



# CLEARSIDE BIOMEDICAL

**Investor Presentation**

**December 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, design 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, Clearside’s Quarterly Report on Form 10-Q filed with the SEC on November 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.

# Delivering on the Potential of the Suprachoroidal Space

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- ✓ **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**



# Promising Pipeline Using Clearside's Suprachoroidal Injection Platform







## Clearside Research and Clinical Development Programs

THERAPEUTIC	MECHANISM	INDICATION	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	APPROVAL	PARTNER
CLS-AX (axitinib)	Tyrosine Kinase Inhibitor	Wet AMD						
Undisclosed	Improve choroidal perfusion	Geographic Atrophy (GA)						
Undisclosed	Modulate pro-inflammatory cells	Geographic Atrophy (GA)						

## Commercial Asset: XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use

THERAPEUTIC	LOCATION	INDICATION	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	APPROVAL	PARTNER
XIPERE®	United States	Uveitic Macular Edema <sup>1</sup>						
XIPERE® / ARCATUS™	Australia and Singapore	Uveitic Macular Edema <sup>2</sup>						
XIPERE® / ARCATUS™	China	Uveitic Macular Edema <sup>2</sup>						
XIPERE® / ARCATUS™	Asia Pacific ex-Japan	Diabetic Macular Edema <sup>2</sup>						

# Multiple Validating Partnerships Expand Utilization of SCS Microinjector® Technology

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					
ABBV-RGX-314	AAV Gene Therapy	Diabetic Retinopathy (DR) Diabetic Macular Edema	ALTITUDE					 
ABBV-RGX-314	AAV Gene Therapy	Wet AMD	AAVIATE					 
Avoralstat	Plasma Kallikrein Inhibitor	Diabetic Macular Edema						



## Ocular Oncology

2024: Actively enrolling Phase 3



## Gene Therapy

Q4 2024:

- Wet AMD: Enrolling new cohort at dose level 4
- DME: Enrolling new cohort at dose level 4

1H 2025: Initiate global pivotal trial in DR



## Plasma Kallikrein Inhibitor

- 2024: Conduct formulation and nonclinical work
- 2025: Begin clinical trials

# Core Competencies in Delivery & Formulation Drive Patented Technology

## KEY INTELLECTUAL PROPERTY COMPONENTS

1. **Comprehensive IP portfolio** that includes protection of: SCS delivery technology, proprietary SCS Microinjector<sup>®</sup>, treatment of various conditions with SCS administration of therapeutic products
2. **28 U.S. and >80 European and International issued patents** with multiple pending patent applications
3. Granted patents provide exclusivity for our delivery technology and product candidates to mid-2030s with pending applications **potentially extending exclusivity beyond 2040**



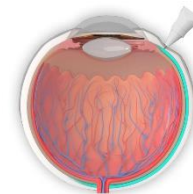
### DEVICE PATENTS

- SCS Microinjector<sup>®</sup> features
- Methods of using SCS Microinjector<sup>®</sup> for drug delivery



### DRUG PATENTS

- Administration of a variety of drugs to the suprachoroidal space by microinjection



### DISEASE PATENTS

- Methods of treating ocular disorders by SCS administration



# Proven Commercial Capabilities in Suprachoroidal Delivery

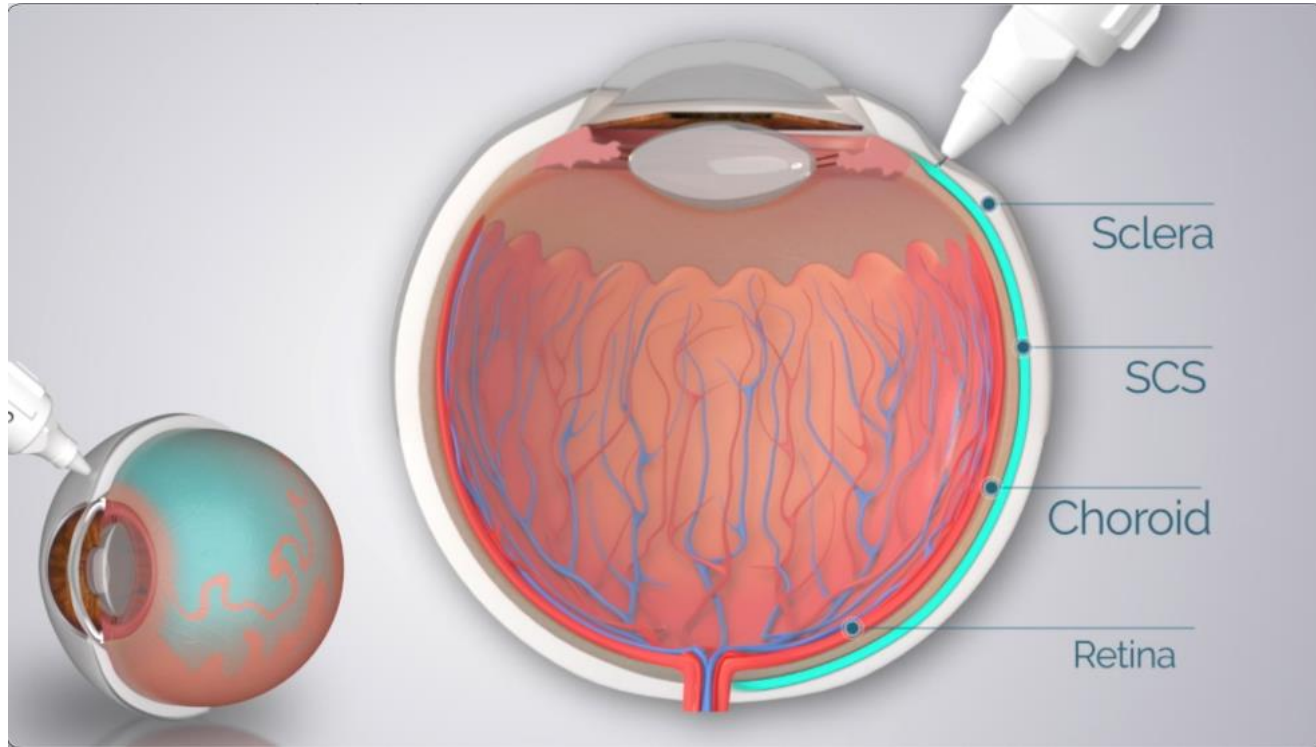


# Suprachoroidal Delivery via SCS Microinjector<sup>®</sup>





# Delivering on the Potential of the Suprachoroidal Space (SCS®): A Novel Approach to Drug Delivery Into the Back of the Eye



