UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): July 24, 2024

Clearside Biomedical, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-37783**	**45-2437375**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
900 North Point Parkway Suite 200 Alpharetta, Georgia		**30005**
(Address of Principal Executive Offices)		**(Zip Code)**

Registrant's Telephone Number, Including Area Code: 678 270-3631

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.001 per share	CLSD	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On July 24, 2024, Clearside Biomedical, Inc. (the "***Company***") will host a virtual Suprachoroidal Delivery KOL Webinar (the "***Webinar***"). [A webcast of the Webinar will be available through the Events and Presentations page of the Investors section of the Company's website.] The Webinar will include a slide presentation. A copy of this slide presentation is furnished herewith as Exhibit 99.1 to this Current Report on Form 8-K.

In accordance with General Instruction B.2. of Form 8-K, the information in this Item 7.01 and Exhibit 99.1 hereto shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "***Exchange Act***"), or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference in any of the Company's filings under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any incorporation language in such a filing, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Exhibit Description
99.1	Company Presentation.
104	The cover page from Clearside Biomedical, Inc.'s Form 8-K filed on July 24, 2024, formatted in Inline XBRL.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: July 24, 2024

CLEARSIDE BIOMEDICAL, INC.

By: /s/ Charles A. Deignan
Name: Charles A. Deignan
Title: Chief Financial Officer

Exhibit 99.1


CLEARSIDE
BIOMEDICAL
Suprachoroidal Space Drug Delivery
July 24, 2024
TM

Forward-Looking Statements

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

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

03 **Pipeline Opportunities**
Victor Chong, MD, MBA, Clearside Chief Medical Officer

04 **Large Practice View of Suprachoroidal Delivery**
David Brown, MD, Director of Research, Retina Consultants Houston

05 **Q&A**

GEORGE LASEZKAY, PharmD, JD

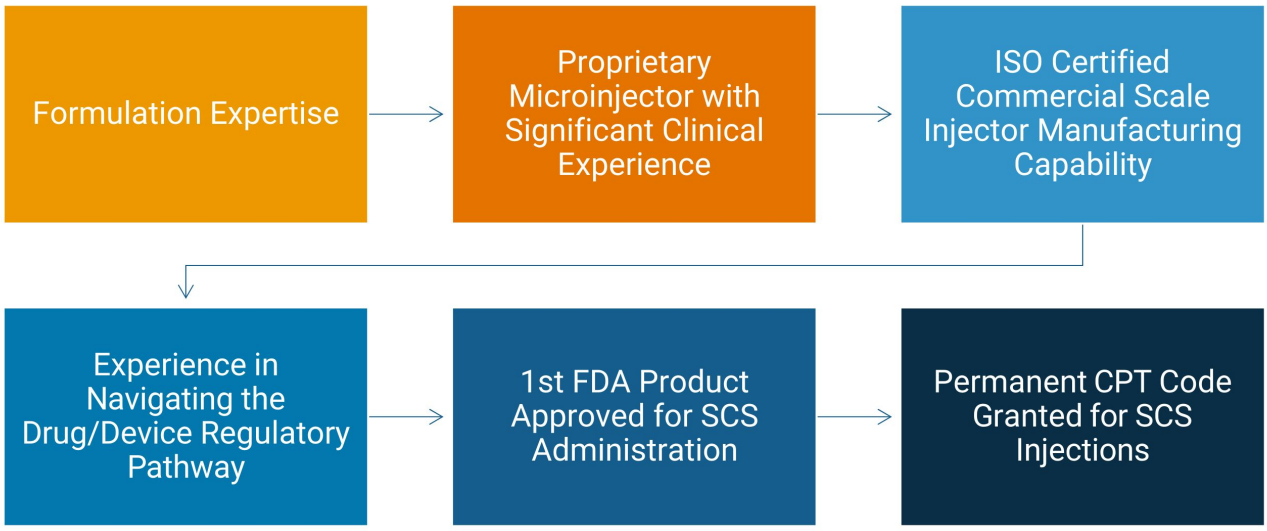
Clearside President & Chief Executive Officer

Versatility of Suprachoroidal Delivery

Delivering on the Potential of the Suprachoroidal Space

- **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[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 (DR)			*ALTITUDE*			REGENXBIO abbvie
ABBV-RGX-314	AAV Gene Therapy	Wet AMD			*AAVIATE*			REGENXBIO abbvie
Avoralstat	Plasma Kallikrein Inhibitor	Diabetic Macular Edema (DME)						bio cryst

CLEARSIDE BIOMEDICAL

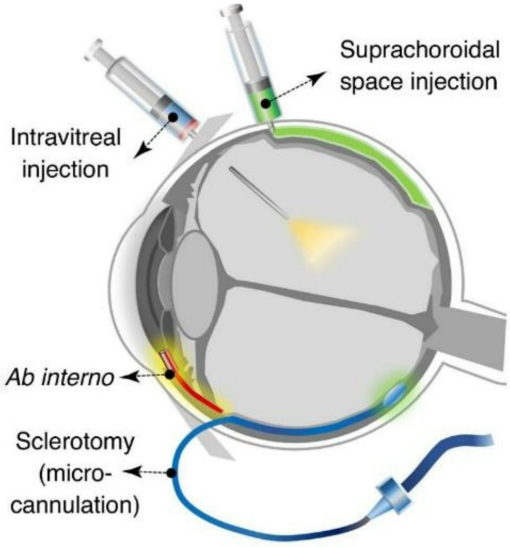
[1]XIPERE® (triamcinolone acetonide injectable suspension), for suprachoroidal use has received U.S. FDA Approval and is being commercialized by Bausch + Lomb.
[2]In China, Arctic Vision is responsible for clinical development of ARCATUS™ (triamcinolone acetonide injectable suspension), formerly referred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

