CLEARSIDE BIOMEDICAL

Eyecelerator Company Showcase
October 17, 2024

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CMO and EVP
Clearside Biomedical, Inc.

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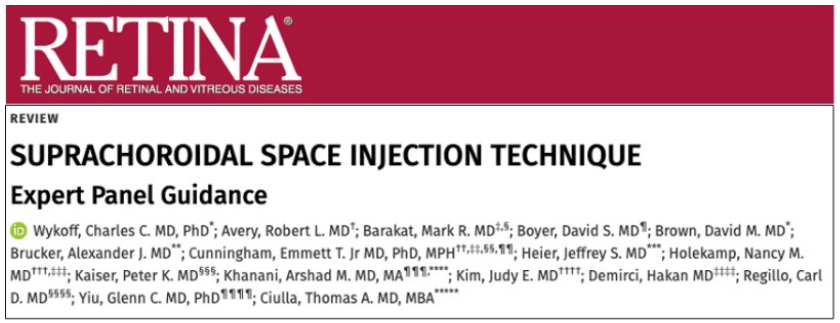
Delivering on the Potential of the Suprachoroidal Space

- **Validated Suprachoroidal Space (SCS) Delivery with Approved Product, Multiple Collaborations, and Comprehensive IP Portfolio**
- **Proven Leader in Suprachoroidal Delivery with Thousands of Injections Performed in the Clinic**
- **Differentiated SCS Clinical Program Targeting Multi-Billion Dollar Wet AMD Market**

Straightforward Suprachoroidal Injection Technique

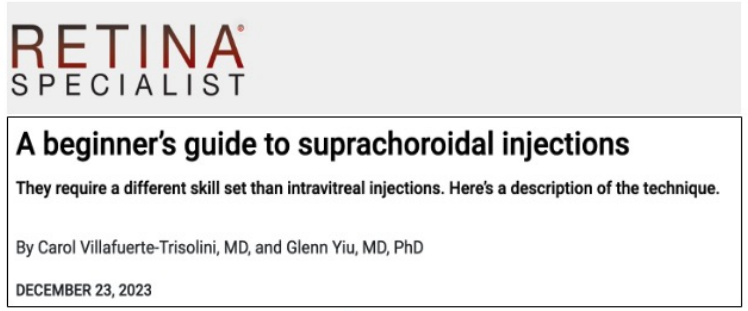

RETINA
THE JOURNAL OF RETINAL AND VITREOUS DISEASES

REVIEW

SUPRACHOROIDAL SPACE INJECTION TECHNIQUE

Expert Panel Guidance

Wykoff, Charles C. MD, PhD*; Avery, Robert L. MD†; Barakat, Mark R. MD‡,§; Boyer, David S. MD¶; Brown, David M. MD*; Brucker, Alexander J. MD**; Cunningham, Emmett T. Jr MD, PhD, MPH††,‡‡,§§,¶¶; Heier, Jeffrey S. MD***; Holekamp, Nancy M. MD†††,‡‡‡; Kaiser, Peter K. MD§§§; Khanani, Arshad M. MD, MA¶¶¶,****; Kim, Judy E. MD††††; Demirci, Hakan MD‡‡‡‡; Regillo, Carl D. MD§§§§; Yiu, Glenn C. MD, PhD¶¶¶¶; Ciulla, Thomas A. MD, MBA*****