# 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



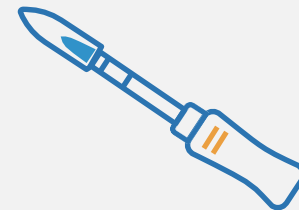
## Injectate Flows to Back of the Eye

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

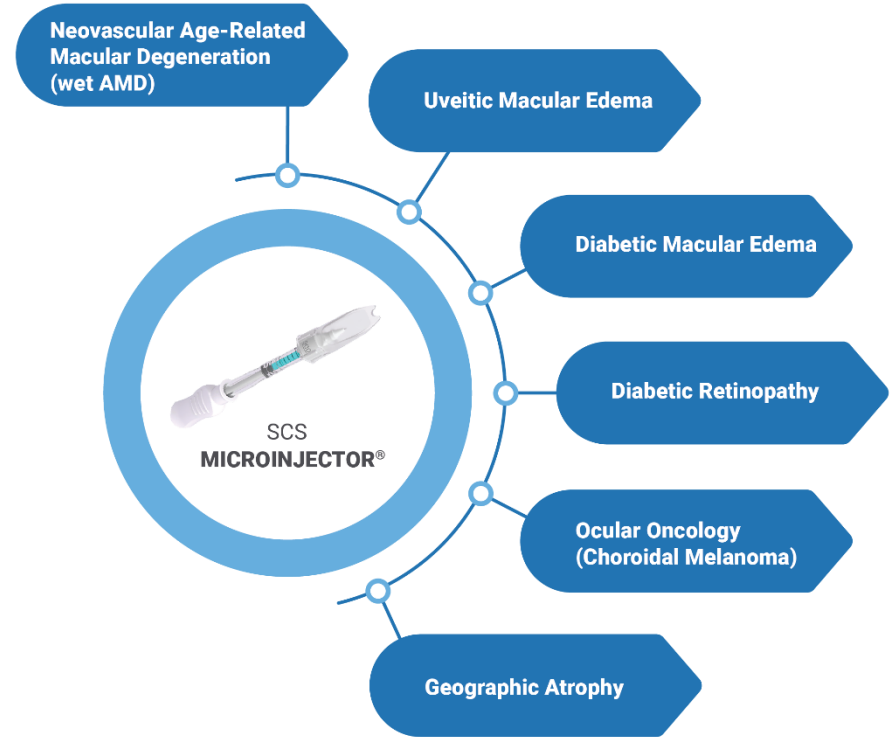


## Injection Similar to Intravitreal

Advanced technology requires only a few seconds longer for each injection

# SCS Microinjector®: Drug/Device Combination with Proven Versatility

- ✓ Demonstrated ability for precise delivery into the suprachoroidal space
- ✓ First and Only FDA-approved SCS product
- ✓ Safety profile of SCS Microinjector comparable to intravitreal injections<sup>1</sup>
- ✓ Well-accepted by retinal physicians with thousands of injections performed



# Straightforward Suprachoroidal Injection Technique

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

REVIEW

**SUPRACHOROIDEAL 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>16,17,18</sup>; Kim, Judy E. MD<sup>19</sup>; Demirci, Hakan MD<sup>20</sup>; Regillo, Carl D. MD<sup>21</sup>; Yiu, Glenn C. MD, PhD<sup>22</sup>; Ciulla, Thomas A. MD, MBA<sup>23</sup>

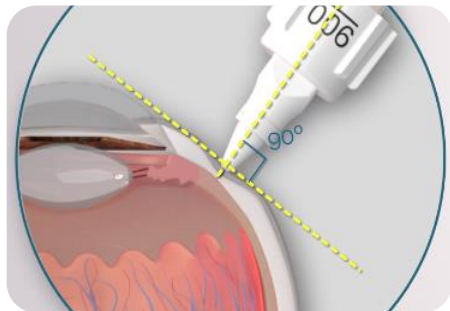
**RETINA**  
SPECIALIST

**A beginner's guide to suprachoroidal injections**

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

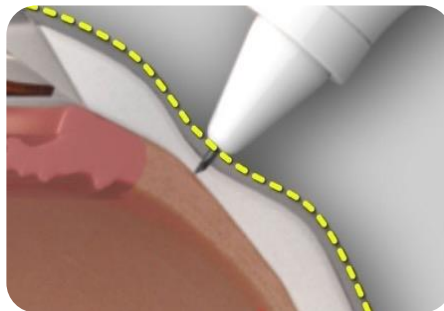
By Carol Villafuerte-Trisolini, MD, and Glenn Yiu, MD, PhD

DECEMBER 23, 2023



**Perpendicular**

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



**Dimple**

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

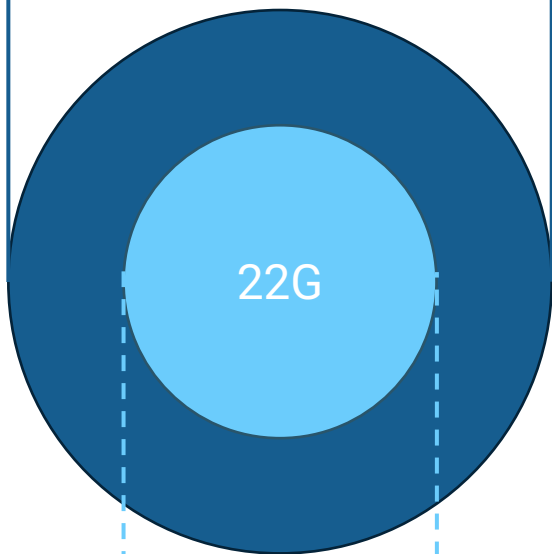


**Slow**

Inject **slowly** over 5 – 10 seconds

# Clearside Needle Size Equivalent to Most Commonly Used Intravitreal Injections and Smaller than Other TKIs in development

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



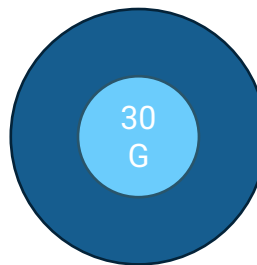
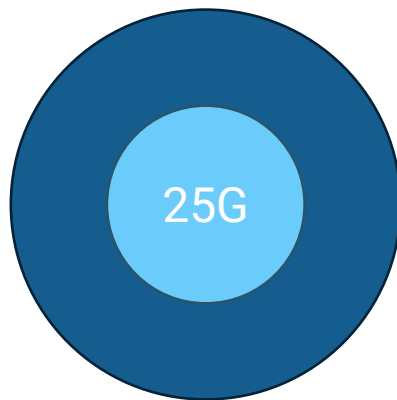
Inner Diameter of the Needle  
*Drug Product Passage*

**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<sup>®</sup>



# CLS-AX

(axitinib injectable suspension)

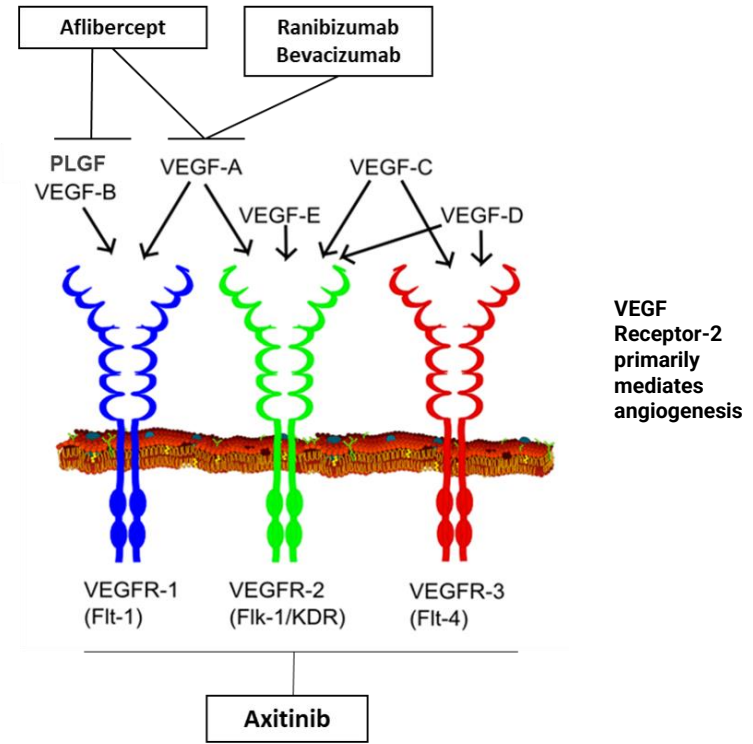
*New mechanism of action with potential  
for longer duration of effect for the  
treatment of wet AMD*



