



CLEARSIDE BIOMEDICAL

July 2025



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. These forward-looking statements include statements regarding Clearside’s plans or intentions relating to product candidates, estimates of market size, the clinical development of CLS-AX, the trial design features and timing of Clearside’s planned Phase 3 trial and its anticipated benefits and impacts, and the commercial potential and addressable market of CLS-AX, if approved. 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 raise additional capital; 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, 2024, filed with the U.S. Securities and Exchange Commission (SEC) on March 27, 2025, 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

- ✓ **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**



Clearside Suprachoroidal Product Development Pipeline Targeting Global Markets

Clearside Research and Clinical Development Programs

THERAPEUTIC	MECHANISM	INDICATION	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	APPROVAL	
CLS-AX (axitinib)	Tyrosine Kinase Inhibitor (TKI)	Wet AMD*	FDA End-of-Phase 2 Meeting Completed					
CLS-TAX [^]	Steroid plus TKI	Diabetic Macular Edema	➔					
Undisclosed	Modulate pro-inflammatory cells	Geographic Atrophy (GA)	➔					
Undisclosed	Improve choroidal perfusion	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 ¹	➔					B+L BAUSCH+LOMB
XIPERE [®] / ARCATUS [™]	Australia and Singapore	Uveitic Macular Edema ²	➔					arctic VISION
XIPERE [®] / ARCATUS [™]	China	Uveitic Macular Edema ²	➔ NDA Under Review					arctic VISION Santen
XIPERE [®] / ARCATUS [™]	Asia Pacific ex-Japan	Diabetic Macular Edema ²	➔					arctic VISION

*Phase 3 plans are in process. [^]CLS-TAX contains triamcinolone acetonide and axitinib;

¹XIPERE[®] (triamcinolone acetonide injectable suspension), for suprachoroidal use has received U.S. FDA Approval and is being commercialized by Bausch + Lomb.

²In licensed territories, Arctic Vision is responsible for clinical development of ARCATUS[™] (triamcinolone acetonide injectable suspension), also known as ARVN001, and known as XIPERE[®] in the U.S.

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					
Sura-vec	AAV Gene Therapy	Diabetic Retinopathy (DR)*	ALTITUDE					
Sura-vec	AAV Gene Therapy	Wet AMD	AAVIATE					
Avoralstat	Plasma Kallikrein Inhibitor	Diabetic Macular Edema						



Ocular Oncology

- Actively enrolling Phase 3



Gene Therapy

- DR: Planning a Phase 3 program to support global regulatory submissions
- ALTITUDE: Enrolling a DME cohort at dose level 4
- AAVIATE: Enrolling new cohort in Wet AMD at dose level 4



Plasma Kallikrein Inhibitor

- First clinical trial for DME granted authorization to proceed in Australia
- Initial data from DME patients expected in 2025

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[®], treatment of various conditions with SCS administration of therapeutic products
2. **34 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**



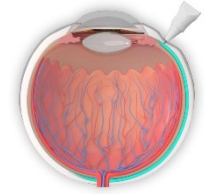
DEVICE PATENTS

- SCS Microinjector[®] features
- Methods of using SCS Microinjector[®] 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

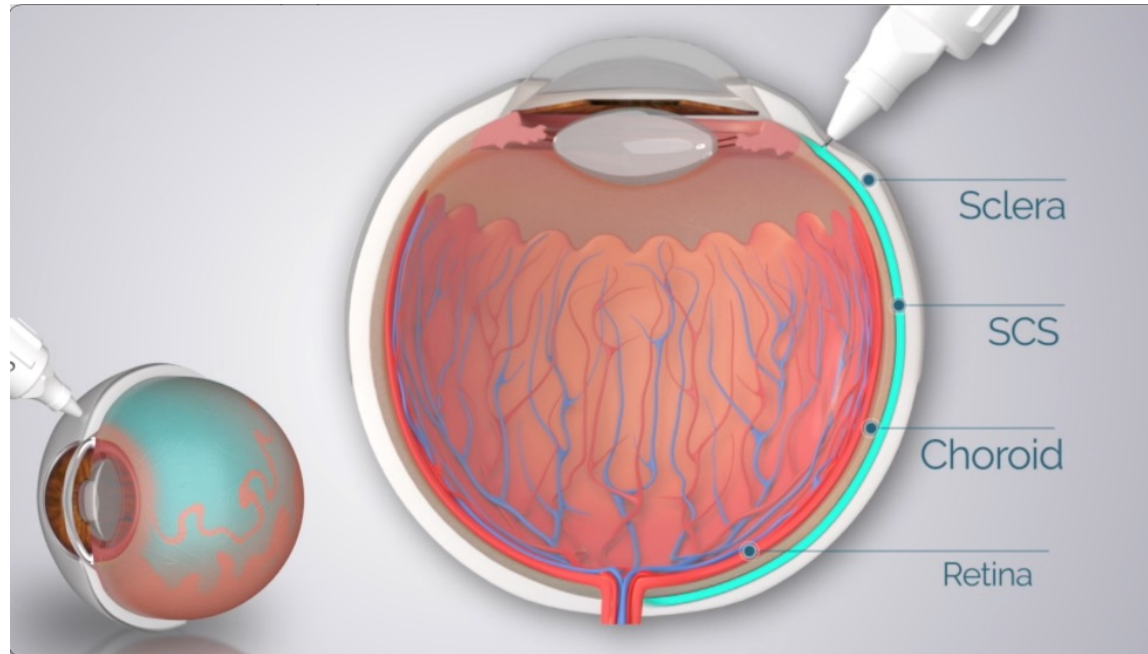


Suprachoroidal Delivery via SCS Microinjector[®]



Delivering on the Potential of the Suprachoroidal Space (SCS®): A Novel Approach to Drug Delivery for Retinal Diseases