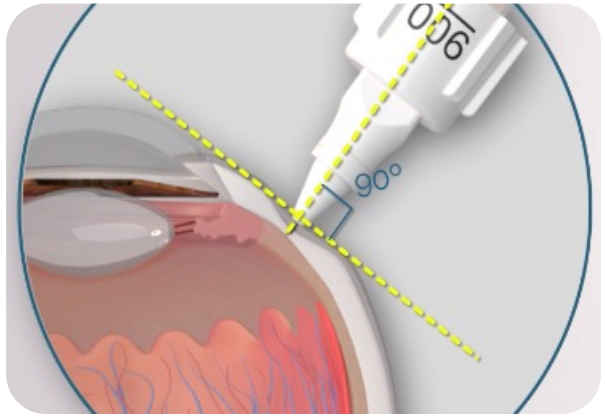

RETINA SPECIALIST

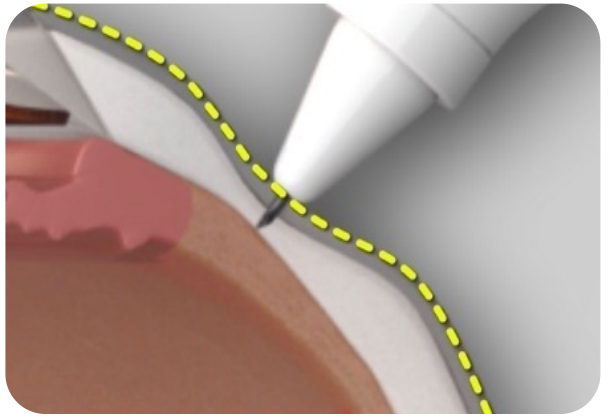
A beginner's guide to suprachoroidal injections

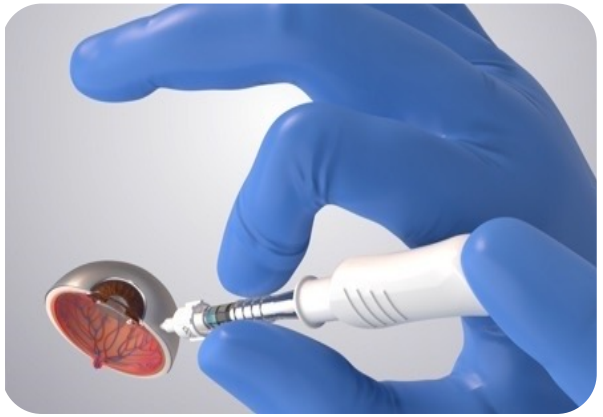
They require a different skill set than intravitreal injections. Here's a description of the technique.

