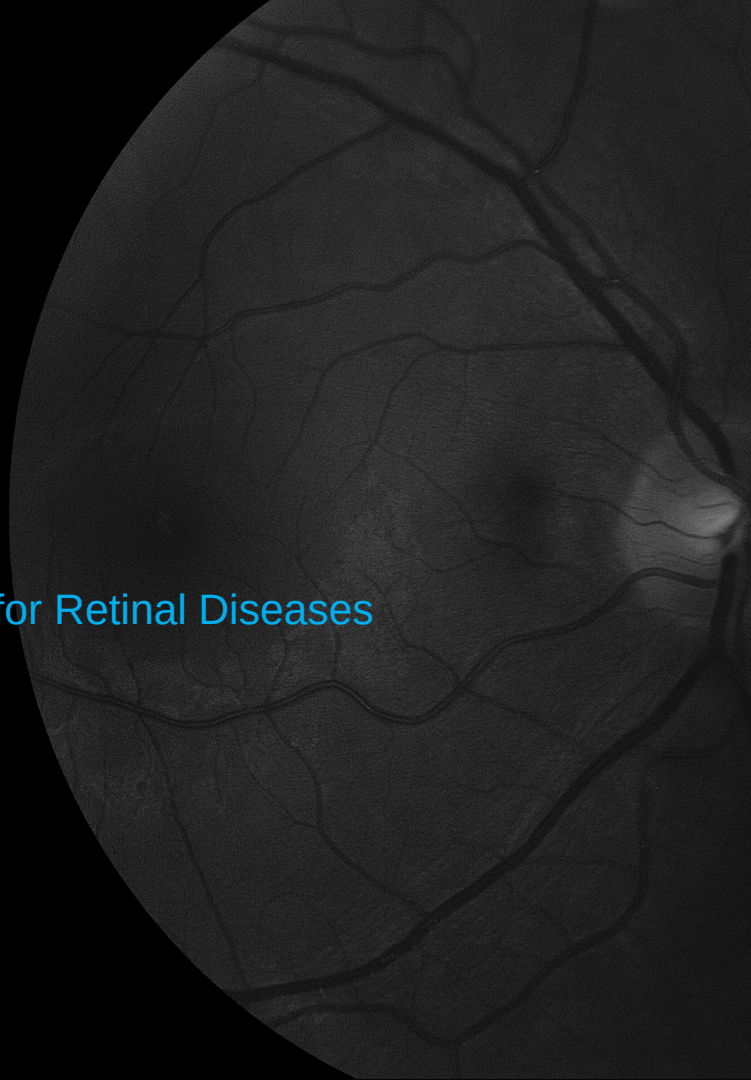
IVERIC bio



Developing Transformative Therapies for Retinal Diseases

August 2020
NASDAQ: ISEE

Forward-looking Statements

Any statements in this presentation about the Company's future 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 and plans and prospects for the Company, 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 the impact of the COVID-19 pandemic on its research and development programs, operations and financial position, its expectations to use its previously announced clinical trial of Zimura for the treatment of geographic atrophy (OPH2003/GATHER1) as a Phase 3 trial, its development strategy for Zimura, the Company's hypotheses regarding complement inhibition as a mechanism of action for the treatment of geographic atrophy, the projected use of cash and cash balances, the periods of marketing exclusivity for its product candidates, the timing, progress and results of clinical trials and other research and development activities, 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 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, the initiation and the progress of research and development programs and clinical trials, availability of data from these programs, reliance on third parties, establishment of manufacturing capabilities, expectations for regulatory 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 will 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.

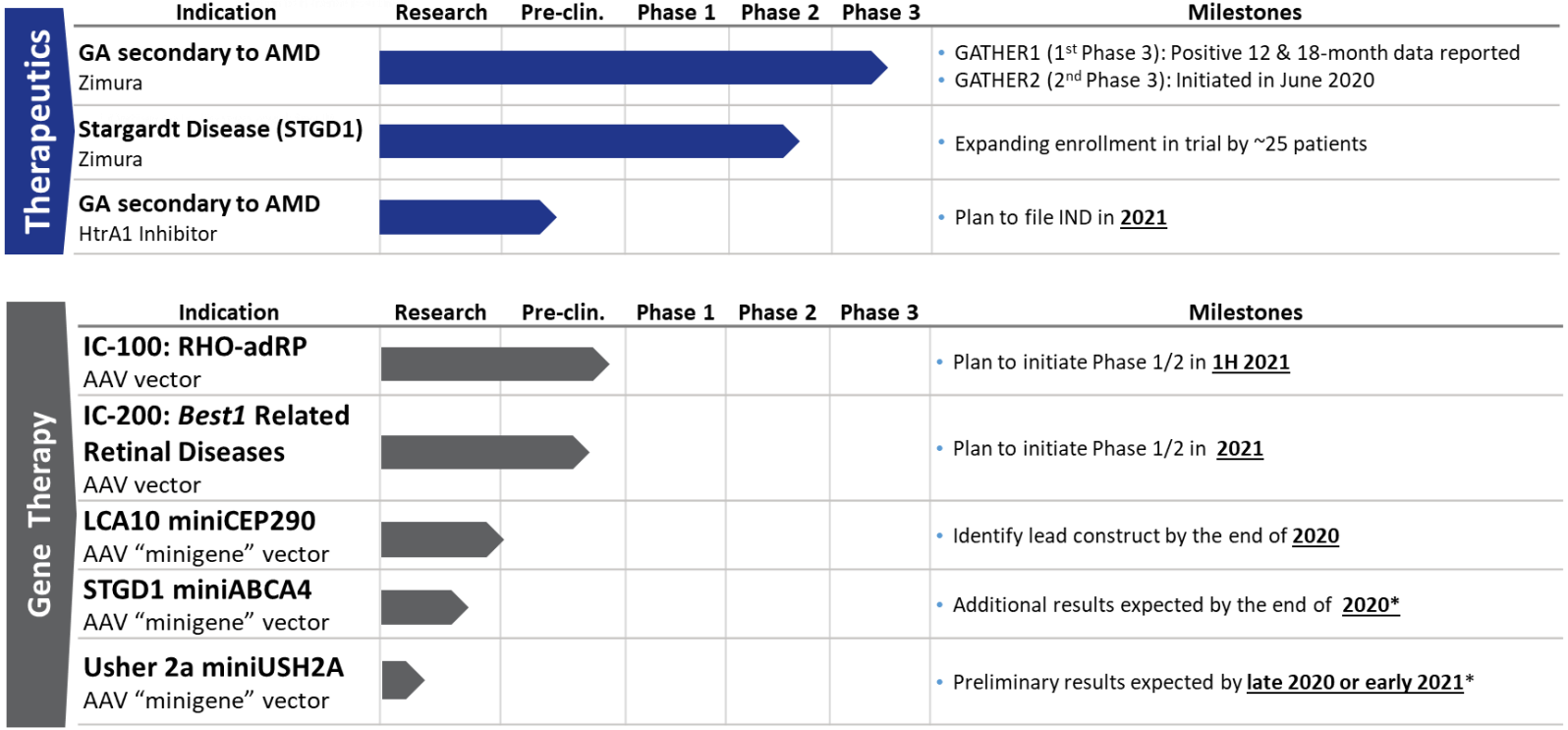
A Diversified Portfolio Focused on Retinal Diseases

- **Therapeutics for Age-Related Retinal Diseases (Large Market)**
  - Zimura: Positive data for the first of two Phase 3 trials (GATHER1)
    - Statistically significant 27% reduction in GA growth over 12 months (primary endpoint achieved)
    - Supported by 18-month results showing continuous treatment effect
    - Favorable safety profile over 18 months
    - Patient enrollment for second Phase 3 trial (GATHER2) initiated in June 2020
    - Potential expansion into intermediate AMD, wet AMD and lifecycle initiatives
  - Multi-billion dollar large market opportunity with no approved therapy in GA
- **Gene Therapy for Retinal Diseases (Orphan)**
  - Broad and diversified Pipeline
    - Novel and cutting edge AAV gene therapy options
    - Five R&D programs in orphan inherited retinal diseases
  - No approved therapies in the targeted diseases
- **Experienced Team with Extensive Drug Development Expertise in Retina**
- **Strong Cash Position and Well-Capitalized**
  - ~$108.4 million in cash and cash equivalents as of 3/31/20
  - Concurrent public offering and private placement with net proceeds of ~$150 million completed in June 2020

Strong Senior Management with Significant Ophthalmology Domain Experience

Key Management	Experience
Glenn Sblendorio *Chief Executive Officer*	The Medicines Company; eyetech; Roche; MPM
Pravin U. Dugel, MD *Chief Strategy and Business Officer*	USC Roski Eye Institute, Keck Medicine of USC; Spectra Eye Institute; UCLA School of Medicine; Columbia University in the City of New York
Kourous A. Rezaei, MD *Chief Medical Officer*	Rush University Medical Center; Illinois Retina Associates, S.C.; University of Cologne; Kresge Eye Institute
Guangping Gao, PhD *Chief Strategist, Gene Therapy*	University of Massachusetts Medical School; Horae (红瑞) Gene Therapy Center; American Society of Gene & Cell Therapy
David F. Carroll *Chief Financial Officer*	The Medicines Company; Genentech, A Member of the Roche Group; Novartis; Bristol-Myers Squibb
Keith Westby *Chief Operating Officer*	Pharmasset; eyetech; Tunnell Consulting, Stronger Performance Ahead; Roche; Pfizer
Abraham Scaria, PhD *Chief Scientific Officer*	Casebia Therapeutics; Sanofi; Genzyme, A Sanofi Company
Evelyn Harrison *Chief Clinical Operations Officer*	eyetech; Roche

IVERIC bio Pipeline



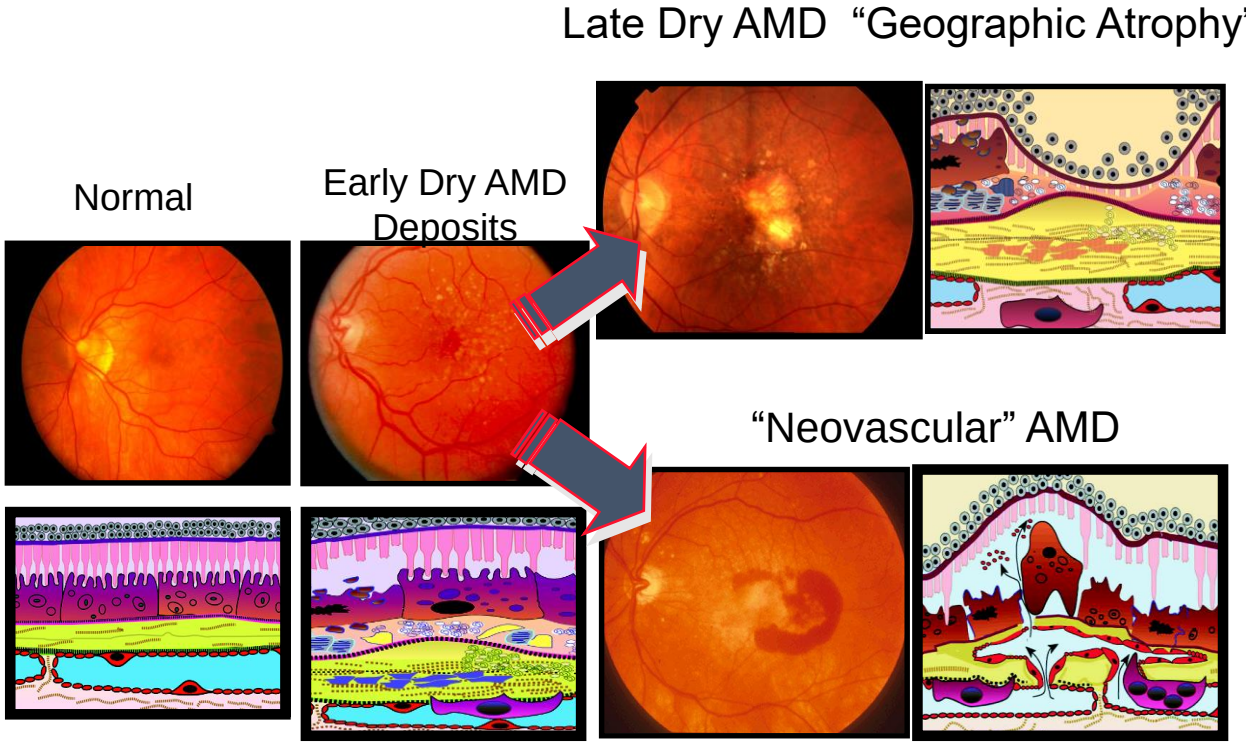
*We have an option to exclusively in-license intellectual property resulting from ongoing sponsored research.

What is Age-Related Macular Degeneration?