Injectate Flows to the Back of the Eye and Diffuses into the Retina



Benefits for Patients and Physicians Using SCS Microinjector[®] Delivery



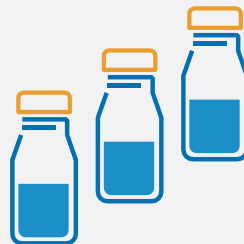
Enhanced Safety

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



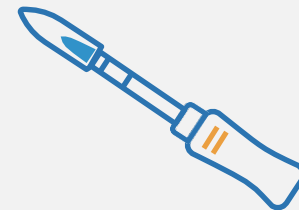
Injectate Flows to Back of the Eye

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

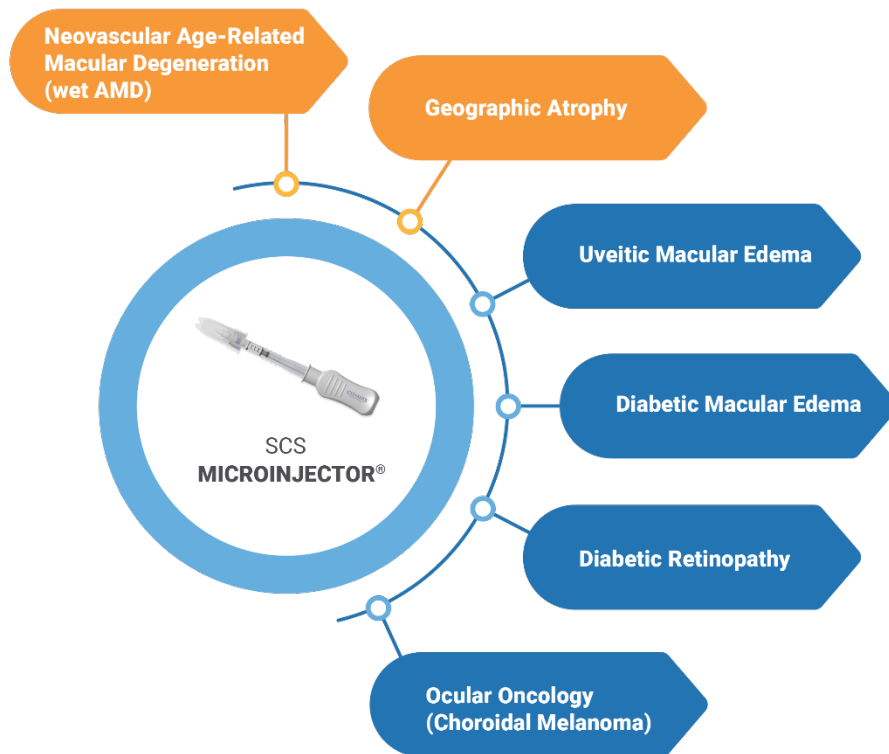


Injection Similar to Intravitreal

Advanced technology requires only a few seconds longer for each injection

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 injections¹
- ✓ Well-accepted by retinal physicians with thousands of injections performed



Straightforward Suprachoroidal Injection Technique

RETINA
THE JOURNAL OF RETINAL AND VITREOUS DISEASES

REVIEW

SUPRACHOROIDSAL SPACE INJECTION TECHNIQUE

Expert Panel Guidance

Wykoff, Charles C. MD, PhD¹; Avery, Robert L. MD²; Barakat, Mark R. MD^{3,4}; Boyer, David S. MD⁵; Brown, David M. MD⁶; Brucker, Alexander J. MD⁷; Cunningham, Emmett T. Jr MD, MPH^{8,9,10,11}; Heier, Jeffrey S. MD¹²; Holekamp, Nancy M. MD^{13,14}; Kaiser, Peter K. MD¹⁵; Khanani, Arshad M. MD, MA^{16,17,18}; Kim, Judy E. MD¹⁹; Demirci, Hakan MD²⁰; Regillo, Carl D. MD²¹; Yiu, Glenn C. MD, PhD²²; Ciulla, Thomas A. MD, MBA²³

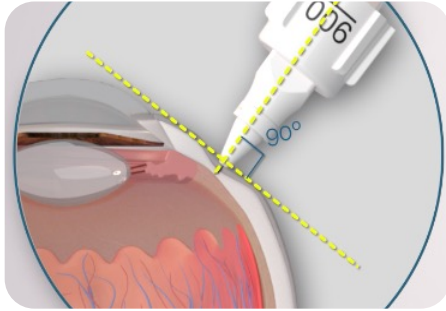
RETINA
SPECIALIST

A beginner's guide to suprachoroidal injections

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

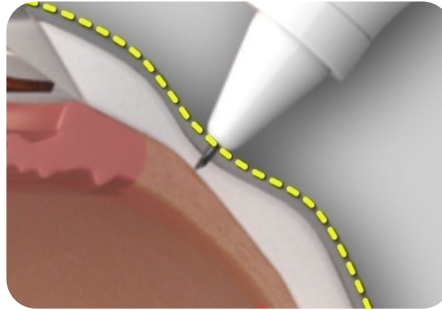
By Carol Villafuerte-Trisolini, MD, and Glenn Yiu, MD, PhD

DECEMBER 23, 2023



Perpendicular

Hold the microinjector
perpendicular
to the ocular surface



Dimple

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

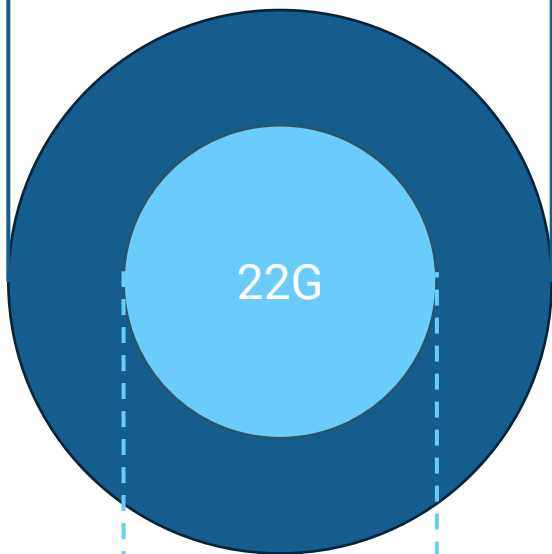


Slow

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



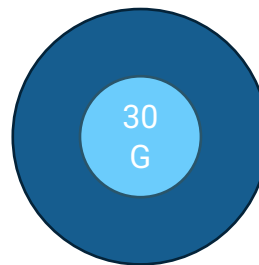
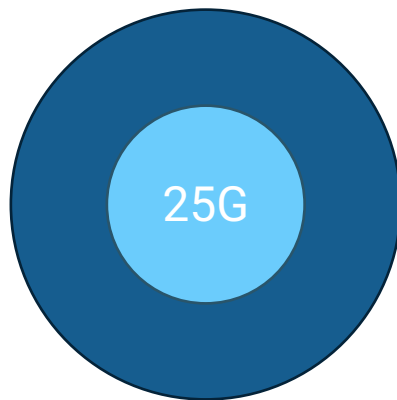
Inner Diameter of the Needle
Drug Product Passage

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[®]



