



CLEARSIDE BIOMEDICAL

ODYSSEY Phase 2b Clinical Trial Results

October 9, 2024



ODYSSEY



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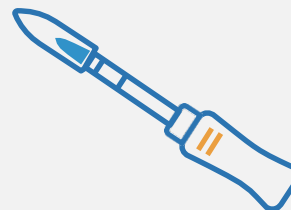
CLS-AX Now Phase 3 Ready Based on Positive ODYSSEY Data in Wet AMD



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



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



**Compelling
Intervention-Free
Rates**



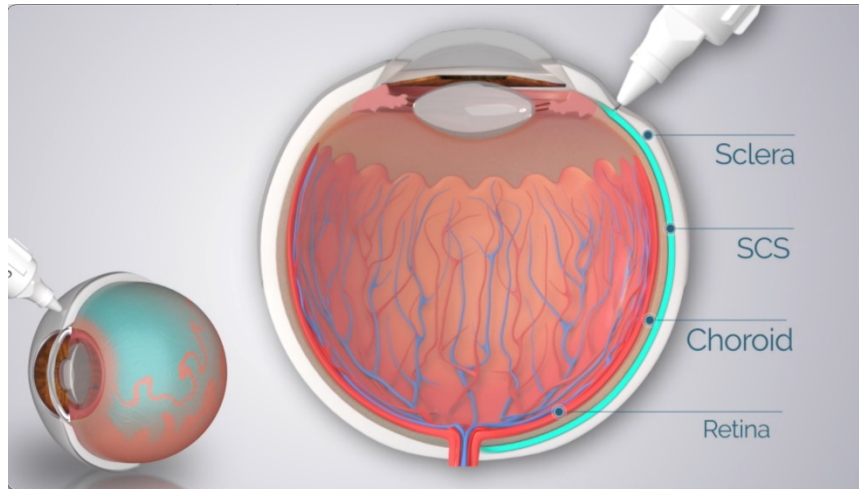
**Positive
Safety Profile
with Repeat
Dosing**

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**



SCS Microinjector®: Drug/Device Combination with Proven Versatility



SUPRACHOROIDSAL SPACE INJECTION

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

- ✓ **First and Only FDA-approved SCS product**
- ✓ **Multiple clinical trials with 4 potential therapies in 5 indications:**
Wet AMD, UME, DME, DR, Choroidal Melanoma
- ✓ **Safety profile of SCS Microinjector comparable to intravitreal injections¹**
- ✓ **Well-accepted by retinal physicians with thousands of injections performed to date**
- ✓ **30-gauge needle equivalent to most commonly used intravitreal injections**
Smaller than tyrosine kinase inhibitor (TKI) competitors in development



CLS-AX for the Treatment of Wet AMD

Leveraging a Highly Potent Pan-VEGF Inhibitor with Suprachoroidal Delivery



01

Axitinib

High potency TKI with pan-VEGF receptor inhibition

02

Proprietary CLS-AX Small Molecule Suspension Formulation

Clearside formulation expertise

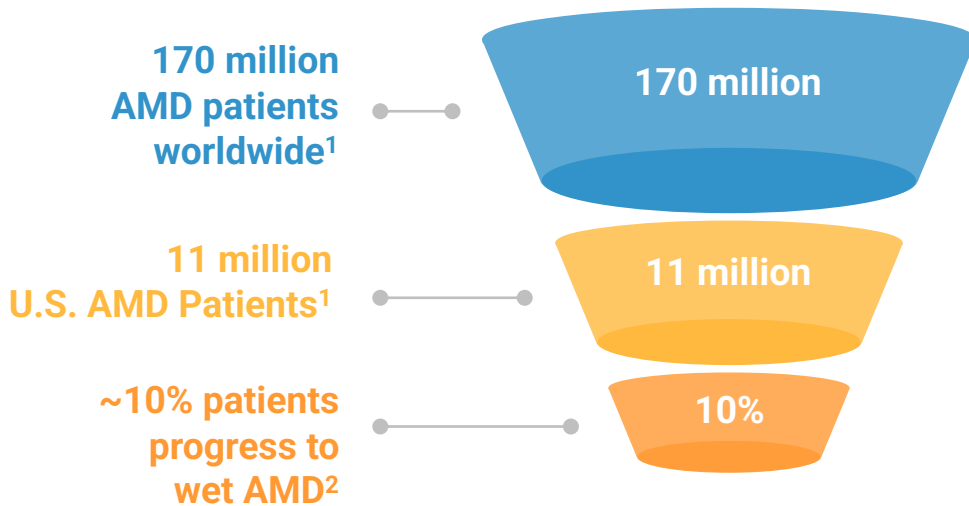
03

Delivery via SCS Microinjector[®]

