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): October 09, 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 October 9, 2024, Clearside Biomedical, Inc. (the "***Company***") will give a presentation describing its positive topline results from ODYSSEY, the Company's Phase 2b clinical trial of CLS-AX for the treatment of wet AMD. The live and archived webcast may be accessed on the Company's website under the "Investors" section. A copy of the presentation is attached as Exhibit 99.1 to this Current Report on Form 8-K. The information contained in, or that can be accessed through, the Company's website is not a part of this filing.

The information in this Item 7.01 of this Current Report on Form 8-K (including Exhibit 99.1) is being furnished and 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 liabilities of that Section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

On October 9, 2024, the Company issued a press release announcing the topline results from the ODYSSEY Phase 2b clinical trial. The full text of the press release is attached as Exhibit 99.2 to this Current Report on Form 8-K and incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Exhibit Description
99.1	Corporate Presentation, dated October 9, 2024.
99.2	Press Release, dated October 9, 2024.
104	Cover Page Interactive Data File (the cover page XBRL tags are embedded within the inline XBRL document)

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.

Clearside Biomedical, Inc.

Date: October 9, 2024

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

Exhibit 99.1


CLEARSIDE
BIOMEDICAL
ODYSSEY Phase 2b Clinical Trial Results
October 9, 2024
ODYSSEY
TM

Forward-Looking Statements

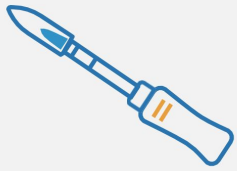
This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. The words “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “target” 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 the clinical development of CLS-AX, the timing of correspondence with regulatory authorities, and the trial design features of a potential Phase 3 trial. 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, , Clearside’s Quarterly Report on Form 10-Q filed with the SEC on August 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. 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.

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

ODYSSEY

Enrolled Only Difficult-to-Treat Participants with Active Disease

Achieved Primary Outcome Maintaining Stable BCVA with Repeat Dosing



Compelling Intervention-Free Rates

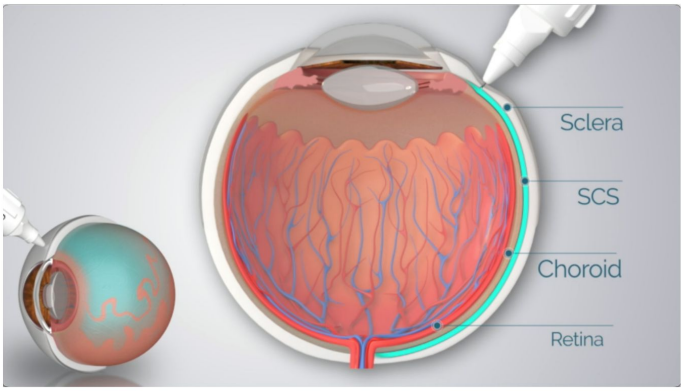
Positive Safety Profile with Repeat Dosing

Abbreviation: Wet AMD = neovascular age-related macular degeneration; BCVA = Best Corrected Visual Acuity

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



SUPRACHOROIDAL SPACE INJECTION

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

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

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

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**

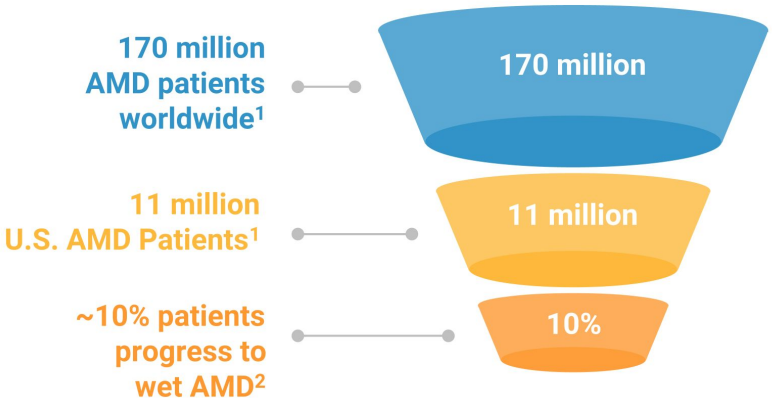
Clearside formulation expertise

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 55[1]
- U.S. prevalence expected to increase to 22 million by the year 2050[1]
- Global prevalence expected to increase to 288 million by the year 2040[1]
- Current treatments require frequent injections and subset of patients experience disappointing visual outcomes[2]
- **Over $12 Billion Market and Growing[3]**