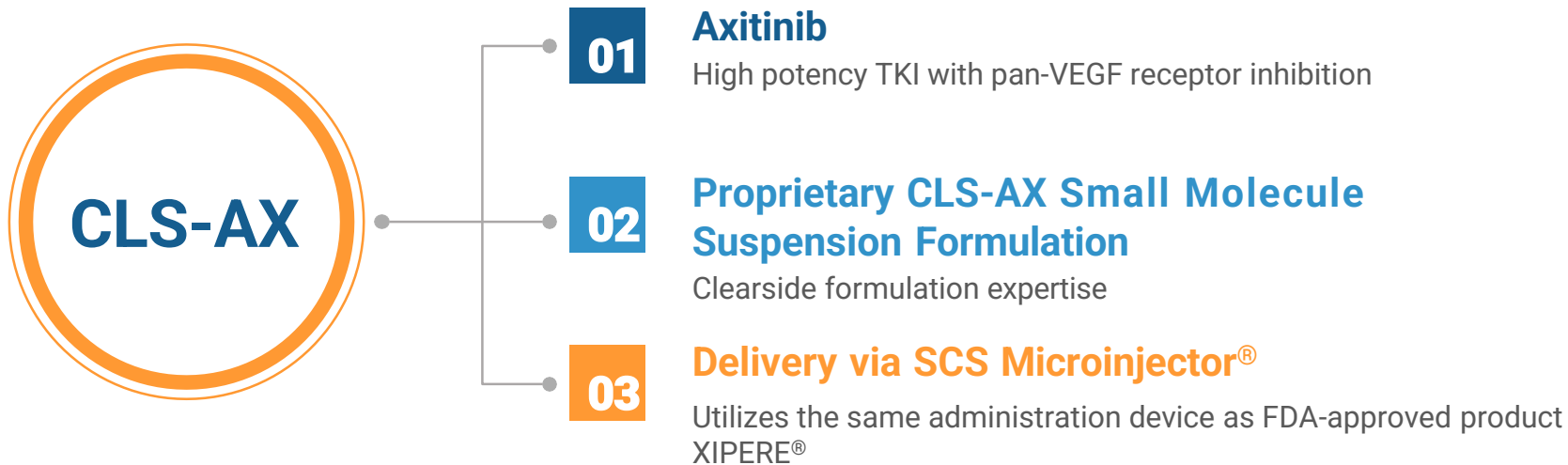


# Axitinib is a Highly Potent, Highly Selective Pan-VEGF Inhibitor

- ✓ **Inhibits ALL VEGF Receptors** (VEGFR-1, VEGFR-2, VEGFR-3)
  - Intrinsic pan-VEGF inhibition through receptor blockade
  - More active than anti-VEGF-A in *in-vitro* angiogenesis model<sup>1-2</sup>
  - Approved AMD treatments are focused VEGF-A inhibitors
- ✓ **Tyrosine kinase inhibitor (TKI) with the highest potency**
  - >10x more potent than other TKIs in *in-vitro* studies<sup>3</sup>
  - Better ocular cell biocompatibility than other TKIs<sup>4</sup>
  - More active than other TKIs for experimental corneal neovascularization in preclinical models
- ✓ **Small molecule formulated into suspension for SCS delivery**
  - Preclinical data showed regression of angiogenesis
  - FDA-approved renal oncology treatment with established mechanism of action

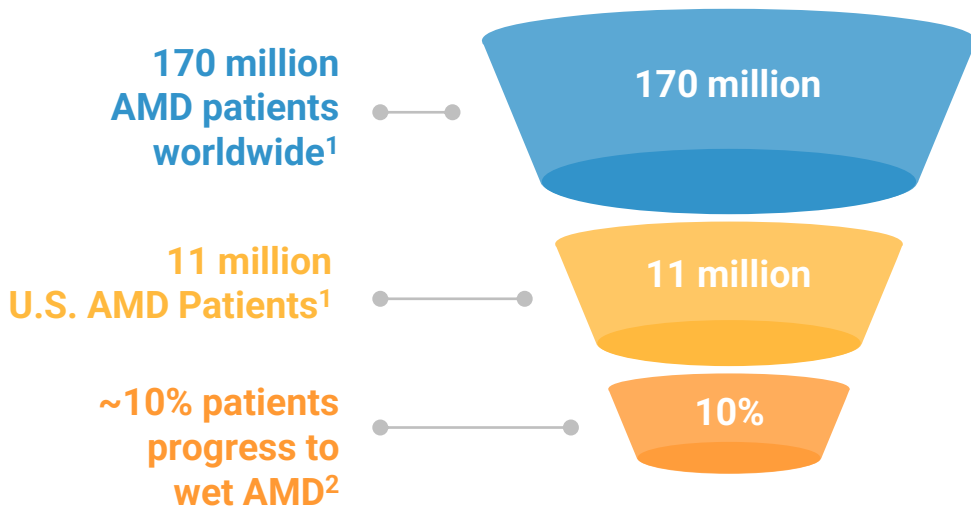


# Leveraging a Highly Potent Pan-VEGF Inhibitor with Suprachoroidal Delivery



# Age-Related Macular Degeneration (AMD) is a Multi-Billion Dollar Market

## A large and growing market opportunity



- ✓ AMD causes a progressive loss of central vision and is the most common cause of blindness in individuals over age 55<sup>1</sup>
- ✓ U.S. prevalence expected to increase to 22 million by the year 2050<sup>1</sup>
- ✓ Global prevalence expected to increase to 288 million by the year 2040<sup>1</sup>
- ✓ Current treatments require frequent injections and subset of patients experience disappointing visual outcomes<sup>2</sup>
- ✓ **Over \$12 Billion Market and Growing<sup>3</sup>**

# Positioning CLS-AX for Real-World Success

## Maintain Vision & Reduce Office Visits

- Objective is to maintain visual acuity and reduce the number of injections; therefore, reducing the number of office visits
- Reduced treatment burden benefits patients, caregivers and payors with improved outcomes

## Ability to Re-dose

- Wet AMD is a chronic disease requiring ongoing treatment
- Goal is a label that allows re-dosing comparable to VABYSMO® and EYLEA HD® in the real-world setting

## Extend Duration Over Currently Approved Drugs

2x - 4x/year maintenance dosing anticipated for CLS-AX compared to approved drugs on label\*:

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

\*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



# Phase 2b Topline Data Summary and Phase 3 Plans

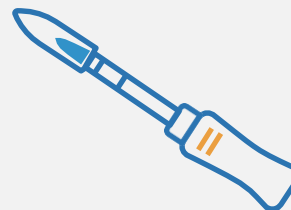
# CLS-AX Now Phase 3 Ready Based on Positive ODYSSEY Data in Wet AMD



**Enrolled Only  
Difficult-to-Treat  
Participants with  
Active Disease**



**Achieved  
Primary Outcome  
Maintaining Stable  
BCVA with Repeat  
Dosing**



**Compelling  
Intervention-Free  
Rates**



**Positive  
Safety Profile  
with Repeat  
Dosing**



# ODYSSEY Phase 2b Clinical Trial



## 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

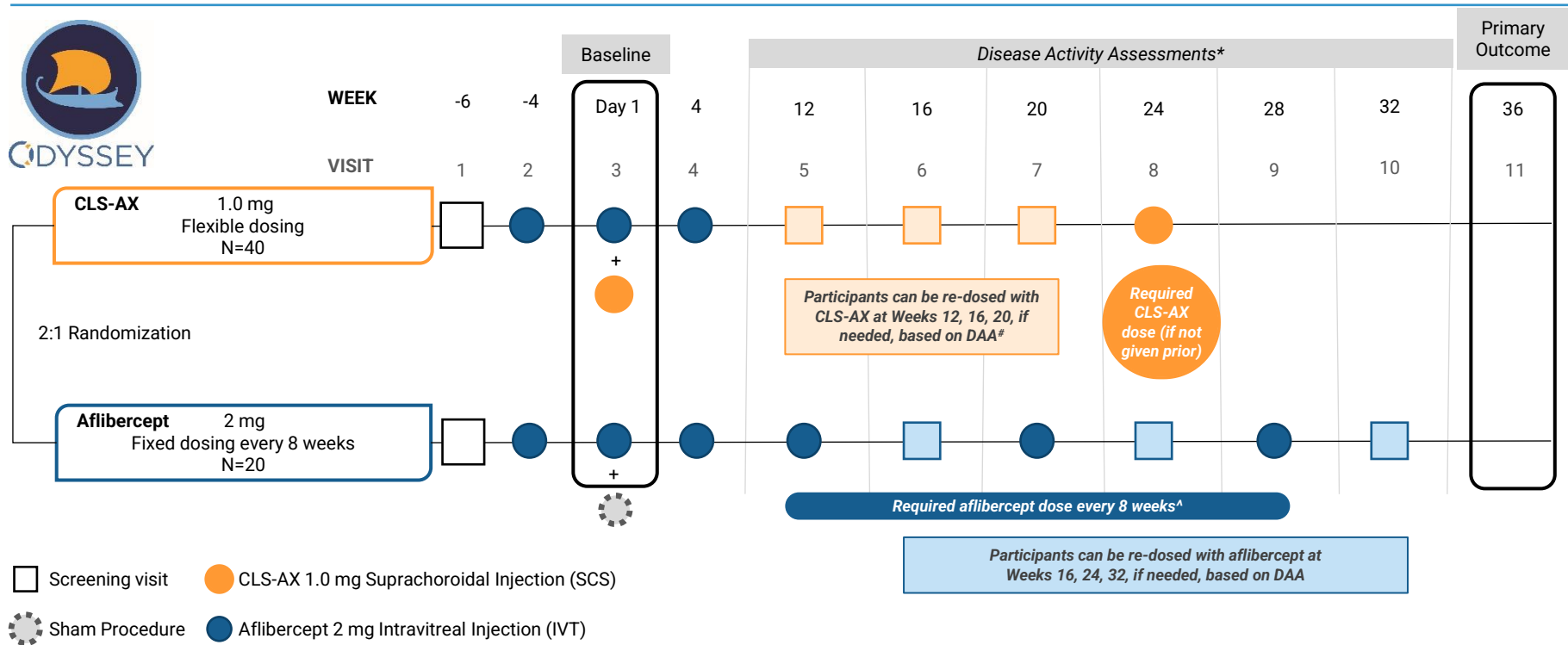


## Participant Profile:

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 requires **re-dosing with CLS-AX** in study arm
  - Participants receive at least 2 doses of CLS-AX
  - Provides important data to plan Phase 3 in chronic disease

# ODYSSEY Trial Design



<sup>#</sup>Participants can be re-dosed with CLS-AX up to every 12 weeks; All arms are sham controlled

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

## Demographics and Baseline Characteristics

Characteristics	CLS-AX	Aflibercept	Overall
No. of participants	40	20	60
Mean age (range), years	76.9 (51-90)	80.3 (54-96)	78.0 (51-96)
Women, no. (%)	25 (62.5)	14 (70.0)	39 (65.0)
Race, no. (%)			
White	37 (92.5)	20 (100)	57 (95.0)
Asian	3 (7.5)	0	3 (5.0)
Median duration of wet AMD diagnosis (range), months	9.65 (1.4-31.1)	10.2 (1.4-20.8)	9.9 (1.4-31.1)
Mean BCVA (range) at screening, ETDRS letters	69.1 (37-80)	69.1 (51-80)	69.1 (37-80)
Mean CST (range) at screening, $\mu\text{m}$	266.8 (175-378)	294.3 (209-592)	276.0 (175-592)
Mean Total Area of CNV (range) at screening, $\text{mm}^2$	6.8 (1.6-26.9)	6.5 (0.5-20.8)	6.7 (0.5-26.9)
Bilateral wet AMD, n	17	6	23
Mean annualized number of prior wet AMD treatments (injections/year) <sup>a</sup> (range)	9.5 (3.2-17.2)	9.2 (4.1-17.2)	9.4 (3.2-17.2)

Abbreviations: AMD = age-related macular degeneration; BCVA = best corrected visual acuity; CNV = choroidal neovascularization; CST = central subfield thickness; ETDRS = Early Treatment Diabetic Retinopathy Study.

<sup>a</sup>Annualized number of prior wet AMD treatments defined as the total number of prior wet AMD treatments divided by the duration of wet AMD diagnosis in years.

