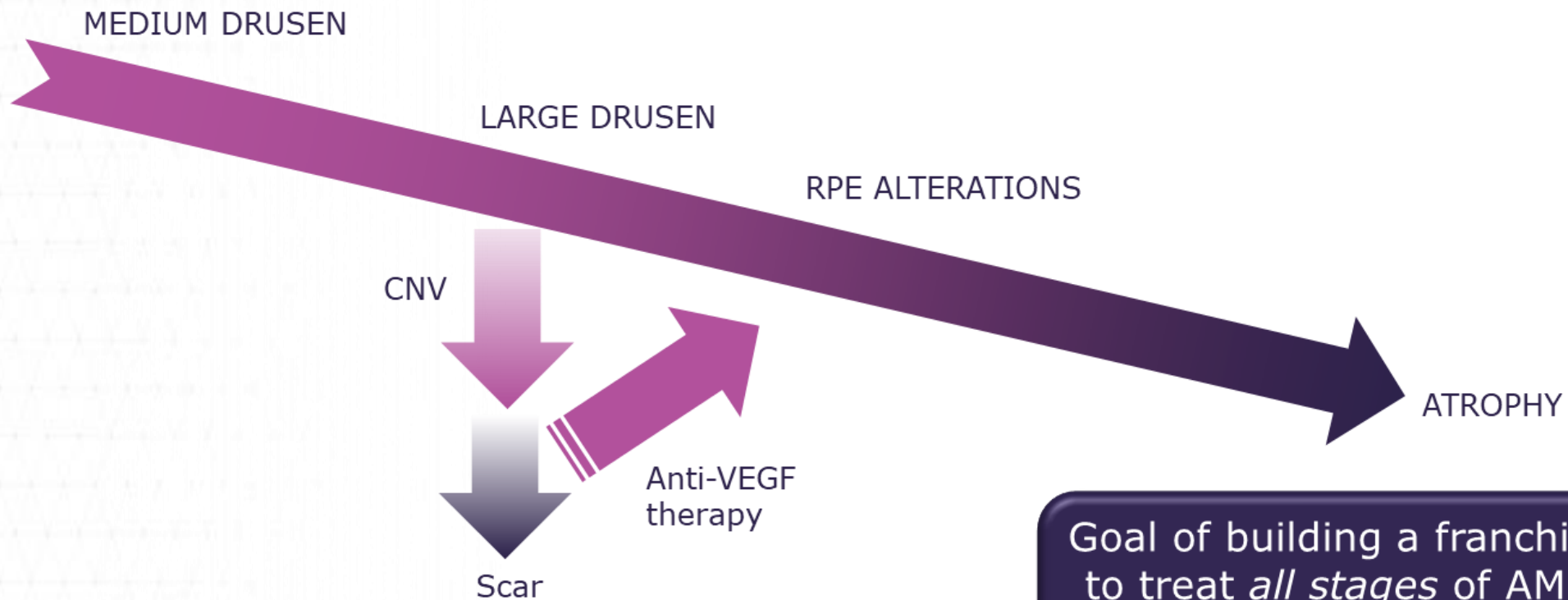
### Prespecified Analysis



### FDA preferred Analysis



# Pathway of AMD disease progression



Goal of building a franchise to treat *all stages* of AMD with Zimura and IC-500 (HtrA1 inhibitor)

## De-risking perspectives on Zimura

- ✓ GATHER1 is the first successful pivotal trial in GA, with an early and continuously increasing treatment effect observed over 18 months
- ✓ Recent Phase 3 data from a competitor suggests inhibiting downstream in the complement cascade is a viable therapeutic approach to addressing GA
- ✓ Data may also suggest that treating earlier (i.e. extrafoveal lesions) with a complement inhibitor may have added benefit as opposed to treating later stage disease (i.e. foveal-involving)
- ✓ GATHER1 post-hoc analyses suggests that Zimura may have the potential to impact AMD earlier in the disease (i.e. drusen, iRORA, cRORA), thereby changing the natural course of the disease

