



# CLEARSIDE BIOMEDICAL

**Suprachoroidal Space Drug Delivery**

**July 24, 2024**



# Forward-Looking Statements

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This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. The words “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “target” or the negative of these terms and other similar words or expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Clearside Biomedical, Inc.’s views as of the date of this presentation about future events and are subject to risks, uncertainties, assumptions, and changes in circumstances that may cause Clearside’s actual results, performance, or achievements to differ significantly from those expressed or implied in any forward-looking statement. Although Clearside believes that the expectations reflected in the forward-looking statements are reasonable, new risks and uncertainties may emerge from time to time, and Clearside cannot guarantee future events, results, performance, or achievements. Some of the key factors that could cause actual results to differ from Clearside’s expectations include its plans to develop and potentially commercialize its product candidates; adverse differences between preliminary or interim data and final data; Clearside’s planned clinical trials and preclinical studies for its product candidates; the timing of and Clearside’s ability to obtain and maintain regulatory approvals for its product candidates; the extent of clinical trials potentially required for Clearside’s product candidates; the clinical utility and market acceptance of Clearside’s product candidates; Clearside’s commercialization, marketing and manufacturing capabilities and strategy; Clearside’s intellectual property position; Clearside’s ability to expand its pipeline; developments and projections relating to Clearside’s competitors and its industry; the impact of government laws and regulations; the timing and anticipated results of Clearside’s preclinical studies and clinical trials and the risk that the results of Clearside’s preclinical studies and clinical trials may not be predictive of future results in connection with future studies or clinical trials and may not support further development and marketing approval; findings from investigational review boards at clinical trial sites and publication review bodies; Clearside’s estimates regarding future revenue, expenses, capital requirements and need for additional financing; and Clearside’s ability to identify additional product candidates with significant commercial potential that are consistent with its commercial objectives. For further information regarding these risks, uncertainties and other factors you should read the “Risk Factors” section of Clearside’s Annual Report on Form 10-K for the year ended December 31, 2023, filed with the U.S. Securities and Exchange Commission (SEC) on March 12, 2024, and Clearside’s subsequent filings with the SEC. Clearside expressly disclaims any obligation to update or revise the information herein, including the forward-looking statements, except as required by law. This presentation also contains estimates and other statistical data made by independent parties and by Clearside relating to market size and growth and other data about its industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of Clearside’s future performance and the future performance of the markets in which Clearside operates are necessarily subject to a high degree of uncertainty and risk.

# Agenda

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01

## Versatility of Suprachoroidal Delivery

George Lasezkay, PharmD, JD, Clearside President & CEO

02

## Real World Use of Suprachoroidal Delivery

Glenn Yiu, MD, PhD, Professor of Ophthalmology, University of California, Davis

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## Pipeline Opportunities

Victor Chong, MD, MBA, Clearside Chief Medical Officer

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## Large Practice View of Suprachoroidal Delivery

David Brown, MD, Director of Research, Retina Consultants Houston

05

Q&A

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# GEORGE LASEZKAY, PharmD, JD

Clearside President & Chief Executive Officer

*Versatility of Suprachoroidal Delivery*

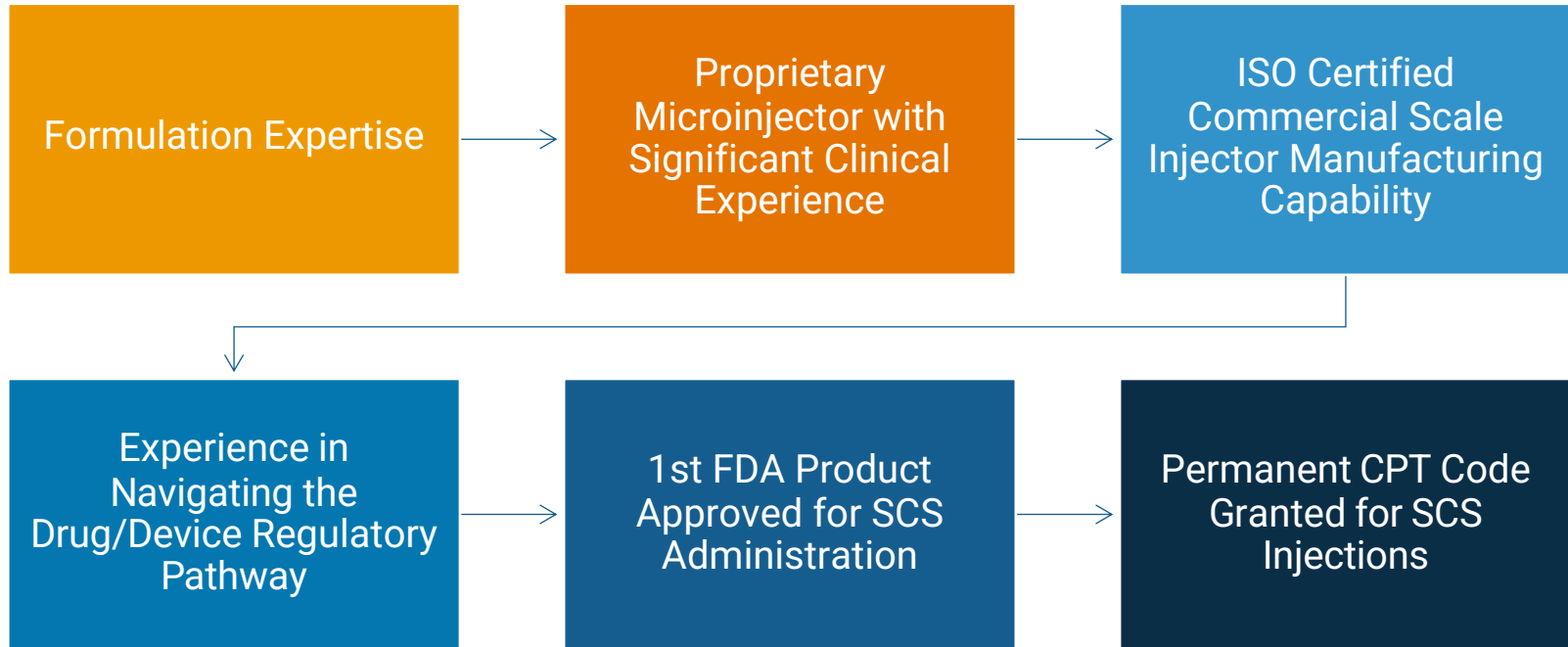
# Delivering on the Potential of the Suprachoroidal Space

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- ✓ **Proven Leader in Suprachoroidal Delivery with Thousands of Injections Performed**
- ✓ **Validated Technology with Approved Product, Multiple Collaborations, and Comprehensive IP Portfolio**
- ✓ **Differentiated Clinical Program Targeting Multi-Billion Dollar Wet AMD Market with Phase 2b Trial Data Expected in Late Q3 2024**



# Proven Leader in Suprachoroidal Delivery





# Diverse Programs Using Clearside's Suprachoroidal Injection Platform

Clearside Developed Programs									
THERAPEUTIC	TYPE	INDICATION	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	APPROVAL	PARTNER	
CLS-AX (axitinib):	Tyrosine Kinase Inhibitor	Wet AMD	Phase 2b			ODYSSEY			
XIPERE®	Corticosteroid (Triamcinolone Acetonide)	Uveitic Macular Edema <sup>1</sup> (U.S. & Canada)						B+L BAUSCH + LOMB	
XIPERE® / ARCATUS™	Corticosteroid (Triamcinolone Acetonide)	Uveitic Macular Edema <sup>2</sup> Diabetic Macular Edema <sup>2</sup> (Asia Pacific ex-Japan)	UME					arctic VISION	
XIPERE® / ARCATUS™	Corticosteroid (Triamcinolone Acetonide)		DME					arctic VISION	
SCS Microinjector® Partner Clinical Development Programs									
THERAPEUTIC	TYPE	INDICATION	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	APPROVAL	PARTNER	
Bel-Sar	Viral-like Drug Conjugate	Choroidal Melanoma	Compass						aura
ABBV-RGX-314	AAV Gene Therapy	Diabetic Retinopathy (DR)	ALTITUDE						REGENXBIO abbvie
ABBV-RGX-314	AAV Gene Therapy	Wet AMD	AAVIATE						REGENXBIO abbvie
Avoralstat	Plasma Kallikrein Inhibitor	Diabetic Macular Edema (DME)							bio crystall