Vision Loss with End-Stage Age-Related Macular Degeneration

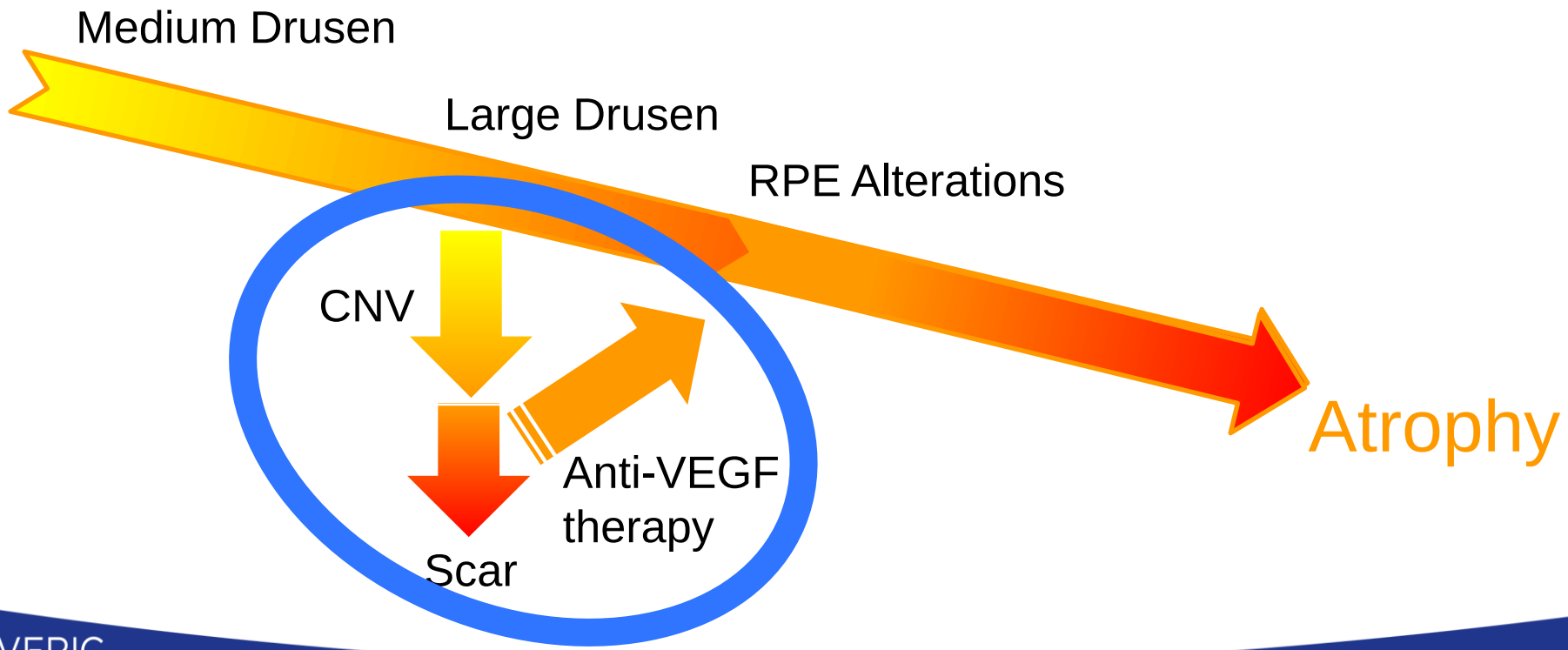
Courtesy of Dr Karl Csaky

Common Perception: Advanced AMD is *either* **Dry** (leading to GA) *or* **Wet**



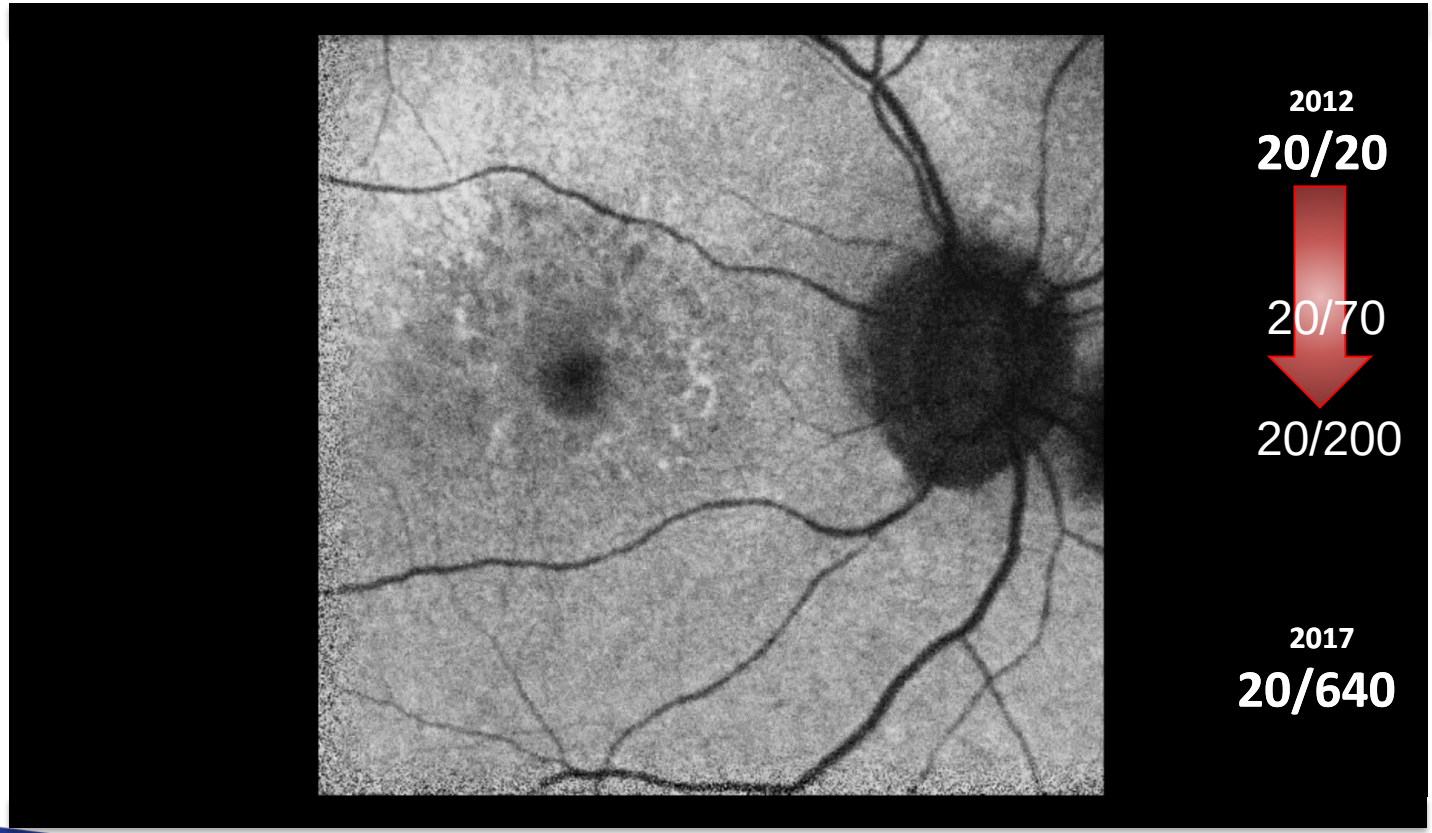
Courtesy of Dr Karl Csaky

Pathway of AMD Disease Progression



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

Geographic Atrophy: Growth Over Time



Lower limit for driving in many US states

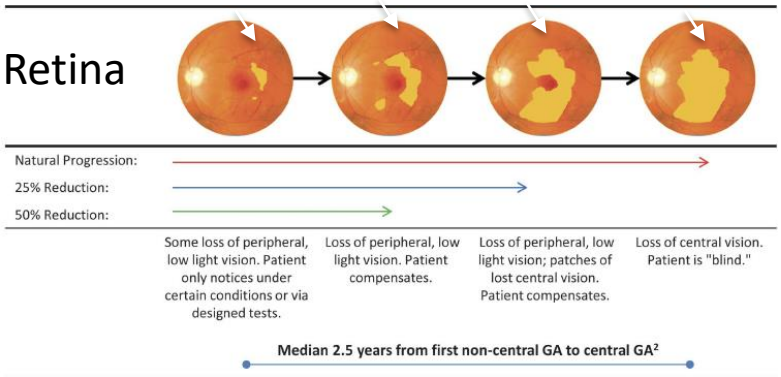
Legal Blindness

Courtesy: Jordi Mones, MD

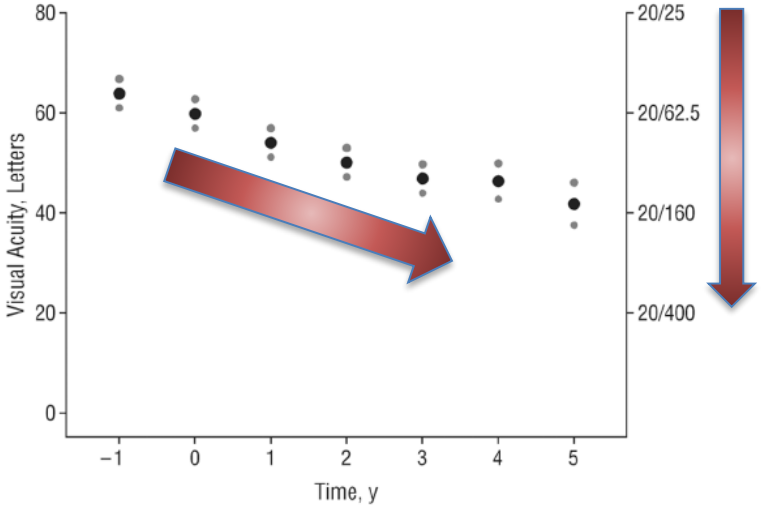
Geographic Atrophy: Growth of Area and Loss of Vision

Geographic Atrophy: Loss of Photoreceptors (Cells that Perceive Light) Over Time

Increase in Area of Degeneration Over Time



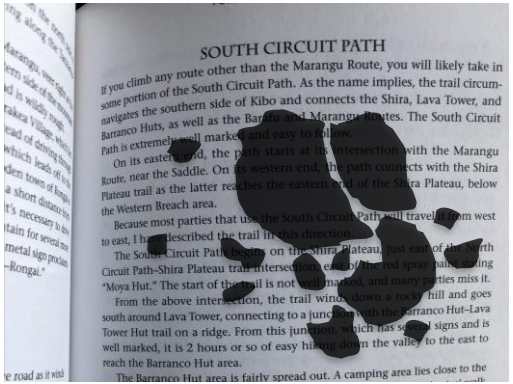
Loss of Vision Over Time



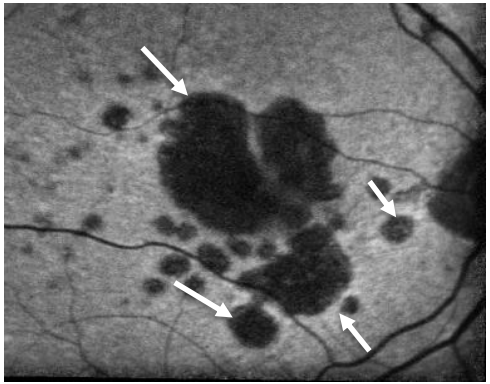
Source: Ophthalmology 2014;121:1079-1091. Retina 2017;27:819-835. Arch Ophthalmol 2009;127:1168-1174.

Geographic Atrophy: Impact on Functional Vision in Daily Life

Treatment Goal: Slow Down the Growth of Geographic Atrophy



Areas of missing vision (scotoma)



Areas of geographic atrophy
(Dead retinal cells)

Areas of missing vision (scotoma)

What does Complement have to do with AMD?

Genetic Link: Complement & AMD

"In individuals homozygous for the risk allele, the likelihood of AMD is increased by a factor of 7.4"

A common haplotype in the complement regulatory gene factor H (*HF1/CFH*) predisposes individuals to age-related macular degeneration

Gregory S. Hageman[a,b,c], Don H. Anderson[b,d], Lincoln V. Johnson[b,d], Lisa S. Hancox[a], Andrew J. Taiber[a], Lisa I. Hardisty[a], Jill L. Hageman[a], Heather A. Stockman[a], James D. Borchardt[a], Karen M. Gehrs[a], Richard J. H. Smith[a], Giulliana Silvestri[f], Stephen R. Russell[a], Caroline C. W. Klaver[g], Irene Barbazetto[h], Stanley Chang[h], Lawrence A. Yannuzzi[h], Gaetano R. Barile[h], John C. Merriam[h], R. Theodore Smith[h], Adam K. Olsh[i], Julie Bergeron[i], Jana Zernant[b], Joanna E. Merriam[b], Bert Gold[j], Michael Dean[j], and Rando Allikmets[b,k,l]

Source: Proc Natl Acad Sci U S A 2005, 102(20), 7227-7232

Complement Factor H Polymorphism and Age-Related Macular Degeneration

Albert O. Edwards,[1*†] Robert Ritter III,[1] Kenneth J. Abel,[2] Alisa Manning,[3] Carolien Panhuysen,[3,6] Lindsay A. Farrer[3,4,5,6,7]

Source: Science 2005, 308(5720), 421-424

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] Josephine Hoh[7†]

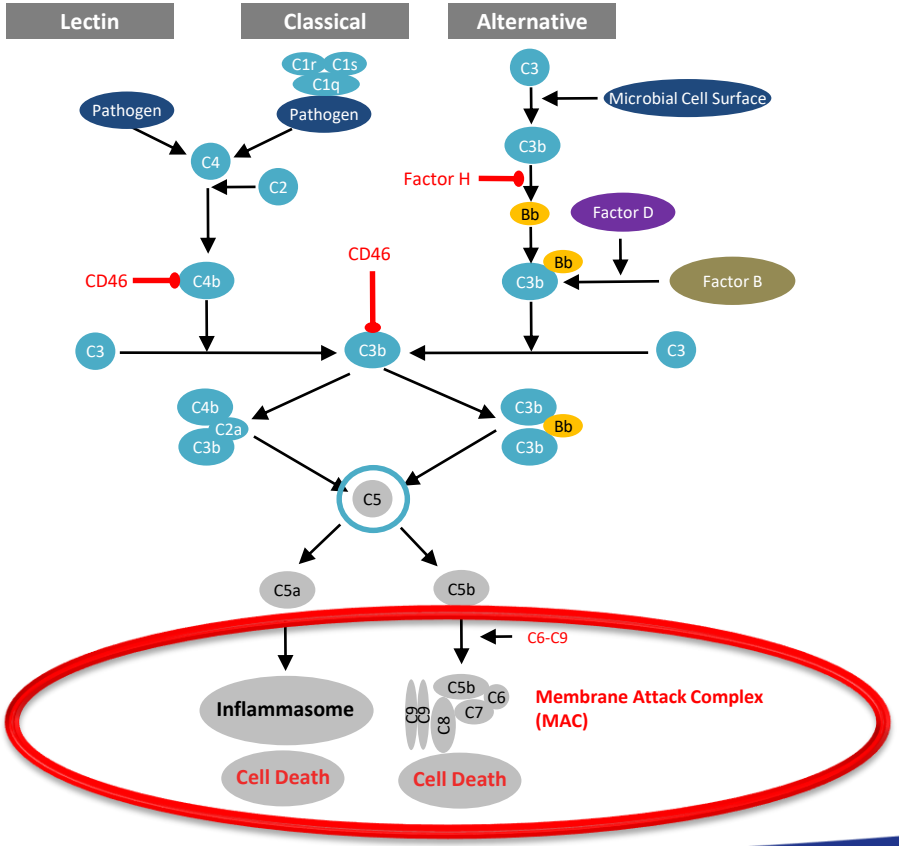
Source: Science. 2005 Apr 15;308(5720):385-389

Complement Factor H Variant Increases the Risk of Age-Related Macular Degeneration

Jonathan L. Haines,[1] Michael A. Hauser,[2] Silke Schmidt,[2] William K. Scott,[2] Lana M. Olson,[1] Paul Gallins,[2] Kylee L. Spencer,[1] Shu Ying Kwan,[2] Maher Noureddine,[2] John R. Gilbert,[2] Nathalie Schnetz-Boutaud,[1] Anita Agarwal,[3] Eric A. Postel,[4] Margaret A. Pericak-Vance[2*]

Source: Science 2005, 308(5720), 419-421

Complement Pathway: Inflammasome & MAC → Cell Death

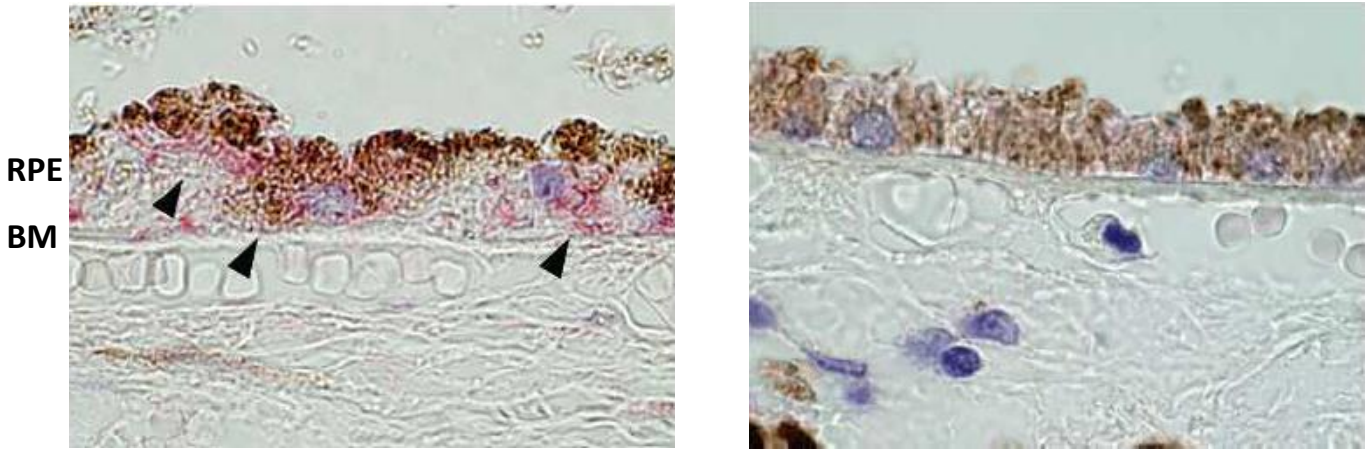


Source: ISEE internal

Inflammasome Activation leading to Cell Death in AMD Affected Eyes

Dry AMD

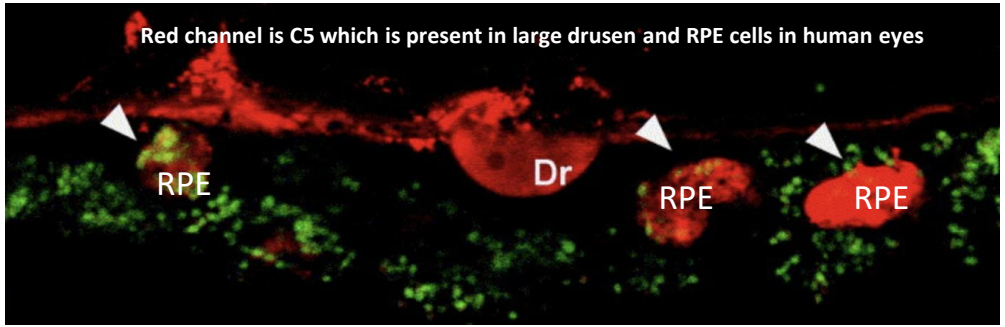
No AMD

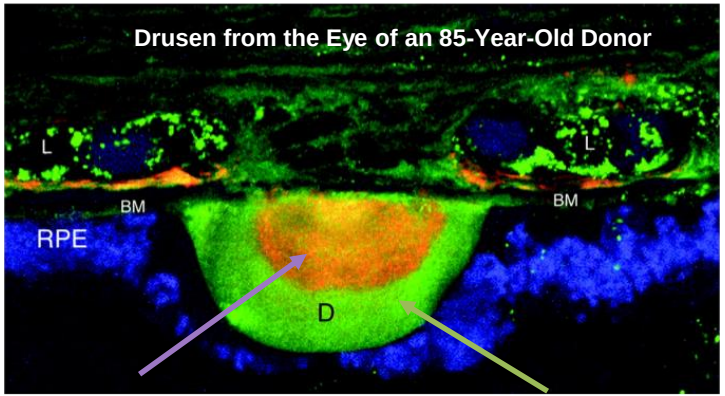


RPE: Retinal pigment Epithelium
BM: Bruch's membrane

Source: Invest Ophthalmol Vis Sci. 2013;54:110–120.

