IVERIC BIO

DEVELOPING TRANSFORMATIVE THERAPIES FOR RETINAL DISEASES

August 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.

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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 September 2022
  - 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: $260 million - $270 million*

*Estimate as of 7/26/22

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STRONG SENIOR TEAM WITH SIGNIFICANT OPHTHALMOLOGY EXPERIENCE

GLENN SBLENDORIO Chief Executive Officer	The Medicines Company; eyetech; Roche; MPM
PRAVIN DUGEL, MD President	USC Roski Eye Institute, Keck Medicine of USC; Spectra Eye Institute; UCLA School of Medicine; Columbia University in the City of New York
DAVID CARROLL Chief Financial Officer	The Medicines Company; Genentech, A Member of the Roche Group; Novartis; Bristol-Myers Squibb
TONY GIBNEY Chief Business & Strategy Officer	fog pharma; Achillion; Leerink; Merrill Lynch
KEITH WESTBY Chief Operating Officer	Pharmasset; eyetech; Tunnell Consulting; Roche; Pfizer
XIAO-PING DAI, PhD Chief Technical Officer	WuXi Advanced Therapies; Celgene; Bristol Myers Squibb; Medarex; Regeneron
CHRISTOPHER SIMMS Chief Commercial Officer	Novartis; Genentech, A Member of the Roche Group; J&J
EVELYN HARRISON Chief Clinical Operations Officer	eyetech; Roche
DHAVAL DESAI, PHARMD Chief Development Officer	Onyx Pharmaceuticals; ThromboGenics; aerpio; Novartis
SNEHAL SHAH, PHARMD Chief Regulatory and Pharmacovigilance Officer	Kyowa Kirin; Noven; Roche

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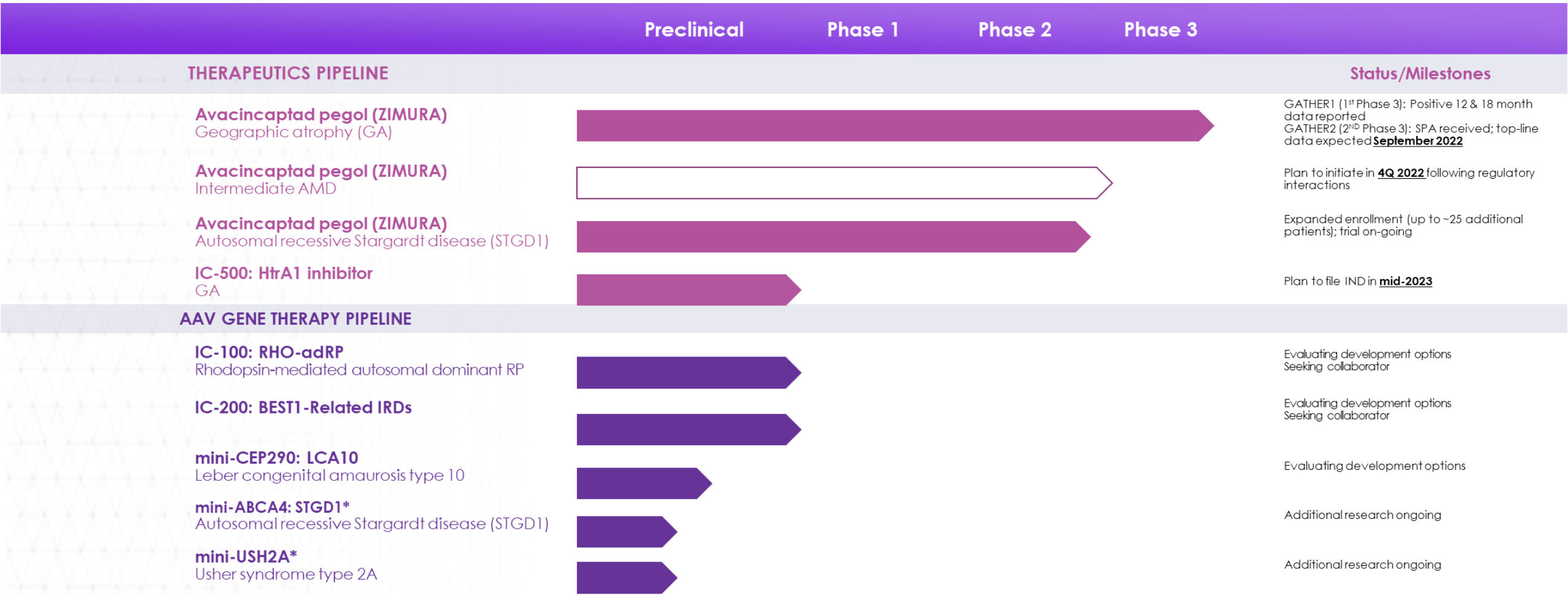
Iveric Bio Pipeline



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

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AGE-RELATED MACULAR DEGENERATION (AMD)

Disease Overview & Market Size

AMD LEADS TO PROGRESSIVE VISION LOSS WITH END-STAGE ATROPHY

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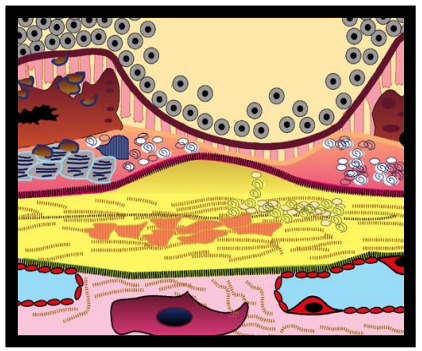
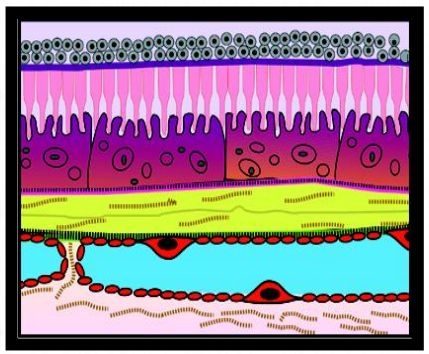
COMMON PERCEPTION: ADVANCED AMD IS EITHER DRY (LEADING TO GA) OR WET

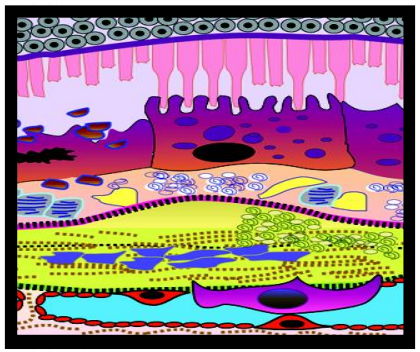
NORMAL

EARLY DRY AMD DEPOSITS

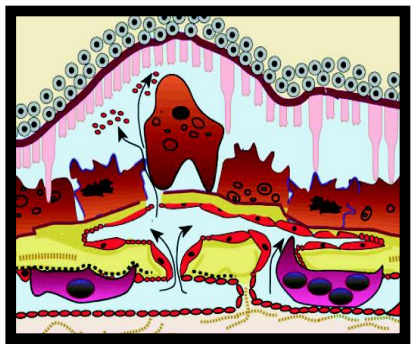
LATE DRY AMD "GEOGRAPHIC ATROPHY"







"NEOVASCULAR" AMD



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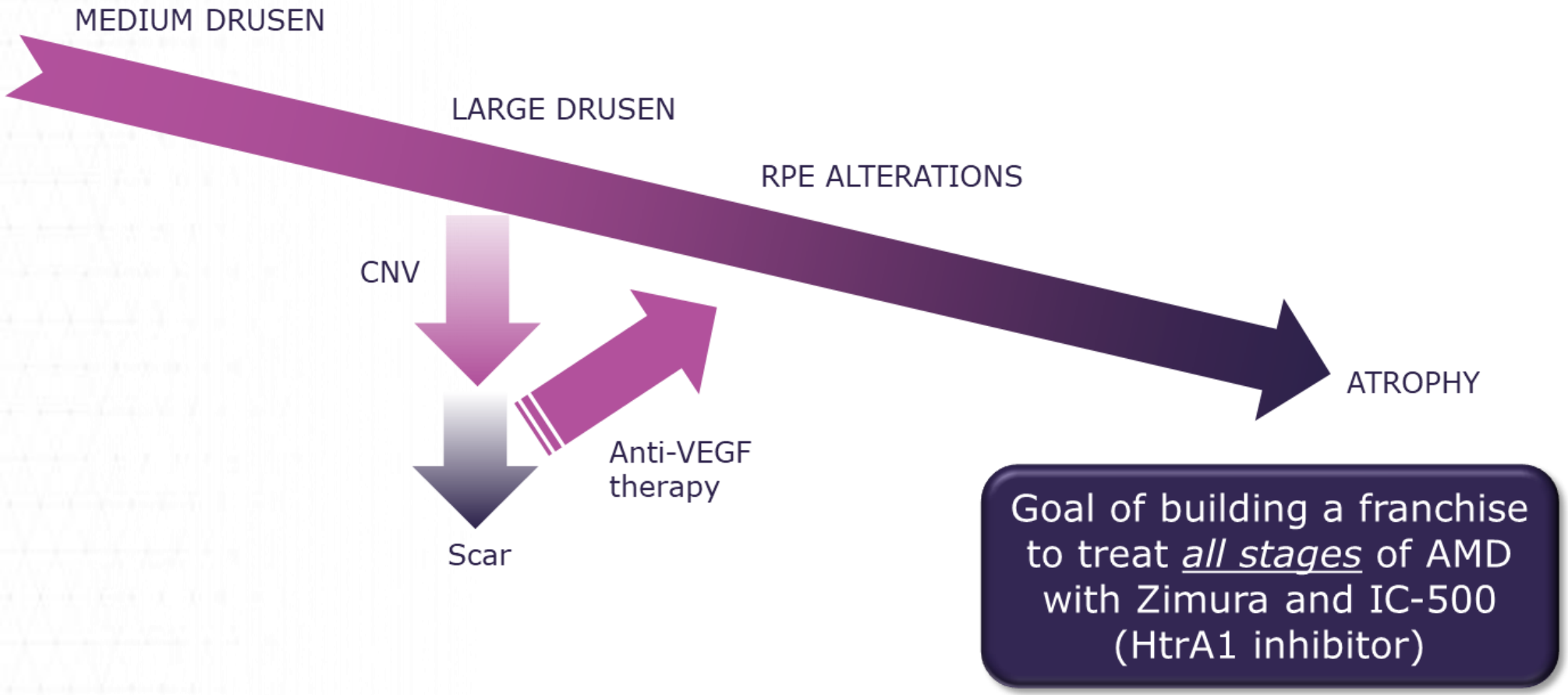
Pathway of AMD disease progression



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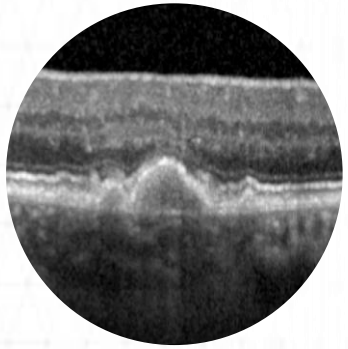
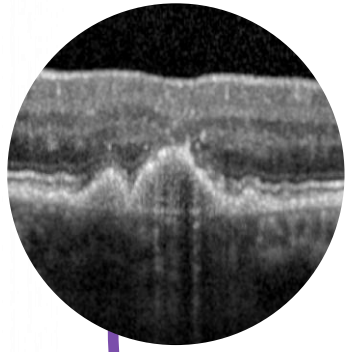
Ophthalmology. 2017 Jan; 124(1): 97–104; Lancet. 2018 Sep 29;392(10153):1147-1159; Retina. 2016 Oct;36(10):1843-50; Am J Ophthalmol. 2015 May;159(5):915-24

Pathway of AMD disease progression

Medium drusen
(Early AMD)

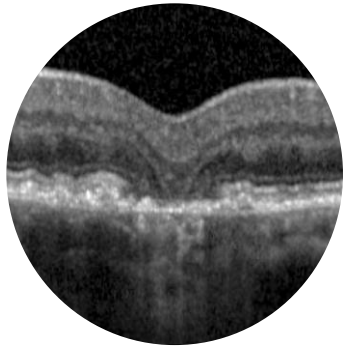


Large drusen
(Intermediate AMD)

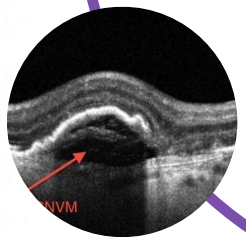


RPE alterations
(iRORA)