# GLENN C. YIU, MD, PhD

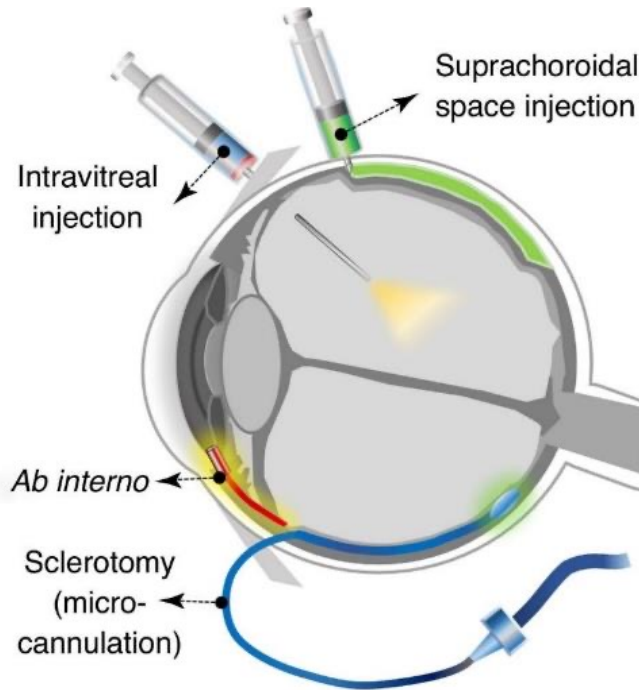
Professor of Ophthalmology, University of California, Davis

*Real World Use of Suprachoroidal Delivery*



# Accessing the suprachoroidal space

## Microcatheter



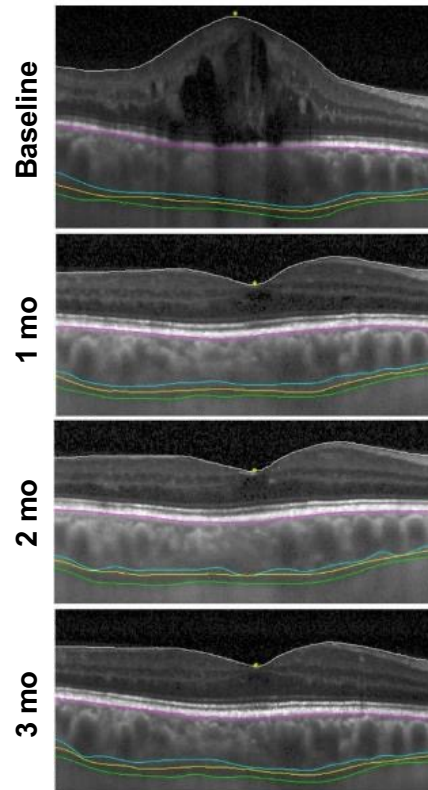
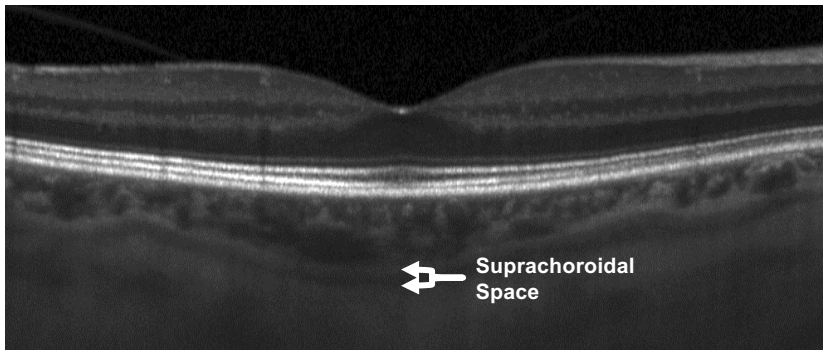
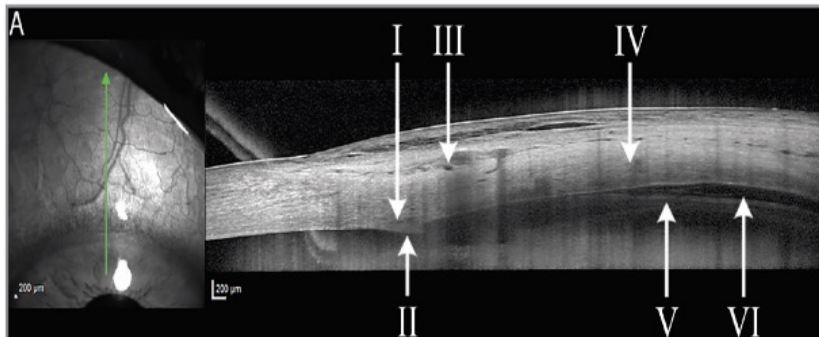
orbitalds.com

## Microneedle



clearsidebio.com

# OCT shows SCS expansion after SC injection in humans



# Suprachoroidally injected triamcinolone acetonide (CLS-TA) for uveitic ME

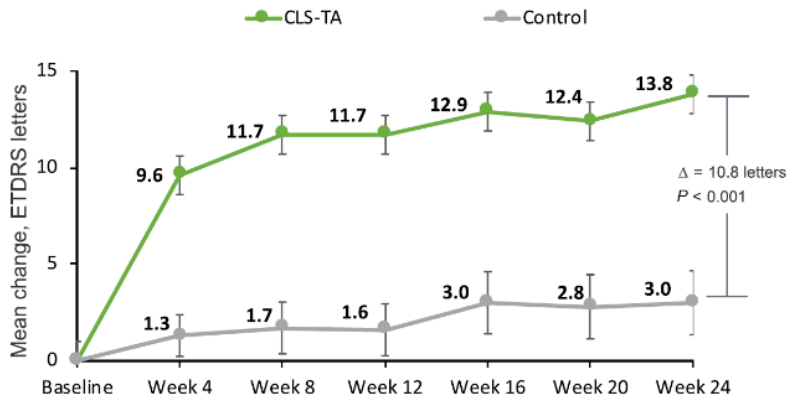


Phase 2 TANZANITE study  
RVO + CME

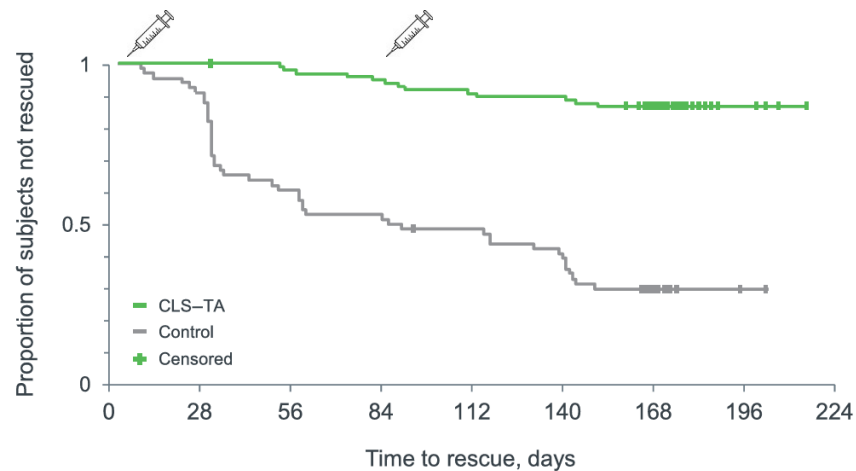
Phase 3 PEACHTREE study  
**Uveitic ME**

Phase 1/2 HULK study  
DME

Phase 1/2 OASIS study  
nAMD



Intention-to-treat population; LOCF imputation. †-test. Differences between the CLS-TA and control arms were significant at each visit.



