
OPHTHOTECH

Corporate Overview

Forward-looking statements

Any statements in this presentation about Ophthotech’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 Ophthotech’s strategy, future operations and future expectations and plans and prospects for Ophthotech, and any other statements containing the words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “goal,” “may,” “might,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions. In this presentation, Ophthotech’s forward looking statements include statements about the implementation of its strategic plan, Ophthotech's projected use of cash and cash balances, the timing, progress and results of clinical trials and other development activities, the potential utility or commercialization of any of Ophthotech’s product candidates and its business development strategy, including any potential in-license or acquisition opportunities. Such forward-looking statements involve substantial risks and uncertainties that could cause Ophthotech’s clinical 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 initiation and conduct of clinical trials, availability of data from clinical trials, expectations for regulatory matters and negotiation and consummation of in-license and/or acquisition transactions, need for additional financing and other factors discussed in the “Risk Factors” section contained in the quarterly and annual reports that Ophthotech files with the Securities and Exchange Commission. Any forward-looking statements represent Ophthotech’s views only as of the date of this presentation. Ophthotech anticipates that subsequent events and developments will cause its views to change. While Ophthotech may elect to update these forward-looking statements at some point in the future, Ophthotech specifically disclaims any obligation to do so except as required by law.

Strategic Objective

*Science driven, retina focused company
with multiple programs concentrated in
orphan and age-related indications*

Timeline/Planned Milestones on the Near Horizon

2017

- ✓ **Set Strategic Plan**
- Stargardt Disease – Zimura**
Initiate program *By end of this year*
- Wet AMD – Zimura**
Initiate Phase 2a trial *By end of this year*
- IPCV – Zimura**
Initiate Phase 2a trial *By end of this year*
- Dry AMD – Zimura**
Phase 2/3 trial ongoing *Strategic decision
(by end of this year)*

2018

- Posterior Uveitis – Zimura** *Planning Phase 2a program*
- Von Hippel Lindau – Fovista** *Initial data*
- Retinoblastoma – Fovista** *Planning pre-clinical program*

Multiple Shots on Goal

Zimura (Complement C5 inhibitor)

Stargardt Disease
(Orphan)



- Plan to initiate program by end of this year
- Engaged with Foundation Fighting Blindness (ProgStar study data)

Wet AMD



- Plan to initiate Phase 2a trial by end of this year
- Assessing a range of dosing regimens in combination with anti-VEGF

Idiopathic Polypoidal Choroidal
Vasculopathy (IPCV)



- Plan to initiate Phase 2a trial by the end of this year

Dry AMD (GA)



- Phase 2/3 monotherapy trial currently ongoing
- Awaiting results of competitor for strategic decision making

Intermediate/Posterior Uveitis
(Orphan)



- Planning Phase 2a trial to initiate in 2018

Fovista (anti-PDGF)

Von Hippel-Lindau Syndrome
(Orphan)



- Phase 1/2 trial is ongoing
- Collaboration with the National Eye Institute

Retinoblastoma
(Orphan)

