DEVELOPING TRANSFORMATIVE THERAPIES
FOR RETINAL DISEASES

March 2021
NASDAQ: ISEE

IVERIC BIO

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 its expectations regarding patient enrollment and retention in its second Phase 3 trial (GATHER2) of Zimura in geographic atrophy secondary to AMD and use of its completed clinical trial of Zimura for the treatment of geographic atrophy secondary to AMD (GATHER1) as a Phase 3 trial, its development and regulatory strategy for Zimura and its other product candidates, including additional indications that the Company may pursue for the development of Zimura and IC-500, 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, the projected use of cash and cash balances, 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, 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, university collaborators and other third parties, establishment of manufacturing capabilities, expectations for regulatory matters, developments from the Company's competitors and the marketplace for the Company's products, 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.

IVERIC BIO

A DIVERSIFIED PORTFOLIO FOCUSED ON RETINAL DISEASES

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)
  - Targeting completion of patient enrollment for second Phase 3 trial (GATHER2) 3Q 2021
  - Potential expansion into intermediate AMD, wet AMD and lifecycle initiatives
- IC-500 (HtrA1 Inhibitor): Complementary MOA adding to development stage AMD franchise

Gene Therapy for Inherited Retinal Diseases (Orphan)

- Broad and diversified pipeline
  - Novel and cutting edge AAV gene therapy options
  - Five programs in orphan inherited retinal diseases w/ no currently approved therapies

Experienced Team with Extensive Drug Development Expertise in Retina

Strong Cash Position and Well-Capitalized

- ~$210 million in cash and marketable securities as of 12/31/20

IVERIC BIO

STRONG SENIOR TEAM WITH SIGNIFICANT OPHTHALMOLOGY EXPERIENCE

GLENN SBLENDORIO Chief Executive Officer	The Medicines Company, eyetech, Roche, MPM
PRAVIN DUGEL, MD Chief Strategy and Business Officer	RA, 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
KEITH WESTBY Chief Operating Officer	Pharmasset, eyetech, Tunnell Consulting, Roche, Pfizer
ABRAHAM SCARIA, PHD Chief Scientific Officer	Casebia Therapeutics, Sanofi, Genzyme A Sanofi Company
EVELYN HARRISON Chief Clinical Operations Officer	eyetech, Roche
DHAVAL DESAI, PHARMD Chief of Staff	Onyx Pharmaceuticals, ThromboGenics, aerpio, Novartis

IVERIC BIO

IVERIC BIO PIPELINE

Therapeutics

AAV Gene Therapies

Indication	Res	Pre-clin	P1	P2	P3	Milestones
Zimura: GA secondary to AMD						• GATHER1 (1st Phase 3): Positive 12 & 18-month data reported • GATHER2 (2nd Phase 3): Target completion of enrollment **3Q 2021**
Zimura: Stargardt Disease						• Expanded enrollment (up to ~25 additional patients) ongoing
IC-500 (anti-HtrA1): GA secondary to AMD						• Plan to file IND in **2H 2022**
IC-100: RHO-adRP						• Plan to initiate Phase 1/2 in **2H 2021**
IC-200: *BEST1*-related IRDs						• Plan to initiate Phase 1/2 in **2H 2021**
miniCEP290: LCA10						• Identify lead construct in **2Q 2021**
miniABCA4: Stargardt Disease*						• Additional results expected in **1H 2021**
miniUSH2A: *USH2A*-related IRDs*						• Preliminary results expected in **1H 2021**

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

IVERIC BIO

WHAT IS AGE-RELATED MACULAR DEGENERATION (AMD)?

IVERIC BIO

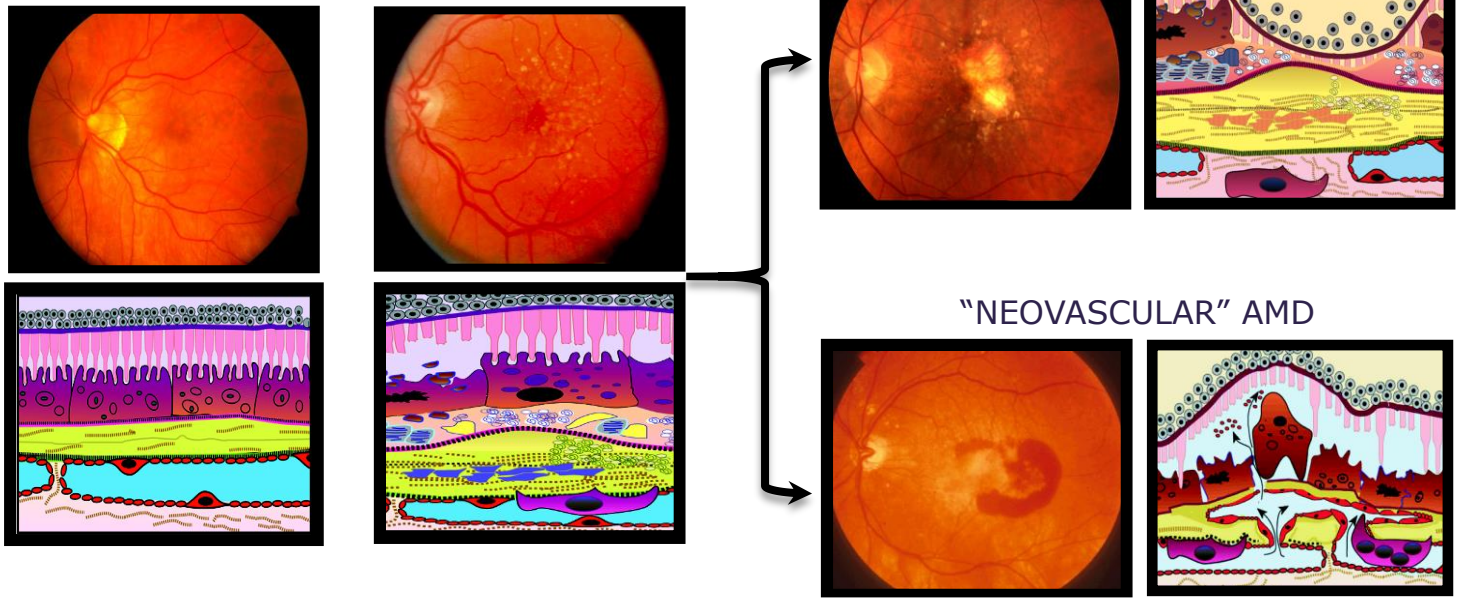
AMD LEADS TO PROGRESSIVE VISION LOSS WITH END-STAGE ATROPHY

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

NORMAL

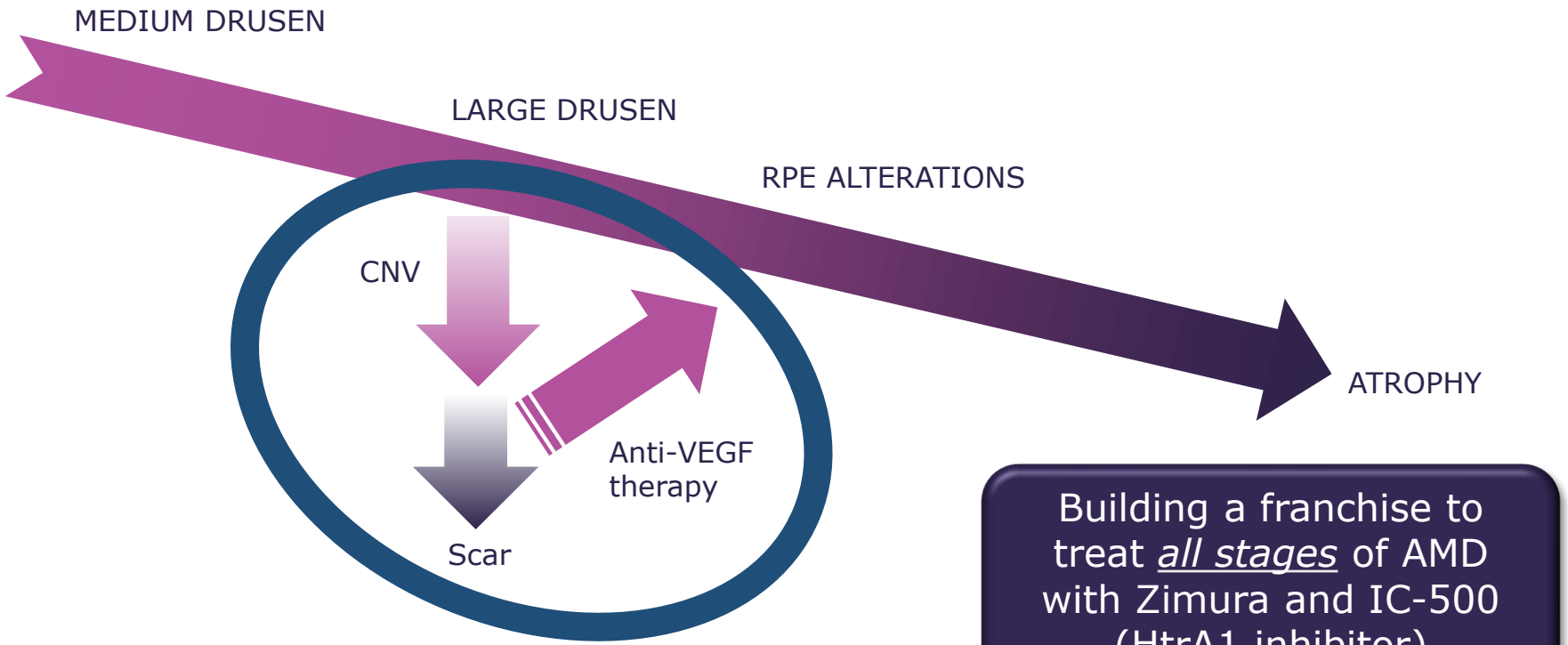
EARLY DRY AMD DEPOSITS

LATE DRY AMD "GEOGRAPHIC ATROPHY"