CLEARSIDE BIOMEDICAL

Sources: [1] Pennington, Katie L and DeAngelis, Margaret M, Eye and Vision, Epidemiology of age-related macular degeneration (AMD): associations with cardiovascular disease phenotypes and lipid factors, Dec 22, 2016.
[2] Prall, F Ryan and Ciulla, Thomas A, Medscape: Exudative (Wet) Age-Related Macular Degeneration (AMD), June 16, 2022.
[3] Annual financial reports from Regeneron Pharmaceuticals, Inc. and Genentech/Roche.

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

*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

ODYSSEY Phase 2b Clinical Trial

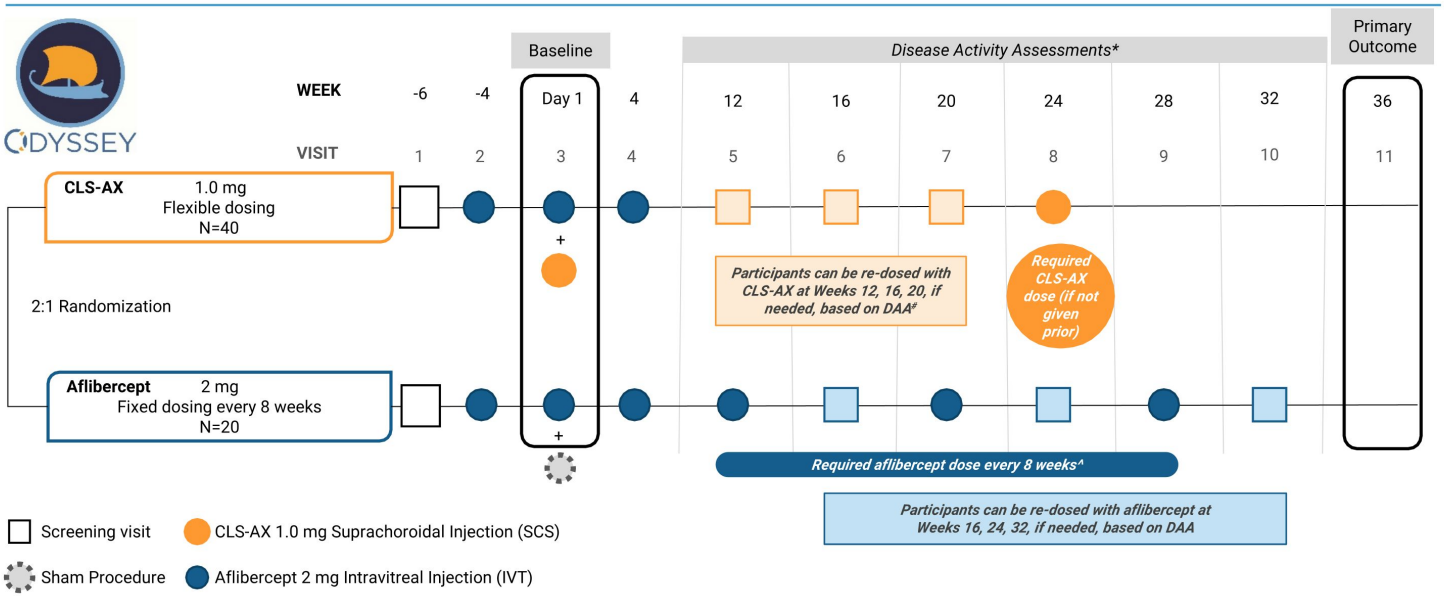
Trial Objectives:
Evaluate safety, efficacy & duration of CLS-AX in participants with wet AMD

- 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

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.