Utilizes the same administration device as FDA-approved product XIPERE[®]

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 55¹
- ✓ U.S. prevalence expected to increase to 22 million by the year 2050¹
- ✓ Global prevalence expected to increase to 288 million by the year 2040¹
- ✓ Current treatments require frequent injections and subset of patients experience disappointing visual outcomes²

✓ **Over \$12 Billion Market and Growing³**

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 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



Phase 2b Topline Data Summary

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

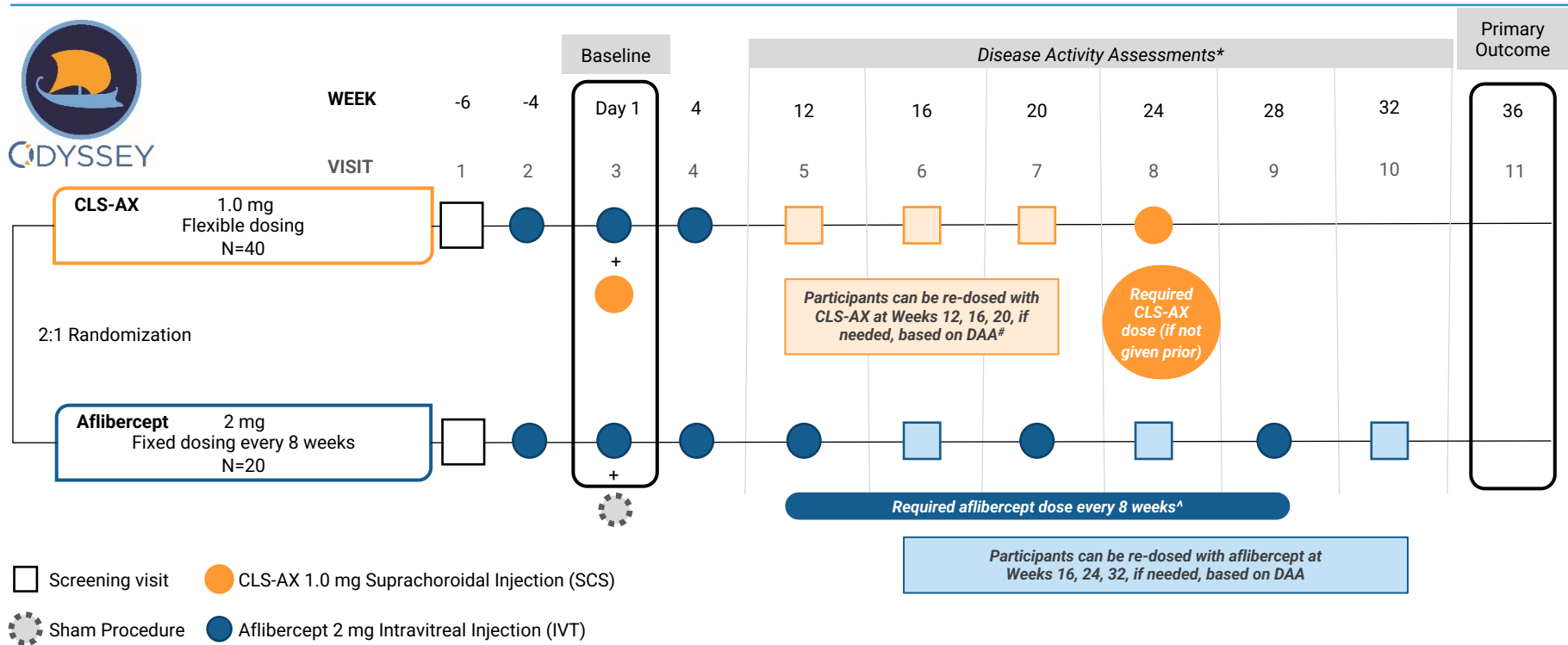


Participant Profile:

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



[#]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.

