

A close-up photograph of a person's eye, showing the iris and eyelashes. The eye is looking slightly to the right. The background is a soft, out-of-focus grey.

# **Advances in Age-Related Macular Degeneration and Diabetic Macular Edema**

## **Pharmacist Focus on Emerging Therapies**

**These slides are meant to be used as an accompaniment to the presentation for note taking purposes, they are not intended as a standalone reference.**



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# Faculty

## **Sheldon J. Rich, RPh, PhD**

Adjunct Assistant Professor

University of Michigan College of Pharmacy

Ann Arbor, MI

President

SJR Associates, LLC

Sarasota, FL



Dr. Rich is President of SJR Associates, LLC, a health care consulting company located in Sarasota, FL. He has over 30 years' experience in the pharmacy field, having practiced in hospital, retail, and managed care pharmacy. He is a nationally recognized lecturer and moderator and provides consulting services to managed care organizations, physician practice groups, employers, and pharmaceutical manufacturers. Dr. Rich earned his pharmacy degree from the University of Michigan and holds a Doctorate in Theocentric Business Ethics. He has held the position of Adjunct Assistant Professor at the University of Michigan since 1982 and has had a dual appointment as an Adjunct Assistant Professor with the Eugene Applebaum College of Pharmacy and Health Sciences at Wayne State University since 1994.

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# Faculty

## **Nancy M. Holekamp, MD**

Director, Retina Services  
Center for Macular Degeneration  
Pepose Vision Institute  
Chesterfield, MO

Dr. Holekamp is Director of Retina Services at the Pepose Vision Institute in St. Louis, Missouri. Previously, she was Professor of Clinical Ophthalmology at the Washington University School of Medicine in St. Louis, Missouri. She has been a principal investigator in more than 38 national clinical trials dealing with age-related macular degeneration, retinal vascular occlusion, and diabetic retinopathy. Her efforts in research have resulted in 80 peer-reviewed publications, 22 book chapters, and more than 120 speaking invitations.







# Disclosures

**Dr. Rich** has no relevant affiliations or financial relationships with a commercial interest to disclose.

**Dr. Holekamp** has disclosed that she has received consulting fees from Apellis, Adverum, Allergan, Clearside Biomedical, Novartis, Regeneron, Genentech, Katalyst, Notal Vision, Annexon, and Spark Therapeutics; and has contracted to do research for Genentech, Gyroscope, Gemini, and Notal Vision.

The clinical reviewer, **Alisa Escano, PharmD, BCPS**, has no relevant affiliations or financial relationships with a commercial interest to disclose.

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**Type of Activity:** Application



# Learning Objectives

- **Describe** the epidemiology, pathogenesis, and burden of age-related macular degeneration (AMD) and diabetic macular edema (DME)
- **Identify** current and emerging treatment options for AMD and DME, including efficacy, safety, and relevant clinical trial data
- **Formulate** approaches for optimal patient counseling on current and emerging AMD and DME treatments to improve outcomes and quality of life



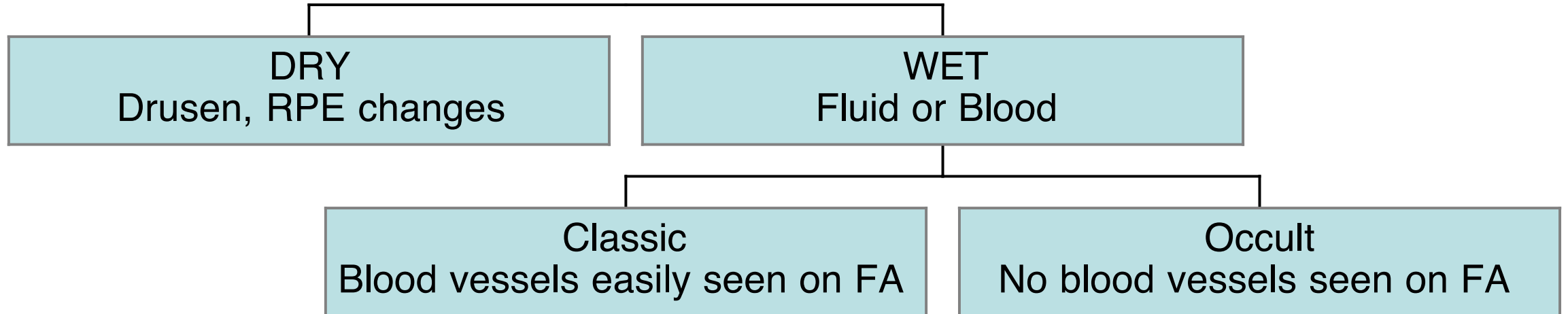
# **Background on AMD and DR/DME**

Nancy M. Holekamp, MD



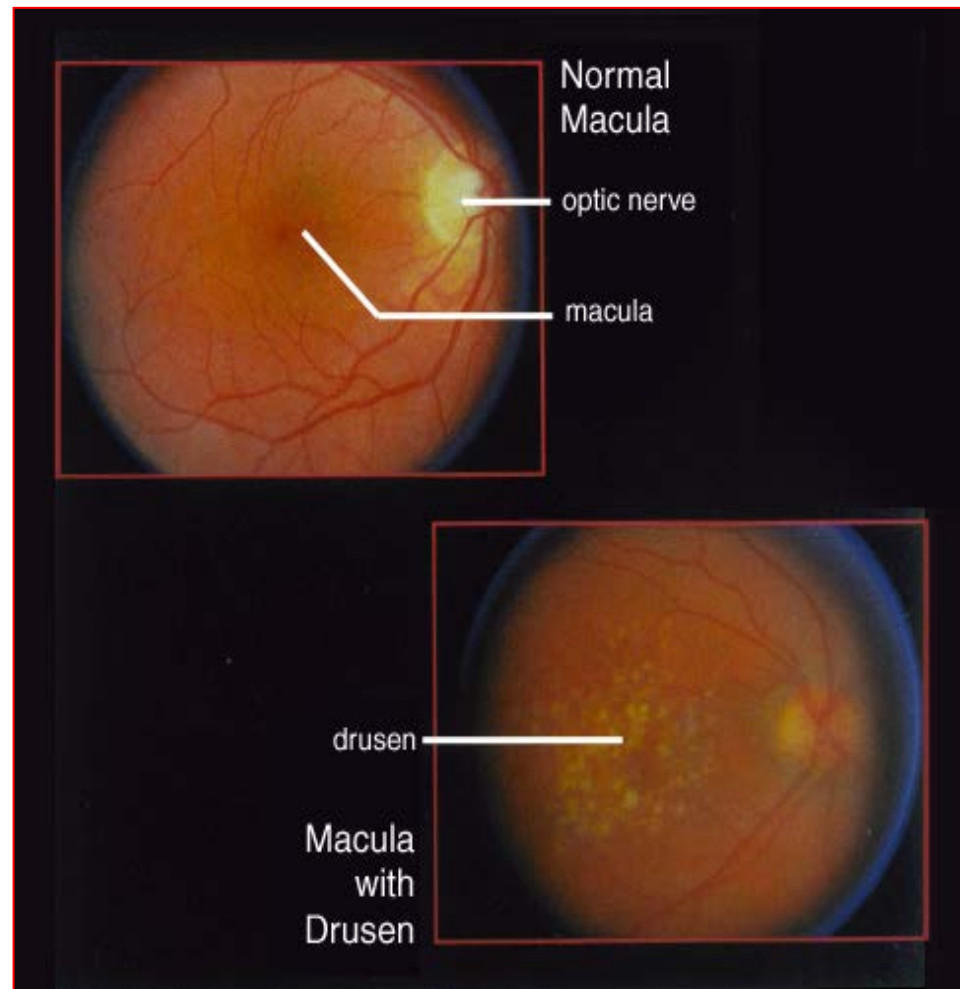
# Age-Related Macular Degeneration (AMD)

## Types of AMD



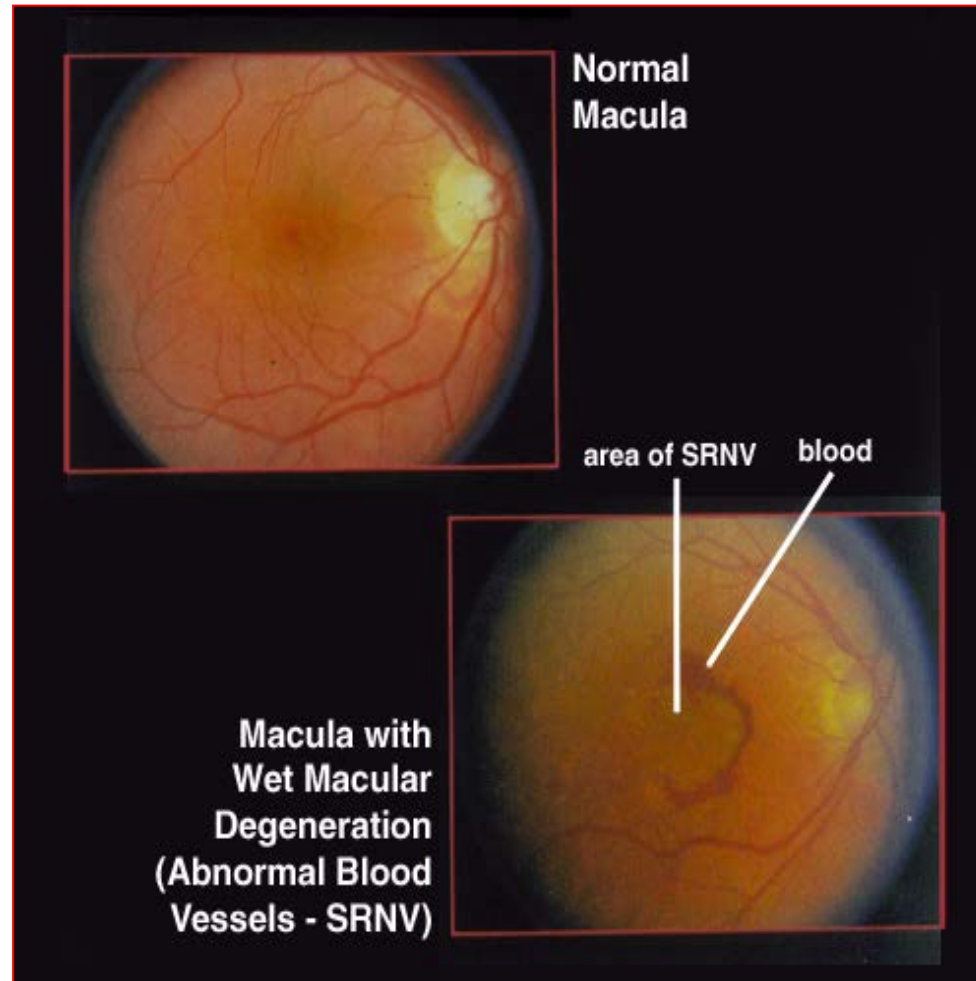
FA, fluorescein angiogram; RPE, retinal pigment epithelium.

# Age-Related Macular Degeneration



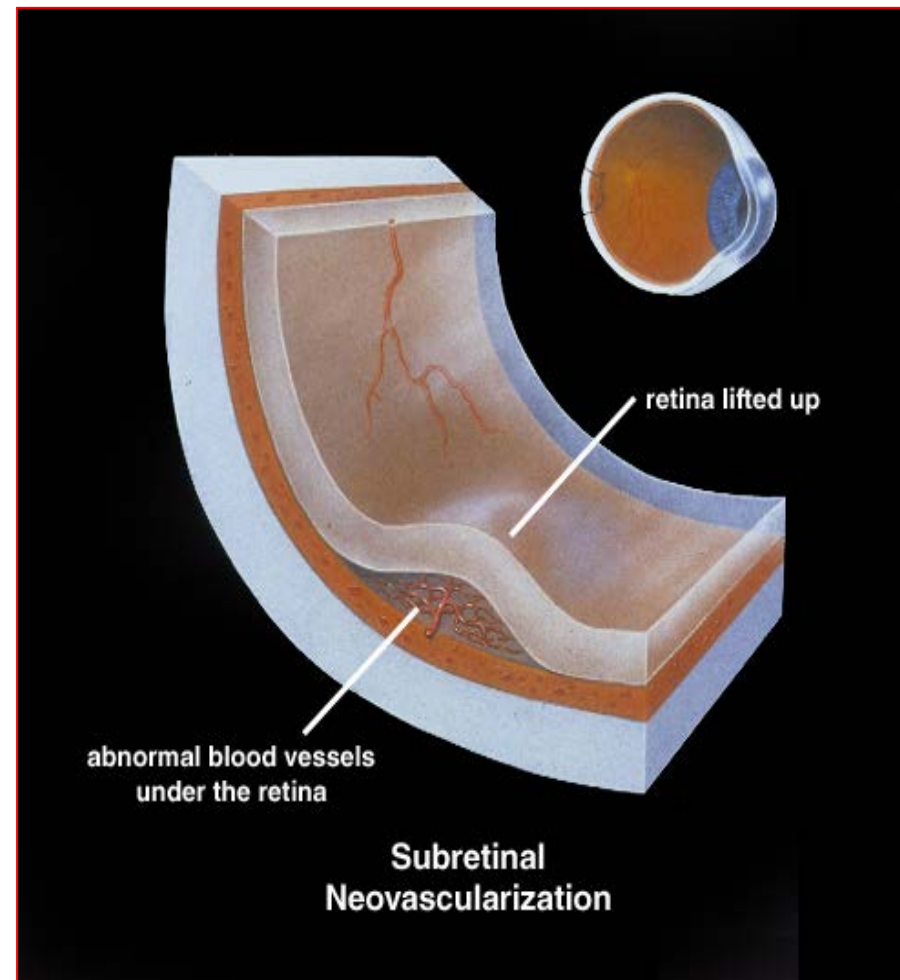
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# Age-Related Macular Degeneration



SRNV, subretinal neovascularization.