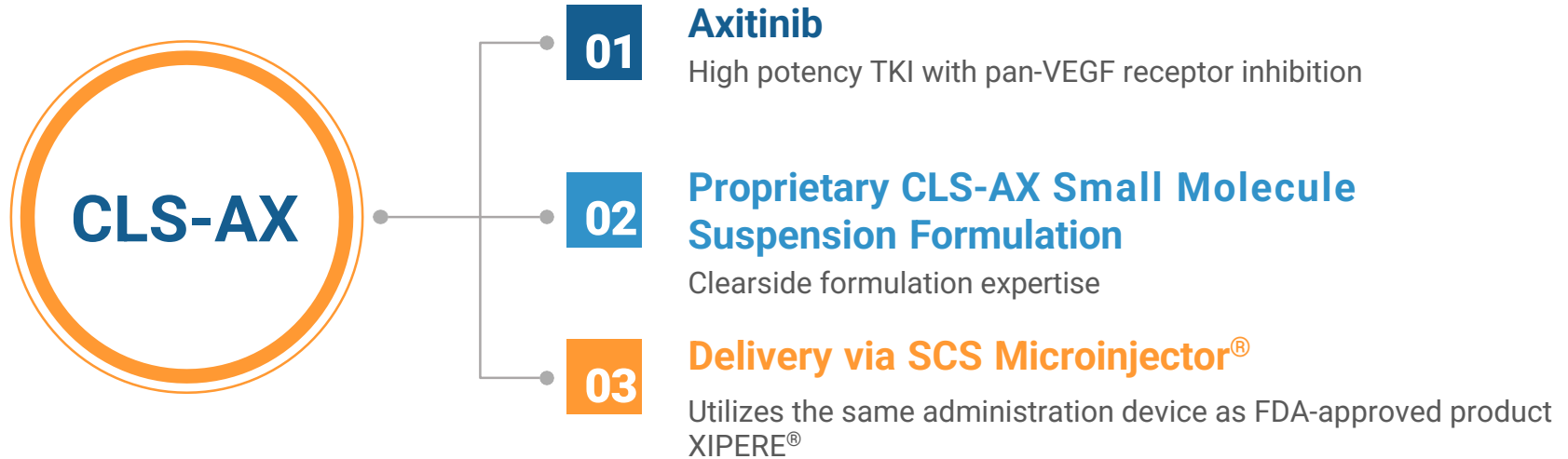
CLS-AX

(axitinib injectable suspension)

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

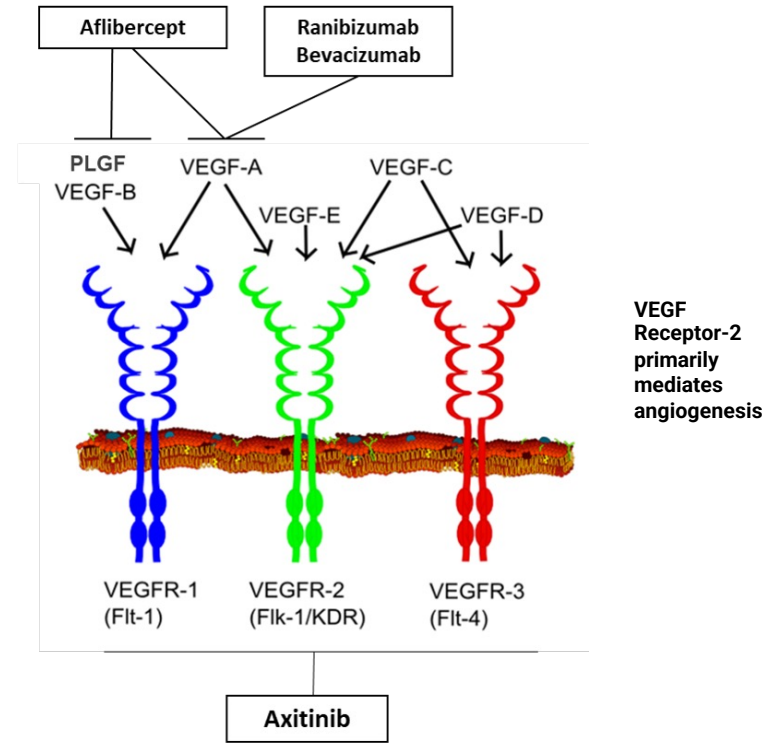


Leveraging a Highly Potent Pan-VEGF Inhibitor with Suprachoroidal Delivery



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 model¹⁻²
 - 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* studies³
 - Better ocular cell biocompatibility than other TKIs⁴
 - 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



Sources: 1. Cabral T et al. Bevacizumab Injection in Patients with Neovascular Age-Related Macular Degeneration Increases Angiogenic Biomarkers. *Ophthalmol Retina*. 2018 January ; 2(1) : 31–37. doi:10.1016/j.oret.2017.04.004. | 2. Lieu et al. The Association of Alternate VEGF Ligands with Resistance to Anti-VEGF Therapy in Metastatic Colorectal Cancer. *PLoS ONE* 8(10): e77117. | 3. Gross-Goupil et al. Axitinib: A Review of its Safety and Efficacy in the Treatment of Adults with Advanced Renal Cell Carcinoma. *Clinical Medicine Insights: Oncology* 2013;7. | 4. Thiele et al. Multikinase Inhibitors as a New Approach in Neovascular Age-Related Macular Degeneration (AMD) Treatment: In Vitro Safety Evaluations of Axitinib, Pazopanib and Sorafenib for Intraocular Use. *Klin Monatsbl Augenheilkd* 2013; 230: 247-254. | Image by Mikael Häggström, used with permission. Häggström, Mikael (2014). "Medical gallery of Mikael Häggström 2014". *WikiJournal of Medicine* 1 (2). DOI:10.15347/wjm/2014.008. ISSN 2002-4436. Public Domain.

Positioning CLS-AX for Real-World Success in the \$12 Billion Dollar Wet AMD Market¹

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 label²:

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

PHASE 2 TOPLINE DATA SUMMARY



ODYSSEY Phase 2b Clinical Trial Overview



Trial Objectives:

Evaluated 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

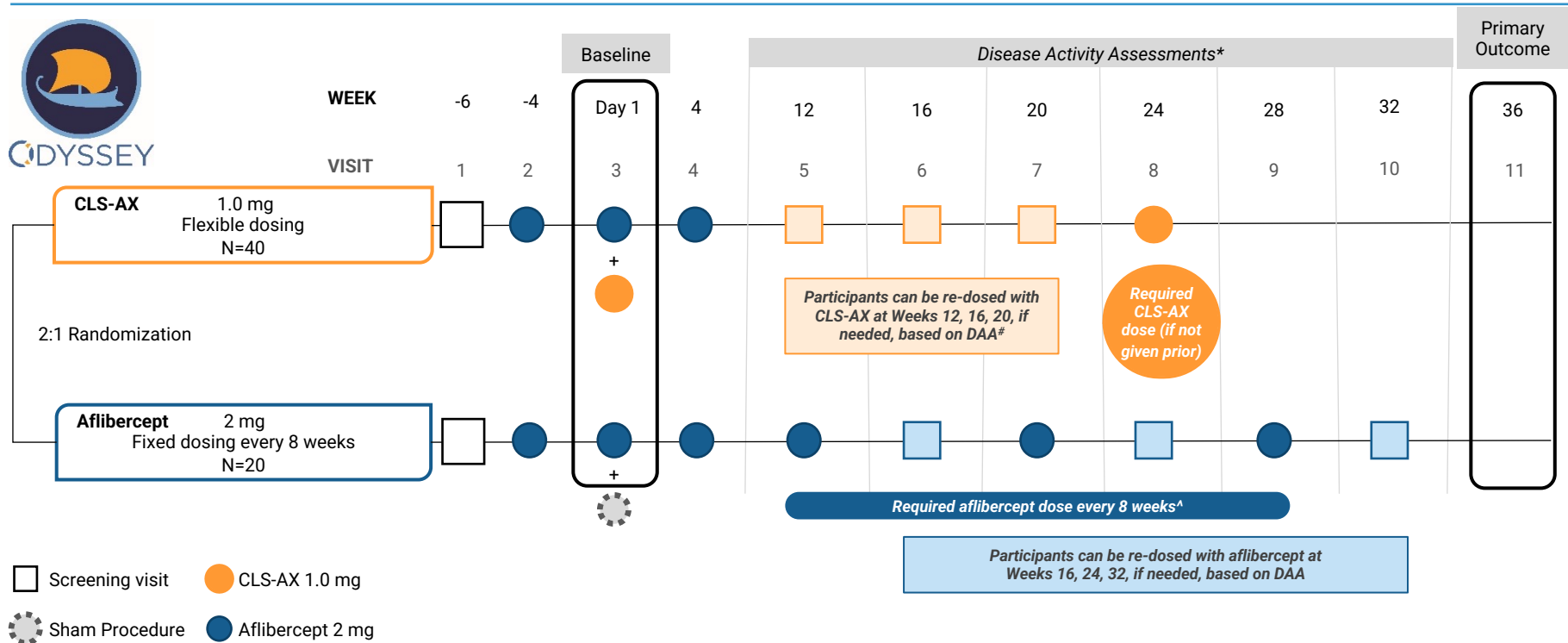


Participant Profile:

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
 - Provided important data to plan Phase 3 in chronic disease

ODYSSEY Trial Design

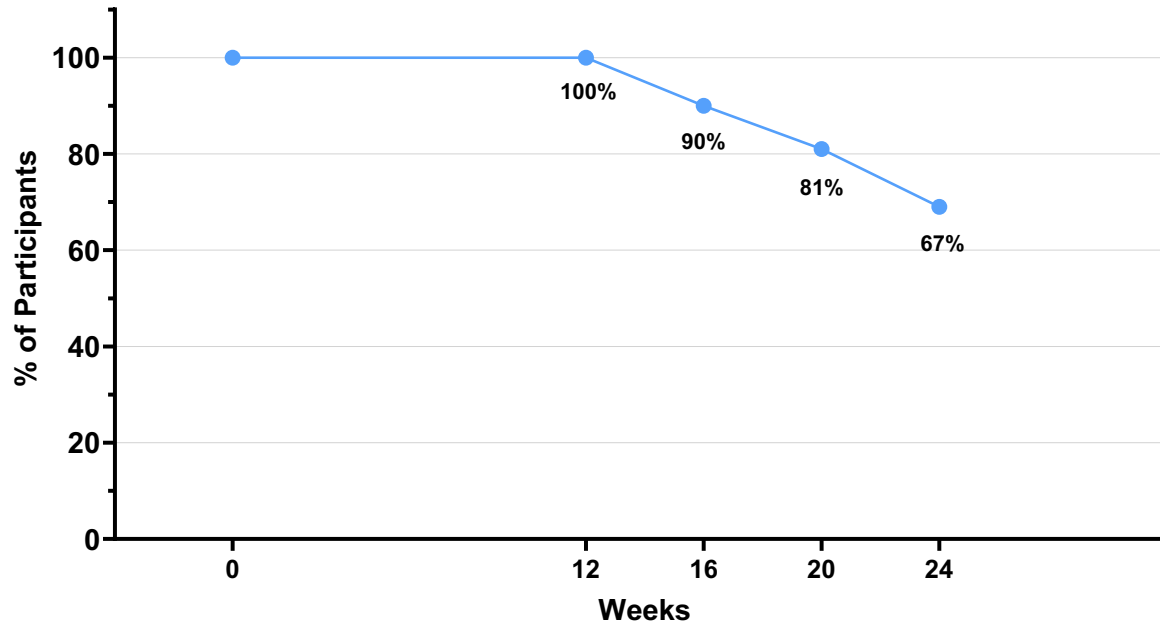


[#]Participants can be re-dosed with CLS-AX up to every 12 weeks; All arms are sham controlled

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

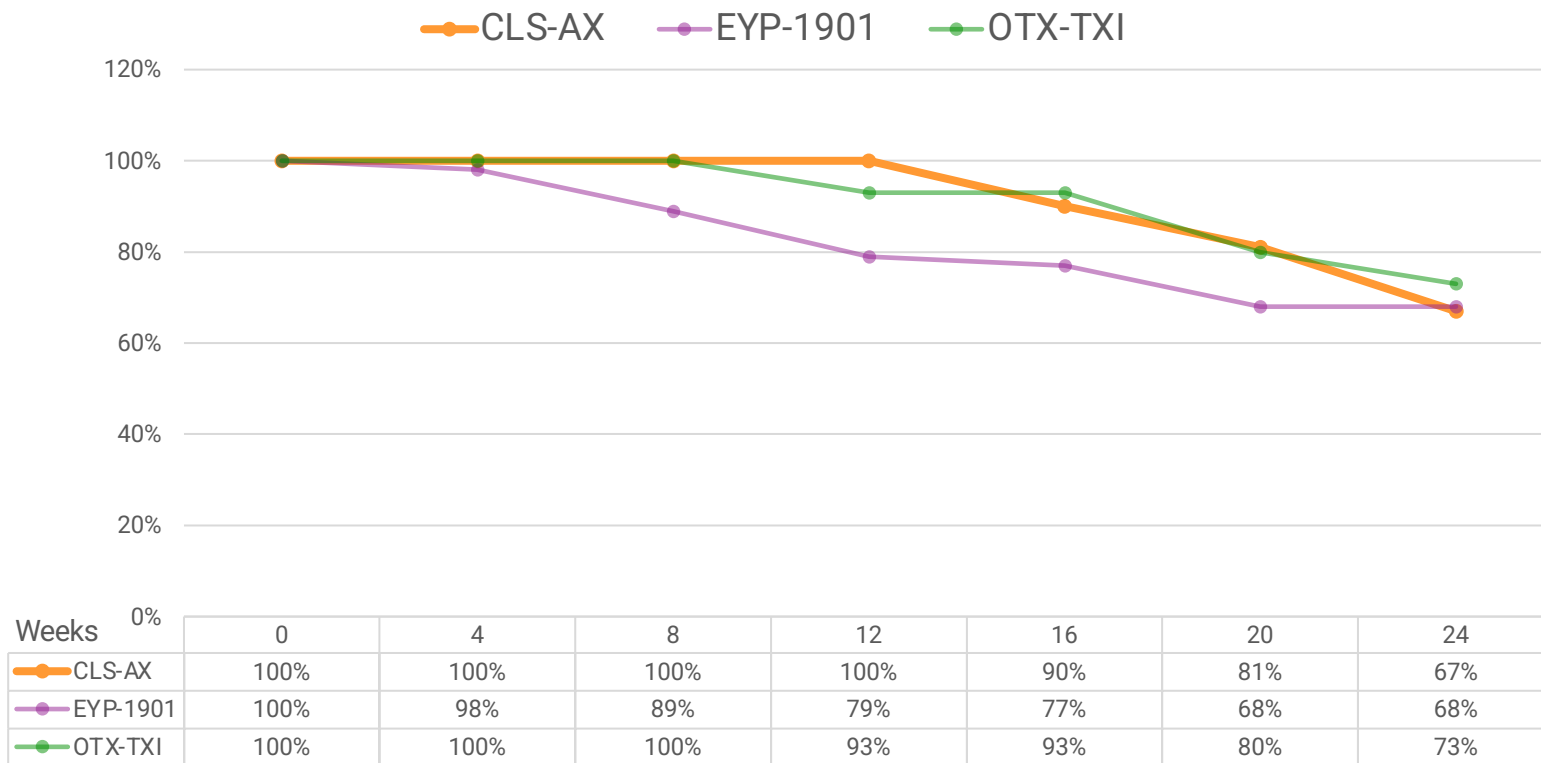
Two-Thirds of Participants Dosed with CLS-AX Reached Six Months Without Additional Treatment