"NEOVASCULAR" AMD

PATHWAY OF AMD DISEASE PROGRESSION

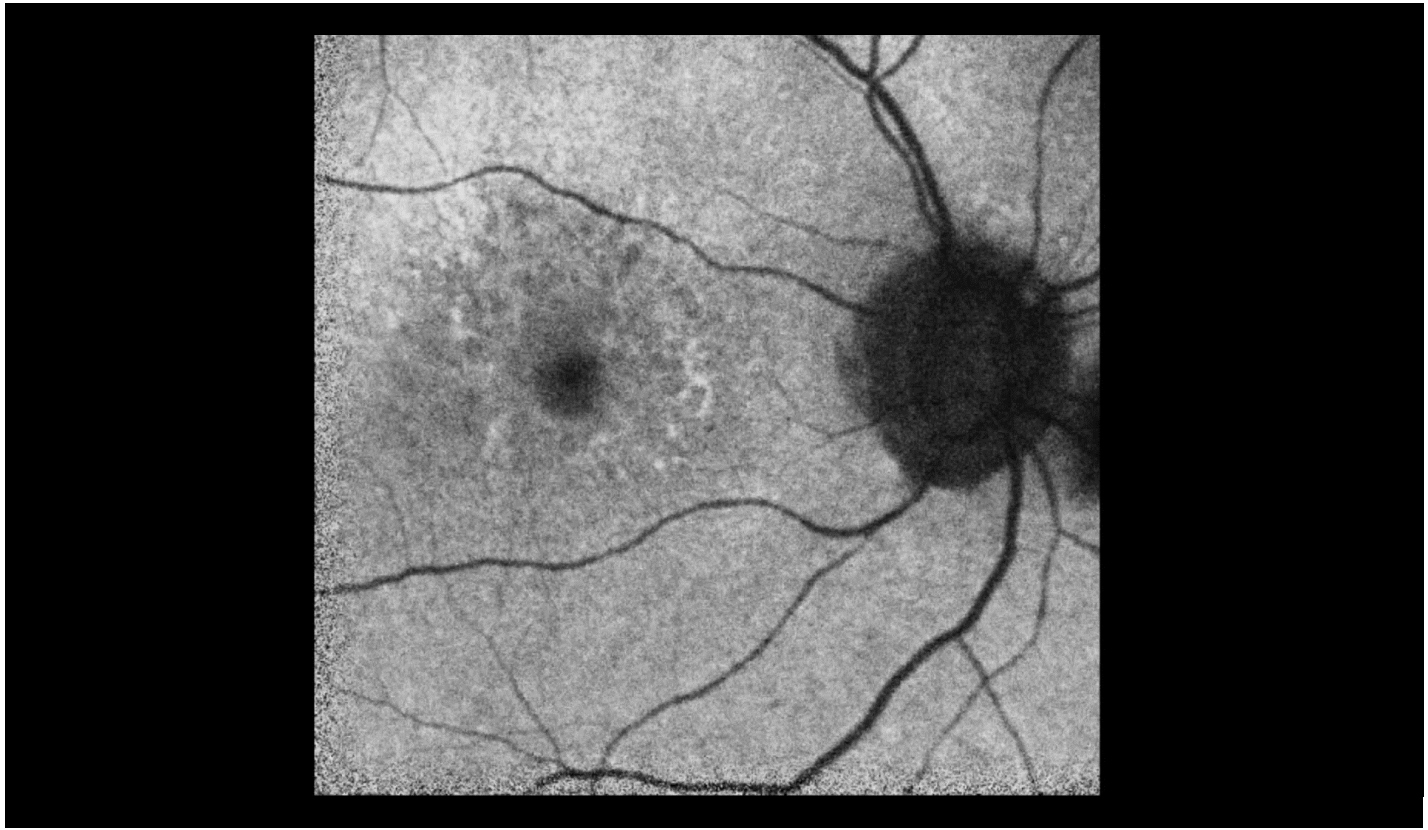


Building a franchise to treat *all stages* of AMD with Zimura and IC-500 (HtrA1 inhibitor)

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

IVERIC BIO

GEOGRAPHIC ATROPHY: GROWTH OVER TIME



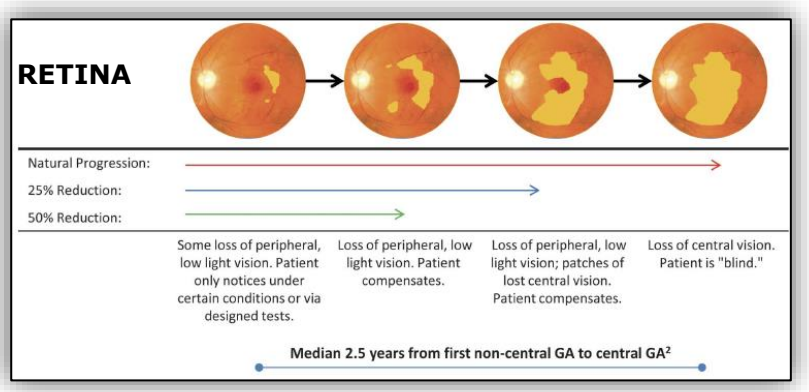
Courtesy: Jordi Mones, MD

IVERIC BIO

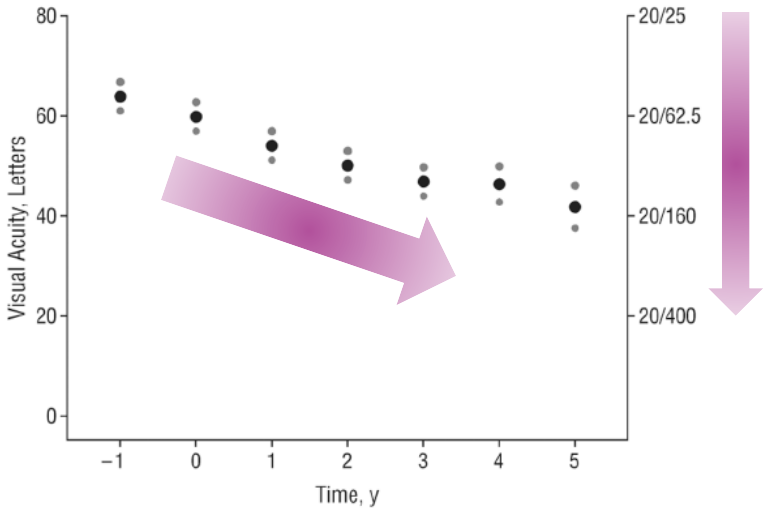
GEOGRAPHIC ATROPHY: GROWTH OF AREA & LOSS OF VISION

GEOGRAPHIC ATROPHY: LOSS OF PHOTORECEPTORS OVER TIME

INCREASE IN AREA OF DEGENERATION OVER TIME



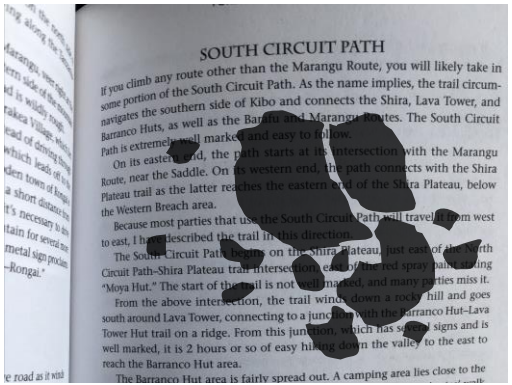
LOSS OF VISION OVER TIME



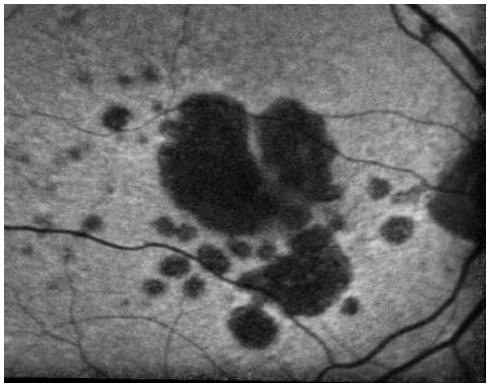
Source: Ophthalmology 2014;121:1079-1091. Retina 2017;27:819-835. Arch Ophthalmol 2009;127:1168-1174.

IVERIC BIO

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)

WHAT DOES COMPLEMENT HAVE TO DO WITH AMD?

IVERIC BIO

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[e], Giuliana 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[h], Joanna E. Merriam[h], Bert Gold[i], Michael Dean[i], and Rando Allikmets[h,k,l]

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

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

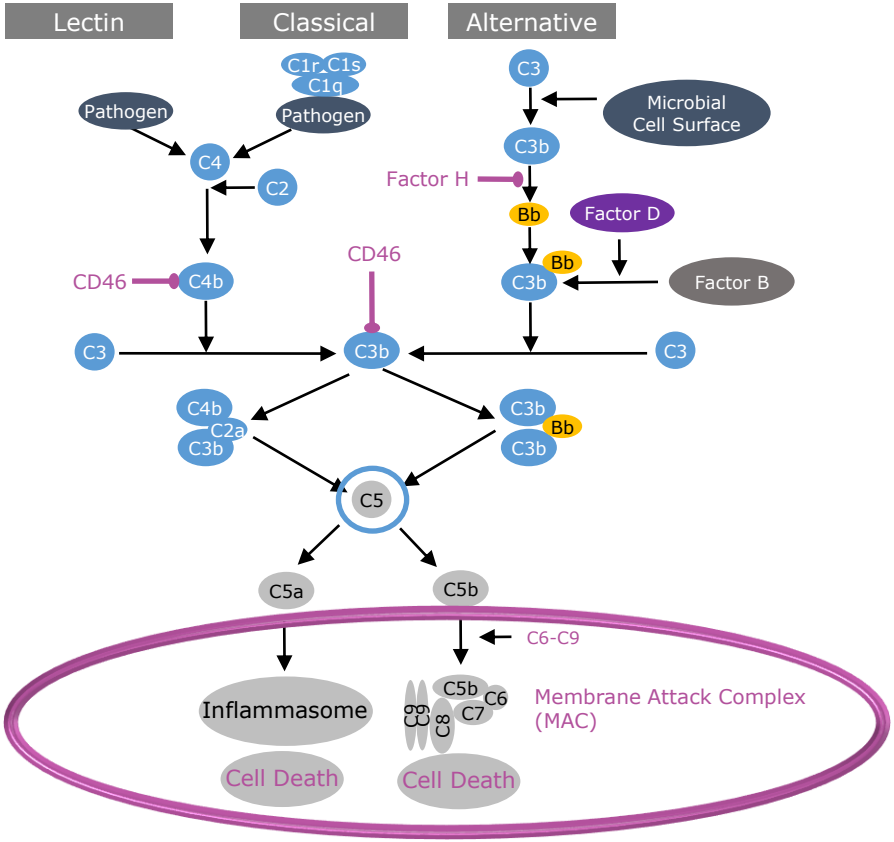
Complement Factor H Polymorphism and Age-Related Macular Degeneration

