# 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): November 09, 2022**

# 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 2.02 Results of Operations and Financial Condition.**

On November 9, 2022, Clearside Biomedical, Inc. (the "***Registrant***") issued a press release announcing its financial results for the quarter ended September 30, 2022, as well as information regarding a conference call to discuss these financial results and the Registrant's recent corporate highlights and the results from the Company's OASIS trial (as discussed below). A copy of this press release is furnished herewith as Exhibit 99.1 to this Current Report and is incorporated herein by reference.

In accordance with General Instruction B.2. of Form 8-K, the information in this Item 2.02, and Exhibit 99.1 hereto, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "***Exchange Act***"), or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference in any of the Registrant's filings under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any incorporation language in such a filing, except as expressly set forth by specific reference in such a filing.

**Item 7.01 Regulation FD Disclosure.**

Also on November 9, 2022, the Registrant issued a press release entitled "Clearside Biomedical Announces Positive Results in Safety, Durability and Biologic Effect in OASIS Phase 1/2a Clinical Trial of Suprachoroidal CLS-AX (axitinib injectable suspension) for the Treatment of Wet AMD." The Company will be discussing the results of the OASIS trial during the conference call noted above. During the conference call, the Company will also be presenting a presentation covering the results of the OASIS trial, which will also be made available on the Registrant's website. A copy of the press release and presentation are furnished herewith as Exhibits 99.2 and 99.3, respectively, to this Current Report on Form 8-K.

The information in this Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.2 and 99.3, is being furnished pursuant to Item 7.01 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, and it shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or under the Exchange Act, whether made before or after the date hereof, except as expressly set forth by specific reference in such filing to this item of this report.

**Item 9.01 Financial Statements and Exhibits.**

**(d) Exhibits**

| Exhibit Number | Exhibit Description |
|---|---|
| 99.1 | Press Release, dated November 9, 2022, titled "Clearside Biomedical Announces Third Quarter 2022 Financial Results and Provides Corporate Update" |
| 99.2 | Press release, dated November 9, 2022, titled "Clearside Biomedical Announces Positive Results in Safety, Durability and Biologic Effect in OASIS Phase 1/2a Clinical Trial of Suprachoroidal CLS-AX (axitinib injectable suspension) for the Treatment of Wet AMD" |
| 99.3 | Presentation, dated November 9, 2022 |
| 104 | Cover Page Interactive Data File (embedded with 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: November 9, 2022

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

# Clearside Biomedical Announces Third Quarter 2022 Financial Results and Provides Corporate Update

*- Favorable Safety Results, Durability and Biologic Effect Observed in Cohorts 3 and 4 of CLS-AX OASIS Phase 1/2a Trial -*

*- Recent Positive Data Presentations Highlight the Potential Safety, Efficacy and Durability Benefits of Suprachoroidal Administration of Small Molecule Suspensions -*

*- Management to Host Webcast and Conference Call on OASIS Data Today at 8:30 A.M. ET -*

ALPHARETTA, Ga., November 9, 2022 -- Clearside Biomedical, Inc. (NASDAQ:CLSD), a biopharmaceutical company revolutionizing the delivery of therapies to the back of the eye through the suprachoroidal space (SCS®), today reported financial results for the third quarter ended September 30, 2022 and provided a corporate update.

“Based on the encouraging data we reported today from our OASIS study, we are now positioned to advance our suprachoroidal CLS-AX program into a larger randomized, controlled Phase 2 trial,” said George Lasezkay, Pharm.D., J.D., Clearside’s President and Chief Executive Officer. “We see significant opportunity across the retinal disease spectrum for CLS-AX, which combines pan-VEGF inhibition from the highly potent tyrosine kinase inhibitor, axitinib, with targeted SCS delivery using our SCS Microinjector. In addition, the growing level of awareness and acceptance of SCS delivery in the retinal medical community is further validating our SCS delivery platform, with recent positive clinical data presented from four other suprachoroidal trials of three different novel therapies each delivered with our proprietary SCS Microinjector.”

**Key Highlights**

- Reported favorable results of safety, durability and biologic effect observed in the higher doses administered in Cohorts 3 and 4 of OASIS, Clearside’s U.S. based, open-label, dose-escalation Phase 1/2a clinical trial of CLS-AX in patients with wet AMD.
- Entered into a Royalty Interest Purchase and Sale Agreement with HealthCare Royalty Partners, in which Clearside received an initial payment of $32.5 million, less certain expenses, with the potential to receive up to $65 million in non-dilutive funding to support ongoing clinical development of Clearside’s pipeline, and pursuant to which HealthCare Royalty Partners will receive certain royalties and milestone payments due to Clearside from XIPERE® (triamcinolone acetonide injectable suspension) and certain SCS Microinjector license agreements.

- Clearside's commercialization partner, Bausch + Lomb, received XIPERE's permanent J-code, a reimbursement code used in the U.S. by commercial insurers and government payers, which became effective for provider billing on July 1, 2022.
- XIPERE was nominated for the 2022 Prix Galien USA Award, which recognizes outstanding achievements in improving the global human condition through the development of innovative drugs, technologies, and other treatments.
- Clearside's proprietary SCS delivery platform was highlighted in multiple presentations and panels at global conferences, including the American Academy of Ophthalmology (AAO) 2022 Annual Meeting, the Retina Society, the Ophthalmology Futures Retina Forum 2022, the American Society of Retina Specialists (ASRS) Annual Meeting, and the Ophthalmology Innovation Source (OIS) Retina Innovation Summit.

**Third Quarter 2022 Financial Results**

Clearside's license and other revenue for the third quarter of 2022 was $0.3 million, compared to $3.1 million for the third quarter of 2021. This decrease was primarily attributable to higher revenue from partner licensing agreements in the third quarter of 2021.

Research and development expenses for the third quarter of 2022 were $4.6 million, compared to $5.1 million for the third quarter of 2021. This decrease was primarily attributable to a decrease in costs in the XIPERE program following approval in October 2021.

General and administrative expenses for the third quarter of 2022 were $2.4 million, compared to $2.8 million for the third quarter of 2021. This decrease was primarily attributable to a $0.3 million decrease in employee related costs related for share-based compensation.

Net loss for the third quarter of 2022 was $7.8 million, or $0.13 per share of common stock, compared to a net loss of $4.9 million, or $0.08 per share of common stock, for the third quarter of 2021. This decrease was primarily attributable to higher revenue from partner licensing agreements in the third quarter of 2021.

As of September 30, 2022, Clearside's cash and cash equivalents totaled $53.4 million. The Company believes this cash balance will provide financial runway into 2024.

**Conference Call & Webcast Details**

Clearside's management will host a webcast and conference call at 8:30 a.m. Eastern Time to provide a corporate update and to discuss results from the OASIS trial. The live and archived webcast 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: 111701. An archive of the webcast will be available for three months.

**About Clearside Biomedical**

Clearside Biomedical, Inc. is a biopharmaceutical company revolutionizing the delivery of therapies to the back of the eye through the suprachoroidal space (SCS®). Clearside's SCS injection platform, utilizing the Company's proprietary 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 and strategically partners its SCS delivery platform with companies utilizing other ophthalmic therapeutic innovations. Clearside's first product, XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use, is commercially available in the U.S. For more information, please visit www.clearsidebio.com.