CLS-AX Demonstrated Positive Efficacy Data in Wet AMD

Overall

Achieved Primary Outcome in participants with confirmed active disease

BCVA

Stable BCVA throughout the trial

Measured as mean change in BCVA from baseline to Week 36

CST

Stable CST throughout the trial

Measured as mean change in CST from baseline to Week 36

Durable Effect

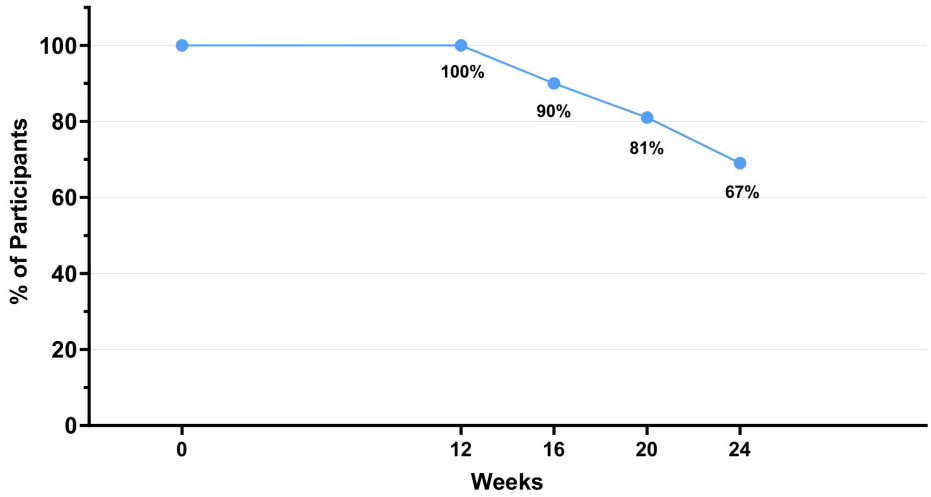
67% of participants did not require any additional treatment for up to 24 weeks (6 months)

Injection frequency reduced by nearly 84% up to 24 weeks

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

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

Intervention–Free Rates By Week Up to Each Visit



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

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

CLS-AX Demonstrated 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

CLEARSIDE BIOMEDICAL

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 36 weeks*	 39 (97.5) 36 (90.0)	 19 (95.0) 17 (85.0)	 58 (96.7) 53 (88.3)

*Discontinuation rate was similar between arms

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 Asian	 37 (92.5) 3 (7.5)	 20 (100) 0	 57 (95.0) 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.
[a]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.

Phase 2b Topline Data Results

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

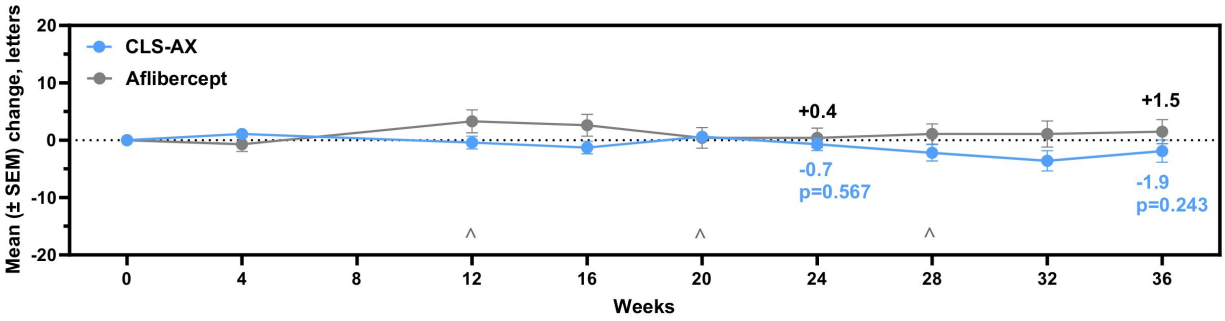
Of the 40 participants in the trial:

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

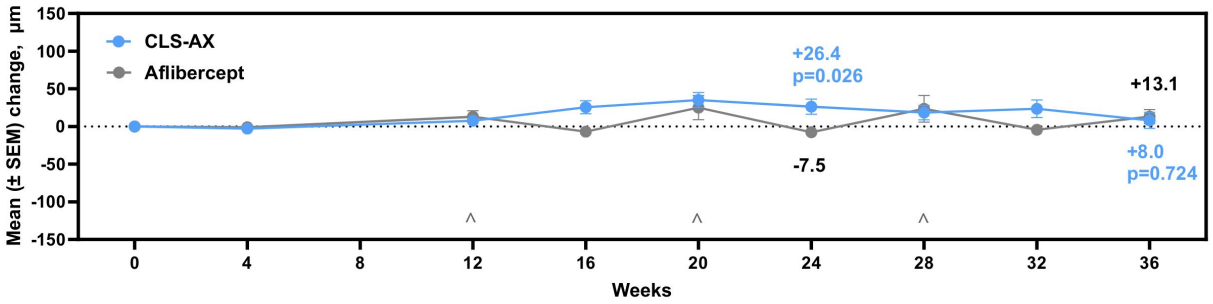


CLS-AX results do not include supplemental therapy with aflibercept

^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

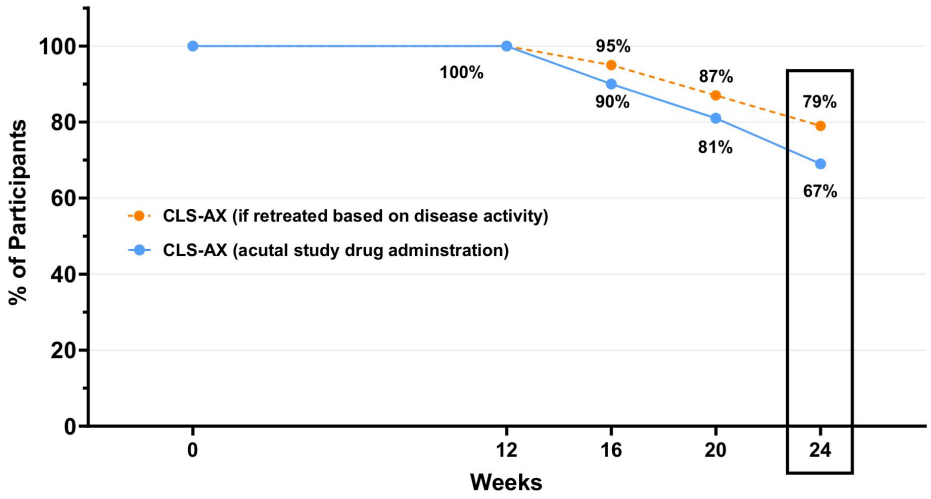


CLS-AX results do not include supplemental therapy with aflibercept

^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%

Injection post Baseline includes re-dosing with CLS-AX and/or supplementary treatment with aflibercept.
Injection frequency reduction calculated by the average number of treatments 24 Weeks prior to Screening Visit as compared to average number of treatments up to 24 Weeks after Baseline Visit.

CLS-AX Demonstrated Positive Safety Profile

No Ocular SAEs and No Treatment-Related SAEs

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

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

Phase 3 Planning

Phase 3 plans are in development and subject to change

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


CLEARSIDE
BIOMEDICAL
Nasdaq: CLSD
TM

Exhibit 99.2

Clearside Biomedical Announces Positive Topline Results from ODYSSEY Phase 2b Trial of Suprachoroidal CLS-AX in Wet AMD Achieving All Primary and Secondary Outcomes

- Maintained Stable Visual Acuity and Anatomical Control Over 9 Months -

- Positive Safety Profile with No Ocular or Treatment-Related Serious Adverse Events -