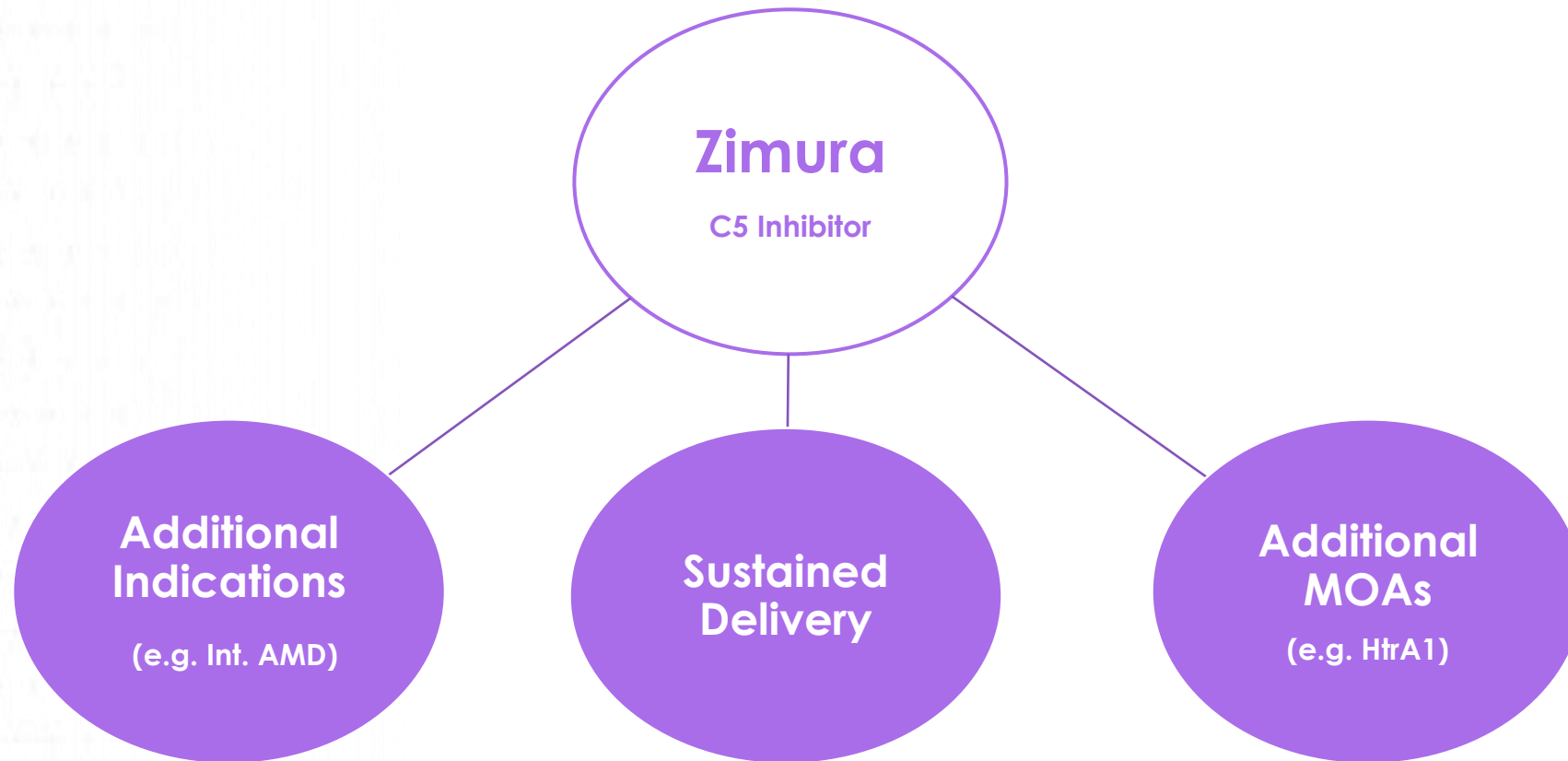
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BUILDING AN AMD  
FRANCHISE

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# Lifecycle Management Strategy



# Intermediate AMD: Planned Trial Design

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- International, randomized, double-masked, sham-controlled, multi-center clinical trial with ~200 patients per treatment group
- Dosing regimens currently under consideration
- Patients treated and followed for 24 months
- Inclusion criteria (definition of “Intermediate AMD”) / primary efficacy endpoint:
  - Based on imaging criteria and anatomic features
- Plans subject to regulatory feedback prior to trial initiation
- Potential to file sNDA/MAA based on results from this pivotal trial and supportive data