**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 the initiation of the Phase 2 clinical trial, the potential benefits of CLS-AX and product candidates using Clearside's SCS Microinjector®, potential future payments under the agreement with HealthCare Royalty Partners and Clearside's ability to fund its operations into 2024. 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, uncertainties regarding the COVID-19 pandemic and other risks and uncertainties that are described in Clearside's Annual Report on Form 10-K for the year ended December 31, 2021, filed with the U.S. Securities and Exchange Commission (SEC) on March 11, 2022, Clearside's Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, 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.

**Investor and Media Contacts:**

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Remy Bernarda
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(678) 430-8206

-Financial Tables Follow-

**CLEARSIDE BIOMEDICAL, INC.**
**Selected Financial Data**
(in thousands, except share and per share data)
(unaudited)

| Statements of Operations Data | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2022 | 2021 | 2022 | 2021 |
| License and other revenue | $ 266 | $ 3,074 | $ 997 | $ 3,888 |
| Operating expenses: | | | | |
| Research and development | 4,637 | 5,147 | 14,603 | 14,697 |
| General and administrative | 2,353 | 2,816 | 8,601 | 8,525 |
| Total operating expenses | 6,990 | 7,963 | 23,204 | 23,222 |
| Loss from operations | (6,724) | (4,889) | (22,207) | (19,334) |
| Other income | 194 | 2 | 220 | 1,001 |
| Non-cash interest expense on liability related the sales of future royalties | (1,297) | — | (1,297) | — |
| Net loss | $ (7,827) | $ (4,887) | $ (23,284) | $ (18,333) |
| Net loss per share of common stock — basic and diluted | $ (0.13) | $ (0.08) | $ (0.39) | $ (0.32) |
| Weighted average shares outstanding — basic and diluted | 60,188,541 | 59,474,346 | 60,134,821 | 58,095,080 |

| Balance Sheet Data | September 30, 2022 | December 31, 2021 |
|---|---|---|
| Cash and cash equivalents | $ 53,381 | $ 30,436 |
| Accounts receivable | 123 | 10,000 |
| Total assets | 55,685 | 42,903 |
| Liability related to the sales of future royalties, net | 31,935 | — |
| Total liabilities | 37,139 | 4,928 |
| Total stockholders' equity | 18,546 | 37,975 |

Source: Clearside Biomedical, Inc.

**Exhibit 99.2**

# Clearside Biomedical Announces Positive Results in Safety, Durability and Biologic Effect in OASIS Phase 1/2a Clinical Trial of Suprachoroidal CLS-AX (axitinib injectable suspension) in Wet AMD Patients

- Primary Safety Endpoint Achieved at all Timepoints with All Doses Well-Tolerated and No Treatment Related or Serious Adverse Events -

- Cohorts 3 and 4 Demonstrated Promising Signs of Durability, Biologic Effect, and a Meaningful Reduction in Treatment Burden -

- Final 6-Month Data from Extension Study Expected in Q1 2023 -

- Expect to Initiate Phase 2 Clinical Trial in Q1 2023 -

- Webcast and Conference Call Today at 8:30 A.M. ET Hosted by Management and Including Key Opinion Leader, Arshad Khanani, M.D. -

ALPHARETTA, Ga., November 9, 2022 -- 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 positive results from its OASIS Phase 1/2a clinical trial of CLS-AX (axitinib injectable suspension) administered by suprachoroidal injection via Clearside's SCS Microinjector® in neovascular age-related macular degeneration (wet AMD) patients. Trial results include final 3-month data from all 4 cohorts, and interim data from the Extension Study that follows participating patients for a total of 6 months after a single dose of CLS-AX.

Thomas A. Ciulla, MD, MBA, Chief Medical Officer and Chief Development Officer, commented, "We are strongly encouraged by the results we reported today which highlight the potential use of CLS-AX, a highly potent tyrosine kinase inhibitor combined with targeted SCS delivery, in serious retinal disease. In the four dose-escalating cohorts of the OASIS trial, we enrolled a total of 27 highly treatment-experienced wet AMD patients with active disease at screening. CLS-AX was well tolerated and demonstrated a positive safety profile across all timepoints and doses. Interim data from the Extension Study in Cohorts 3 and 4 showed the supplemental anti-VEGF injection-free rate up to each visit was 88% (7 of 8 patients) to Month 5 and 75% (3 of 4 patients) to Month 6 and at least a 90% reduction in treatment burden to date compared to the patients' 6-month anti-VEGF therapy prior to receiving CLS-AX. In addition, there were observable signs of

biologic effect with stable mean Best Corrected Visual Acuity (BCVA) and stable mean Central Subfield Thickness (CST) throughout OASIS and the Extension Study at all timepoints to date."

"The positive safety results seen in all four cohorts, combined with evidence that CLS-AX showed biologic effect in a difficult to treat patient population, supports our belief that CLS-AX has the potential to treat retinal diseases with a repeatable, reliable, and validated in-office delivery approach using our SCS Microinjector. We are finalizing the optimal path forward for CLS-AX in retinal diseases including wet AMD and/or diabetic retinopathy. We are actively preparing for and expect to initiate a randomized, controlled Phase 2 clinical trial in the first quarter of 2023," Dr. Ciulla concluded.

"Real world outcomes in patients with wet AMD continue to be poor due to high treatment burden and missed visits, which drives retinal specialists to look for better treatment options that are safe, effective, and provide a better quality of life for our patients. This CLS-AX data is quite promising as the optical coherence tomography (OCT) images show a biologic effect while extending the time for retreatment out for several months. CLS-AX, combined with the convenience and reliability of the suprachoroidal injection procedure, may be a valid future approach for treating a variety of retinal disorders," added Arshad M. Khanani, MD, MA, FASRS, Managing Partner, Director of Clinical Research, and Director of Fellowship at Sierra Eye Associates, and Clinical Associate Professor at the University of Nevada, Reno School of Medicine.

**Summary of OASIS Data**

The OASIS 3-month open-label, dose-escalation Phase 1/2a trial is complete. There is an ongoing additional 3-month Extension Study, for a total of 6 months of follow-up after a single dose of CLS-AX in patients from Cohorts 2, 3 and 4. All patients enrolled in OASIS were heavily anti-VEGF treatment experienced with active disease[1] at screening, which was confirmed by an independent reading center. Patient demographics and wet AMD treatment history are summarized in the following chart:

| Wet AMD Disease Characteristics | COHORT 1: 0.03 mg | COHORT 2: 0.1 mg | COHORT 3: 0.5 mg | COHORT 4: 1.0 mg | All Cohorts |
|---|---|---|---|---|---|
| No. of participants | 6 | 5 | 8 | 8 | 27 |
| Mean age (range), years | 81.8 (66-93) | 78.2 (65-90) | 86.3 (75-97) | 76.5 (66-83) | 80.9 (65-97) |
| Mean baseline best corrected visual acuity (range), letters | 59.0 (29-74) | 65.6 (52-75) | 58.5 (37-74) | 65.8 (50-74) | 62.1 (29-75) |
| Mean baseline central subfield retinal thickness (range), µm | 231.2 (208-294) | 209.4 (184-227) | 202.0 (175-238) | 218.8 (152-295) | 214.8 (152-295) |
| Mean duration of wAMD diagnosis (range), months | 50.13 (12.4-110.3) | 49.78 (24.7-81.3) | 66.64 (6.8-102.1) | 48.21 (4.5-132.8) | 54.39 (4.5-132.8) |
| Number of anti-VEGF injections reported prior to CLS-AX administration on Day 1, mean (range) | 26.8 (7-41) | 24.2 (12-39) | 37.0 (6-90) | 28.8 (5-89) | 29.9 (5-90) |
| Annualized number of anti-VEGF injections prior to CLS-AX administration on Day 1, mean (range) | 9.36 (6.3-12.7) | 9.54 (5.4-12.2) | 8.47 (4.9-11.8) | 11.96 (8.9-13.6) | 9.90 (4.9-13.6) |