- 67% of CLS-AX Participants Did Not Require Any Additional Treatment up to 6 Months -

- Reduced Treatment Burden by 84% Over 6 Months -

- Webcast and Conference Call Today at 8:00 A.M. ET with Management and Key Opinion Leader and Board-Certified Retinal Specialist, Roger Goldberg, M.D., MBA -

ALPHARETTA, Ga., October 9, 2024 -- Clearside Biomedical, Inc. (Nasdaq: CLSD), a biopharmaceutical company revolutionizing the delivery of therapies to the back of the eye through the suprachoroidal space (SCS®), announced today that the ODYSSEY Phase 2b clinical trial of CLS-AX (axitinib injectable suspension) for the treatment of neovascular age-related macular degeneration (wet AMD) achieved both its primary and secondary outcomes. In participants who received CLS-AX delivered suprachoroidally, best corrected visual acuity (BCVA) and ocular anatomy (central subfield thickness) were stable up to 6 months compared to participants who received aflibercept. In addition, CLS-AX demonstrated a well-tolerated safety profile to Week 36 inclusive of mandatory re-dosing of CLS-AX at Week 24.

“We are very excited to report positive topline data from our successful ODYSSEY Phase 2b trial,” said George Lasezkay, PharmD, JD, President and Chief Executive Officer, Clearside Biomedical. “These encouraging results strongly support advancing our CLS-AX wet AMD program into Phase 3 development and provide further evidence of the potential benefits of delivering medicines to the back of the eye using our proprietary SCS Microinjector®. We achieved our primary outcome of maintaining stable BCVA throughout the trial as measured by the mean change in BCVA from baseline to Week 36. CLS-AX consistently reduced the frequency of injections after the initial dose of CLS-AX with approximately 90% of CLS-AX participants not requiring any additional treatment up to 4 months, 81% not requiring any additional treatment up to 5 months, and 67% not requiring any additional treatment up to 6 months before mandatory re-dosing at Week 24. We believe this data supports our goal to potentially provide a safe, convenient wet AMD treatment

option with the advantage of a flexible maintenance dosing regimen between 3 to 6 months. We look forward to continuing to analyze the results and share additional data analysis with the retina community at upcoming medical meetings."

Victor Chong, M.D., MBA, Chief Medical Officer of Clearside, added, "CLS-AX demonstrated extended duration and stable vision and anatomic measures throughout the trial in a difficult-to-treat patient population with reading center confirmed active disease early in their treatment journey. ODYSSEY confirmed the ability to administer multiple doses of CLS-AX from 12 weeks up to 36 weeks with a well-tolerated safety profile. We believe the ability to deliver multiple doses as needed between 12 and 36 weeks is a key differentiator from other treatments in development. In the trial, we observed that CLS-AX, delivered into the suprachoroidal space using our SCS Microinjector®, can be flexibly dosed similar to current biologic treatments, but has the potential to last longer because it is a highly potent tyrosine kinase inhibitor that achieves pan-VEGF blockade. Our goal is to provide a new and important treatment option with meaningful efficacy, safety, and delivery benefits for patients and retina specialists. These topline results provide valuable data in wet AMD with repeat dosing data to better inform our planned Phase 3 program design."

David M. Brown, M.D., Director of Research, Retina Consultants Houston, commented, "These data are encouraging and demonstrate that suprachoroidal CLS-AX may have sustained durability beyond our currently approved agents. The positive safety profile, potential flexible dosing and delivery of CLS-AX directly to the back of the eye via Clearside's SCS Microinjector has the potential to improve the treatment landscape for patients and physicians looking for a long-acting treatment for wet AMD."