N = 160 patients with uveitic CME  
Suprachoroidally injected CLS-TA vs. sham (3:2) at day 0 & week 12

# IRIS study of real-world durability of suprachoroidally injected triamcinolone acetonide for uveitic ME

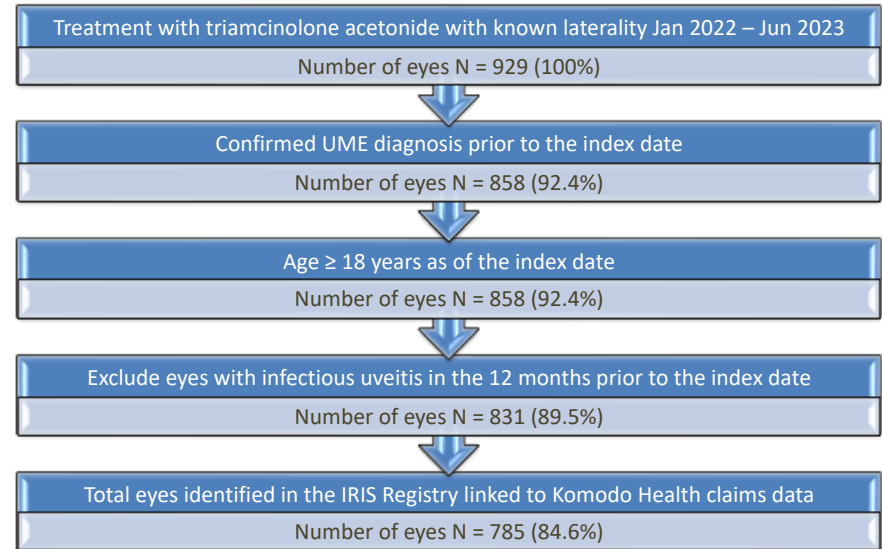
## Inclusion criteria

- Age  $\geq 18$  years
- Diagnosis of non-infectious UME
- Suprachoroidal injection of triamcinolone acetonide

## Study Design

- Dates: Jan 2022 to Jun 2023
- Index date: first suprachoroidal triamcinolone acetonide injection
- Rescue: any injectable, implanted, or topical cortical steroids
- Follow-up: 24 weeks

IRIS<sup>®</sup> Registry (Intelligent Research in Sight) linked to Komodo open-source claims data using the Datavant token to identify corticosteroid use



# Study demographics & comorbidities



Total eyes	831 (100.0%)
<b>Age</b>	
Mean (SD)	68.2 (13.6)
<b>Sex</b>	
Female	55.7%
Male	44.3%
<b>Race</b>	
Asian	1.7%
Black or African American	9.4%
White	65.8%
Other races	8.3%
Unknown	14.8%
<b>Ethnicity</b>	
Hispanic	4.8%
Non-Hispanic	64.7%
Unknown	30.4%
<b>Insurance / payer type</b>	
Medicare	53.4%
Medicare Advantage	9.7%
Medicaid	4.6%
Commercial	26.0%
Other/Unknown	6.3%

Abbreviations: SD, standard deviation

<b>Ocular comorbidities</b>	
Glaucoma/Ocular Hypertension	41.8%
Cataract	24.7%
nAMD	2.3%
DR with DME	3.5%
DR without DME	4.3%
ME from CRVO	1.6%
ME from BRVO	2.6%
Retinal Detachment	14.4%
Posterior uveitis	81.1%
Panuveitis	14.6%

Abbreviations: DR, diabetic retinopathy; DME, diabetic macular edema; ME, macular edema; CRVO, central retinal vein occlusion; BRVO, branch retinal vein occlusion

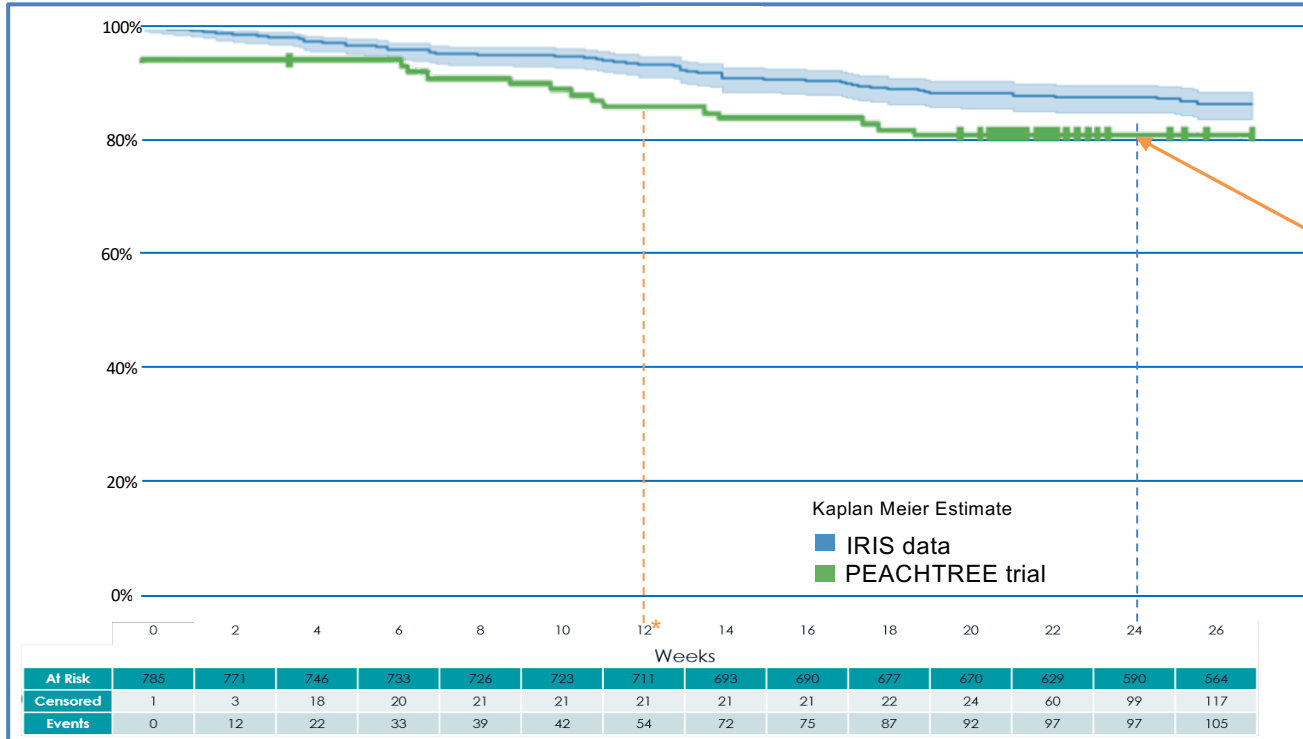
<b>Treating provider subspecialty</b>	
Retina/Vitreous Specialist	86.3%
Cataract/Anterior Segment Specialist	5.9%
Other/Unknown	7.9%

<b>Prior corticosteroid use*</b>	
Injectable/implantable with or without topical	35.2%
Topical only	17.3%

\* This was only evaluated in the 786 patients whose data could be linked to claims

41.8% of patients had glaucoma or ocular hypertension prior to suprachoroidal injection of triamcinolone acetonide