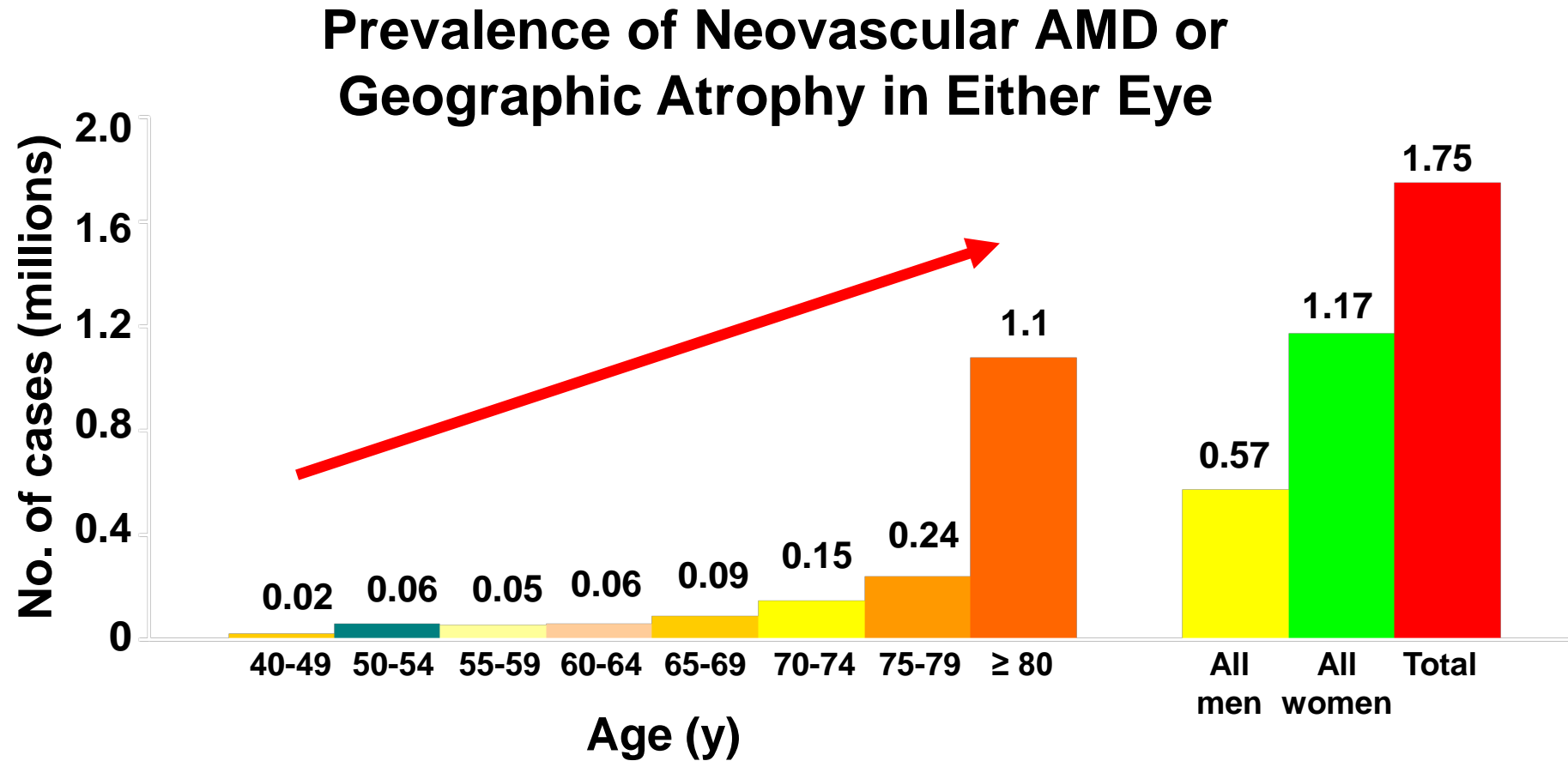
# Age-Related Macular Degeneration



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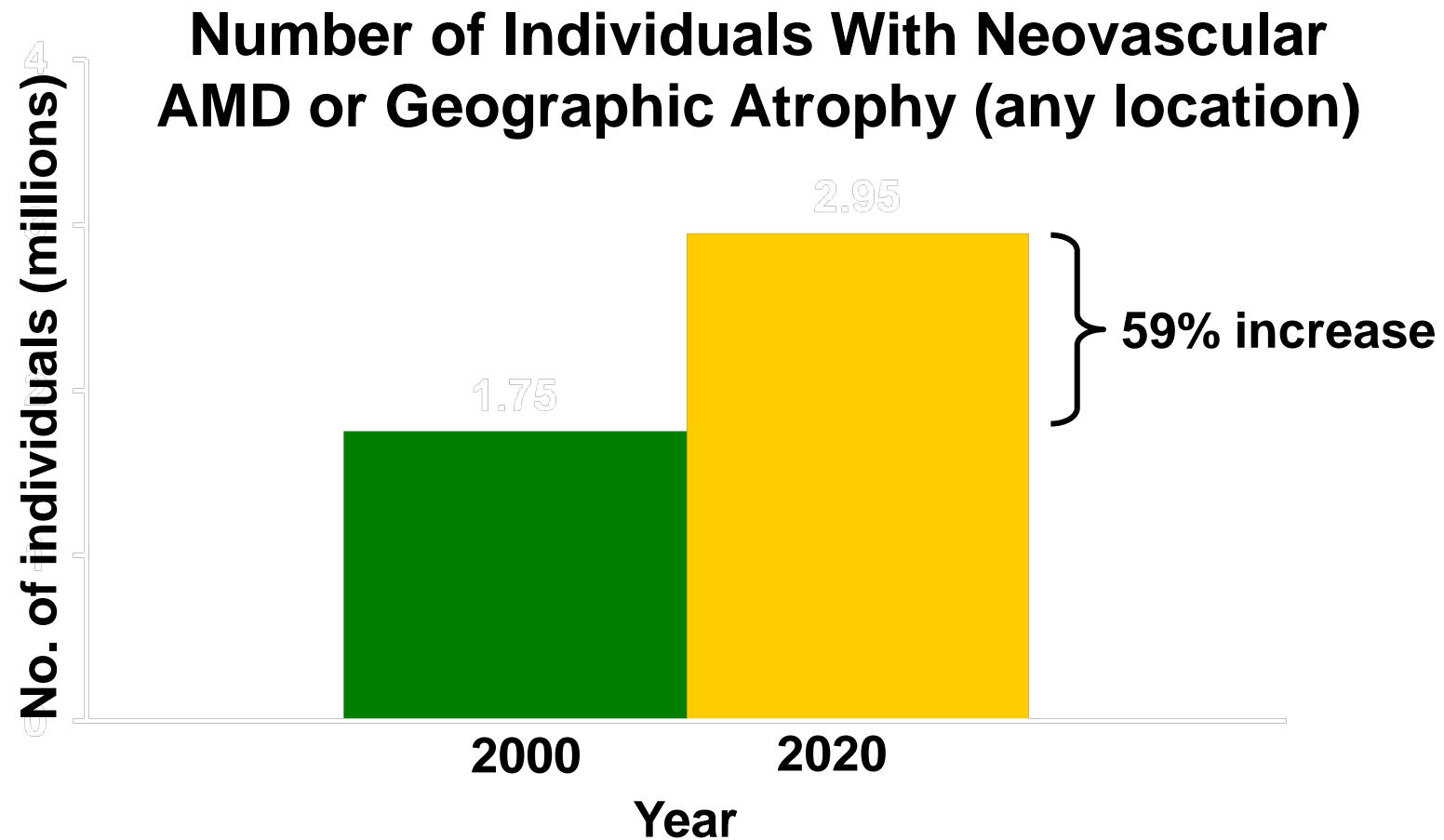
# Estimated Prevalence of US Adults With Advanced AMD by Age and Gender



Based on US Census 2000. Friedman et al. *Arch Ophthalmol.* 2004;122:564.

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# Increasing Prevalence of Advanced AMD



Friedman et al. *Arch Ophthalmol.* 2004;122:564.

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# AMD Decreases Quality of Life

- Increased incidence of depression in advanced AMD<sup>1</sup> (depression increases mortality risk)
- Increased mortality risk among individuals with advanced AMD
- Greater need for assistance with daily living activities versus older adults without AMD<sup>2</sup>

1. Brody et al. *Ophthalmology*. 2001;108:1893; 2. Williams et al. *Arch Ophthalmol*. 1998;116:514.



# AMD Decreases Quality of Life

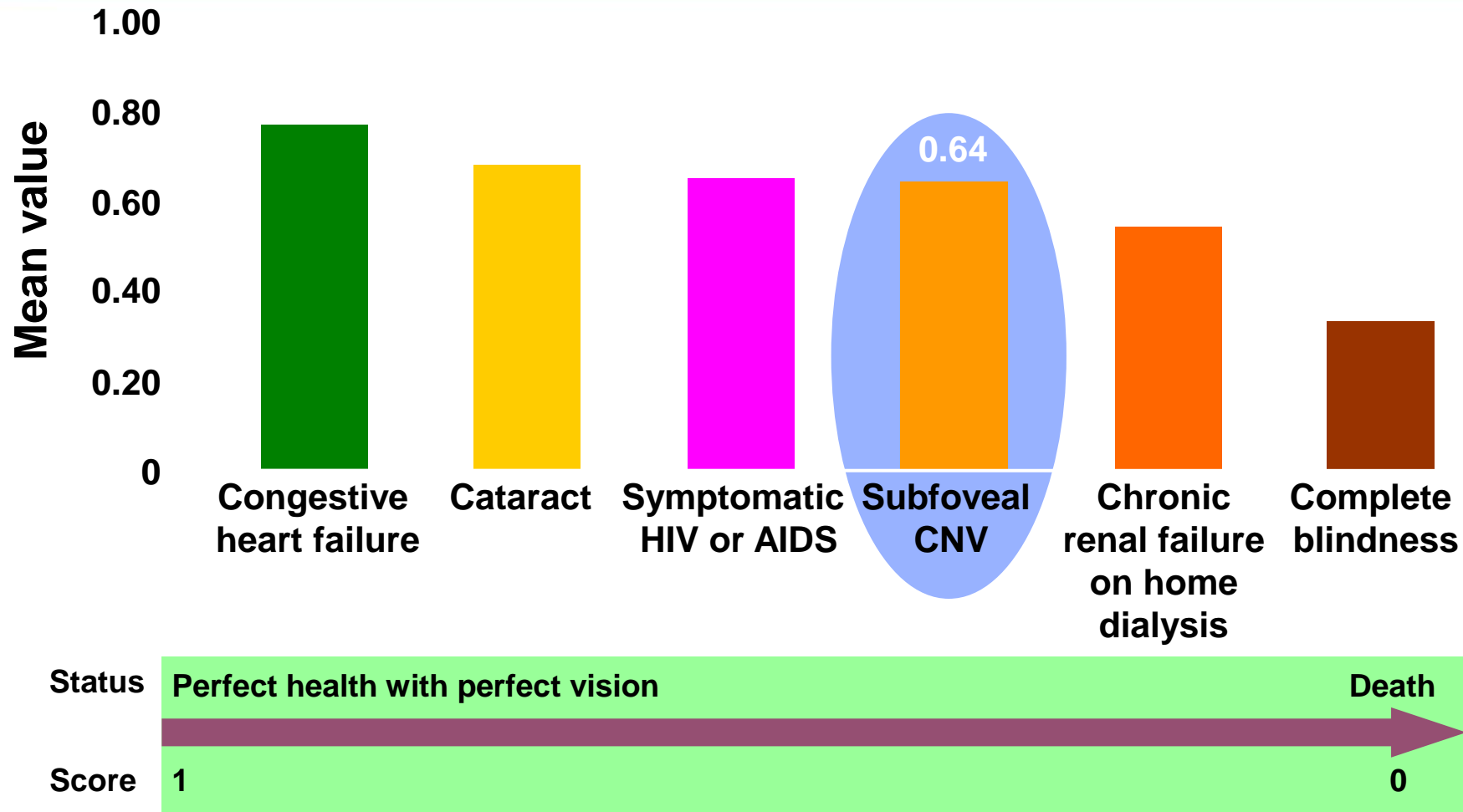
- Both intermediate and advanced AMD negatively impact quality of life<sup>1,2</sup>
  - General vision
  - Near activities
  - Distance vision
  - Driving
  - Mental health
  - Role difficulties
  - Dependency
  - Peripheral vision

1. Berdeaux et al. *Am J Ophthalmol.* 2005;139:271; 2. Clemons et al. *Arch Ophthalmol.* 2003;121:211.

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# QOL Ratings for Chronic Diseases



QOL, quality of life; CNV, choroidal neovascularization. Submacular Surgery Trials Research Group. *Arch Ophthalmol.* 2004;122:1856.

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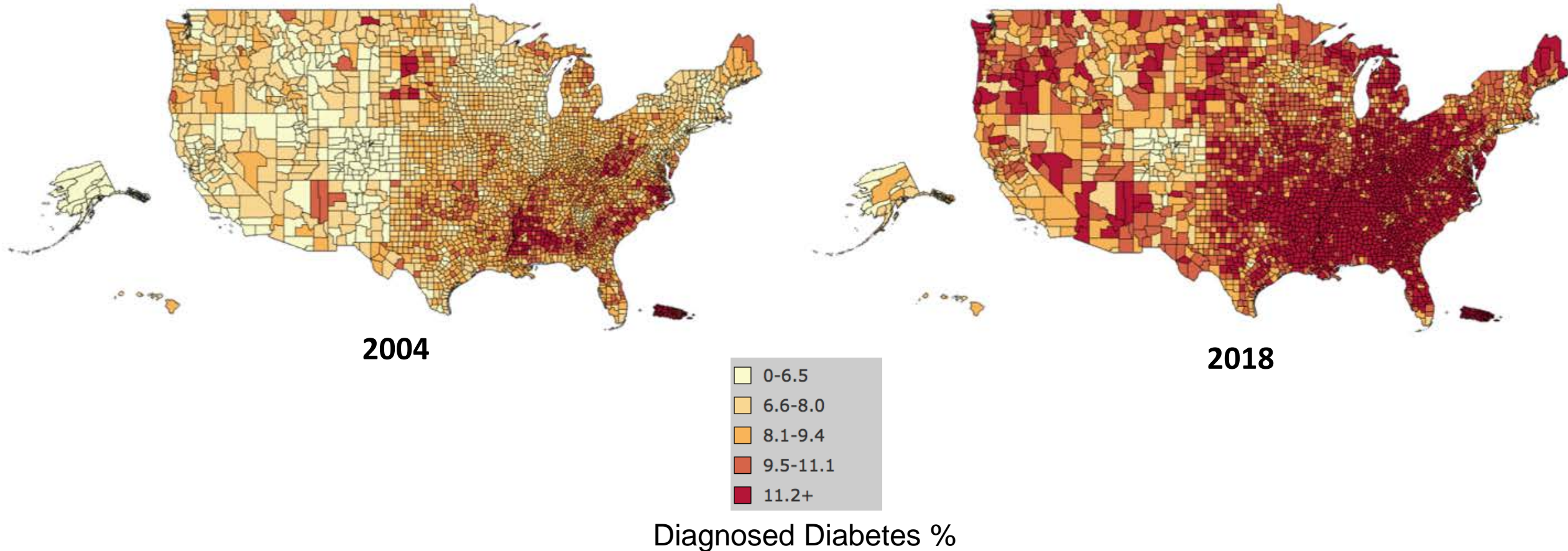


# Prevalence of Diabetes in the US

- Approximately 39 million people of all ages (11% of the US population) had diabetes in 2018
- 7.2 million people have undiagnosed diabetes
- In adults, there are race/ethnicity differences
  - American Indians/Alaska Natives have highest prevalence of diagnosed diabetes (~15%)
  - Non-Hispanic Blacks and Hispanics (12%) have higher prevalence than non-Hispanic Whites and Asians (8%)
- Varies based on socioeconomic status and education level
- **All** people with diabetes are at risk of developing eye complications
- About 1 in 3 people with diabetes have **diabetic retinopathy (DR)**

CDC. National Diabetes Statistics Report 2020. Atlanta, GA. CDC. US Dept. of Health and Human Services; 2020.

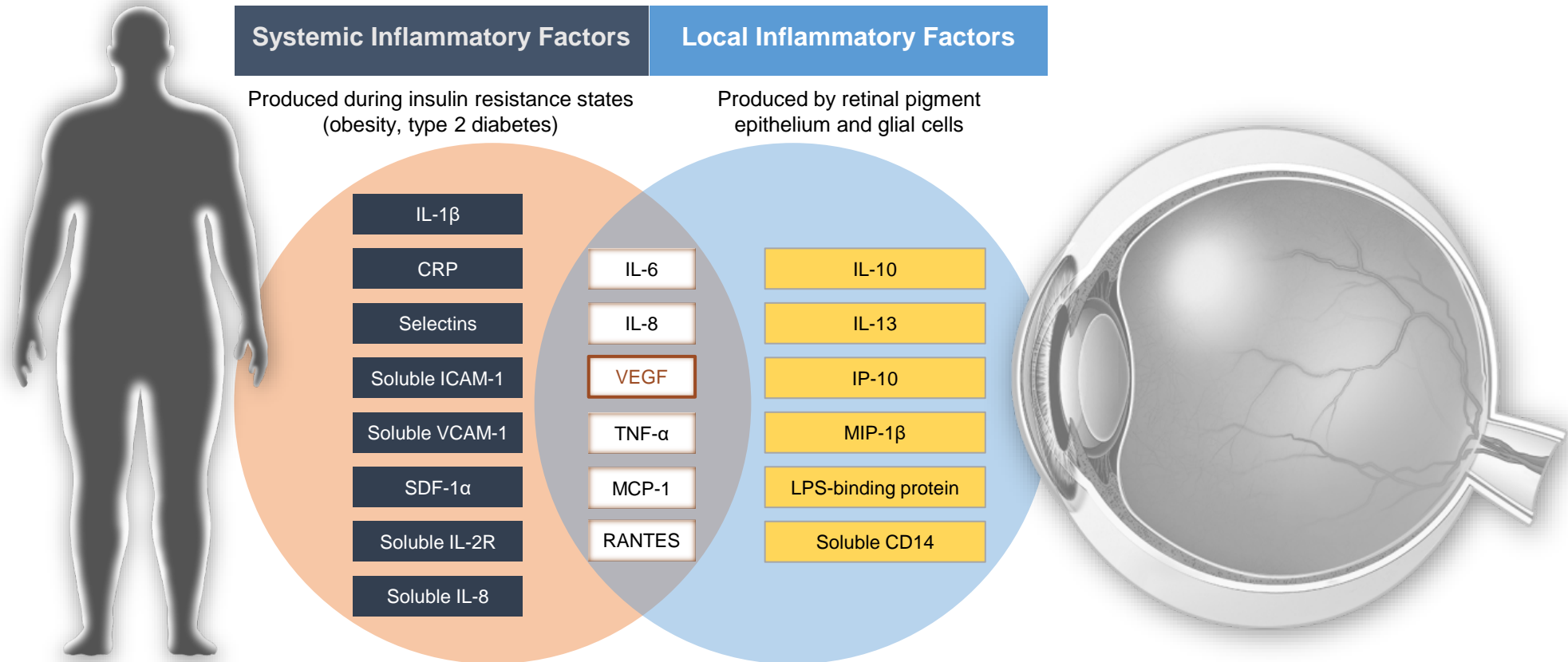
# Increasing Prevalence of Diagnosed Diabetes Among Adults 20 Years or Older



CDC. National Diabetes Statistics Report 2020. Atlanta, GA. CDC. US Dept. of Health and Human Services; 2020.

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# Many Systemic and Local Inflammatory Factors May Contribute to DR and DME



CD14, cluster of differentiation 14; CRP, c-reactive protein; ICAM-1, intercellular adhesion molecule 1; IL, interleukin; IP-10, interferon gamma-induced protein 10; LPS, lipopolysaccharide; MCP, monocyte chemotactic protein; MIP-1 $\beta$ , macrophage inflammatory protein 1 beta; SDF-1 $\alpha$ , stromal cell-derived factor 1 alpha; TNF, tumor necrosis factor; VCAM-1, vascular cell adhesion molecule 1; VEGF, vascular endothelial growth factor; RANTES, regulated on activation, normal T cell expressed and secreted. Rangasamy et al. *Middle East Afr J Ophthalmol.* 2012;19:52.