CLS-AX Demonstrated Positive Efficacy Data in Wet AMD

Overall

Achieved Primary Outcome in participants with confirmed active disease

BCVA

Stable BCVA throughout the trial

Measured as mean change in BCVA from baseline to Week 36

CST

Stable CST throughout the trial

Measured as mean change in CST from baseline to Week 36

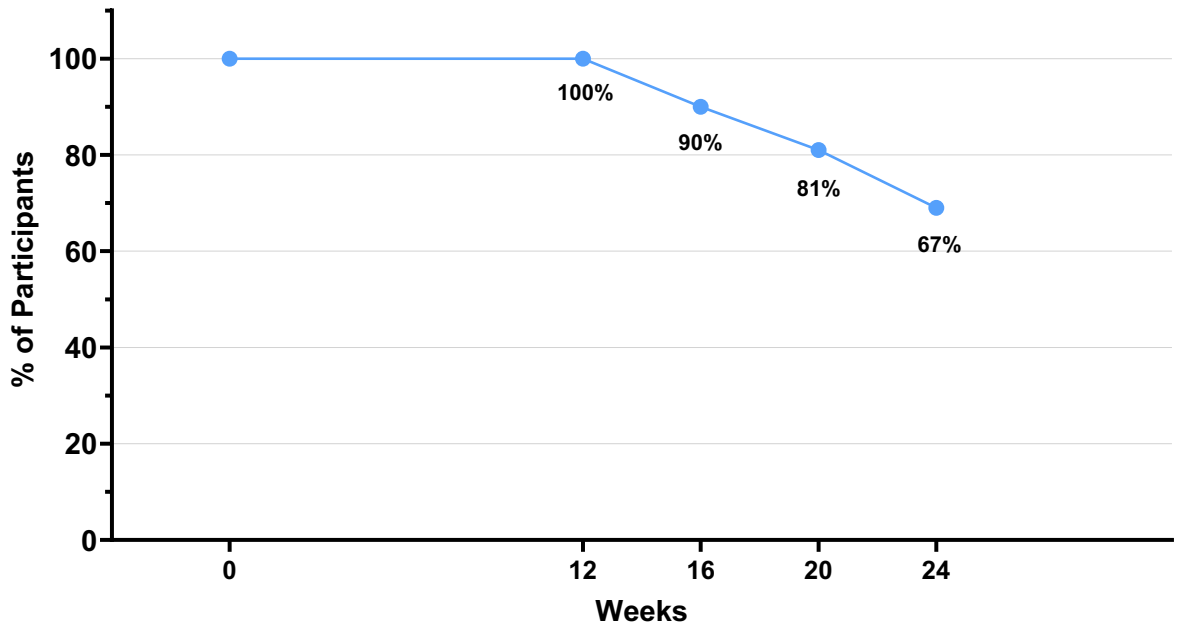
Durable Effect

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

Injection frequency reduced by nearly 84% up to 24 weeks

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 Demonstrated A Positive Safety Profile

Safety Profile

Excellent 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



Phase 2b Trial Participant Characteristics

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[#]

Dosing Regimen

- **Participants in both arms received 3 aflibercept (2 mg) loading doses (2nd 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.
[#] Using the Early Treatment Diabetic Retinopathy Study (ETDRS) measurement.
Abbreviations: SD-OCT (Spectral Domain Optical Coherence Tomography).

Rapid Enrollment Demonstrates Investigator Interest in Suprachoroidal TKI Delivery

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)

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, μm	266.8 (175-378)	294.3 (209-592)	276.0 (175-592)
Mean Total Area of CNV (range) at screening, 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) ^a (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.

^aAnnualized 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.