Presence of C5 and MAC Activation leading to Cell Death in AMD





C5-9 membrane attack complex of complement

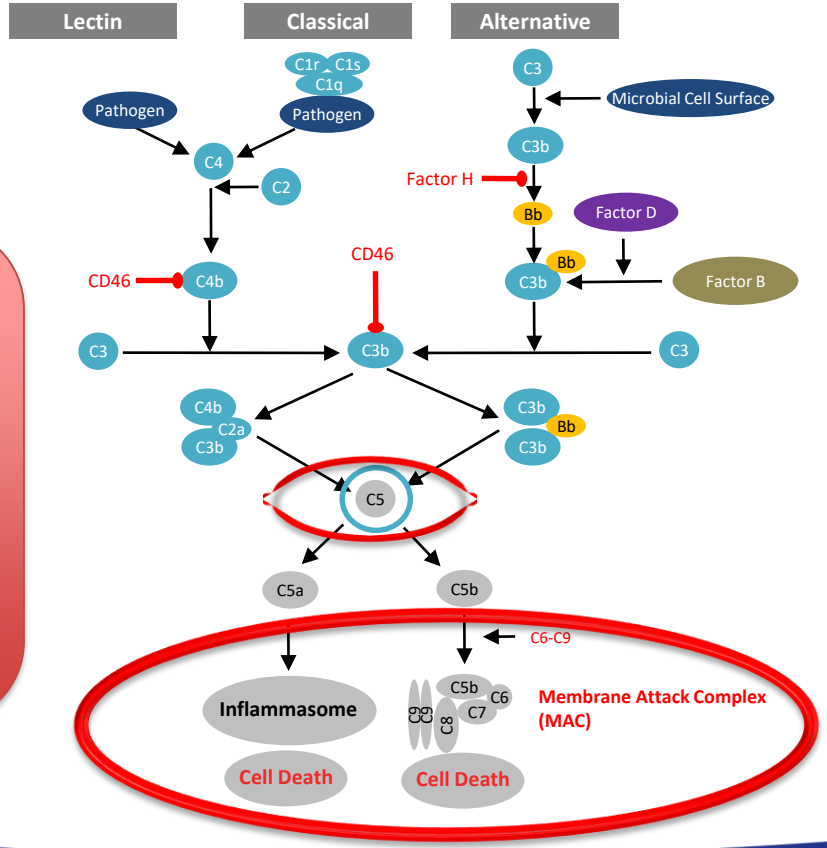
Complement factor H

Source: Am J Ophthalmol 2002;134:411–431. Proc Natl Acad Sci USA. 2005, 102(20), 7053-7054

Why is Zimura® Important?

Complement Pathway

Inhibit the 2 “Killers,” But Preserve the Rest



Zimura (Avacincaptad Pegol)

- 39-mer – oligonucleotide conjugated to 40 kDa PEG
- Formulation: sterile, preservative free solution for intravitreal injection (100 µL)

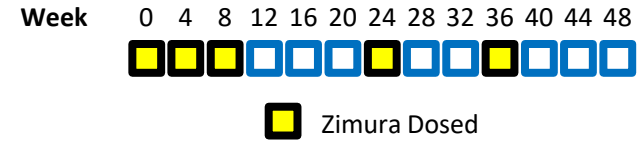
Source: ISEE internal

Do we have evidence of Zimura's efficacy in GA?

Zimura Phase 1/2a Dry AMD (GA) – Completed*

Study Design

Intravitreal Zimura was administered for a maximum of 5 injections at one of two dose levels (0.3 mg/eye or 1mg/eye)



47 Patients Enrolled

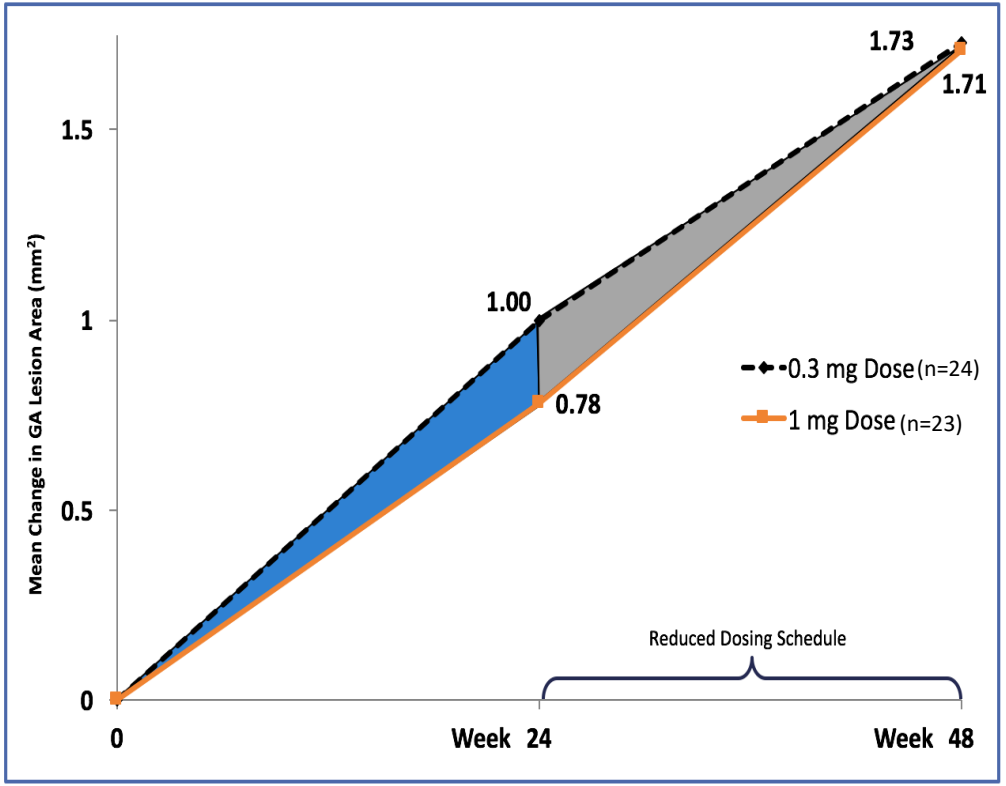
0.3 mg dose group (n=24)

1 mg dose group (n=23)

*Uncontrolled safety trial; small sample size

Zimura Phase 1/2a Dry AMD (GA) – Completed*

- Potential efficacy signal(s)
  - Presence of a dose-response trend with “on-off effect”
- Safety
  - No Zimura related adverse events
  - Zero incidence of wet AMD in eyes treated with Zimura



*Uncontrolled safety trial; small sample size

ZIMURA PHASE 3 PROGRAM IN GEOGRAPHIC ATROPHY SECONDARY TO AMD

GATHER1 & GATHER2

(**G**eographic **A**trophy **THER**apy Trials)

GATHER1 (OPH2003): Phase 3 Trial Design

- Screening trial: designed similar to a traditional Phase 3 but with fewer patients
- **Minimized bias**: patient, evaluating physician, reading center, sponsor are all masked
- Valid control: sham control arm
- Independent masked reading center reviewing the images; images for each visit were evaluated independently
- Robust statistical analysis: prespecified statistical analysis plan (SAP) and detailed sensitivity testing
- Prespecified strength of evidence needed to meet the standard requirement of a **0.0125 one-sided false positive error rate** (incorporating an adjustment for multiplicity arising from comparing each dose with the Sham control) to achieve statistical significance

GATHER1: Prespecified Screening Trial

Designed as a registration trial with three potential outcomes:

- Negative Trial:
  - Low level or no benefit observed: would not move forward with a subsequent trial
- Positive Phase 2 Trial:
  - Moderate, clinically relevant benefit but without statistically significant p-value: move forward with two larger Phase 3 clinical trials
- **Positive Phase 3 Trial:**
  - **Statistically significant benefit (as observed in both Zimura 2 mg and 4 mg groups): trial could potentially serve as a registration trial and only one more Phase 3 trial would be required for regulatory approval**

Source: Fleming & Richrdson, J Infectious Diseases. 2004;190:666-74.

GATHER1: Trial Design

- Randomized, double masked (quadruple masked), sham controlled clinical trial
- Cohorts included in the pre-specified statistical analysis of the primary endpoint at Month 12*:
  - Zimura 4 mg dose
  - Zimura 2 mg dose
  - Sham
- 286 subjects were enrolled for monthly treatment with Zimura or Sham for 18 months
  - ~75% of the patients were enrolled in the US
- Primary efficacy endpoint: Mean rate of change in GA over 12 months measured by fundus autofluorescence (FAF) at three time points: Baseline, Month 6, and Month 12 (square root transformation of GA lesion)

*Descriptive analysis was performed for the Zimura 1mg cohort

Duke Reading Center: Imaging Analysis Overview

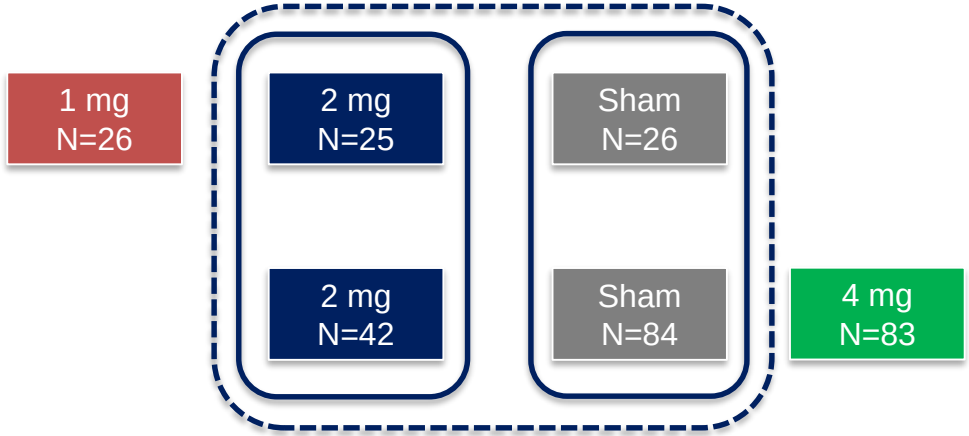
- Completely masked assessment
- Images for each visit evaluated independently
- Two experienced primary readers analyze the GA lesion size on FAF with RegionFinder
- > 10% discrepancy will be arbitrated by Reading Center Director: Glenn Jaffe, MD
- Supportive modalities: OCT and NIR imaging

Source: Duke Reading Center

GATHER1: Dose Groups

Masked Throughout the Entire process

Randomization

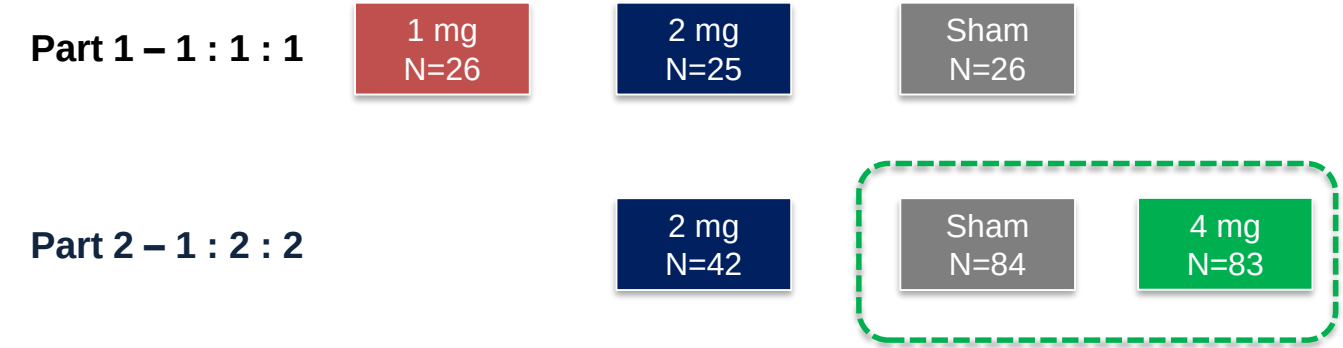


Efficacy Evaluation Based on Prespecified Statistical Analysis Plan (SAP):

- Zimura 2 mg vs. Sham: subjects randomized from Part 1 were combined with the subjects randomized from Part 2, where the analysis included a regression factor by part

GATHER1: Dose Groups

Randomization

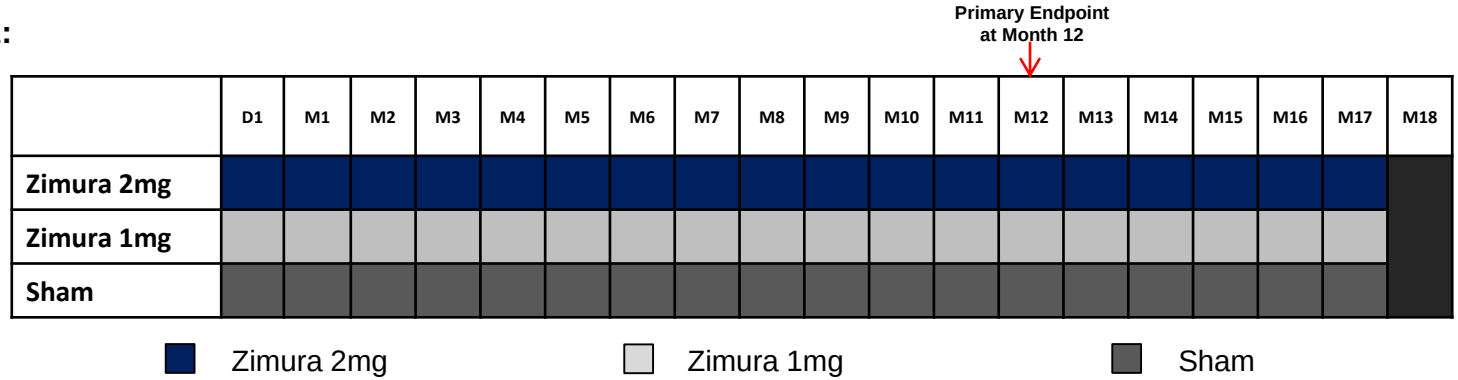


Efficacy Evaluation Based on Prespecified Statistical Analysis Plan (SAP):