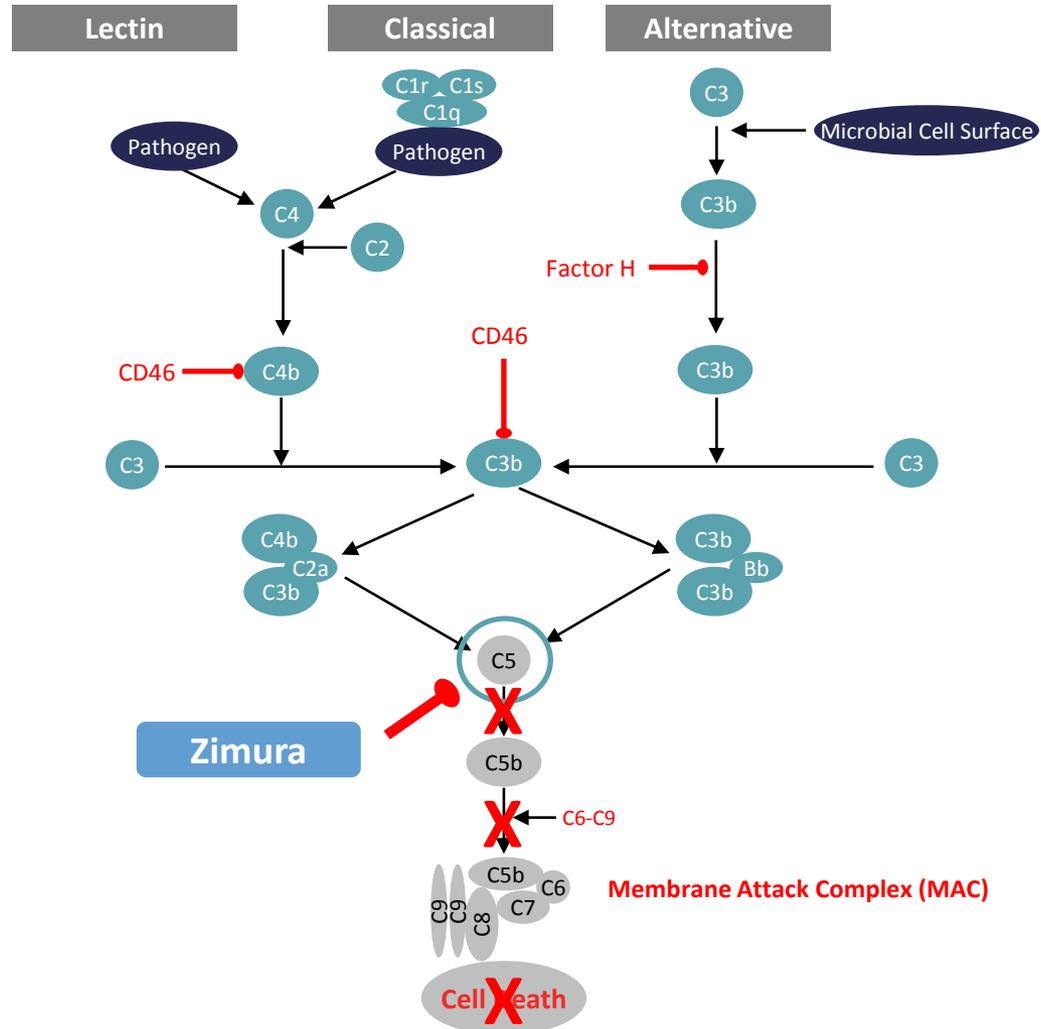


- Planning pre-clinical program

Zimura, C5 Complement Inhibitor

Ophthalmic Orphan and Age-Related Eye Diseases

Complement Pathway



Source: OPHT internal

Zimura, C5 Complement Inhibitor

**Stargardt Disease
(Orphan Indication)**

Rationale for Development of Zimura in Stargardt

A devastating inherited retinal orphan disease that causes vision loss during childhood/adolescence with no FDA approved treatment

- High unmet medical need
 - Estimated prevalence (US) of ~32,000 - 41,000 patients⁽¹⁾
 - No FDA approved treatment available
- Scientific evidence⁽²⁾
 - Bisretinoids (visual cycle waste) activate complement
 - Complement inhibition rescues photoreceptor cells in a Stargardt animal model
 - Anti-C5 improved RPE cell viability in bisretinoid/complement cell culture model
- Orphan disease
 - May have potential for priority review voucher
 - Seven year exclusivity
- OPHT plans to initiate program by the end of this year
 - Randomized, control clinical trial
 - Identified and engaged potential trial sites

Sources:

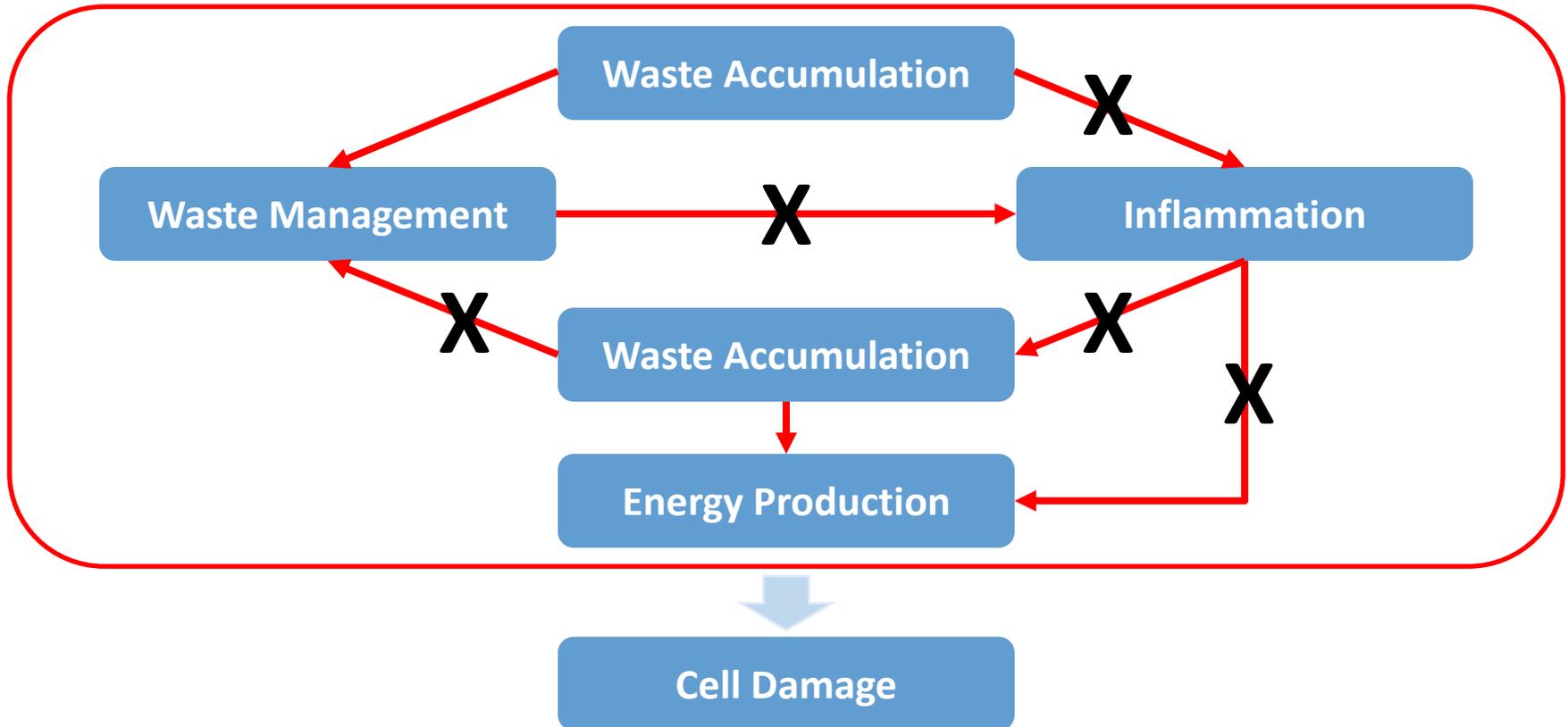
- 1) Blacharski PA . Fundus flavimaculatus. In: Newsome DA ed. Retinal Dystrophies and Degenerations. New York: Raven Press; 1988:135–159.
- 2) The Journal of Biological Chemistry. 2011; 286(21): 18593–18601. Proc Natl Acad Sci U S A. 2017; 114(15):3987-3992. Invest Ophthalmol Vis Sci. 2013;54:2669-2677