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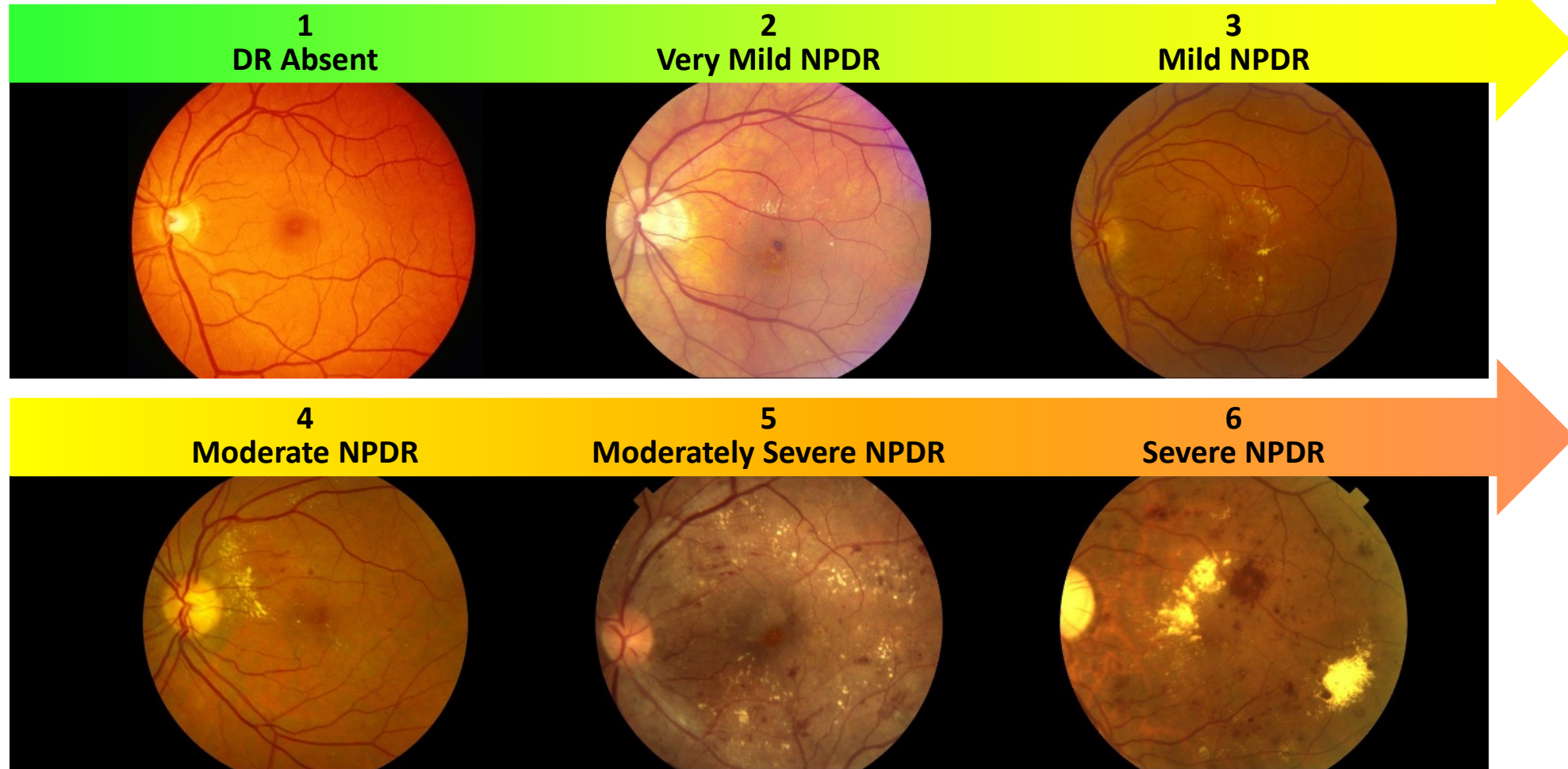




# Etiology and Pathogenesis

- Chronic exposure to hyperglycemia triggers biochemical and physiological changes, resulting in microvascular damage
- DR is a microvascular complication of diabetes that leads to the development of leaky blood vessels in the retina
- Chemical inflammatory cytokines **including VEGF** play a critical role in the onset of DR and DME
- As DR develops, there may be bleeding (DR) in the retina as well as increased fluid in the macula (DME)
- Patients may have DR and DME without experiencing deficiencies in visual acuity
  - More impairment in central vision with higher permeability in blood vessels
  - Thickening and swelling of macula distorts vision

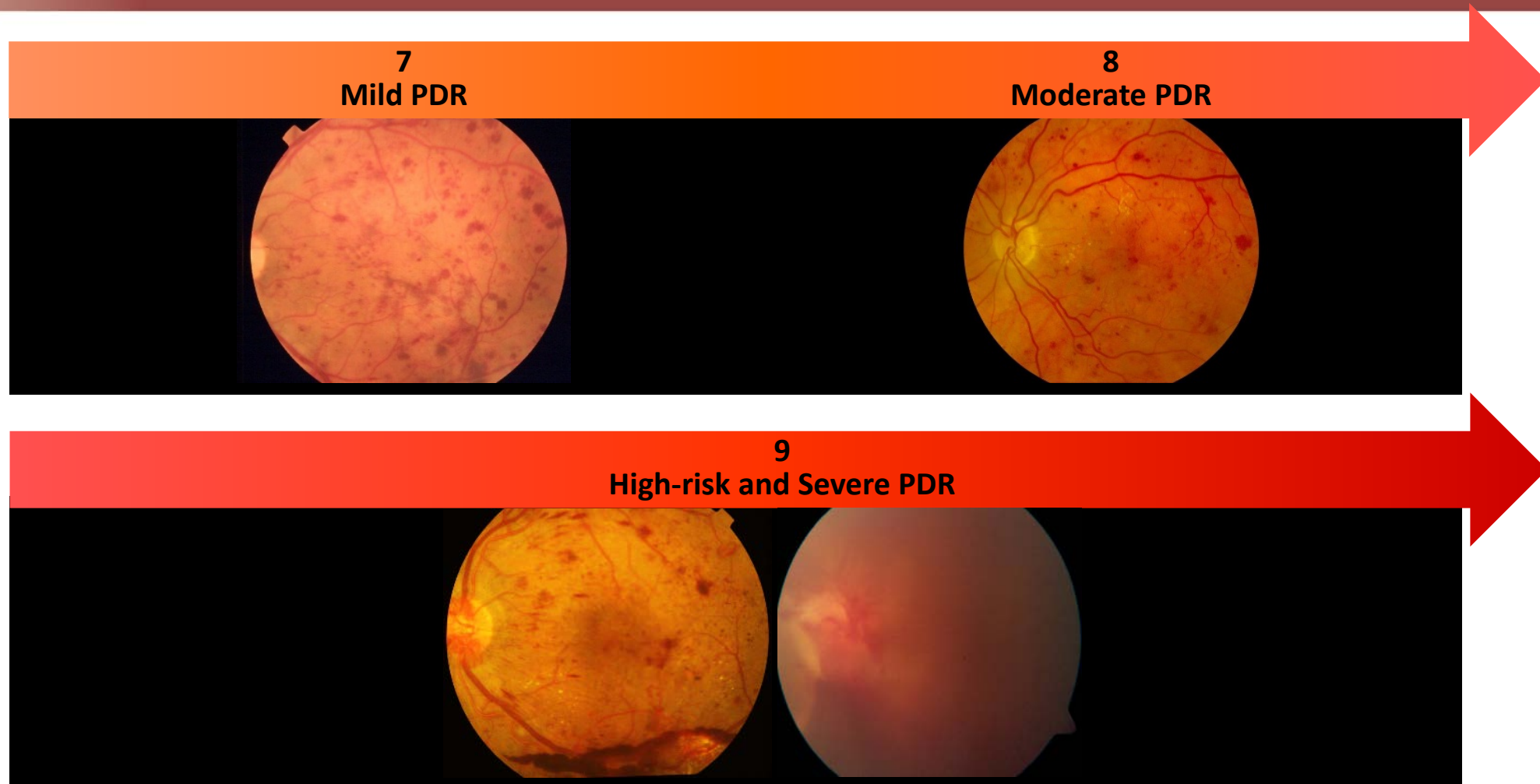
# Nonproliferative Diabetic Retinopathy (NPDR)



1. ETDRS. *Ophthalmology*. 1991;98:823; 2. Ip et al. *Arch Ophthalmol*. 2012;130:1145; 3. Scott et al. *Diabetes and Ocular Disease*. 2nd ed. Oxford University Press; 2010.

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# Proliferative Diabetic Retinopathy (PDR)



1. ETDRS. *Ophthalmology*. 1991;98:823. 2. Ip et al. *Arch Ophthalmol*. 2012;130:1145. 3. Scott et al. *Diabetes and Ocular Disease*. 2nd ed. Oxford University Press; 2010.

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# Disease Burden of DR and DME

- Often patients have other chronic diseases as well (eg, depression, cardiovascular disease)
- Vision-related functional burden is high in people with more severe eye disease
  - ~50% have difficulty with at least 1 visual function task (driving, reading, walking)
- Prevention is important to stop progression in this at-risk population
  - As many as 50% of patients are not getting their eyes examined or are diagnosed too late for treatment to be effective

National Diabetes Statistics Report, 2017. Atlanta, GA: National Center for Chronic Disease Prevention and Health Promotion. National Eye Institute. Accessed April 8, 2021. <https://nei.nih.gov/health/diabetic/retinopathy>

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# **The Journey of Anti-VEGF Inhibition**





# Anti-VEGF Therapies

- Anti-VEGF therapies have revolutionized the care of patients with retinal diseases—namely nAMD and DR/DME

*Adoption of intravitreal anti-VEGF therapy as the standard of care has resulted in a*

**~50% decrease**

*in the number of people becoming legally blind owing to nAMD*

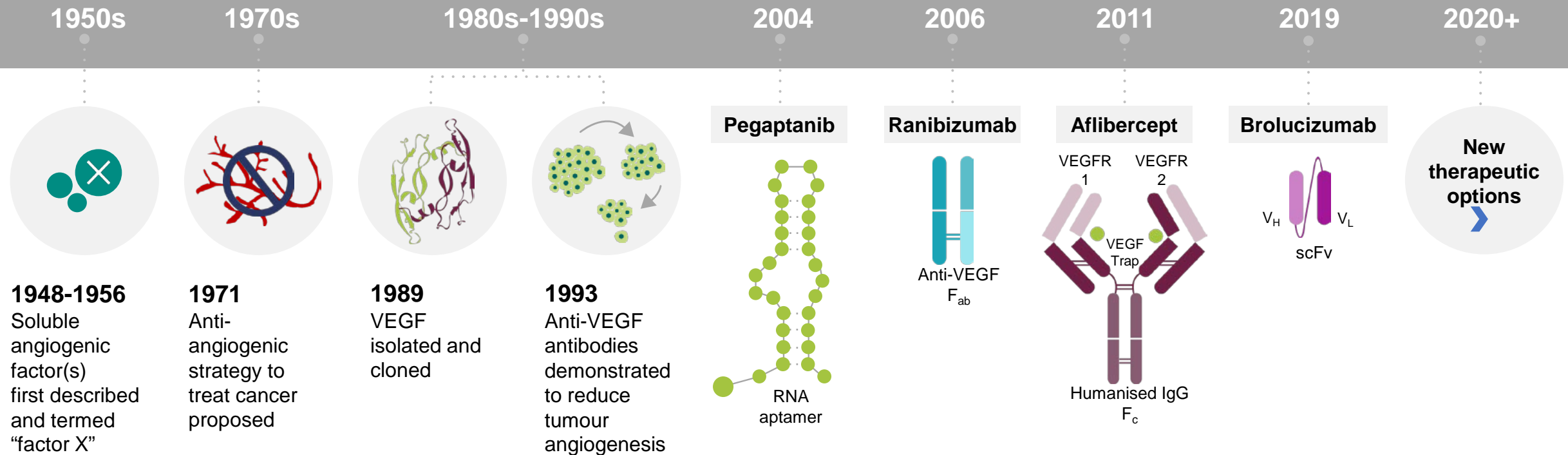
nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.  
Adamis et al. *Eye (Lond)*. 2020;34:1966.

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# Anti-VEGF Therapies: History

## Historical timeline of VEGF discovery<sup>1</sup>

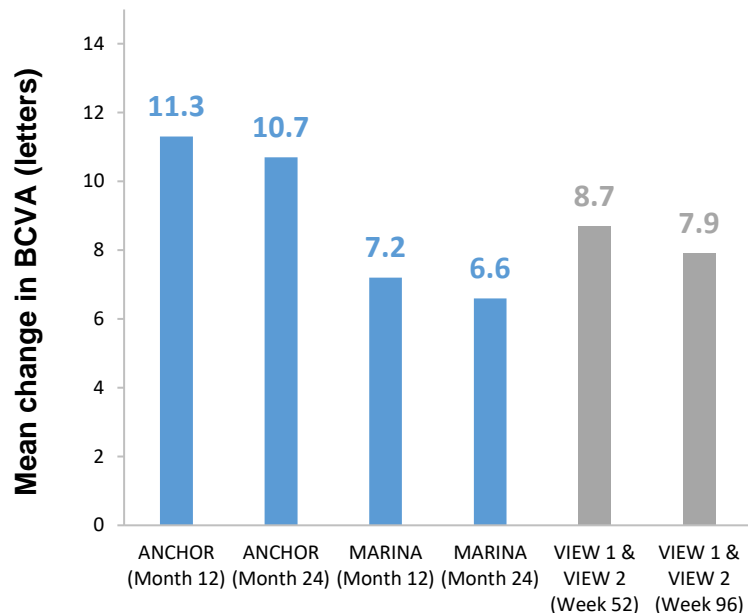
## The evolution of anti-VEGF therapies for retinal disease management<sup>2-6,\*</sup>



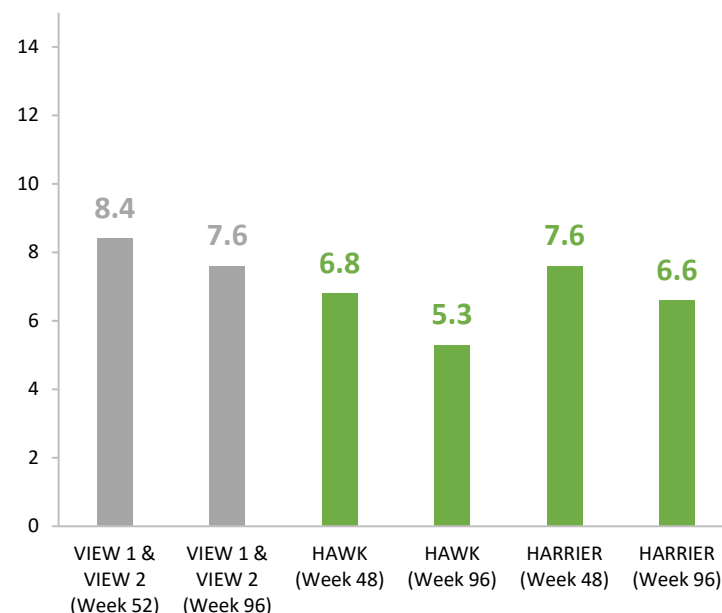
\*Images adapted with permission from Springer Nature. Sharma et al. *Eye (Lond)*. 2020;34:611. 1. Apte et al. *Cell*. 2019;176:1248; 2. Sharma et al. *Eye (Lond)*. 2020;34:611; 3. Adamis et al. *Eye (Lond)*. 2020;34:1966; 4. Lucentis (ranibizumab) PI; 2006. 5. Eylea (aflibercept) PI; 2011. 6. Beovu (brolucizumab) PI; 2019.