Safety and Tolerability Results (in All Four Cohorts, n=27)

- CLS-AX met the trial's primary endpoint, demonstrating a positive safety profile at all doses and timepoints.
- There were no serious adverse events, no treatment emergent adverse events, no dose limiting toxicities, no adverse events related to inflammation, vasculitis or vascular occlusion.
- There were no vitreous "floaters" or dispersion of CLS-AX into the vitreous, no retinal detachments or endophthalmitis, and no adverse events related to intraocular pressure.

Durability (in Cohorts 3 & 4)

In OASIS to the 3-month timepoint (n=16):

- 69% of patients did not receive additional therapy
- 92% of patients did not receive additional therapy per protocol criteria
- ≥73% reduction in treatment burden from the average monthly injections in the three months before CLS-AX administration

In the ongoing Extension Study, based on interim data as of 10/27/22 (n=12):

- Supplemental anti-VEGF injection-free rate up to each visit
  - To Month 5: 88% (7/8) of patients did not receive additional therapy
  - To Month 6: 75% (3/4) of patients did not receive additional therapy
- ≥ 90% reduction in treatment burden from the average monthly injections in the six months before CLS-AX administration
- 8 patients remain in the Extension Study with final 6-month data expected in Q1 2023

Biologic Effect (in Cohorts 3 & 4)

- In OASIS, CLS-AX showed signs of biologic effect with stable mean BCVA and stable mean CST to the 3-month timepoint.
- In the ongoing Extension Study, CLS-AX showed signs of biologic effect with stable mean BCVA and stable mean CST to the 6-month timepoint (based on interim data as of 10/27/22).
- On OCT, anatomical signs of TKI biologic effect were observed in anti-VEGF treatment experienced sub-responders.

[1]Active persistent disease defined as active subfoveal choroidal neovascularization (CNV) secondary to AMD in the study eye confirmed by an independent reading center as leakage from a subfoveal CNV on fluorescein angiography and intra-retinal or sub-retinal fluid on OCT central subfield).

**Conference Call & Webcast Details**

Clearside will host a webcast and conference call with accompanying slides today at 8:30 a.m. ET, including comments by management and retinal expert, Dr. Arshad Khanani. The live and archived webcast 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: 111701.

**OASIS Phase 1/2a Clinical Trial Design**

OASIS is an open-label, dose-escalation Phase 1/2a trial in wet AMD patients to assess the safety and tolerability of a single dose of CLS-AX administered by suprachoroidal injection via Clearside's SCS Microinjector®. Eligible patients were those who demonstrated stable visual acuity following two or more previous injections with an intravitreal anti-VEGF agent. All enrolled patients underwent diagnostic imaging on screening, followed by masked reading center confirmation of persistent active disease.

The study included four cohorts totaling 27 patients at the following doses: Cohort 1 at 0.03 mg; Cohort 2 at 0.1 mg; Cohort 3 at 0.5 mg; Cohort 4 at 1.0 mg. Enrolled patients received aflibercept at the first visit followed by a single dose of CLS-AX at the second visit one month later. The primary endpoint for the trial was assessment of the safety and tolerability of CLS-AX for the 3 months following the administration of CLS-AX, and secondary endpoints evaluated the pharmacokinetics, visual function, ocular anatomy, and the need for additional treatment with intravitreal aflibercept.

A 3-month Extension Study to follow patients in Cohorts 2, 3 and 4 is ongoing. Additional information on the Phase 1/2a trial can be found on clinicaltrials.gov NCT04626128 and the extension study can be found at NCT05131646.

**About CLS-AX (axitinib injectable suspension)**

CLS-AX (axitinib injectable suspension) is a proprietary suspension of axitinib for suprachoroidal injection. Axitinib is a tyrosine kinase inhibitor (TKI) currently approved to treat renal cell cancer 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 a Phase 1/2a clinical

trial. With suprachoroidal administration of axitinib, there is the potential to achieve prolonged duration and targeted delivery to affected tissue layers. Clearside is developing CLS-AX as a long-acting therapy for the treatment of retinal diseases.

**About Neovascular Age-Related Macular Degeneration (wet 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. 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. In the U.S., approximately 11 million patients are living with AMD, and about 20% have the wet form. 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.

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

Clearside's patented, 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 proprietary SCS Microinjector® can be used to inject a wide variety of drug candidates that are specifically formulated to be delivered via suprachoroidal injection. The SCS Microinjector provides targeted delivery to potentially improve efficacy and compartmentalization of medication to reduce or eliminate toxic effects on non-diseased cells. The SCS Microinjector is composed of a syringe and two 30-gauge hollow microneedles of varying lengths, each less than 1.2 millimeters, within a custom-designed hub that optimizes insertion and suprachoroidal administration of drugs.

**About Clearside Biomedical**

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(triamcinolone acetonide injectable suspension) for suprachoroidal use, is commercially available in the U.S. For more information, please visit www.clearsidebio.com.

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Source: Clearside Biomedical, Inc.

Exhibit 99.3


CLEARSIDE
BIOMEDICAL
OASIS
OASIS Phase 1/2a Clinical Trial Results
November 9, 2022

# 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" and similar 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, 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; 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; 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, 2021, filed with the SEC on March 11, 2022, and Clearside's other Periodic Reports filed 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.

# OASIS (3 Month) and Extension Study (6 Month, Interim Data) Cohorts 3 and 4: Promising CLS-AX Safety Results, Durability and Biologic Effect

## SAFETY RESULTS

- Excellent safety profile at all doses and timepoints
- No Serious Adverse Events
- No dose limiting toxicities
- No Adverse Events from inflammation

## DURABILITY

**In OASIS, to 3 months:**

- ≥73% reduction in treatment burden

**In Extension Study, to 6 months (interim data):**

- ≥90% reduction in treatment burden


## BIOLOGIC EFFECT

- Stable mean Best Corrected Visual Acuity (BCVA)
- Stable mean Central Subfield Thickness (CST)
- On optical coherence tomography (OCT), anatomical signs of tyrosine kinase inhibitor (TKI) biologic effect were observed in anti-VEGF treatment-experienced sub-responders