# CLS-AX Demonstrated Positive Clinical Activity 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

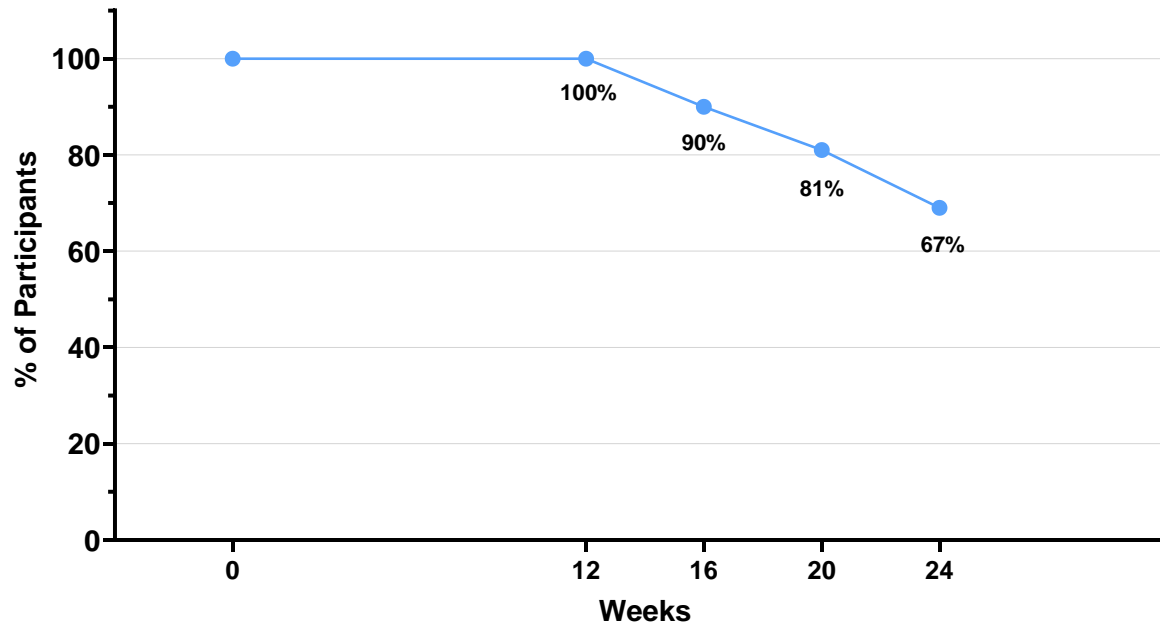
## Durable Effect

**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

# 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%)

# CLS-AX Consistently Reduced the Frequency of Injections

## Comparison of Wet AMD Treatments Pre- and Post- Randomization

### 24 Weeks Before and After

Average number of treatments  
24 Weeks prior to Screening Visit:  
**2.95 injections**

Average number of treatments  
up to 24 Weeks after Baseline Visit:  
**0.475 injections**

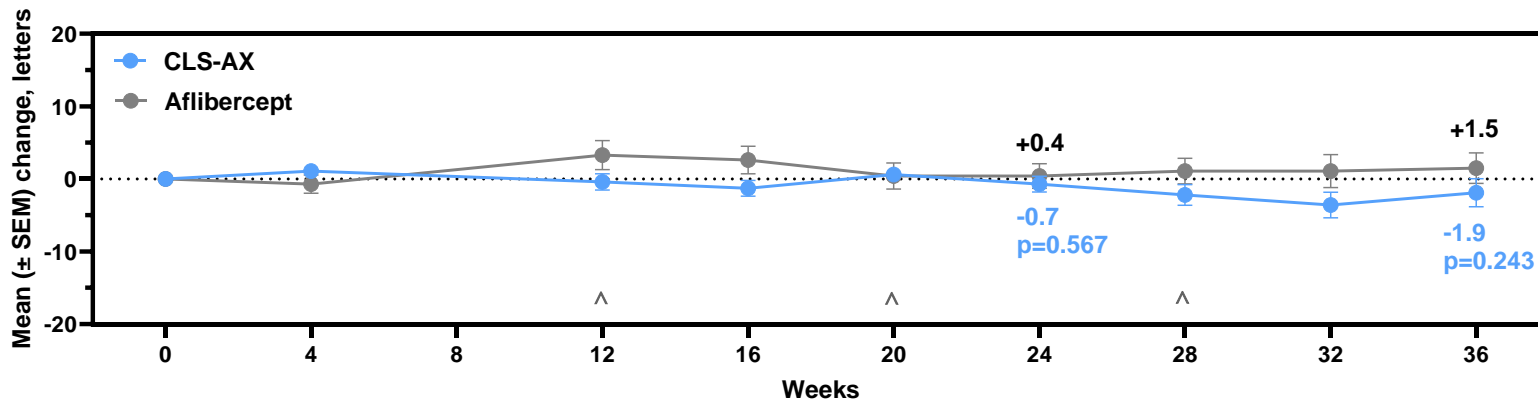
Reduced injection frequency by

**84%**



# Stable Best Corrected Visual Acuity (BCVA) Over 36 Weeks

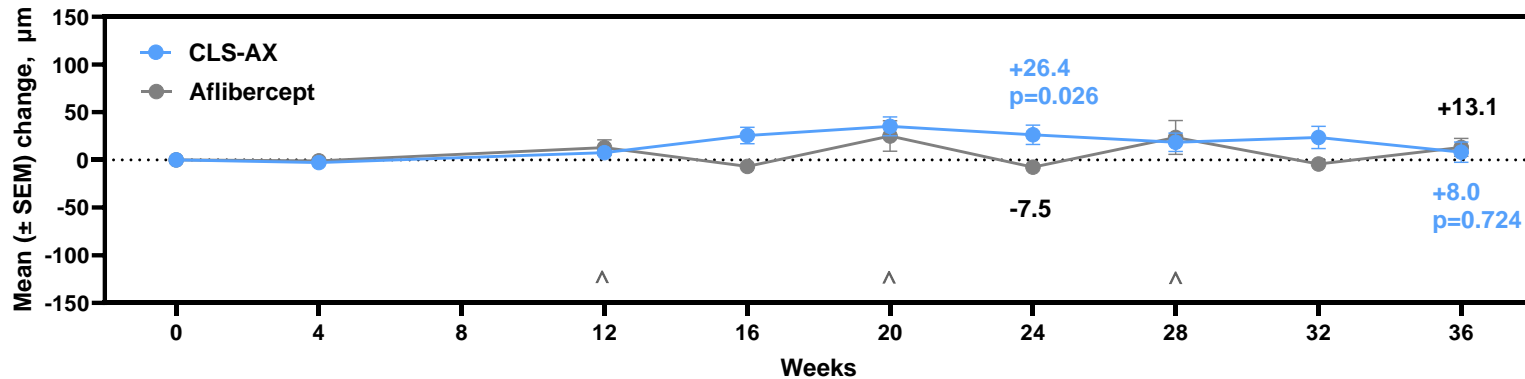
## BCVA Within 2 Letters From Baseline at Both Week 24 and Week 36 in CLS-AX Arm



*CLS-AX results do not include supplemental therapy with aflibercept*

# Stable Central Subfield Retinal Thickness (CSRT) Over 36 Weeks as Verified by Independent Reading Center

## CLS-AX Demonstrates Stable Anatomical Control and Reduces Fluctuation



*CLS-AX results do not include supplemental therapy with aflibercept*

# CLS-AX Demonstrated A Positive Safety Profile

## Safety Profile

**Well-tolerated safety profile through 36 weeks** including after mandatory re-dosing of CLS-AX at Week 24

## No Serious Adverse Events (SAEs)

**No ocular SAEs** or treatment-related SAEs:

- No drug or procedure related ocular SAEs
- No reported drug or procedure related systemic SAEs
- No endophthalmitis
- No retinal vasculitis

## Positive Adverse Event (AE) Profile

Ocular AEs were considered **clinically mild** in both arms

- Only one reported incident related to mild eye pain out of 84 total CLS-AX injections (1.2%)

## Discontinuation Rates

**Similar discontinuation rates** between treatment and comparator groups

## CLS-AX Now Phase 3 Ready Based on Positive ODYSSEY Data

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**Achieved Primary Objective: Stable BCVA to Week 36**  
Difficult-to-treat Wet AMD participants with confirmed activity