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

DECEMBER 23, 2023







Perpendicular

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

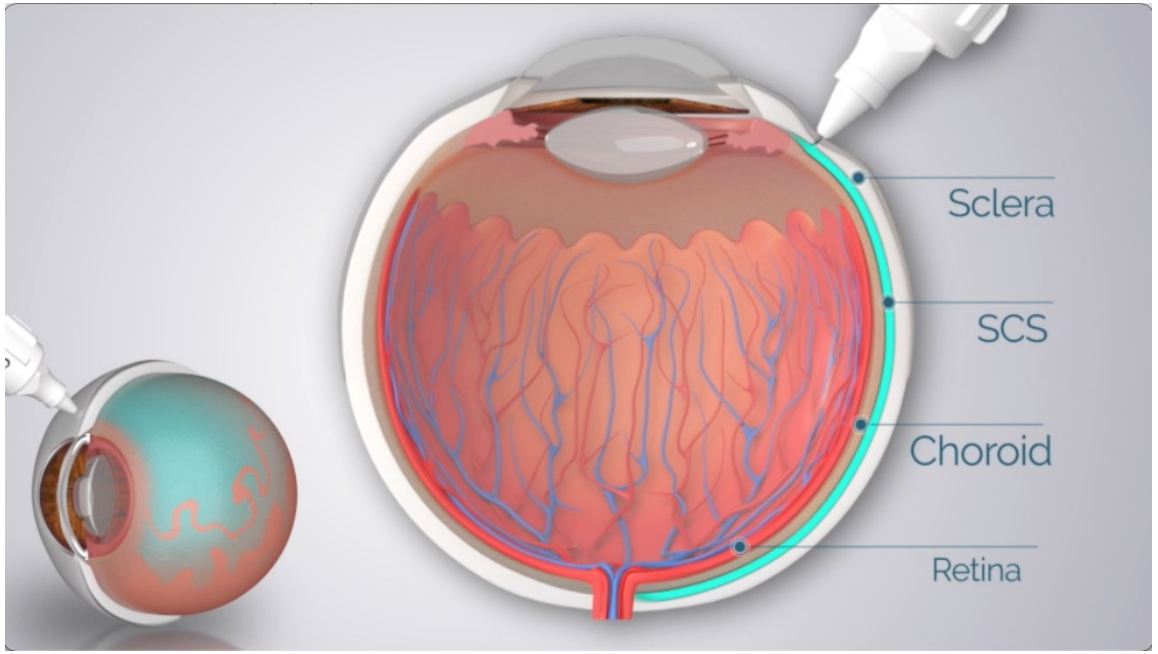
Dimple

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

Slow

Inject **slowly** over 5 – 10 seconds

SCS Microinjector®: Drug/Device Combination with Proven Versatility



SUPRACHOROIDAL SPACE INJECTION

Novel SCS Microinjector® shows a demonstrated ability for precise delivery into the suprachoroidal space

- **First and Only FDA-approved SCS product**
- **Multiple clinical trials with 4 potential therapies in 5 indications:**
  Wet AMD, UME, DME, DR, Choroidal Melanoma
- **Safety profile of SCS Microinjector comparable to intravitreal injections[1]**
- **Well-accepted by retinal physicians with thousands of injections performed to date**
- **30-gauge needle equivalent to most commonly used intravitreal injections**
  Smaller than tyrosine kinase inhibitor (TKI) competitors in development

Abbreviations: UME = uveitic macular edema; DME = diabetic macular edema; DR = diabetic retinopathy;
Sources: Clearside data on file | [1]Kurup, et. al, Macula Society 2021 *Safety of the Suprachoroidal Injection Procedure Utilizing SCS Microinjector® across Three Retinal Disorders.*

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 - Completed			CDYSSEY
XIPERE®	Corticosteroid *(Triamcinolone Acetonide)*	Uveitic Macular Edema[1] *(U.S. & Canada)*						B+L BAUSCH+LOMB
XIPERE® / ARCATUS™	Corticosteroid *(Triamcinolone Acetonide)*	Uveitic Macular Edema[2] Diabetic Macular Edema[2] *(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 Diabetic Macular Edema			ALTITUDE			REGENXBIO abbvie
ABBV-RGX-314	AAV Gene Therapy	Wet AMD			AAVIATE			REGENXBIO abbvie
Avoralstat	Plasma Kallikrein Inhibitor	Diabetic Macular Edema						bio cryst

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[1]XIPERE® (triamcinolone acetonide injectable suspension), for suprachoroidal use has received U.S. FDA Approval and is being commercialized by Bausch + Lomb.
[2]In China, Arctic Vision is responsible for clinical development of ARCATUS™ (triamcinolone acetonide injectable suspension), formerly referred to as ARVN001, and known as XIPERE® in the U.S.

Phase 2b Topline Data Results

ODYSSEY Phase 2b Clinical Trial

ODYSSEY

Trial Objectives:
Evaluate safety, efficacy & duration of CLS-AX in participants with wet AMD

- Primary Outcomes: Mean change in BCVA from Baseline to **Week 36**; Safety & tolerability
- Secondary Outcomes: Other changes in visual function and retinal imaging, including CST; Need for supplemental treatment; Treatment burden as measured by total injections

Participant Profile:
60 total with 2:1 randomization (40 in CLS-AX arm & 20 in aflibercept arm)

- Treatment experienced participants with reading center confirmation of **persistent active disease**
- Protocol required **re-dosing with CLS-AX** in study arm
  - Participants received at least 2 doses of CLS-AX
  - Provides important data to plan Phase 3 in chronic disease