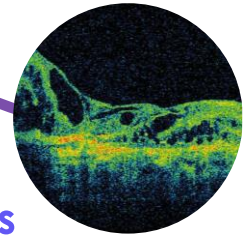
Atrophy
(cRORA)



CNV
(Wet AMD)



Anti-VEGF therapy



Fibrosis

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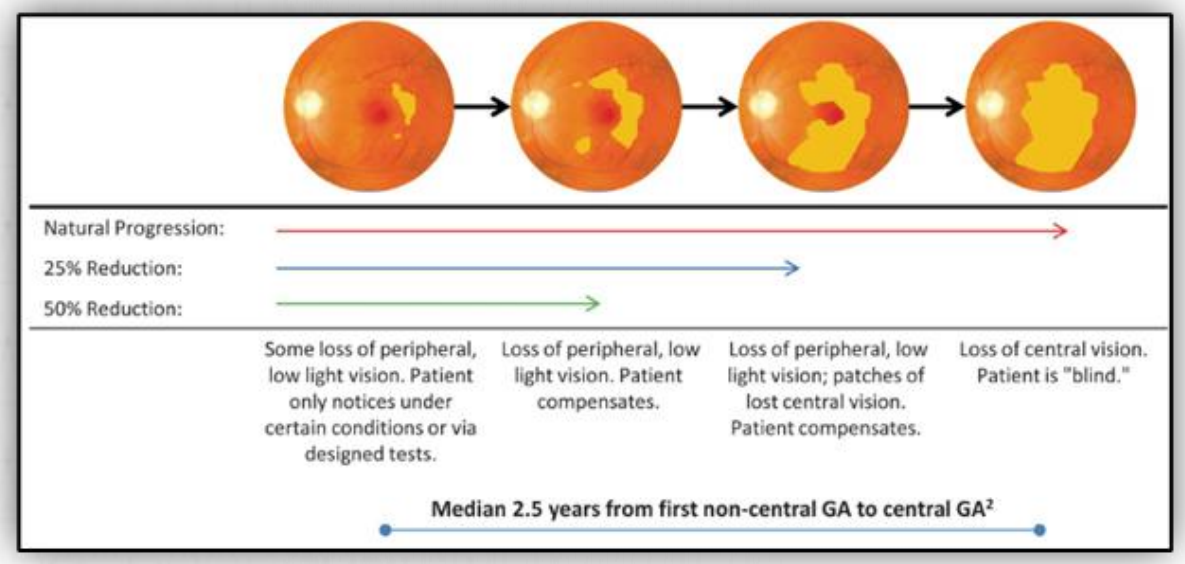
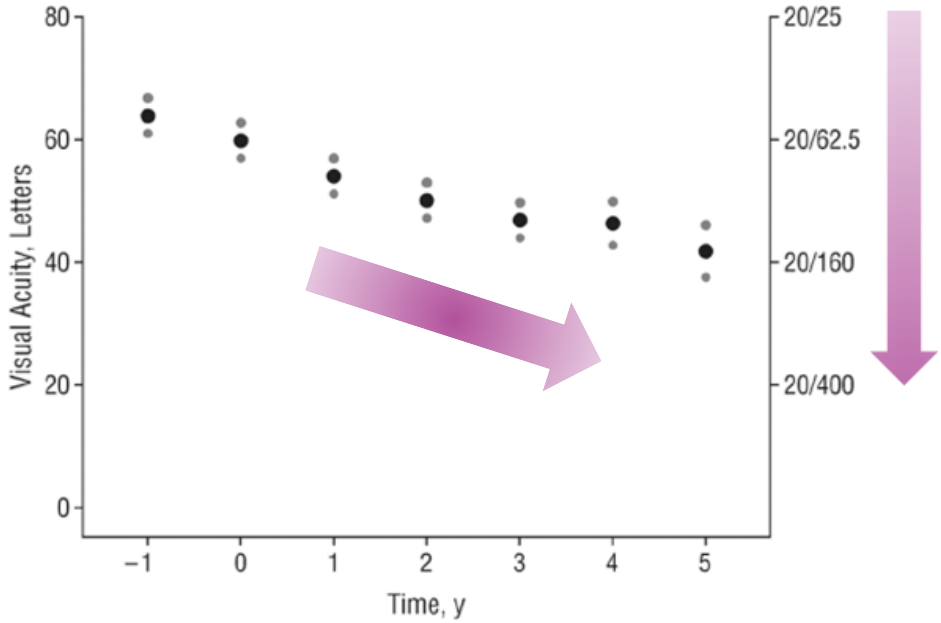
Growth rate and loss of vision depend on GA location

Geographic Atrophy: loss of photoreceptors over time

Increase In Area of Degeneration Over Time



Loss of Vision Over Time



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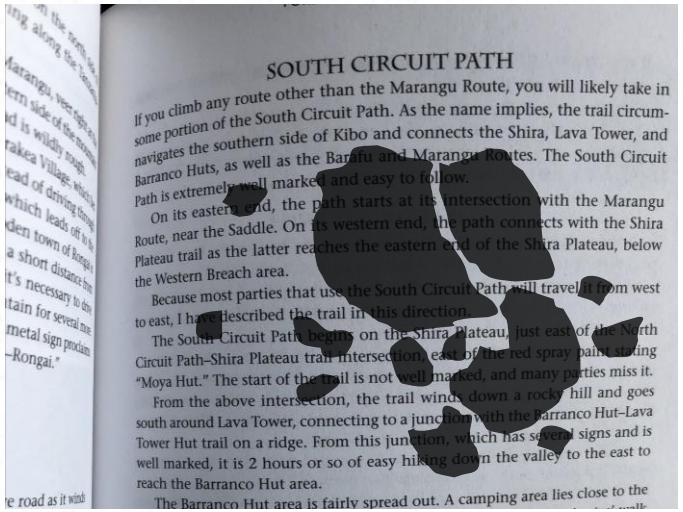
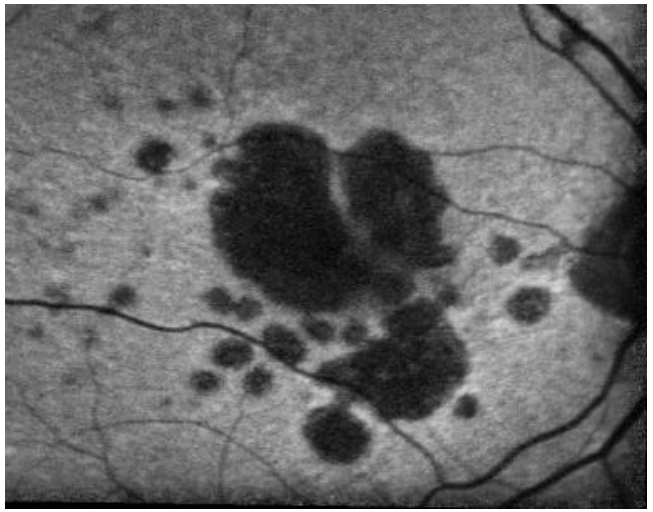
Source: Ophthalmology 2014;121:1079-1091. Retina 2017;27:819-835. Arch Ophthalmology 2009;127:1168-1174.

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)

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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[1]

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[2]

Early signs of retinal changes are seen in individuals as young as **30–40 years old**[3]

Studies show **GA severity increases with age**[1]

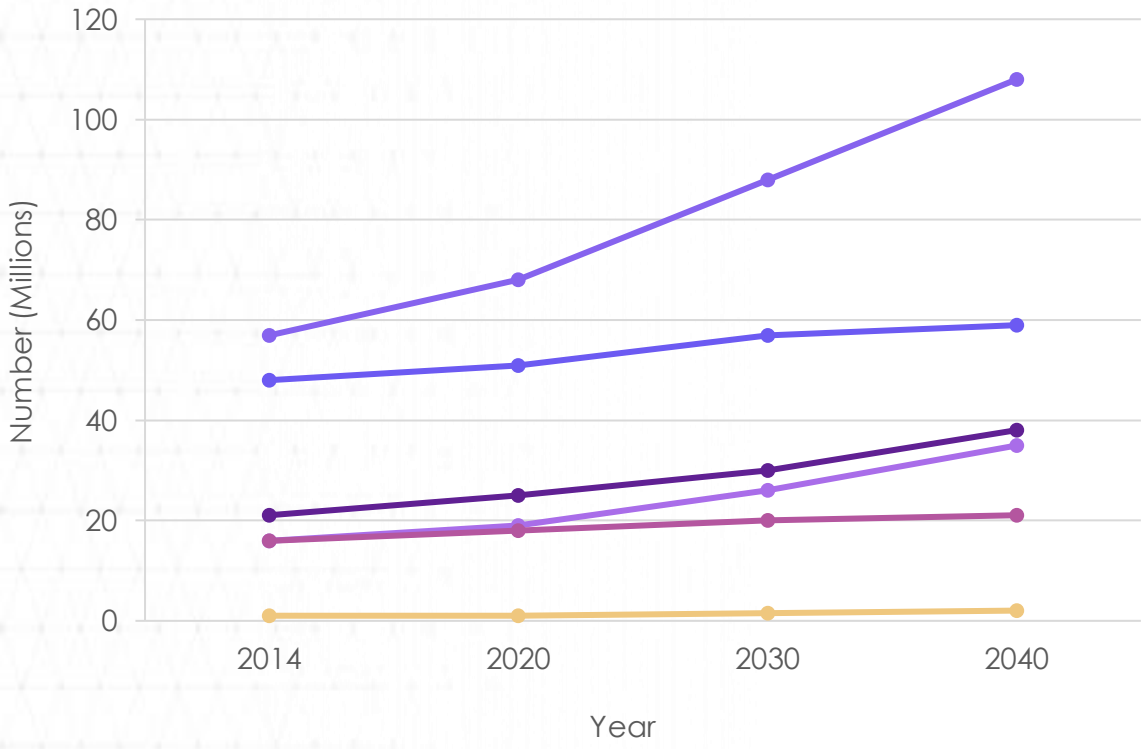
One-third of the population is affected by GA by the time individuals are 80 years old[3]

1. Ferris FL, Wilkinson CP, Bird A, Chakravarthy U, Chew E, Csaky K, et al. Clinical Classification of Age-related Macular Degeneration. *Ophthalmology*. 2013;120(4):844-851. **2.** Boyer DS, Schmidt-Erfurth U, van Lookeren Campagne M, Henry EC, Brittain C. The pathophysiology of geographic atrophy secondary to age-related macular degeneration and the complement pathway as a therapeutic target. *Retina*. 2017;37(5):819-835. **3.** Ratnayaka JA, Lotery AJ. Challenges in studying geographic atrophy (GA) age-related macular degeneration: the potential of a new mouse model with GA-like features. *Neural Regen Res*. 2020;15(5):863-864. doi:10.4103/1673-5374.268972.

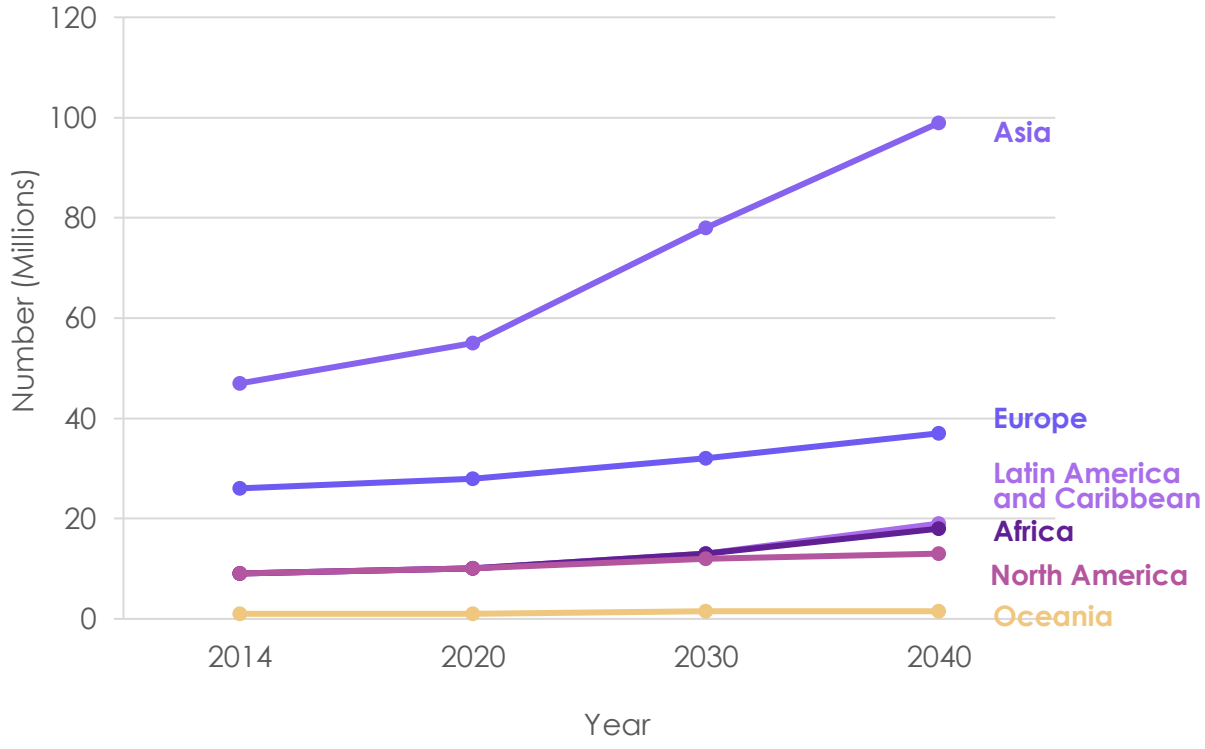
AMD is projected to increase in global prevalence

Projected number of individuals with AMD by region[1]

Early AMD



Late AMD



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1. Wong WL, Su X, Li X, et al. *Lancet Glob Health*. 2014;2(2):e106-e116.