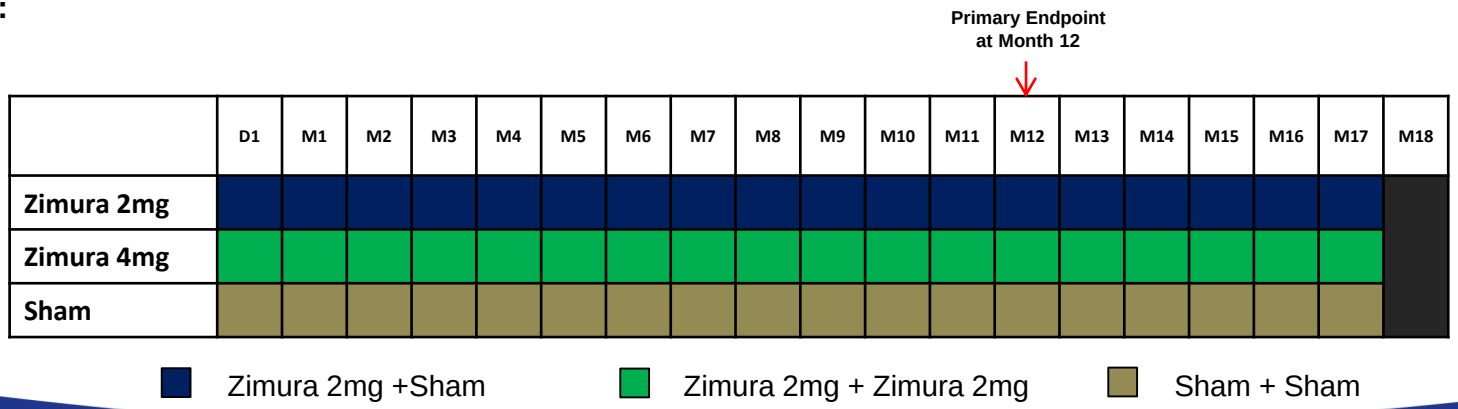
- Zimura 4 mg vs. Sham: based only on subjects randomized in Part 2

GATHER1: Dosing Regimen

Part 1:



Part 2:



GATHER1: Key Ophthalmic Inclusion Criteria (Study Eye)

- **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

GATHER1: Primary Efficacy Endpoint Achieved for Both Zimura 2mg and 4mg

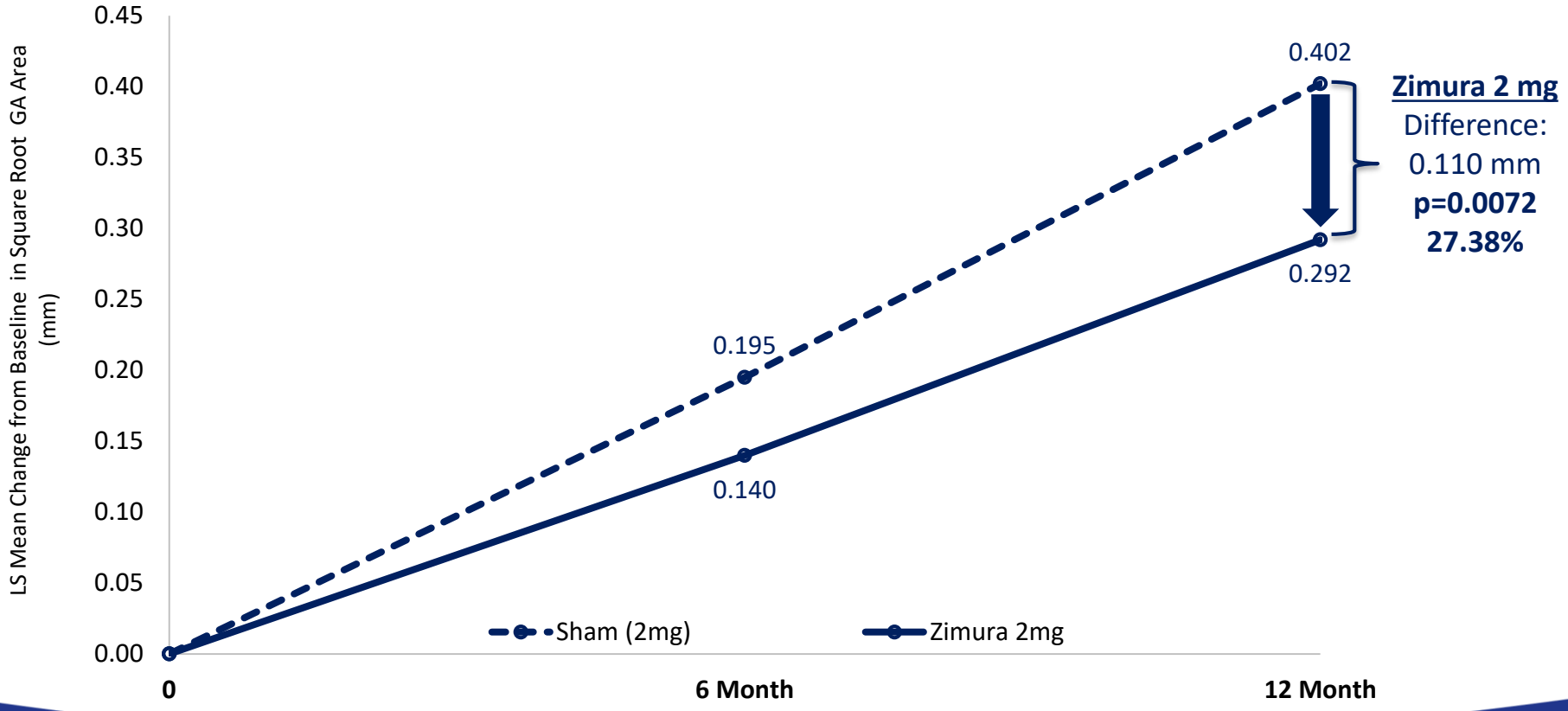
Mean Rate of Change in Geographic Atrophy (GA) Area from Baseline to Month 12
(MRM Analysis) (Square Root Transformation, ITT Population)

Cohort	Zimura 2mg (N=67)	Sham 2mg (N=110)	Difference	P-value	% Difference
Mean Change in GA[a] (mm)	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] (mm)	0.321	0.444	0.124	0.0051[b]	27.81%

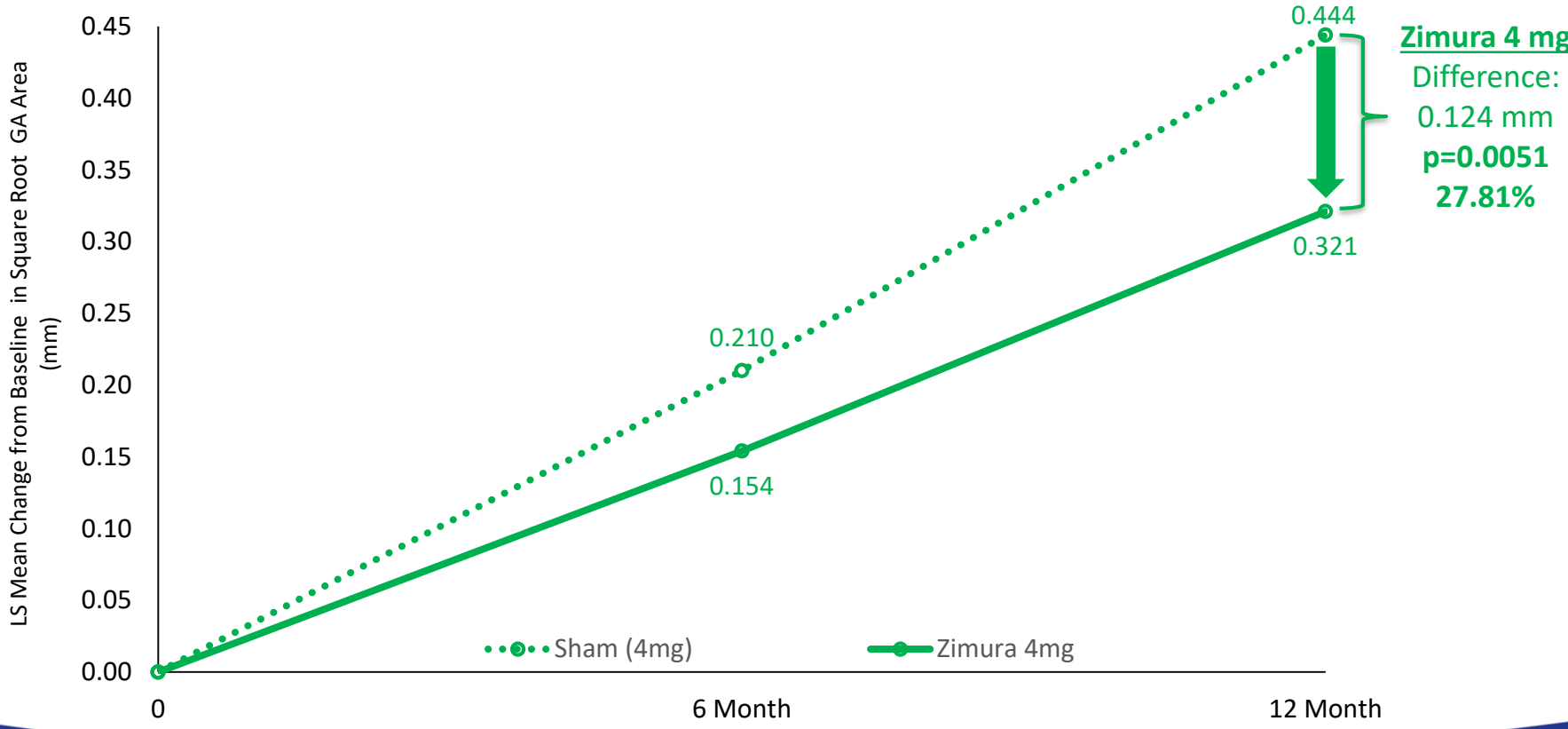
(a) = based on the least squares means from the MRM model
(b) = reflects statistically significant p-value; Hochberg procedure was used for significance testing
(c) = these least squares means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization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

GATHER1: Primary Efficacy Endpoint Achieved: Zimura 2 mg vs. Sham



Based on LSMEANS from MRM Model; ITT Population Hochberg procedure used for significance testing. 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.

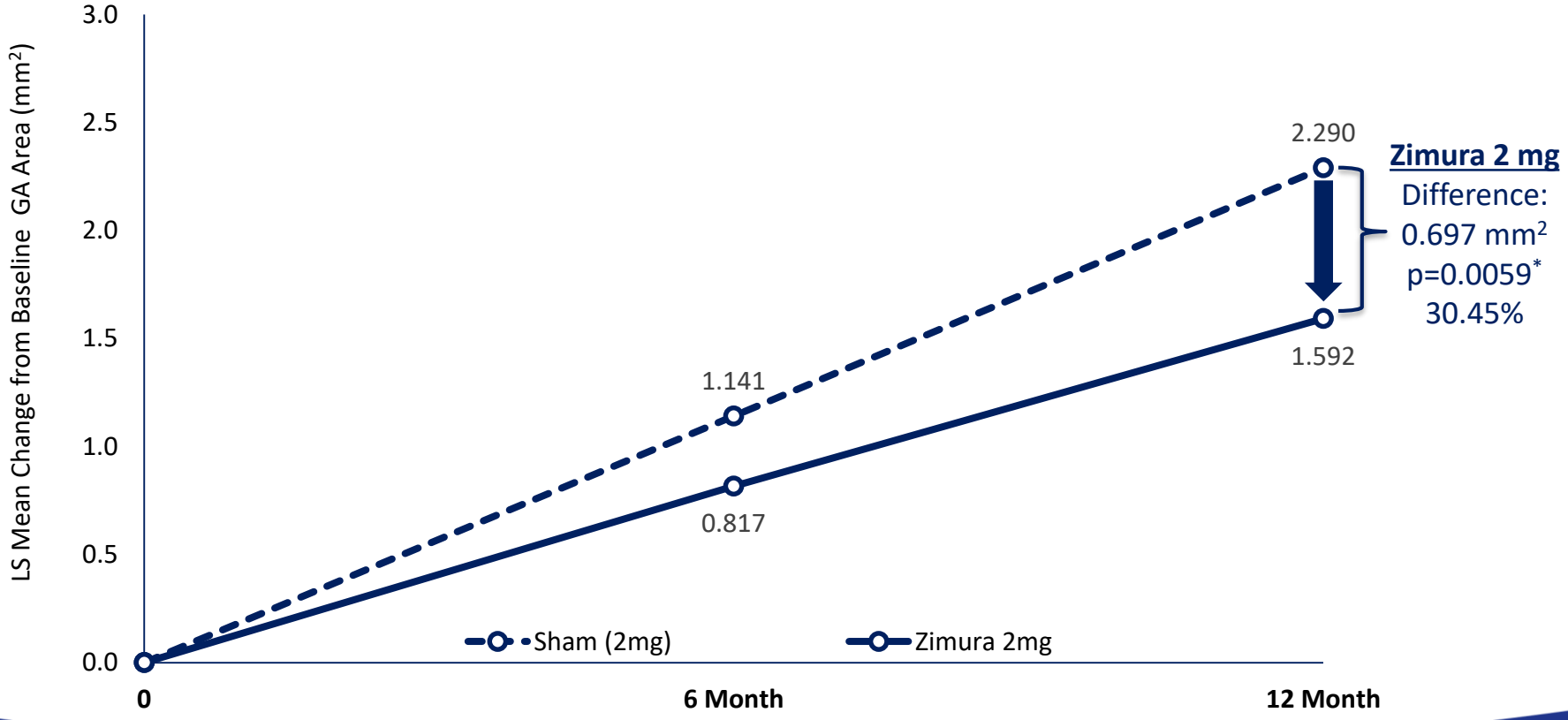
GATHER1: Primary Efficacy Endpoint Achieved: Zimura 4 mg vs. Sham



Based on LSMEANS from MRM Model; ITT Population Hochberg procedure used for significance testing

GATHER1: Supportive Efficacy Endpoint: Zimura 2 mg vs. Sham

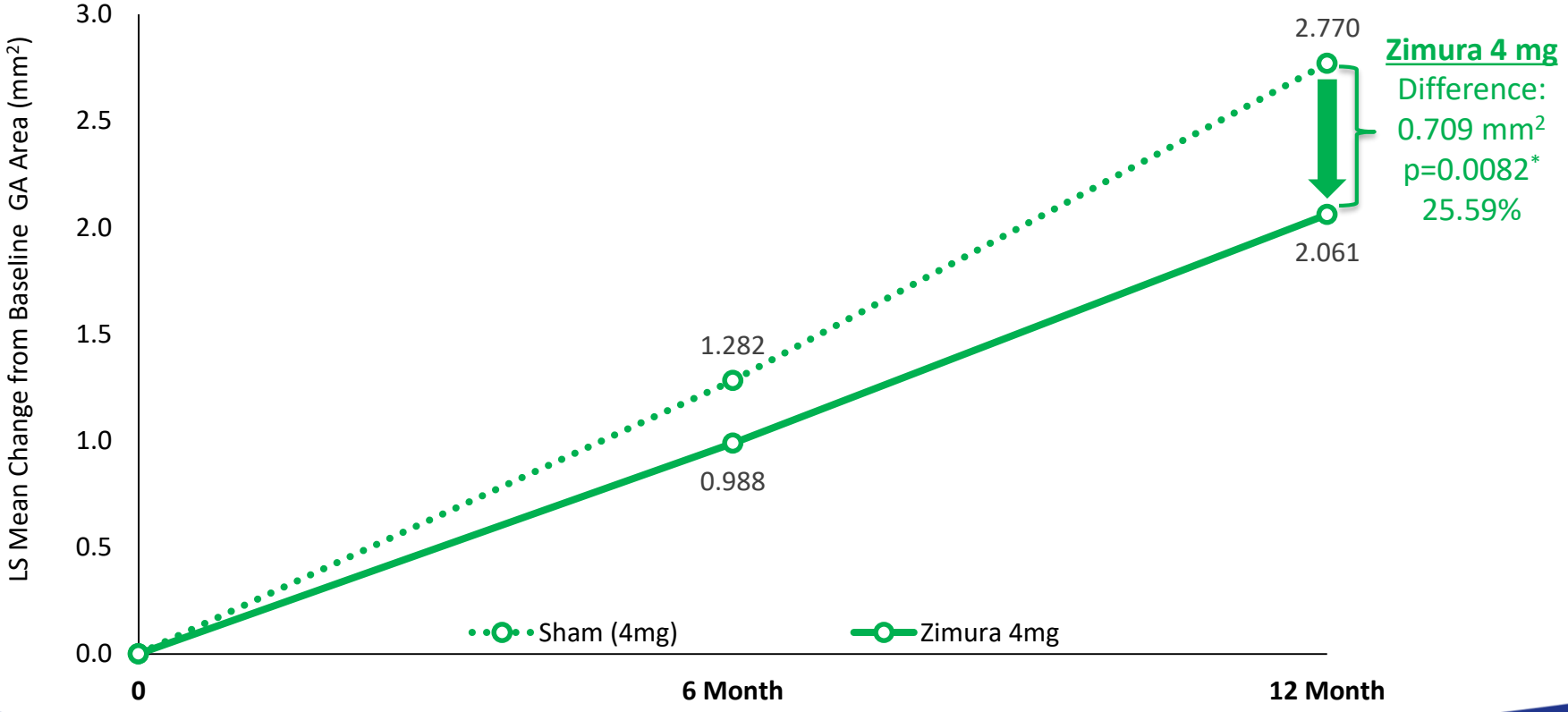
(Non-Square Root)



Based on LSMEANS from MRM Model; ITT Population Hochberg procedure used for significance testing. 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. *Prespecified and descriptive analysis.