GLENN C. YIU, MD, PhD
Professor of Ophthalmology, University of California, Davis

Real World Use of Suprachoroidal Delivery

Accessing the suprachoroidal space

Microcatheter



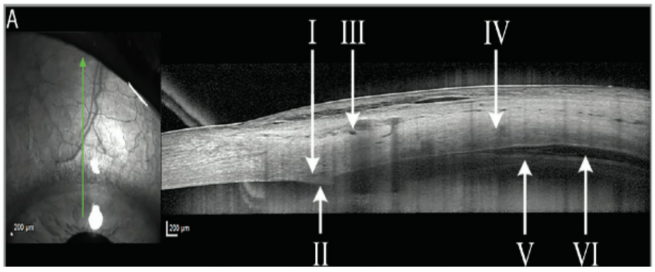
orbitsds.com

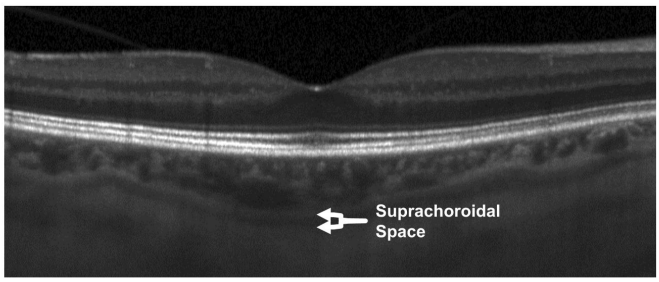
Microneedle

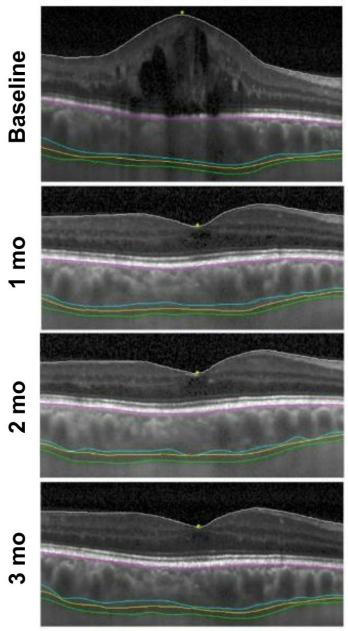
clearsidebio.com

Jung et al., *Drug Discovery Today*, 2019
Naftali & Moisseiev, *Pharmaceutics*, 2021

OCT shows SCS expansion after SC injection in humans







Lampen et al. OSLI Retina, 2018
Yiu et al., Am J Ophthalmol, 2018

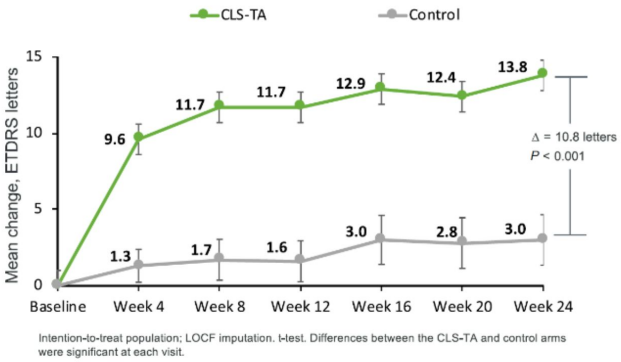
Suprachoroidally injected triamcinolone acetonide (CLS-TA) for uveitic ME