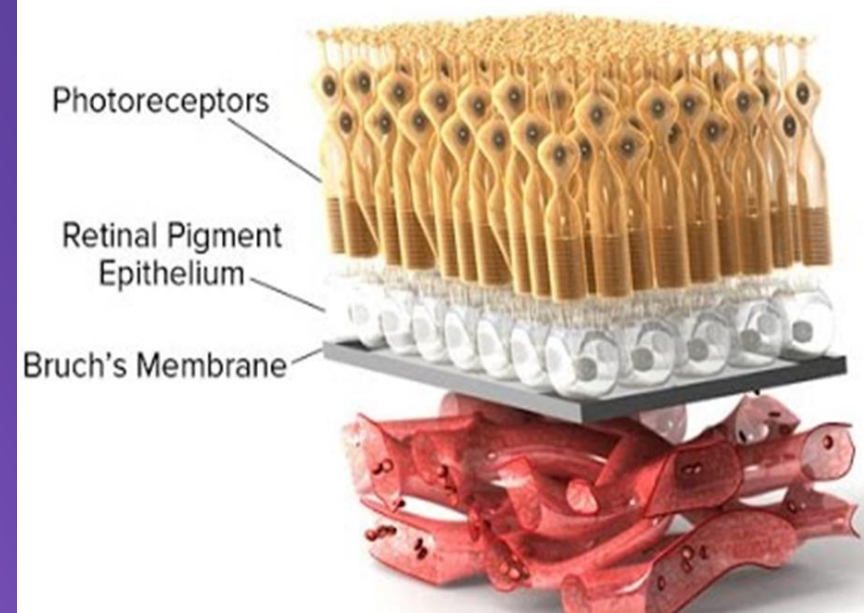
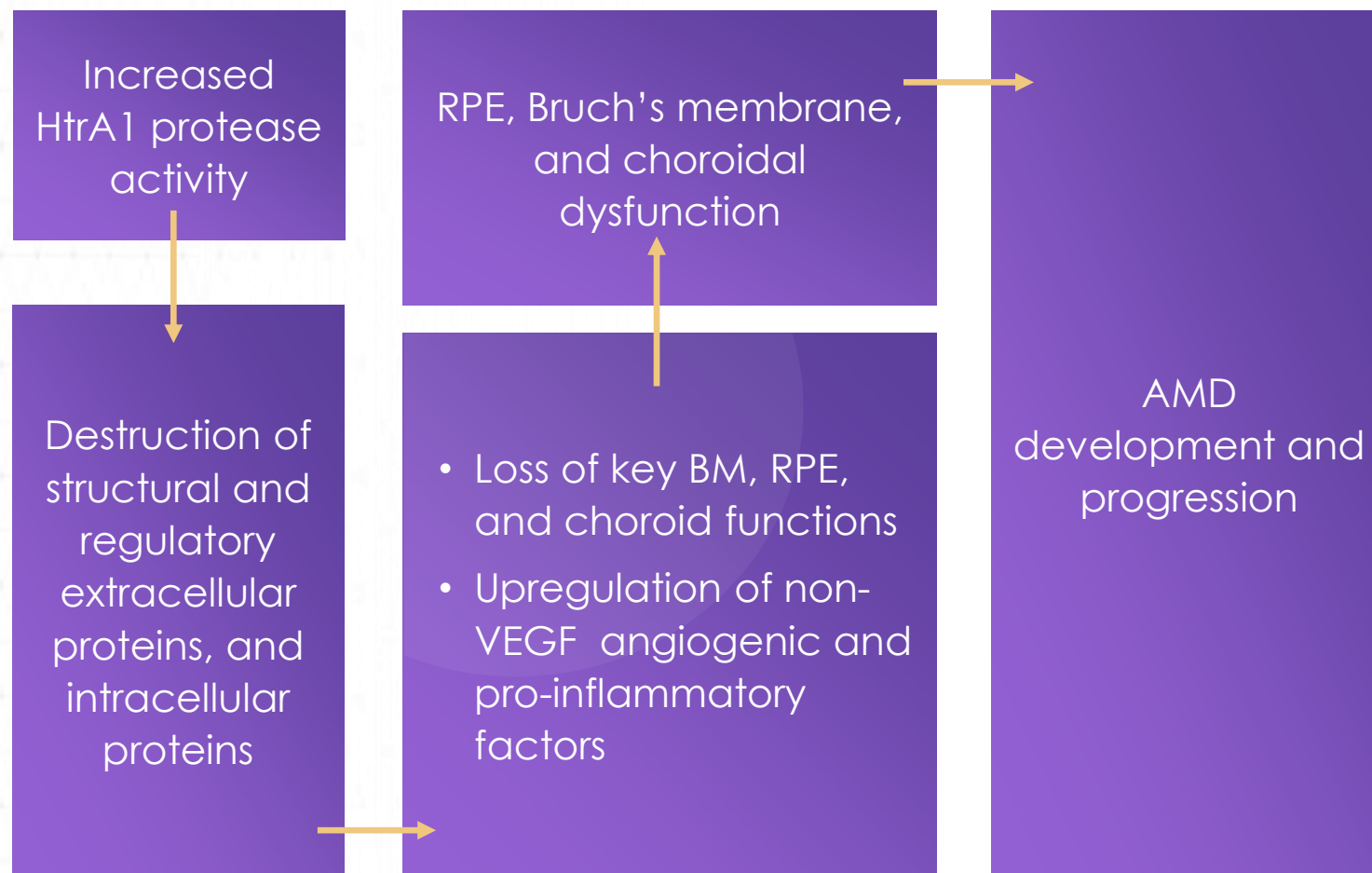
# Evidence for the role of HtrA1 in AMD pathogenesis