GATHER1: Supportive Efficacy Endpoint: Zimura 4 mg vs. Sham

(Non-Square Root)



Based on LSMEANS from MRM Model; ITT Population Hochberg procedure used for significance testing. *Prespecified and descriptive analysis.

GATHER1: Secondary Endpoints

Trial not designed to demonstrate differences in mean changes in BCVA or LL BCVA with statistical significance

- Mean change in best corrected visual acuity (ETDRS letters) from Baseline to Month 12

Cohort	Zimura 2mg (N=67)	Sham 2mg (N=110)	Difference
Mean Change in BCVA[a]	-7.90[b]	-9.29[b]	1.39

Cohort	Zimura 4mg (N=83)	Sham 4mg (N=84)	Difference
Mean Change in BCVA[a]	-3.79	-3.51	-0.28

- Mean change in low luminance best corrected visual acuity (ETDRS letters) from Baseline to Month 12

Cohort	Zimura 2mg (N=67)	Sham 2mg (N=110)	Difference
Mean Change in LL BCVA[a]	-1.03[b]	-1.41[b]	0.38

Cohort	Zimura 4mg (N=83)	Sham 4mg (N=84)	Difference
Mean Change in LL BCVA[a]	1.53	2.97	-1.44

(a) Based on the least squares means from the MRM model; ITT population.

(b) 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: Safety Analysis Through Month 12*

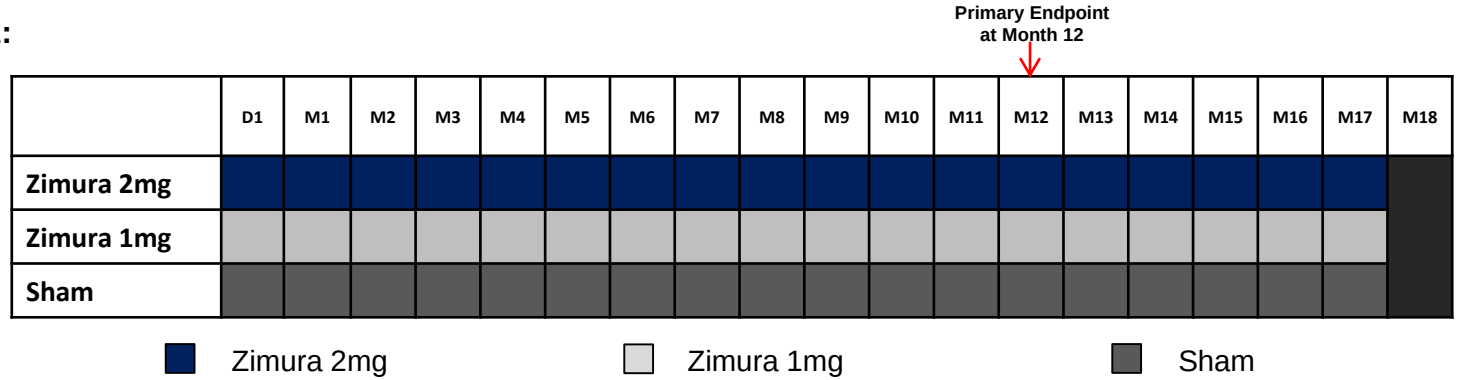
- Zimura was generally well tolerated after 12 months of administration
- No Zimura related adverse events
- No Zimura related inflammation
- No drug related discontinuations from the trial attributed to Zimura
- No serious ocular adverse events in the study eye related to Zimura
- No cases of endophthalmitis reported in the clinical trial
- The most frequently reported ocular adverse events were related to the injection procedure
- Incidence of CNV in the untreated fellow eyes was 10 patients (3.5%) and in the study eyes was 3 patients (2.7%) in the sham group, 1 patient (4.0%) in the Zimura 1mg group, 6 patients (9.0%) in the Zimura 2mg group, and 8 patients (9.6%) in the Zimura 4mg group

Favorable Safety Profile To Date

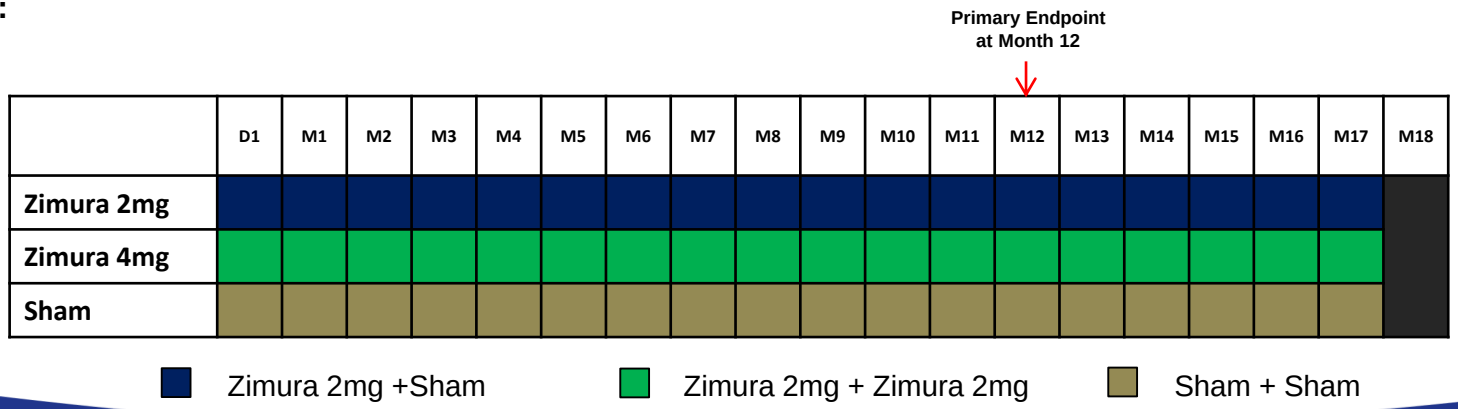
*Based on Investigator Reported Safety Events

GATHER1: Dosing Regimen

Part 1:

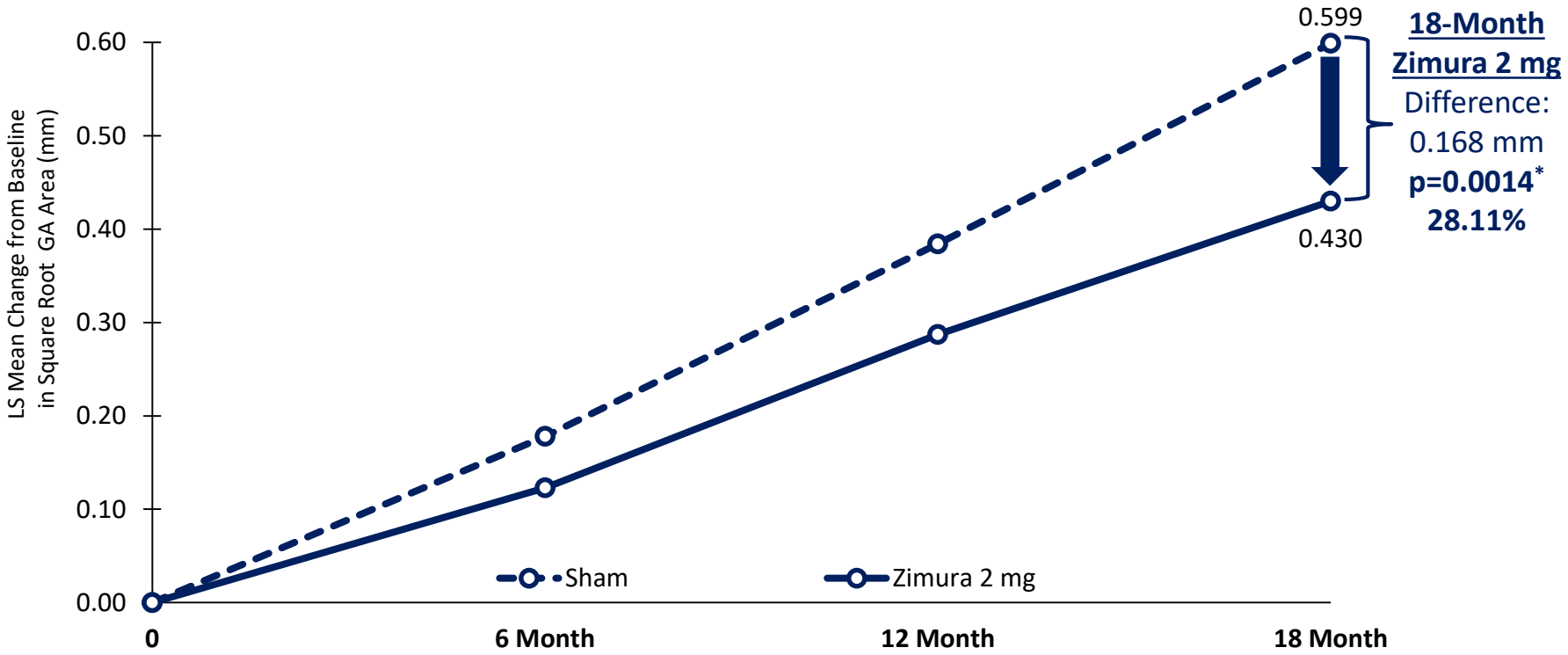


Part 2:



GATHER1: Decrease in GA Growth over 18 Months

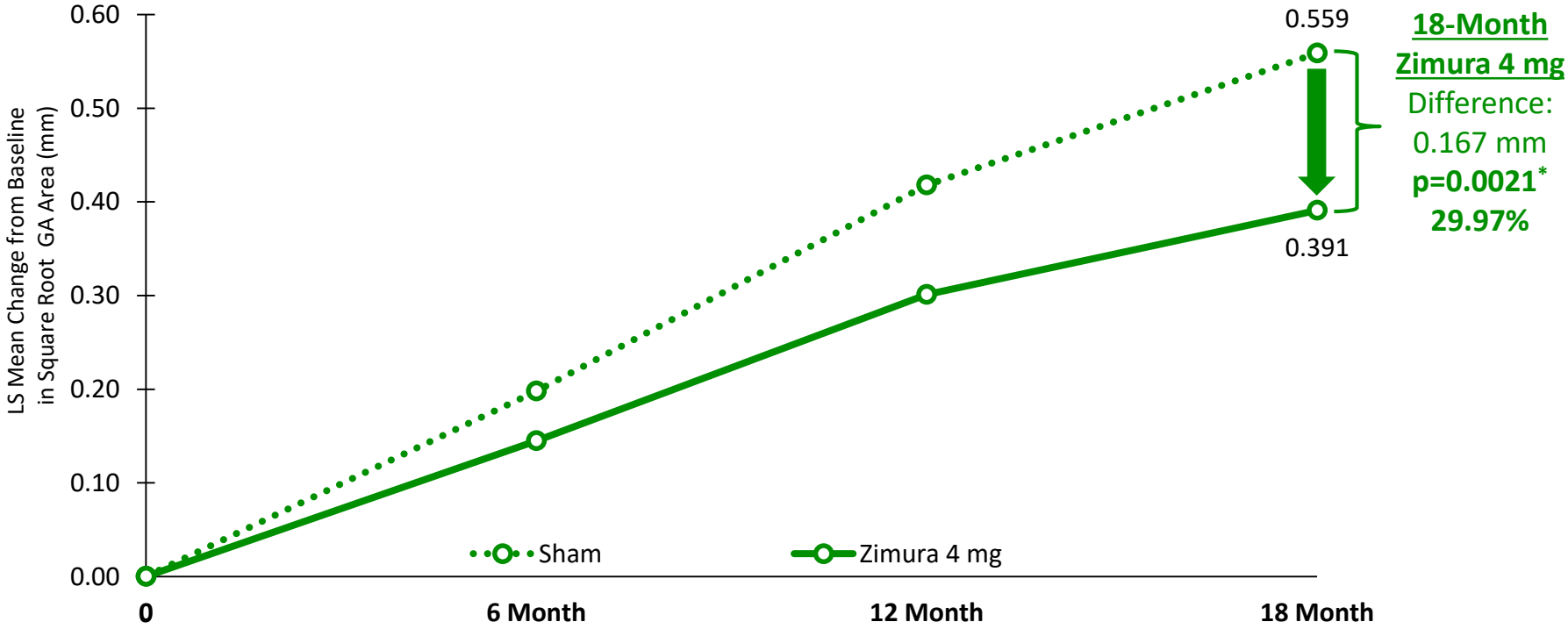
Zimura 2 mg vs. Sham (square root transformation)



ITT Population; Based on LSMEANS from 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; Prespecified and descriptive analysis. *18 month p values are descriptive in nature.