# Time to rescue with injectable / implantable corticosteroid

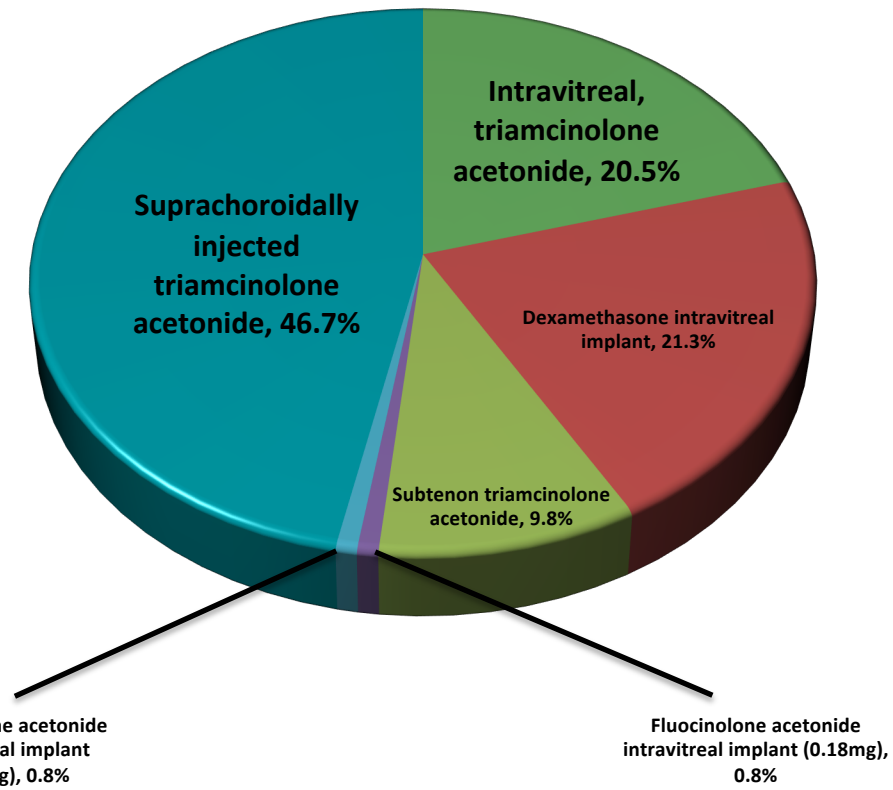


In PEACHTREE 86.5% did not require rescue therapy by week 24

\*In PEACHTREE, all subjects had a second injection at week 12

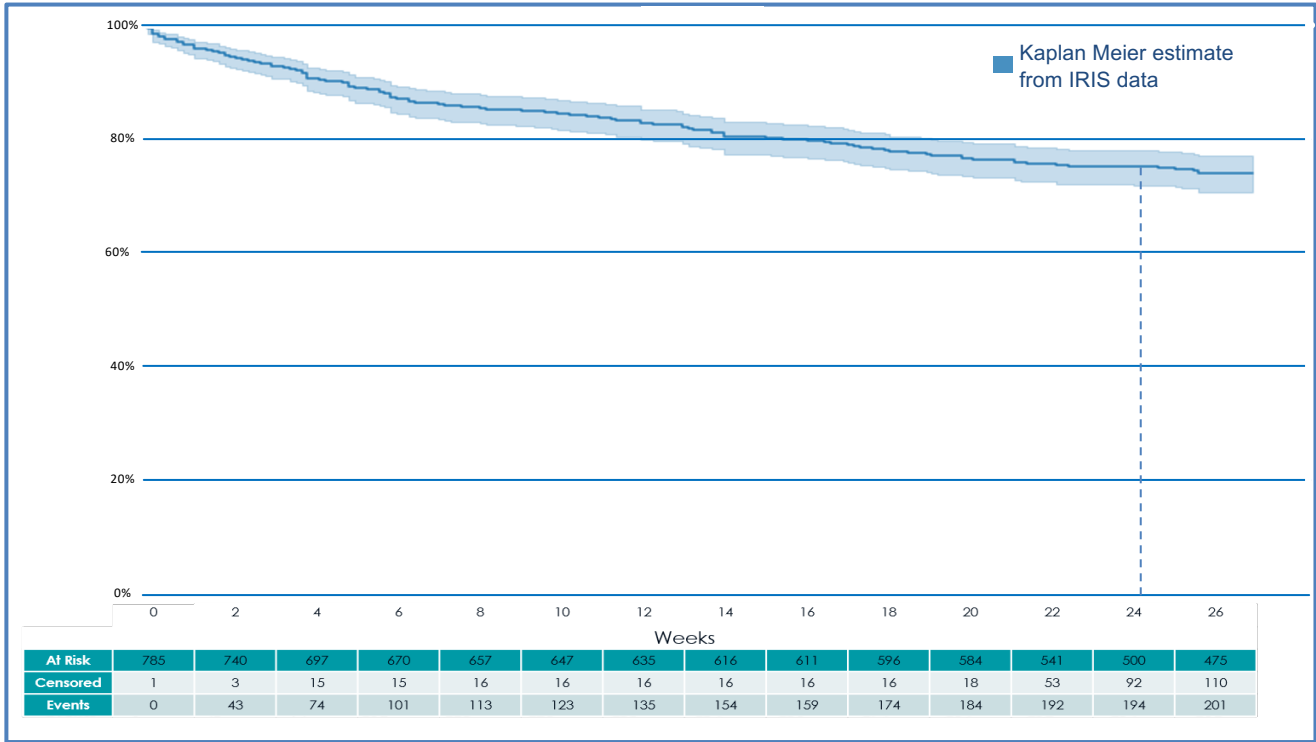
87.7% of eyes did not require an injected or implanted corticosteroid by week 24

# Types of injected / implanted rescue therapy





# Time to rescue with any corticosteroid (including topical)



**75.4% of eyes did not require any corticosteroid by week 24**

# Patient considerations for suprachoroidal injections

## Patient Selection

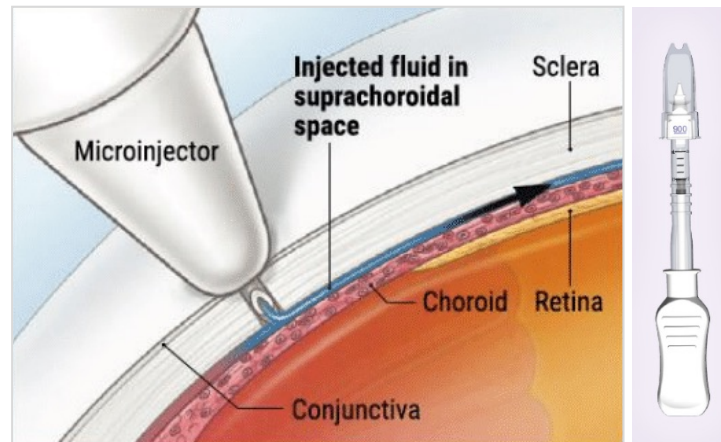
- High myopia or axial length
- Known scleral thinning
- History of glaucoma or hypotony
- History of ocular surgery (esp. trabeculectomy or glaucoma shunt)

## Patient Expectations

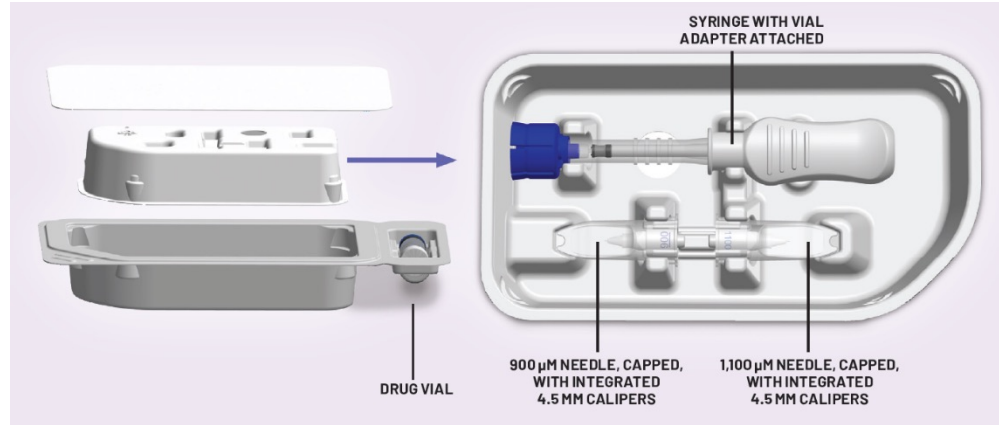
- Sensation of “pressure wave”
- Longer duration of procedure
- Possible change in needle or injection site