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

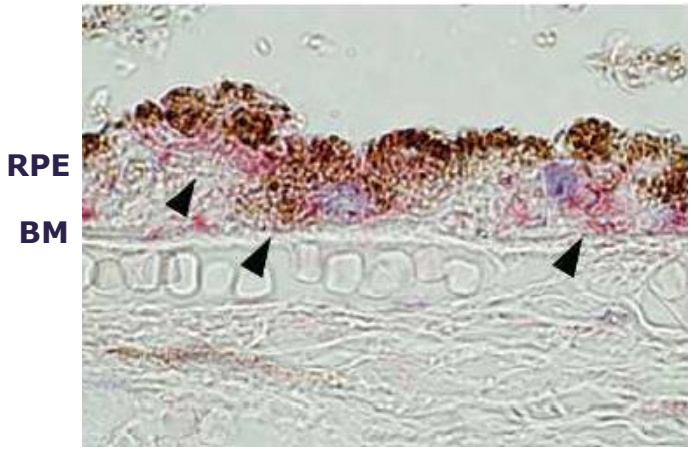
IVERIC BIO

COMPLEMENT PATHWAY: INFLAMMASOME AND MAC → CELL DEATH

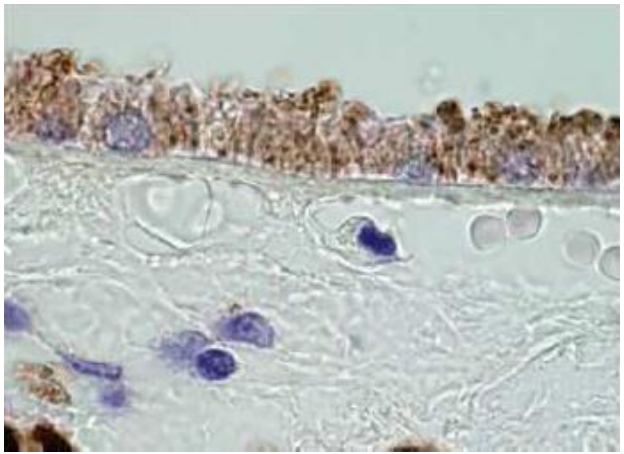


INFLAMMASOME ACTIVATION LEADING TO CELL DEATH IN AMD AFFECTED EYES

DRY AMD



NO AMD

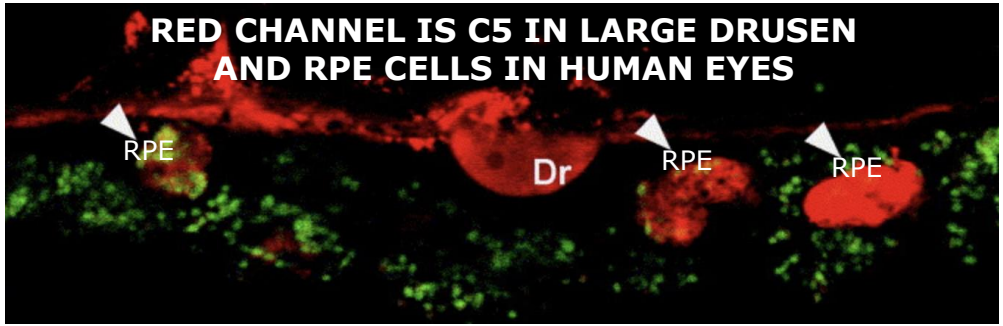


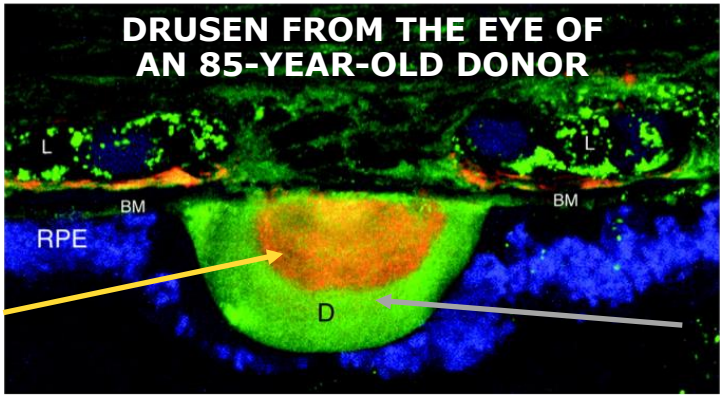
RPE: Retinal pigment Epithelium
BM: Bruch's membrane

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

IVERIC BIO

PRESENCE OF C5 AND MAC ACTIVATION LEADING TO CELL DEATH IN AMD





C5-9 membrane attack complex of complement

Complement factor H

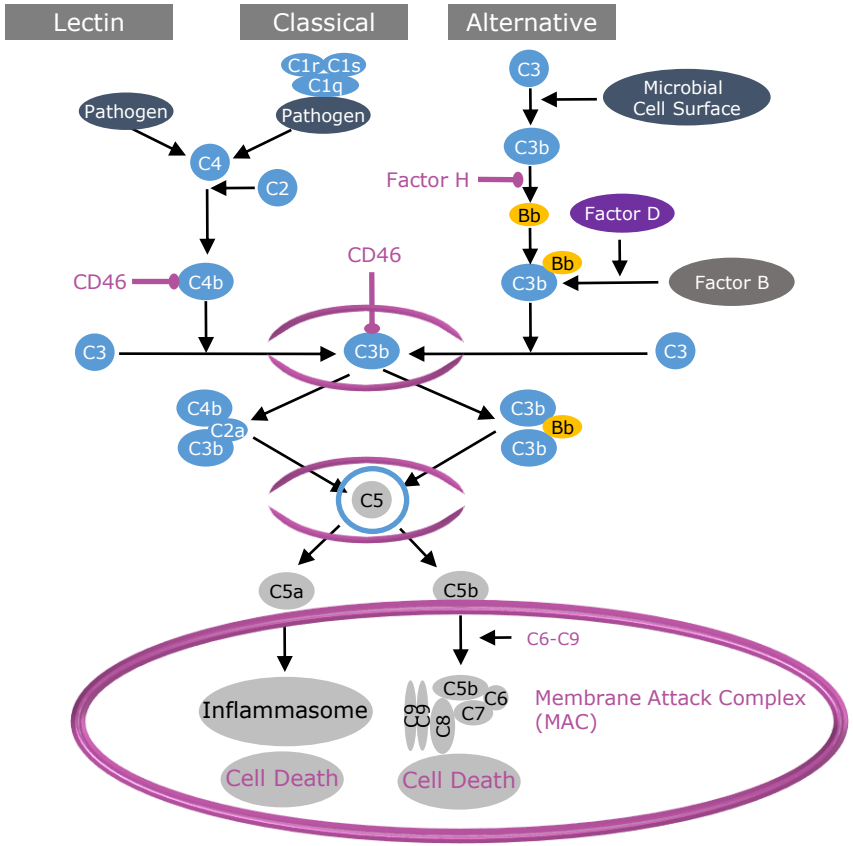
Source: Am J Ophthalmol 2002;134:411–431. Proc Natl Acad Sci USA. 2005, 102(20), 7053-7054.

IVERIC BIO

WHY IS ZIMURA® IMPORTANT?

COMPLEMENT PATHWAY

Inhibit the 2 triggers of cell death, preserving the remainder of pathway



DO WE HAVE EVIDENCE OF ZIMURA'S EFFICACY IN GA?

IVERIC BIO

ZIMURA PHASE 1/2A DRY AMD (GA) – COMPLETED*

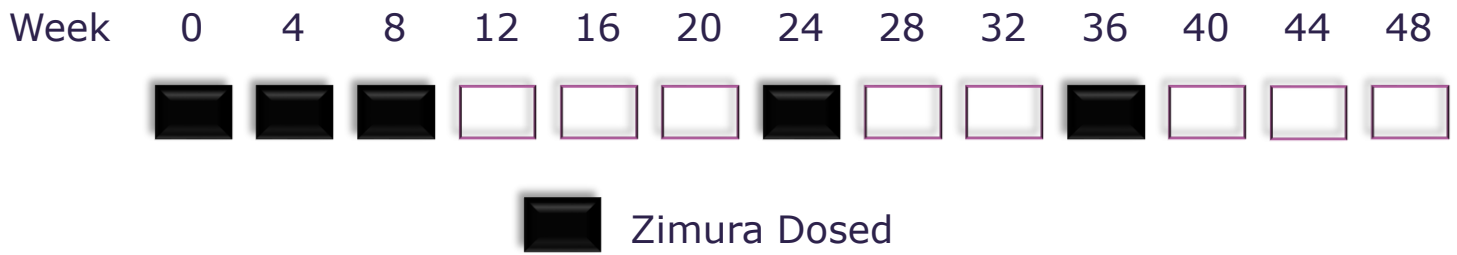
STUDY DESIGN

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

IVERIC BIO

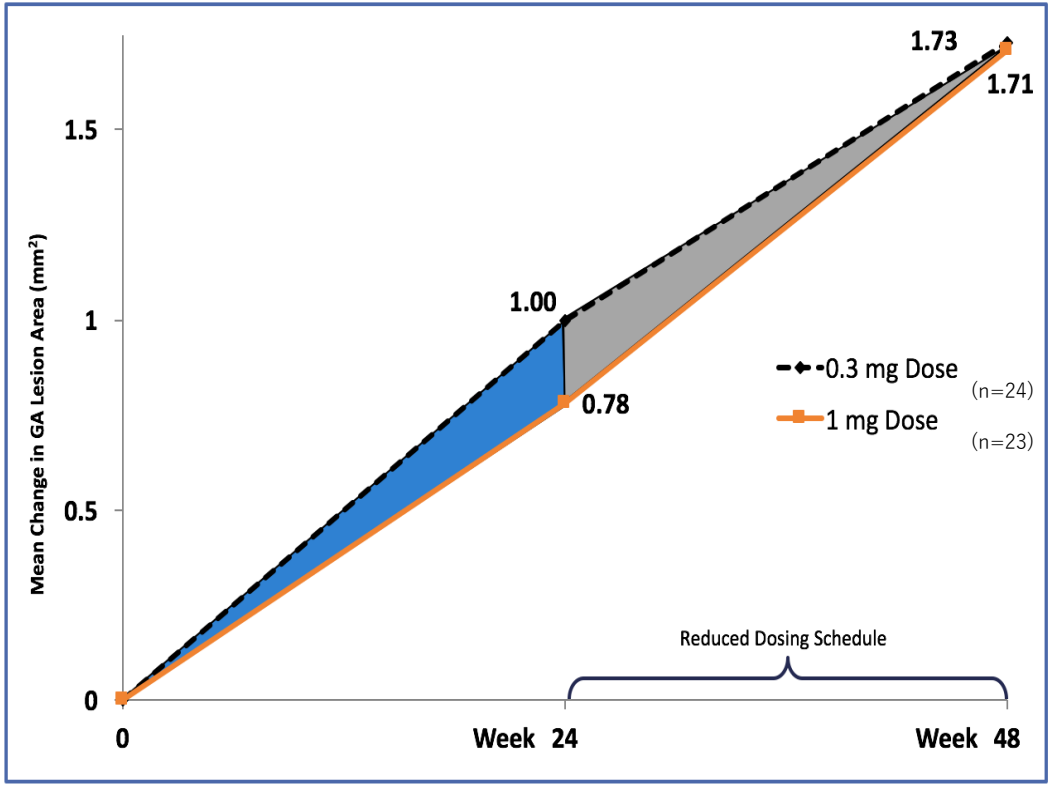
ZIMURA PHASE 1/2A DRY AMD (GA) – COMPLETED

POTENTIAL EFFICACY SIGNAL

- 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

IVERIC BIO

ZIMURA PHASE 3 PROGRAM IN GEOGRAPHIC ATROPHY SECONDARY TO AMD

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

(Geographic Atrophy Therapy Trials)

IVERIC BIO

GATHER1 (OPH2003): 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

IVERIC BIO

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 & Richardson, J Infectious Diseases. 2004;190:666-74.