CLS-AX Demonstrated Positive Efficacy Data in Wet AMD

Overall

Achieved Primary Outcome in participants with confirmed active disease

BCVA

Stable BCVA throughout the trial

Measured as mean change in BCVA from baseline to Week 36

CST

Stable CST throughout the trial

Measured as mean change in CST from baseline to Week 36

Durable Effect

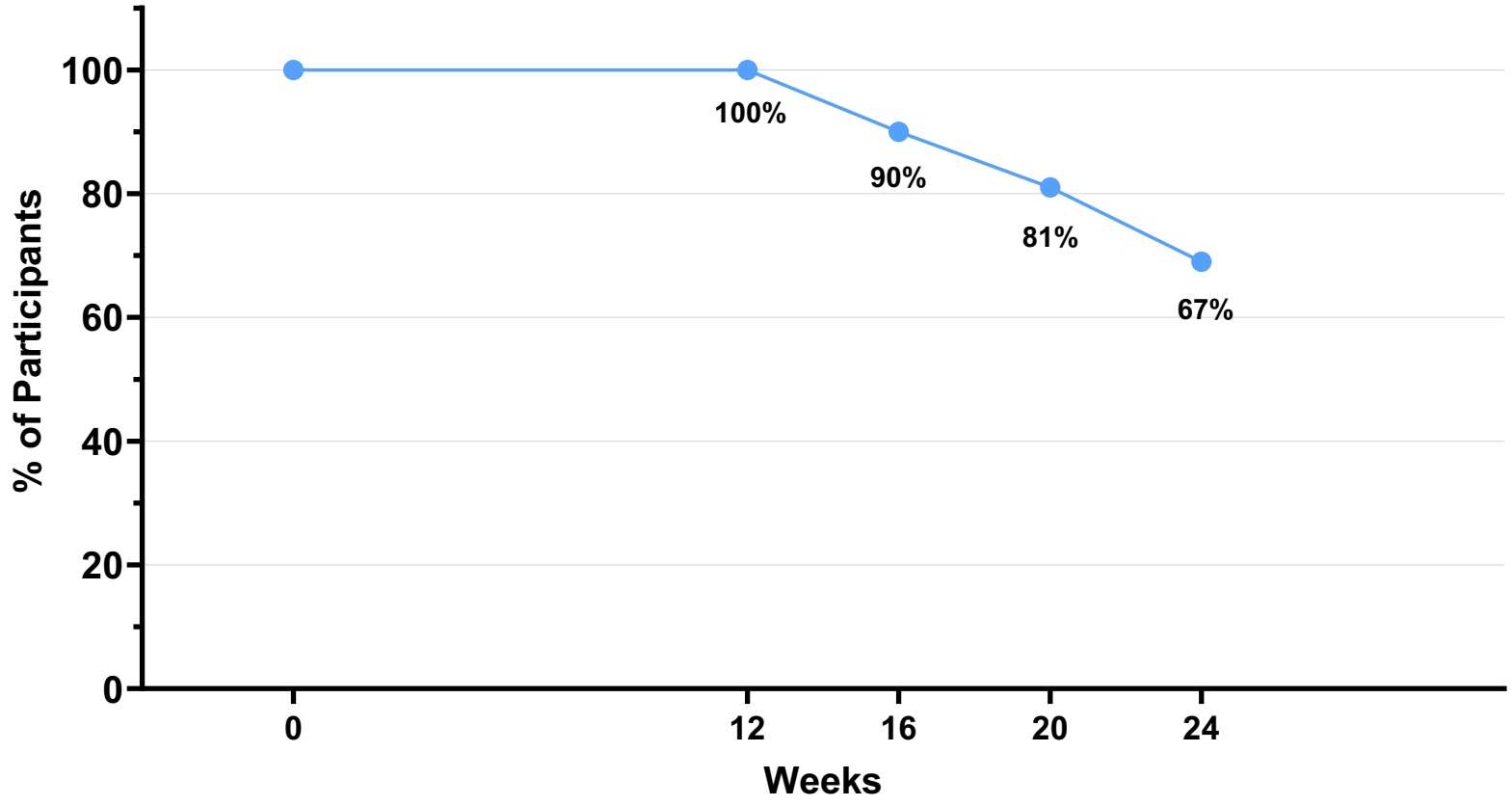
67% of participants did not require any additional treatment for up to 24 weeks (6 months)

Injection frequency reduced by nearly 84% up to 24 weeks

Abbreviations: CST=Central Subfield Thickness
Injection frequency reduction calculated by the average number of treatments 24 Weeks prior to Screening Visit as compared to Average number of treatments up to 24 Weeks after Baseline Visit.