## Patient Preparation

- Patient in supine position with head support
- Topical or subconjunctival anesthetic
- Povidone-iodine antiseptic
- Lid speculum recommended



# Needle lengths & injection locations



Two needle lengths:  
900 μm & 1,100 μm

Preferred locations:  
Superotemporal or  
Inferotemporal

# Suprachoroidal injection technique

**RETINA**  
THE JOURNAL OF RETINAL AND VITREOUS DISEASES

REVIEW

### SUPRACHOROIDSAL SPACE INJECTION TECHNIQUE

#### Expert Panel Guidance

Wykoff, Charles C. MD, PhD<sup>1</sup>; Avery, Robert L. MD<sup>2</sup>; Barakat, Mark R. MD<sup>3,4</sup>; Boyer, David S. MD<sup>5</sup>; Brown, David M. MD<sup>6</sup>; Brucker, Alexander J. MD<sup>7</sup>; Cunningham, Emmett T. Jr MD, PhD, MPH<sup>8,9,10,11</sup>; Heier, Jeffrey S. MD<sup>12</sup>; Holekamp, Nancy M. MD<sup>13,14</sup>; Kaiser, Peter K. MD<sup>15</sup>; Khanani, Arshad M. MD, MA<sup>16,17</sup>; Kim, Judy E. MD<sup>18</sup>; Demirci, Hakan MD<sup>19</sup>; Regillo, Carl D. MD<sup>20</sup>; Yiu, Glenn C. MD, PhD<sup>21</sup>; Ciulla, Thomas A. MD, MBA<sup>22</sup>

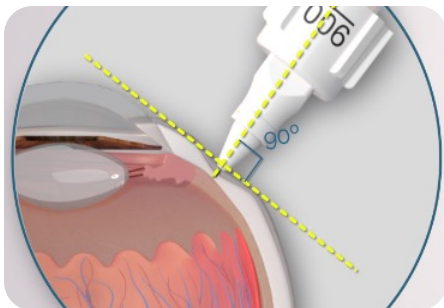
**RETINA**  
SPECIALIST

### A beginner's guide to suprachoroidal injections

They require a different skill set than intravitreal injections. Here's a description of the technique.

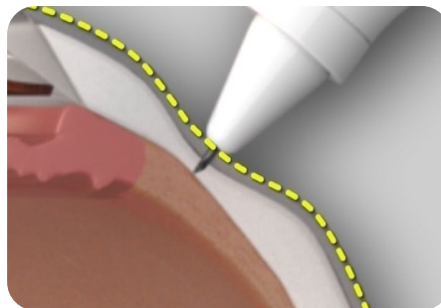
By Carol Villafuerte-Trisolini, MD, and Glenn Yiu, MD, PhD

DECEMBER 23, 2023



**Perpendicular**

Hold the microinjector **perpendicular** to the ocular surface



**Dimple**

Ensure firm contact with sclera by maintaining a **dimple** throughout injection



**Slow**

Inject **slowly** over 5 – 10 seconds

# Gene Therapy Drug Development for Geographic Atrophy

- To date, intravitreal biologics have failed in geographic atrophy (GA)
- Biofactory gene therapy uses retinal cells to produce biologics
- Intravitreal delivery: gene therapy mostly transfects inner retina and non retinal cells, so would be similar to intravitreal biologics
- Subretinal delivery: even for wet AMD, it has been difficult for patient acceptance; therefore, may be even more difficult for GA without foveal involvement and good vision
- Suprachoroidal delivery: could be the preferred way to go



# Key Takeaways

- SCS Microinjector® enables targeted in-office delivery to the suprachoroidal space
- Clearside is the leader with FDA-approved product, XIPERE® (triamcinolone acetonide injectable suspension), for suprachoroidal use to treat uveitic macular edema
- Durability of suprachoroidally injected triamcinolone acetonide in the real-world is comparable to Phase 3 trial results, with only ~12% needing subsequent corticosteroid within 24 weeks
- Suprachoroidal delivery represents a new and innovative technique that has many potential applications beyond delivering steroids, including angiogenesis inhibitors and gene therapies

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# VICTOR CHONG, MD, MBA

Clearside Chief Medical Officer

*Pipeline Opportunities*

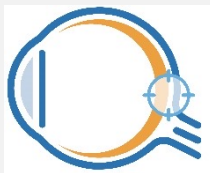


# Benefits for Patients and Physicians Using SCS Microinjector<sup>®</sup> Delivery



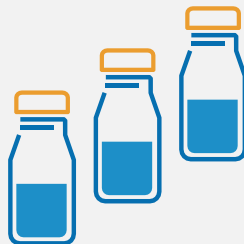
## Enhanced Safety

Much lower risk of endophthalmitis as direct contact to immune system vs intravitreal injection



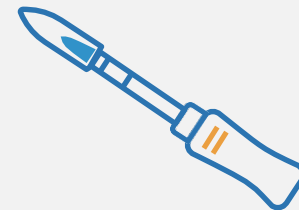
## Injectate Flows to Back of the Eye

Reduced risk of floaters, snow globe effect, or other visual disturbances



## No Implants or Devices in the Vitreous

Can be easily re-dosed for potentially longer durability



## Injection Similar to Intravitreal

Advanced technology requires only a few seconds longer for each injection

# Competitive Advantage in Needle Gauge Diameter

Outer Diameter of the Needle  
*Relative to the Ocular Tissue*

22G

Inner Diameter of the Needle  
*Drug Product Passage*

**30G needle results in less damage to the ocular tissue**

wound size to the ocular tissue is

>4x greater with 22G Needle

>2x greater with 25G Needle

25G

30  
G

Clearside  
SCS Microinjector®



# CLS-AX: Wet AMD Clinical Development Program



# Leveraging a Highly Potent Pan-VEGF Inhibitor with Suprachoroidal Delivery



# Differentiated Approach to Targeting Wet AMD

CLS-AX target profile: maintain visual acuity without need for retreatment for potentially up to 6 months

## Key CLS-AX Program Features

Opportunity for treatments that may have longer duration of action in multi-billion-dollar market



## Potential CLS-AX Competitive Advantages

2 - 3x/year maintenance dosing compared to approved drugs\*:

LUCENTIS®: 12x/year | VABYSMO®: 3 - 6x/year  
EYLEA®: 6x/year | EYLEA HD®: 3 - 4x/year

Utilizes the same SCS Microinjector device as FDA-approved product XIPERE



Competitors' delivery devices differ from their approved products

Objective is to maintain efficacy and reduce the number of injections and required visits