## NEXT STEPS

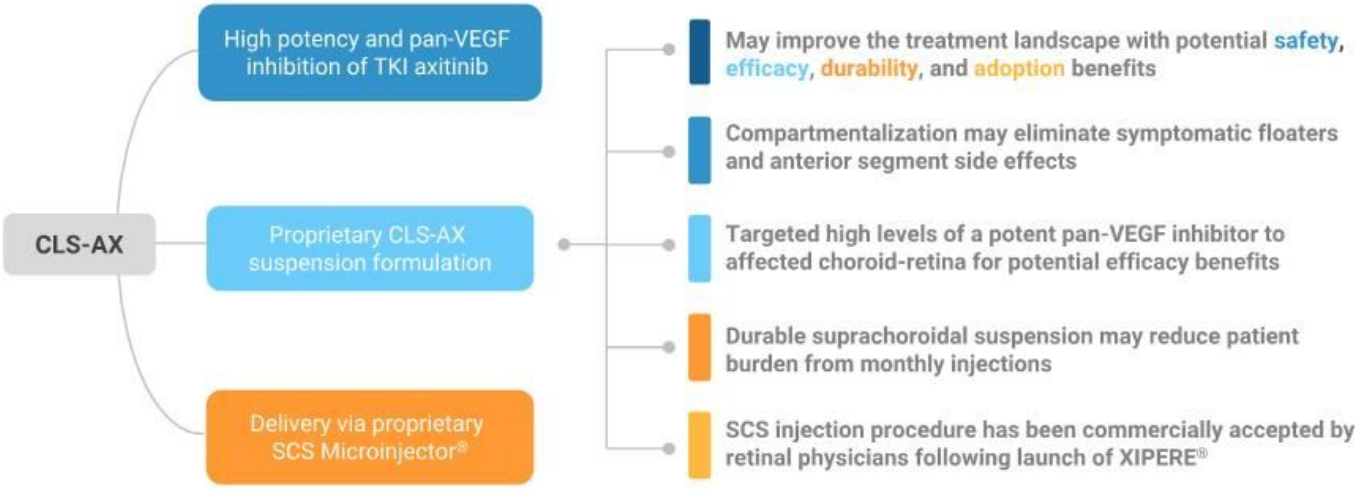
- Follow remaining patients in Extension Study with final data expected in Q1 2023
- Initiate Phase 2 clinical trial in Q1 2023



Source: Clearside data on file. | Extension Study interim data as of October 27, 2022.

# CLS-AX (axitinib injectable suspension) for Suprachoroidal Use

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



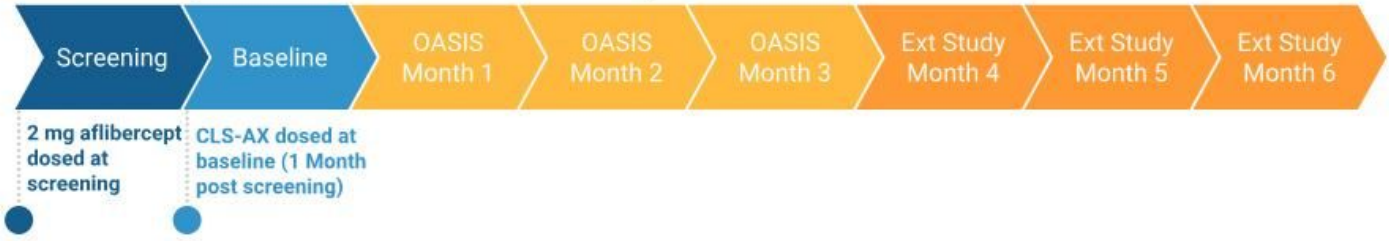



Axitinib is a tyrosine kinase inhibitor (TKI) | XIPERE® (triamcinolone acetonide injectable suspension), for suprachoroidal use has received U.S. FDA Approval. Please see Important Safety Information for XIPERE in the Full Prescribing Information: https://www.bauschhealth.com/Portals/25/Pdf/PI/XIPERE-PI.pdf. | Source: Viral S. Kansara, Leroy W. Muya, Thomas A. Ciulla; Evaluation of Long-Lasting Potential of Suprachoroidal Axitinib Suspension Via Ocular and Systemic Disposition in Rabbits. *Trans. Vis. Sci. Tech.* 2021;10(7):19.

# OASIS and Extension Study: CLS-AX Phase 1/2a Clinical Trial in Treatment-Experienced Wet AMD Patients with Active Disease at Screening

## TRIAL DESIGN AND OBJECTIVES

- Open-label study with a primary endpoint to evaluate safety and tolerability of escalating single doses of CLS-AX administered through suprachoroidal injection following IVT aflibercept
- Wet AMD patients with ≥2 anti-VEGF treatments in the prior 4 months, reading center confirmation of persistent active disease
- Dose-escalation of CLS-AX (in mg): Cohort 1 at 0.03; Cohort 2 at 0.1; Cohort 3 at 0.5; Cohort 4 at 1.0
- Secondary endpoints: visual function, ocular anatomy, and need for additional treatment
- Monthly assessment for additional treatment with aflibercept: loss from best measurement of ≥10 letters in BCVA with exudation; increase in CST >75 microns; a vision-threatening hemorrhage
- 6-Month follow-up after CLS-AX via a 3-month Extension Study




CLEARSIDE BIOMEDICAL

Note: aflibercept is dosed via intravitreal injection (IVT); CLS-AX is dosed via suprachoroidal injection | clinicaltrials.gov NCT# 04626128
Active Disease definition: Active subfoveal choroidal neovascularization (CNV) secondary to AMD in the study eye confirmed by an independent reading center as leakage from a subfoveal CNV on fluorescein angiography and intra-retinal or sub-retinal fluid on OCT central subfield)

# OASIS Enrolled Heavily anti-VEGF Treatment-Experienced Wet AMD Patients

## Patients were sub-responders with active disease at screening confirmed by reading center

**Why target this patient population instead of treatment naïve or patients with controlled disease?**

- Patients have a high need for effective therapy with lower treatment burden
- Minimizes the risk of false signals of biologic effect
- Facilitates assessment for biological effect in a difficult-to-treat nAMD patient population
- Facilitates assessment of an appropriate dose, not only based on both safety but also on biologic effect
- Represents a significant number of patients in clinical practice, with >30% sub-responders
- De-risks future clinical studies

**Desired outcomes in this heavily treated patient population:**

- Demonstrate safety and tolerability of CLS-AX
- Maintain stability of visual acuity and central subfield thickness with lower treatment burden

Enrolling difficult to treat anti-VEGF sub-responders allowed observation of possible signs of biologic effect while minimizing false signals



Core et at. Predominantly Persistent Intraretinal Fluid in the Comparison of Age-related Macular Degeneration Treatments Trials. Ophthalmol Retina. 2022 Sep;6(9):771-785. | Waldstein et al. Morphology and visual acuity in aflibercept and ranibizumab therapy for neovascular age-related macular degeneration in the VIEW trials. Ophthalmology 2016;123:1521-1529.