**Compelling injection free rates up to 6 months**  
Injection frequency reduced by nearly 84%



**Positive safety profile**  
No ocular SAEs or treatment-related SAEs  
CLS-AX was well-tolerated after re-dosing



**Only Phase 2 trial in wet AMD with repeat TKI dosing data to better inform  
and potentially de-risk Phase 3 design**

# CLS-AX Phase 3 Program Current Plans



# CLS-AX Flexible Dosing of a Biologic with the Duration of a TKI

## Phase 3 Program Summary

Two pivotal, non-inferiority trials

Two arms with ~225 participants per arm: CLS-AX 1mg vs aflibercept 2mg

Similar to Phase 3 trial design of EYLEA HD and VABYSMO in maintenance phase

Phase 3 flexible dosing data will be differentiated from other TKI programs

End-of-Phase 2 Meeting expected in Q1 2025

Expect to initiate both trials in 2H 2025

# CLS-AX Phase 3 Non-Inferiority Study Design in Wet AMD Designed to Optimize Success

Target patient population:

- **Treatment naïve** → **Potentially increase commercial value**
- **No more than 1 previous injection of anti-VEGF** → **Easier recruitment anticipated**

Two strategies to reduce variability to enhance success in non-inferiority trial:

- **At Screening**
  - Participants must have 20/80 to 20/32 AND CST <500 at diagnosis
  - **Minimizes enrollment of highly variable participants**→ **Intended to increase probability of success**
- **Prior to Randomization**
  - At Visit 4 (Wk -4) following three aflibercept loading doses, eliminate:**
  - Participants with  $\geq 10$  letter change from Visit 3 (Wk -12) OR
  - CST (AI assessment) increases by  $\geq 100$  microns→ **Intended to increase probability of more consistent results**

# Flexible Dosing to Support Commercial Success

*Personalized Treatment Interval (PTI) assessment enables physicians to use “real world” approach with flexible dosing schedule based on participant needs*

## Re-Dosing Criteria with CLS-AX

- **Improve consistency in assessing need for re-dosing** by using OCT biomarkers (IRF and SRF) determined in office using AI tool

## Rescue Criteria with Aflibercept

- $\geq 10$  letter loss AND
- $\geq 100$  microns in 2 consecutive visits

Rationale based on learnings from ODYSSEY

- TKIs may take longer to act, thus some participants need to be re-dosed earlier
- There is variability in physician’s approach to providing rescue treatment



# Year 1 Study Designed to Maximize Commercial and Competitive Potential in Wet AMD

						R/BL									PE				
Week	-20	-16	-12	-8	-4	D1	4	8	12	16	20	24	28	32	36	40	44	48	52
Visit	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Activity					EC				PTI	PTI	PTI					PTI	PTI	PTI	PTI
CLS-AX FLEX	A	A	A		A	C	S					C	S	S	S	S	S	C	S
												C	S	S	S	S	C	S	S
												C	S	S	C	S	S	C	S
												C	S	S	C	S	S	C	S
Aflibercept Q8W	A	A	A		A	S	A		A	S	A	S	A	S	C	S	S	S	C

Reduce variability

A, Aflibercept 2mg; C, CLS-AX 1 mg; S, Sham injection; R/BL, Randomization/Baseline; PE, Primary Endpoint; EC, Exclusion Criteria; PTI, Personalized Treatment Interval assessment by AI tool: IRF and/or SRF changes from Visit 6 (Baseline, Day 1).

→ **EC: At Week -4, participants with high variation will be discontinued from the study.** At Weeks 12-20, participants meeting PTI criteria will be dosed at that visit and will continue on q12w, q16w or q20w until the primary endpoint. Participants not meeting PTI criteria at these visits will be dosed at Week 24 and will continue on q24w until the primary endpoint.

# Study Design Intended to Provide Additional Safety and Efficacy Data After Primary Endpoint

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## After 36-Week Primary Endpoint:

- Aflibercept arm moves to CLS-AX every 16 weeks (q16w)
  - To maintain masking
  - To collect more safety data
  - To collect efficacy data for q16w CLS-AX in year 2
- CLS-AX arm stays on the original assignment after PTI assessment
  - Allows readjustment of dosing in CLS-AX arm (close to **real world** situation)
    - Similar to EYLEA HD and VABYSMO study designs

# Year 2 Evaluation After Primary Endpoint

Week		40	44	48	52	56	60	64	68	72	76	80	84	88	92	96
Visit		16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Activity		PTI	PTI	PTI	PTI	PTI	PTI	PTI	PTI	PTI	PTI	PTI	PTI	PTI	PTI	EOS
CLS-AX FLEX	Q24W	S	S	C <sup>a</sup>	S	S	S	S	S	C <sup>a</sup>	S	S	S	S	S	
	Q20W	C <sup>a</sup>	S	S	S	S	C <sup>a</sup>	S	S	S	S	C	S	S	S	
	Q16W	S	S	C <sup>a</sup>	S	S	S	C <sup>a</sup>	S	S	S	C <sup>a</sup>	S	S	S	
	Q12W	S	S	C	S	S	C	S	S	C	S	S	C	S	S	
Aflibercept Q8W		S	S	S	C	S	S	S	C	S	S	S	C	S	S	

C, CLS-AX 1 mg; S, Sham injection; EOS, End of Study.  
For masking purposes, PTI assessments will be performed in all participants at all visits starting at Week 40.

<sup>a</sup> For participants randomized to CLS-AX on a dosing interval of q24w, q20w, or q16w after Week 36, if PTI criteria are met at an active injection visit, then the next dosing interval will be reduced by 4 weeks, to a minimum of q12w.