ODYSSEY Topline Data Summary

ODYSSEY was a randomized, double-masked, parallel-group, active-controlled, multicenter, 36-week, Phase 2b clinical trial in participants with wet AMD previously treated with intravitreal anti-vascular endothelial growth factor (VEGF) standard of care therapy. A total of 60 participants were treated for 36 weeks and randomized to either CLS-AX (1 mg) or aflibercept (2 mg) with a 2:1 randomization schedule (40 participants in CLS-AX arm and 20 participants in aflibercept arm). CLS-AX was administered by suprachoroidal injection via Clearside's SCS Microinjector, and aflibercept was administered via intravitreal injection. Participants in the trial were determined to have active disease with a median duration of wet AMD diagnosis of 9.9 months. Eligible participants underwent diagnostic imaging at their screening visit, followed by masked reading center confirmation of persistent active disease.

Primary and Secondary Outcomes

The ODYSSEY trial achieved its primary and secondary outcomes including the mean change from baseline in BCVA, changes from baseline in visual function and ocular anatomy, the need for supplemental treatment, treatment burden as measured by total injections over the trial duration, and safety measures.

CLS-AX Efficacy Results

- Maintained stable BCVA throughout the trial as measured by the mean change in BCVA from baseline to Week 36.
- Maintained stable central subfield retinal thickness (CSRT) throughout the trial as measured by the mean change in CSRT from baseline to Week 36, as confirmed by the independent reading center.

CLS-AX Durability Results

- CLS-AX participants not requiring any additional treatment:
  - 100% up to 12 weeks (3 months); n=40/40
  - 90% up to 16 weeks (4 months); n=35/39
  - 81% up to 20 weeks (5 months); n=30/37
  - 67% up to 24 weeks (6 months) before mandatory re-dosing at Week 24; n=26/39
- Reduced injection frequency by approximately 84% compared to the average monthly injections in the 24 weeks prior to screening

CLS-AX Safety and Tolerability Results

- Well-tolerated safety profile through 36 weeks that included mandatory re-dosing of CLS-AX at Week 24
- No ocular serious adverse events (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 profile
- Similar discontinuation rates between treatment and comparator groups

Conference Call & Webcast Details

Clearside will host a webcast and conference call with accompanying slides today at 8:00 A.M. ET, including comments by management and key opinion leader Roger Goldberg, M.D., MBA, who is a board-certified retinal surgeon at the Bay Area Retinal Associates Medical Group. The live and archived webcast with slides may be accessed on the Clearside

website under the Investors section: Events and Presentations. The live call can be accessed by dialing (888) 506-0062 (domestic) or (973) 528-0011 (international) and entering conference code: 494679.

About CLS-AX (axitinib injectable suspension)

Clearside is developing CLS-AX as a longer-acting therapy for the treatment of retinal diseases. CLS-AX (axitinib injectable suspension) is a proprietary suspension of axitinib for suprachoroidal injection. Axitinib is a tyrosine kinase inhibitor (TKI), currently approved as an oral tablet formulation to treat advanced renal cell carcinoma, that achieves pan-VEGF blockade, directly inhibiting VEGF receptors-1, -2, and -3 with high potency and specificity. Clearside believes this broad VEGF blockade may have efficacy advantages over existing retinal therapies by acting at a different level of the angiogenesis cascade and may benefit patients who sub-optimally respond to current, more narrowly focused anti-VEGF therapies. Suprachoroidal injection of this proprietary suspension of axitinib has demonstrated meaningful potential in preclinical studies in multiple species, and in both Phase 1/2a and Phase 2b wet AMD clinical trials in which CLS-AX was well tolerated and demonstrated a positive safety profile. With suprachoroidal administration of axitinib, there is the potential to achieve prolonged duration and targeted delivery to affected tissue layers by compartmentalizing axitinib behind the retina, thereby limiting drug exposure to the front of the eye.