# Intravitreal anti-VEGF Therapies in nAMD Have Evolved to Increase Fixed-Dose Treatment Intervals Without Compromising Efficacy

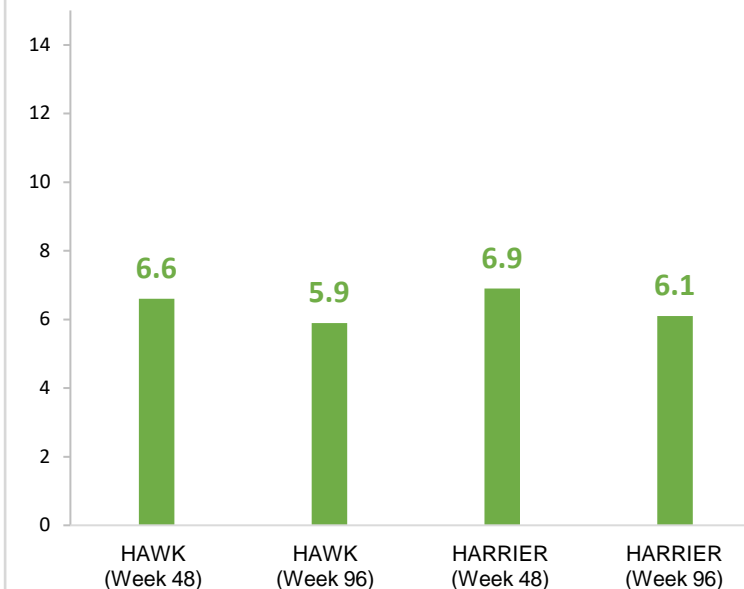
## Ranibizumab<sup>1,2</sup> Q4W (0.5 mg)



## Aflibercept<sup>2,3</sup> Q8W\* (2.0 mg)



## Brolucizumab<sup>3</sup> Q8W/Q12W<sup>†</sup> (6.0 mg)

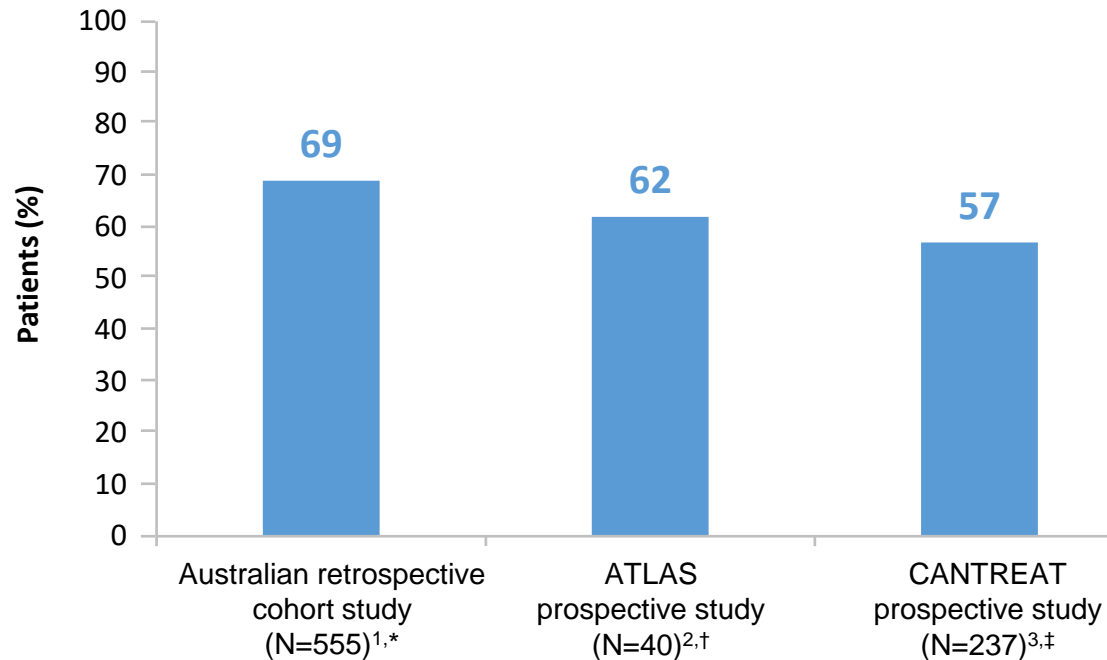


BCVA, best-corrected visual acuity; ; nAMD, neovascular age-related macular degeneration; QxW, every x weeks.

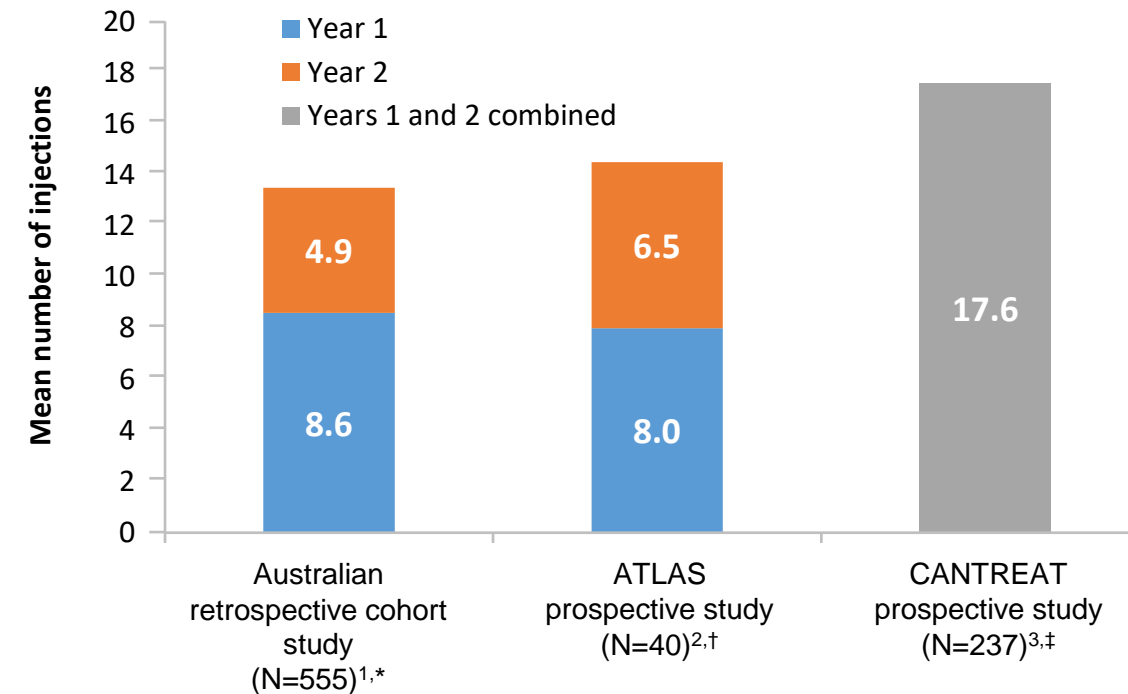
\*Following 3 monthly loading doses; <sup>†</sup>After 3 monthly doses, patients receiving brolucizumab were treated Q12W with the option of adjusting to a dosing interval Q8W based on disease activity. 1. Lucentis (ranibizumab) summary of product characteristics (SmPC), 2020; 2. Eylea (aflibercept) SmPC, 2020; 3. Beovu (brolucizumab) SmPC, 2020.

# While T&E Regimens May Increase Treatment Intervals, Most Pts With nAMD Still Require Injections More Than Every 12 Weeks

### Patients requiring a T&E treatment interval of <12 weeks



### Mean number of injections, regardless of T&E treatment interval



IVT, intravitreal; nAMD, neovascular age-related macular degeneration; Pts, patients; T&E, treat and extend.

\*Pts treated with IVT injections of ranibizumab, bevacizumab, or aflibercept (data based on 632 eyes from 555 pts); †Pts treated with IVT injections of aflibercept; ‡Pts treated with IVT injections of ranibizumab. 1. Skelly et al. *Vision (Basel)*. 2019;3:41; 2. DeCroos et al. *Am J Ophthalmol*. 2017;180:142; 3. Kertes et al. *JAMA Ophthalmol*. 2020;138:244.

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# Burden Associated With Frequent IVT Injections for nAMD and DR/DME May Result in Undertreatment

Over 4 to 5 years, patients with nAMD and DR/DME have a **high risk** of loss to follow-up or treatment discontinuation<sup>1-3</sup>



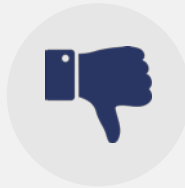
## Most common reasons for patients lost to follow-up\* (% of patients)



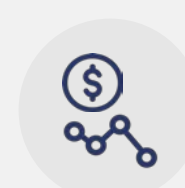
**Distance from home to hospital**  
(51.7%)



**Burden of follow-up visits**  
(24.1%)



**Dissatisfaction with IVT benefit**  
(34.5%)



**Financial burden**  
(8.6%)

**Patients' lives are filled with frequent clinic visits, which places a heavy burden on them and their caregivers<sup>1,4-6</sup>**

IVT, intravitreal. \*Retrospective chart review and follow-up telephone survey.

1. Boulanger-Scemama et al. *J Fr Ophthalmol*. 2015;38:620; 2. Obeid et al. *JAMA Ophthalmol*. 2018;136:1251; 3. Gillies et al. *Ophthalmology*. 2015;122:1837; 4. Gohil et al. *PLoS One*. 2019;10:e0129361; 5. Wolf et al. *Graefes Arch Clin Exp Ophthalmol*. 2014;252:647; 6. McCloud et al. *Eye (Lond)*. 2015;29:1561.





# Anti-VEGF 2.0

# New Strategies to Relieve the Burden of Frequent Monitoring and Treatment in nAMD and DR/DME

The goal: Increase treatment durability and thereby reduce treatment burden and improve real-world outcomes<sup>1</sup>



**Gene therapy**<sup>1-3</sup>

**ADVM-022**  
(Phase 1)

**RGX-314**  
(Phase 1/2/3)



**Slow-release formulation**<sup>1,4</sup>

**GB-102**  
(Phase 2)



**Slow-clearing large molecule**<sup>1,5</sup>

**KSI-301**  
(Phase 2/3)



**New molecular target**<sup>1,6</sup>

**Faricimab**  
(Phase 3)



**Continuous delivery drug-device combination technology**<sup>1,6</sup>

**PDS**  
(Phase 3)

PDS, Port Delivery System with ranibizumab.

1. Adams et al. *Eye (Lond)*. 2020;34:1966; 2. Adverum Biotechnologies. <https://adverum.com/pipeline/#wet-AMD>; 3. RegenXBio. <https://regenxbio.gcs-web.com/news-releases/news-release-details/regenxbio-announces-additional-positive-interim-phase-iii-a-0>; 4. Graybug Vision. <https://www.graybug.vision/our-technologies-and-pipeline/#gb102>; 5. Kodiak. <https://kodiak.com/our-pipeline/>; 6. Roche. [https://www.roche.com/research\\_and\\_development/who\\_we\\_are/how\\_we\\_work/pipeline.htm](https://www.roche.com/research_and_development/who_we_are/how_we_work/pipeline.htm).

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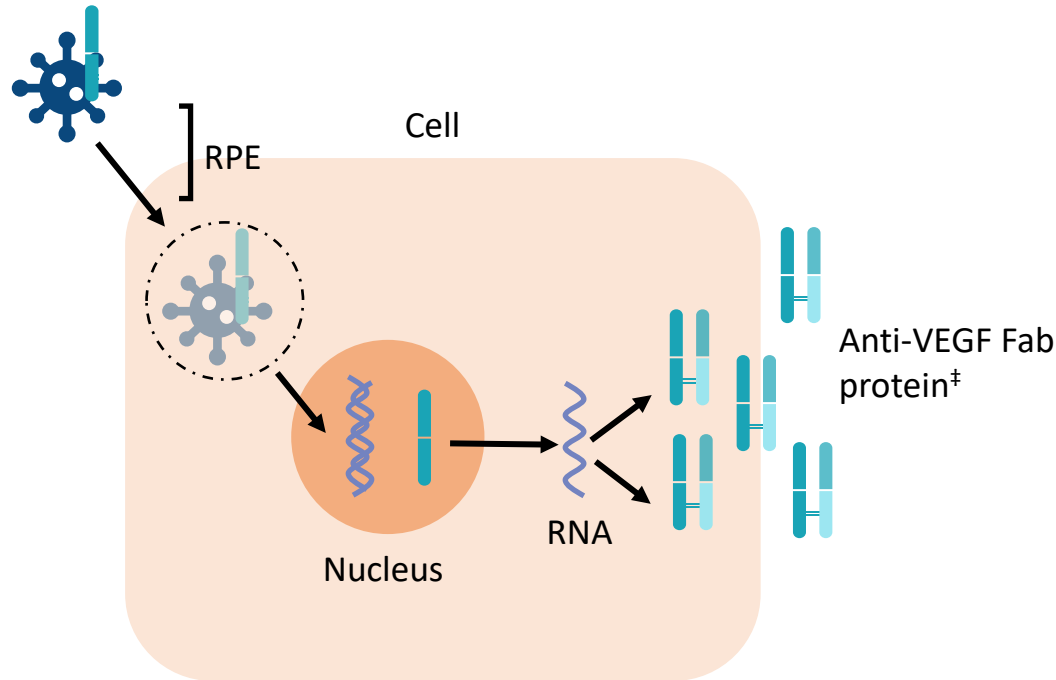
# RGX-314: An Investigational Gene Therapy in Phase 1/2/3



**Vector:** AAV8



**Gene:** anti-VEGF Fab



## Indications Investigated<sup>1-4</sup>

nAMD and DME/DR

## Class

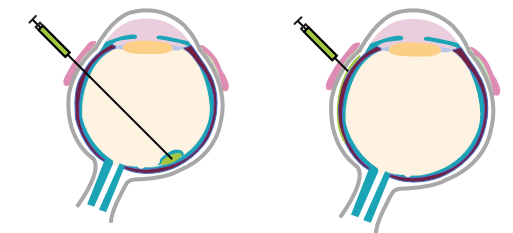
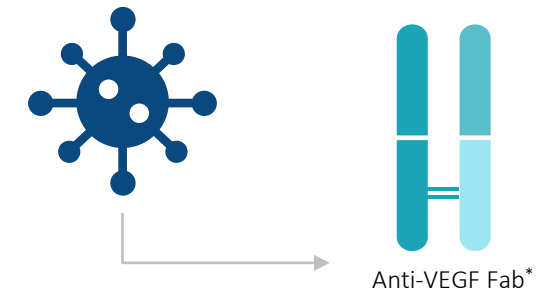
Gene therapy

## MOA<sup>4</sup>

Reducing leakage and edema by giving ocular cells the ability to produce an anti-VEGF Fab

## Route of Administration<sup>1,3,5</sup>

Subretinal or suprachoroidal<sup>‡</sup>



AAV, adeno-associated virus; Fab, fragment antigen binding; MOA, mechanism of action; RNA, ribonucleic acid; RPE, retinal pigment epithelium.

\*Image adapted with permission from Springer Nature: Sharma et al. *Eye (Lond)*. 2020;34:611; †Image adapted from de Guimaraes et al. *Br J Ophthalmol*. 2021;105:151; ‡Image redrawn based on data from *Retinal Physician*. <https://www.retinalphysician.com/issues/2020/special-edition-2020/gene-therapy-for-neovascular-amd>.

1. Regenxbio. <https://regenxbio.gcs-web.com/news-releases/news-release-details/regenxbio-announces-additional-positive-interim-phase-iii-a-0>; 2. AAVIATE clinical trial (NCT04514653); 3. ALTITUDE clinical trial (NCT04567550); 4. Heier et al. Presented at AAO Retina Subspecialty Day 2019; 5. de Guimaraes et al. *Br J Ophthalmol*. 2021;105:151.

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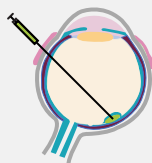
# RGX-314 Phase 1/2a Informs the Design of New Studies in nAMD and DME/DR<sup>1-7</sup>

## Clinical Trials Ongoing

### Phase 1/2a

#### 5-year LTFU<sup>1,\*</sup>

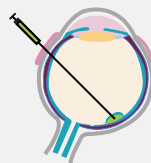
- ➔ **RGX-314**  
(single **subretinal** delivery)
- ➔ In patients with **nAMD**



### Phase 2/3

#### ATMOSPHERE<sup>2,3</sup>

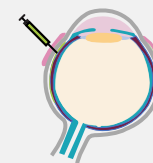
- 6.4×10<sup>10</sup> gc/eye  
1.3×10<sup>11</sup> gc/eye
- ➔ **RGX-314**  
(single **subretinal** delivery)  
vs **ranibizumab** (Q4W)
  - ➔ In patients with **nAMD**



### Phase 2b

#### AAVIATE<sup>4,5</sup>

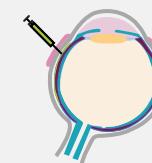
- 2.5×10<sup>11</sup> gc/eye  
5.0×10<sup>11</sup> gc/eye
- ➔ **RGX-314**  
(1 or 2 **suprachoroidal** injections)  
vs **ranibizumab** (Q4W)
  - ➔ In patients with **nAMD**



### Phase 2

#### ALTITUDE<sup>6,7</sup>

- 2.5×10<sup>11</sup> gc/eye  
5.0×10<sup>11</sup> gc/eye
- ➔ **RGX-314**  
(1 or 2 **suprachoroidal** injections)
  - ➔ In patients with **DR**  
**without CI-DME**



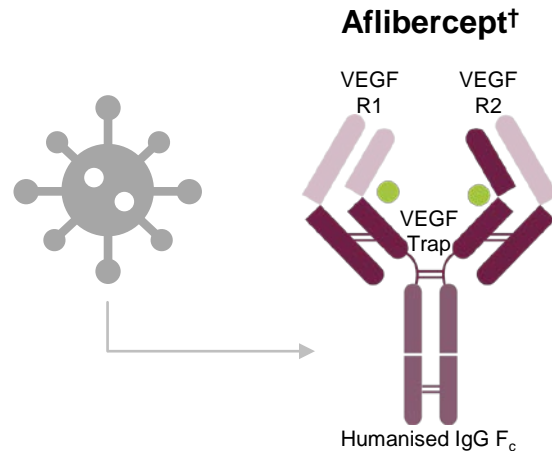
CI-DME, centre-involved diabetic macular edema; gc, gene copy; LTFU, long-term follow-up; QxW, every x weeks. \*3-year data of cohort 3 recently announced; †Image adapted from de Guimaraes et al. *Br J Ophthalmol.* 2021;105:151. 1. RGX314-LTFU clinical trial (NCT03999801); 2. ATMOSPHERE clinical trial (NCT04704921); 3. Regenxbio. <http://ir.regenxbio.com/news-releases/news-release-details/regenxbio-announces-update-rgx-314-and-pivotal-program-treatment>; 4. AAVIATE clinical trial (NCT04514653); 5. Regenxbio. <http://ir.regenxbio.com/news-releases/news-release-details/regenxbio-announces-dosing-first-patient-phase-ii-aaviatetm/>; 6. ALTITUDE clinical trial (NCT04567550); 7. Regenxbio. <http://ir.regenxbio.com/news-releases/news-release-details/regenxbio-announces-dosing-first-patient-phase-ii-altitudetm>.