# Pipeline Expansion Opportunity in Geographic Atrophy



# 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

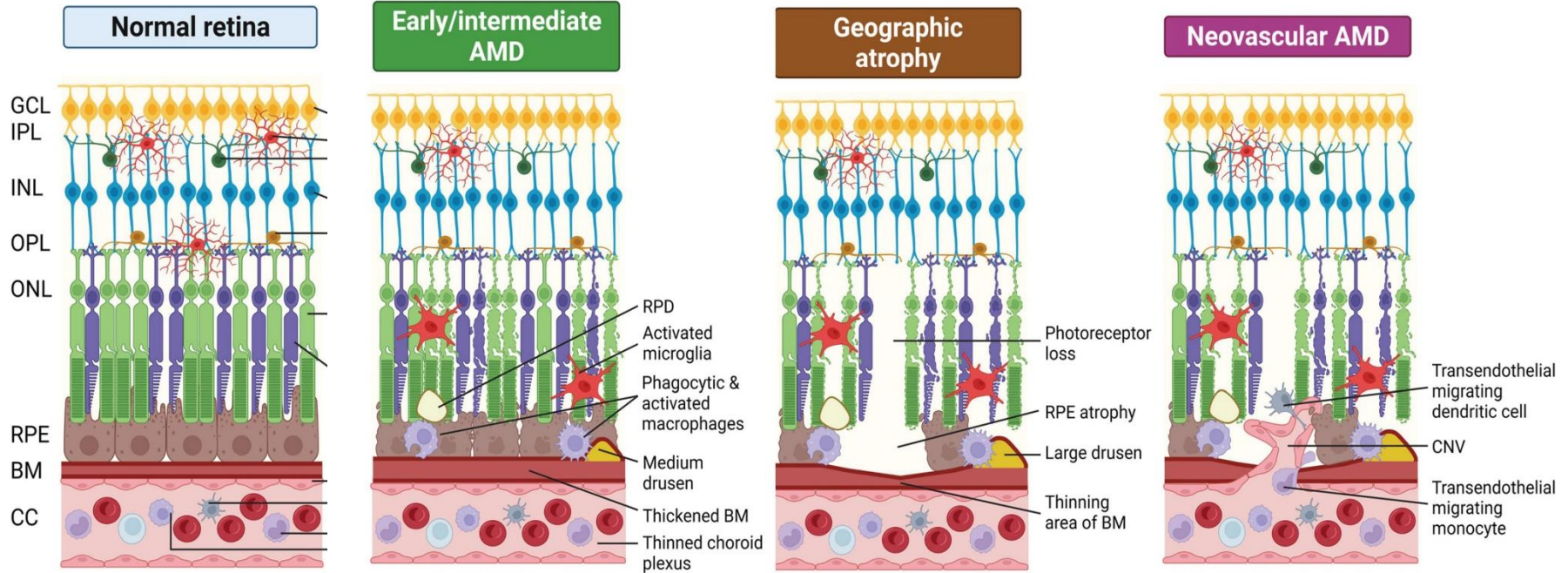
## Less invasive, in-office procedure

- 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

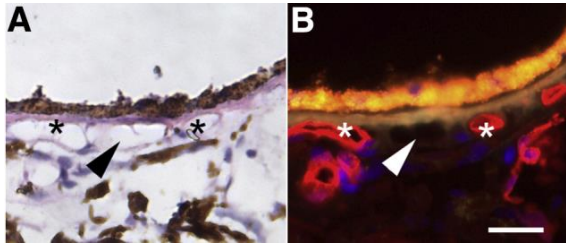
# Pathology of Age-Related Macular Degeneration (AMD)



# Geographic Atrophy is a Choroidal Disease

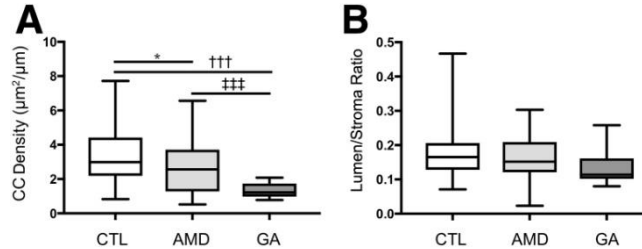
## Choroidal Hypoxia Theory and Choriocapillaris are Damaged First

1



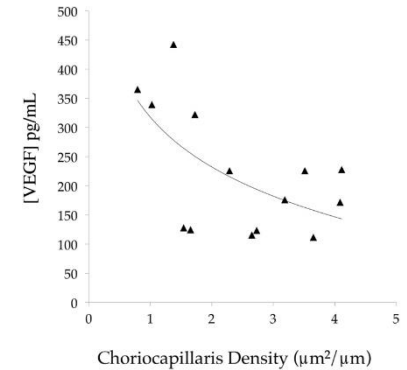
Choriocapillaris endothelial cells damage with ghost vessels before any significant RPE changes

2



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

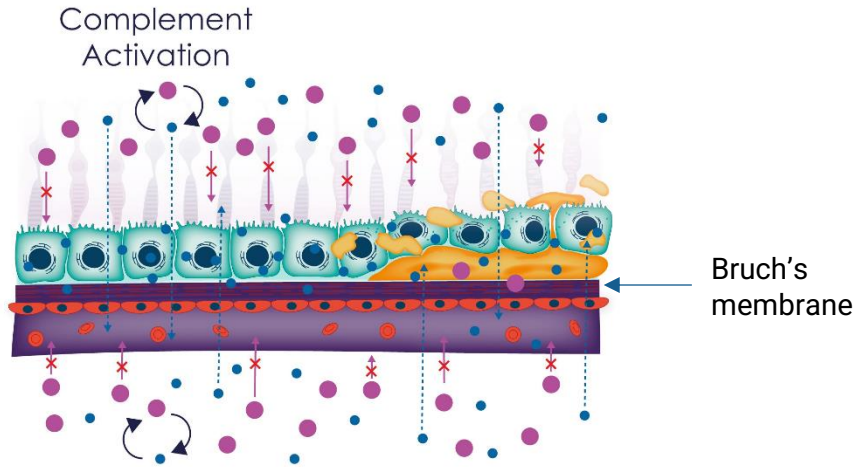
3



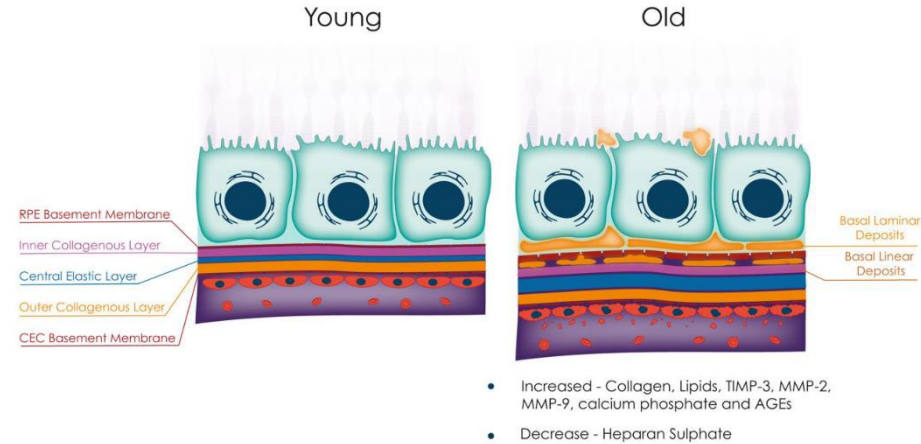
VEGF level increased with low vascular density support the choroidal hypoxia theory