OPHT Engages Foundation Fighting Blindness

- OPHT entered into an agreement with Foundation Fighting Blindness (FFB)
 - Highly-distinguished organization recognized for its scientific commitment to orphan inherited retinal diseases
 - Established network of scientists and a robust patient registry
- OPHT gains access to FFB's publicly available **ProgStar** study
 - Largest Natural History Study of Stargardt Disease
 - OPHT plans to leverage information in the design of Zimura Stargardt study

Gene Mutation: Waste Accumulation ~~X~~ Inflammation

Complement inhibition may potentially lead to healthier RPE cells = Better ability to process and recycle the waste and therefore slow down the progression of Stargardt disease ⁽¹⁾



(1) Sources: FASEB J. 2004 Mar;18(3):562-4. Graefe's Arch Clin Exp Ophthalmol (2002) 240:983-988. The Journal of Biological Chemistry. 2011; 286(21): 18593–18601. Proc Natl Acad Sci U S A. 2017; 114(15):3987-3992. Invest Ophthalmol Vis Sci. 2013;54:2669-2677

Autosomal Recessive Stargardt Disease (STGD1): Disease Overview

Progressive damage to the macula and retina caused by mutations in the ABCA4 gene

- ABCA4 gene makes a protein that normally helps clear away vitamin A byproducts inside photoreceptors
- Lack of the needed protein leads to the accumulation of bisretinoids/lipofuscin/A2E (“wear and tear” pigment: waste)
- Accumulation of waste and associated inflammation (complement activation) in the RPE cells leads to the death of photoreceptors and loss of vision

Complement Inhibition Rescues Light Perceiving Cells

Expression of Complement Inhibitory Protein (CRRY)



Normalized Complement Activity



**~2 fold decrease in
bisretinoid accumulation**



**~30% increase in the number
of photoreceptor nuclei**

PNAS

Complement modulation in the retinal pigment epithelium rescues photoreceptor degeneration in a mouse model of Stargardt disease

Tamara L. Lenis^{h1}, Shanta Sarfare^{h1,2}, Zhichun Jiang^{h1}, Marcia B. Lloyd^{h1}, Dean Bok^{h1}, and Roxana A. Radu^{h1,3}