Phase 2b Topline Data Results

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

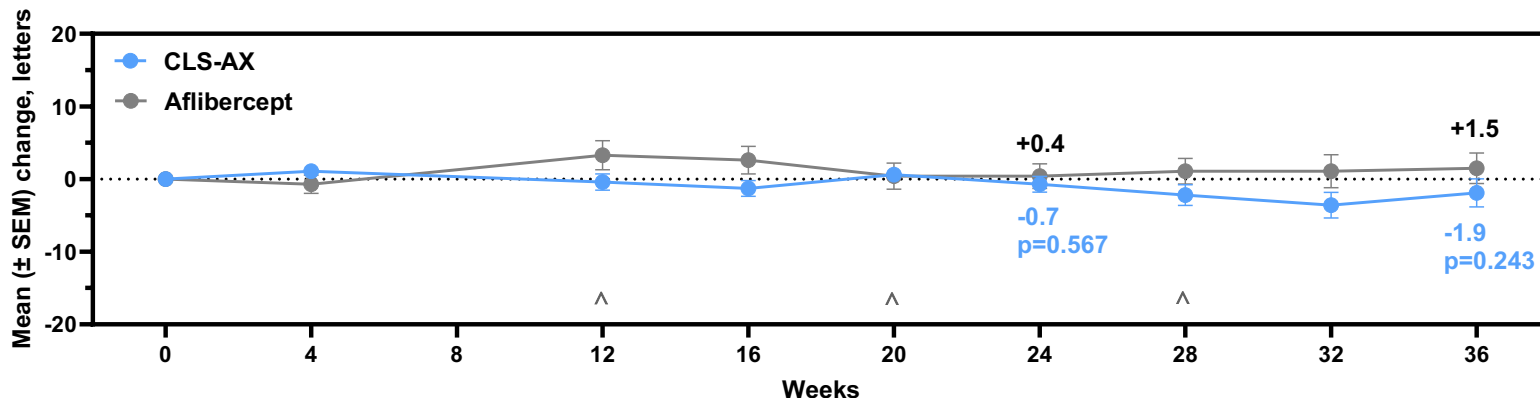
Of the 40 participants in the trial:

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%

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

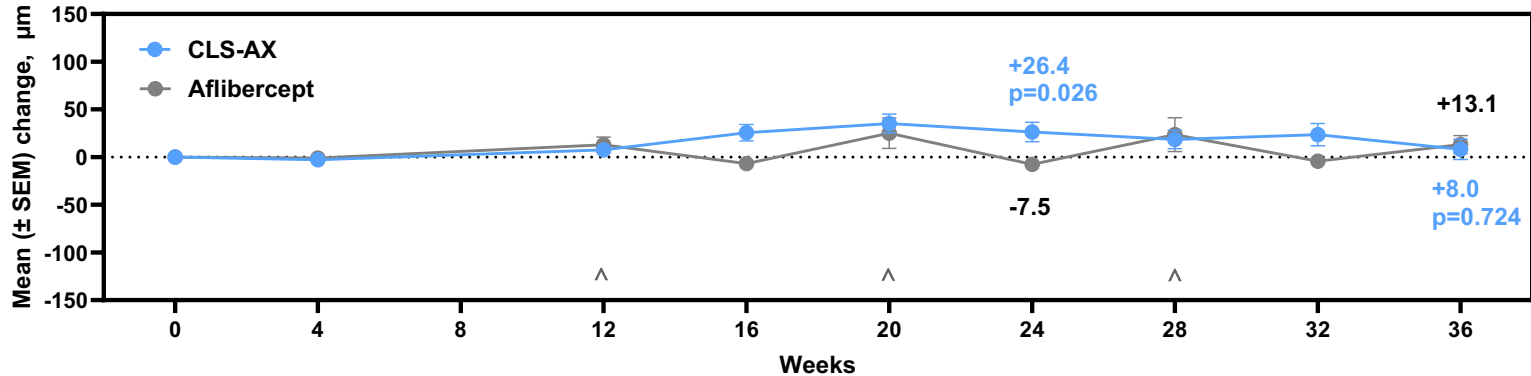


CLS-AX results do not include supplemental therapy with aflibercept

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

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

CLS-AX Demonstrates Stable Anatomical Control and Reduces Fluctuation

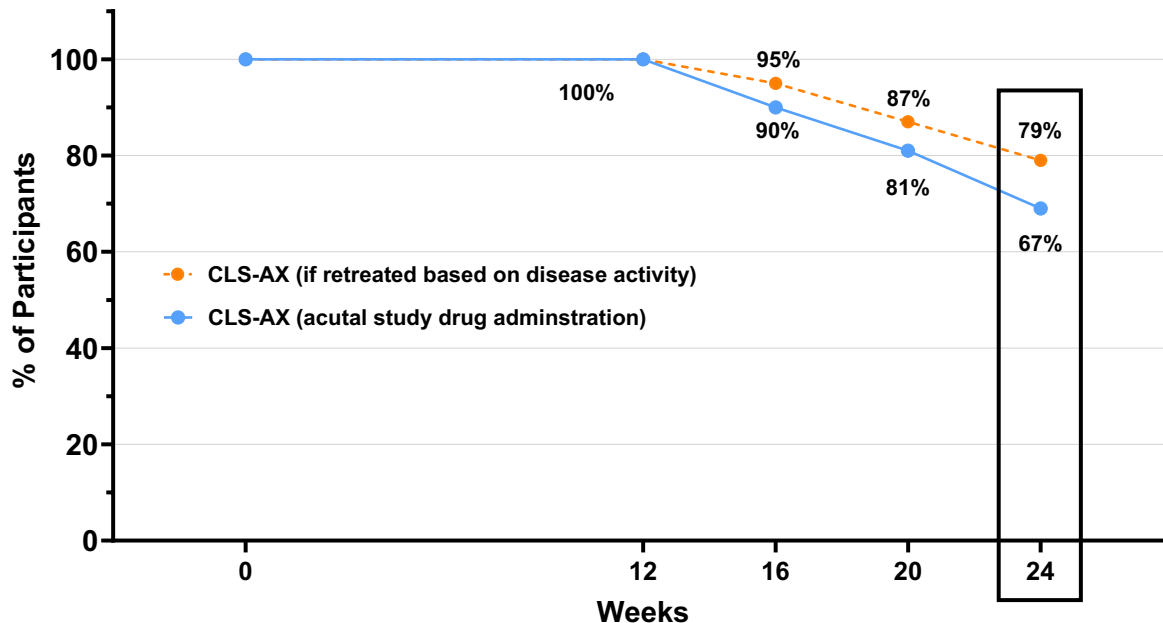


CLS-AX results do not include supplemental therapy with aflibercept

^Study drug administration for aflibercept participants given at Weeks 12, 20 and 28.
Abbreviations: CSRT = central subfield retinal 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 .

More Participants May Have Been Intervention Free at Every Time Point if DAA Criteria Strictly Applied

No Participants Met the DAA Criteria Per Reading Center Confirmation at Week 24, but They Received Mandatory Re-Dosing Per the Protocol



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

DAA = Disease Activity Assessment. Actual treatments compared to reading center confirmation. Active disease-free rate calculation: if participant had active disease at a study visit, those were reflected in the count at the following study visit. N = number of participants assessed at a study visit; n = number of participants active disease-free up to a visit. Active disease presence based on BCVA and CSRT as graded by the central reading center.

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 Positive Safety Profile

No Ocular SAEs and No Treatment-Related SAEs

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



Phase 3 Planning

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

Goal for Label: Flexible Wet AMD Maintenance Dosing Regimen Between 3 Months and 6 Months

Next Steps

Continue analysis of ODYSSEY results including expert assessments

Conduct **End-of-Phase 2 meeting** with U.S. FDA in early 2025

Phase 3 Current Planning Considerations

- Design Phase 3 to produce data supportive of a label with **dosing between 3 – 6 months** to align with wet AMD treatment approach desired by most retinal physicians
- **Repeat CLS-AX dosing data** in ODYSSEY will inform the Phase 3 design and improve overall data to support NDA submission

Likely Trial Design Features*

Two Phase 3 studies with aflibercept 2 mg as comparator

Treatment-naïve participants

- Consistent with aflibercept high dose and faricimab Phase 3 trials
- As a group, not considered as difficult to treat by most retinal physicians

Non-inferiority and flexible dosing design

- Similar to recently approved intravitreal wet AMD therapies
- Provides easy transition to real-world clinical setting for commercial success



Results Summary

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



**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**

Roger A. Goldberg, MD, MBA

Bay Area Retina Associates





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Nasdaq: CLSD



TM