IVERIC BIO

GATHER1: TRIAL DESIGN

- Randomized, masked (patient, evaluating physician, reading center, sponsor), 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 on the Zimura 1 mg cohort

IVERIC BIO

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

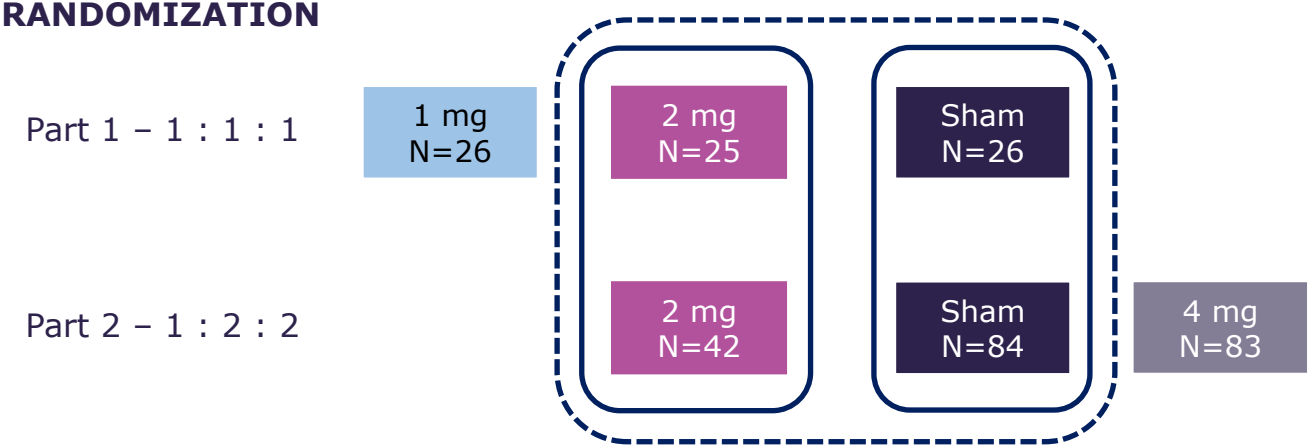
Source: Duke Reading Center

IVERIC BIO

GATHER1: DOSE GROUPS

MASKED THROUGHOUT THE ENTIRE PROCESS

RANDOMIZATION

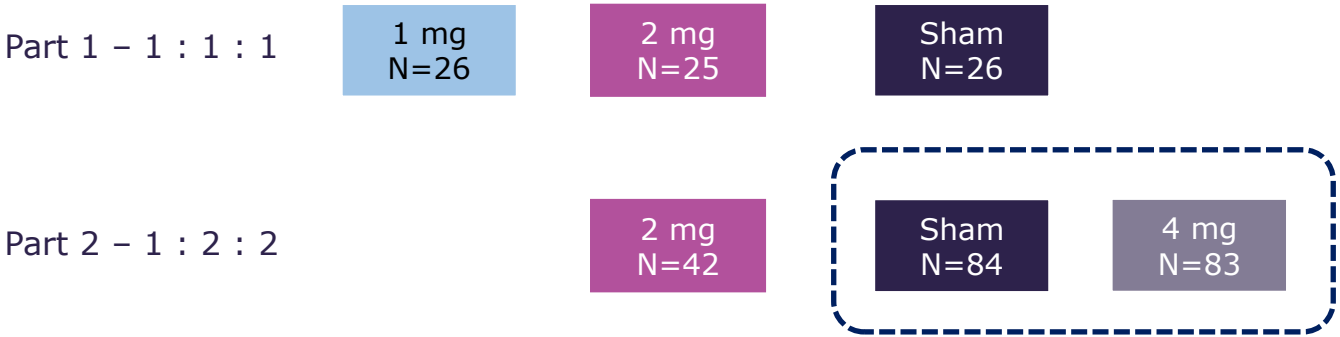


EFFICACY EVALUATION BASED ON PRESPECIFIED STATISTICAL ANALYSIS PLAN (SAP):

- 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:

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																			
Zimura 1mg																			
Sham																			

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																			
Zimura 4mg																			
Sham																			

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

IVERIC BIO

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

IVERIC BIO

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)

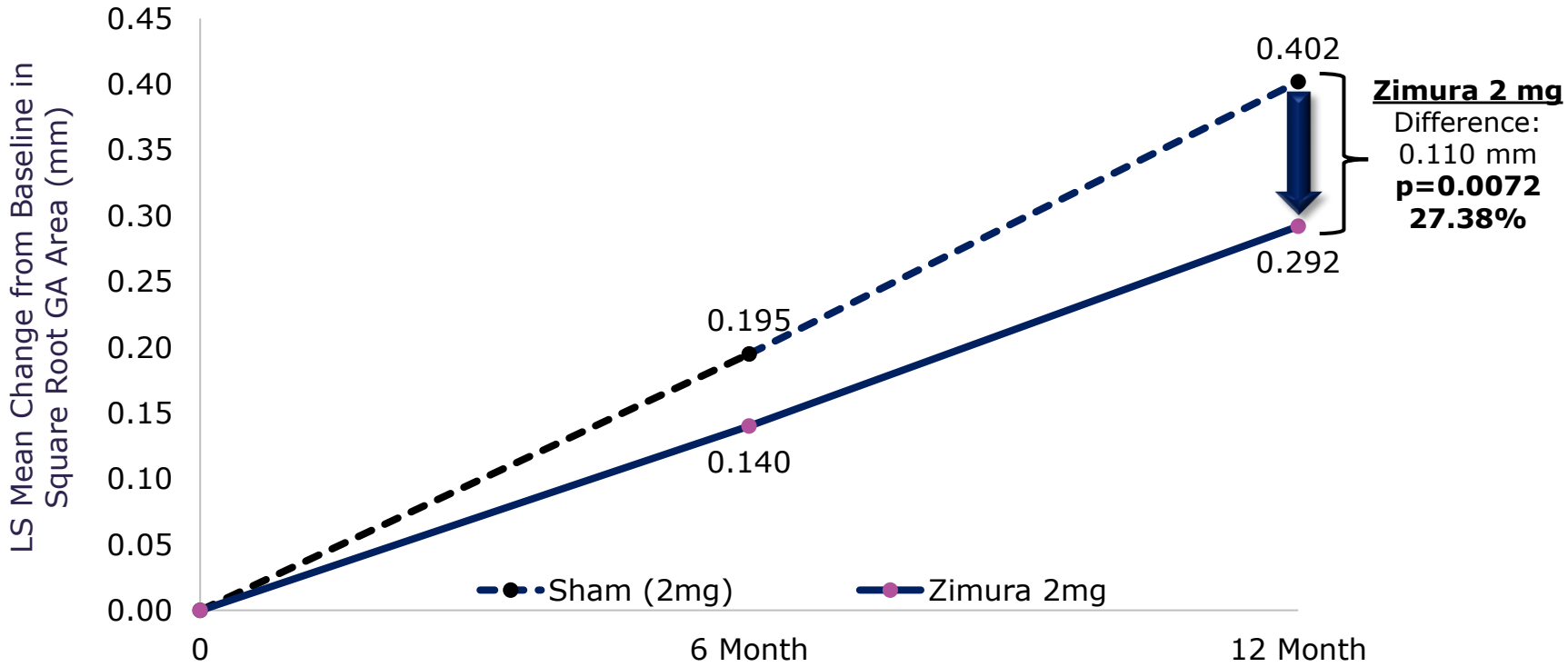
Cohort	Zimura 2mg (N=67)	Sham 2mg (N=110)	Difference	P-value	% Difference
Mean Change in GA[a]	0.292[c]	0.402[c]	0.110	0.0072[b]	27.38%

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%

(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

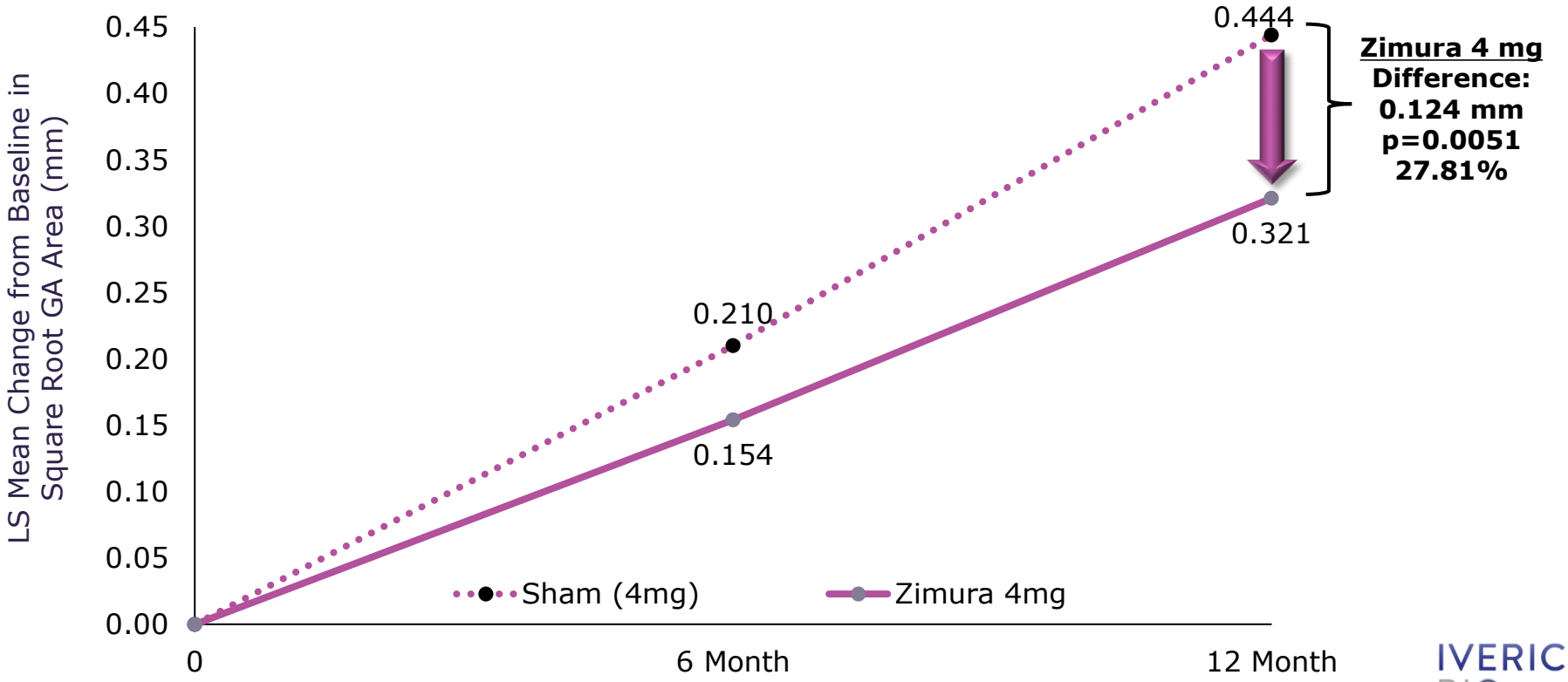
IVERIC BIO

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.