Two-Thirds of Participants Dosed with CLS-AX Reached Six Months Without Additional Treatment

Intervention–Free Rates By Week Up to Each Visit



Week 12: 40/40 (100%)
Week 16: 35/39 (89.7%)
Week 20: 30/37 (81.1%)
Week 24: 26/39 (66.7%)

Calculation accounts for missed treatments; time of initial administration of study drug shown as month 0 on figure. Intervention-free rate calculation: if participant received intervention at a study visit, those were reflected in the count at the following study visit.

CLS-AX Demonstrated Positive Safety Profile

No Ocular SAEs and No Treatment-Related SAEs

- No drug or procedure-related ocular SAEs
- No reported drug or procedure-related systemic SAEs
- No endophthalmitis
- No retinal vasculitis
- Four cases of intraocular inflammation all deemed clinically mild by the Safety Review Committee
  - Two cases had minimal clinical signs that resolved
  - Two cases were potentially related to drug administration
  - In all four cases, the inflammation was no longer detected at or before Week 36

Abbreviations: AE = adverse event; SAE = serious adverse event; TEAE = treatment-emergent adverse event.

Pipeline Expansion
Opportunity in Geographic Atrophy

Focusing on Choroidal Health and Capillary Homeostasis

Differentiated and Promising Approach

Complement inhibition

- Clinically validated
- Approved therapies have limited efficacy

Neuroprotection

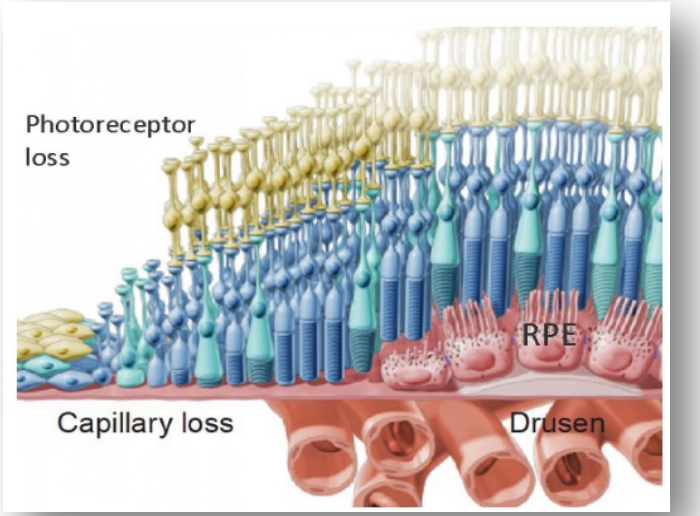
- Promising preclinical evidence
- Limited clinical success

Lipid pathway

- Complex lipid metabolism pathways
- Clinical effectiveness likely to require removal of lipid from Bruch's

Extracellular matrix modulation (HTRA1, TIMP3 & MMPs)

- Molecular mechanism is not controversial
- Anti-HTRA1 failed in clinical trial



Visual cycle modulation

- Lacks robust clinical efficacy
- Multiple failed trials

Reduce choriocapillaris degeneration & improve choroidal perfusion

- Choriocapillaris degeneration precedes RPE and PR loss
- Implicated in the pathophysiology of AMD
- Warrants further clinical investigation

Control proinflammatory microenvironment

- Well-studied inflammatory pathways (macrophages, microglia, mast cells)
- Controls multiple disease-triggering insults

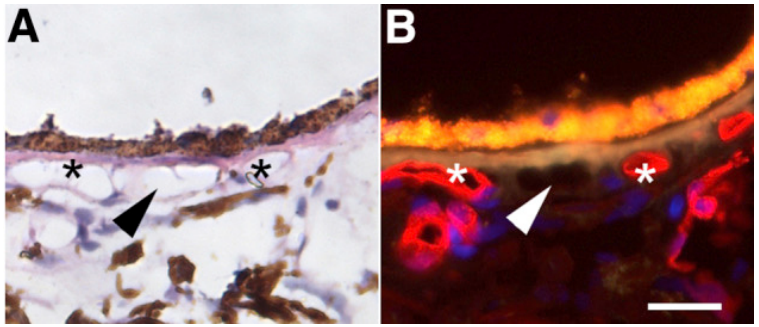
HTRA1: High-Temperature Requirement Factor A1
TIMP3:tissue inhibitor of metalloproteinases 3
MMPs: Matrix Metalloproteinases