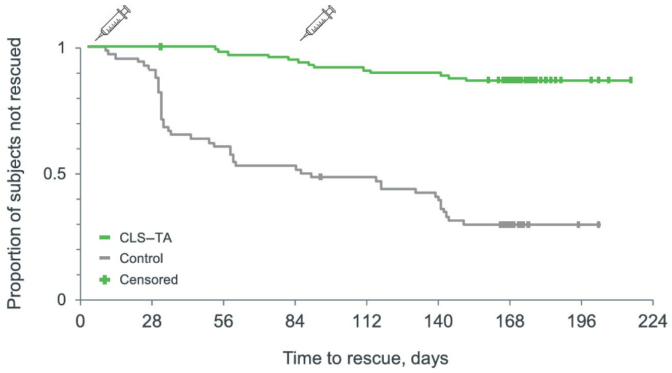
Phase 2 TANZANITE study
RVO + CME

Phase 3 PEACHTREE study
Uveitic ME

Phase 1/2 HULK study
DME

Phase 1/2 OASIS study
nAMD





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

Yeh et al., Ophthalmology, 2020

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

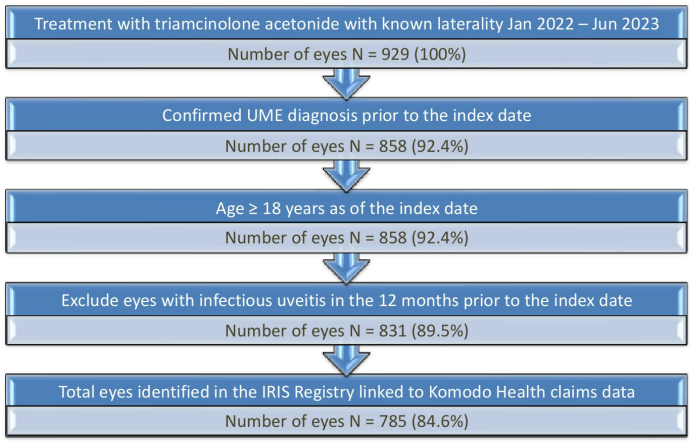
Inclusion criteria

- Age ≥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® Registry (Intelligent Research in Sight) linked to Komodo open-source claims data using the Datavant token to identify corticosteroid use



Singer, et al. Macula Society 2024. Durability with suprachoroidal injection of triamcinolone acetonide injectable suspension for uveitic macular edema and use of rescue therapy in clinical practice.

Study demographics & comorbidities

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

Abbreviations: SD, standard deviation

Ocular comorbidities	
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

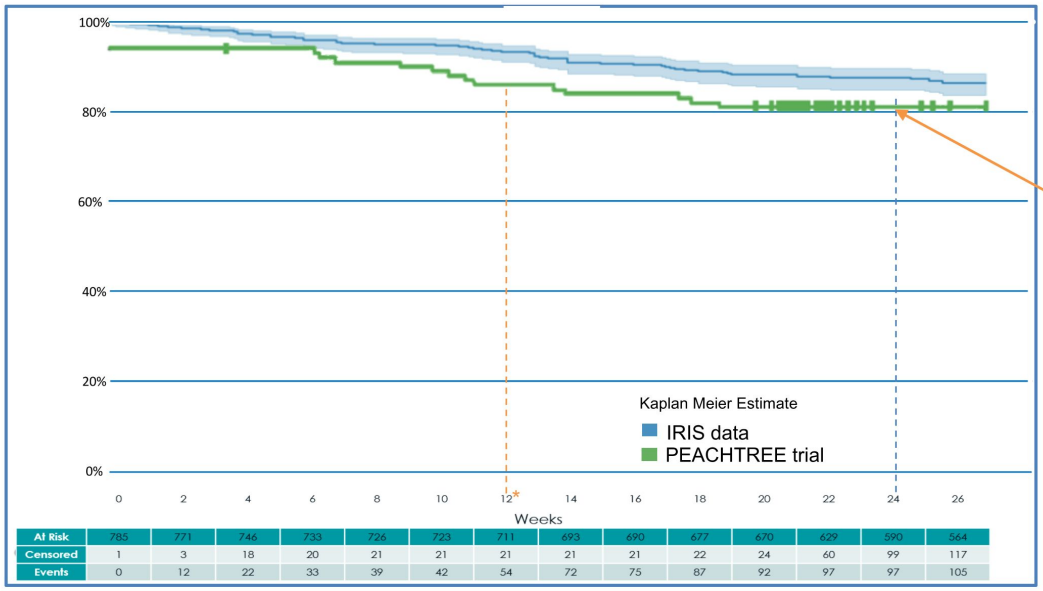
Treating provider subspecialty	
Retina/Vitreous Specialist	86.3%
Cataract/Anterior Segment Specialist	5.9%
Other/Unknown	7.9%

Prior corticosteroid use*	
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



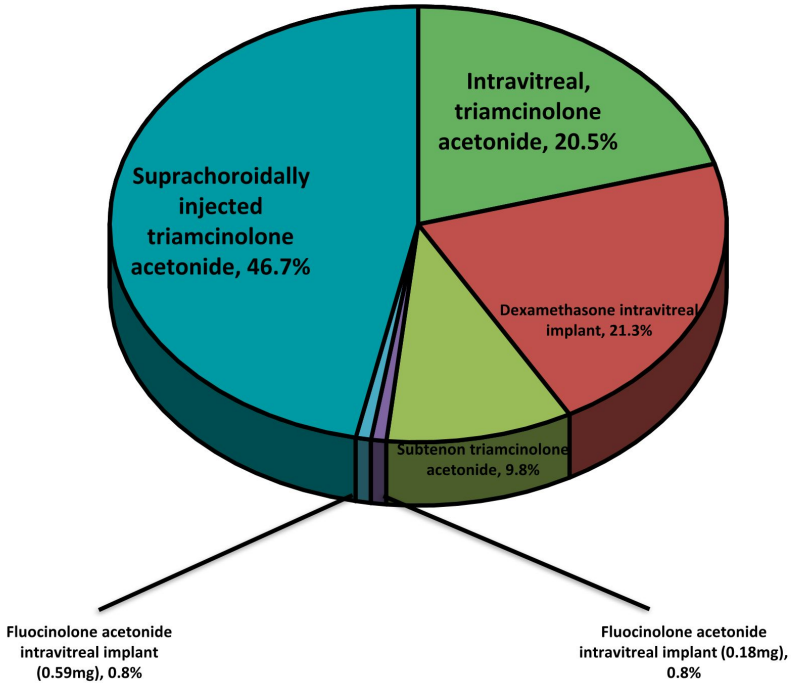
At Risk	785	771	746	733	726	723	711	693	690	677	670	629	590	564
Censored	1	3	18	20	21	21	21	21	21	22	24	60	99	117
Events	0	12	22	33	39	42	54	72	75	87	92	97	97	105