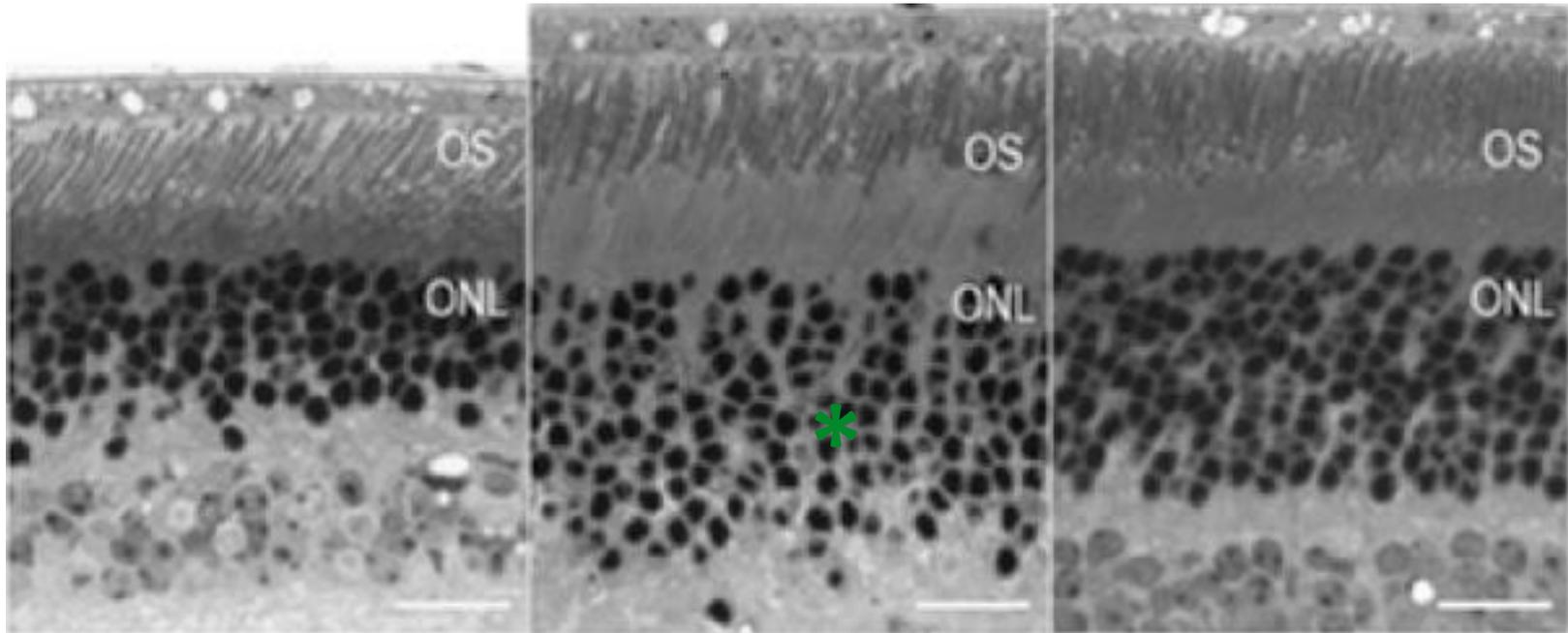
Source: Proc Natl Acad Sci U S A. 2017; 114(15):3987-3992.