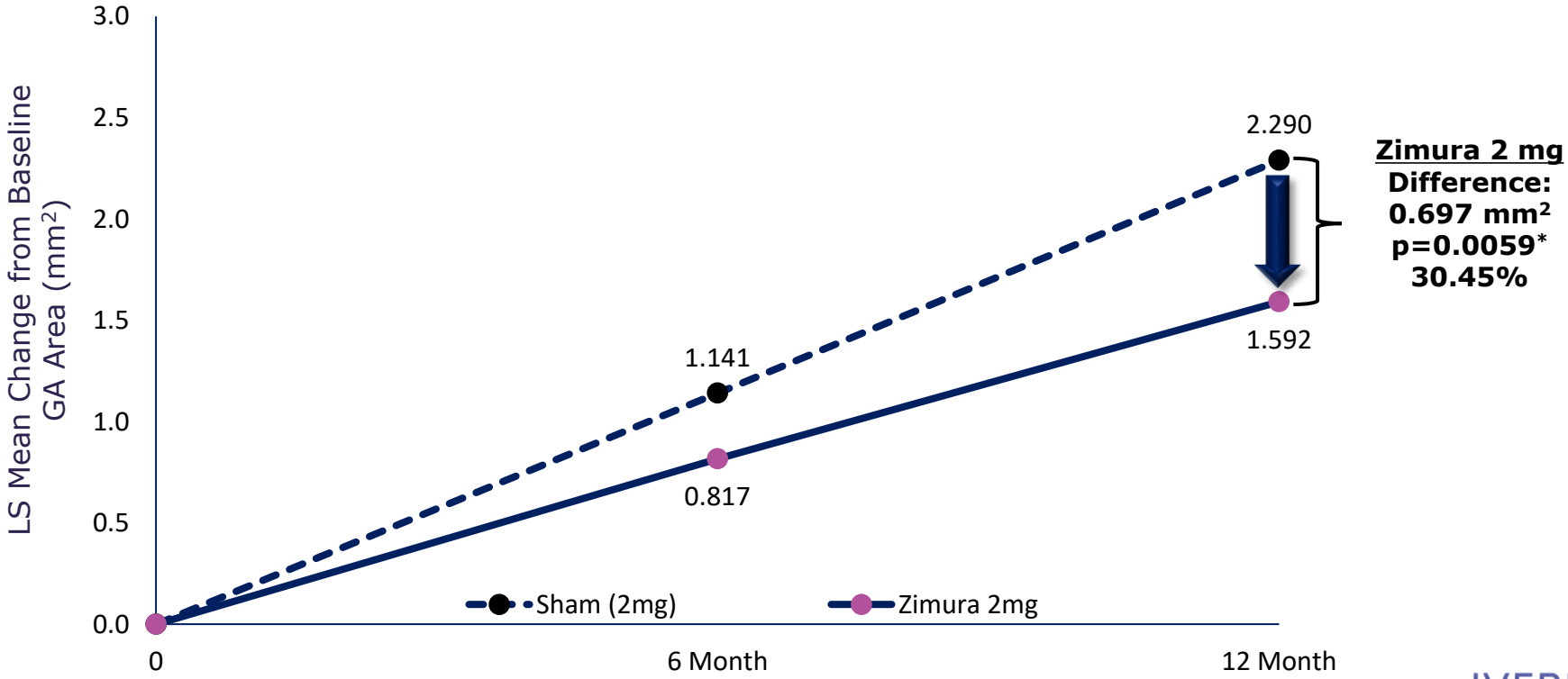
GATHER1: PRIMARY EFFICACY ENDPOINT ACHIEVED: ZIMURA 4 MG VS. SHAM



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

IVERIC BIO

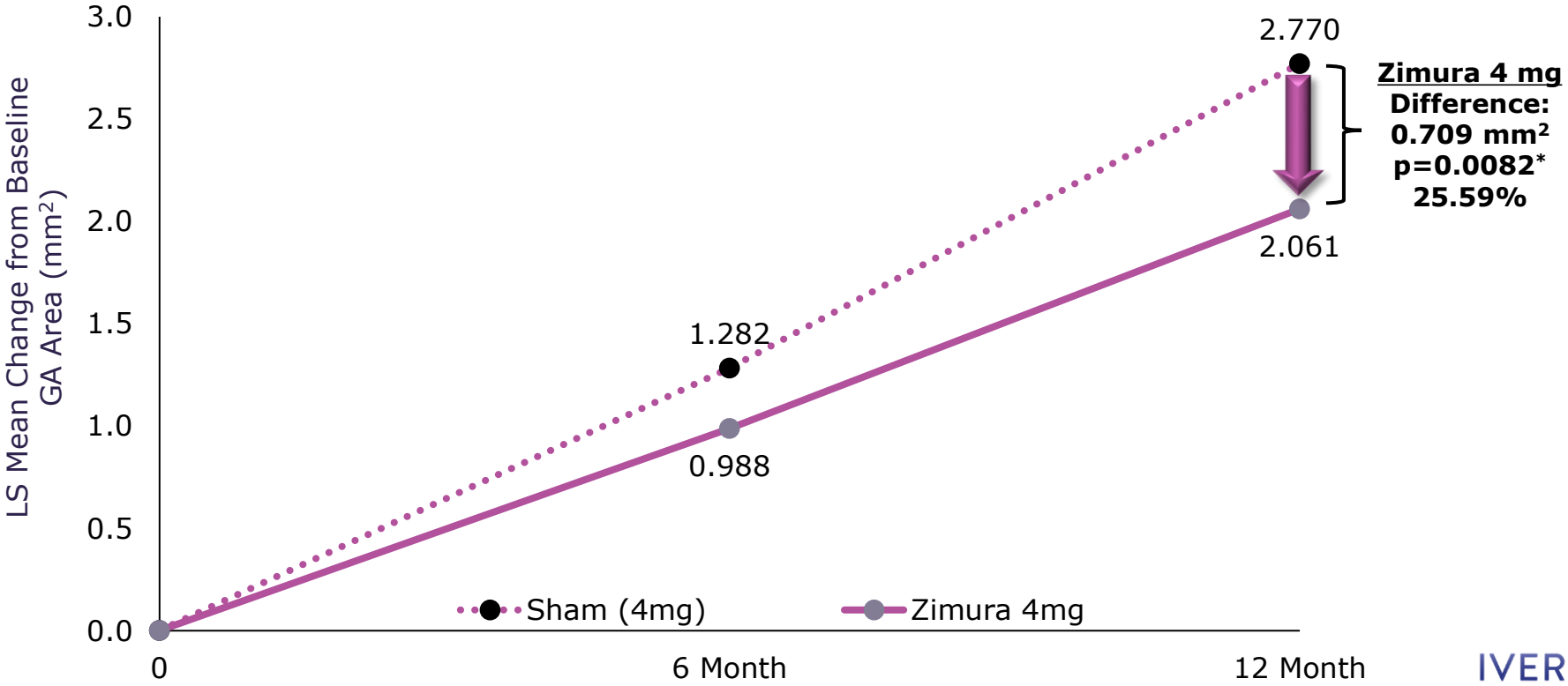
GATHER1: SUPPORTIVE EFFICACY ENDPOINT: ZIMURA 2 MG VS. SHAM (NON-SQUARE ROOT)



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.

IVERIC BIO

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.

IVERIC BIO

GATHER1: PRELIMINARY SAFETY ANALYSIS THROUGH MONTH 12*

FAVORABLE SAFETY PROFILE TO DATE

- 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 eye was 10 patients (3.5%), and in the study eye was 3 patients (2.7%) in the sham control group, 1 patients (4.0%) in the Zimura 1 mg group, 6 patients (9.0%) in the Zimura 2 mg group, and 8 patients (9.6%) in the Zimura 4 mg group.

IVERIC BIO

*Based on Investigator Reported Safety Events

GATHER1: DOSING REGIMEN

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																			
Zimura 1mg																			
Sham																			

Zimura 2mg Zimura 1mg Sham

PART 2:

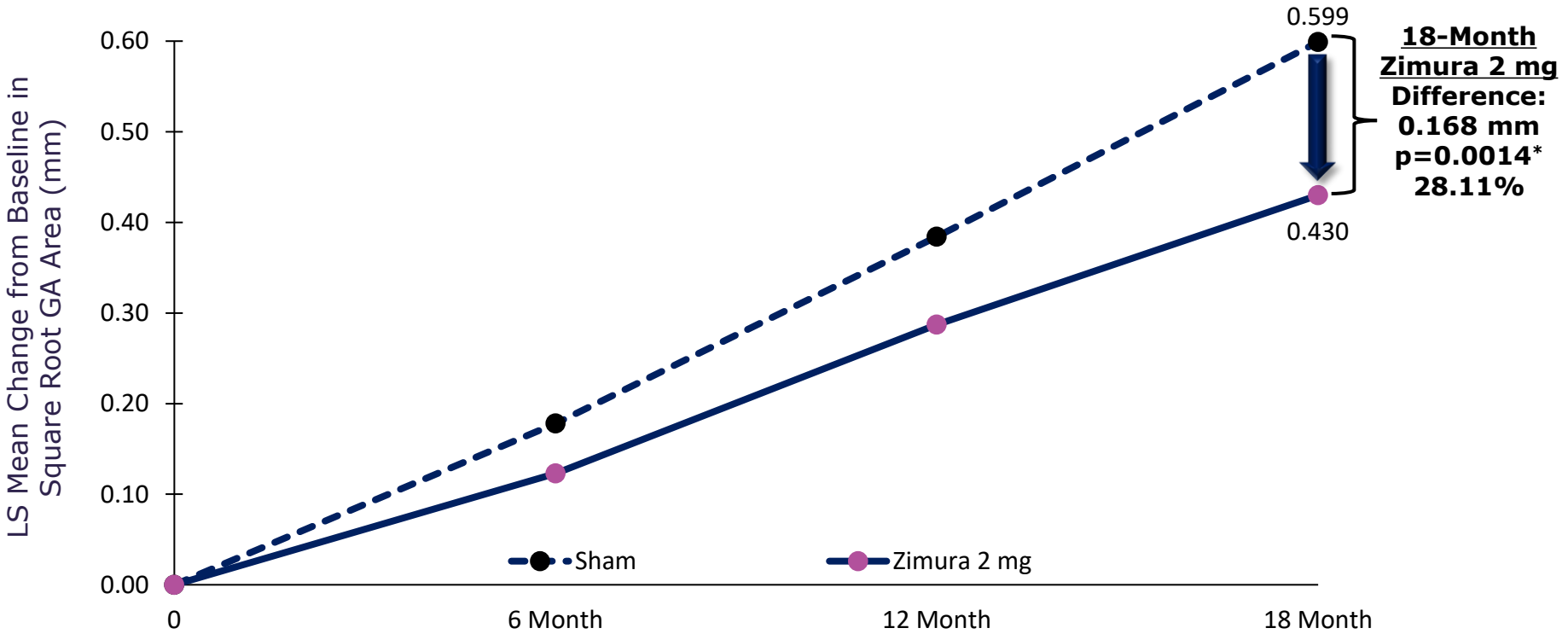
Primary Endpoint at Month 12

	D1	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18
Zimura 2mg																			
Zimura 4mg																			
Sham																			