Image source: NEI

Geographic Atrophy is a Choroidal Disease

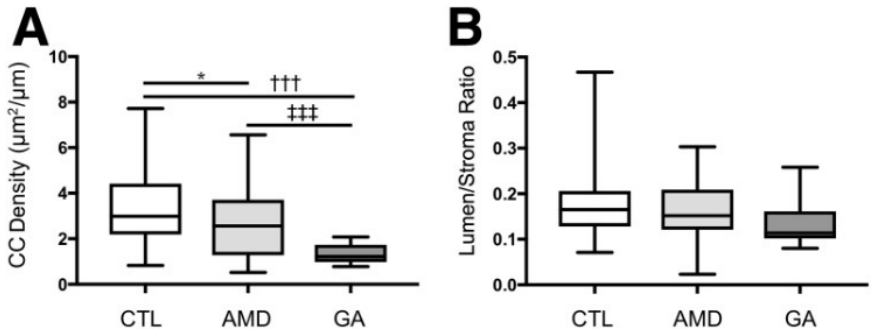
Choroidal Hypoxia Theory and Choriocapillaris are Damaged First

1



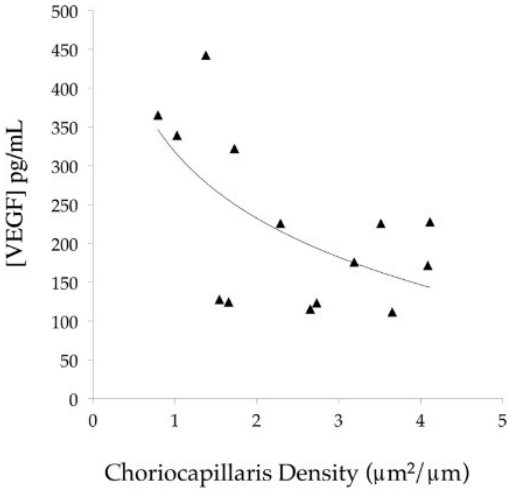
Choriocapillaris endothelial cells damage with ghost vessels before any significant RPE changes