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

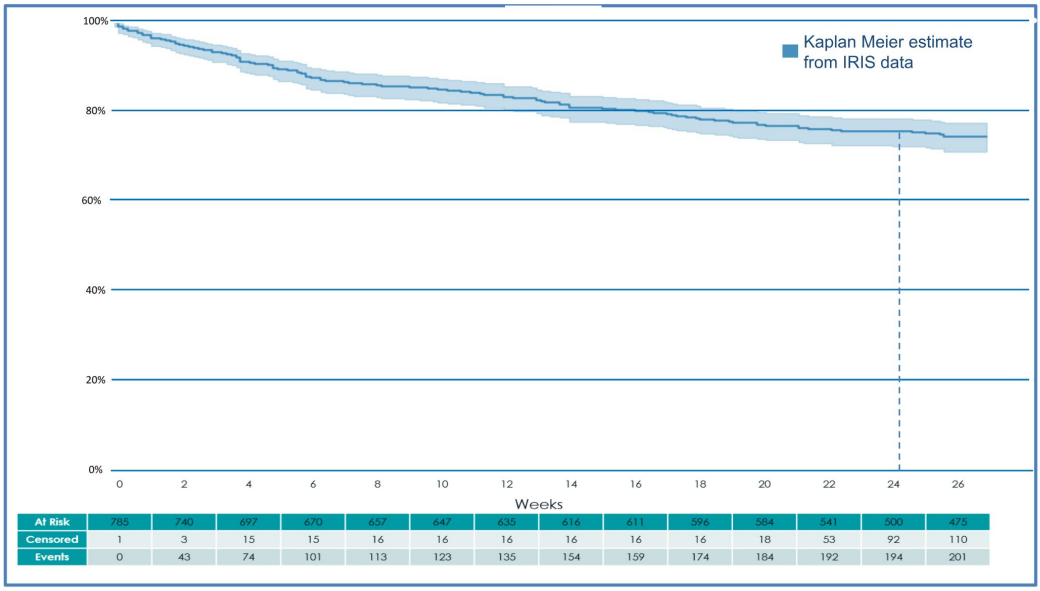
*In PEACHTREE, all subjects had a second injection at week 12

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)



At Risk	785	740	697	670	657	647	635	616	611	596	584	541	500	475
Censored	1	3	15	15	16	16	16	16	16	16	18	53	92	110
Events	0	43	74	101	113	123	135	154	159	174	184	192	194	201

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

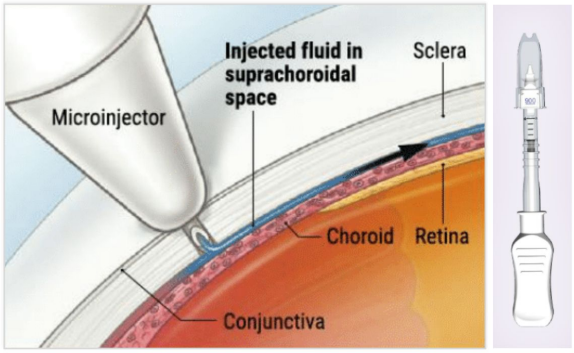
(esp. trabeculectomy or glaucoma shunt)

Patient Expectations

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

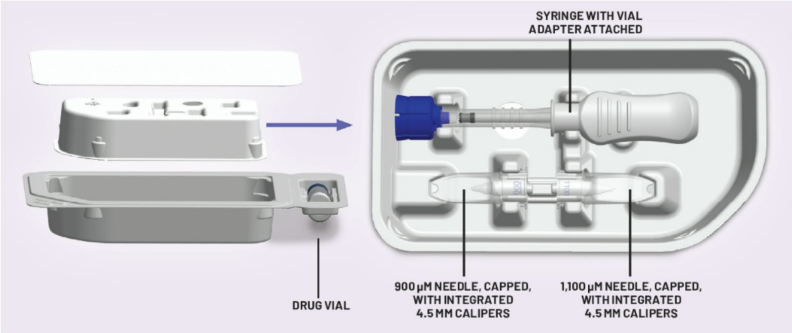
Patient Preparation

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



Wykoff CC, Avery RL, Barakat MR, Boyer DS, Brown DM, Brucker AJ, Cunningham ET, Heier JS, Holekamp NM, Kaiser PK, Khanani AM, Kim JE, Demirci H, Regillo CD, Yiu G, Ciulla TA. Suprachoroidal Space Injection Technique: Expert Panel Guidance. Retina | Image courtesy of Bausch & Lomb