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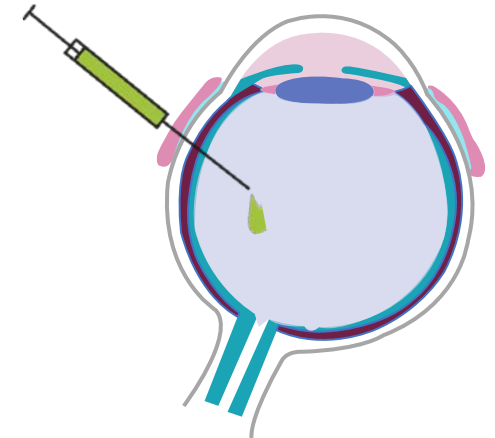
# ADVM-022: An Investigational Gene Therapy in Early-Stage Development\*

Gene therapies for nAMD aim to provide continuous expression of anti-VEGF in the retina with a single treatment<sup>1,2</sup>

ADVM-022 utilizes an AAV gene therapy vector (AAV.7m8) carrying an **aflibercept** coding sequence<sup>1</sup>



ADVM-022 is delivered by **intravitreal injection**<sup>‡,1,3</sup>



## Ongoing Phase 1 Trial: OPTIC<sup>1</sup>

- Assessing **single intravitreal administration** of ADVM-022
- In patients responsive to anti-VEGF treatment who **require frequent anti-VEGF injections**

AAV, adeno-associated virus; IgG, immunoglobulin G. \*Not currently licensed; †Image adapted with permission from Springer Nature: Sharma et al. *Eye (Lond)*, 2020;34:611; ‡image adapted from de Guimaraes et al. *Br J Ophthalmol*. 2021;105:151. 1. Adverum Biotechnologies. <https://www.globenewswire.com/en/news-release/2020/05/04/2027131/32452/en/Adverum-Biotechnologies-Reports-Positive-Interim-Data-from-Cohorts-1-3-of-OPTIC-Phase-1-Trial-of-ADVM-022-Intravitreal-Gene-Therapy-for-Wet-AMD.html>. 2. Kiss et al. *Mol Ther Methods Clin Dev*. 2020;18:345. 3. de Guimaraes et al. *Br J Ophthalmol*. 2021;105:151.

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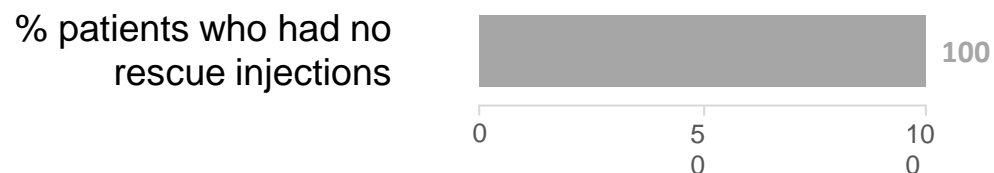
# Initial Data From Gene Therapy Trials in nAMD Patients Show Potential for Long-Term Durability

## ADVM-022<sup>1,\*</sup>

### Ongoing Phase 1 Trial: OPTIC

- ➡ A multicenter, open-label, dose-ranging trial in patients responsive to anti-VEGF treatment who **require frequent anti-VEGF injections**
- ➡ Assessing the safety and efficacy of a **single intravitreal administration**

### Phase 1 interim efficacy results for patients in the highest dose cohort after 1 year (n=6)



## RGX-314<sup>2,\*</sup>

### Ongoing Phase 1/2a Trial<sup>2,3</sup>

- ➡ A multicenter, open-label, multiple-cohort, dose-escalation study in patients responsive to anti-VEGF therapy and who **require frequent anti-VEGF injections**
- ➡ Assessing the safety and efficacy of a **single treatment**

### Phase 1/2 interim efficacy results for patients in the highest dose cohort after 1 year (n=11)<sup>2</sup>



\*Not currently licensed. 1. Adverum Biotechnologies. <https://www.globenewswire.com/en/news-release/2020/05/04/2027131/32452/en/Adverum-Biotechnologies-Reports-Positive-Interim-Data-from-Cohorts-1-3-of-OPTIC-Phase-1-Trial-of-ADVM-022-Intravitreal-Gene-Therapy-for-Wet-AMD.html>. 2. RegenXBio. <https://regenxbio.gcs-web.com/news-releases/news-release-details/regenxbio-announces-additional-positive-interim-phase-iiia-0>; 3. Heier et al. Presented at AAO Retina Subspecialty Day 2019.

# GB-102: A Slow-Release Formulation of Encapsulated Sunitinib Malate in Early-Stage Development\*

GB-102 is designed to sustain therapeutic levels of sunitinib in the ocular tissues for up to 6 months<sup>1</sup>



- GB-102 is a **microparticle depot formulation of encapsulated sunitinib malate**
- Sunitinib malate **blocks tyrosine kinase activities** of VEGF receptors
- GB-102 is delivered by **intravitreal injection**

## Completed Phase 1/2a trial: ADAGIO<sup>1,2</sup>

Dose-finding study in patients responsive to **anti-VEGF therapy**

Patients received a **single intravitreal dose** of GB-102

## Ongoing Phase 2b trial: ALTISSIMO<sup>1</sup>

A 12-month, multicenter, prospective, masked, randomized study in patients **responsive to anti-VEGF**

Comparing treatment with **GB-102 every 6 months vs aflibercept every 2 months**

\*Not currently licensed. 1. Graybug Vision. <https://www.globenewswire.com/news-release/2020/03/18/2002492/0/en/Graybug-Vision-Concludes-Patient-Enrollment-in-its-Phase-2b-Clinical-Trial-of-GB-102-in-Wet-Age-Related-Macular-Degeneration-and-Accelerates-Trial-Read-out-by-Approximately-Six-Mon.html>; 2. Graybug Vision. <https://www.graybug.vision/graybug-vision-presents-top-line-results-of-phase-1-2a-adagio-study-at-hawaiian-eye-retina-2019/>.

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# Preliminary Data for GB-102\* Suggest 6-Month Durability in Many Patients With nAMD

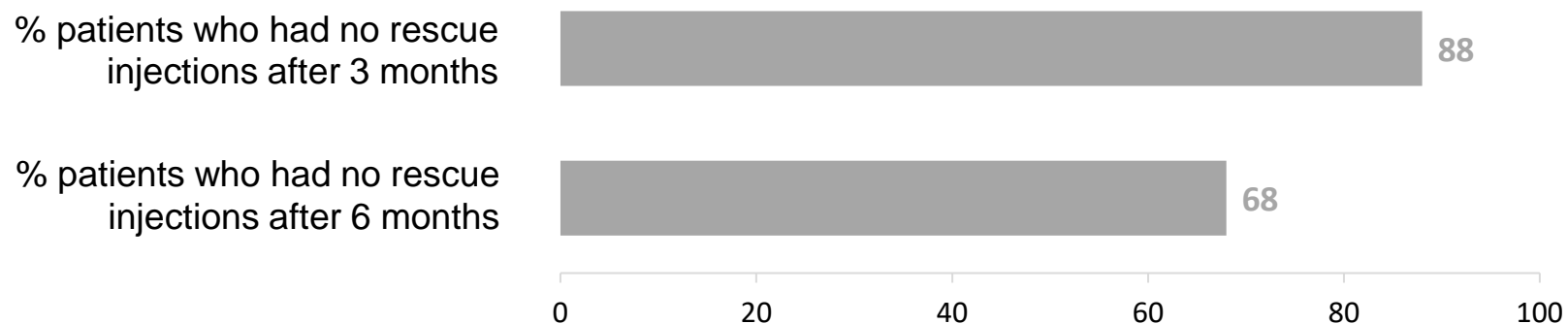
## Completed Phase 1/2a Trial: ADAGIO<sup>1,2</sup>



A multicenter, open-label, multiple-cohort study in patients **responsive to anti-VEGF therapy**



Patients (n=32) received a **single intravitreal dose** of GB-102 (0.25, 0.5, 1 or 2 mg) and were followed monthly for 8 consecutive months



The percentage of patients who had no rescue injections ranged from 50% to 88%, depending on dose

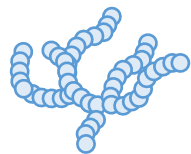
\*Not currently licensed. 1. Graybug Vision. <https://www.globenewswire.com/news-release/2020/03/18/2002492/0/en/Graybug-Vision-Concludes-Patient-Enrollment-in-its-Phase-2b-Clinical-Trial-of-GB-102-in-Wet-Age-Related-Macular-Degeneration-and-Accelerates-Trial-Read-out-by-Approximately-Six-Mon.html> ; 2. Graybug Vision. <https://graybug.com/graybug-vision-presents-top-line-results-of-phase-1-2a-adagio-study-at-hawaiian-eye-retina-2019/>.

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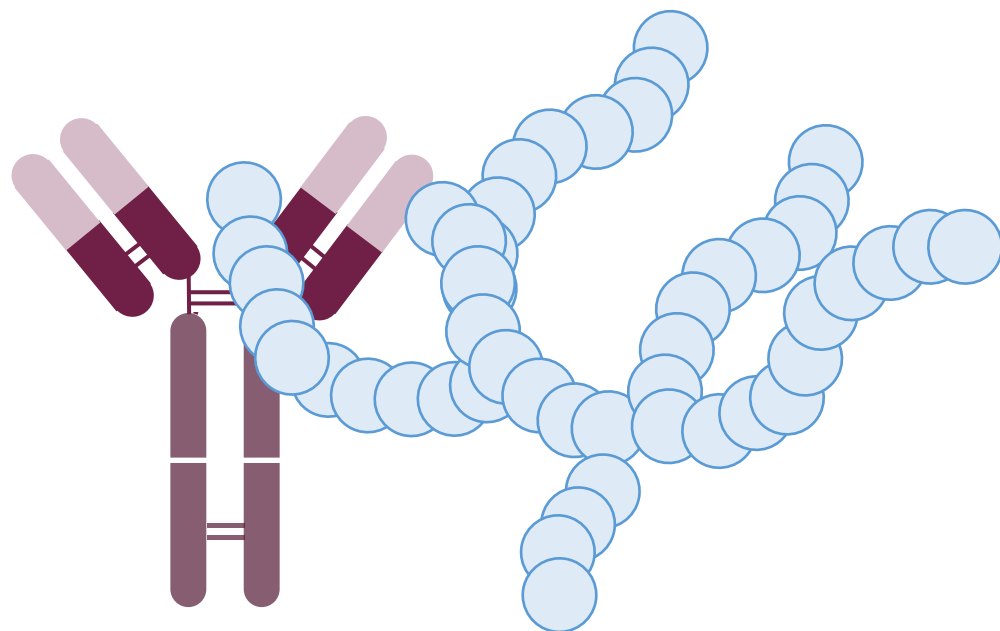
# KSI-301: A Slow-Clearing VEGF Antibody-Polymer Conjugate in Phase 1/2/3



Antibody: IgG1



Polymer: phosphorylcholine<sup>†</sup>



## Indications Investigated<sup>1-4</sup>

nAMD, DME, DR, and RVO

## Class

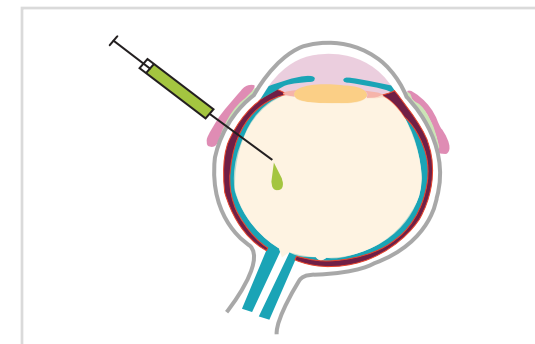
Antibody-polymer conjugate

## MOA<sup>5-7</sup>

Anti-VEGF antibody biopolymer conjugate (950 kDa) designed to provide sustained inhibition of VEGF-A for up to 6 months

## Route of Administration

Intravitreal injection\*



RVO, retinal vein occlusion. \*Image adapted from de Guimaraes et al. *Br J Ophthalmol.* 2021;105;151; †Image redrawn based on data from Barakat et al. Presented at ASRS 2020. <http://ir.kodiak.com/static-files/0138e555-b238-4df6-86c6-5149636645eb>. 1. DAZZLE clinical trial (NCT04049266); 2. GLEAM clinical trial (NCT04611152); 3. GLIMMER clinical trial (NCT04603937); 4. BEACON clinical trial (NCT04592419); 5. Barakat et al. Presented at ASRS 2020. <http://ir.kodiak.com/static-files/0138e555-b238-4df6-86c6-5149636645eb>; 6. Kodiak. <https://ir.kodiak.com/news-releases/news-release-details/kodiak-sciences-announces-new-longer-term-safety-efficacy-and>; 7. ADCReview. <https://www.adcreview.com/clinical-trials-update/phase-ib-study-shows-safety-efficacy-and-durability-of-ksi-301/>.

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# KSI-301 Phase 1b Informs the Design of New Pivotal Studies in nAMD, DME, DR, and RVO<sup>1-5</sup>

## Ongoing Clinical Trials

## Future Clinical Trials

### Phase 2/3

#### DAZZLE<sup>1</sup>

➡ **KSI-301** (Q12, 16, 20W\*)  
vs **aflibercept** (Q8W\*)

➡ In patients with  
**treatment-naïve nAMD**

### Phase 3

#### GLEAM/GLIMMER<sup>2,3</sup>

➡ **KSI-301** (Q8W–Q24W\*)  
vs **aflibercept** (Q8W<sup>†</sup>)

➡ In patients with  
**treatment-naïve DME**

### Phase 3

#### BEACON<sup>4</sup>

➡ **KSI-301** (≥Q8W<sup>‡</sup>)  
vs **aflibercept** (QW4)

➡ In patients with  
**treatment-naïve DME  
due to RVO**

### Phase 3

#### GLOW<sup>5</sup>

➡ **KSI-301**  
(Q16W or Q24W<sup>‡</sup>)

➡ In patients with  
**NPDR without DME**

NPDR, nonproliferative diabetic retinopathy; RVO, retinal vein occlusion; QxW, every x weeks.

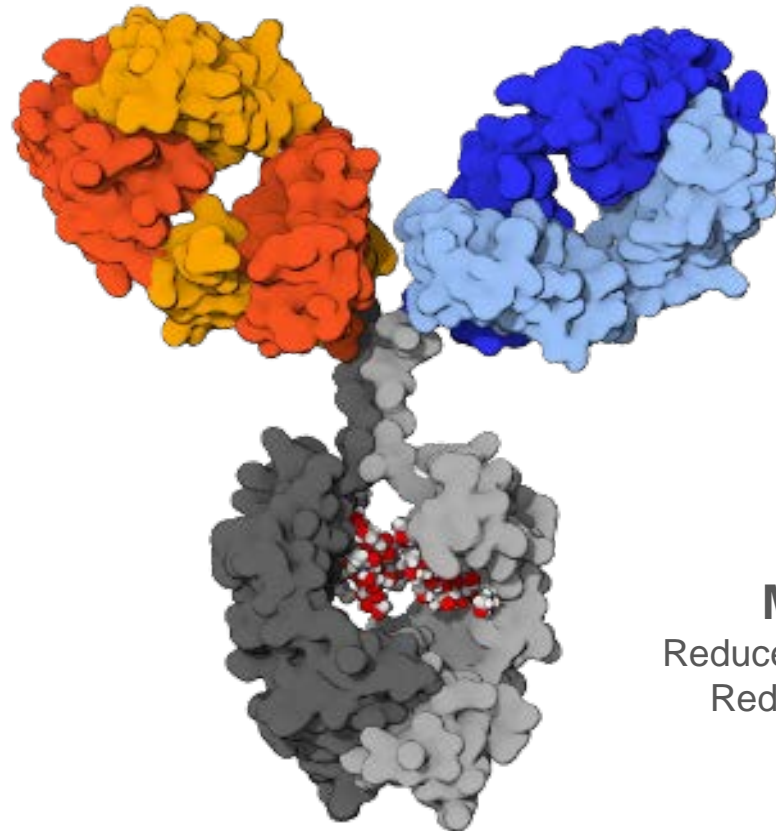
\*After 3 monthly doses; † After 5 monthly doses; ‡After 2 bimonthly doses. 1. DAZZLE clinical trial (NCT04049266); 2. GLEAM clinical trial (NCT04611152); 3. GLIMMER clinical trial (NCT04603937); 4. BEACON clinical trial (NCT04592419). 5. Barakat et al. Presented at ASRS 2020. <http://ir.kodiak.com/static-files/0138e555-b238-4df6-86c6-5149636645eb>.



# Faricimab: Not Anti-VEGF Monotherapy But A New Era

## One Molecule – Two Targets

**Anti-Ang-2 Fab**  
Enhances vascular stability  
Reduces inflammation and  
vascular leakage



**Anti-VEGF-A Fab**  
Inhibits vascular leakage  
and neovascularization

**Modified Fc**  
Reduces systemic exposure  
Reduces inflammatory  
potential

Note: CrossMAb molecule representative of faricimab.

Ang-2, angiopoietin-2; Fab, fragment antigen binding; Fc, fragment crystallizable; VEGF-A, vascular endothelial growth factor-A.

Regula et al. *EMBO Mol Med.* 2016;8:1265, with correction in Regula JT et al. *EMBO Mol Med.* 2019;11:e10666.