2



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

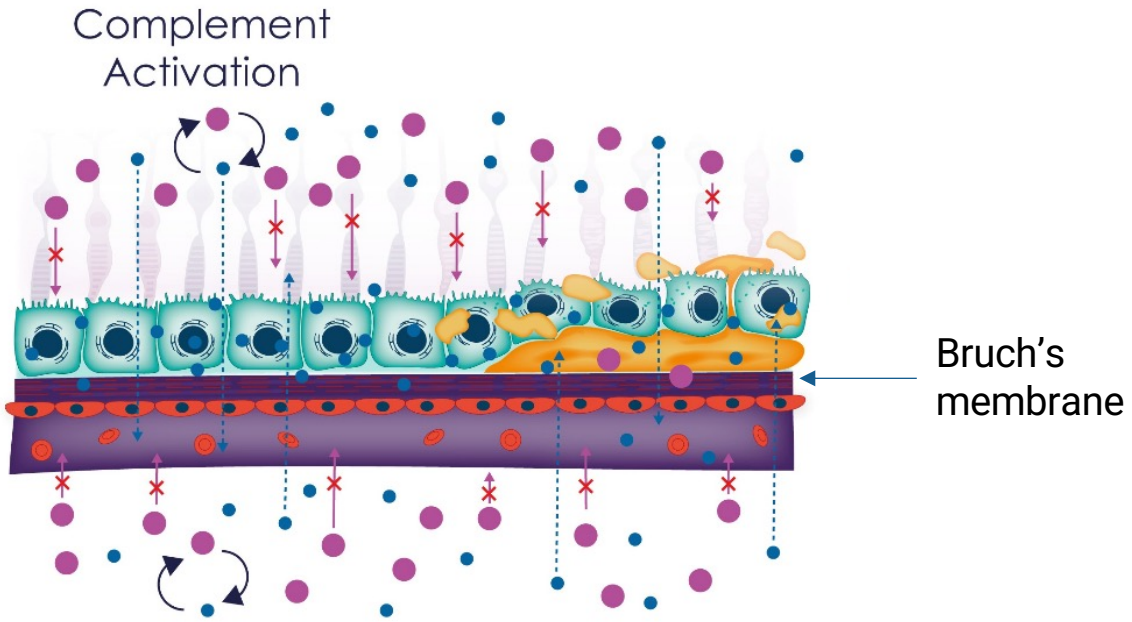
3

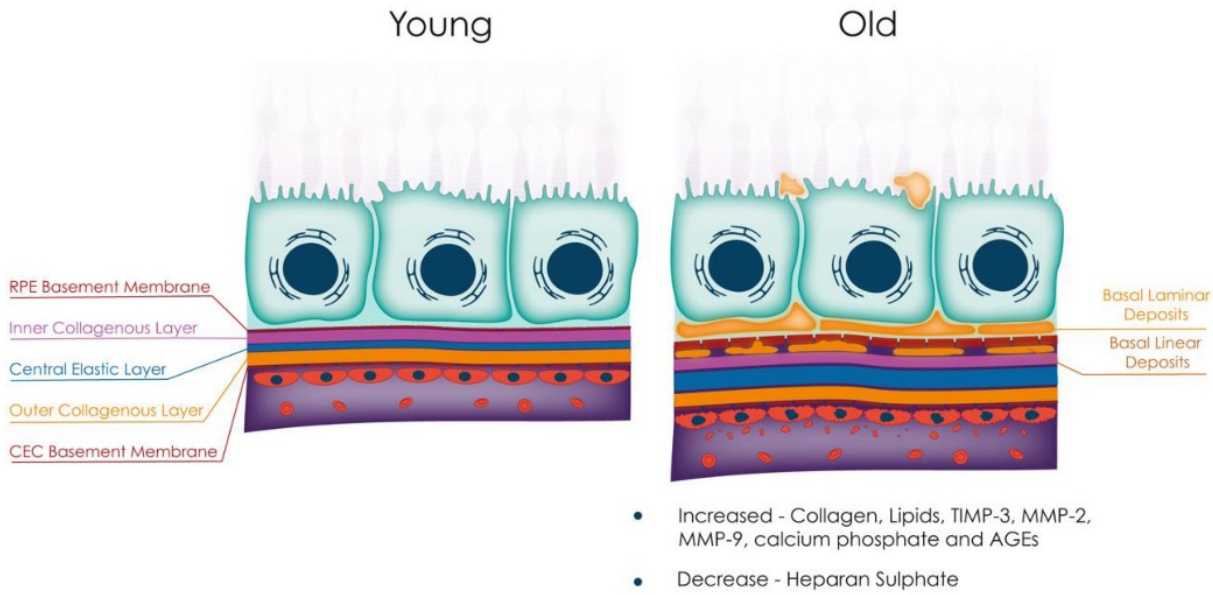


VEGF level increased with low vascular density support the choroidal hypoxia theory

RPE = Retinal Pigment Epithelium
Images modified from Sohn EH et al., Am J Path 2019: 189: 1473-80