GATHER1: Decrease in GA Growth over 18 Months

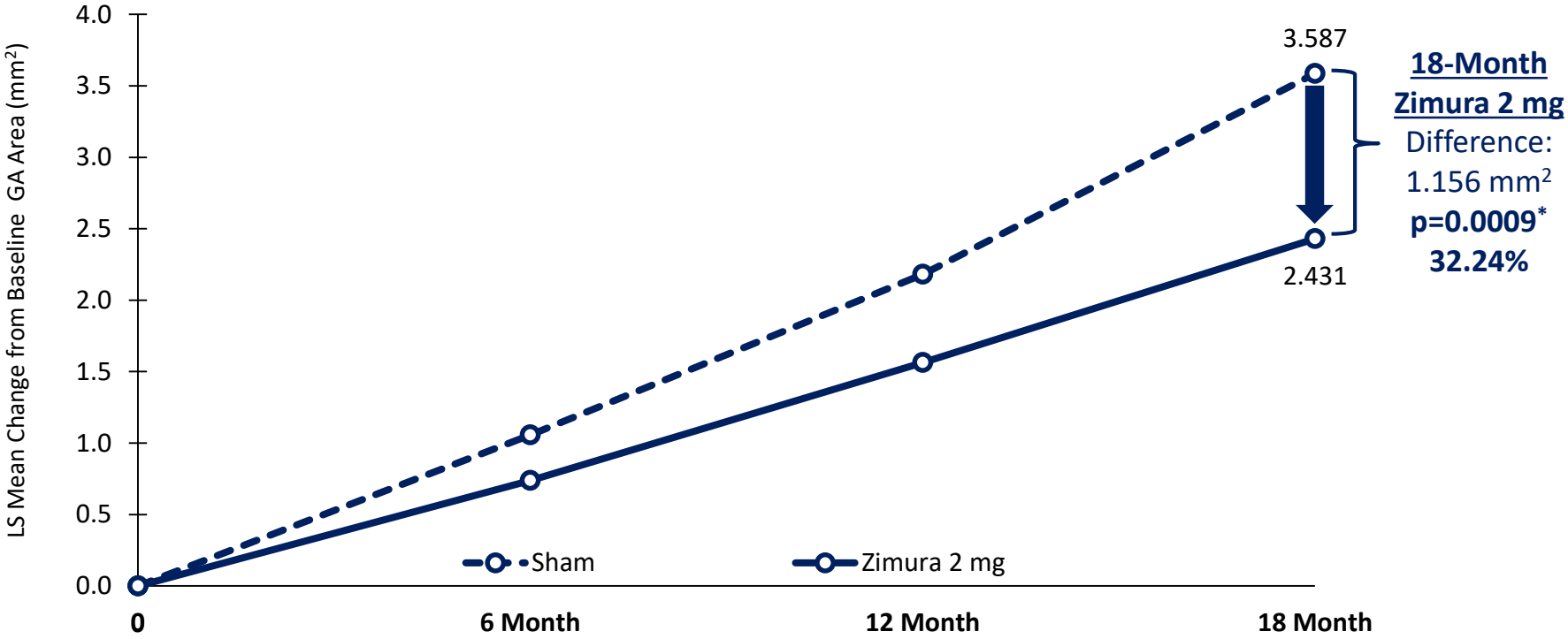
Zimura 4 mg vs. Sham (square root transformation)



ITT Population; Based on the least squares means from the MRM Model drawing on all available data; Prespecified and descriptive analysis. *18 month p values are descriptive in nature.

GATHER1: Decrease in GA Growth over 18 Months

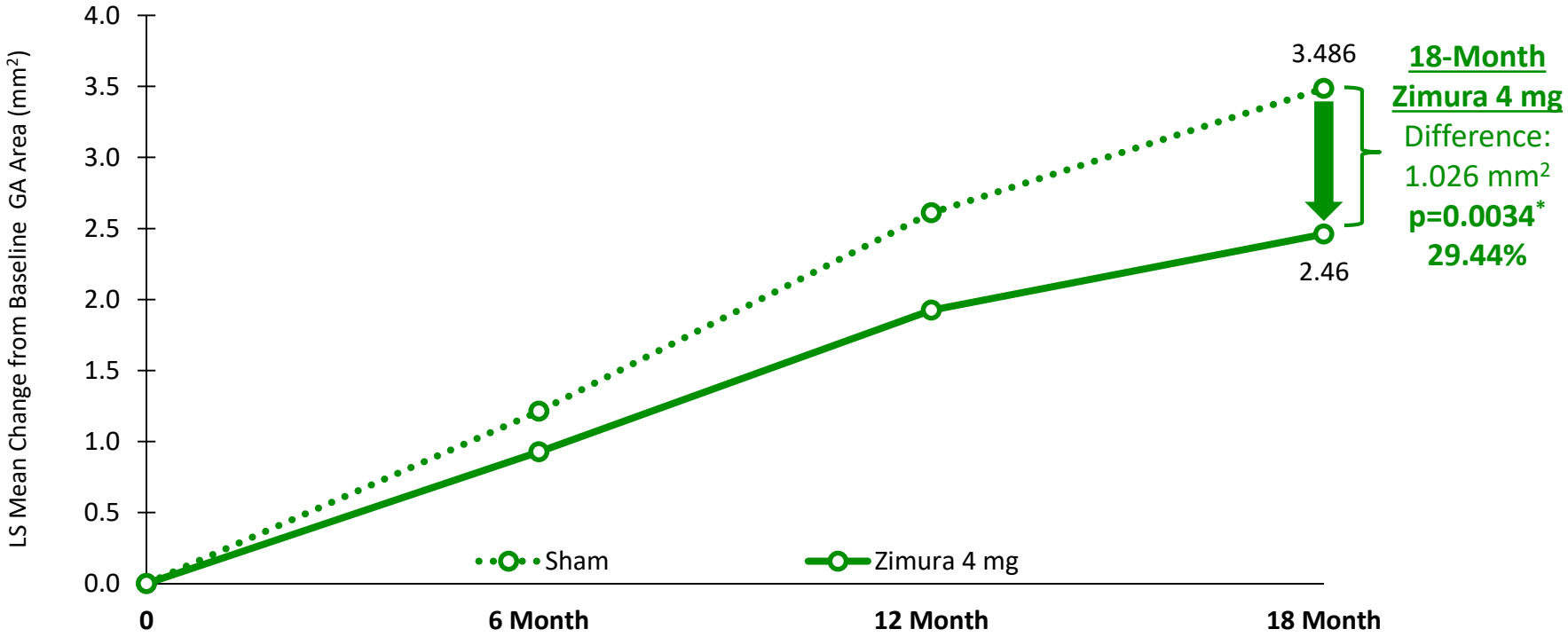
Zimura 2 mg vs. Sham (non-square root)



ITT Population; Based on LSMEANS from 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; Prespecified and descriptive analysis. *18 month p values are descriptive in nature.

GATHER1: Decrease in GA Growth over 18 Months

Zimura 4 mg vs. Sham (non-square root)



ITT Population; Based on the least squares means from the MRM Model drawing on all available data; Prespecified and descriptive analysis. *18 month p values are descriptive in nature.

GATHER1: Preliminary Safety Analysis Through Month 18*

- Zimura was generally well tolerated after 18 months of administration
- No Zimura related adverse events
- No Zimura related inflammation
- No drug related discontinuations from the trial attributed to Zimura
- No serious ocular adverse events in the study eye related to Zimura
- No cases of endophthalmitis reported in the clinical trial
- The most frequently reported ocular adverse events were related to the injection procedure
- Incidence of CNV in the untreated fellow eye was 11 patients (3.8%), and in the study eye was 3 patients (2.7%) in the sham control group, 8 patients (11.9%) in the Zimura 2 mg group, and 13 patients (15.7%) in the Zimura 4 mg group.

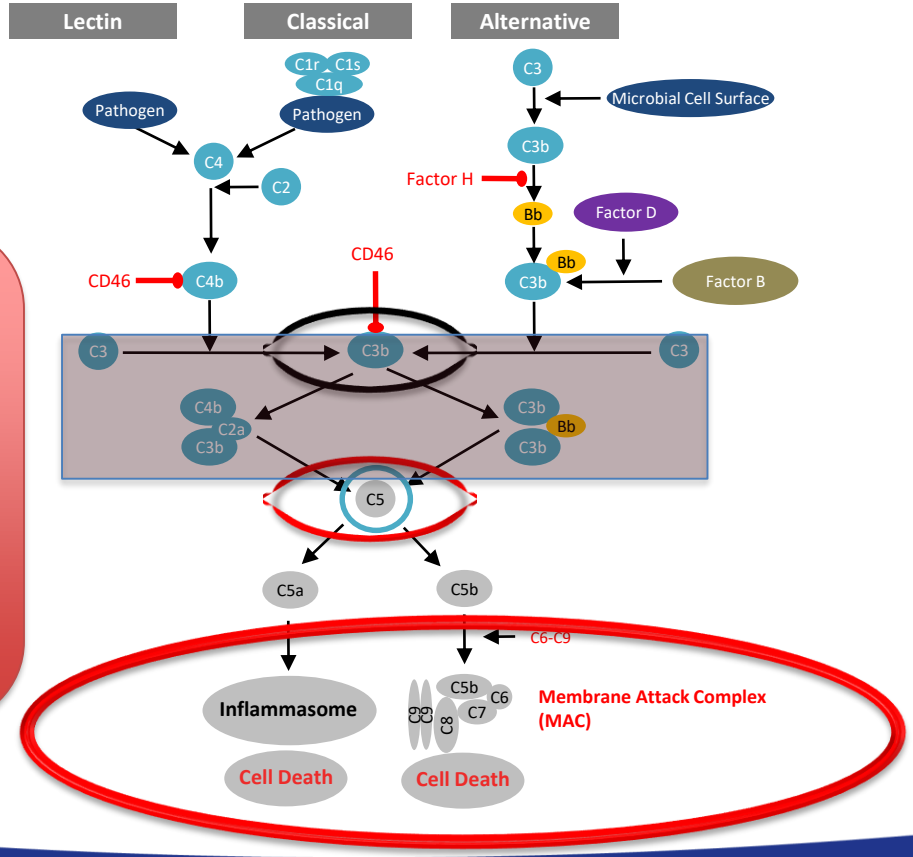
Favorable Safety Profile To Date

*Based on Investigator Reported Safety Events

What are the Potential Advantages of Inhibiting at the C5 Level?

Complement Pathway

Inhibit the 2 “Killers,” But Preserve the Rest



Source: ISEE internal

C5 Inhibition: 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

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.

C5 Inhibition: Potential Safety Advantages

C3 Inhibition: Potential for Neurotoxicity

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.

"Deficiency of C3 or CR3 decreased microglial phagocytosis of apoptotic photoreceptors and increased microglial neurotoxicity to photoreceptors,…"

J. Exp. Med. 2019 Vol. 216 No. 8; 1925-1943

What is the Level of Statistical Confidence for this Pivotal Trial?

GATHER1: Analyzed Geographic Atrophy Data

Data from 85% of the patients were included in the month 12 analysis

	N (%) [1]
Missing at baseline[2]	1 (<1%)
Missing at 6 months and at 12 months[2]	36 (14%)
Missing at 6 months only	11 (4%)
Missing at 12 months only	30 (12%)
No missing	182 (70%)
	260 (100%)

[1]Sham, 2mg and 4mg groups. [2]*Excluded from model for 2mg and 4mg*

GATHER1: Prespecified Month 12 Sensitivity Analyses

Replace missing data using multiple imputations, with an added “shift” increase until significance is lost

Data Imputation Method	Zimura 2mg vs. Sham		Zimura 4mg vs. Sham	
	Difference**	*P*	Difference**	*P*
No imputation (primary analysis)	0.110	0.0072*	0.124	0.0051*
Impute mean value of same arm	0.119	0.0005*	0.152	<0.0001*
Impute mean value of opposite arm	0.075	0.0309*	0.107	0.0033*
Impute mean value of both arms	0.097	0.0047*	0.129	0.0003*
Impute mean value of sham arm	**0.093**	**0.0056***	**0.120**	**0.0008***

** Statistically significant (without adjustment for multiplicity)*
*** Difference in means of GA area (square root transformation)*

GATHER1: Sensitivity Analysis at Month 12

Statistical interpretation:

- All analyses showed small impact of missing data on our overall conclusion on the primary endpoint
- The shift imputation analyses showed that statistical significance would only be lost for large shifts (~40% of observed treatment effect)
- Analysis results were robust to missing data

What Distinguishes the GATHER1 data in a post-COVID world?

GA Studies Post-COVID

- ***We believe GATHER1 is the only pre-COVID positive Phase 3 dataset for GA***

- New environment for clinical trial execution: Recruitment / Retention

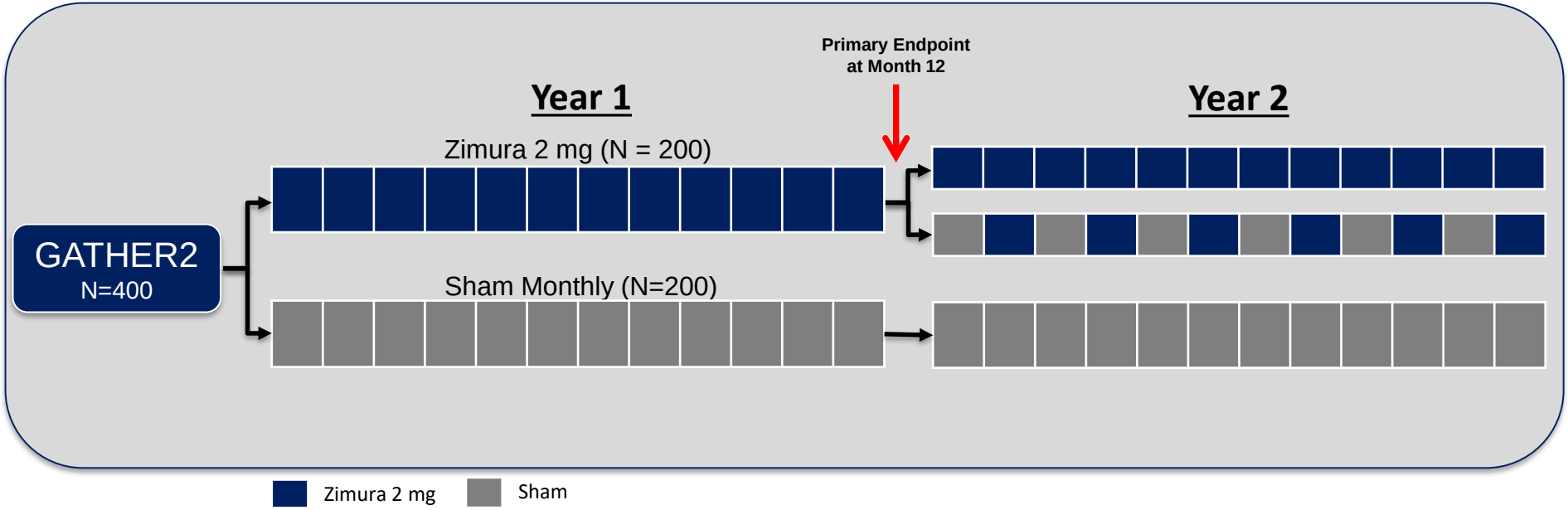
- Proactive strategies to maximize data integrity / interpretability for GATHER2

GATHER2 Clinical Trial

A Phase 3 Multicenter, Randomized, Double-Masked, Sham Controlled Clinical Trial to Assess the Safety and Efficacy of Intravitreal Administration of Zimura (Complement C5 Inhibitor) in Subjects with Geographic Atrophy Secondary to Age-Related Macular Degeneration

GATHER2 (ISEE2008): Trial Design

Primary Efficacy Endpoint: Mean rate of change in GA over 12 months measured by fundus autofluorescence (FAF) at three time points: Baseline, Month 6, and Month 12 (square root transformation)



GATHER2: Key Ophthalmic Inclusion Criteria (Study Eye)

- **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

GATHER2: Key Ophthalmic Exclusion Criteria

- GA secondary to any condition other than AMD in either eye (e.g., drug-induced)
- Any prior treatment for AMD or any prior intravitreal treatment for any indication in either eye, except oral supplements of vitamins and minerals
- Evidence of CNV in either eye
- If subject develops CNV in the SE during the course of the trial, the subject remains in the study and continues to receive Zimura/Sham treatment (in addition to the standard of care anti-VEGF)
- Any ocular condition in the SE that would progress during the course of the study that could affect central vision or otherwise be a confounding factor

GATHER1: Strengths

- Patient criteria
  - Non-foveal GA: faster growing lesions as compared to foveal lesions
- Appropriate masking for Phase 3 trial
  - patients; investigators; reading center; sponsor
- Pre-specified statistical threshold for “positive” Phase 3 clinical trial
  - One-sided significance level of $p < 0.0125$ in either arm (adjusted for multiplicity based on trial design)
- Early and continuous positive treatment effect over 18 months
- Favorable safety profile with 18 months of continuous treatment

Source: Ophthalmology, Volume 123, Issue 2, 361-368

IVERIC bio Pipeline

Therapeutics

Indication	Research	Pre-clin.	Phase 1	Phase 2	Phase 3	Milestones
GA secondary to AMD Zimura						• GATHER1 (1st Phase 3): Positive 12 & 18-month data reported • GATHER2 (2nd Phase 3): Initiated in June 2020
Stargardt Disease (STGD1) Zimura						• Expanding enrollment in trial by ~25 patients
GA secondary to AMD HtrA1 Inhibitor						• Plan to file IND in **2021**

Gene Therapy

Indication	Research	Pre-clin.	Phase 1	Phase 2	Phase 3	Milestones
IC-100: RHO-adRP AAV vector						• Plan to initiate Phase 1/2 in **1H 2021**
IC-200: *Best1* Related Retinal Diseases AAV vector						• Plan to initiate Phase 1/2 in **2021**
LCA10 miniCEP290 AAV "minigene" vector						• Identify lead construct by the end of **2020**
STGD1 miniABCA4 AAV "minigene" vector						• Additional results expected by the end of **2020***
Usher 2a miniUSH2A AAV "minigene" vector						• Preliminary results expected by **late 2020 or early 2021***

*We have an option to exclusively in-license intellectual property resulting from ongoing sponsored research.