Needle lengths & injection locations



Two needle lengths:
900 µm & **1,100 µm**

Preferred locations:
Superotemporal or **Inferotemporal**

Image courtesy of Bausch & Lomb

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*****

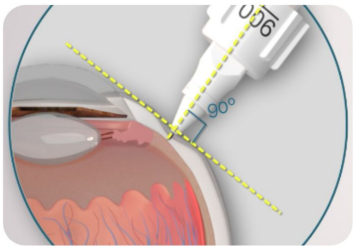
RETINA SPECIALIST

A beginner's guide to suprachoroidal injections

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

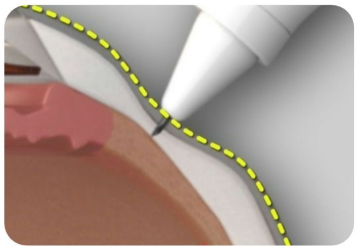
By Carol Villafuerte-Trisolini, MD, and Glenn Yiu, MD, PhD

DECEMBER 23, 2023



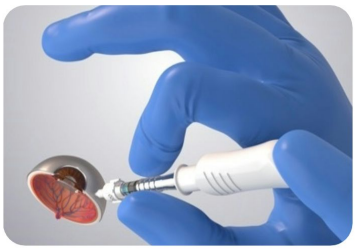
Perpendicular

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

Images courtesy of Bausch & Lomb

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 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

Singer, et al. Macula Society 2024. Durability with suprachoroidal injection of triamcinolone acetonide injectable suspension for uveitic macular edema and use of rescue therapy in clinical practice.

VICTOR CHONG, MD, MBA

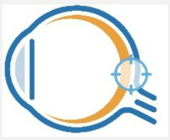
Clearside Chief Medical Officer

Pipeline Opportunities

Benefits for Patients and Physicians Using SCS Microinjector® Delivery

Enhanced Safety

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

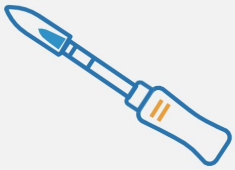


Injectate Flows to Back of the Eye

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

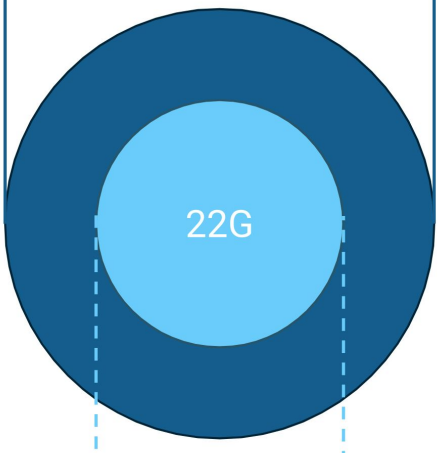


Injection Similar to Intravitreal

Advanced technology requires only a few seconds longer for each injection

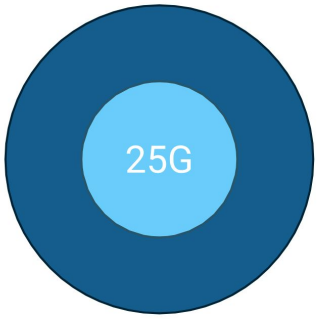
Competitive Advantage in Needle Gage Diameter

Outer Diameter of the Needle
Relative to the Ocular Tissue

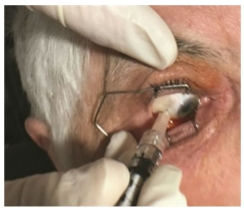


Inner Diameter of the Needle
Drug Product Passage

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



Clearside
SCS Microinjector®



Gustavo Barreto Melo, et al. Progress in Retinal and Eye Research. "Critical analysis of techniques and materials used in devices, syringes, and needles used for intravitreal injections". https://doi.org/10.1016/j.preteyeres.2020.100862

CLS-AX: Wet AMD Clinical Development Program

Leveraging a Highly Potent Pan-VEGF Inhibitor with Suprachoroidal Delivery

01 **Axitinib**

High potency TKI with pan-VEGF inhibition

02 **Proprietary CLS-AX Suspension Formulation**

Clearside formulation expertise

03 **Delivery via SCS Microinjector®**

Compartmentalization may eliminate treatment related floaters, haze, and anterior segment side effects