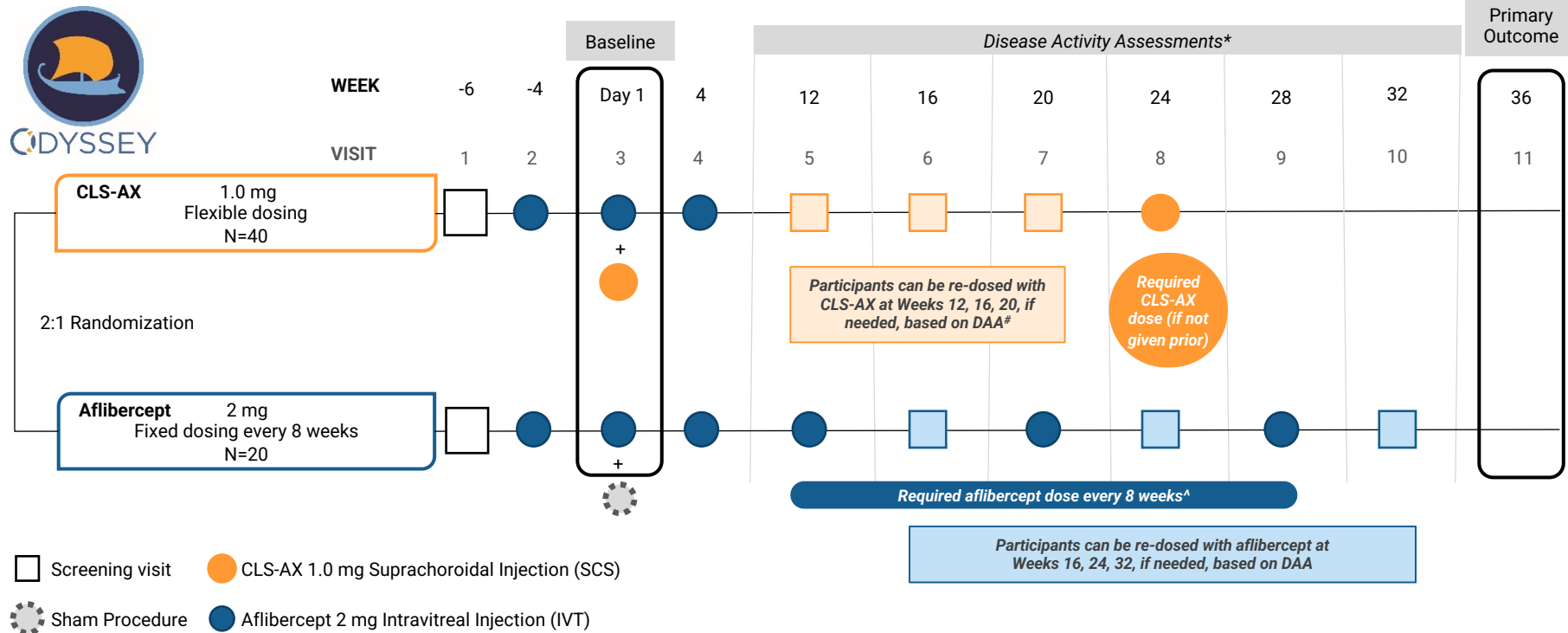
Reduced treatment burden benefits patients, caregivers and payors with improved outcomes

Re-dosing incorporated in Phase 2b design to provide insight for Phase 3 program



Allowing re-dosing comparable to VABYSMO® and EYLEA HD® in real-world setting

# Multiple Dosing Requirement To Help Inform Phase 3 Development Program



<sup>#</sup>Participants can be re-dosed with CLS-AX up to every 12 weeks

\* Disease Activity Assessments (DAA): Conducted at Week 12 through 32 to determine need for supplemental treatment.

# In CLS-AX arm, following 3 loading doses of aflibercept and initial dose of CLS-AX at Baseline, participants will receive CLS-AX at least every 24 weeks unless more frequently required based on DAA; if disease is active and participant is <12 weeks since last CLS-AX injection, participant receives dose of aflibercept; if disease is active and participant is >12 weeks since last CLS-AX injection, participant receives dose of CLS-AX.

<sup>^</sup> In aflibercept arm, following 3 loading doses of aflibercept, participants will receive aflibercept on fixed dosing regimen every 8 weeks unless more frequently required based on DAA; if disease is active, participant receives dose of aflibercept.

## ODYSSEY Phase 2b Key Differences

### Re-dosing with CLS-AX

Every patient in the CLS-AX group will be re-dosed at least once

### 36 Week Treatment Duration

Anticipated primary endpoint duration of Phase 3 wet AMD study based on FDA draft guidance

### Other longer duration therapies (other TKIs, gene therapy) need rescue with anti-VEGF

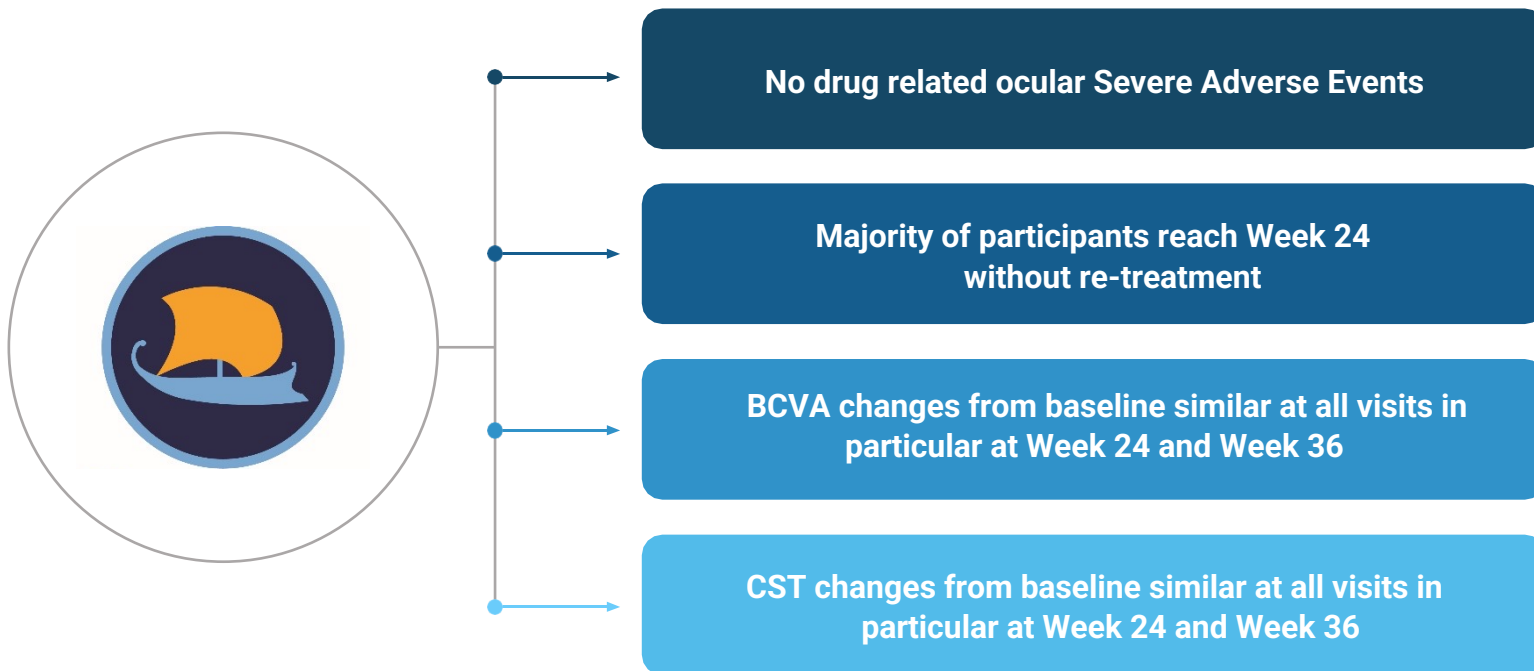
Harder to implement in clinical practice as patients do not want to come in for a scan every 4 weeks as in clinical trials



## ODYSSEY Update

- All participants in the study have completed 6 months of treatment
- Participants in the CLS-AX arm have received two doses of CLS-AX per protocol
- In July 2024 meeting, the ODYSSEY Safety Review Committee (SRC) reviewed masked safety data and recommended that the trial continue as planned without modifying the protocol or unmasking of the participants
- SRC noted that there have been no drug-related Serious Adverse Events (SAEs) in masked study treatments observed to date, including no endophthalmitis or retinal vasculitis
- On-track to release top-line data in late Q3 2024