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

Images modified from Hammadi et al JCM 2023, 12 (8), 2870

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

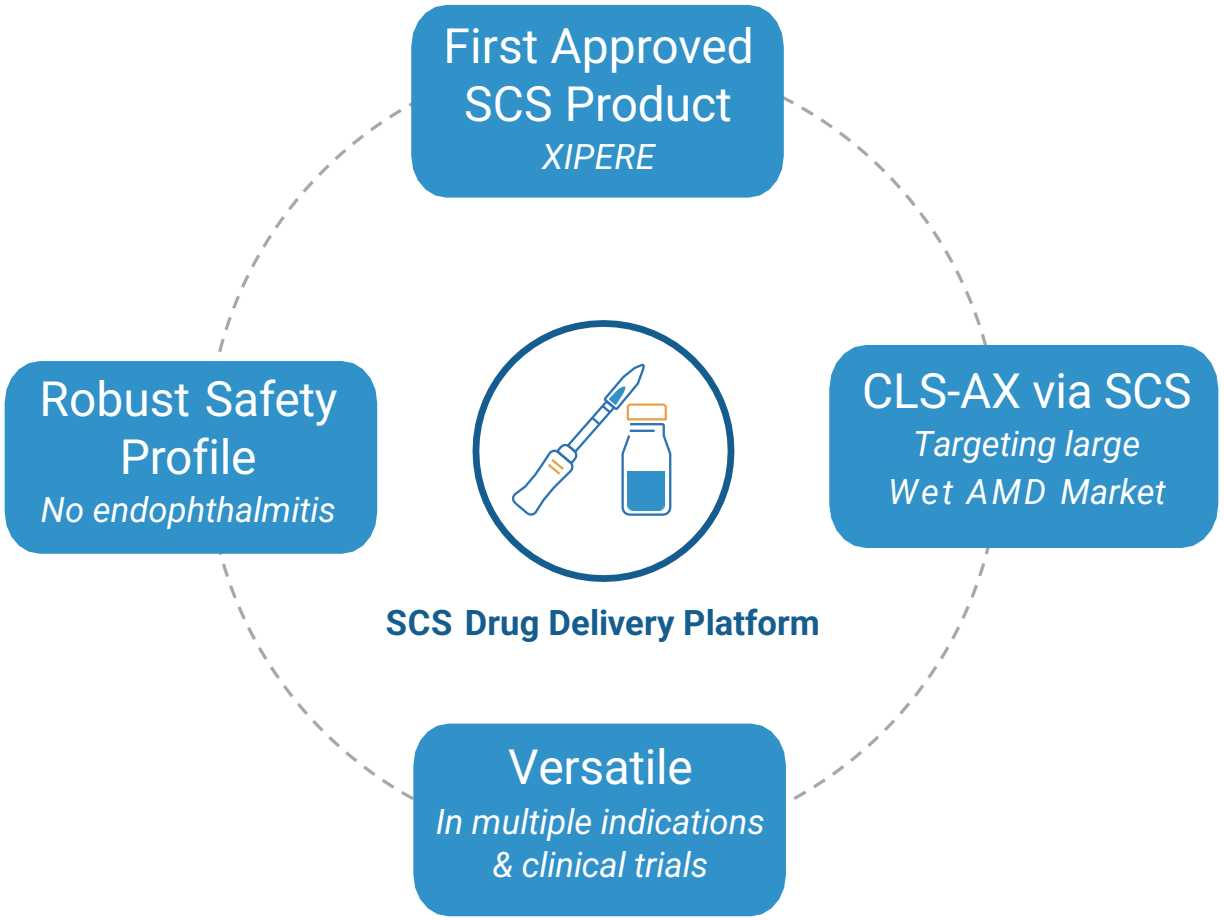
Small molecules may have better efficacy than current therapies
- Potential to treat complement activation in both RPE and choroid

Suprachoroidal gene therapy – potentially better efficacy and might be safer
- Intravitreal gene therapy may not achieve efficacy
- Subretinal gene therapy has additional risks

Less invasive, in-office procedure with potential of longer duration (3 to 6 months)
- 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 ocular adverse events

Innovative and Experienced Leader in Suprachoroidal Drug Delivery



Upcoming Potential Catalysts

CLS-AX (axitinib injectable suspension)

- ✓ **October 9, 2024: ODYSSEY Phase 2b Top Line Results**
- ▪ **H2 2024:** Phase 3 Planning

Medical/Scientific meeting presentations

- ✓ **Q1 2024:** Macula Society; Next Generation Ophthalmic Drug Delivery Summit
- ✓ **Q2 2024:** Retina World Congress; Clinical Trials at the Summit
- ▪ **Q4 2024:** AAO; Asia-Pacific Vitreo-Retina Society; Ophthalmology Innovation Summit

Publications

- ✓ **Q2 2024:** Expert panel practice guidelines on SCS® delivery in *Retina*
- ✓ **H2 2024:** OASIS Data in *Ophthalmology Science*