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

IVERIC BIO

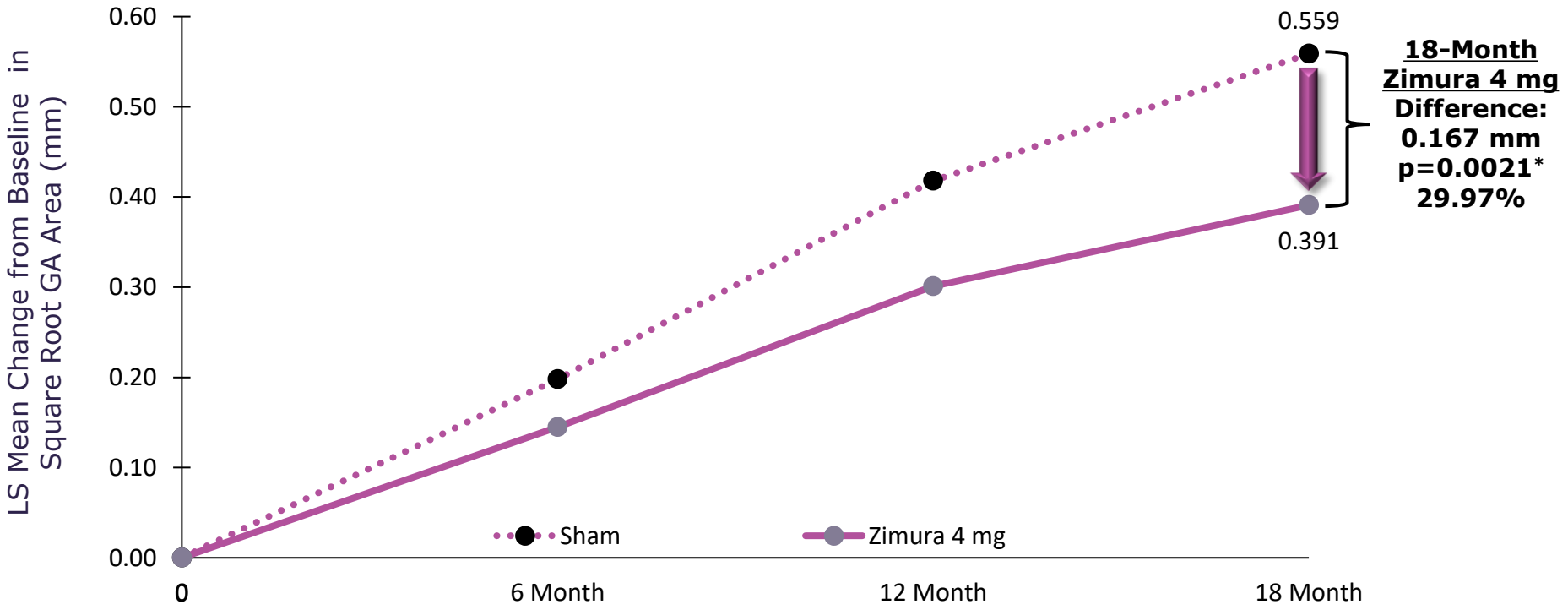
GATHER1: DECREASE IN GA GROWTH OVER 18 MONTHS ZIMURA 2 MG VS. SHAM (SQUARE ROOT TRANSFORMATION)



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.

IVERIC BIO

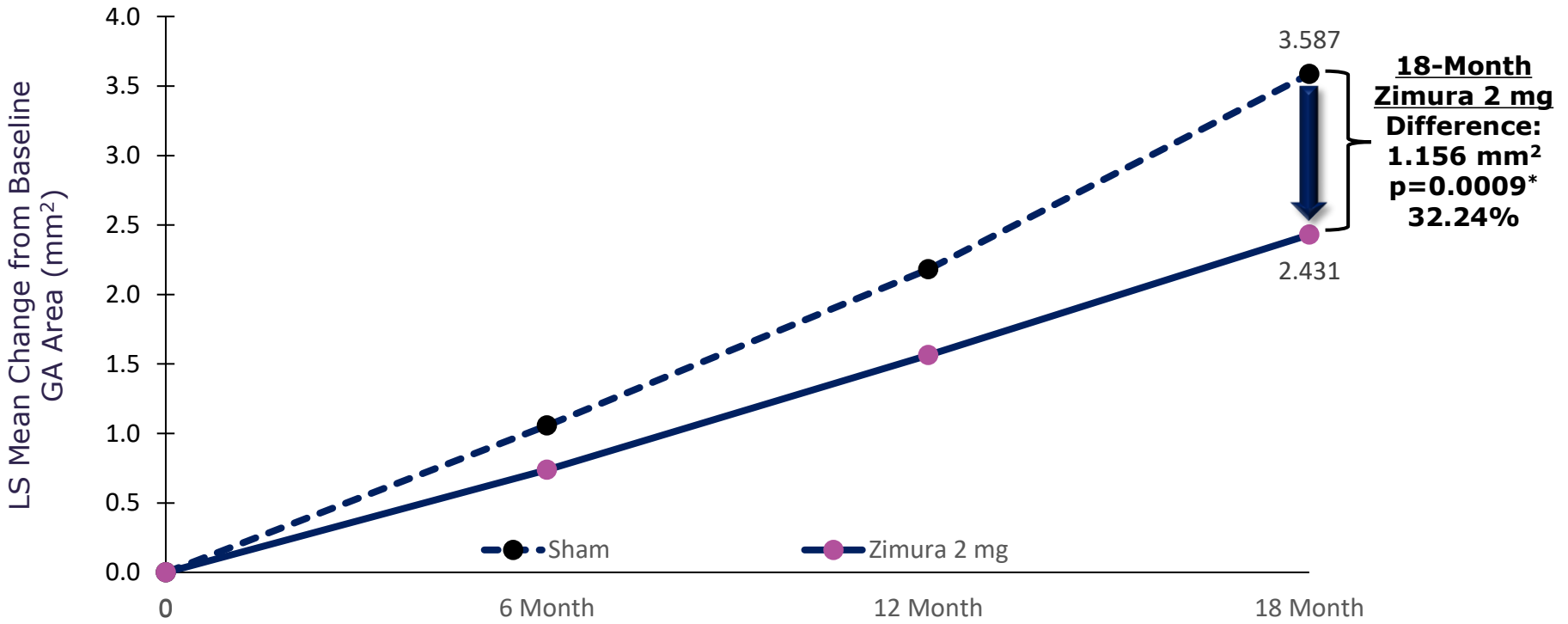
GATHER1: DECREASE IN GA GROWTH OVER 18 MONTHS ZIMURA 4 MG VS. SHAM (SQUARE ROOT TRANSFORMATION)



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.

IVERIC BIO

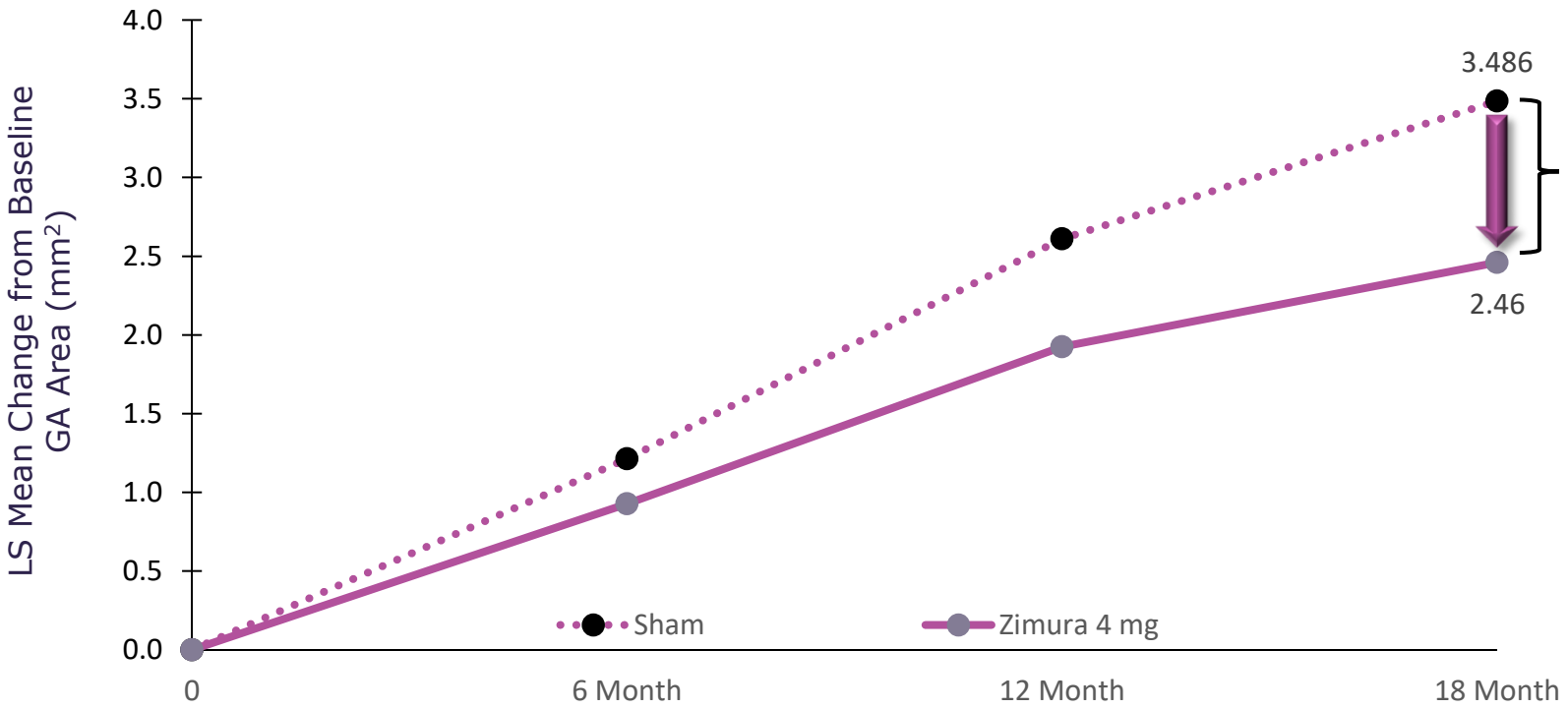
GATHER1: DECREASE IN GA GROWTH OVER 18 MONTHS ZIMURA 2 MG VS. SHAM (NON-SQUARE ROOT)



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.

IVERIC BIO

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.

IVERIC BIO

GATHER1: PRELIMINARY SAFETY ANALYSIS THROUGH MONTH 18*

FAVORABLE SAFETY PROFILE TO DATE

- 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, 2 patients (7.7%) in the Zimura 1 mg group, 8 patients (11.9%) in the Zimura 2 mg group, and 13 patients (15.7%) in the Zimura 4 mg group.

IVERIC BIO

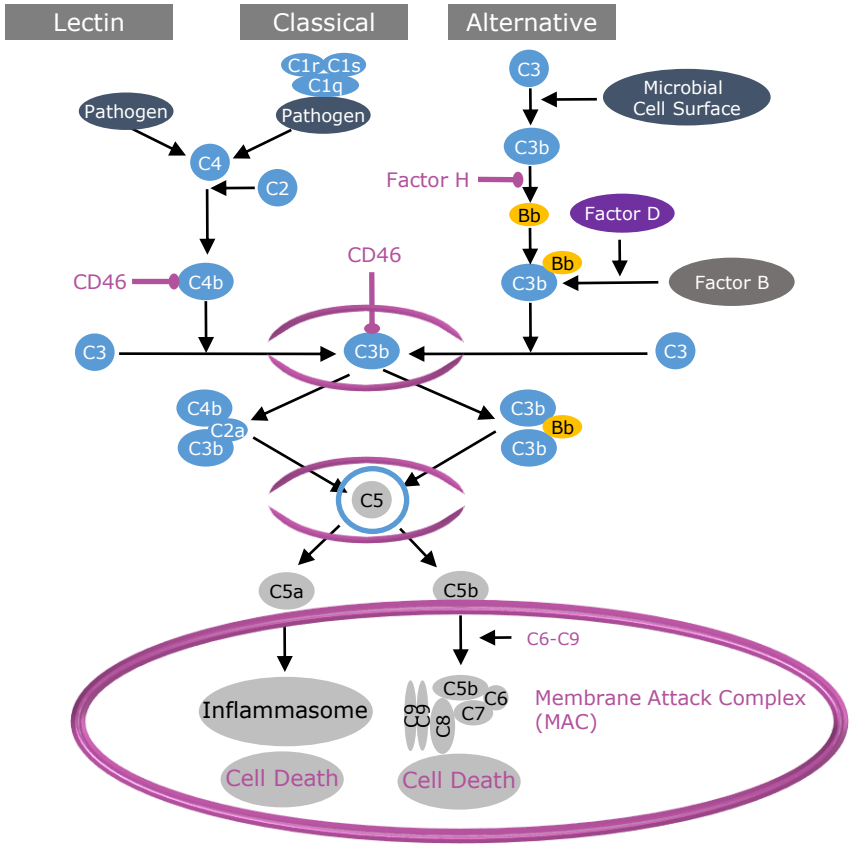
*Based on Investigator Reported Safety Events

WHAT ARE THE POTENTIAL ADVANTAGES OF INHIBITING AT THE C5 LEVEL?