Target backed by strong human genetic and pre-clinical/clinical evidence

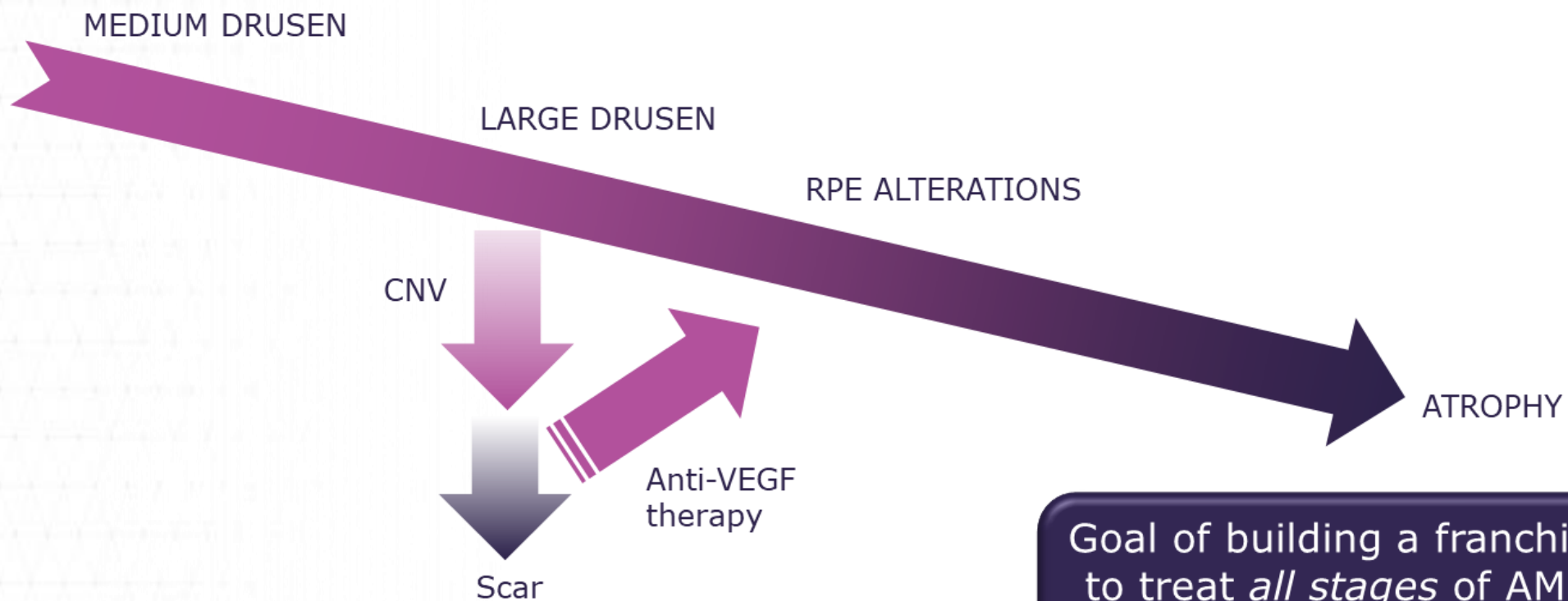
- ✓ Strong human genetic evidence associates ocular HtrA1 overexpression with geographic atrophy and all neovascular forms of AMD
- ✓ Compelling preclinical and clinical evidence for role of HtrA1 in AMD
- ✓ HtrA1 is non-overlapping and could augment the effects of targeting other AMD treatment pathways