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COMPLEMENT ACTIVATION IN GA

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

"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,[1] Anna Machalinska,[2,3] Dorota Roginska,[1] and Boguslaw Machalinski[1]

Complement Activation Levels Are Related to Disease Stage in AMD

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

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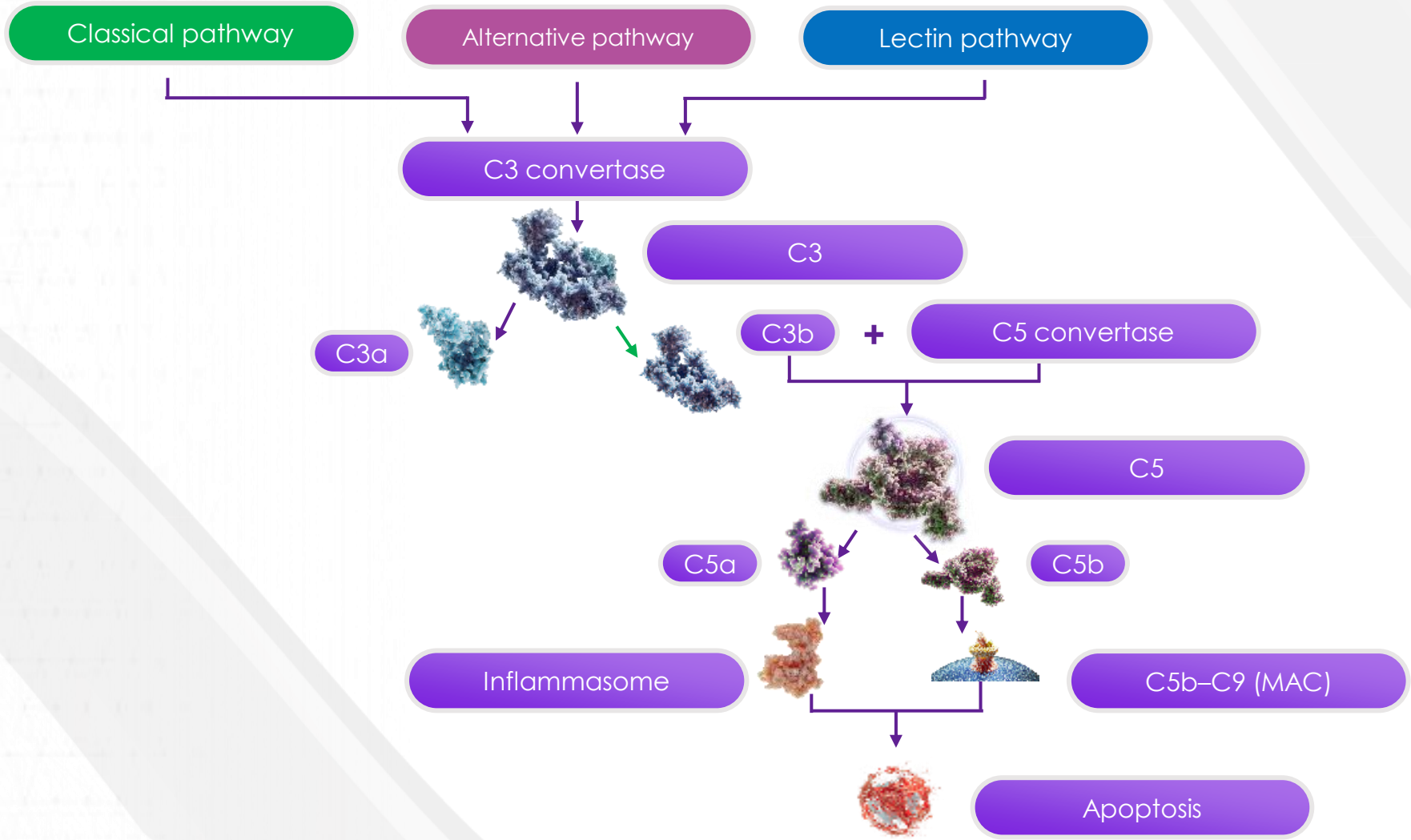
* Quotation from: Klein, et al. Complement Factor H Polymorphism in Age-Related Macular Degeneration. *Science*. 2005 April 15; 308(5720): 385-389.

Activated complement leads to inflammation and cell death



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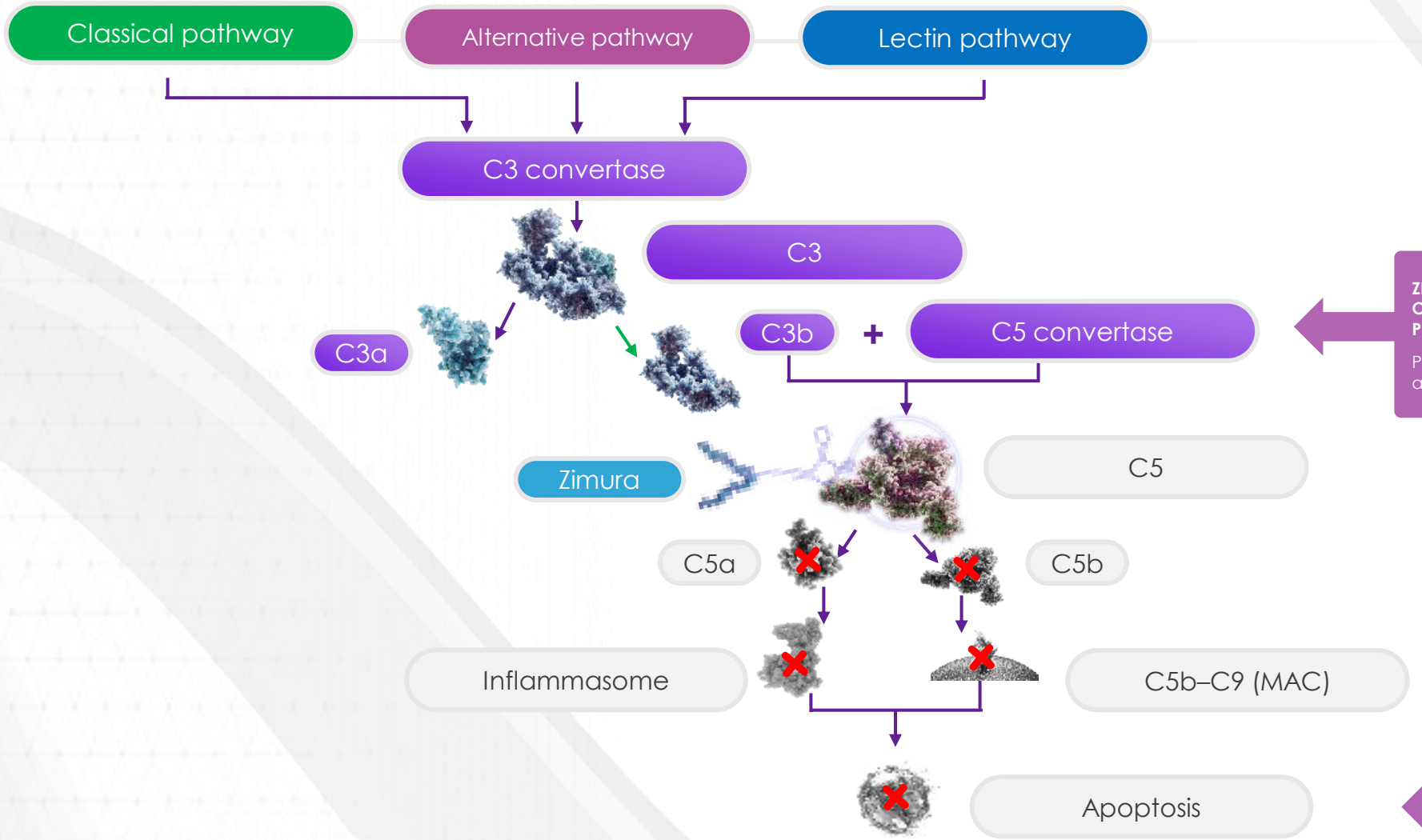
WHY IS ZIMURA® IMPORTANT?

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



ZIMURA BYPASSES C3, PRESERVING OPSONIZATION AND PERFUSION WHILE PROVIDING NEUROPROTECTION

Promotes phagocytosis of antigens and apoptotic cells

BY INHIBITING C5, ZIMURA IS HYPOTHESIZED TO PREVENT APOPTOSIS

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Xu H, Chen M. Targeting the complement system for the management of retinal inflammatory and degenerative diseases. *European Journal of Pharmacology*. 2016;787:94-104.

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ZIMURA® PHASE 3 PROGRAM IN GA SECONDARY TO AMD

GATHER 1 Geographic Atrophy Therapy Trial

GATHER 2 Geographic Atrophy Therapy Trial

(Geographic Atrophy Therapy Trials)

GATHER1 Dosing Regimen

Geographic Atrophy Therapy Trial

PART 1:

Primary Endpoint at Month 12

	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

PART 2:

Primary Endpoint at Month 12

	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

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GATHER1: Key Inclusion Criteria

- Non-foveal GA secondary to dry AMD
- Total GA area ≥ 2.5 and ≤ 17.5 mm^2 (1 and 7 disk areas [DA] respectively), determined by screening images of FAF
- If GA is multifocal, at least one focal lesion should measure ≥ 1.25 mm^2 (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

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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[a]	0.292[c]	0.402[c]	0.110	0.0072[b]	27.38%

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

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(a) = mm, based on the least squares means from the MRM model
(b) = reflects statistically significant p-value; Hochberg procedure was used for significance testing
(c) = these least squares means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data

GATHER1 Dosing Regimen

Geographic Atrophy Therapy Trial

PART 1:

Primary Endpoint at Month 12

	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

PART 2:

Primary Endpoint at Month 12

	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

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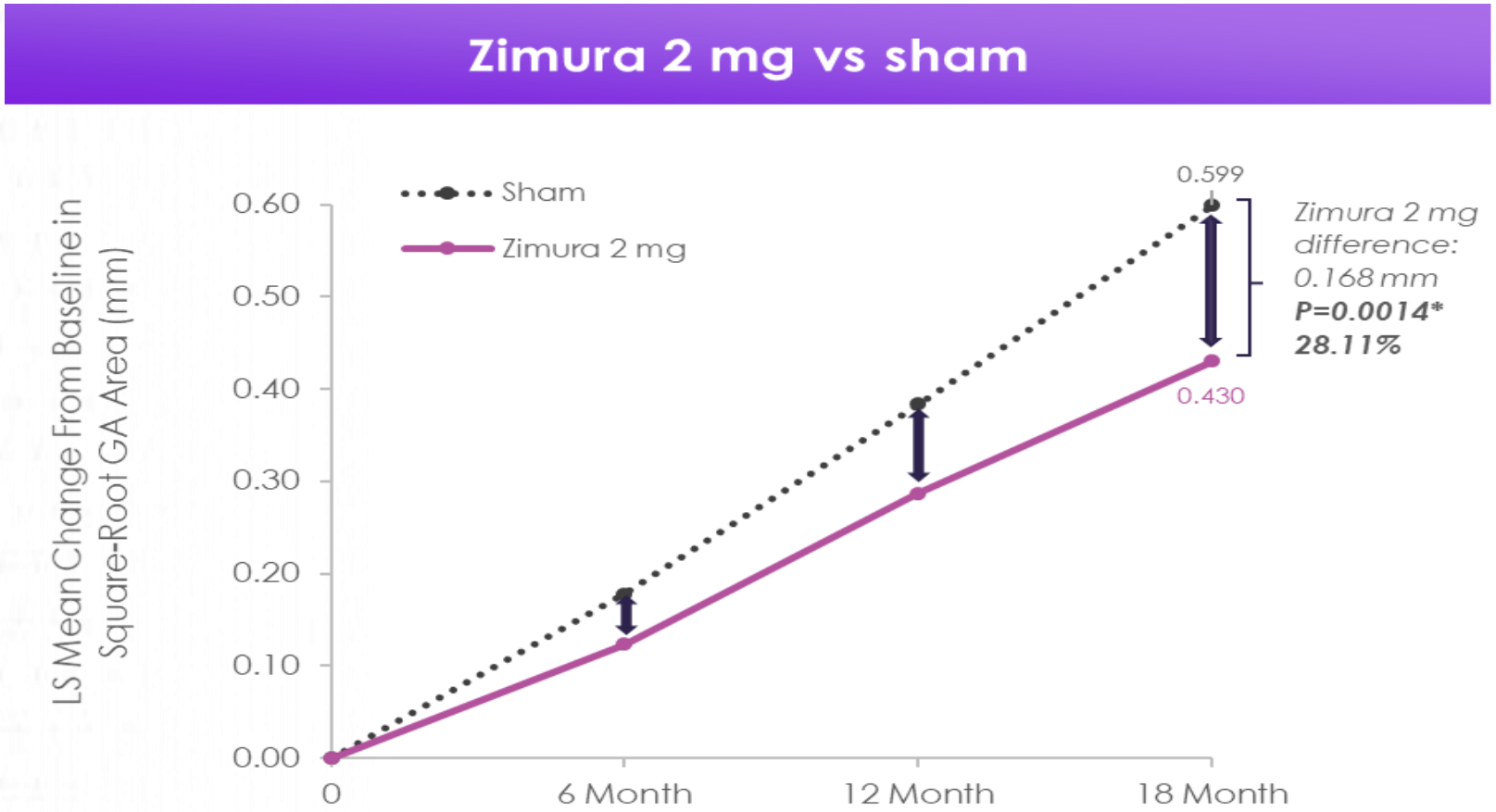
GATHER1: Decrease in GA growth over 18 months Zimura 2 mg vs. Sham (square root transformation)

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



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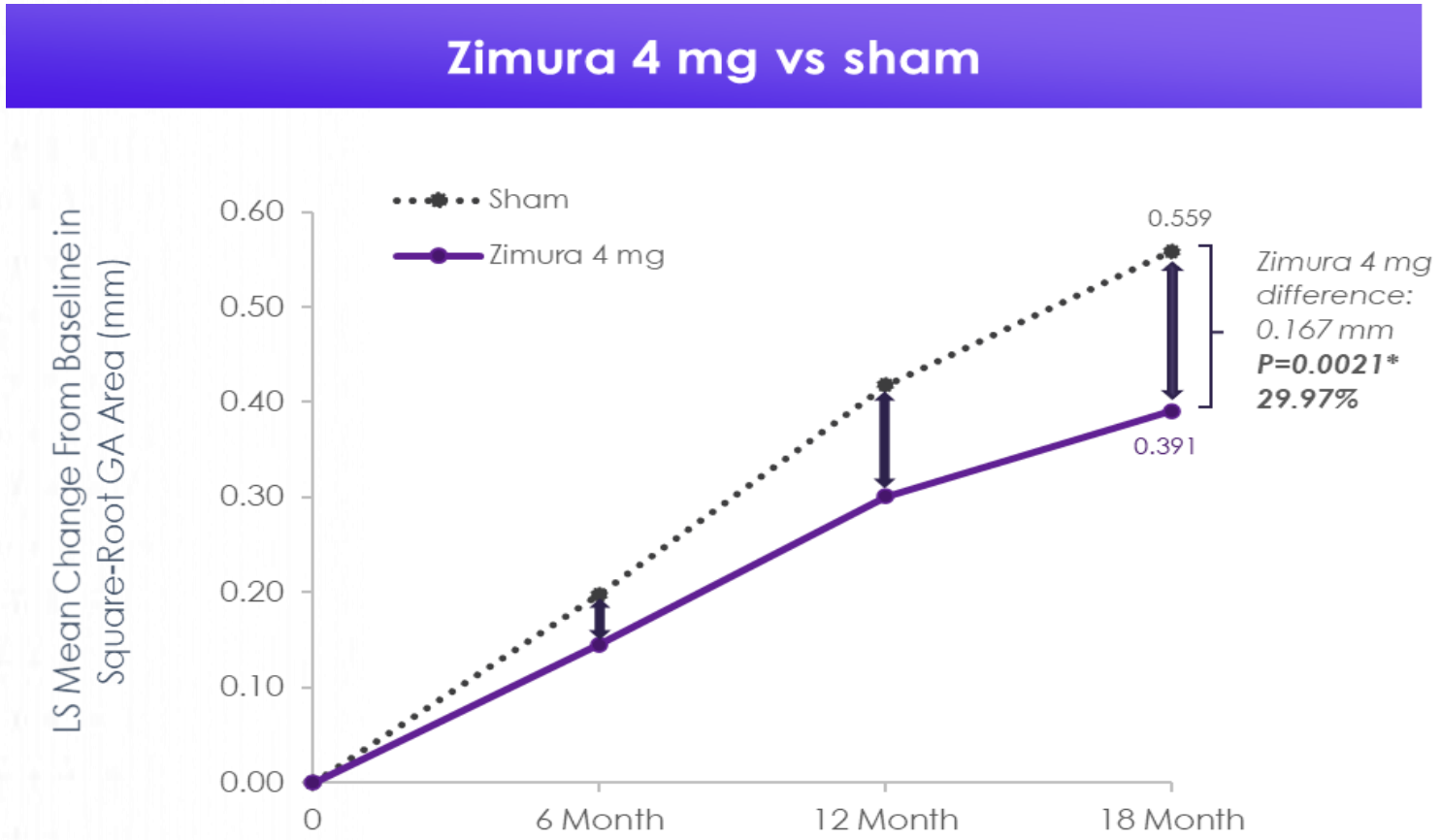
Based on LSMEANS from MRM model; ITT population Hochberg procedure was used for significance testing; prespecified and descriptive analysis. These least squares means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.
*18-month P values are descriptive in nature.

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



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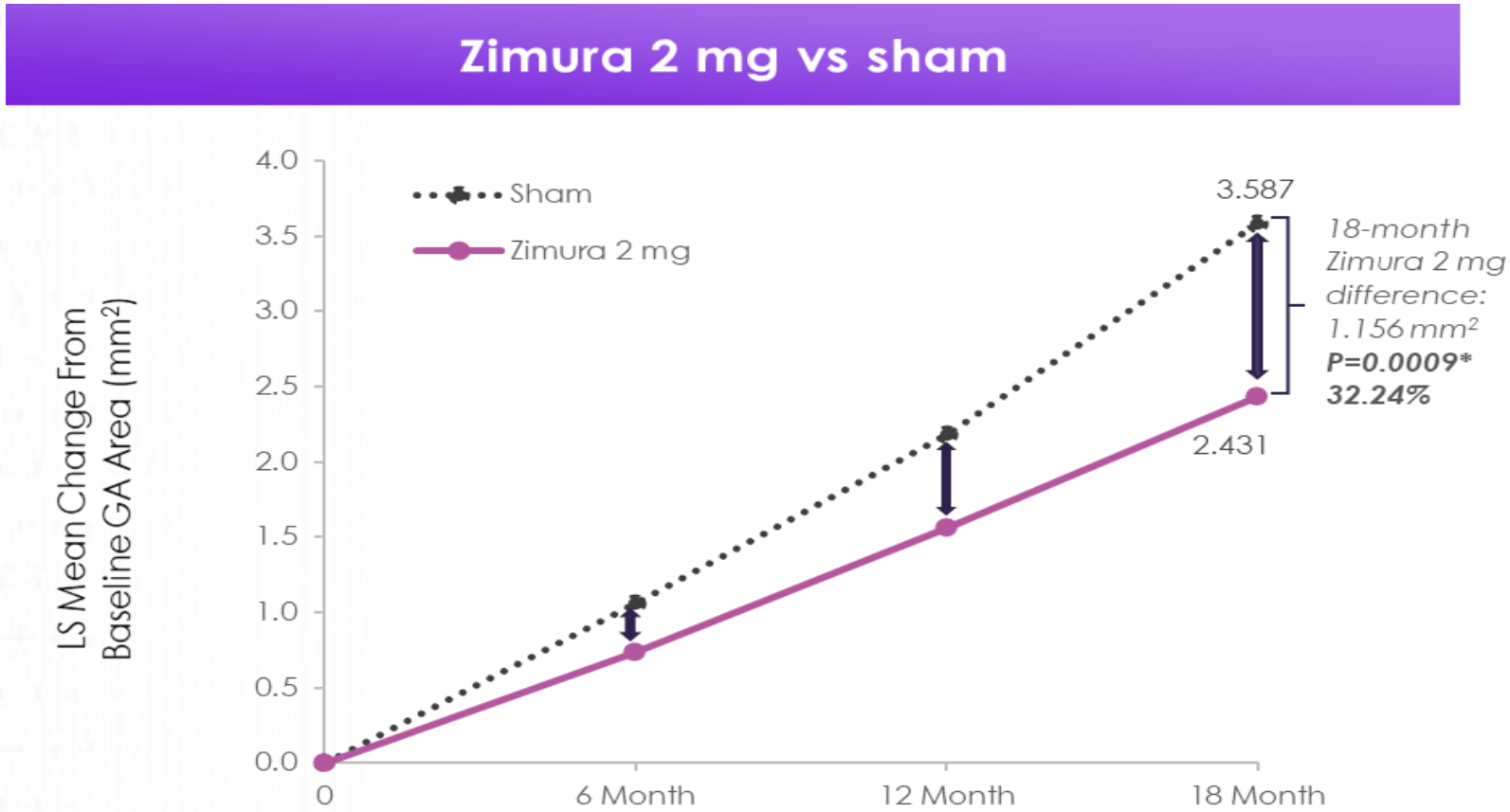
Based on LSMEANS from MRM model; ITT population Hochberg procedure was used for significance testing; prespecified and descriptive analysis. These least squares means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.
*18-month P values are descriptive in nature.