Decreased Complement Activity: Rescued Photoreceptors

AAV-Null

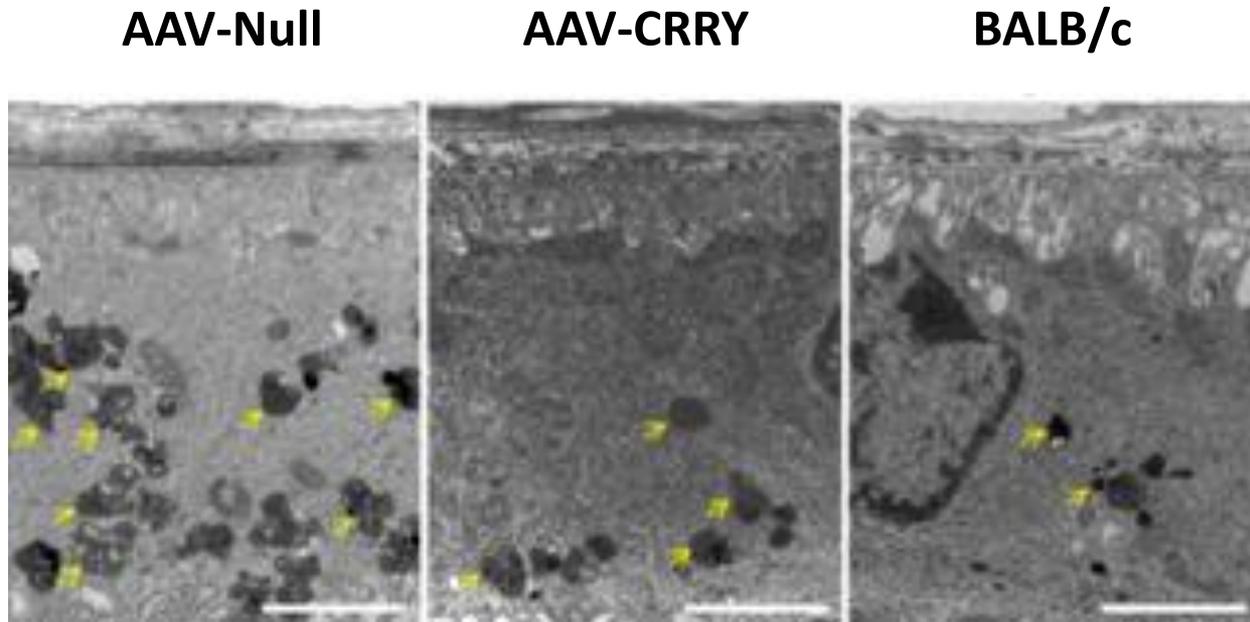
AAV-CRRY

BALB/c



1 Year old Albino $Abca4^{-/-}$ or BALB/c Mice

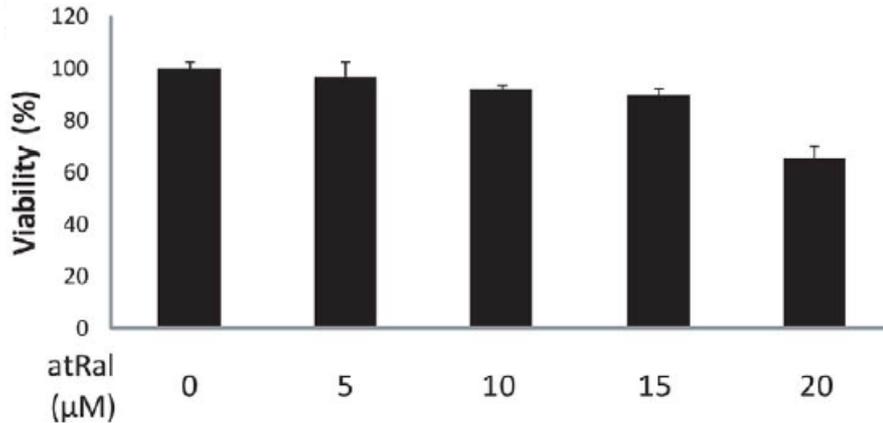
Decreased Complement Activity: Decreased Lipofuscin Accumulation



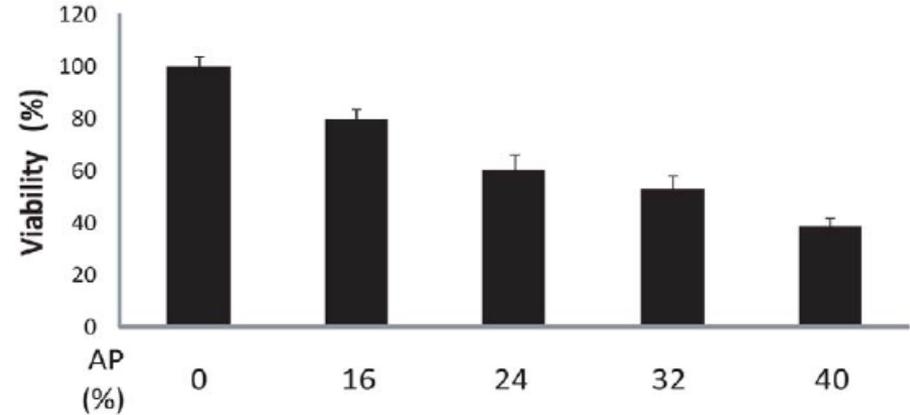
1 Year old Albino Abca4^{-/-} or BALB/c Mice

Waste + Complement Activation: Significant Reduction in RPE Viability

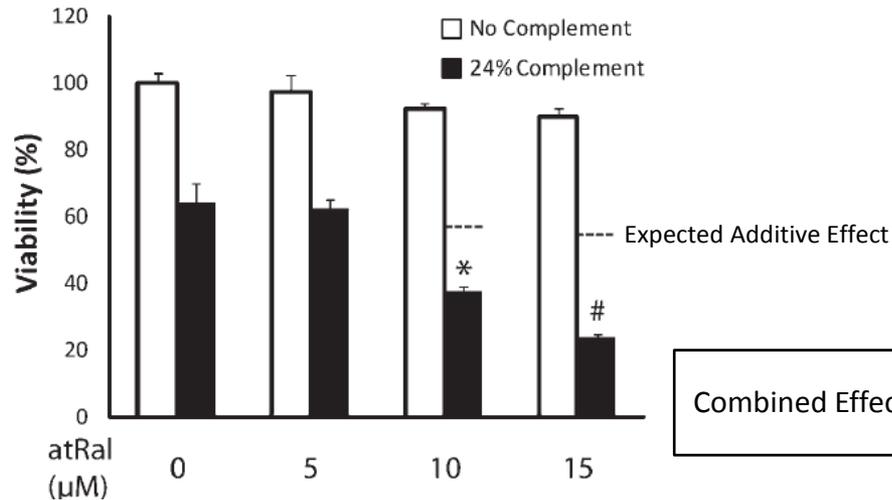
Waste: all-Trans-Retinal (atRal)