# Proposed mechanism of HtrA1 activity in AMD

Destruction of extracellular matrix proteins leads to epithelium dysfunction



# Multiple shots on goal in AMD



Goal of building a franchise to treat *all stages* of AMD with Zimura and IC-500 (HtrA1 inhibitor)

# Planned and recent milestones

- ✓ GATHER2 topline data readout (3Q 2022)
- ✓ Initiate clinical trial of Zimura in intermediate AMD (4Q 2022)
- ✓ IC-500 IND submission (mid-2023)
- ✓ GATHER2 enrollment completed (July 2021)
- ✓ Hired Chief Commercial Officer (August 2021)



# Summary

- ✓ GATHER1 is the first known successful pivotal trial for GA
- ✓ If positive, we expect GATHER2 will be the final pivotal trial required for FDA and EMA approval for GA
- ✓ Zimura has the potential to impact earlier stages of AMD
- ✓ We believe we are well positioned to expand Zimura's indications, build an AMD franchise and, subject to regulatory approval, commercialize Zimura for GA as a market leader

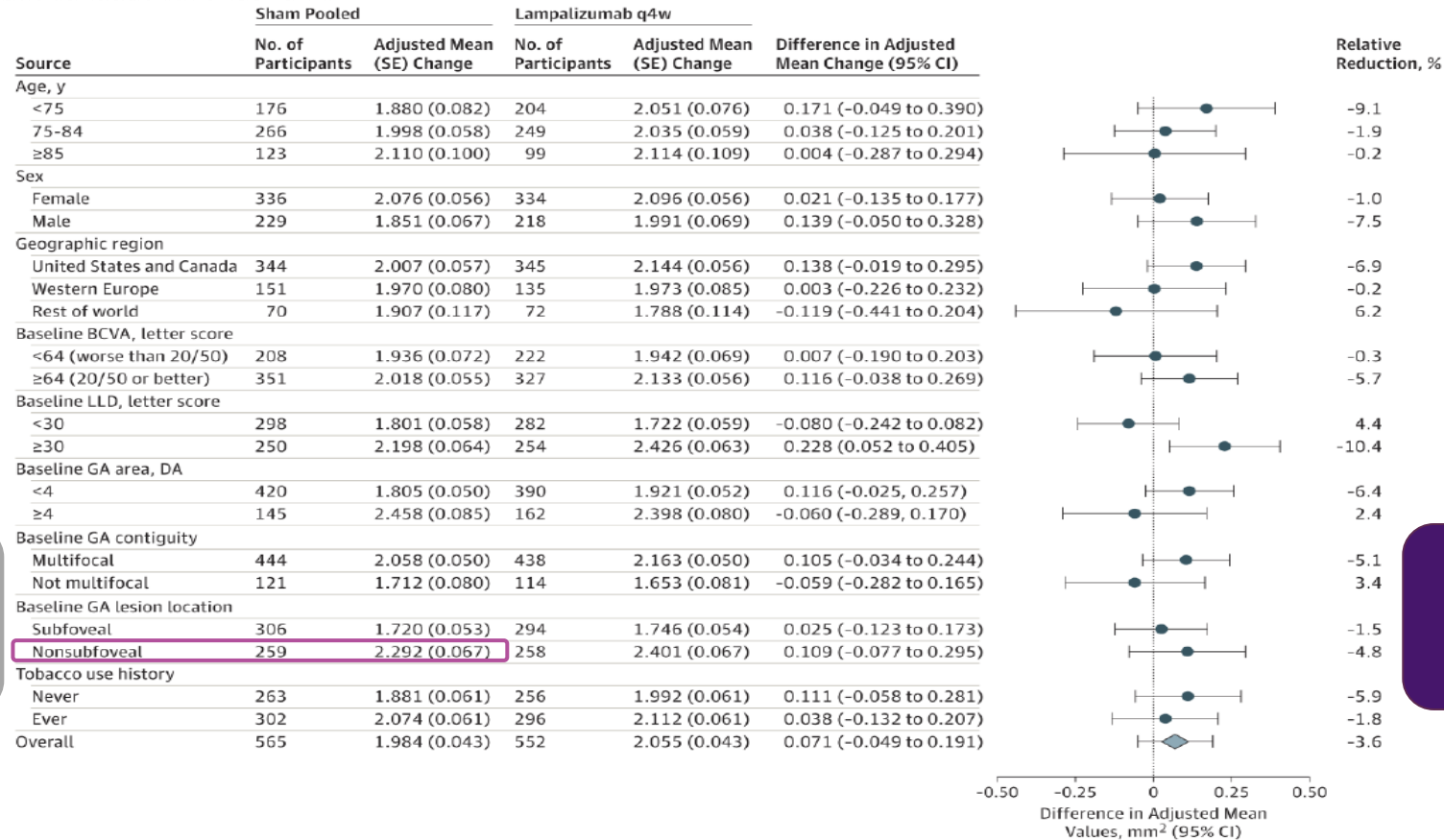
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APPENDIX