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

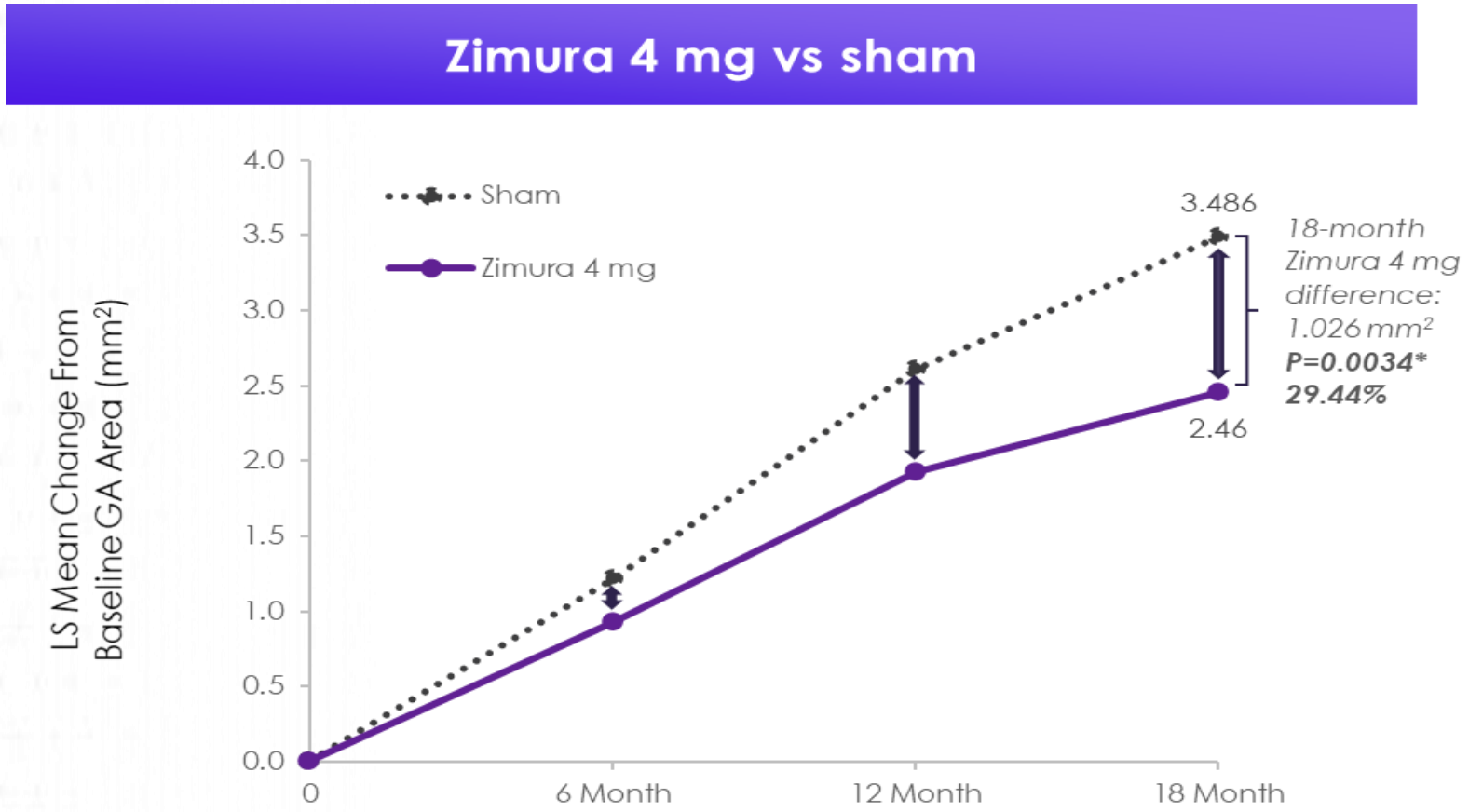
MEAN RATE OF GROWTH IN GA AREA AS MEASURED BY NON-SQUARE-ROOT GA LESION AREA OVER 18 MONTHS



Based on LSMEANS from MRM model; ITT population Hochberg procedure was used for significance testing; prespecified and descriptive analysis. These least squares means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.
*18-month P values are descriptive in nature.

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



Based on LSMEANS from MRM model; ITT population Hochberg procedure was used for significance testing; prespecified and descriptive analysis. These least squares means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.
*18-month P values are descriptive in nature.

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%)
Zimura 2mg	**6 (9.0%)**	**8 (11.9%)**
Zimura 4mg	8 (9.6%)	13 (15.7%)

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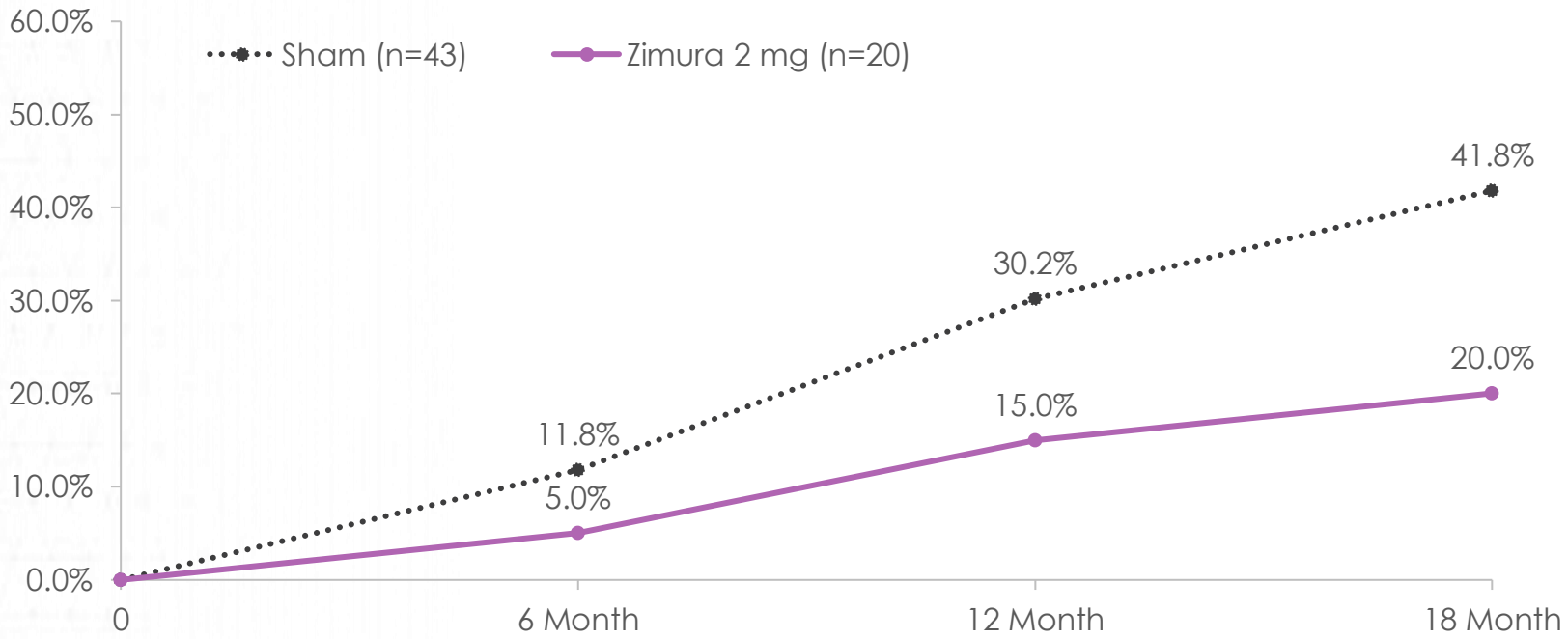
Based on investigator-reported safety events.

Progression of iRORA to cRORA

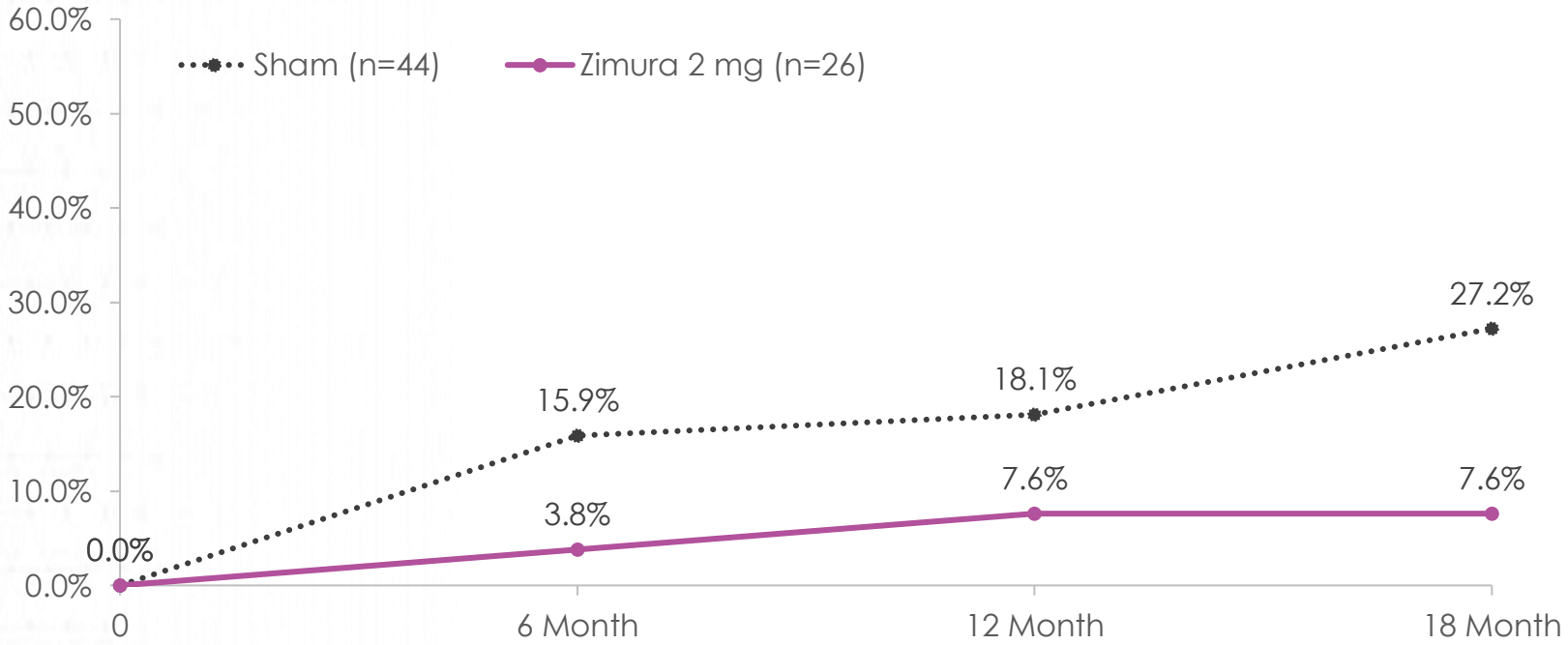
Proportion of patients that progress from iRORA to cRORA (Zimura 2 mg vs. Sham) (post-hoc analysis)



*iRORA: Incomplete RPE + Outer Retinal Atrophy; cRORA: Complete RPE + Outer Retinal Atrophy
GA is a subset of cRORA (excludes region of CNV)

Progression of Drusen to iRORA/cRORA

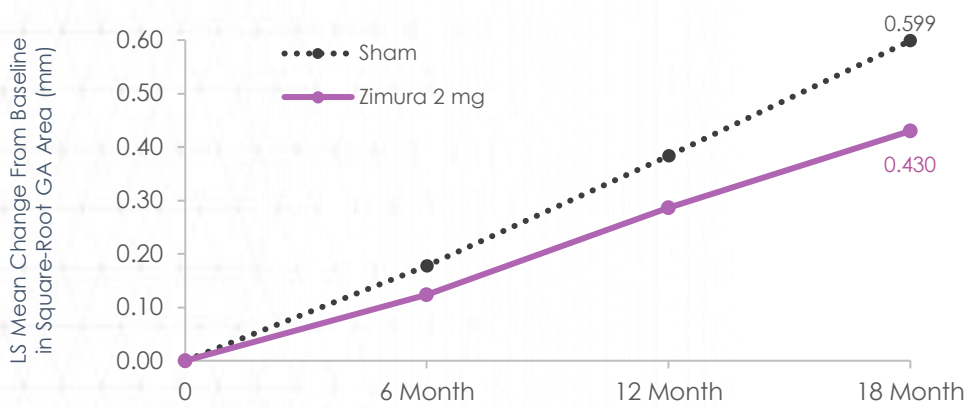
Proportion of patients that progress from drusen to iRORA or cRORA (Zimura 2 mg vs. Sham) (post-hoc analysis)



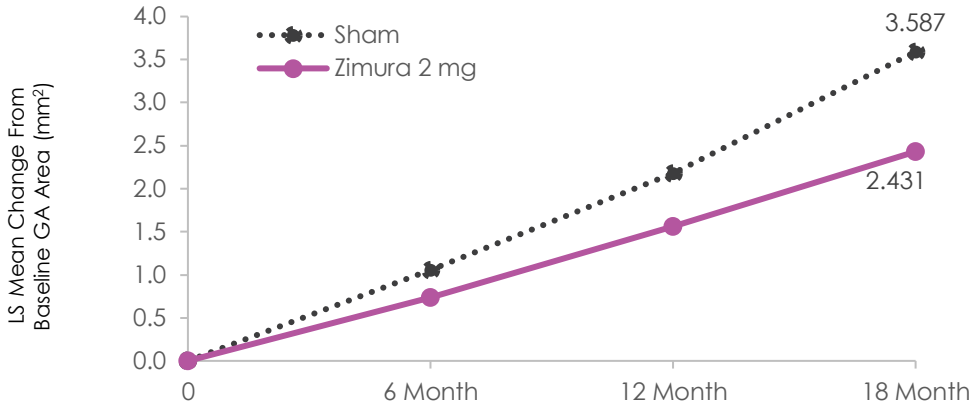
*iRORA: Incomplete RPE + Outer Retinal Atrophy; cRORA: Complete RPE + Outer Retinal Atrophy
GA is a subset of cRORA (excludes region of CNV)