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%)

Comparative TKI Intervention Free Rate Over 6 Months



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

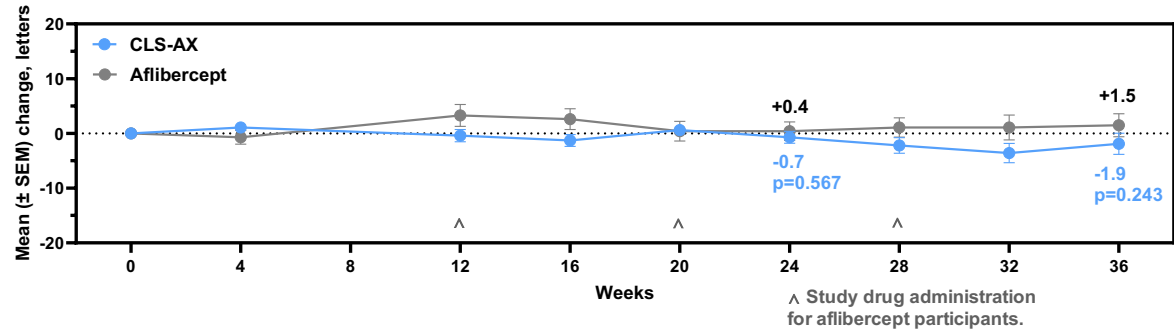
Average number of treatments
up to 24 Weeks after Baseline Visit:
0.475 injections

Reduced injection frequency by

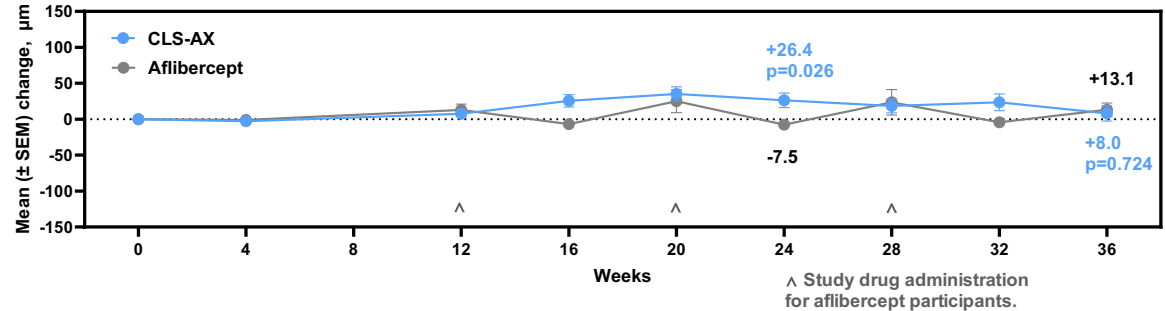
84%

CLS-AX Demonstrated Stable BCVA and CST Over 36 Weeks

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



CLS-AX Demonstrates Stable Anatomical Control and Reduces Fluctuation



CLS-AX results do not include supplemental therapy with aflibercept

[^]Study drug administration for aflibercept participants given at Weeks 12, 20 and 28.
 Abbreviations: BCVA = best corrected visual acuity; CST = central subfield thickness as reported by the reading center; SEM = standard error of the mean
 P-value based on a 2-sample t-test between treatment groups .

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

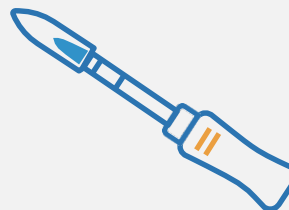
CLS-AX Now Phase 3 Ready Based on Positive ODYSSEY Data in Wet AMD



**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**

CLS-AX Phase 3 Program Current Plans

*Phase 3 plans are in development and
subject to change*



CLS-AX Phase 3 To Feature the Flexible Dosing of a Biologic with the Duration of a TKI

Two pivotal, non-inferiority trials in treatment naïve participants

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

Employ more “real world” clinical practice re-dosing criteria for CLS-AX

CLS-AX flexible dosing is an important differentiation vs other TKI programs

Successful End-of-Phase 2 FDA Meeting confirms Phase 3 program

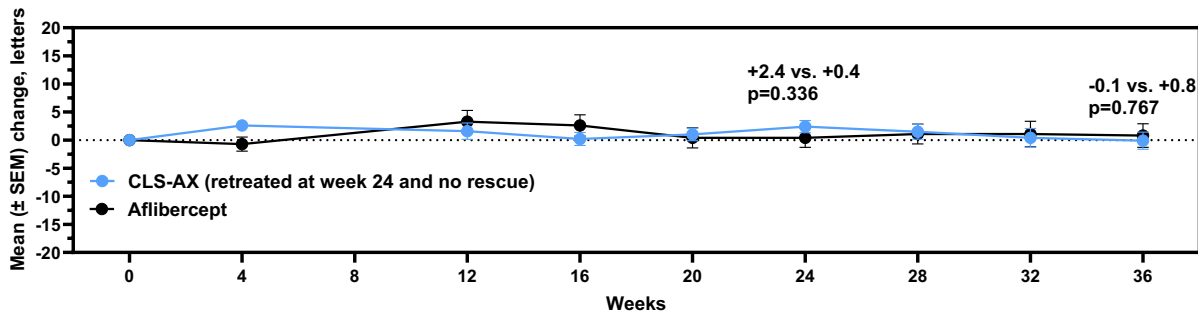
Preparations for Phase 3 program ongoing



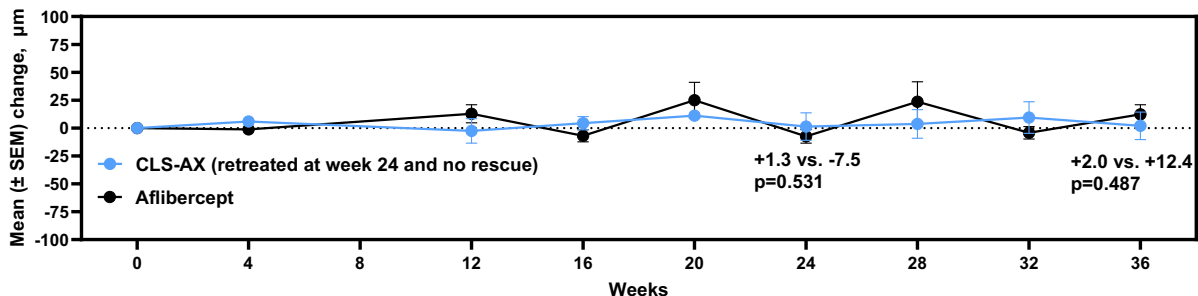
Sub-Group Analysis: Supports Enrolling Treatment Naïve Patients in the Phase 3 Program

Participants Solely Re-Dosed with CLS-AX at Week 24 Without Prior Intervention

BCVA



CST



Key Insights for Phase 3

- **ODYSSEY:** 67% of CLS-AX participants did not require rescue or re-dosing until the 6-month mandatory CLS-AX re-dosing in more difficult-to-treat patients.
- **Sub-group:** Stable BCVA and CST in participants who did not require aflibercept rescue or CLS-AX re-dosing prior to Week 24
- **Phase 3:** By targeting treatment naïve there may be an even greater percentage reaching 6-months without the need for any intervention.