IVERIC BIO

COMPLEMENT PATHWAY

Inhibit the 2 triggers of cell death, preserving the remainder of pathway



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.

IVERIC BIO

C5 INHIBITION: POTENTIAL SAFETY ADVANTAGES

C3 INHIBITION: POTENTIAL FOR NEUROTOXICITY

"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.

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

IVERIC BIO

WHAT IS THE LEVEL OF STATISTICAL CONFIDENCE FOR THIS PIVOTAL TRIAL?

IVERIC BIO

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

IVERIC BIO

GATHER1: PRESPECIFIED MONTH 12 SENSITIVITY ANALYSES

REPLACE MISSING DATA USING MULTIPLE IMPUTATIONS, WITH AN ADDED "SHIFT" INCREASE UNTIL SIGNIFICANCE IS LOST

	Zimura 2mg vs. Sham		Zimura 4mg vs. Sham	
Data Imputation Method	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)

IVERIC BIO

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

IVERIC BIO

WHAT DISTINGUISHES THE GATHER1 DATA IN A POST-COVID WORLD?

IVERIC BIO

GA TRIALS POST-COVID

- We believe GATHER1 is the only pre-COVID positive Phase 3 trial for GA
- New environment for clinical trial execution: Recruitment/retention

IVERIC BIO

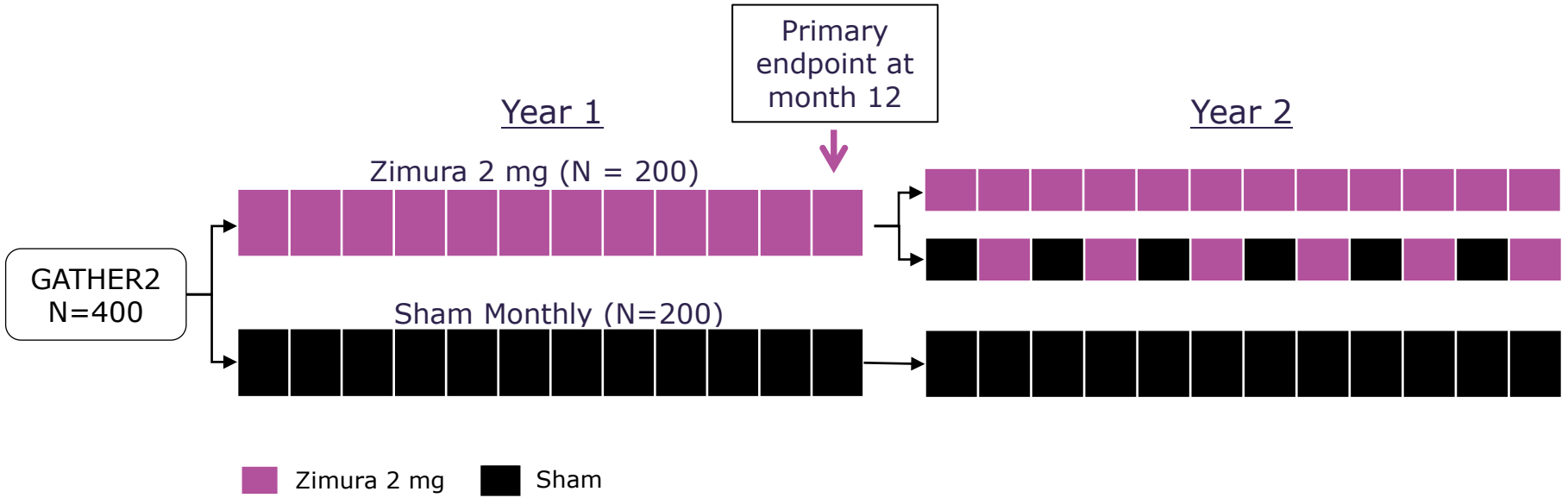
GATHER2 CLINICAL TRIAL

GATHER 2
Geographic Atrophy Therapy Trial

IVERIC BIO

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

IVERIC BIO

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

IVERIC BIO

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

	Indication	Res	Pre-clin	P1	P2	P3	Milestones
Therapeutics	**Zimura:** GA secondary to AMD						• GATHER1 (1st Phase 3): Positive 12 & 18-month data reported • GATHER2 (2nd Phase 3): Target completion of enrollment **3Q 2021**
	Zimura: Stargardt Disease						• Expanded enrollment (up to ~25 additional patients) ongoing
	IC-500 (anti-HtrA1): GA secondary to AMD						• Plan to file IND in **2H 2022**
AAV Gene Therapies	**IC-100:** RHO-adRP						• Plan to initiate Phase 1/2 in **2H 2021**
	IC-200: *BEST1*-related IRDs						• Plan to initiate Phase 1/2 in **2H 2021**
	miniCEP290: LCA10						• Identify lead construct in **2Q 2021**
	miniABCA4: Stargardt Disease*						• Additional results expected in **1H 2021**
	miniUSH2A: *USH2A*-related IRDs*						• Preliminary results expected in **1H 2021**

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

IVERIC BIO

STARGARDT DISEASE

IVERIC BIO

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
- Expanded enrollment (up to ~25 additional patients) ongoing

IVERIC BIO

IC-500
HtrA1 Inhibitor

IVERIC BIO

HTRA1 IN AMD

High Temperature Requirement A Serine Peptidase 1/ HtrA1

Compelling target for Geographic Atrophy and other forms of AMD

- AMD is highly heritable
  - Genetic component may account for 46-71% of risk
- Genome-Wide Association Studies (GWAS) highlight HtrA1 and complement pathway as the major genetic contributors to disease
- HtrA1 risk alleles
  - Most compelling known genetic risk for early and late AMD

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

IC-500 OVERVIEW

- Rationale
  - Strong genetic link to age-related macular degeneration
  - HtrA1 expression and function
- HtrA1 target
  - RPE expression and protease function
- IC-500
  - Highly potent/specific inhibitor with favorable properties (e.g., inhibition of both intracellular and extracellular HtrA1)
  - Lead candidate currently in pre-clinical development

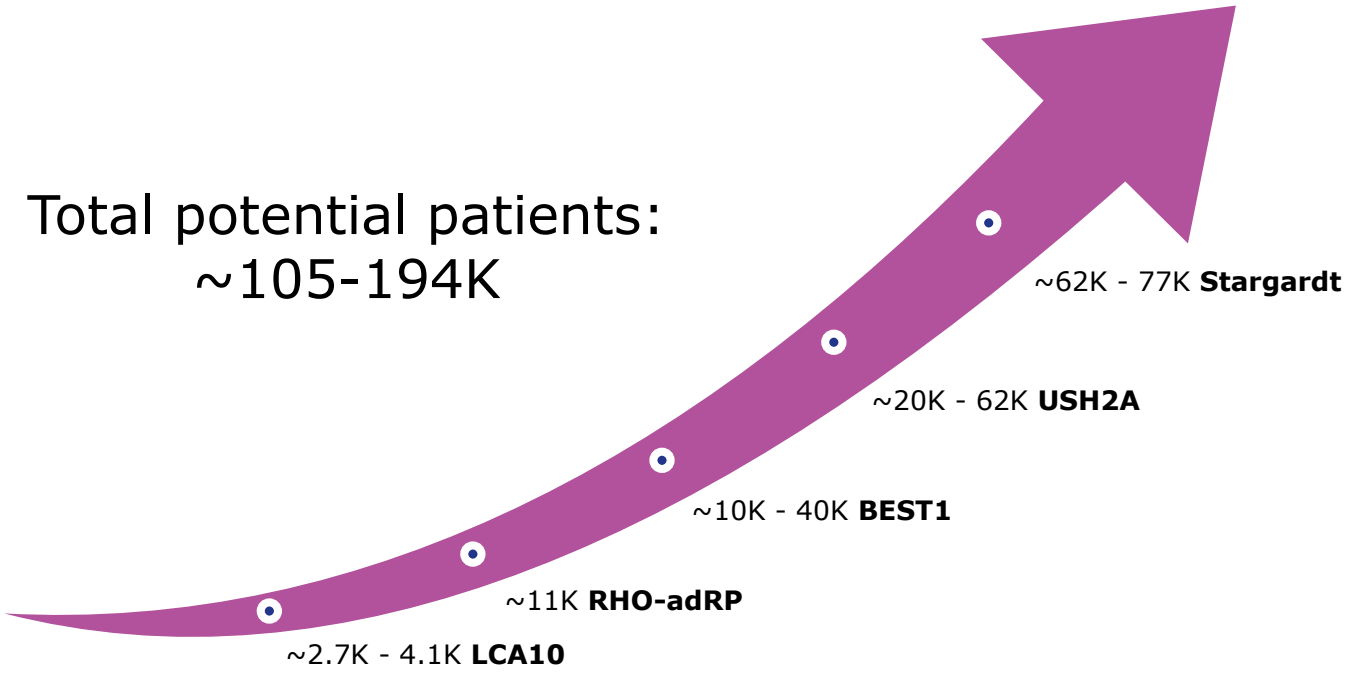
Source: Ophthalmology, Volume 123, Issue 2, 361-368

GENE THERAPY

IVERIC BIO

LARGE POTENTIAL FOR PATIENTS WITH INHERITED RETINAL DISEASES (IRD)[1,2]

Total potential patients:
~105-194K



[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

- Mutation agnostic approach
  - >150 identified rhodopsin (RHO) gene mutations
- Knockdown and replacement with a single AAV vector
  - Suppression of endogenous mutant, toxic rhodopsin protein
  - Replacement 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
- Phase 1/2 planned to initiate in 2H 2021

Sources: PNAS September 4, 2018 115 (36) E8547-E8556. Human Gene Therapy 23:356–366 (April 2012).