Potential to alter natural history of disease

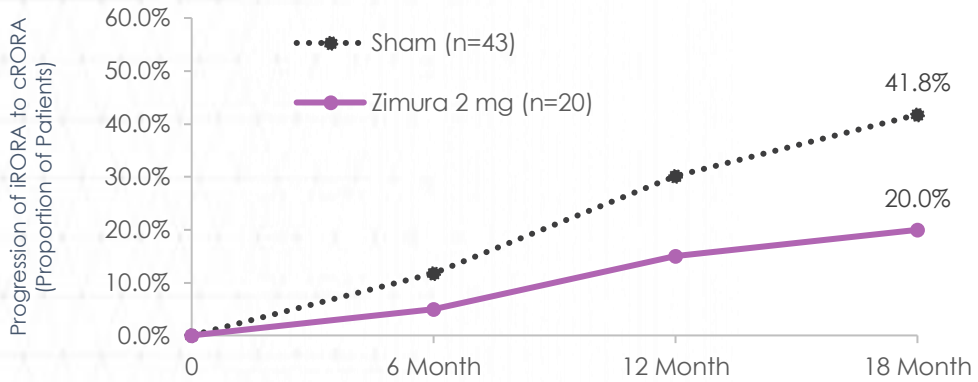
Zimura 2 mg vs sham (square root transformation)



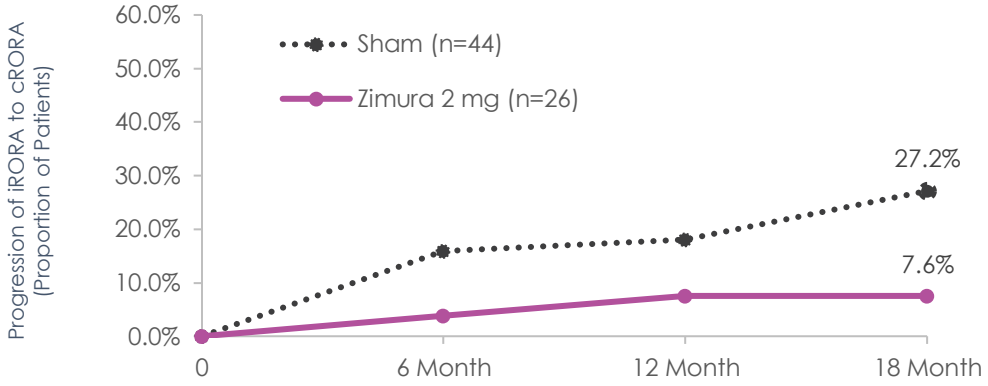
Zimura 2 mg vs sham (non-square root transformation)



Progression of iRORA to cRORA (post-hoc analysis)



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



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Based on LSMEANS from MRM model; ITT population Hochberg procedure was used for significance testing; prespecified and descriptive analysis. These least-squares means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.
iRORA & drusen analysis are post-hoc

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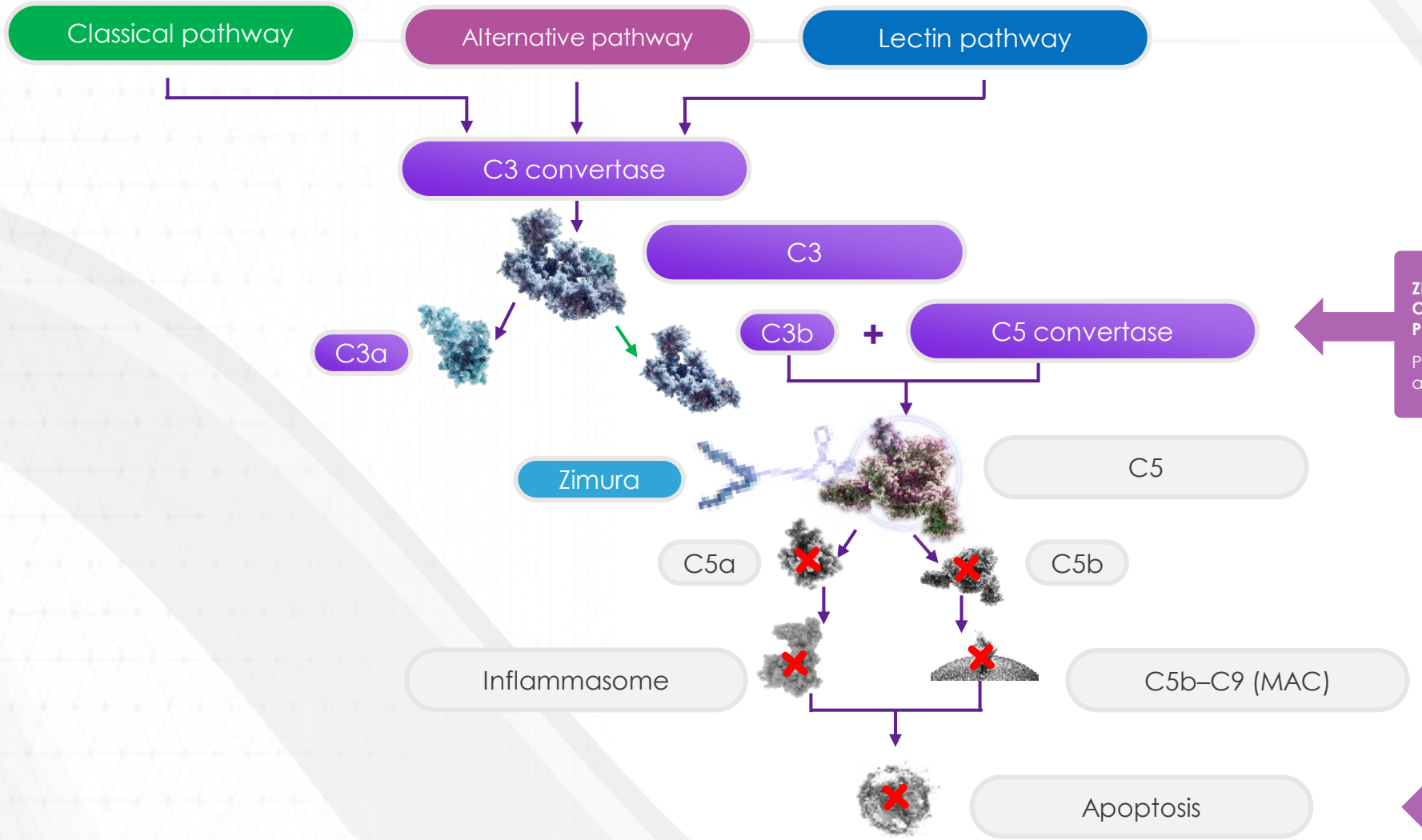
INHIBITION OF C5

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



ZIMURA BYPASSES C3, PRESERVING OPSONIZATION AND PERFUSION WHILE PROVIDING NEUROPROTECTION

Promotes phagocytosis of antigens and apoptotic cells

BY INHIBITING C5, ZIMURA IS HYPOTHESIZED TO PREVENT APOPTOSIS

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Xu H, Chen M. Targeting the complement system for the management of retinal inflammatory and degenerative diseases. *European Journal of Pharmacology*. 2016;787:94-104.

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

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Source: J. Exp. Med. 2019 Vol. 216 No. 8 1925–1943. J Immunol 2006; 176:4315-4322. J Immunol 2015;194: 3542–3548.
Wu et al., 2013, PNAS; Brennan et al., 2019, JCI Insight. Woodruff unpublished data.

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

JEM Journal of Experimental Medicine

Sean M. Silverman, Wenxin Ma, Xu Wang, Lian Zhao, and Wai T. Wong

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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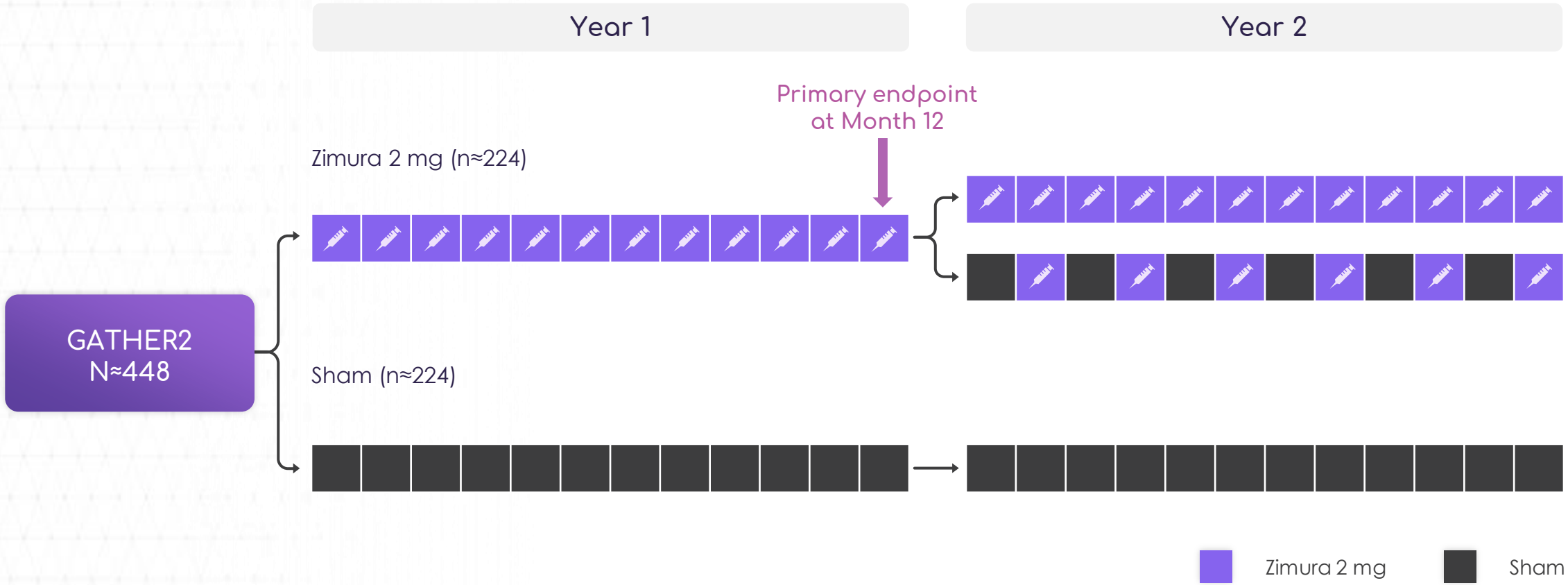
GATHER 2

Geographic Atrophy Therapy Trial

Second Pivotal Clinical Trial of Zimura in GA

GATHER2 Primary endpoint at Month 12



Jaffe EG, Westby K, Csaky KG, et al. *Ophthalmology*. 2020. doi:10.1016/j.ophtha.2020.08.027.