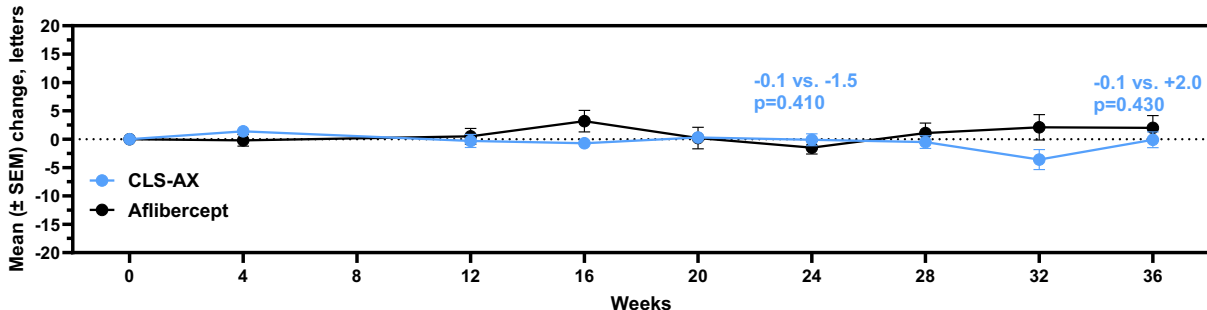


Sub-Group Analysis: Supports Phase 3 Design that Excludes Participants with Non-Disease Related Changes in Visual Acuity Prior to Randomization

DYSSEY

Excluding Observations with ≥ 10 Letter Change from the Previous Visit in BCVA Without a Corresponding 25 Micron Change in CST

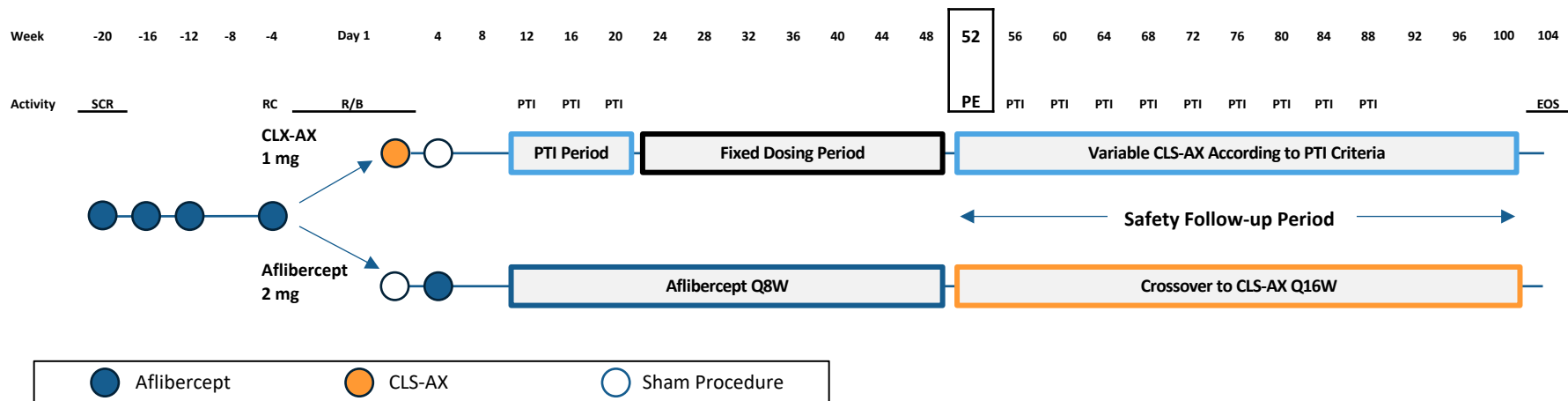
BCVA



Key Insights for Phase 3

- BCVA changes without OCT changes may not be disease related
- **Sub-group:** compelling BCVA results provide evidence that excluding participants with ≥ 10 letter changes prior to randomization may:
 - Reduce BCVA variability unrelated to Wet AMD activity
 - Better ensure data reflects real world treatment practices

CLS-AX Phase 3 Program Designed to Potentially Reduce Regulatory Risk and Maximize Commercial Opportunity in Wet AMD



- Participants will be randomized 1:1 to CLS-AX 1 mg or aflibercept 2 mg on Day 1.
- Personalized Treatment Interval (PTI) Assessment: At Weeks 12, 16, and 20, participants will undergo an assessment of disease activity based on PTI criteria. If the criteria were not met, the participants will be given CLS-AX every 24 weeks.
- Fixed Dosing Period: Once the treatment interval is determined in the PTI period, the participants will stay at that interval until week 52 (primary endpoint). For instance, if the participants met the PTI criteria at week 16, they will be given CLS-AX every 16 weeks in the fixed dosing period.
- For participants randomized to CLS-AX on a dosing interval of q24w, q20w, or q16w on or after Week 52, 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.

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

Key Elements:

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

Anticipated
Impact

- Addresses more general wet AMD population
- Increased commercial value, if approved

Strategies to Reduce Variability:

- Minimize enrollment of highly variable participants at Screening
 - Participants must have 20/80 to 20/32 AND CST <500 at diagnosis
- At Week -4 following three aflibercept loading doses, eliminate variability during treatment prior to randomization:
 - Participants with ≥ 10 letter change from Week -12 OR
 - CST (AI assessment) increases by ≥ 100 microns

Anticipated
Impact

- Intended to increase probability of success
- Strict participant screening to reduce variability in visual acuity is important in non-inferiority trials

Unique Ability to Re-Dose CLS-AX vs Rescue Supports Regulatory & Commercial Strategy



Why Flexible Dosing Matters

- Wet AMD is a chronic disease requiring numerous injections to maintain vision and stabilize the disease
- We know from clinical experience that patients require differing frequency of treatment to stabilize their disease
- Payer research confirmed reimbursement with a 3 to 6-month label to be on par with competitors
- Other TKIs in development initiated Phase 3 trials without multi-dose data and are only re-dosing at 6 months ("rescues" expected)



Planned Phase 3 Approach

- **Personalized Treatment Interval (PTI)** assessment enables physicians to use a "real world" approach with flexible dosing schedule based on participant needs
- **Minimal to No "rescues" expected** due to PTI defined CLS-AX re-dosing every 3 to 6 months
- **Employ in-office OCT biomarkers** (IRF and SRF) determined using AI tool to improve consistency in assessing need for re-dosing

IRF = intraretinal fluid; SRF = subretinal fluid; AI = artificial intelligence

Disease control and dosing based on publicly available information provided by each company as of March 2025.
EYLEA is a registered trademarks of Regeneron Pharmaceuticals. VABYSMO is a registered trademark of Genentech.