Complement Activation

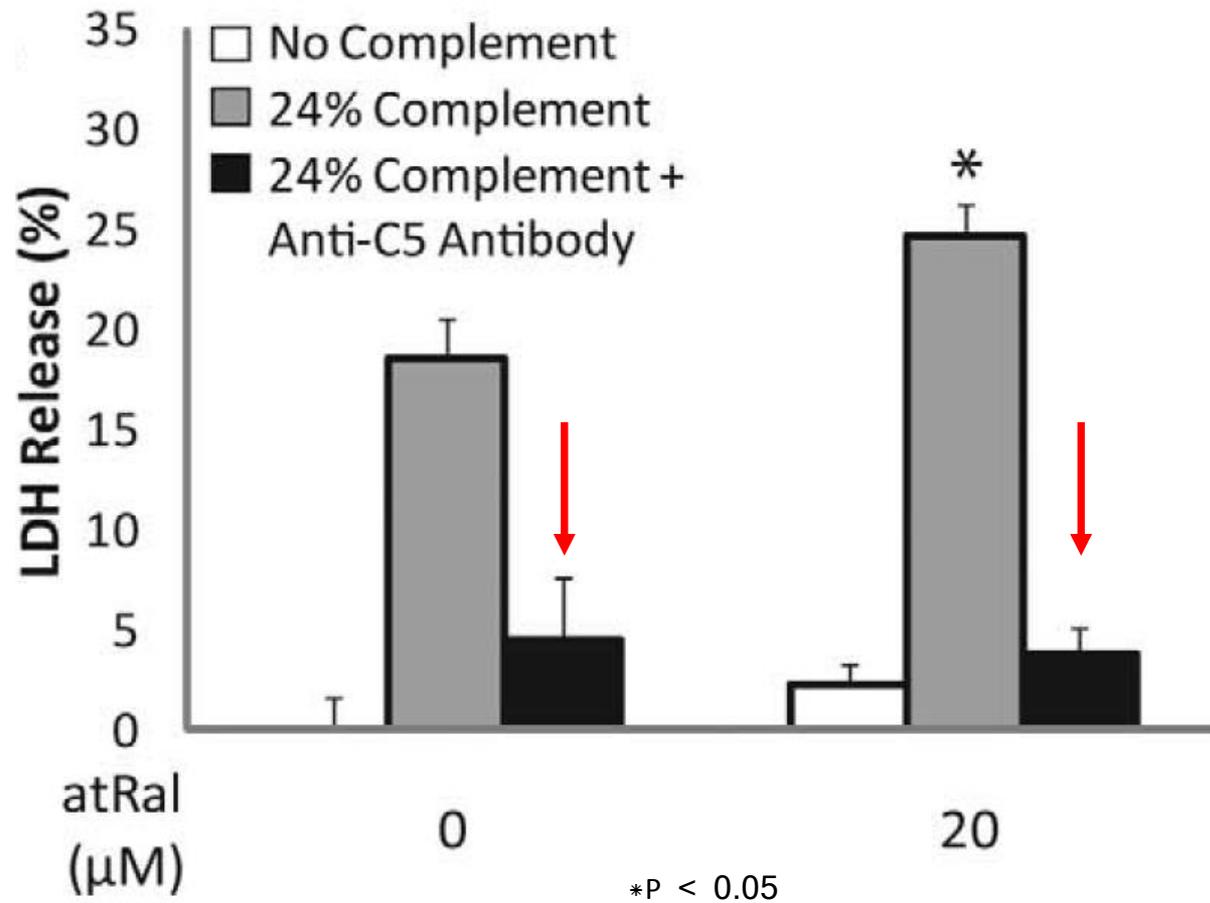


atRal + Complement



Source: Invest Ophthalmol Vis Sci. 2013;54:2669-2677

Anti-C5 Inhibits atRal/Complement Induced Cell Toxicity



Source: Invest Ophthalmol Vis Sci. 2013;54:2669-2677

Zimura, C5 Complement Inhibitor

Wet and Dry Age-Related Macular Degeneration

Rationale for Development of Zimura in Wet AMD

A disease characterized by abnormal neovascularization into the retina, which leads to central vision loss

- Unmet medical need – major market opportunity:
 - Anti-VEGF monotherapy
 - Shown to reach a ceiling effect
 - Majority of patients do not reach a visual acuity of > 20/40
 - In the real world most patients lose vision over time
- Patients receiving anti-VEGF monotherapy may develop geographic atrophy: 20% at two years and ~38% at 5 years have geographic atrophy (CATT study) ⁽¹⁾
- New developments in the role of complement in anti-VEGF therapy
 - VEGF upregulates complement factor H, which is a complement inhibitory factor (Research from Scripps Laboratories in San Diego) ⁽²⁾
- Completed Zimura Phase 1/2a
- Phase 2a trial to initiate by the end of this year