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EXECUTION AND REGULATORY CLARITY

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 -

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Injection fidelity is the most meaningful marker of patient retention

GATHER1

12-Month Injection Fidelity Rate

87%

GATHER2

12- Month Injection Fidelity Rate

92.5%

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

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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 -

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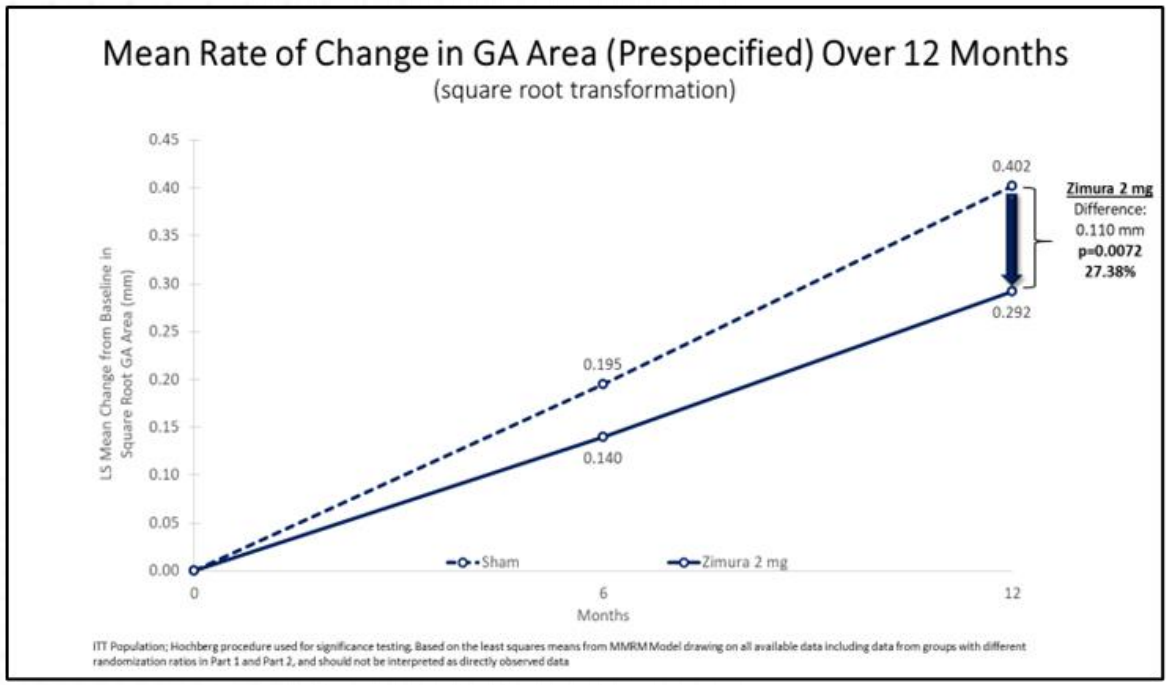
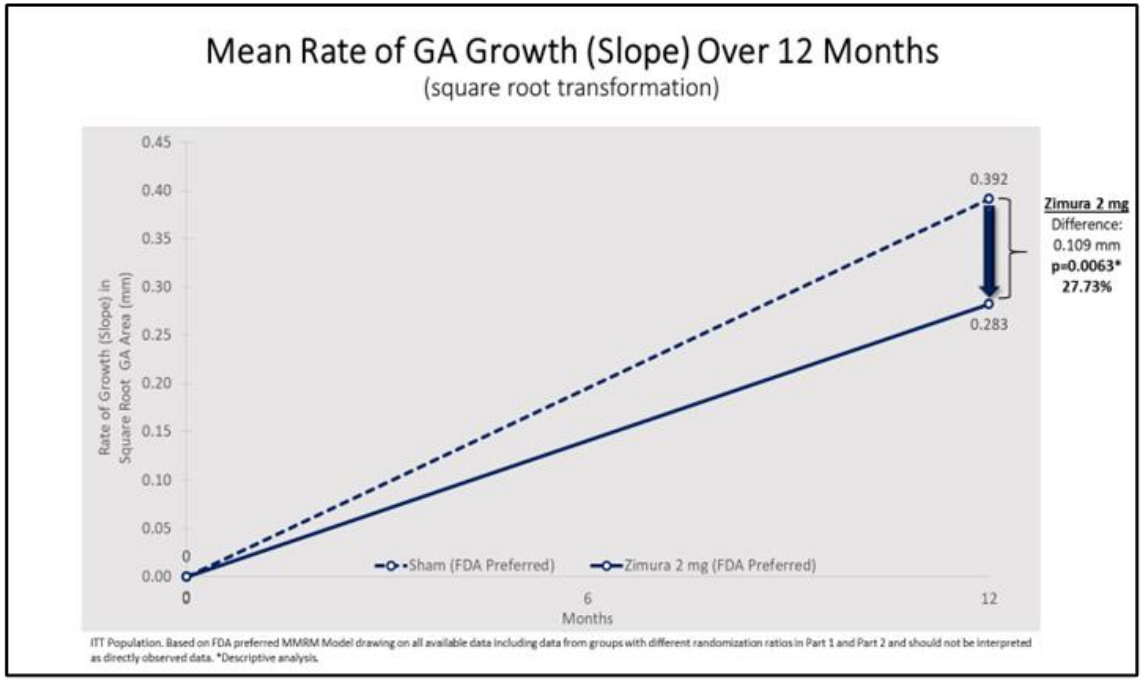
GATHER1: 2mg vs. sham mean rate of change in GA area (pre-specified) and mean rate of GA growth (slope) (post-hoc)

FDA Preferred Analysis Supports Prespecified Analysis

Prespecified Analysis



FDA preferred Analysis



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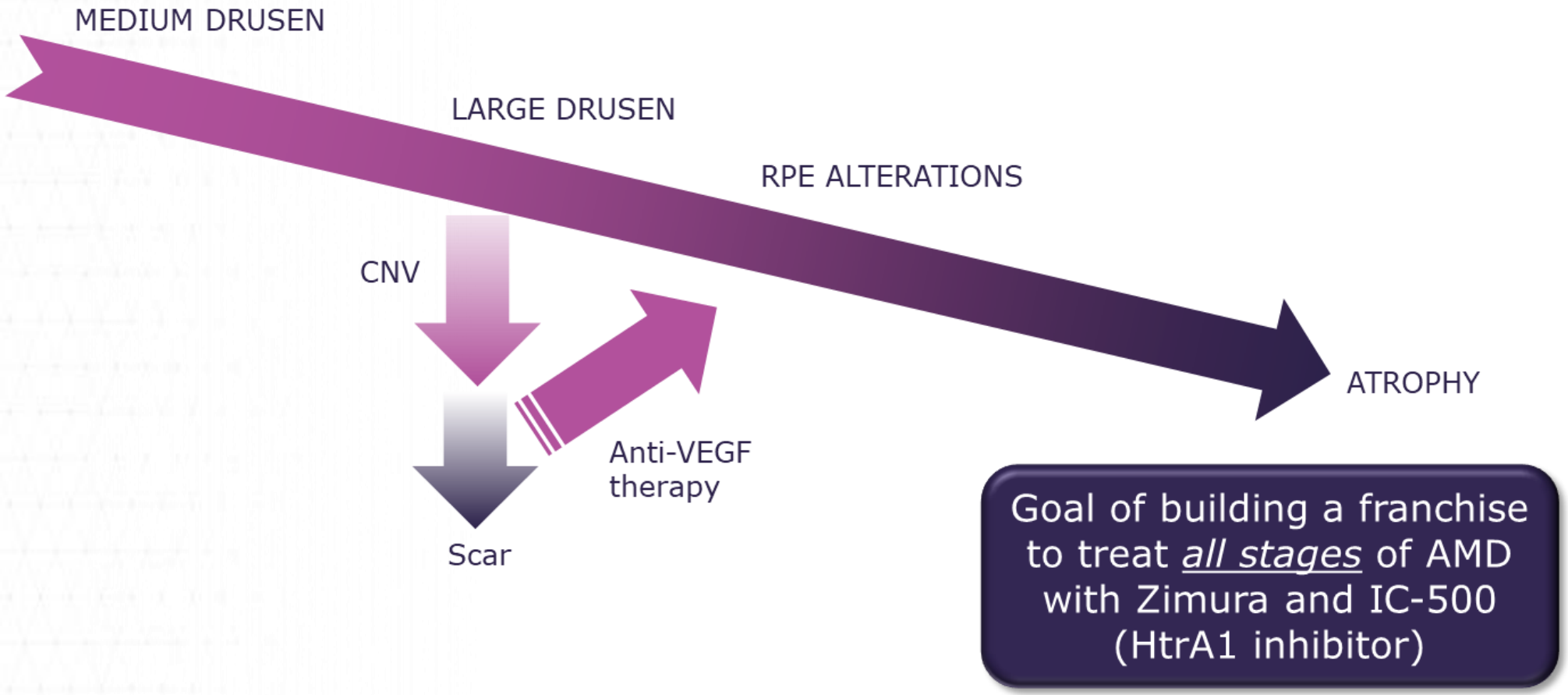
Pathway of AMD disease progression



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Ophthalmology. 2017 Jan; 124(1): 97–104; Lancet. 2018 Sep 29;392(10153):1147-1159; Retina. 2016 Oct;36(10):1843-50; Am J Ophthalmol. 2015 May;159(5):915-24

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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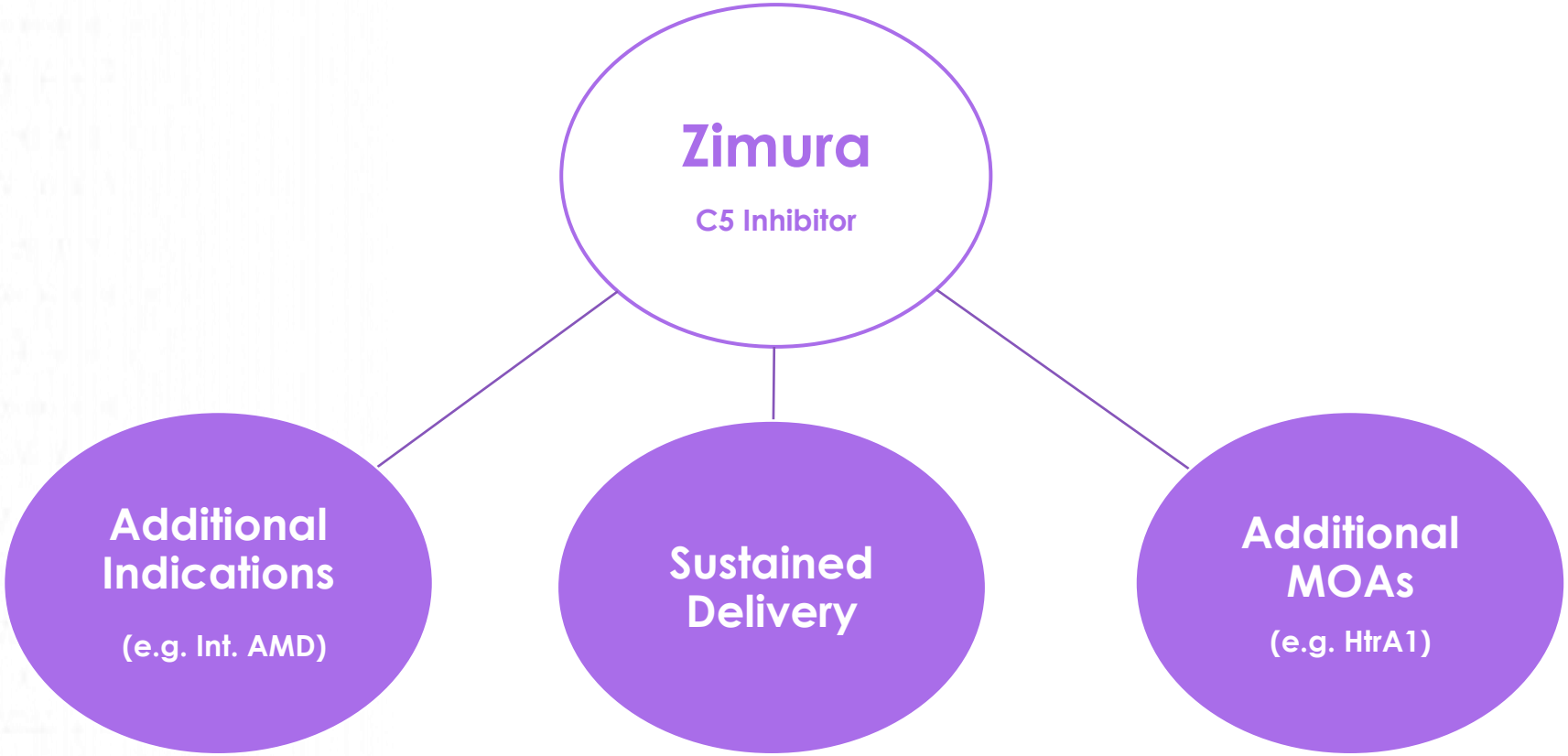
BUILDING AN AMD FRANCHISE

Lifecycle Management Strategy



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Intermediate AMD: Planned Trial Design

- 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

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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

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Proposed mechanism of HtrA1 activity in AMD