Utilizes the same device as FDA-approved product XIPERE®

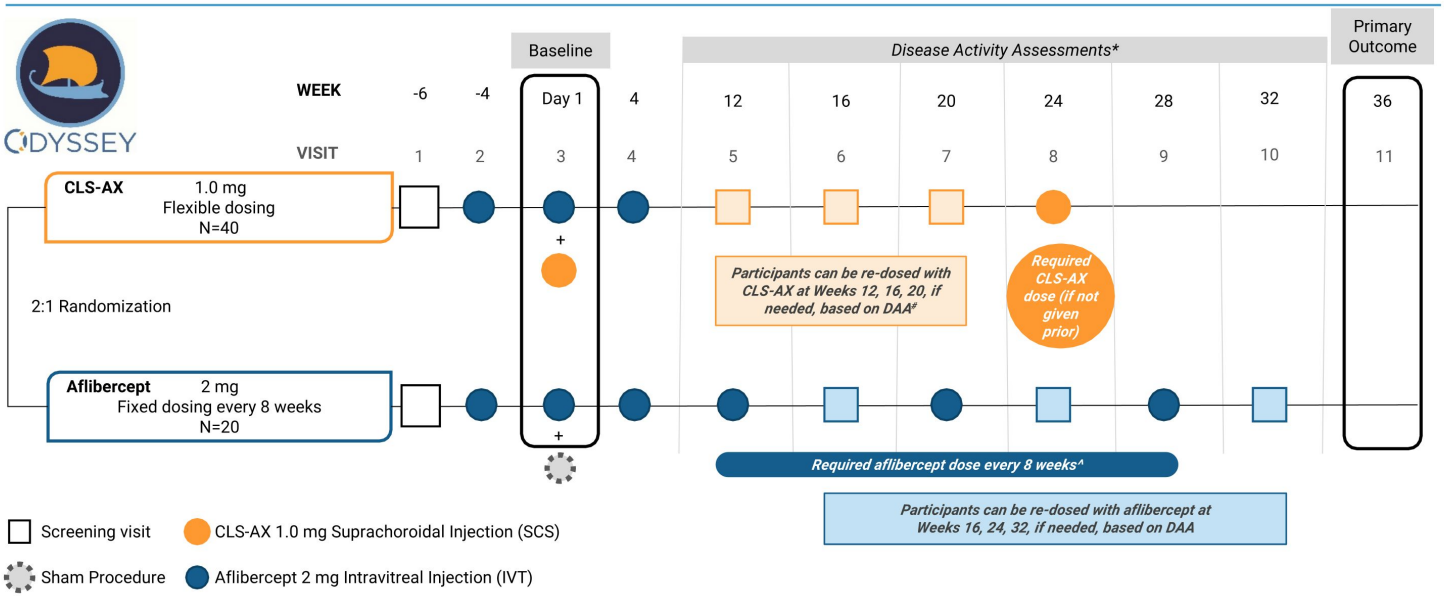
Differentiated Approach to Targeting Wet AMD

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

Key CLS-AX Program Features	Potential CLS-AX Competitive Advantages
Opportunity for treatments that may have longer duration of action in multi-billion-dollar market	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

*Dosing regimens are per respective product labels | EYLEA® and EYLEA HD® are registered trademarks of Regeneron Pharmaceuticals| LUCENTIS® and VABYSMO® are registered trademarks of Genentech/Roche

Multiple Dosing Requirement To Help Inform Phase 3 Development Program



#Participants can be re-dosed with CLS-AX up to every 12 weeks

CLEARSIDE BIOMEDICAL

* 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.
^ 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

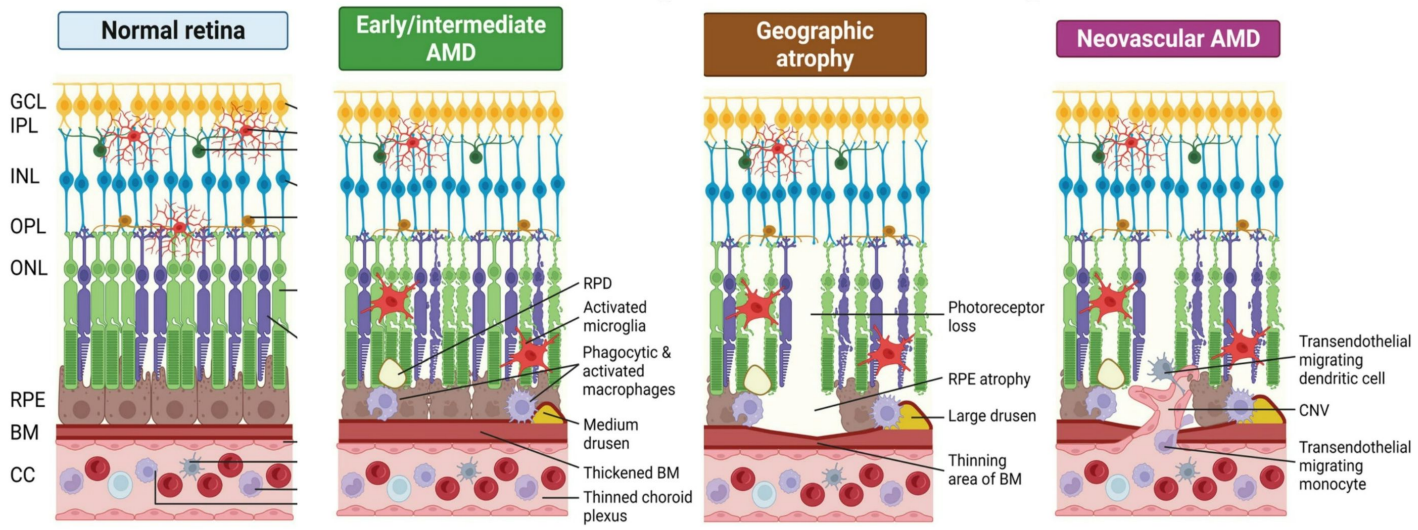
- All participants in the study have completed 6 months of treatment
- Participants in the CLS-AX arm have received two doses of CLS-AX per protocol
- In July 2024 meeting, the ODYSSEY Safety Review Committee (SRC) reviewed masked safety data and recommended that the trial continue as planned without 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