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# Extrafoveal Sham Growth: Chroma/Spectri & GATHER1

## NON-SQUARE-ROOT TRANSFORMATION



**Chroma/Spectri**

Mean change in  
extrafoveal GA  
2.292-2.401

**GATHER1**

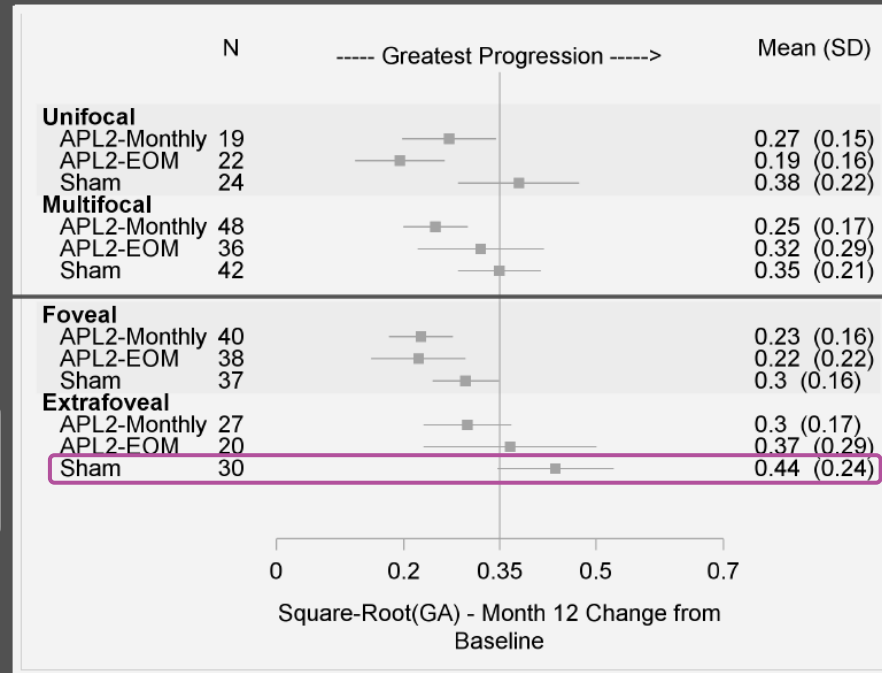
Mean change in  
extrafoveal GA  
2.29-2.77

**eFigure 2.** Adjusted Mean Change in Geographic Atrophy (GA) Area From Baseline to Week 48 in the Study Eye by Clinical Subgroup, Chroma and Spectri Pooled

# Nonsubfoveal/Extrafoveal Sham Growth: Chroma/Spectri/Filly

## SQUARE-ROOT TRANSFORMATION

### Change in GA Lesion Size at Month 12 Baseline GA Lesion Characteristics



Mean change in Sham (extrafoveal)  
Filly: 0.44

Mean change in Sham (extrafoveal)  
GATHER1: 0.42-0.44

Evaluation of Baseline Risk Factors on Progression in Geographic Atrophy

Post-hoc Analysis from the Filly Study  
Nathan Steinle, MD<sup>1</sup>, Mohamed Hamdani<sup>2</sup>

<sup>1</sup>California Retina Consultants  
<sup>2</sup>Apellis Pharmaceuticals

## Mixed-Effect Repeated Measures Model

- Used to assess the differences between Zimura 2mg or 4mg dose and their corresponding sham in rate of change of GA area (square-root transformation) over 12 months
- The model included the following fixed and random effects:
  - Treatment: Sham vs dose
  - Study part (1 vs 2): only for 2 mg
  - Baseline VA:  $< 50$  letters vs  $\geq 50$  letters
  - Size of baseline GA:  $< 4$  disc area vs  $\geq 4$  disc area
  - Pattern of FAF at the junctional zone of GA: none/focal vs banded/diffuse
  - Visit (0, 6 mos or 12 mos) with unstructured correlation
  - Interaction terms between visit and all other factors