Active Disease definition: Active subfoveal choroidal neovascularization (CNV) secondary to AMD in the study eye confirmed by an independent reading center as leakage from a subfoveal CNV on fluorescein angiography and intra-retinal or sub-retinal fluid on OCT central subfield)

# Enrolled Patients All with Active Disease at Screening and Confirmed by Independent Reading Center

Demographics and Wet AMD History

| Wet AMD Disease Characteristics | COHORT 1: 0.03 mg | COHORT 2: 0.1 mg | COHORT 3: 0.5 mg | COHORT 4: 1.0 mg |
|---|---|---|---|---|
| No. of participants | 6 | 5 | 8 | 8 |
| Mean age (range), years | 81.8 (66-93) | 78.2 (65-90) | 86.3 (75-97) | 76.5 (66-83) |
| Mean baseline best corrected visual acuity (range), letters | 59.0 (29-74) | 65.6 (52-75) | 58.5 (37-74) | 65.8 (50-74) |
| Mean baseline central subfield retinal thickness (range), µm | 231.2 (208-294) | 209.4 (184-227) | 202.0 (175-238) | 218.8 (152-295) |
| **Mean duration of wAMD diagnosis (range), months** | **50.13 (12.4-110.3)** | **49.78 (24.7-81.3)** | **66.64 (6.8-102.1)** | **48.21 (4.5-132.8)** |
| **Number of anti-VEGF injections reported prior to CLS-AX administration on Day 1, mean (range)** | **26.8 (7-41)** | **24.2 (12-39)** | **37.0 (6-90)** | **28.8 (5-89)** |
| **Annualized number of anti-VEGF injections prior to CLS-AX administration on Day 1, mean (range)** | **9.36 (6.3-12.7)** | **9.54 (5.4-12.2)** | **8.47 (4.9-11.8)** | **11.96 (8.9-13.6)** |



Source: Clearside data on file.


Safety Results

# CLS-AX Demonstrated a Positive Safety Profile in All Four Cohorts

## 3-Month Final Data & 6-Month Interim Data

**SAFETY RESULTS**

### Excellent Safety Profile at all doses and timepoints

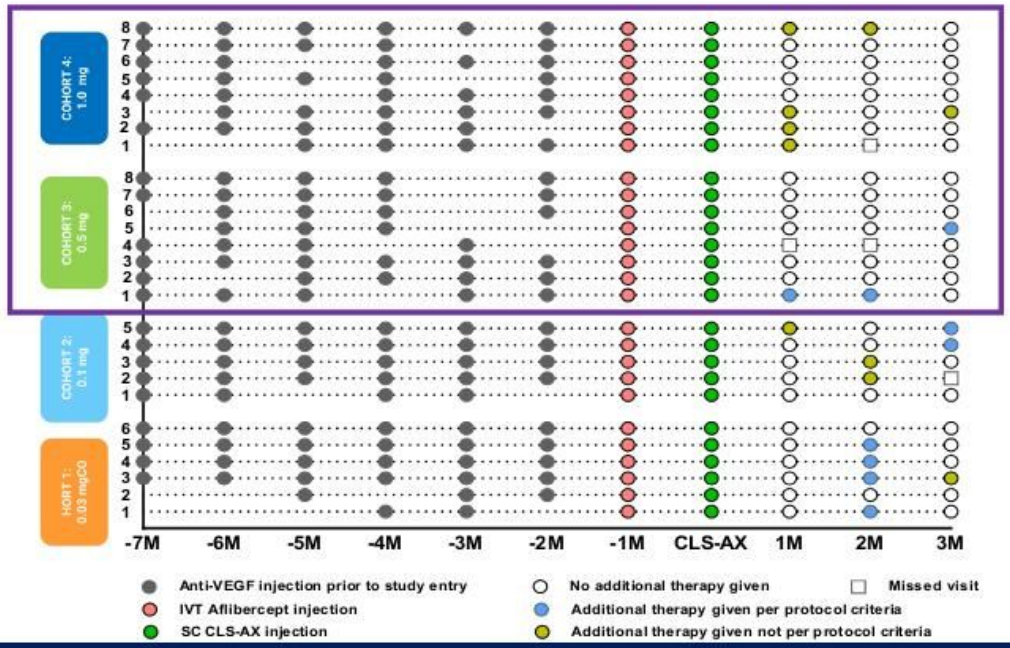
- No serious adverse events (SAEs)
- No treatment emergent adverse events (TEAEs) related to study treatment
- No dose limiting toxicities
- No adverse events related to inflammation, vasculitis or vascular occlusion
- No vitreous "floaters" or dispersion of CLS-AX into the vitreous
- No retinal detachment
- No endophthalmitis
- No adverse events related to intraocular pressure



Source: Clearside data on file. | Extension Study interim data as of October 27, 2022.

# Durability

# OASIS (3 Month):
# Prior Anti-VEGF Therapies and All Additional Therapies

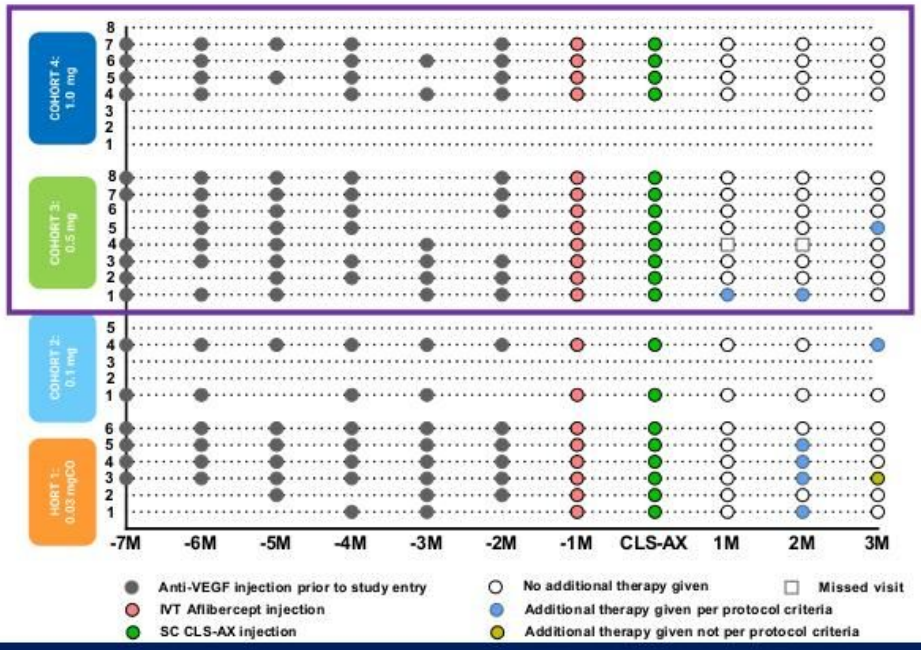



**DURABILITY**

Cohorts 3 & 4:

11/16 (69%) of patients did not receive additional therapy to 3 months

# OASIS (3 Month):
# Prior Anti-VEGF Therapies and Additional Therapies Per Protocol Criteria




**DURABILITY**

Cohorts 3 & 4:

11/12 (92%) of patients did not receive additional therapy to 3 months

CLEARSIDE BIOMEDICAL

Excludes patients whose first additional therapy was not per protocol-defined criteria.
Source: Clearside data on file.