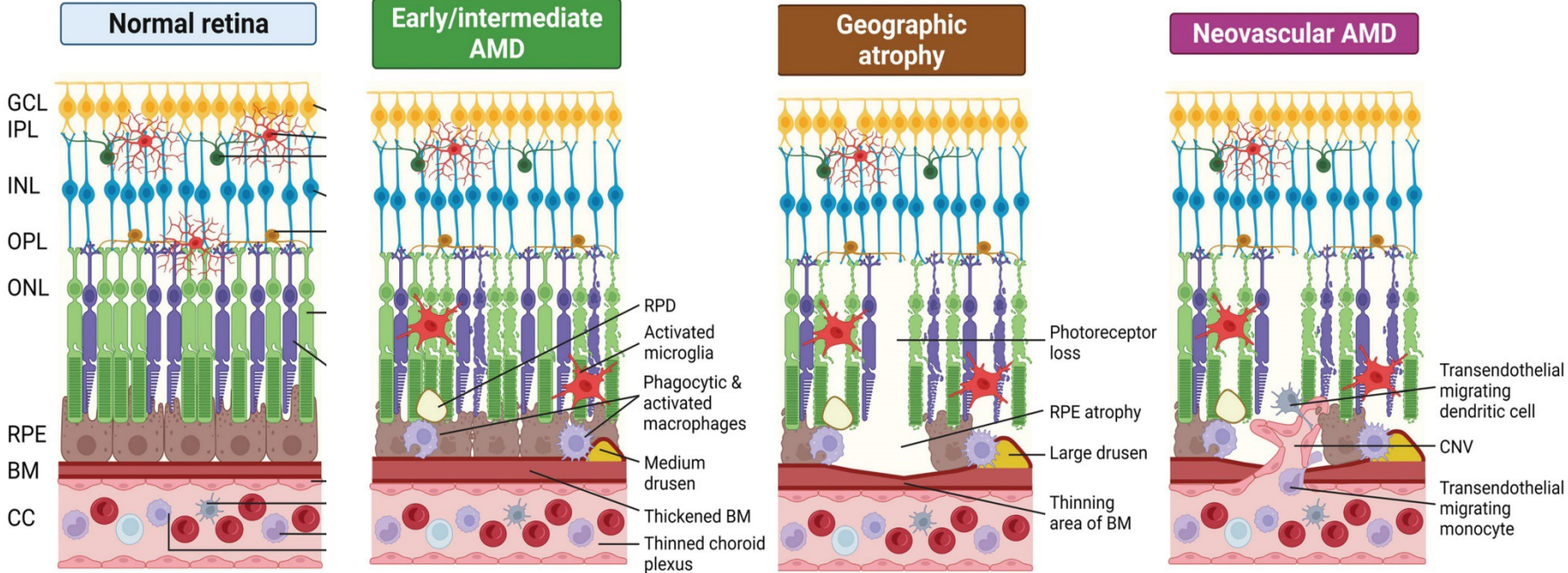
## Our Target Success Measures for ODYSSEY



# Pipeline Expansion Opportunity in Geographic Atrophy



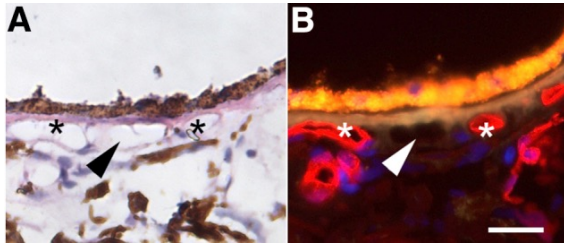
# Pathology of Age-Related Macular Degeneration (AMD)



# Geographic Atrophy is a Choroidal Disease

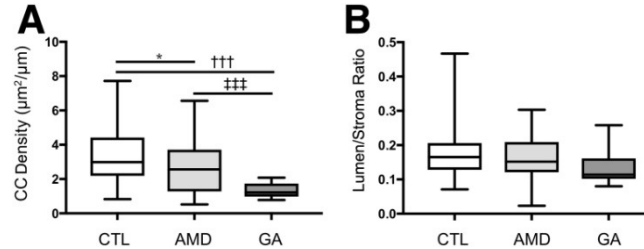
## Choroidal Hypoxia Theory and Choriocapillaris are Damaged First

1



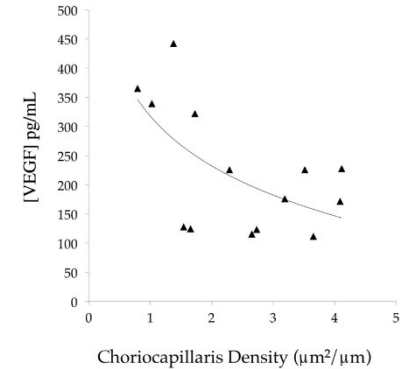
Choriocapillaris endothelial cells damage with ghost vessels before any significant RPE changes

2



- Choriocapillaris (CC) vascular density is significantly lower in GA donor
- No meaningful differences in vascular lumen area / stroma area

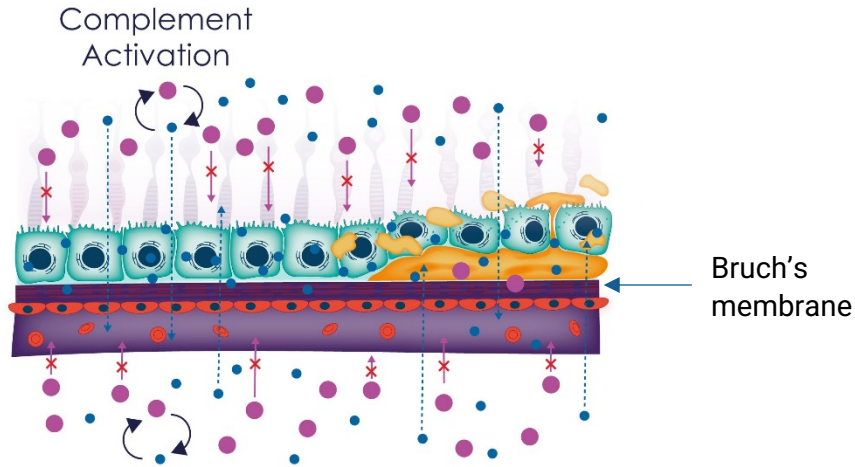
3



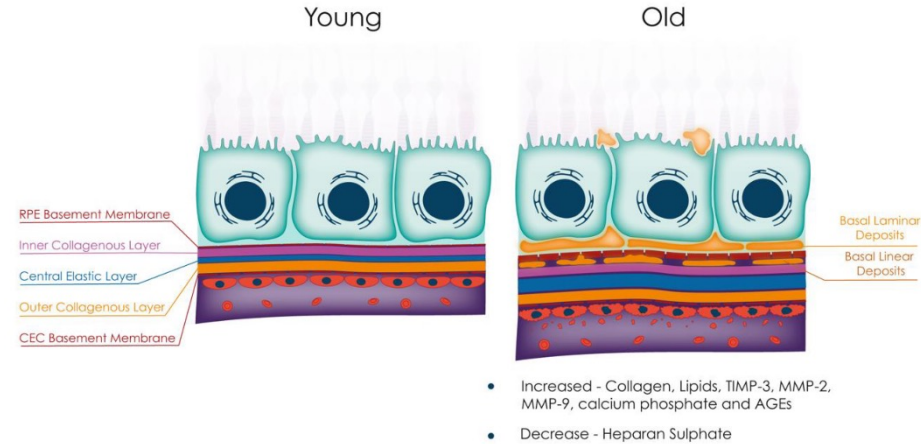
VEGF level increased with low vascular density support the choroidal hypoxia theory