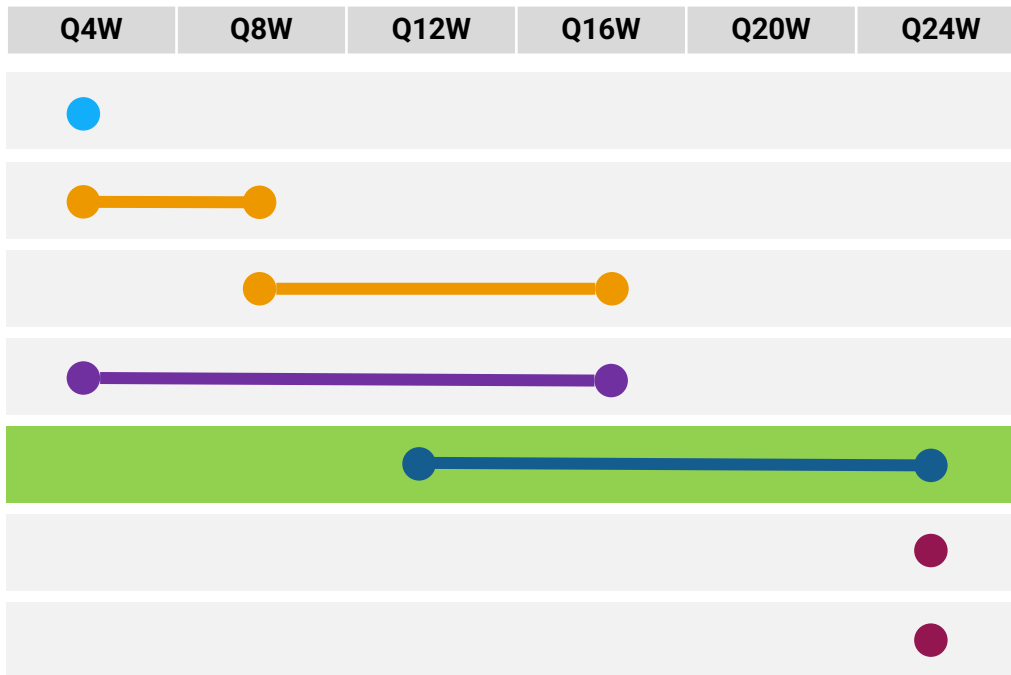
CLS-AX Phase 3 Designed to Compete with Currently Approved Drugs

Phase 3 Clinical Trial Design Comparison

	VABYSMO®	CLS-AX	OTX-TKI	EYP-1901
Non-inferiority	2	2	1	2
Multiple dosing	2	2	1	2
Flexible dosing	Y	Y	N	N
Tested Interval in Months	2 to 4	3 to 6	6	6
Rescue / Redosing	Redosing	Redosing	Rescue	Rescue
Study population optimization	N	Y	Y	N

CLS-AX Potentially Versatile and Commercially Appealing Label with Large Total Addressable Market Based on Planned 3-6 Month Dosing Flexibility

WET AMD Intended Dosing Interval Range (Weeks)



- Low Durability
- Less Flexible Dosing Regimen

- Moderate Durability
- Flexible Dosing Regimen

- High Durability - up to 6 mo
- Flexible Dosing Regimen

- High Durability up to 6 mo
- Fixed Dosing Regimen
- Needs anti-VEGF Rescue



Dosing based on publicly available information provided by each company as of March 2025.

LUCENTIS and VABYSMO are registered trademarks of Genentech. EYLEA and EYLEA HD are registered trademarks of Regeneron Pharmaceuticals. Clearside Biomedical is developing CLS-AX. Ocular Therapeutix is developing OTX-TKI. EyePoint Pharmaceuticals is developing EYP-1901.

Why We Believe CLS-AX Should Be the “Preferred TKI”



Efficacy Profile vs. Other TKIs

- Equivalent 6-month Duration of Effect as EYPT and OCUL
- Equivalent Intervention Free Rates despite more rigorous intervention criteria
- Equivalent reduction in treatment burden
- More potent API vs EYPT, Same API as OCUL



Potential SCS Safety Advantages

- Very low risk of endophthalmitis since CLS-AX not injected into vitreous
- No implant floating in vitreous
- No evidence TKI implants fully dissolved in vitreous at 6 months
- Same gauge injection needle as EYLEA/VABYSMO; EYPT and OCUL each use larger needle gauges to inject implants



Rigorous Phase 2 Trial Design Should Reduce Phase 3 Risks facing other TKIs

- ODYSSEY enrolled only participants with active disease vs OCUL whose participants had to be inactive (dry)
- ODYSSEY more sensitive re-treatment/rescue criteria yet similar durability of effect to other TKIs
- CLS-AX may have even better results if using same inclusion/re-treatment criteria as other TKIs
- OCUL did not conduct Phase 2 trial (only limited Phase 1 data in 15 active arm participants)



Physician/Commercially Preferred Target Label (3 - 6 months)

- As flexible as VABYSMO and EYLEA HD and as durable as other TKIs – potentially translatable to a larger market share
- EYPT and OCUL must “rescue” with anti-VEGF biologics
- Physicians prefer re-dose with same product for harder to treat patients
- CLS-AX may be re-dosed as often as every 3 months
- CPT code for SCS administration reimburses physicians at a higher rate than IVT

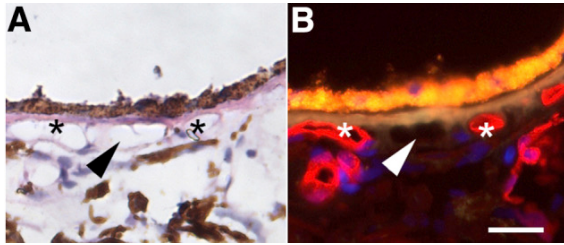
Pipeline Expansion Opportunity in Geographic Atrophy



Geographic Atrophy is a Choroidal Disease and an Advanced Form of Age-Related Macular Degeneration (AMD)

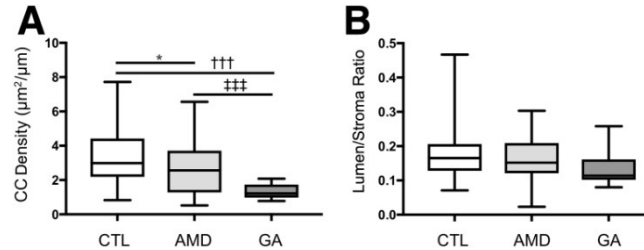
Choroidal Hypoxia Theory and Choriocapillaris are Damaged First