# OASIS (3 Month):
# CLS-AX Reduced Treatment Burden Across All Cohorts

## Reduction in Treatment Burden
All Therapies

| Cohort | Number of Participants | Avg Monthly Injections Before CLS-AX Administration | Avg Monthly Injections After CLS-AX Administration | % Reduction |
|---|---|---|---|---|
| 4 | 8 | 0.88 | 0.25 | **72.9** |
| 3 | 8 | 0.75 | 0.13 | **79.2** |
| 2 | 5 | 0.93 | 0.37 | 63.3 |
| 1 | 6 | 0.94 | 0.28 | 69.4 |

## Reduction in Treatment Burden
Therapies Per Protocol Criteria

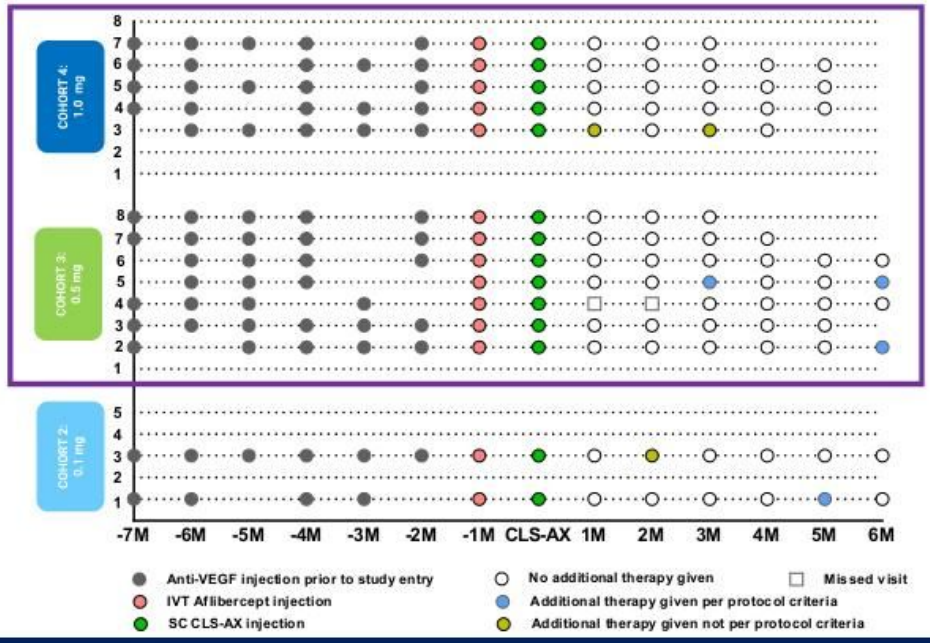
| Cohort | Number of Participants | Avg Monthly Injections Before CLS-AX Administration | Avg Monthly Injections After CLS-AX Administration | % Reduction |
|---|---|---|---|---|
| 4 | 4 | 0.83 | 0 | **100** |
| 3 | 8 | 0.75 | 0.13 | **79.2** |
| 2 | 2 | 0.83 | 0.17 | 83.3 |
| 1 | 6 | 0.94 | 0.28 | 69.4 |

73 – 100% Reduction in Treatment Burden in Cohorts 3 and 4

CLEARSIDE BIOMEDICAL

Note: Average Monthly Injections Before CLS-AX Administration = # treatments three months prior / 3.
Average Monthly Injections After CLS-AX Administration = # treatments / # months of follow-up.
% Reduction = Average of individual reductions calculated as (after – before) / before × 100%.
Source: Clearside data on file.

# Extension Study (6 Month, Interim Data): Prior Anti-VEGF Therapies and All Additional Therapies



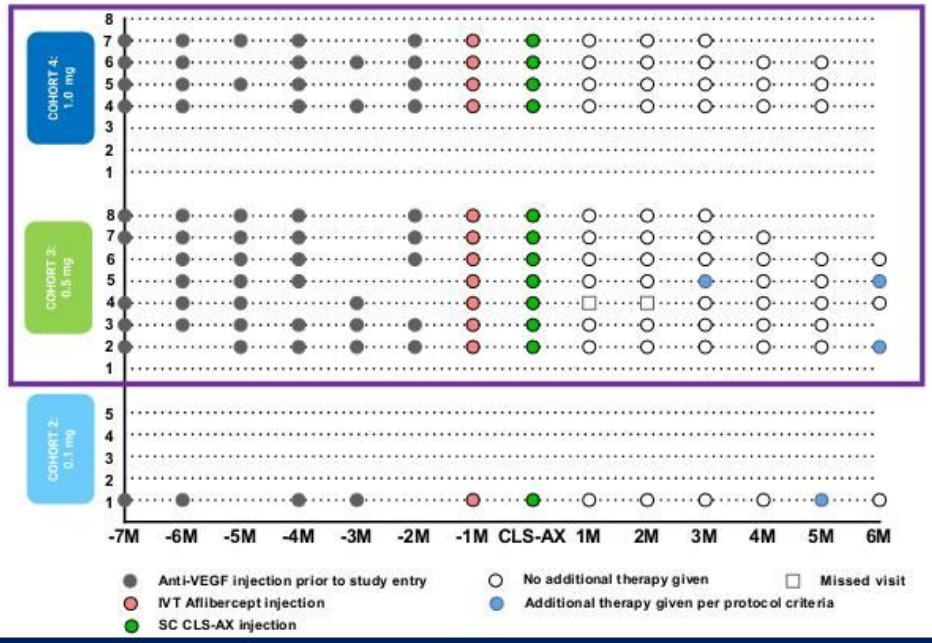

**DURABILITY**

Cohorts 3 & 4

No Additional Therapy

To Month 4: 8/10
To Month 5: 7/8
To Month 6: 3/4

# Extension Study (6 Month, Interim Data): Prior Anti-VEGF Therapies and Additional Therapies Per Protocol Criteria




**DURABILITY**

Cohorts 3 & 4

No Additional Therapy

To Month 4: 8/9

To Month 5: 7/8

To Month 6: 3/4

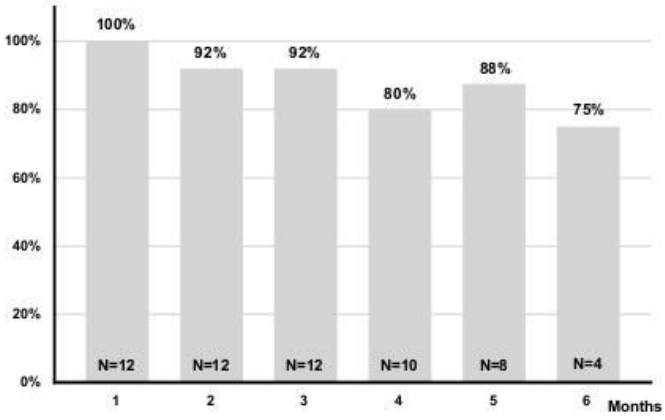


Excludes patients whose first additional therapy was not per protocol-defined criteria.
Source: Clearside data on file. | Extension Study interim data as of October 27, 2022.

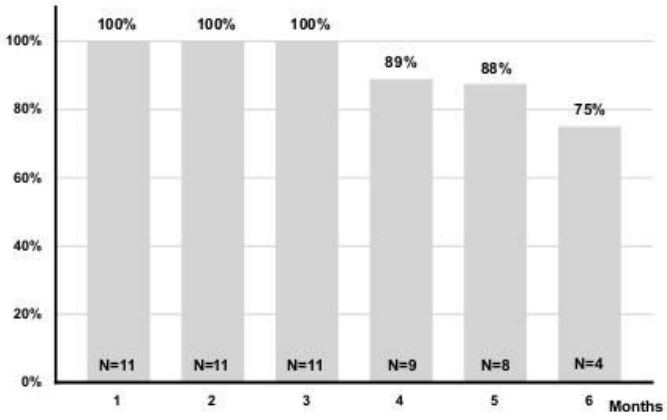
# Extension Study (6 Month, Interim Data): Supplemental Anti-VEGF Injection-Free Rate up to Each Visit in Cohorts 3 and 4

Extension Study Interim Data: 75% of Patients with No Additional Therapy to Month 6

## All Therapies




## Therapies Per Protocol Criteria






Source: Clearside data on file. | Extension Study interim data as of October 27, 2022.