Stargardt Disease

OPH2005: Zimura in Autosomal Recessive Stargardt Disease – Ongoing

The most common inherited macular dystrophy in both children and adults

- Phase 2b, randomized, double masked, sham controlled screening clinical trial
- Two arms:
  - Zimura 4mg
  - Sham
- ~ 95 subjects were previously enrolled for treatment with Zimura or Sham for 18 months
- Primary Efficacy Endpoint
  - Mean rate of change over 18 months in the area of ellipsoid zone defect measured by en face SD-OCT
- **Expanding enrollment in trial by ~25 patients**

HtrA1 Inhibitor

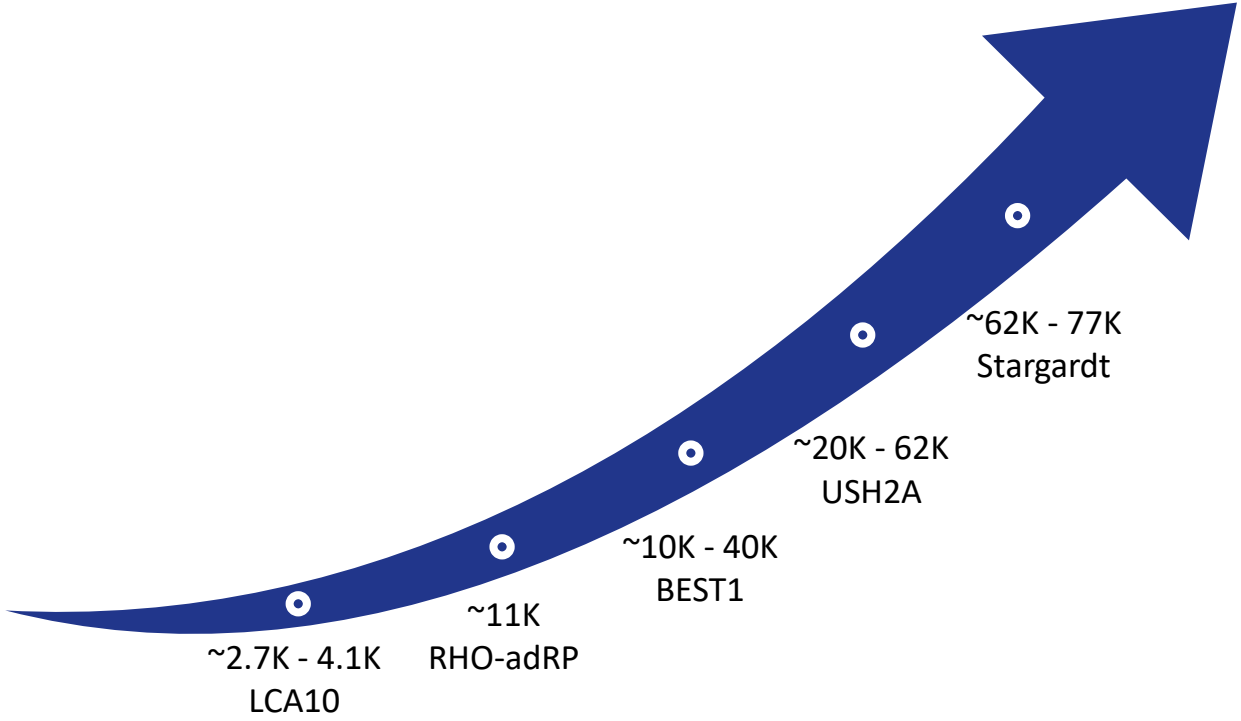
HtrA1 Inhibitor Program for AMD: Small Molecules with High Affinity and Specificity for HtrA1

- Potential targets: dry AMD, including GA, as well as potentially other age-related retinal diseases, such as wet AMD and IPCV
- Plan to file IND in 2021
- Strong genetic link between HtrA1 & AMD
  - Homozygotes have ~8.2 fold increased risk
- AMD patients overexpress HtrA1
  - Increased intracellular expression of HtrA1 inside the RPE cells of AMD patients
  - Increased HtrA1 staining in a majority of drusen of AMD patients' donor eyes
  - Increased HtrA1 protein level in aqueous humor of wet AMD patients
- Overexpression of HtrA1 protein contributes to AMD
  - Damages the extracellular matrix and Bruch's membrane
  - Alters and disrupts RPE cells
  - Upregulates complement
  - Leads to drusen formation
  - Interferes with RPE cell function and secondarily impacting photoreceptors

Sources: Human Molecular Genetics, 2005: 14, 3227–3236. Arch Ophthalmol. 2007;125:55-62. Aging Cell. 2018 May 5:e12710. doi: 10.1111/acel.12710. [Epub ahead of print]. Investigative Ophthalmology & Visual Science January 2017, Vol.58, 162-167. EBioMedicine 27 (2018) 258–274. Science 2006; 314 (5801), 992-993. Cell Cycle 6:9, 1122-1125, 1 May 2007]. Scientific Reports | 7: 14804 | DOI:10.1038. Invest Ophthalmol Vis Sci. 2010;51:3379–3386. PLoS One. 2011;6(8):e22959. doi: 10.1371/journal.pone.0022959. Invest Ophthalmol Vis Sci. 2010;51:3379–3386.

Gene Therapy

Program Portfolio: Multi-billion $ Cumulative Net Sales Potential [1,2]



[1] **Estimated combined patient populations in US and EU5 for each indication based on published literature:**

RHO-adRP estimate based on data from *Arch Ophthalmol*ogy 2007 Feb; 125(2): 151–158./ *BEST1*-related estimate based on data from Ophthalmic Genet. 2017 ; 38(2): 143–147. doi:10.1080/13816810.2016.1175645 / LCA10 estimate based on data from various sources including Genetics Home Reference; *Am J Hum Genet* 2006 Sep; 79(3) 556-561; *Gene Reviews,* Leber Congenital Amaurosis, Last update May 2, 2013; *Human Mutation,* Mutation in Brief #956(2007) / Stargardt data from National Eye Institute, Genetics Home Reference and Progstar Natural History Study / *USH2A* estimates based on data from Experimental Eye Research Vol 79, Issue 2, Aug 2004: 167-173.

[2] Non risk-adjusted

IC-100: RHO-adRP Program Summary

- **Potentially best-in-class**
- **Mutation independent strategy**
  - >150 identified rhodopsin (RHO) gene mutations
- **Knockdown and replacement with a single AAV vector**
  - Suppression of endogenous mutant toxic rhodopsin protein
  - Replace with healthy rhodopsin protein
- **Proof-of-concept in two animal models (canine and mouse)**
  - Naturally occurring canine disease model
  - Long-term preservation of retinal anatomy and function
- **No clinical stage gene therapy competition**
- **Path to IND submission**
  - Completed: pre-IND FDA meeting
  - Ongoing: IND enabling activities and natural history studies
  - Paragon engaged as manufacturer for Phase 1/2 clinical trial (GMP slots secured); CMC strategy in place
- **Phase 1/2 planned to initiate in 1H 2021**

Sources: PNAS September 4, 2018 115 (36) E8547-E8556. HUMAN GENE THERAPY 23:356–366 (April 2012).

IC-200: BEST1 Program Summary

- **Potentially first-in-class and best-in-class**
- **No clinical stage competition currently**
- **Proof of concept established in the naturally occurring autosomal recessive BEST1 canine model**
  - 3 different mutations
  - Long-term preservation of retinal structure
- **Path to IND submission**
  - Completed: pre-IND FDA meeting
  - Ongoing: IND enabling activities and natural history studies
  - Paragon engaged as manufacturer for Phase 1/2 clinical trial (GMP slots secured); CMC strategy in place
- **Phase 1/2 planned to initiate in 2021**

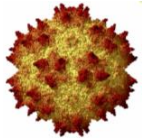
Sources: PNASMarch 20, 2018 115 (12) E2839-E2848; first published March 5, 2018 https://doi.org/10.1073/pnas.1720662115

Minigene Programs

AAV Vectors Preferred for Ocular Gene Therapy

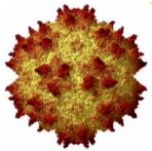
- FDA Approved (Luxturna®)
- Extensive experience with intraocular application in both humans and animal models
- Well documented safety profile
- Tropism for retinal tissue
- Alternative technologies have inherent challenges (e.g. Lentivirus)

- Limited packaging capacity of < 5kb



The minigene solution:

Engineer AAV-amenable genes that encode functionally optimized proteins



Current Minigene Programs

- **Leber Congenital Amaurosis (LCA10): miniCEP290**
  - Estimated Prevalence: ~2.7K - 4.1K in US & EU5 combined
- **Autosomal Recessive Stargardt Disease: miniABCA4**
  - Estimated Prevalence: ~62K - 77K US & EU5 combined
- **Usher Syndrome Type 2A & USH2A related nonsyndromatic Autosomal Recessive RP: miniUSH2A**
  - Estimated Combined Prevalence: ~20K - 62K US & EU5 combined

LCA10 estimate based on data from various sources including Genetics Home Reference; *Am J Hum Genet* 2006 Sep; 79(3) 556-561; *Gene Reviews,* Leber Congenital Amaurosis, Last update May 2, 2013; *Human Mutation,* Mutation in Brief #956(2007) / Stargardt estimate based on data from National Eye Institute, Genetics Home Reference and Progstar Natural History Study / *USH2A* estimates based on data from Experimental Eye Research Vol 79, Issue 2, Aug 2004: 167-173. / USH2A estimate based on data from Experimental Eye Research 79 (2004):167-173. J R Soc Med 2006;99:189-191. https://nei.nih.gov/health/ushers/ushers. Otology & Neurology 2018; 40:121-129.

miniCEP290: LCA10 Potential Product Candidate

- **Significant Unmet Medical Need**
  - Estimated Prevalence: ~2.7K - 4.1K in US & EU5 combined[1]
  - Most common cause of LCA with early onset of vision loss in both eyes
- **Potentially best-in-class**
- **Mutation independent strategy**
- **Replacement of the mutated gene with a novel *miniCEP290* in AAV**
- **Preliminary proof-of-concept in mouse model**
  - Preservation of retinal structure and function
  - ~ 4.6x improvement in prolonging the functional rescue measured by ERG, extending the benefit from 3 to 14 weeks of age (ongoing)
- **Converted Option to Worldwide Exclusive License in July 2019**
  - Encouraging results from POC study provide additional support for the potential of minigene in LCA10
  - Next steps: Continue to optimize constructs with the goal of identifying a lead construct by the end of 2020

[1]LCA10 estimate based on data from various sources including Genetics Home Reference; *Am J Hum Genet* 2006 Sep; 79(3) 556-561; *Gene Reviews,* Leber Congenital Amaurosis, Last update May 2, 2013; *Human Mutation,* Mutation in Brief #956(2007)

A Diversified Portfolio Focused on Retinal Diseases

- **Therapeutics for Age-Related Retinal Diseases (Large Market)**
  - Zimura: Positive data for the first of two Phase 3 trials (GATHER1)
    - Statistically significant 27% reduction in GA growth over 12 months (primary endpoint achieved)
    - Supported by 18-month results showing continuous treatment effect
    - Favorable safety profile over 18 months
    - Patient enrollment for second Phase 3 trial (GATHER2) initiated in June 2020
    - Potential expansion into intermediate AMD, wet AMD and lifecycle initiatives
  - Multi-billion dollar large market opportunity with no approved therapy in GA
- **Gene Therapy for Retinal Diseases (Orphan)**
  - Broad and diversified Pipeline
    - Novel and cutting edge AAV gene therapy options
    - Five R&D programs in orphan inherited retinal diseases
  - No approved therapies in the targeted diseases
- **Experienced Team with Extensive Drug Development Expertise in Retina**
- **Strong Cash Position and Well-Capitalized**
  - ~$108.4 million in cash and cash equivalents as of 3/31/20
  - Concurrent public offering and private placement with net proceeds of ~$150 million completed in June 2020

IVERIC bio

Developing Transformative Therapies For Retinal Diseases

APPENDIX

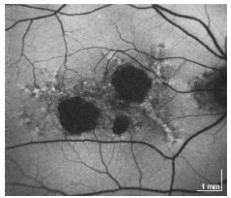
Age-Related Macular Degeneration: A Leading Cause of Visual Disability

All AMD: Estimated Prevalence

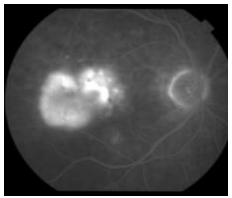
Worldwide: ~170 Million → Year 2040 → ~288 Million

United States: ~11 Million → Year 2050 → ~22 Million

GA Secondary to Dry AMD: Estimated Prevalence in 2020 ~1.5 Million in the US



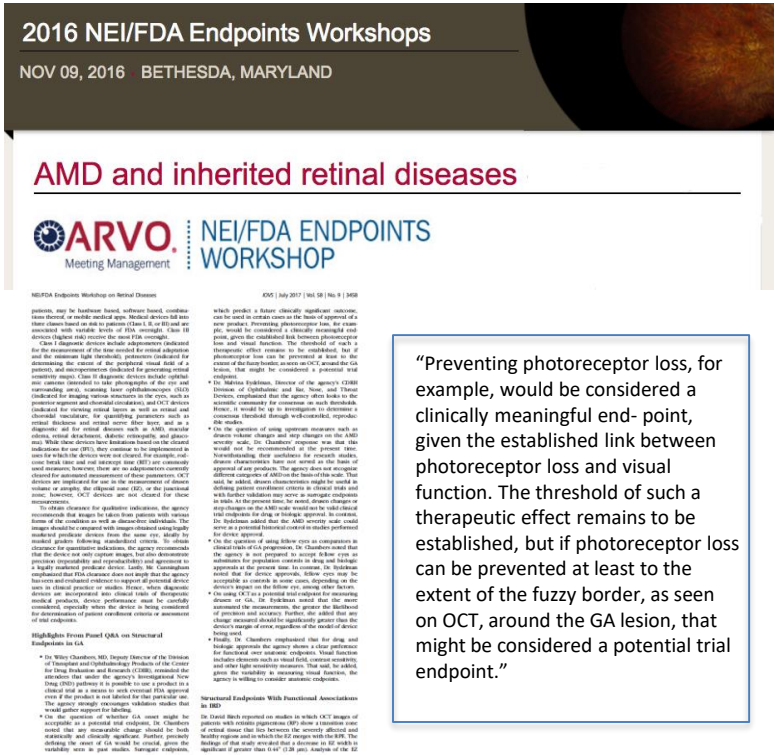
Incidence of GA
~159,000/ Year (US)



Incidence of Wet AMD
~150,000/ Year (US)

Source for all AMD: Eye Vis (Lond) 2016;22;3:34.
Source for GA and wet AMD: Am J Ophthalmol 2015; 160:85-9. Arch Ophthalmol. 2004;122(4):564-572.3.