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# Four FDA Phase 3 Studies Released Simultaneously for nAMD and DME

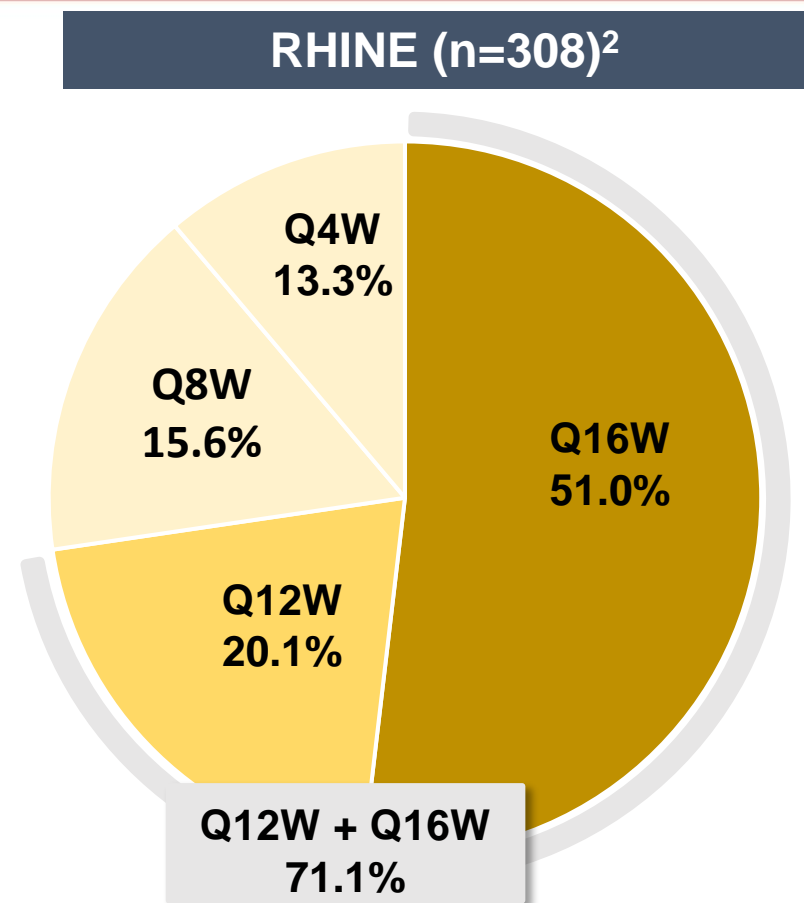
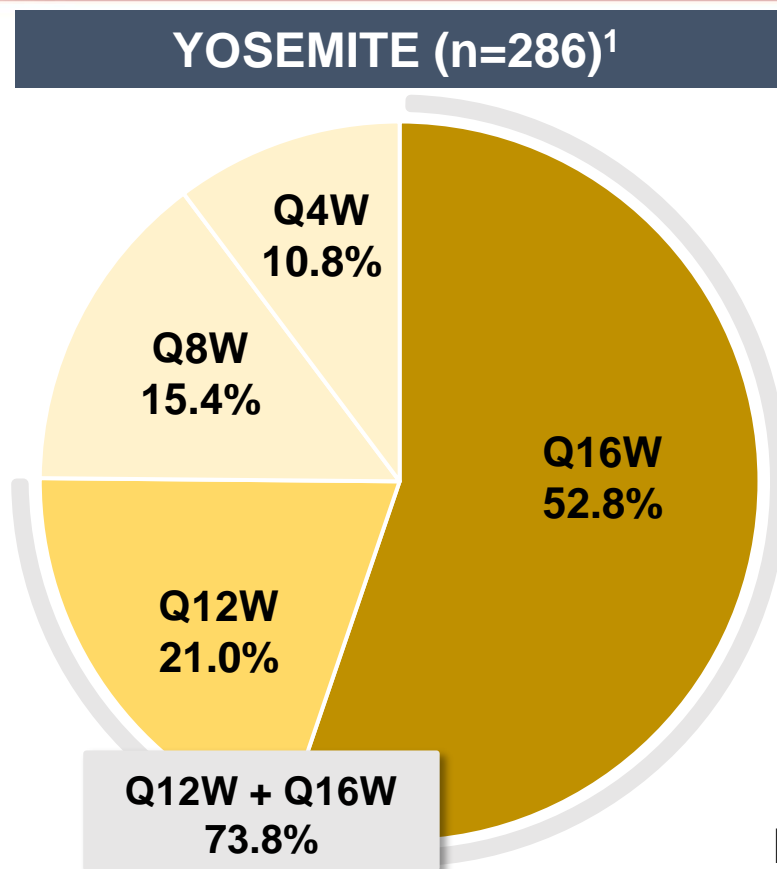
	DME YOSEMITE <sup>1</sup> /RHINE <sup>2</sup>	nAMD TENAYA <sup>3</sup> /LUCERNE <sup>4</sup>
<b>Primary Endpoint</b>	<b>BCVA change from baseline*:</b> <ul style="list-style-type: none"> <li>Non-inferiority achieved for faricimab up to Q12W or Q16W vs aflibercept dosed Q8W</li> </ul>	<b>BCVA change from baseline†:</b> <ul style="list-style-type: none"> <li>Noninferiority achieved for faricimab up to Q16W vs aflibercept dosed Q8W</li> </ul>
	<ul style="list-style-type: none"> <li>Consistent results between both sets of studies: YOSEMITE/RHINE and TENAYA/LUCERNE</li> <li>Secondary analysis results consistent with main analysis</li> </ul>	
<b>Secondary Endpoint: Durability</b>	<ul style="list-style-type: none"> <li>~50% PTI* patients on Q16W</li> <li>~70% PTI* patients on at ≥Q12W at Week 52</li> </ul>	<ul style="list-style-type: none"> <li>~45% of patients on Q16W dosing interval</li> <li>~80% of patients on ≥Q12W dosing interval</li> </ul>
<b>Safety</b>	<ul style="list-style-type: none"> <li>Faricimab was generally well-tolerated, with no new or unexpected safety signals identified</li> <li>No intraocular inflammation associated with retinal vasculitis or retinal occlusive events</li> </ul>	

BCVA, best-corrected visual acuity; PTI, personalized treatment interval; QxW, every x weeks.

\*Averaged over Weeks 48, 52, 56; †Averaged over Weeks 40, 44, 48; data quality and integrity of acceptable standard for filing despite the COVID-19 pandemic.

1. YOSEMITE clinical trial (NCT03622580); 2. RHINE clinical trial (NCT03622593); 3. TENAYA clinical trial (NCT03823287); 4. LUCERNE clinical trial (NCT03823300).

# nAMD: Unparalleled Durability With Faricimab Through Year 1\*



**ITT Population**

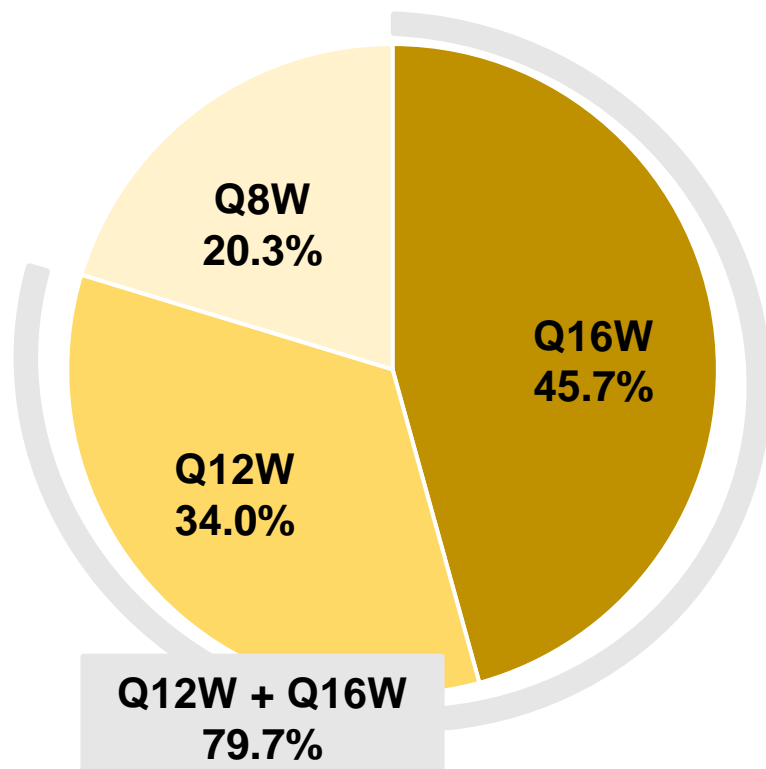
ITT, intent-to-treat population; PTI, personalized treatment interval. \*N = Number of patients in PTI arm with evaluable data at week 52. Treatment interval at a given visit is defined as the treatment interval decision made at that visit. Percentages are based on the number of patients who have not discontinued the study at the visit.

1. YOSEMITE clinical trial (NCT03622580); 2. RHINE clinical trial (NCT03622593).

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# DME: Unparalleled Durability With Faricimab Through Year 1\*

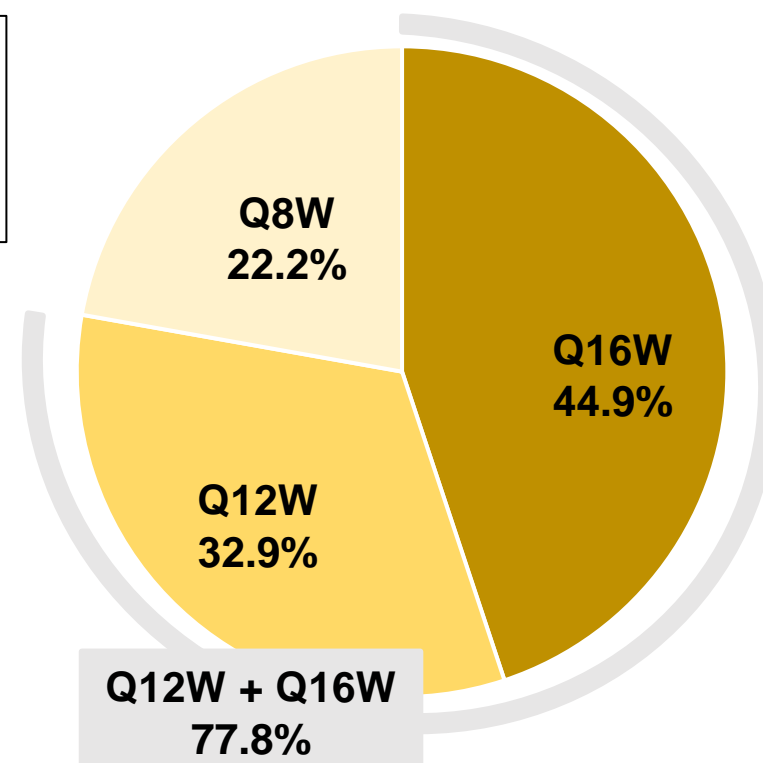
TENAYA (n = 334)<sup>1</sup>



**Median Number of Injections**

Faricimab: 6  
Aflibercept: 8

LUCERNE (n = 331)<sup>2</sup>



ITT Population

\*Percentages are based on number of patients randomized to the faricimab arm who have not discontinued the study at Week 48. Treatment interval at Week 48 is defined as the treatment interval decision followed at that visit. 1. TENAYA clinical trial (NCT03823287); 2. LUCERNE clinical trial (NCT03823300).

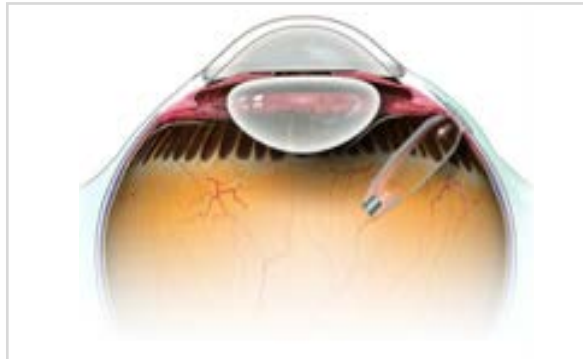
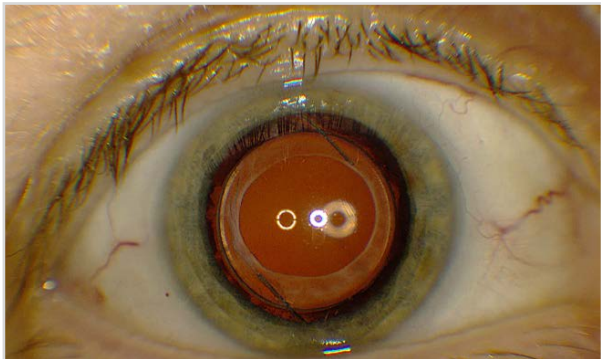
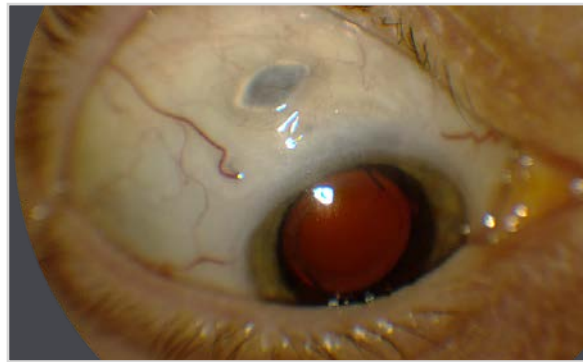
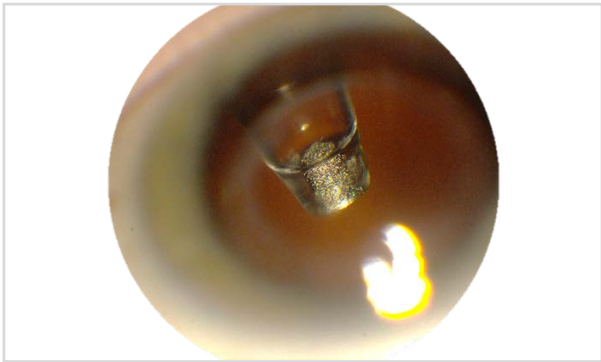
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# Summary: Faricimab Is Very Likely What Is Coming Next

TOPIC	ARGUMENTS
<b>Safety</b>	<ul style="list-style-type: none"><li>• Faricimab did not have any intraocular inflammation (IOI) associated with retinal vasculitis or retinal occlusive events</li><li>• Overall, faricimab showed a comparable safety profile to aflibercept</li><li>• Roche/Genentech already have a safe and trusted drug in the anti-VEGF space (eg, Lucentis)</li></ul>
<b>Efficacy</b>	<ul style="list-style-type: none"><li>• Noninferiority of BCVA change from baseline was achieved in faricimab up to Q12W or Q16W for both indications over aflibercept dosed at Q8W</li></ul>
<b>Durability</b>	<ul style="list-style-type: none"><li>• Up to 50% of the patients were extended to Q16W interval for both indications</li><li>• Over 70% of patients were extended to Q12W or longer for both indications</li><li>• Durability data is reproducible and has been shown by 4 trials in over 3000 patients</li></ul>
<b>Anatomical Endpoints</b>	<ul style="list-style-type: none"><li>• More patients showing absence of DME and intraretinal fluid (IRF) for aflibercept in YOSEMITE/RHINE</li><li>• Reductions in CST favor faricimab for both indications</li></ul>
<b>Dual MOA</b>	<ul style="list-style-type: none"><li>• There are theoretical advantages to faricimab being a bispecific antibody</li><li>• RUBY study validates the Ang-2 target in DME</li></ul>
<b>Ang-2 Contribution</b>	<ul style="list-style-type: none"><li>• Ang-2 might play a role in increased durability rather than Diabetic Retinopathy Severity Scale (DRSS) improvement</li><li>• There is evidence that Ang-2 is upregulated in several retinal diseases, including AMD and DR</li></ul>
<b>Other</b>	<ul style="list-style-type: none"><li>• Could avoid Step Therapy</li><li>• Could avoid Biosimilars intrusion in the market</li><li>• Being an injection makes it easy to adopt (versus PDS)</li></ul>

# The Port Delivery System (PDS) With Ranibizumab\*

PDS provides continuous delivery of ranibizumab into the vitreous

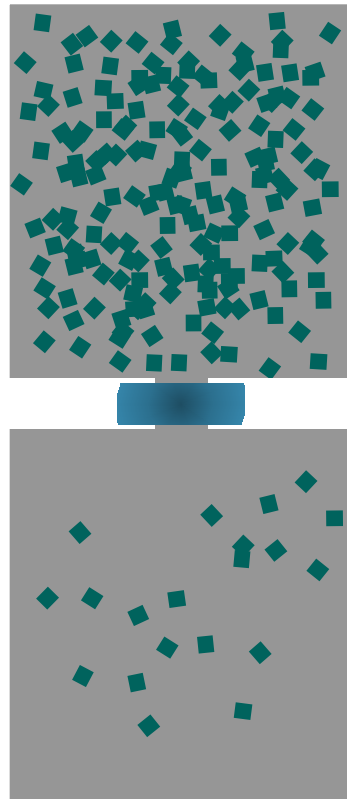
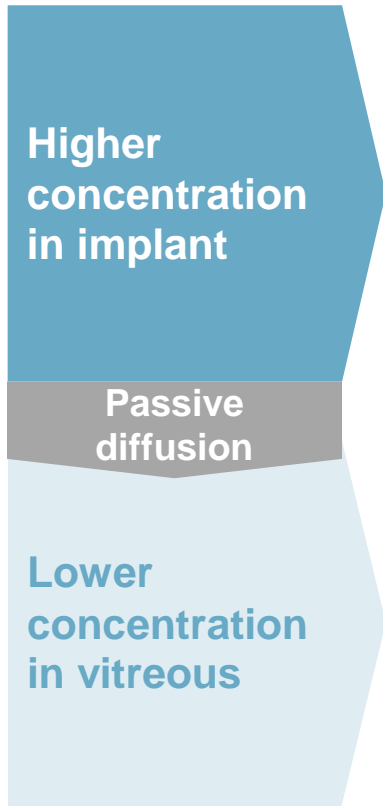


\*PDS with ranibizumab has not yet received regulatory approval in any country.  
Video reproduced from Campochiaro PA, et al. *Ophthalmology*. 2019;126:1141, with permission from Elsevier.