# Extension Study (6 Month, Interim Data): CLS-AX Reduced Treatment Burden Across Cohorts

## Reduction in Treatment Burden
All Therapies

| Cohort | Number of Participants | Avg Monthly Injections Before CLS-AX Administration | Avg Monthly Injections After CLS-AX Administration | % Reduction |
|---|---|---|---|---|
| 4 | 5 | 0.87 | 0.10 | **90.0** |
| 3 | 7 | 0.81 | 0.07 | **90.0** |
| 2 | 2 | 0.83 | 0.17 | 79.2 |

## Reduction in Treatment Burden
Therapies Per Protocol Criteria

| Cohort | Number of Participants | Avg Monthly Injections Before CLS-AX Administration | Avg Monthly Injections After CLS-AX Administration | % Reduction |
|---|---|---|---|---|
| 4 | 4 | 0.83 | 0 | **100** |
| 3 | 7 | 0.81 | 0.07 | **90.0** |
| 2 | 1 | 0.67 | 0.17 | 75.0 |

90 – 100% Reduction in Treatment Burden in Cohorts 3 and 4

CLEARSIDE BIOMEDICAL

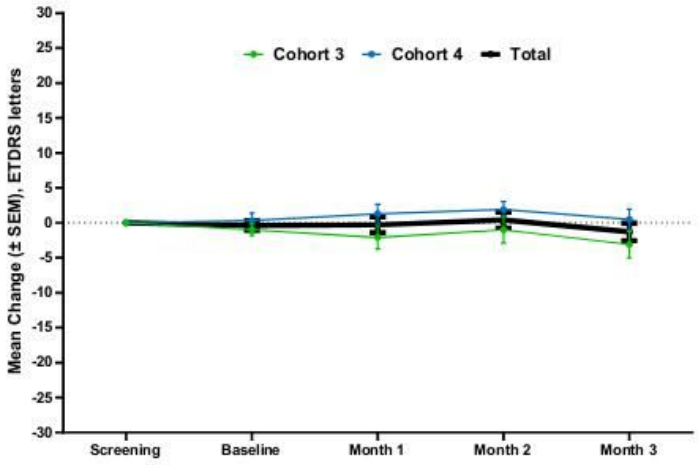
Note: Average Monthly Injections Before CLS-AX Administration = # treatments six months prior/ 6.
Average Monthly Injections After CLS-AX Administration = # treatments / # months of follow-up.
% Reduction = Average of individual reductions calculated as (after – before) / before × 100%.
Source: Clearside data on file. | Extension Study interim data as of October 27, 2022.


Biologic Effect in
Cohorts 3 & 4

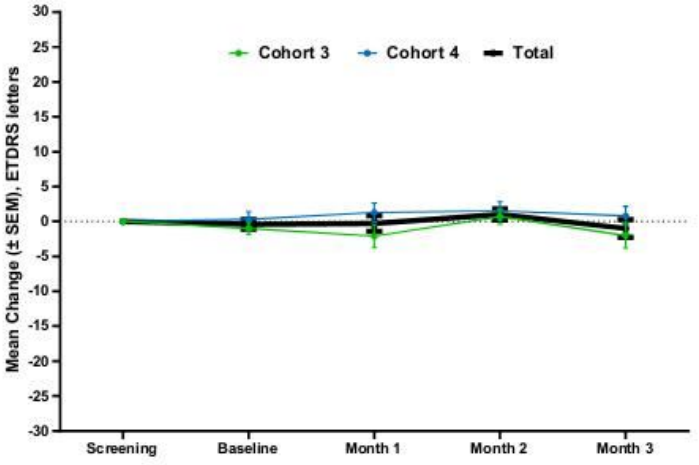
# OASIS (3 Months): Stable Visual Acuity

Mean Best Corrected Visual Acuity Letter Score, Change from Screening

**All Data**




**Excluding Data After Additional Treatment**



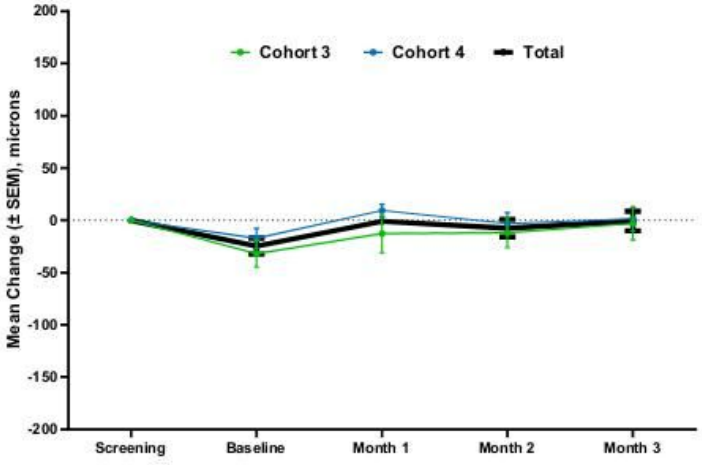



Source: Clearside data on file.

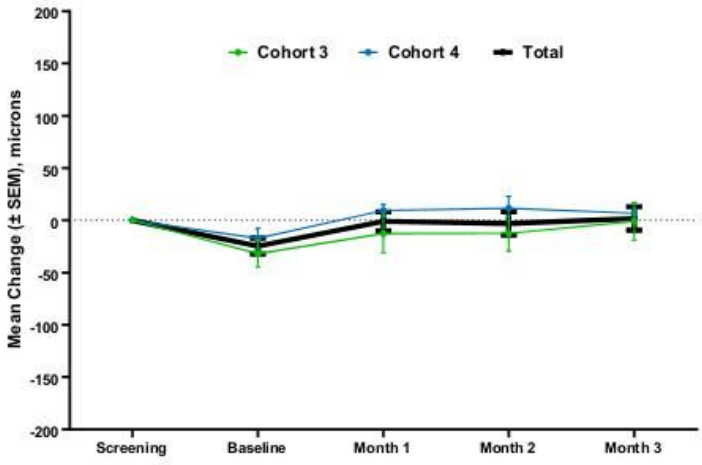
# OASIS (3 Months): Stable Central Subfield Thickness

Mean Central Subfield Thickness, Change from Screening

**All Data**




**Excluding Data After Additional Treatment**



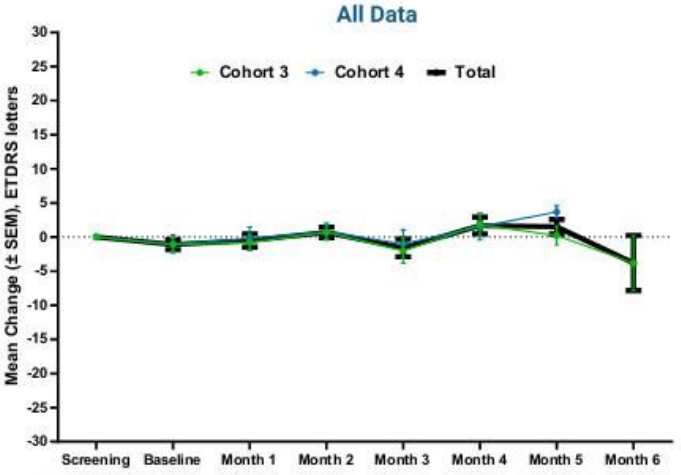

CLEARSIDE BIOMEDICAL

Source: Clearside data on file.