Destruction of extracellular matrix proteins leads to epithelium dysfunction

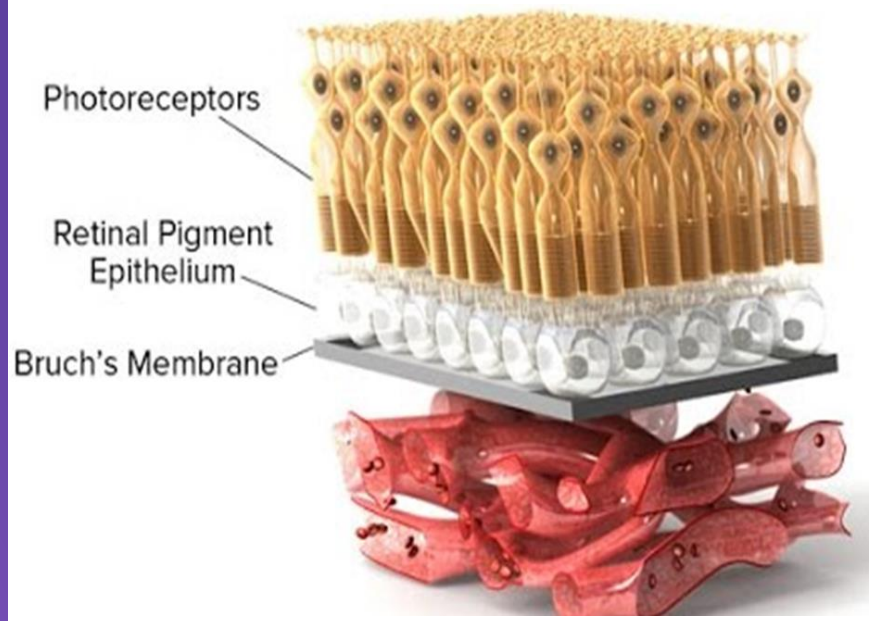
Increased HtrA1 protease activity

Destruction of structural and regulatory extracellular proteins, and intracellular proteins

- Loss of key BM, RPE, and choroid functions
- Upregulation of non-VEGF angiogenic and pro-inflammatory factors

RPE, Bruch's membrane, and choroidal dysfunction

AMD development and progression



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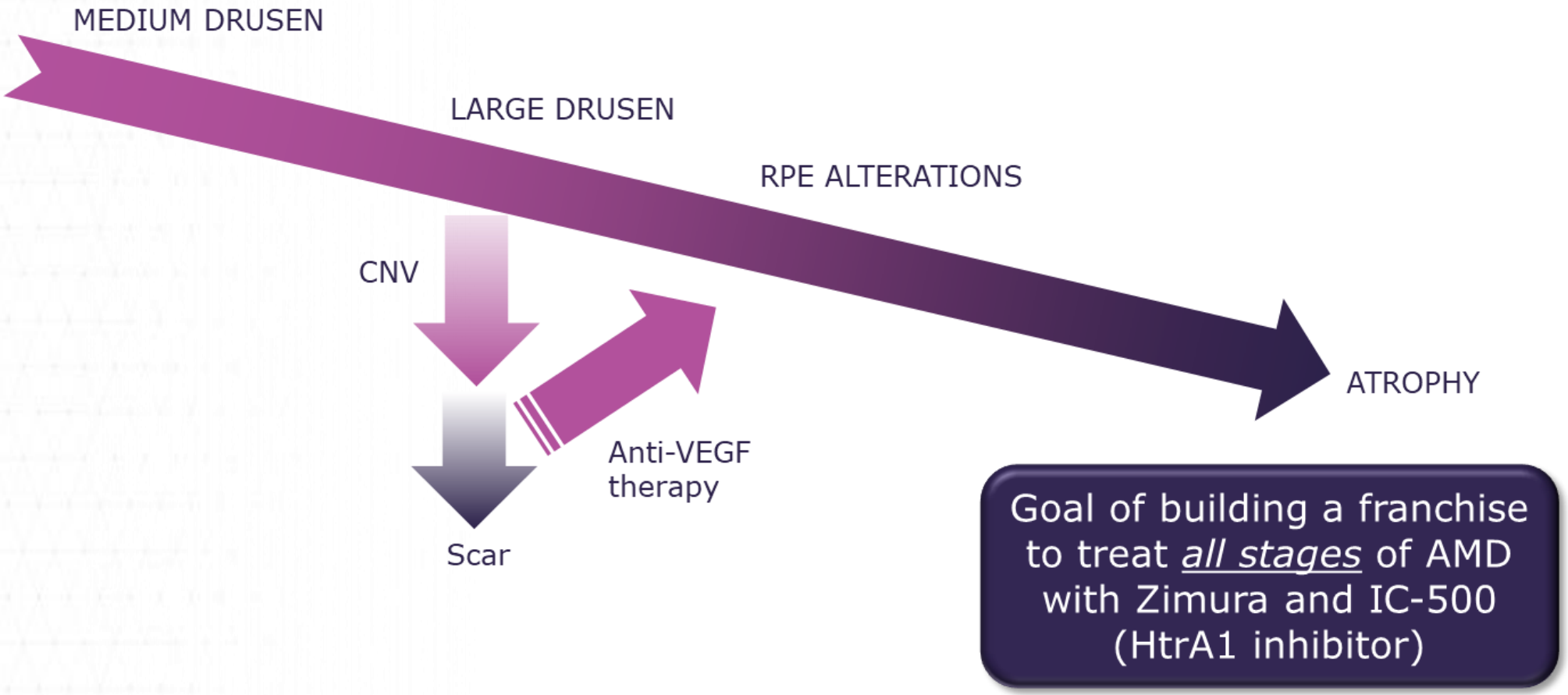
Multiple shots on goal in AMD



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Ophthalmology. 2017 Jan; 124(1): 97–104; Lancet. 2018 Sep 29;392(10153):1147-1159; Retina. 2016 Oct;36(10):1843-50; Am J Ophthalmol. 2015 May;159(5):915-24

Planned and recent milestones

- ✔ GATHER2 topline data readout (September 2022)
- ✔ Initiate clinical trial of Zimura in intermediate AMD (4Q 2022)
- ✔ IC-500 IND submission (mid-2023)

- ✔ Signed license agreement with DelSiTech for Sustained Release for Zimura (June 2022)
- ✔ GATHER2 enrollment completed (July 2021)
- ✔ Hired Chief Commercial Officer (August 2021)

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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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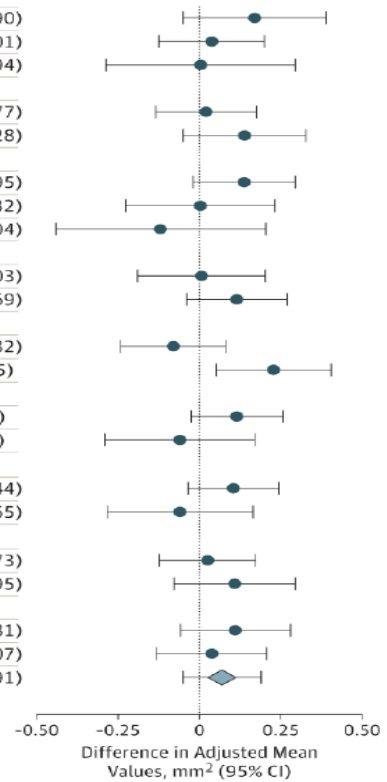
APPENDIX

Extrafoveal Sham Growth: Chroma/Spectri & GATHER1

NON-SQUARE-ROOT TRANSFORMATION

Source	Sham Pooled No. of Participants	Sham Pooled Adjusted Mean (SE) Change	Lampalizumab q4w No. of Participants	Lampalizumab q4w Adjusted Mean (SE) Change	Difference in Adjusted Mean Change (95% CI)	Relative Reduction, %
Age, y						
<75	176	1.880 (0.082)	204	2.051 (0.076)	0.171 (-0.049 to 0.390)	-9.1
75-84	266	1.998 (0.058)	249	2.035 (0.059)	0.038 (-0.125 to 0.201)	-1.9
≥85	123	2.110 (0.100)	99	2.114 (0.109)	0.004 (-0.287 to 0.294)	-0.2
Sex						
Female	336	2.076 (0.056)	334	2.096 (0.056)	0.021 (-0.135 to 0.177)	-1.0
Male	229	1.851 (0.067)	218	1.991 (0.069)	0.139 (-0.050 to 0.328)	-7.5
Geographic region						
United States and Canada	344	2.007 (0.057)	345	2.144 (0.056)	0.138 (-0.019 to 0.295)	-6.9
Western Europe	151	1.970 (0.080)	135	1.973 (0.085)	0.003 (-0.226 to 0.232)	-0.2
Rest of world	70	1.907 (0.117)	72	1.788 (0.114)	-0.119 (-0.441 to 0.204)	6.2
Baseline BCVA, letter score						
<64 (worse than 20/50)	208	1.936 (0.072)	222	1.942 (0.069)	0.007 (-0.190 to 0.203)	-0.3
≥64 (20/50 or better)	351	2.018 (0.055)	327	2.133 (0.056)	0.116 (-0.038 to 0.269)	-5.7
Baseline LLD, letter score						
<30	298	1.801 (0.058)	282	1.722 (0.059)	-0.080 (-0.242 to 0.082)	4.4
≥30	250	2.198 (0.064)	254	2.426 (0.063)	0.228 (0.052 to 0.405)	-10.4
Baseline GA area, DA						
<4	420	1.805 (0.050)	390	1.921 (0.052)	0.116 (-0.025, 0.257)	-6.4
≥4	145	2.458 (0.085)	162	2.398 (0.080)	-0.060 (-0.289, 0.170)	2.4
Baseline GA contiguity						
Multifocal	444	2.058 (0.050)	438	2.163 (0.050)	0.105 (-0.034 to 0.244)	-5.1
Not multifocal	121	1.712 (0.080)	114	1.653 (0.081)	-0.059 (-0.282 to 0.165)	3.4
Baseline GA lesion location						
Subfoveal	306	1.720 (0.053)	294	1.746 (0.054)	0.025 (-0.123 to 0.173)	-1.5
Nonsubfoveal	259	2.292 (0.067)	258	2.401 (0.067)	0.109 (-0.077 to 0.295)	-4.8
Tobacco use history						
Never	263	1.881 (0.061)	256	1.992 (0.061)	0.111 (-0.058 to 0.281)	-5.9
Ever	302	2.074 (0.061)	296	2.112 (0.061)	0.038 (-0.132 to 0.207)	-1.8
Overall	565	1.984 (0.043)	552	2.055 (0.043)	0.071 (-0.049 to 0.191)	-3.6



Chroma/Spectri

Mean change in extrafoveal GA 2.292-2.401

GATHER1

Mean change in extrafoveal GA 2.29-2.77

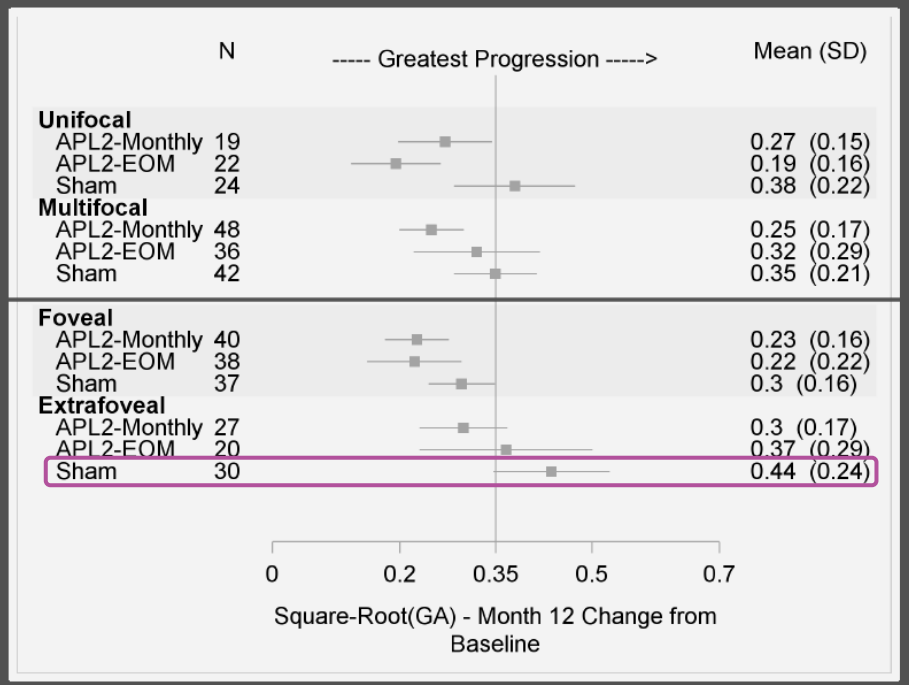
eFigure 2. Adjusted Mean Change in Geographic Atrophy (GA) Area From Baseline to Week 48 in the Study Eye by Clinical Subgroup, Chroma and Spectri Pooled

Source: JAMA Ophthalmol. 2018 Jun 1;136(6):666-677. www.apellis.com

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[1], Mohamed Hamdani[2]

[1]California Retina Consultants
[2]Apellis Pharmaceuticals

Source: JAMA Ophthalmol. 2018 Jun 1;136(6):666-677. www.apellis.com

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 ≥ 50 letters
  - Size of baseline GA: < 4 disc area vs ≥ 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