# 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

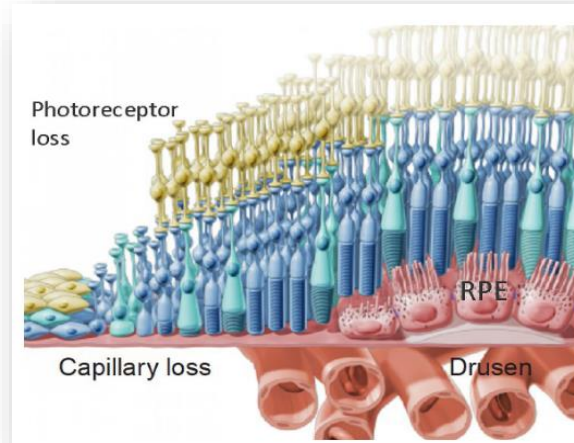


# A Differentiated and Promising Approach Focusing on Choroidal Health and Capillary Homeostasis

- 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

## Complement inhibition

- Clinically validated
- Approved therapies have limited efficacy



## Reduce choriocapillaris degeneration & improve choroidal perfusion

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

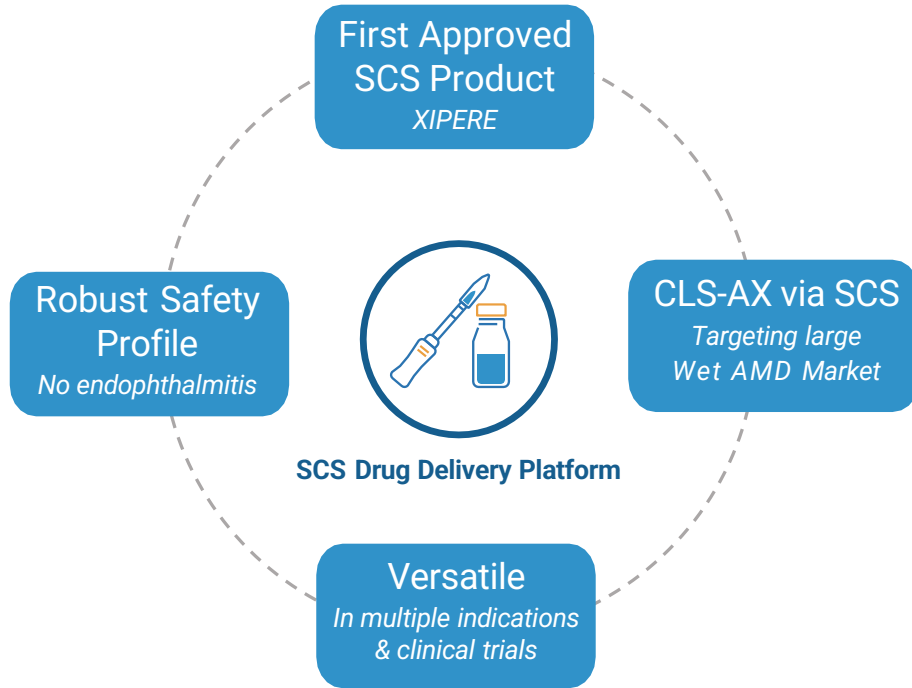
## Control proinflammatory microenvironment

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

# Summary



# Innovative and Experienced Leader in Suprachoroidal Drug Delivery



## Upcoming Potential Catalysts

### CLS-AX (axitinib injectable suspension)

- ✓ **ODYSSEY Phase 2b Topline Results**
  - **Q4 2024:** Phase 3 Planning
  - **Q1 2025:** End-of-Phase 2 meeting with FDA

### 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; Floretina

### Publications

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



# CLEARSIDE BIOMEDICAL

Nasdaq: CLSD





# Appendix



# ODYSSEY Trial Focused on Participants with Active Disease

## Key Inclusion Criteria

- Diagnosed with neovascular AMD (wet AMD) within 36 months of screening
- History of 2 to 4 anti-VEGF treatments in 6 months before screening and response to prior anti-VEGF treatment for wet AMD
- **Reading center confirmation of persistent active disease**; BCVA of 20 to 80 letters<sup>#</sup>

## Dosing Regimen

- **Participants in both arms received 3 aflibercept (2 mg) loading doses (2<sup>nd</sup> dose = Baseline visit)**
- **CLS-AX arm received one dose of CLS-AX (1.0 mg) at Baseline visit**
- Unless DAA required more frequent dosing, **CLS-AX arm dosed at least every 24 weeks** & aflibercept arm dosed every 8 weeks

## Disease Activity Assessments (DAA)

- **Monthly DAA: Weeks 12 through 32 in both arms** to determine if there is need for supplemental treatment
- Supplemental treatment criteria: Decrease in BCVA, increase in CST, or new or worsening vision-threatening hemorrhage due to wet AMD

## Criteria for Supplemental Treatment

- BCVA reduction of >10 letters from Baseline measurement
- Increase in CST of >100 microns on SD-OCT from Baseline measurement
- BCVA reduction of > 5 letters from Baseline measurement AND increase in CST of >75 microns on SD-OCT from Baseline measurement
- Presence of new or worsening vision-threatening hemorrhage

Aflibercept is dosed via intravitreal injection (IVT); CLS-AX is dosed via suprachoroidal injection.

<sup>#</sup> Using the Early Treatment Diabetic Retinopathy Study (ETDRS) measurement.

Abbreviations: SD-OCT (Spectral Domain Optical Coherence Tomography).

# ODYSSEY Trial Enrolled Rapidly

32 SITES ACTIVATED

158 PARTICIPANTS SCREENED

60 PARTICIPANTS RANDOMIZED



Required Independent Reading  
Center Confirmation of  
Active Disease

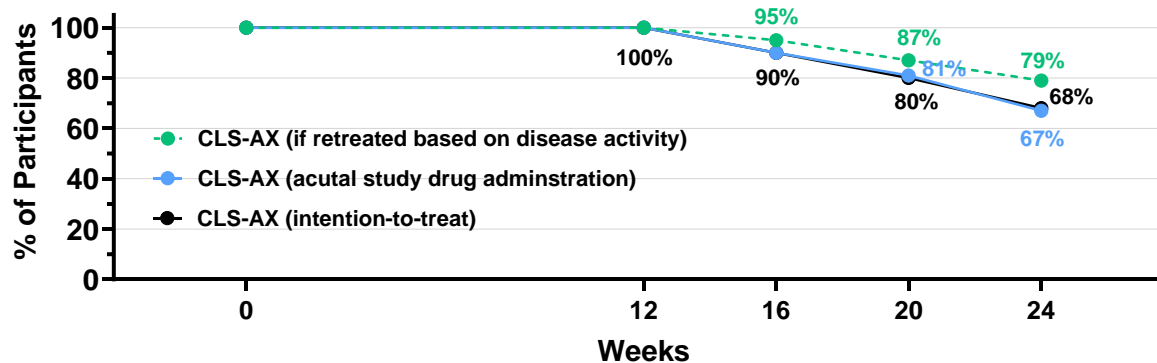
Study Activity	Date
First Participant Randomized	July 12, 2023
Last Participant Randomized	December 13, 2023

Disposition	CLS-AX	Aflibercept	Overall
Enrolled, n			158
Randomized, n	40	20	60
Completed, n (%)			
24 weeks	39 (97.5)	19 (95.0)	58 (96.7)
36 weeks*	36 (90.0)	17 (85.0)	53 (88.3)

\*Discontinuation rate was similar between arms

# Two-Thirds of Participants Dosed with CLS-AX Reached 6 Months Without Supplemental Therapy

## Intervention-Free Rates By Week Up to Each Visit



### Based on disease activity<sup>1</sup>

Week 12: 40/40 (100%)  
 Week 16: 37/39 (94.9%)  
 Week 20: 32/37 (86.5%)  
 Week 24: 30/38 (78.9%)

### Actual study drug administration<sup>1</sup>

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

### Intention-to-Treat

Week 12: 40/40 (100%)  
 Week 16: 36/40 (90.0%)  
 Week 20: 32/40 (80.0%)  
 Week 24: 27/40 (67.5%)



# ODYSSEY Confirmed the Ability to Administer Multiple Doses of CLS-AX with a Well-Tolerated Safety Profile

Of the 40 participants in the trial on study drug:  
32 received two doses of CLS-AX and 6 received three doses of CLS-AX

Multi-Dosing Data		
CLS-AX Doses Received Including Baseline		
# Doses	# Participants	% of total enrolled (n=40)
1	2	5%
2	32	80%
3	6	15%