“Preventing Photoreceptor Loss”: “Clinically Meaningful End-point”

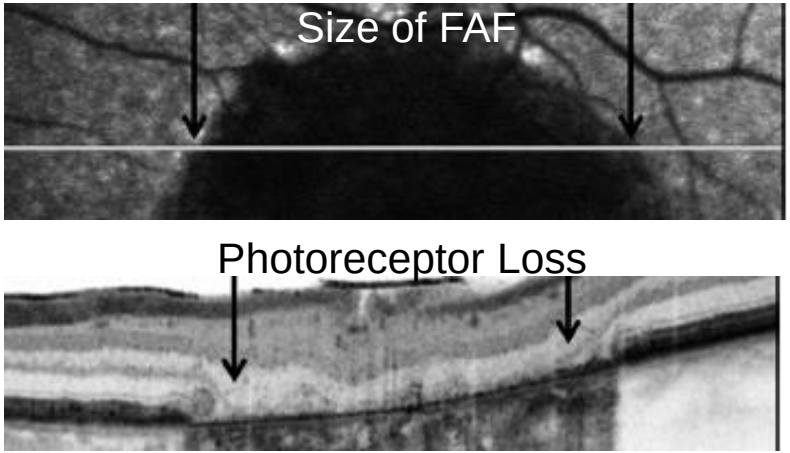


“Preventing photoreceptor loss, for example, would be considered a clinically meaningful end- point, given the established link between photoreceptor loss and visual function. The threshold of such a therapeutic effect remains to be established, but if photoreceptor loss can be prevented at least to the extent of the fuzzy border, as seen on OCT, around the GA lesion, that might be considered a potential trial endpoint.”

Research Opportunities

Report From the NEI/FDA Endpoints Workshop on Age-Related Macular Degeneration and Inherited Retinal Diseases

Karl Csaky,[1] Frederick Ferris III,[2] Emily Y. Chew,[2] Prashant Nair,[3] Janet K. Cheetham,[4] and Jacque L. Duncan[5]



Source: Investigative Ophthalmology & Visual Science January 2011, Vol.52, 1-6. Investigative Ophthalmology & Visual Science 2017 Jul 1;58(9):3456-3463.

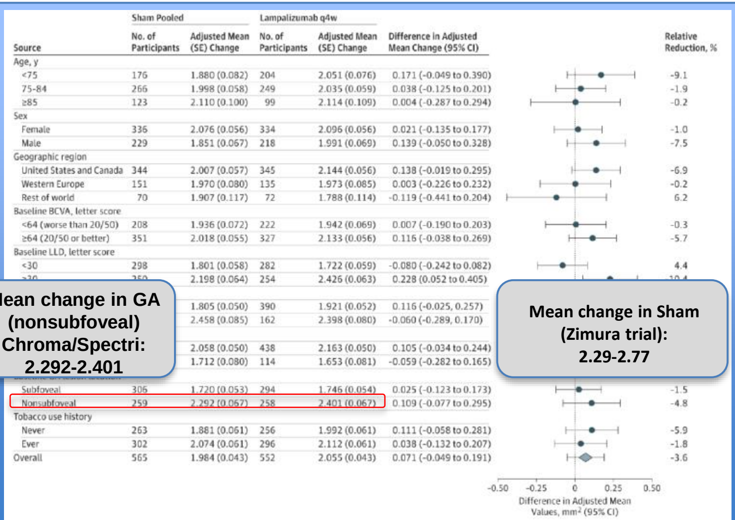
GATHER1 Baseline Characteristics: Generally Balanced Across Cohorts*

	Zimura 2mg N = 67	Sham for 2mg arm N = 110	Zimura 4mg N = 83	Sham for 4mg arm N = 84
Mean Age, Years	78.8	78.2	79.2	78.2
Female Gender, Number (%)	45 (67.2%)	79 (71.8%)	58 (69.9%)	61 (72.6%)
Active smoker, Number (%)	25 (37.3%)	36 (32.7%)	26 (31.3%)	29 (34.5%)
Non-Subfoveal GA, Number (%)	62 (92.5%)	104 (94.5%)	81 (97.6%)	82 (97.6%)
Mean GA Area, mm^2	7.33	7.42	7.90	7.45
Mean SQ Root GA Area, mm	2.62	2.63	2.72	2.64
Bilateral GA, Number (%)	67 (100%)	108 (98.2%)	83 (100%)	83 (98.8%)
Hyper Autofluorescence (%)	66 (98.5%)	109 (99.1%)	82 (98.8%)	83 (98.8%)
Mean BCVA (ETDRS Letters)	70.2	69.0	69.5	68.3
Mean LL BCVA (ETDRS Letters)	36.7	34.5	36.8	33.9
Low Luminance Deficit (BCVA-LL BCVA)	33.5	34.5	32.7	34.4

*Detailed baseline characteristics based on part 1 and part 2 are available online

Nonsubfoveal/Extrafoveal Sham Growth: Chroma/Spectri/Filly

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	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
[illegible]	[illegible]	2.198 (0.064)	254	2.426 (0.063)	0.228 (0.052 to 0.405)	[illegible]
[illegible]						
[illegible]	[illegible]	1.805 (0.050)	390	1.921 (0.052)	0.116 (-0.025, 0.257)	[illegible]
[illegible]	[illegible]	2.458 (0.085)	162	2.398 (0.080)	-0.060 (-0.289, 0.170)	[illegible]
[illegible]						
[illegible]	[illegible]	2.058 (0.050)	438	2.163 (0.050)	0.105 (-0.034 to 0.244)	[illegible]
[illegible]	[illegible]	1.712 (0.080)	114	1.653 (0.081)	-0.059 (-0.282 to 0.165)	[illegible]
[illegible]						
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

Mean change in GA (nonsubfoveal) Chroma/Spectri: 2.292-2.401

Mean change in Sham (Zimura trial): 2.29-2.77

Non-Square Root Transformation

Evaluation of Baseline Risk Factors on Progression in Geographic Atrophy

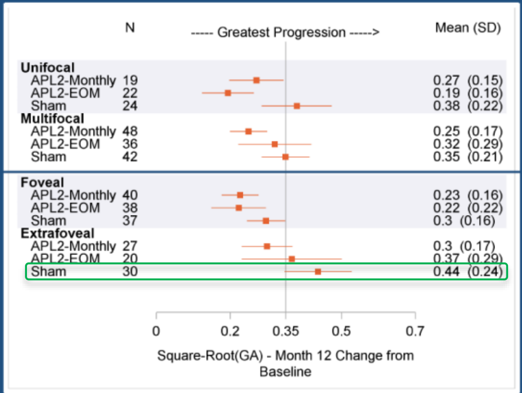
Post-hoc Analysis from the FILLY Study

Nathan Steinle, MD[1], Mohamed Hamdani[2]

[1]California Retina Consultants
[2]Apellis Pharmaceuticals

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

FILLY



Mean change in Sham (extrafoveal) Filly: 0.44

Mean change in Sham (Zimura trial): 0.42-0.44

Square Root Transformation

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

GATHER1: Statistical Analysis

- A Mixed-Effects Repeated Measures (MRM) model was 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*

GATHER1: Mean Rate of Change in GA for Zimura 2 mg by Part

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

Cohort		Zimura 2mg (N = 25)	Sham 2mg (N = 26)	Difference
Part 1	Mean Change in GA[(a)] (mm)	0.329	0.422	0.093

(a) = based on the least squared means from the MRM model

Cohort		Zimura 2mg (N = 42)	Sham 2mg (N = 84)	Difference
Part 2	Mean Change in GA[(a)] (mm)	0.308	0.422	0.114

(a) = based on the least squared means from the MRM model

Least square means are estimates from 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: Sensitivity Analysis

Several pre-specified sensitivity analyses conducted for primary endpoint:

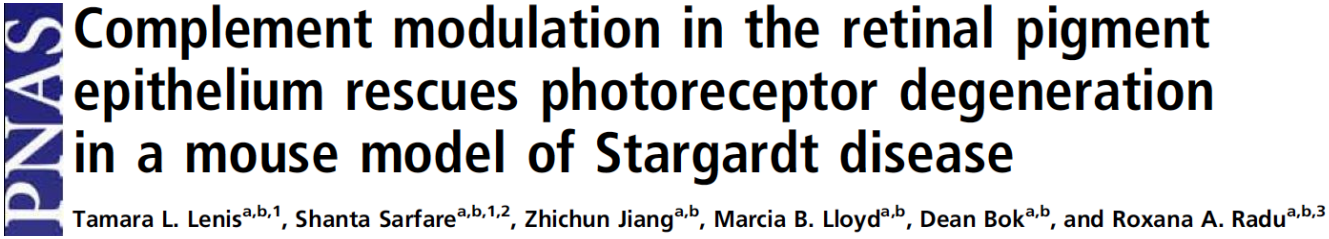
- Replaced missing data using multiple imputations, with an added “shift” increased until significance is lost
- Replaced missing data by
  - mean value of same treatment arm
  - mean value of opposite treatment arm
  - mean value of both treatment arms
  - mean value of sham arm
- Replaced missing data using “pattern mixture model” (useful to investigate “missing not at random” assumptions)

Stargardt: Pathophysiology and Prevalence

- Stargardt disease is most commonly inherited in an autosomal recessive manner caused by mutations in the ABCA4 gene (STGD1)
- Estimated US & EU5 Prevalence: ~62K - 77K
- The ATP binding cassette (ABC) transporters are the largest and most diverse membrane transport system and associated with many important biological processes as well as various severe pathological conditions
- ABCA4, also known as ABCR, is a 250-kDa glycoprotein and a member of the ABCA subfamily of ABC. During the visual cycle, in absence of ATP, ABCA4 binds with high affinity and clears N-retinylidene-phosphatidylethanolamine

Sources: Sources: Nat Genet. 1997; 15(3):236-46. BMC Med Genet. 2012; 3;13:67. Mol Med Rep. 2012; 6(5):1045-9. Annu Rev Cell Biol. 1992; 8:67-113. J Biol Chem. 2004; 279(52):53972-9. Estimate from National Eye Institute, Genetics Home Reference and Progstar Natural History Study

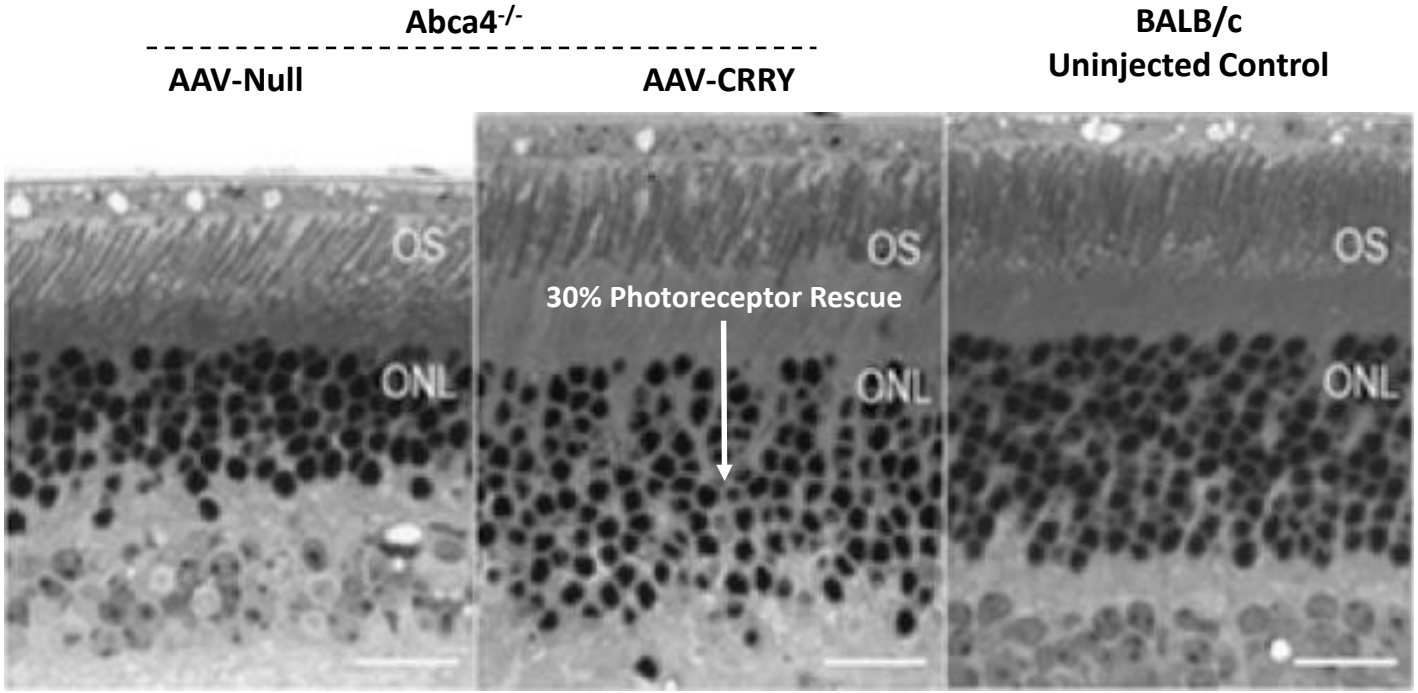
Decreased Complement Activity: Rescued Photoreceptors



- "In this study, we attempted to protect cells against complement attack by increasing expression of CRRY in the RPE of Abca4$^{-/-}$ mice"
- "CRRY is an important Complement **Negative** Regulatory Protein (CRP) in the mouse eye"

Source: Proc Natl Acad Sci U S A. 2017; 114(15):3987-3992.

Complement Inhibition Rescues Photoreceptors

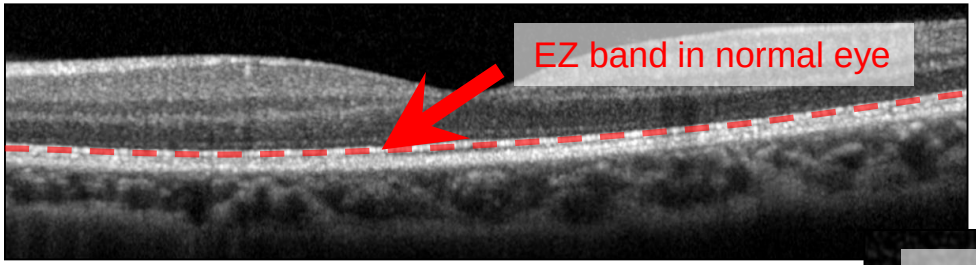


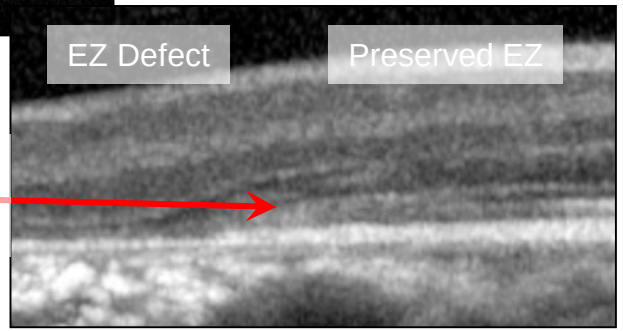
Representative retinal images from 1 Year old Albino Abca4$^{-/-}$ or BALB/c Mice

Source: Proc Natl Acad Sci U S A. 2017; 114(15):3987-3992.

OCT – Inclusion/Exclusion Criteria

- There is at least one location of ≥ 250 µm EZ defect within the ETDRS subfields
- There are no areas of EZ loss outside the ETDRS subfields





Likely the A-scan threshold between absent/preserved EZ