- No drug related ocular Severe Adverse Events
- Majority of participants reach Week 24 without re-treatment
- BCVA changes from baseline similar at all visits in particular at Week 24 and Week 36
- CST changes from baseline similar at all visits in particular at Week 24 and Week 36

Pipeline Expansion Opportunity in Geographic Atrophy

Pathology of Age-Related Macular Degeneration (AMD)

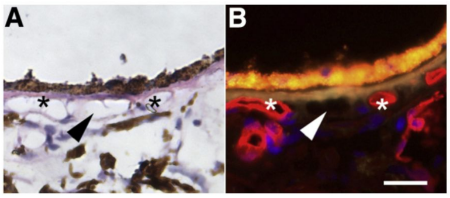


Wong JHC et al., Front Neurosci 16: 1009599

Geographic Atrophy is a Choroidal Disease

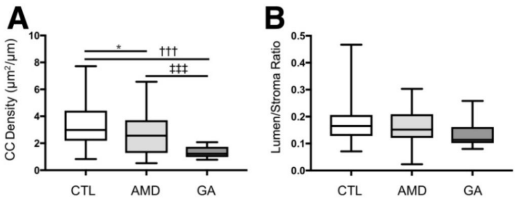
Choroidal Hypoxia Theory and Choriocapillaris are Damaged First

1



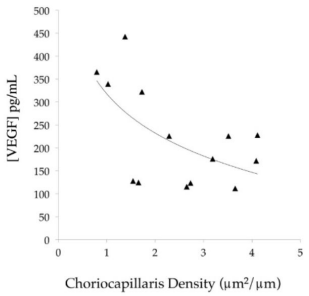
Choriocapillaris endothelial cells damage with ghost vessels before any significant RPE changes

2



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

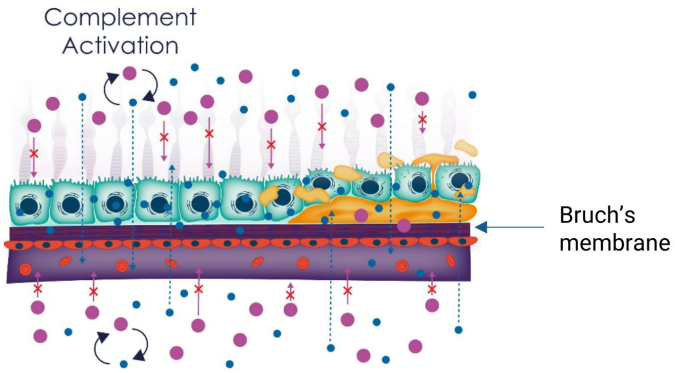
3

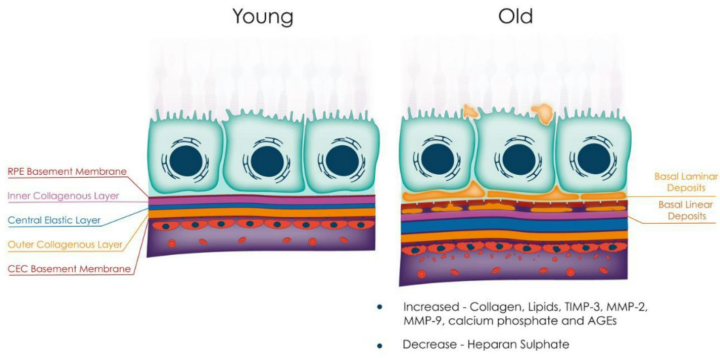


VEGF level increased with low vascular density support the choroidal hypoxia theory

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





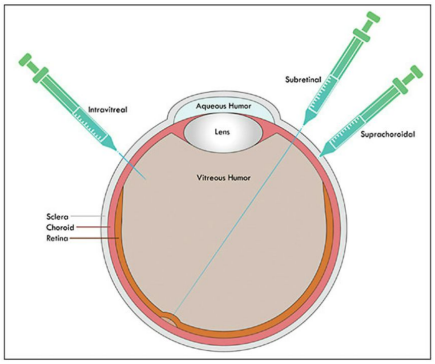
Larger molecules cannot get through Bruch's membrane