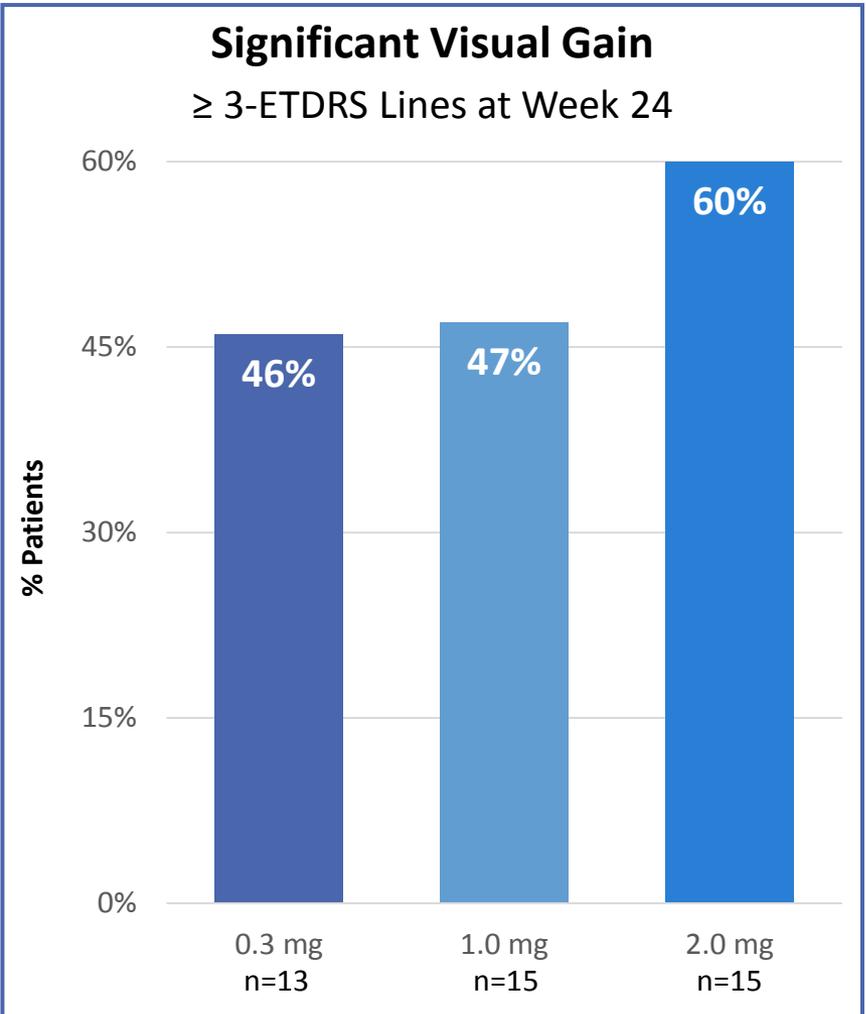
Sources:

1) Ophthalmology 2014;121:150-161.

2) J Clin Invest. 2017;127(1):199–214.

Zimura Phase 1/2a Wet AMD – Completed

- Inclusion:
 - Treatment Naïve subjects
 - All CNV subtypes
- Design:
 - Six monthly doses of Zimura in combination with 0.5mg Lucentis
- Safety:
 - All doses well tolerated; no safety concerns were identified



Rationale for Development of Zimura in Dry AMD

Geographic Atrophy, a disease characterized by atrophy of the retina, which leads to central vision loss

- An unmet medical need – major market opportunity
- Phase 2/3 clinical trial of monotherapy Zimura is ongoing
- Strategic decision based on the competitor's study outcome available in the second half of 2017

Conclusion: Large market with no available treatment options supports a second to market therapy

Zimura, C5 Complement Inhibitor
Idiopathic Polypoidal Choroidal Vasculopathy (IPCV)

Rationale for Development of Zimura in Idiopathic Polypoidal Choroidal Vasculopathy

A retinal disease involving the choroidal vasculature characterized by the presence of polypoidal lesions, which leads to vision loss

- Unmet medical need
 - Estimated prevalence (U.S.) ~80,000 – 160,000 ⁽¹⁾
- Scientific rationale ⁽²⁾
 - Response to anti-VEGF monotherapy may be limited
 - Anti-VEGF treatment may lead to complement activation
- Plan to initiate Phase 2a trial by the end of this year

Sources:

1) OPHT Estimate based on published data

2) J Clin Invest. 2017;127(1):199–214. Br J Ophthalmol, 2010; 94(3), 297-301. Br J Ophthalmol. 2008 Jan;92(1):70-3.