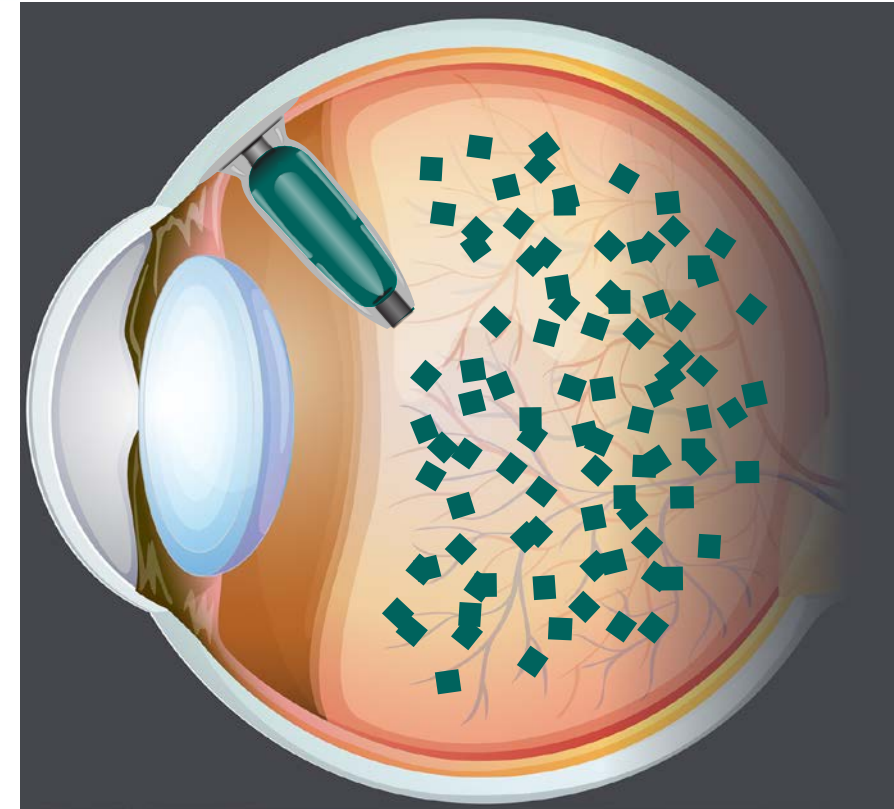
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# PDS\* Mechanism of Continuous Delivery: Passive Diffusion

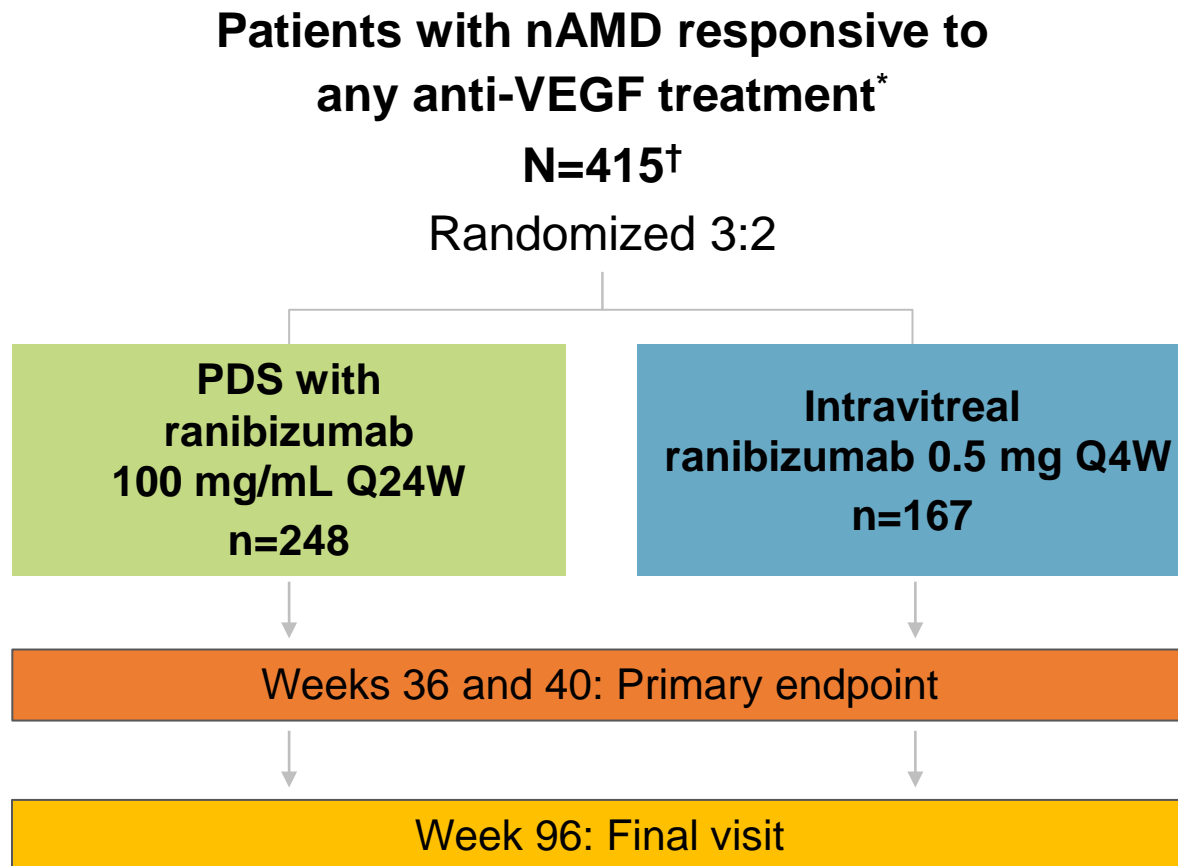


- Continuous delivery mediated by passive diffusion across a concentration gradient
- Rate of diffusion is concentration dependent and decreases over time
- Follows Fick's law



\*PDS with ranibizumab has not yet received regulatory approval in any country. Campochiaro et al. Ophthalmology. 2019;126:1141.

# Archway Trial: Designed to Evaluate the Efficacy and Safety of PDS for the Treatment of nAMD



## Primary Objective

Evaluate noninferiority and equivalence of PDS 100 mg/mL Q24W vs intravitreal ranibizumab 0.5 mg Q4W

## Primary Endpoint

Change in BCVA score from baseline averaged over Weeks 36 and 40

## Secondary Endpoints

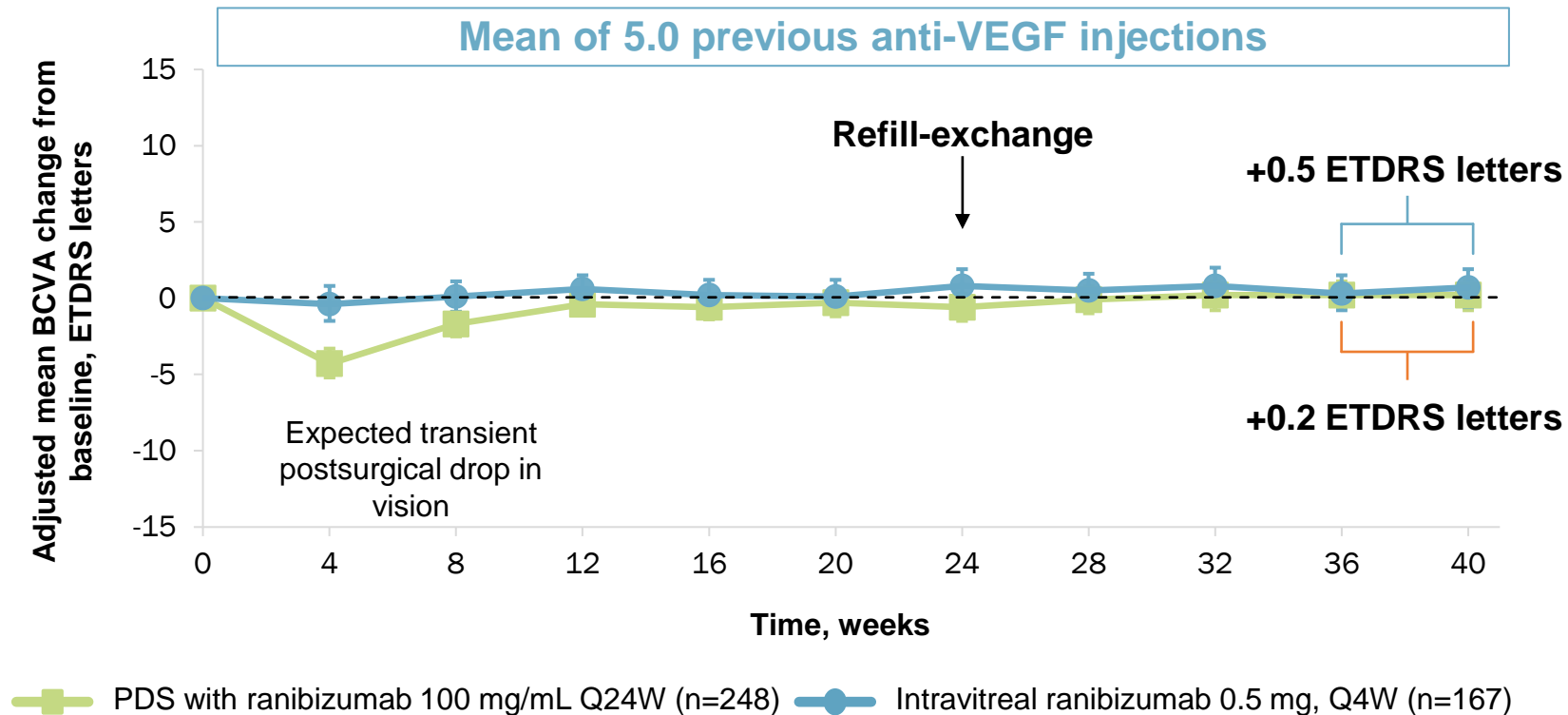
- Change in BCVA score from baseline over time
- Change in CPT from baseline over time and at Week 36
- Percentage of PDS-treated patients who received supplemental treatment during first refill-exchange interval
- Incidence and severity of ocular and systemic AEs, SAEs, and ocular AEs of special interest

AE, adverse events; BCVA, best-corrected visual acuity; CPT, centre point thickness; SAE, serious adverse events. \*nAMD in study eye diagnosed within 9 months of screening;  $\geq 3$  intravitreal injections of any anti-VEGF agent within previous 6 months; †efficacy- and safety-evaluable population. 418 total patients were enrolled, with 251 and 167 patients randomized to the PDS 100 mg/mL Q24W and intravitreal ranibizumab 0.5 mg Q4W arms, respectively; 3 patients in the PDS arm did not receive study treatment and were excluded from the efficacy- and safety-evaluable population. Archway clinical trial (NCT03677934). Campochiaro et al. Presented at the American Society of Retina Specialists (ASRS) 2020.

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# Primary Endpoint: PDS Q24W Noninferior and Equivalent to Monthly Ranibizumab for Long-Term Maintenance

## Adjusted mean BCVA change from baseline\*



### Primary Endpoint

Change in BCVA from baseline averaged over Weeks 36 and 40

Difference in adjusted means, 95% CI  
**-0.3 (-1.7, +1.1)**

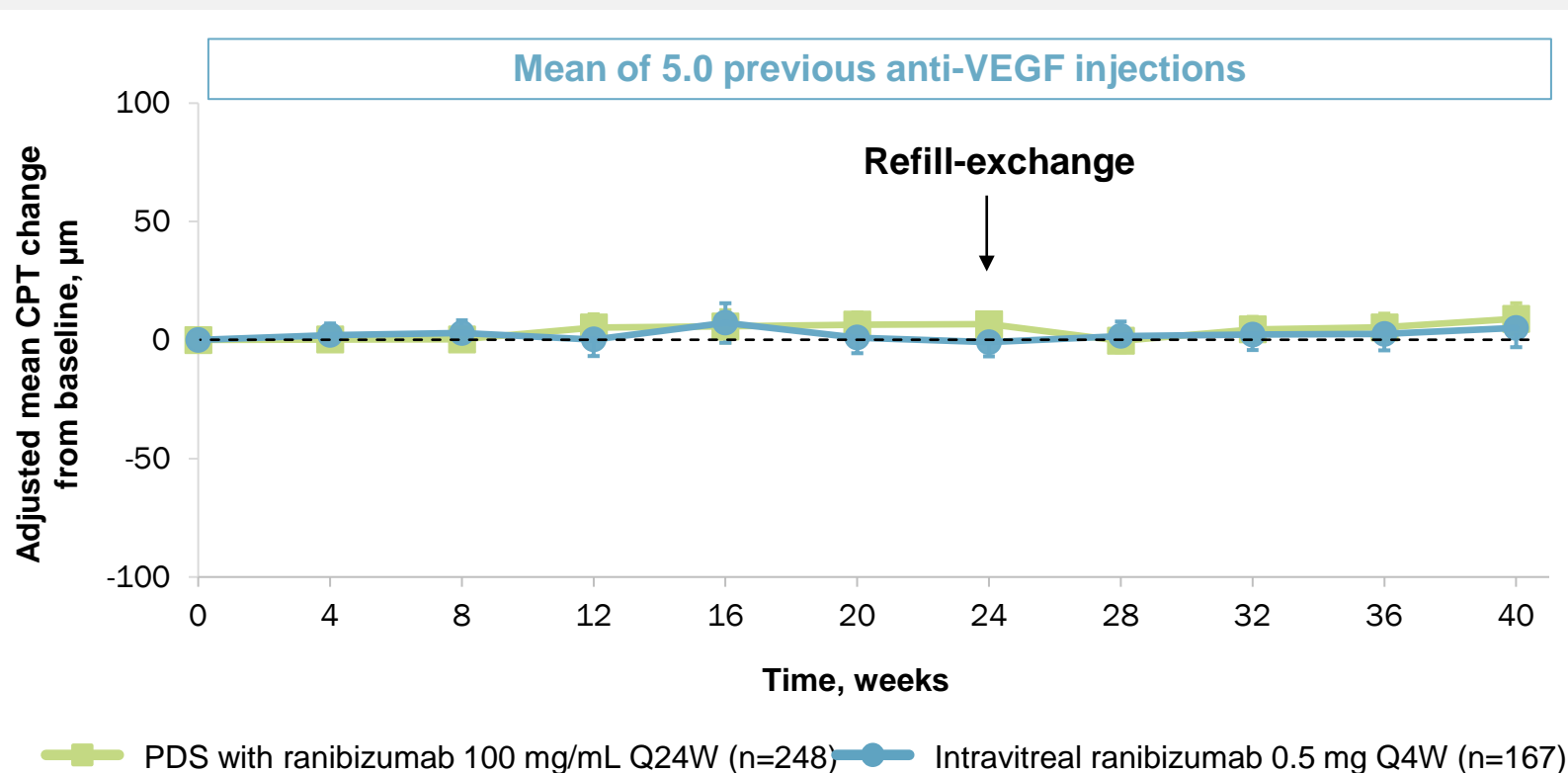
**PDS equivalent to monthly treatment**

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study. \*Adjusted means from a mixed-effect model for repeated measures (MMRM) analysis and vertical bars represent 95% CI. 95% CI is a rounding of 95.03% CI; the type 1 error was adjusted for interim safety monitoring. Adjusted means estimated using a MMRM with adjustment for change from baseline in BCVA as the response and included terms for treatment group, visit, treatment-by-visit interaction, and baseline BCVA (<74 ETDRS letters vs ≥74 ETDRS letters). Campochiaro et al. Presented at ASRS 2020.