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

Suprachoroidal Administration Could Be Preferred Delivery Method



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

Images modified from Kasetty VM et al. Retinal Physician Aug 1, 2022, 19-23

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

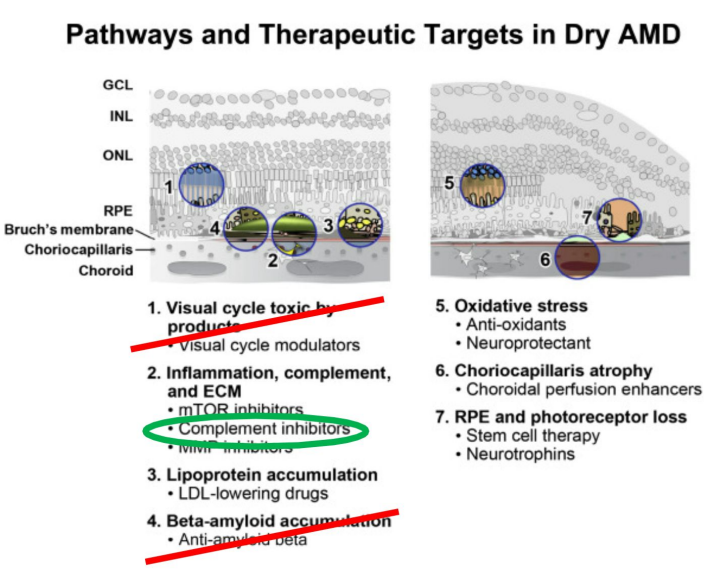
Small molecules may have better efficacy than current therapies
- Potential to treat complement activation in both RPE and choroid

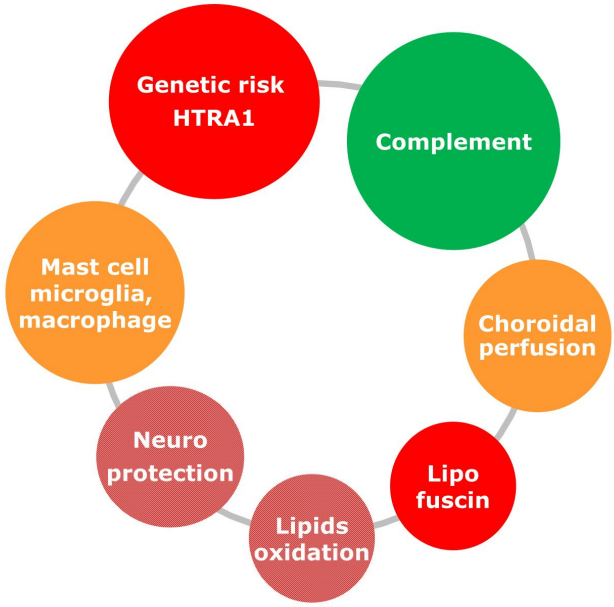
Suprachoroidal suspension/gene therapy may have longer duration (3 to 6 months)
- Intravitreal gene therapy may not achieve efficacy
- Subretinal has additional risks

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





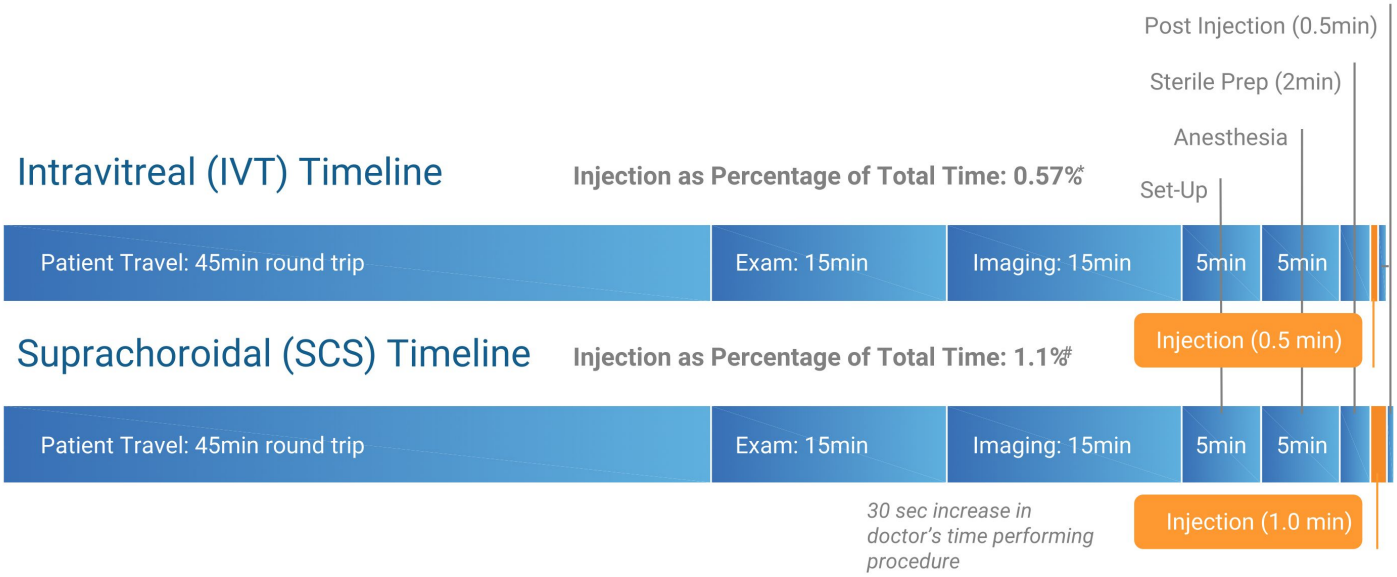
Holz FG et al. Ophthalmology 2014, 1079-91

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



*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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