1



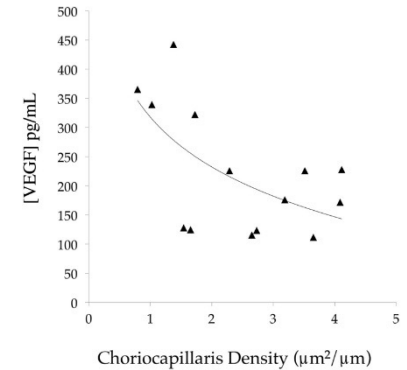
Choriocapillaris endothelial cells damage with ghost vessels before any significant RPE changes

2



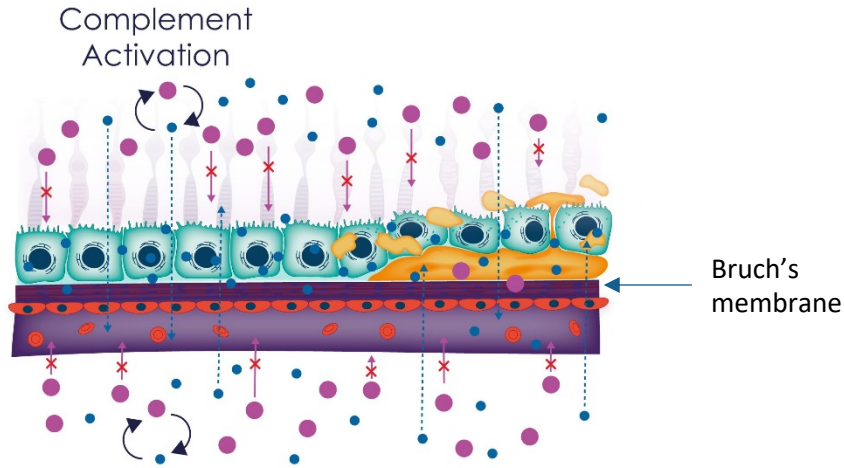
- Choriocapillaris (CC) vascular density is significantly lower in GA donor
- No meaningful differences in vascular lumen area / stroma area

3

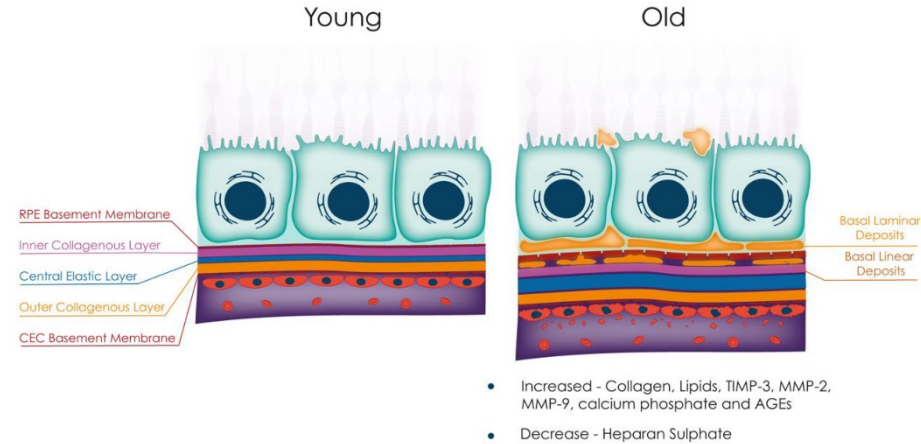


VEGF level increased with low vascular density support the choroidal hypoxia theory

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



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



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

Potential Advantages of Suprachoroidal Delivery in Geographic Atrophy



● **Able to reach the choroid first**

● **Small molecules may have better efficacy than current therapies**

● **In-office procedure**

● **Targeted delivery compartmentalized to the posterior segment**

● **SCS may be ideal delivery for gene therapy as subretinal is too invasive and intravitreal delivery lacks efficacy with a high risk of inflammation**

Geographic Atrophy Program Focused on Small Molecule Suspensions

Evaluating Two Mechanisms That Could Potentially Be Used as Add On to Complement-Based Therapies

Small Molecule Suspensions

- Can treat both sides of the Bruch's membrane (Retina, RPE and Choroid)
- Higher concentration of drug in the choroid

1. Improve choroidal perfusion

Blood flow improvement can improve retinal function directly and slow progression

2. Modulate pro-inflammatory cells

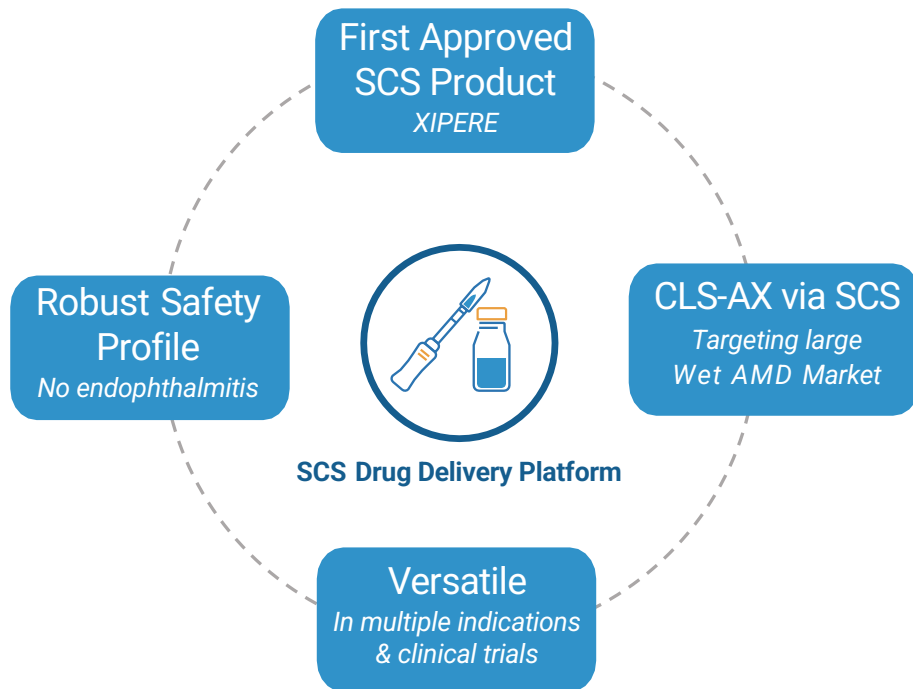
Inflammatory cells manipulation can reduce the root cause of complement activation

Summary



Innovative and Experienced Leader in Suprachoroidal Drug Delivery

- Differentiated late-stage ophthalmology company with a platform of assets
- Patented SCS Microinjector[®] delivers agents directly to the back of the eye
- Validated technology with multiple partners
- Aligned with the FDA on the Phase 3 program designed to support a commercially appealing label
- Potential pipeline expansion in geographic atrophy, diabetic retinopathy, and the combination of CLS-AX and a steroid (CLS-TA) for DME





CLEARSIDE BIOMEDICAL

Nasdaq: CLSD



TM