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# PDS Controlled nAMD Disease Activity Through Week 40 Similar to Monthly Ranibizumab

Adjusted mean CPT change from baseline (BL)\*



Prespecified Secondary Endpoint (Week 36)

Baseline	Week 36	Week 36 change from BL
176.9 $\mu\text{m}$	182.3 $\mu\text{m}$	+5.4 $\mu\text{m}$
177.4 $\mu\text{m}$	180.0 $\mu\text{m}$	+2.6 $\mu\text{m}$

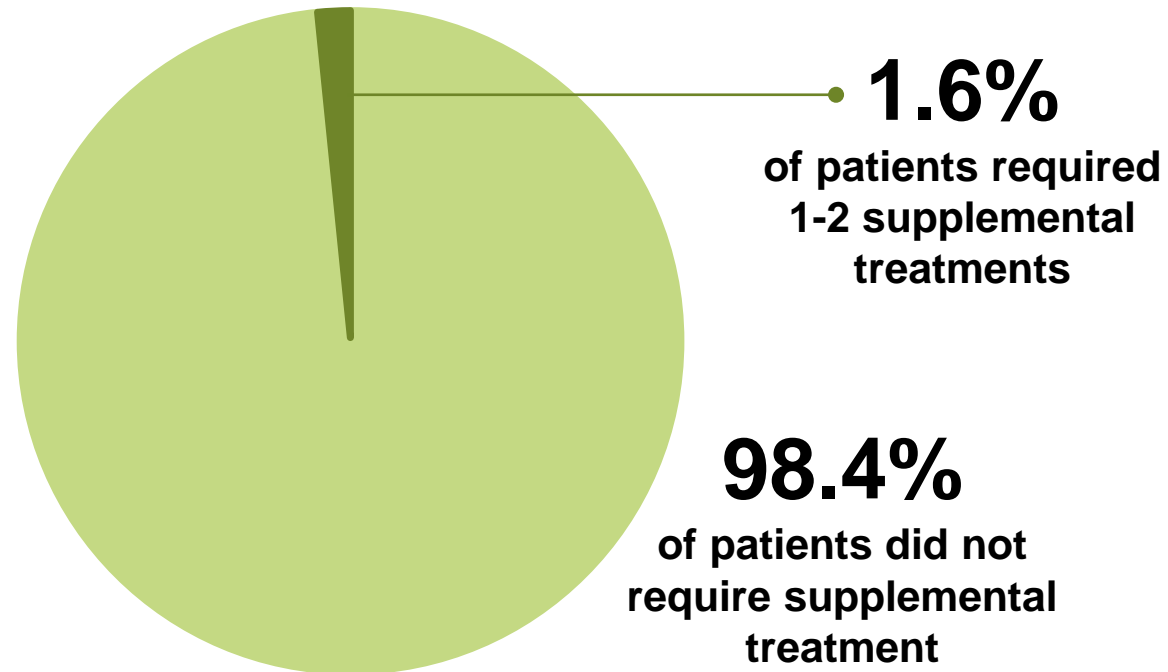
\*CPT (center point thickness) defined as retinal thickness in the center of the fovea measured between the inner limiting membrane and the inner third of the retinal pigment epithelium layer. Adjusted means were estimated using a mixed-effect model for repeated measures with adjustment for change from baseline in CPT score as the response and included terms for treatment group, visit, treatment-by-visit interaction, and baseline BCVA (<74 ETDRS letters vs  $\geq$ 74 ETDRS letters). ETDRS, Early Treatment Diabetic Retinopathy Study. Campochiaro et al. Presented at ASRS 2020.

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# ~98% of PDS-treated Patients Did Not Receive Supplemental Treatment During First Refill-Exchange Interval

Percentage of PDS patients who received supplemental treatment before first refill-exchange at Week 24

PDS patients received  
**~5x fewer treatments**  
through **Week 40**  
vs patients receiving  
monthly ranibizumab  
intravitreal



Campochiaro et al. Presented at ASRS 2020.

# Ocular Adverse Events of Special Interest Associated With a Surgical Procedure

MedDRA Preferred Term, n (%) <sup>†</sup>	PDS with ranibizumab 100 mg/mL Q24W (n=248)			Intravitreal ranibizumab 0.5 mg Q4W (n=167)
	Time from surgery		Total <sup>‡</sup>	Total <sup>‡</sup>
	≤1 month	>1 month		
Conjunctival bleb/ conjunctival filtering bleb leak	11 (4.4)	6 (2.4)	16 (6.5)	0
Vitreous haemorrhage	12 (4.8)	1 (0.4)	13 (5.2)	4 (2.4)
Cataract <sup>§</sup>	1 (0.4)	9 (3.6)	10 (4.0)	6 (3.6)
Conjunctival erosion	1 (0.4)	5 (2.0)	6 (2.4)	0
Conjunctival retraction	1 (0.4)	4 (1.6)	5 (2.0)	0
Endophthalmitis	0	4 (1.6)	4 (1.6)	0
Rhegmatogenous retinal detachment	1 (0.4)	1 (0.4)	2 (0.8)	0
Hyphema	1 (0.4)	0	1 (0.4)	0

All cases of vitreous haemorrhage resolved spontaneously – no cases required vitrectomy

1 of 248 PDS-treated patients had irreversible vision loss due to an adverse event (*E. faecalis* endophthalmitis)

1 PDS patient experienced device dislocation into the eye during a refill-exchange procedure; following removal, the patient's vision returned to baseline

\*Protocol-defined ocular adverse events of special interest potentially related to the PDS implant or implant procedure; <sup>†</sup>Frequency counts by preferred term. Multiple occurrences of the same adverse event in an individual are counted only once for each column; <sup>‡</sup>All data through Week 40. <sup>§</sup>Includes the following terms: cataract, cataract nuclear, cataract cortical, cataract subcapsular. Observed data, all treated patients who received ≥1 dose of study drug according to the actual treatment. Month 1 visit includes data up to 37 days (monthly study visit + 7 days). MedDRA, Medical Dictionary for Regulatory Activities. Campochiaro P, et al. Presented at ASRS 2020.

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# Summary of PDS

- Phase 3 clinical trial completed in nAMD
- PDS for nAMD submitted to FDA
  - Waiting on reply from FDA
- PDS currently in Phase 3 trials for DME and NPDR

DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration; nonproliferative NPDR, nonproliferative diabetic retinopathy; PDS, Port Delivery System with ranibizumab.

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# Summary of Anti-VEGF 2.0 for nAMD and DME/DR

- There are multiple strategies being investigated to increase treatment durability and reduce treatment burden for patients with nAMD
- Preliminary data indicate that treatment intervals of 4 to 6 months may be achievable for most patients with these investigational therapies
- Gene therapies have potential for even longer-term durability



# Pharmacist Considerations

Sheldon J. Rich, RPh, PhD



# Patient-Centered Therapy Selection

- Developed at the Department of Family Medicine at Western University in Ontario, Canada in 1968
- Changes in the mindset of clinicians
  - The notion that the professional is in charge and the patient is passive does not hold
    - To be patient-centered, the practitioner must be able to empower the patient and share the power in the relationship
  - Maintaining an exclusively objective stance in relation to patients produces an unacceptable insensitivity to human suffering
    - To be patient-centered requires a balance between the subjective and the objective, a bringing together of the mind and body

Stewart et al. *Patient-Centered Medicine: Transforming the Clinical Method*. 3rd ed. CRC Press; 2014.

# The Four Interactive Components of the Patient-Centered Clinical Method

## 1. Exploring Health, Disease, and the Illness Experience

- Unique perceptions and experiences of health (meanings and aspirations)
- History, physical, lab
- Dimensions of the illness experience (feelings, ideas, effects on function and expectations)

## 2. Understanding the Whole Person

- The person (eg, life history, personal and developmental issues)
- The proximal context (eg, family, employment, social support)
- The distal context (eg, culture, community, ecosystem)

## 3. Finding Common Ground

- Problems and priorities
- Goals of treatment and/or management
- Roles of patient and doctor

## 4. Enhancing the Patient-Centered Relationship

- Compassion and empathy
- Power
- Healing and hope
- Self-awareness and practical wisdom
- Transference and countertransference

Stewart et al. *Patient-Centered Medicine: Transforming the Clinical Method*. 3rd ed. CRC Press; 2014.



# Goals of the Interactive Components

## 1. Exploring Health, Disease, and the Illness Experience

**GOAL:** To explore disease and patients' perceptions of health and illness. Clinicians need to understand the patients' perception of health and unique experience of illness

## 2. Understanding the Whole Person

**GOAL:** Integration of these concepts with an understanding of the whole person

## 3. Finding Common Ground

**GOAL:** Define the problem, establish goals of treatment, and identify the roles to be assumed by the patient and clinician

## 4. Enhancing the Patient-Centered Relationship

**GOAL:** Each patient contact should build on the patient-clinician relationship with compassion, empathy, a sharing of power, healing and hope

Stewart et al. *Patient-Centered Medicine: Transforming the Clinical Method*. 3rd ed. CRC Press; 2014.

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A close-up photograph of a person's face, focusing on the eye and nose area. The image is partially obscured by a dark red banner at the top and a white text area on the right.

# Patient Education and Compliance Improvement

- Identify patients at risk
- Refer all patients with diabetes for complete, routine eye exams
- Encourage adherence to eye exam visit schedule for those with DR or DME
- Encourage treatment adherence
- Initiate preventive strategies
- Initiate patient education
- Evaluate treatment
- Assess adherence



# Patient Education and Compliance Improvement

- Explain therapy requirements (frequent visits), cost, and possible adverse effects
- Monitor therapy safety and efficacy
- Describe what to expect with therapy
- Stopping vision loss
- Vision improvement expectations



# Patient Education and Compliance Improvement

- Importance and Monitoring of Treatment Adherence
  - Slow progression of DME
  - Prevent vision loss or blindness
  - Emphasize importance of ongoing treatment
  - Follow up with patients to ensure they are adhering to therapy
    - If not adhering to therapy, find out why and try to help address the issue
  - Possibly offer less expensive alternatives or less complicated treatment regimens
  - Provide assistance with cost of care whenever possible



# Coping Strategies for Vision Loss

- Low vision applications for mobile devices
- Special lighting
- Vision rehabilitation specialist
- Vision loss support groups

A close-up photograph of a woman's face, focusing on her eyes and nose. A white horizontal bar is superimposed across the middle of the image, partially obscuring her eyes and nose. The text "Patient Assistance Programs" is centered on this bar.

# Patient Assistance Programs

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# Patient Assistance Programs

- Most programs include:
  - Verification of patient-specific insurance benefits
  - Pre-submission claims review and support
  - Prior authorization assistance
  - Coding and billing guidance
  - Payer research
  - Denied and underpaid claims assistance
  - Patient assistance program for qualified patients

National Comprehensive Cancer Network (NCCN). <https://www.nccn.org/business-policy/business/virtual-reimbursement-resource-room-and-app>.

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# Patient Assistance Programs

- **Patient Assistance Programs**

- American Society of Retina Specialists

<https://www.asrs.org/patients/patient-assistance-resources>

- Good Days Assistance Program

<http://www.mygooddays.org/apply/>

- Patient Access Network (PAN) Foundation

<https://www.panfoundation.org/disease-funds/macular-diseases/>

- **Patient Resources**

- American Society of Retina Specialists

<https://www.asrs.org/patients/retina-health-information>

- Prevent Blindness

<https://preventblindness.org/>



# Formulary and Payer Considerations

- Studies involving anti-VEGF therapies need to translate to clinical practice
- Compliance with 9 injections during first year of treatment is difficult
- Ability to read 1 additional line on an eye chart may/may not have meaningful functional value
- Lack of evidence for treatment of nonresponders
- Necessary DME-related services such as screening, diagnosis, treatment, and ongoing care may not be covered by insurance providers
- Precise data on DME financial impact to individual and society are needed to justify costs

International DME Expert Summit White Paper; June 2014. <https://www.angio.org/wp-content/uploads/2014/02/DME-Intl-Summit-White-Paper-Report.pdf>.

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# Formulary and Payer Considerations

- Cost (AWP<sup>1</sup>) of anti-VEGF therapies
  - Aflibercept 2.0 mg (Eylea) Q4W
    - \$2,220 per 0.05 mL
  - Bevacizumab 1.25 mg (Avastin; used off label) Q4W
    - ~\$50-\$75 per dose (\$73.20 for the Fagron Sterile Services product→)
  - Brolucizumab 6.0 mg (Beovu) Q8/12W
    - \$2,220 per 0.05 mL
  - Ranibizumab 0.5 mg (Lucentis) Q4W
    - \$2,340 per 0.05 mL
- Copayments under Medicare Part B are typically 20% of drug plus physician services<sup>3</sup>



1. Average wholesale price (AWP). *Micromedex Red Book*. <https://www.ibm.com/products/micromedex-red-book>. Accessed September 8, 2021;  
2. Bevacizumab (Avastin) injection solution. <https://www.fagronsterile.com/avastin>; 3. Shah et al. *Dev Ophthalmol*. 2016;55:376.

A close-up photograph of a woman's face, focusing on her eye and the bridge of her nose. The image is split horizontally by a white band containing text. The top half shows her eye with greenish-brown irises and dark eyeliner. The bottom half shows her nose and lips. The background is a soft, out-of-focus grey.

# Prior Authorization

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# Consensus Statement on Improving the Prior Authorization Process

- Participants:
  - American Hospital Association (AHA), America's Health Insurance Plans (AHIP), American Medical Association (AMA), American Pharmacists Association (APhA), BlueCross BlueShield Association (BCBS), Medical Group Management Association (MGMA)
- Opportunities for improvement:
  - Selective application of prior authorization
  - Prior authorization program review and volume adjustment
  - Transparency and communication regarding prior authorization
  - Continuity of patient care
  - Automation to improve transparency and efficiency

Consensus statement on improving the prior authorization process. <https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc-public/prior-authorization-consensus-statement.pdf>.



# Selective Application of Prior Authorization

- Encourage the use of programs that selectively implement prior authorization requirements based on stratification of health care providers' performance and adherence to evidence-based medicine
- Encourage (1) the development of criteria to select and maintain health care providers in these selective prior authorization programs with the input of contracted health care providers and/or provider organizations; and (2) making these criteria transparent and easily accessible to contracted providers
- Encourage appropriate adjustments to prior authorization requirements when health care providers participate in risk-based payment contracts

Consensus statement on improving the prior authorization process. <https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc-public/prior-authorization-consensus-statement.pdf>.



# Prior Authorization Program Review and Volume Adjustment

- Encourage review of medical services and prescription drugs requiring prior authorization on at least an annual basis, with the input of contracted health care providers and/or provider organizations
- Encourage revision of prior authorization requirements, including the list of services subject to prior authorization, based on data analytics and up-to-date clinical criteria
- Encourage the sharing of changes to the lists of medical services and prescription drugs requiring prior authorization via (1) provider-accessible websites; and (2) at least annual communications to contracted health care providers

Consensus statement on improving the prior authorization process. <https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc-public/prior-authorization-consensus-statement.pdf>.

# Transparency and Communication Regarding Prior Authorization

- Improve communication channels between health plans, health care providers, and patients
- Encourage transparency and easy accessibility of prior authorization requirements, criteria, rationale, and program changes to contracted health care providers and patients/enrollees
- Encourage improvement in communication channels to support:
  - 1) Timely submission by health care providers of the complete information necessary to make a prior authorization determination as early in the process as possible
  - 2) Timely notification of prior authorization determinations by health plans to impacted health care providers (both ordering/rendering physicians and dispensing pharmacists) and patients/enrollees

Consensus statement on improving the prior authorization process. <https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc-public/prior-authorization-consensus-statement.pdf>.



# Continuity of Patient Care

- Encourage sufficient protections for continuity of care during a transition period for patients undergoing an active course of treatment when there is a formulary or treatment coverage change or change of health plan that may disrupt their current course of treatment
- Support continuity of care for medical services and prescription medications for patients on appropriate, chronic, stable therapy through minimizing repetitive prior authorization requirements
- Improve communication between health care providers, health plans, and patients to facilitate continuity of care and minimize disruptions in needed treatment

Consensus statement on improving the prior authorization process. <https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc-public/prior-authorization-consensus-statement.pdf>.

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# Automation to Improve Transparency and Efficiency

- Encourage health care providers, health systems, health plans, and pharmacy benefit managers to accelerate use of existing national standard transactions for electronic prior authorization (ie, National Council for Prescription Drug Programs ePA transactions and X12 278)
- Advocate for adoption of national standards for the electronic exchange of clinical documents (ie, electronic attachment standards) to reduce administrative burdens associated with prior authorization

Consensus statement on improving the prior authorization process. <https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc-public/prior-authorization-consensus-statement.pdf>.

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# Automation to Improve Transparency and Efficiency

- Advocate that health care provider and health plan trading partners, such as intermediaries, clearinghouses, electronic health records (EHR), and practice management system vendors, develop and deploy software and processes that facilitate prior authorization automation using standard electronic transactions
- Encourage the communication of up-to-date prior authorization and step therapy requirements, coverage criteria and restrictions, drug tiers, relative costs, and covered alternatives:
  - 1) To EHR, pharmacy system, and other vendors to promote the accessibility of this information to health care providers at the point-of-care via integration into ordering and dispensing technology interfaces
  - 2) Via websites easily accessible to contracted health care providers

Consensus statement on improving the prior authorization process. <https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc-public/prior-authorization-consensus-statement.pdf>.



A close-up photograph of a woman's face, focusing on her eyes and nose. A white horizontal band is superimposed over the middle of the image, partially obscuring her eyes and nose. The word "Discussion" is written in large, bold, black letters across this white band.

# Discussion



A close-up photograph of a woman's face, showing her eyes, nose, and mouth. A white horizontal bar is superimposed over the middle of the image, partially obscuring her eyes and nose. The text "Questions & Answers" is centered on this bar.

# Questions & Answers

A close-up photograph of a woman's face, focusing on her eyes and nose. A white horizontal bar is superimposed across the middle of the image, partially obscuring her eyes and nose. The text "Thank You!" is centered on this white bar.

**Thank You!**