IVERIC BIO

IC-200: *BEST1* PROGRAM SUMMARY

- Only known gene therapy currently in development for *BEST1*-related IRDs
- Therapy provides replacement for dysfunctional *BEST1* gene allowing production of normal bestrophin protein
- Proof-of-concept established in naturally occurring autosomal recessive *BEST1* canine model
- Phase 1/2 planned to initiate in 2H 2021

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

IVERIC BIO

MINIGENE PROGRAMS

IVERIC BIO

MINIGENE STRATEGY

- AAV Vectors
  - Extensive experience with intraocular application in both humans and animal models
  - Well-documented safety profile
  - Limited packaging capacity of <5kb

- Minigene Solution
  - Allows for the potential treatment of genetic diseases previously not amenable to AAV approach by delivering a smaller but still functional gene

IVERIC BIO

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
- Construct provides replacement for mutated *CEP290* gene with a novel minigene
- 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

[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)

IVERIC BIO

2021 GOALS

- Complete enrollment for GATHER2 in 3Q 2021
- Investigate multiple dosing schedules for IC-500 (HtrA1) as part of expanding development-stage AMD franchise
- Advance IC-100 (RHO-adRP) and IC-200 (*BEST1*-related IRDs) into the clinic
- Continue to strengthen leadership team through strategic hiring

IVERIC BIO

DEVELOPING TRANSFORMATIVE THERAPIES
FOR RETINAL DISEASES

March 2021
NASDAQ: ISEE

IVERIC BIO

APPENDIX

IVERIC BIO

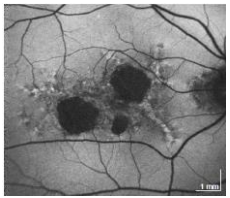
AGE-RELATED MACULAR DEGENERATION: A LEADING CAUSE OF VISUAL DISABILITY

ALL AMD: ESTIMATED PREVALENCE

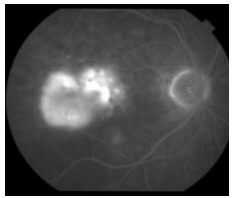
Worldwide: ~170 Million → **YEAR 2040** → ~288 Million

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)

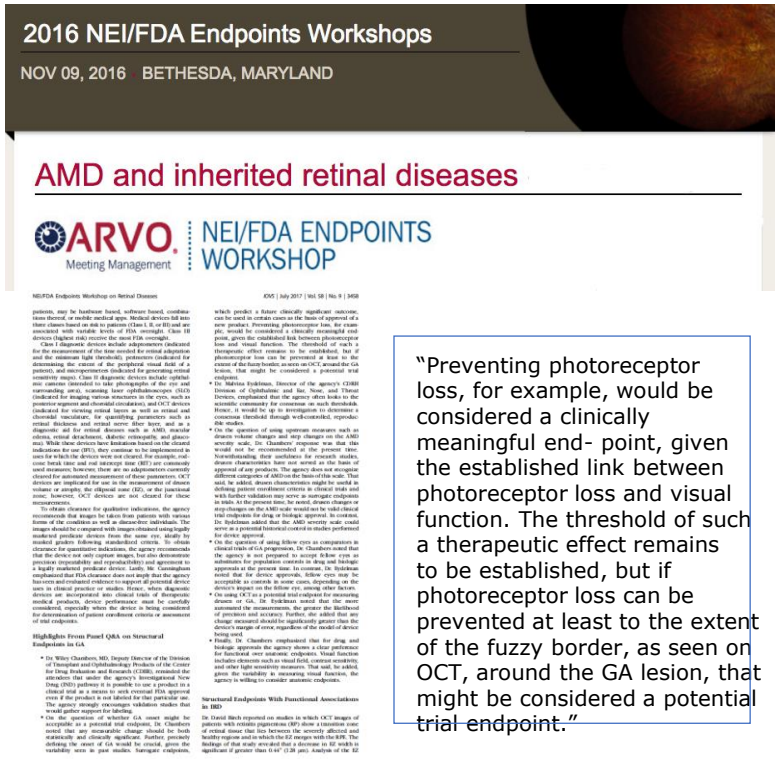


Incidence of Wet AMD
~150,000/ Year (US)

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.

IVERIC BIO

"PREVENTING PHOTORECEPTOR LOSS": "CLINICALLY MEANINGFUL END-POINT"

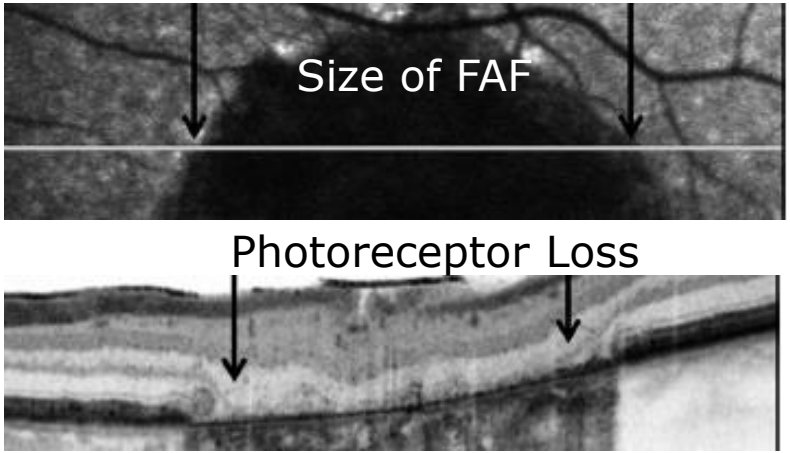


"Preventing photoreceptor loss, for example, would be considered a clinically meaningful end- point, given the established link between photoreceptor loss and visual function. The threshold of such a therapeutic effect remains to be established, but if photoreceptor loss can be prevented at least to 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.

IVERIC BIO

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

IVERIC BIO

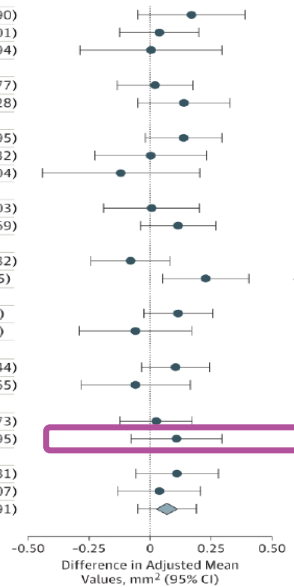
EXTRAFOVEAL SHAM GROWTH: CHROMA/SPECTRI & GATHER1

NON-SQUARE ROOT TRANSFORMATION

Chroma/Spectri

Mean change in extrafoveal GA 2.292-2.401

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



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

GATHER1

Mean change in extrafoveal GA 2.29-2.77

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

IVERIC BIO

NONSUBFOVEAL/EXTRAFOVEAL SHAM GROWTH: CHROMA/SPECTRI/FILLY

SQUARE ROOT TRANSFORMATION

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

FILLY

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*

	N	Mean (SD)
Unifocal		
APL2-Monthly	19	0.27 (0.15)
APL2-EOM	22	0.19 (0.16)
Sham	24	0.38 (0.22)
Multifocal		
APL2-Monthly	48	0.25 (0.17)
APL2-EOM	36	0.32 (0.29)
Sham	42	0.35 (0.21)
Foveal		
APL2-Monthly	40	0.23 (0.16)
APL2-EOM	38	0.22 (0.22)
Sham	37	0.3 (0.16)
Extrafoveal		
APL2-Monthly	27	0.3 (0.17)
APL2-EOM	20	0.37 (0.29)
Sham	30	0.44 (0.24)

----- Greatest Progression ----->

0 0.2 0.35 0.5 0.7

Square-Root(GA) - Month 12 Change from Baseline

Mean change in Sham (extrafoveal) Filly: 0.44

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

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

IVERIC BIO

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

IVERIC BIO

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)

IVERIC BIO

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

IVERIC BIO

DECREASED COMPLEMENT ACTIVITY: RESCUED PHOTORECEPTORS

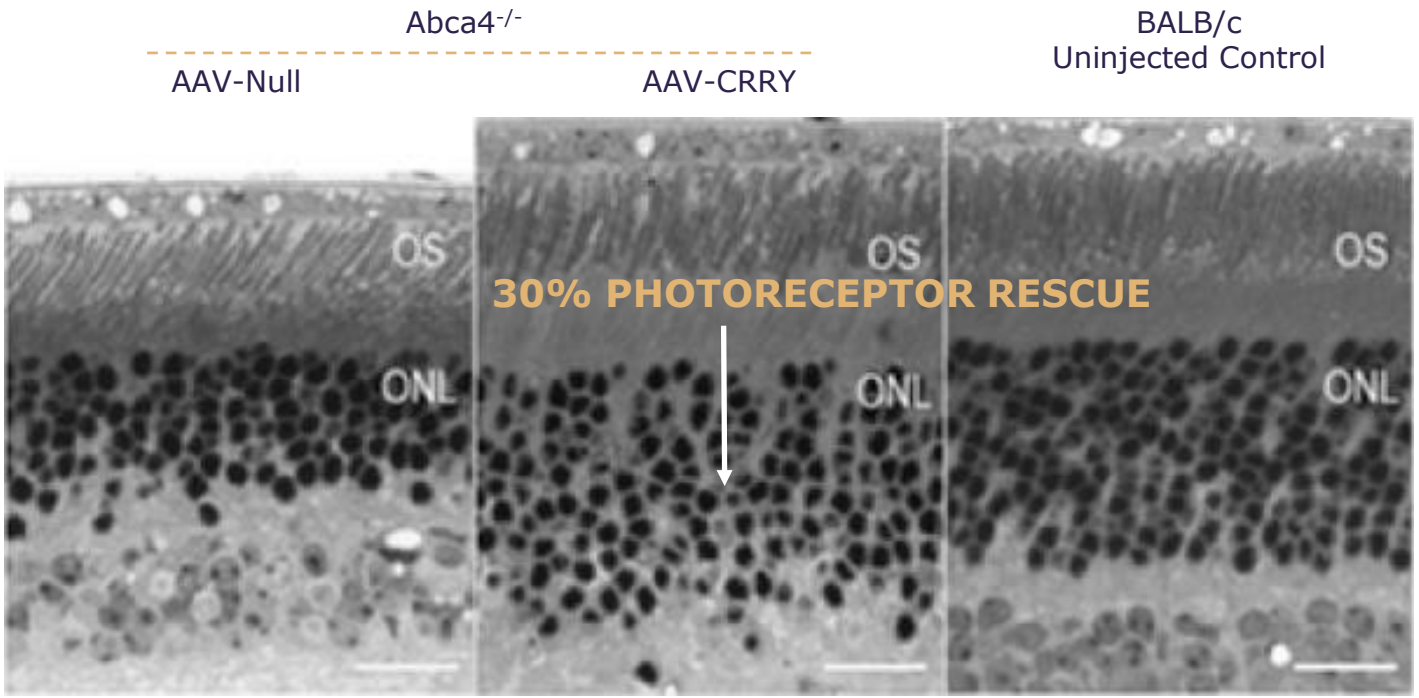
- "In this study, we attempted to protect cells against complement attack by increasing expression of CRRY in the RPE of Abca4$^{-/-}$ mice"
- "CRRY is an important Complement Negative Regulatory Protein (CRP) in the mouse eye"

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

IVERIC BIO

COMPLEMENT INHIBITION RESCUES PHOTORECEPTORS

REPRESENTATIVE RETINAL IMAGES FROM 1 YEAR OLD ALBINO ABCA4$^{-/-}$ OR BALB/C MICE

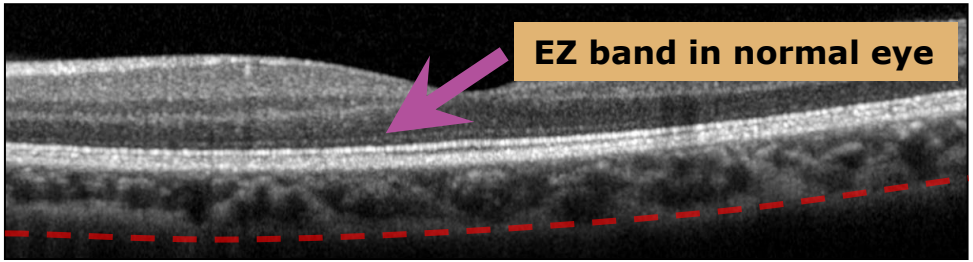


Source: Proc Natl Acad Sci U S A. 2017; 114(15):3987-3992.

IVERIC BIO

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