About Age-Related Macular Degeneration (AMD)

Age-related macular degeneration causes a progressive loss of central vision and is the most common cause of legal blindness in individuals over age 55. Neovascular AMD (wet AMD) is generally caused by abnormal blood vessels that leak fluid or blood into the macula, the part of the retina responsible for central vision, and accounts for the majority of vision loss in patients with this disorder. Approximately 11 million patients in the U.S. are living with AMD[1], and about 10% of all patients with AMD have the wet form[2]. Current treatments require life-long, frequent injections to maintain efficacy. This treatment regimen tends to cause a treatment burden for patients resulting in reduced compliance and under-treatment leading to potentially limited outcomes. In the U.S., the total economic impact of late-stage AMD is estimated to be approximately $49 billion, with the majority of costs attributed to lower productivity related to job loss or job reduction due to the condition[3].

Sources

[1] Pennington, Katie L and DeAngelis, Margaret M, Eye and Vision, Epidemiology of age-related macular degeneration (AMD): associations with cardiovascular disease phenotypes and lipid factors, Dec 22, 2016.

[2] Prall, F Ryan and Ciulla, Thomas A, Medscape: Exudative (Wet) Age-Related Macular Degeneration (AMD), June 16, 2022.

[3] Retina International, The Socio-economic Impact of Age-related Macular Degeneration (AMD) in Bulgaria, Germany, and USA, Oct 12, 2022.

About Clearside's Suprachoroidal Space (SCS®) Injection Platform and SCS Microinjector®

Clearside's patent protected, proprietary suprachoroidal space (SCS®) injection treatment approach offers unprecedented access to the back of the eye, where sight-threatening disease often occurs. The Company's unique platform is inherently flexible and intended to work with established and new formulations of medications. Clearside's patented SCS Microinjector® can deliver a wide variety of drug candidates into the suprachoroidal space, providing targeted delivery to potentially improve efficacy and compartmentalization of medication to reduce or eliminate toxic effects on non-diseased cells. The SCS Microinjector system comprises a syringe, a custom-designed hub, and two 30-gauge hollow microneedles of varying lengths, each approximately one millimeter, optimizing insertion and suprachoroidal administration of drugs.

About Clearside Biomedical, Inc.

Clearside Biomedical, Inc. is a biopharmaceutical company revolutionizing the delivery of therapies to the back of the eye through the suprachoroidal space (SCS®) to improve patient outcomes. Clearside's SCS injection platform, utilizing the Company's patented SCS Microinjector®, enables an in-office, repeatable, non-surgical procedure for the targeted and compartmentalized delivery of a wide variety of therapies to the macula, retina, or choroid to potentially preserve and improve vision in patients with sight-threatening eye diseases. Clearside is developing its own pipeline of small molecule product candidates for administration via its SCS Microinjector. The Company's lead program, CLS-AX (axitinib injectable suspension), for the treatment of neovascular age-related macular degeneration (wet AMD), recently completed a Phase 2b clinical trial, and planning for a Phase 3 program is underway. Clearside developed and gained approval for its first product, XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use, which is available in the U.S. through a commercial partner. Clearside also strategically partners its SCS injection platform with companies utilizing other ophthalmic therapeutic innovations. For more information, please visit clearsidebio.com or follow us on LinkedIn.

Cautionary Note Regarding Forward-Looking Statements

Any statements contained in this press release that do not describe historical facts may constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. These statements may be identified by words such as "believe", "expect", "may", "plan", "potential", "will", and similar expressions, and are based on Clearside's current beliefs and expectations. These forward-looking statements include statements regarding the clinical development of CLS-AX (including any future clinical trials), and the potential benefits of CLS-AX, Clearside's suprachoroidal delivery technology and Clearside's SCS Microinjector®. These statements involve risks and uncertainties that could

cause actual results to differ materially from those reflected in such statements. Risks and uncertainties that may cause actual results to differ materially include uncertainties inherent in the conduct of clinical trials, Clearside's reliance on third parties over which it may not always have full control and other risks and uncertainties that are described in 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 for the quarter ended June 30, 2024, filed with the SEC on August 12, 2024, and Clearside's other periodic reports filed with the SEC. Any forward-looking statements speak only as of the date of this press release and are based on information available to Clearside as of the date of this release, and Clearside assumes no obligation to, and does not intend to, update any forward-looking statements, whether as a result of new information, future events or otherwise.

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