# Small Molecule Can Access the Diseased Area of the RPE and Choroid

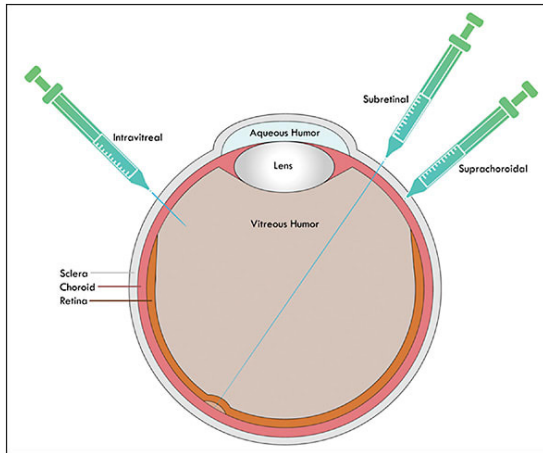


Larger molecules cannot get through Bruch's membrane  
So, if given intravitreally, it can only treat the RPE side



Aging intensifies disease actions and even peptides might not be able to get through

# Suprachoroidal Administration Could Be Preferred Delivery Method



	Setting	Distribution	Deliver large molecules	Deliver small molecules	Gene therapy
<b>Suprachoroidal</b>	Office	Posterior segment	Not used	Suspension	RPE and <b>Choroid</b>
Intravitreal	Office	Widespread in eye	Standard	Implant	Mostly ganglion cells
Subretinal	Operating room	Localized to treatment bleb	Not used	Not used	Photoreceptor and RPE
Systemic	Home	Whole body	Need injection	Oral	Liver



# Potential Advantages of Suprachoroidal Delivery in Geographic Atrophy

Potential Target Product Profile (TPP) Aligns with SCS Suspension or SCS Gene Therapy



## Able to reach the choroid first

- Fluid spreads circumferentially and posteriorly when injected within the suprachoroidal space, bathing the choroid, RPE, retina and adjacent areas with drug

## Small molecules may have better efficacy than current therapies

- Potential to treat complement activation in both RPE and choroid

## Suprachoroidal suspension/gene therapy may have longer duration (3 to 6 months)

- Intravitreal gene therapy may not achieve efficacy
- Subretinal has additional risks

## Less invasive, in-office procedure

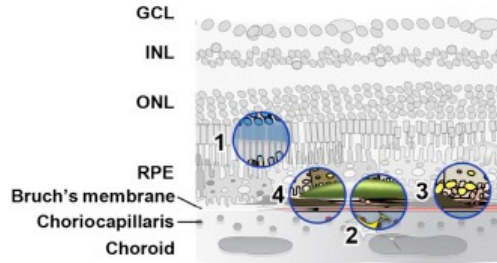
- Systemic therapy may be effective, but potential infection risks in this elderly population
- Local ocular therapy may have fewer adverse events

## Targeted delivery compartmentalized to the posterior segment

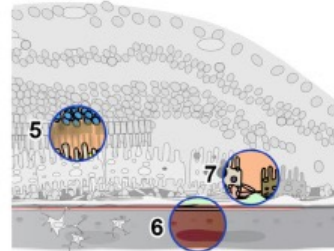
- Potentially fewer adverse events

# Traditional Target Pathways for Geographic Atrophy

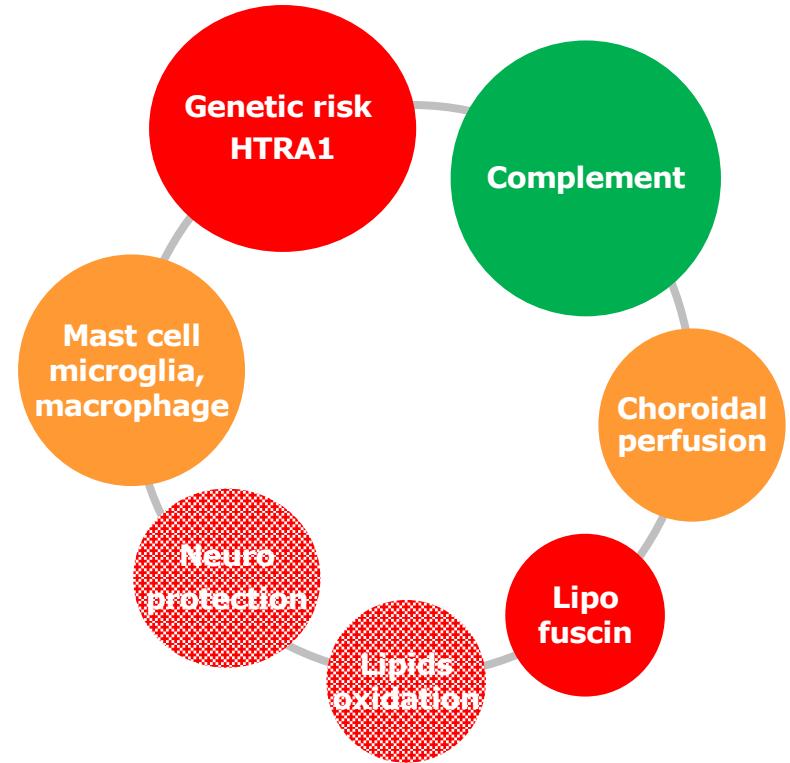
## Pathways and Therapeutic Targets in Dry AMD



- ~~1. Visual cycle toxic by products~~
  - Visual cycle modulators
2. Inflammation, complement, and ECM
  - mTOR inhibitors
  - Complement inhibitors
  - MMP inhibitors
3. Lipoprotein accumulation
  - LDL-lowering drugs
- ~~4. Beta-amyloid accumulation~~
  - Anti-amyloid beta



5. Oxidative stress
  - Anti-oxidants
  - Neuroprotectant
6. Choriocapillaris atrophy
  - Choroidal perfusion enhancers
7. RPE and photoreceptor loss
  - Stem cell therapy
  - Neurotrophins



# DAVID M. BROWN, MD

Director of Research, Retina Consultants Houston

*Large Practice View of Suprachoroidal Delivery*

# IVT vs SCS Procedure Time Comparison in Optimized High-Volume Practice

## Intravitreal (IVT) Timeline

Injection as Percentage of Total Time: 0.57%\*

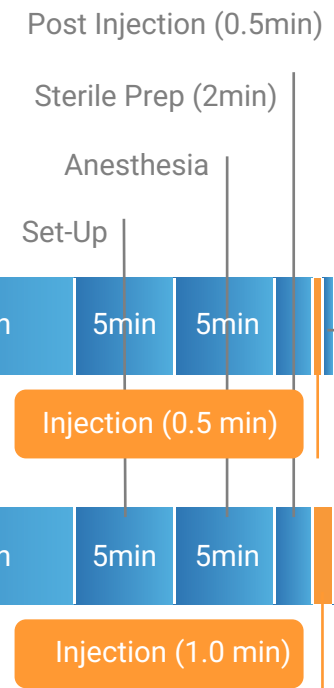


## Suprachoroidal (SCS) Timeline

Injection as Percentage of Total Time: 1.1%#



30 sec increase in doctor's time performing procedure



\*IVT Injection as % of Total Time: 0.5 min / (45 + 15 + 15 + 5 + 5 + 2 + 0.5 + 0.5) min = 0.57%

#SCS Injection as % of Total Time: 1.0 min / (45 + 15 + 15 + 5 + 5 + 2 + 1.0 + 0.5) min = 1.1%

## Learning from Phase 3 Designs of Aflibercept 8mg and Faricimab

- Understanding wet AMD patients have variable dosing frequency requirements
- Aflibercept 8mg and Faricimab extension criteria are not typically used in clinical practice
  - However, physicians are using them as a replacement of other anti-VEGF in Treat and Extend
- Ideal Phase 3 design for longer duration wet AMD therapy
  - Re-treatment extension criteria closer to clinical practice
  - Treatment naïve patients: to allow more direct comparison to established therapy

# Discussion with Dr. Brown



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