Zimura, C5 Complement Inhibitor

**Non-Infectious Intermediate/Posterior Uveitis
(Orphan Indication)**

Rationale for Development of Zimura in Uveitis

Non-infectious intermediate/posterior uveitis: A rare inflammatory disease of the back of the eye

- Unmet medical need
 - Need for effective intermediate/posterior uveitis treatments with minimal local and systemic adverse events
 - Estimated total Uveitis prevalence (U.S.)*: 38 in 100,000, or about ~120,000 ⁽¹⁾
- Scientific rationale ⁽²⁾
 - Anti-C5, sCRRY inhibits uveitis in Experimental Autoimmune Uveitis (EAU) model
 - C5 knock-out mice had decreased uveitis severity compared with wild-type mice
 - C3aR/C5aR deficient mice resistant to EAU
 - Complement Factor B inhibition decreases EAU in mouse model
- Planning to initiate Phase 2a trial in 2018

Conclusion: Reduction of complement activity may lead to a decrease in inflammation

Sources:

- 1) Orphanet J Dis. 2012; 7: 57. Published online 2012 Aug 29. doi:10.1186/1750-1172-57
- 2) Clin Exp Immunol. 2010 Mar;159(3):303-14. Exp Eye Res. 2006 Mar;82(3):389-94. ARVO2017; program 536, Board #: B0091. Eur J Immunol. 2010 Oct;40(10):2870-81.

* Intermediate/posterior uveitis are forms of uveitis found in the vitreous and retina; prevalence for these forms are less than the total uveitis prevalence

Fovista, Anti-PDGF

Von Hippel-Lindau Syndrome

(Orphan Indication)

and

Retinoblastoma

(Orphan Indication)

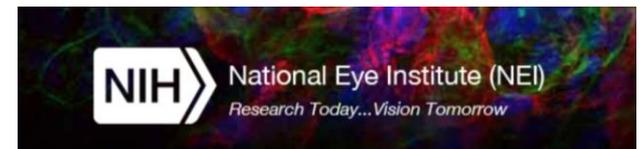
Rationale for Development of Fovista in Von Hippel-Lindau Syndrome

An orphan disease where the ocular manifestation presents as retinal capillary hemangiomas that may leak, induce traction and cause vision loss

- Unmet medical need
 - No optimal treatment option available
 - Estimated Prevalence (U.S.): ~7,000 ⁽¹⁾
- Scientific rationale
 - PDGF and VEGF are involved in the proliferation of the capillary hemangioma ⁽²⁾
 - Anti-VEGF + anti-PDGF combination therapy has the potential to slow down the progression of the disease
- Collaboration with National Eye Institute
 - Phase 1/2a trial ongoing

Sources:

- 1) Surv Ophthalmol. 2001 Sep-Oct;46(2):117-42.
- 2) Annu Rev Pathol. 2007;2:145-73.



Rationale for Development of Fovista in Retinoblastoma

An orphan cancer in children resulting from the growth of immature retinal cells leading to loss of vision, eye, and death

- Unmet medical need
 - No optimal treatment for metastatic tumor
 - Potential to be first to market to prevent or decrease the likelihood of metastasis
 - Estimated Prevalence (U.S.): 1 out of every 20,000 births per year /200 new cases a year ⁽¹⁾
- Scientific rationale
 - Retinoblastoma cell lines express PDGF receptor ⁽²⁾
 - Planning pre-clinical program

Sources:

1) Int J Ophthalmol.2011; 4(1): 103–109. Published online 2011 Feb 18. doi: 10.3980/j.issn.2222-3959.2011.01.24

2) Eye. 2013; 27: 92-99

Diversified Ophthalmic Company

- Positioned to identify value driven solutions for ophthalmic diseases with significant unmet need
- Orphan Ophthalmology (3 current or planned clinical programs, 1 planned pre-clinical) led by a program for Stargardt Disease
 - Significant need to treat underserved patients with rare ophthalmic diseases
 - Potential for faster, less costly clinical trials
 - Limited product competition
 - Regulatory exclusivity for 7 years in US/10 years in EU
- Age-related Ophthalmology for wet and dry AMD currently ongoing
 - Multi-billion dollar market opportunities
- Continue business development strategy
 - Focus on retina & orphan; opportunistic in other ocular diseases
- Significant cash position
 - \$196M in cash, cash equivalents and available for sales securities as of June 30, 2017
 - Expect 2017 year-end cash balance to range between \$145 million to \$160 million*
- Ophthalmic drug development expertise
 - Multiple retina specialists
 - Experienced clinical development team

* Excluding any potential business development activities or any other changes to the Company's current clinical development programs

Timeline/Planned Milestones on the Near Horizon

2017



Set Strategic Plan



Stargardt Disease – Zimura

Initiate program

By end of this year



Wet AMD – Zimura

Initiate Phase 2a trial

By end of this year



IPCV – Zimura

Initiate Phase 2a trial

By end of this year



Dry AMD – Zimura

Phase 2/3 trial ongoing

*Strategic decision
(by end of this year)*

2018



Posterior Uveitis – Zimura

Initiate Phase 2a program



Von Hippel Lindau – Fovista

Initial data



Retinoblastoma – Fovista

Planning pre-clinical