# Extension Study (6 Month, Interim Data): Stable Visual Acuity

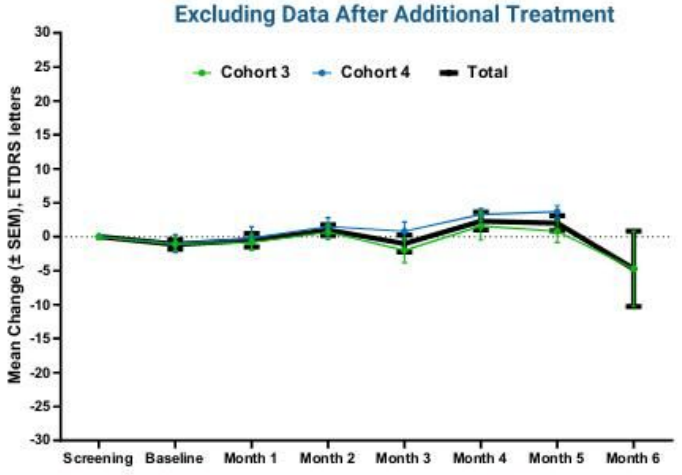
Mean Best Corrected Visual Acuity Letter Score, Change from Screening

## All Data




| Cohort, n | Scr | Bl | Mth 1 | Mth 2 | Mth 3 | Mth 4 | Mth 5 | Mth 6 |
|---|---|---|---|---|---|---|---|---|
| 3 | 7 | 7 | 6 | 6 | 7 | 6 | 5 | 4 |
| 4 | 5 | 5 | 5 | 5 | 5 | 4 | 3 | 0 |

## Excluding Data After Additional Treatment




| Cohort, n | Scr | Bl | Mth 1 | Mth 2 | Mth 3 | Mth 4 | Mth 5 | Mth 6 |
|---|---|---|---|---|---|---|---|---|
| 3 | 7 | 7 | 6 | 6 | 7 | 5 | 4 | 3 |
| 4 | 5 | 5 | 5 | 4 | 4 | 3 | 3 | 0 |

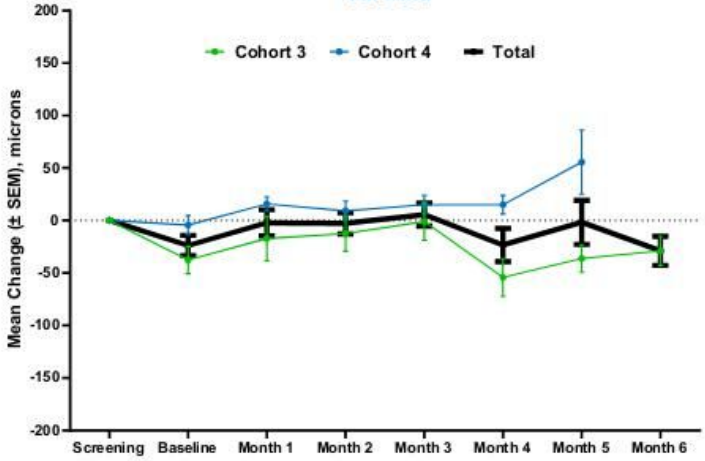
CLEARSIDE BIOMEDICAL

Source: Clearside data on file. | Extension Study interim data as of October 27, 2022.

# Extension Study (6 Month, Interim Data): Stable Central Subfield Thickness

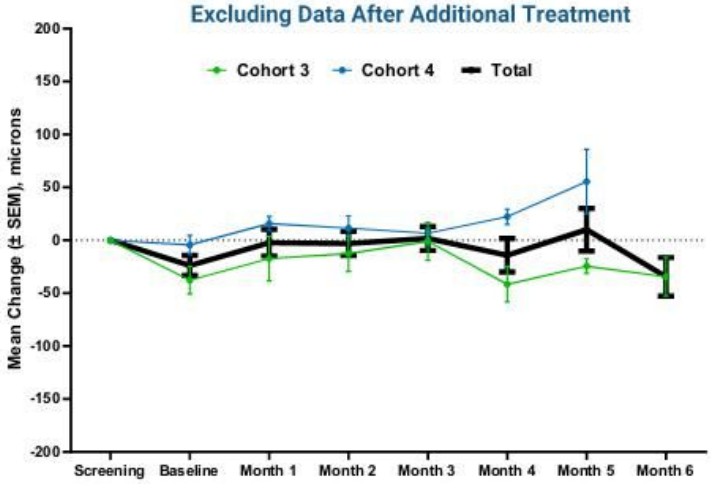
## Mean Central Subfield Thickness, Change from Screening

### All Data




| Cohort, n | Scr | Bl | Mth 1 | Mth 2 | Mth 3 | Mth 4 | Mth 5 | Mth 6 |
|---|---|---|---|---|---|---|---|---|
| 3 | 7 | 7 | 6 | 6 | 7 | 5 | 5 | 4 |
| 4 | 5 | 5 | 5 | 5 | 5 | 4 | 3 | 0 |

### Excluding Data After Additional Treatment



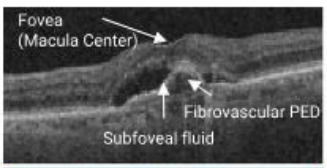

| Cohort, n | Scr | Bl | Mth 1 | Mth 2 | Mth 3 | Mth 4 | Mth 5 | Mth 6 |
|---|---|---|---|---|---|---|---|---|
| 3 | 7 | 7 | 6 | 6 | 7 | 4 | 4 | 3 |
| 4 | 5 | 5 | 5 | 4 | 4 | 3 | 3 | 0 |


Case Studies

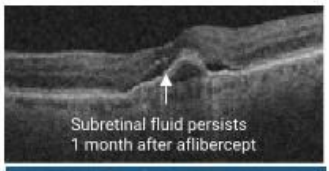
# 6 Month Case Study:
# CLS-AX Demonstrated Biologic Effect in anti-VEGF Sub-responder

Cohort 3, Subject 2: 89 prior anti-VEGF injections with persistent subfoveal fluid 1 month after aflibercept at screen

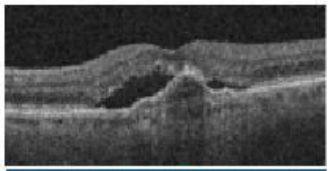
Subretinal fluid gradually resolves through 4 months after CLS-AX with stable BCVA and improved CST



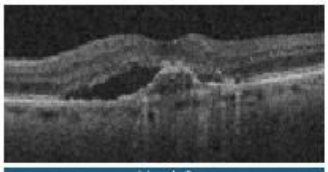

Screening: Aflibercept
BCVA 75, CST 265



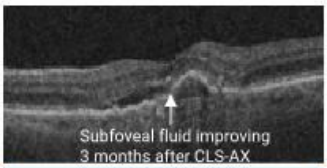

Baseline: CLS-AX
BCVA 73, CST 218



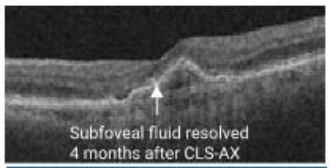
Month 1
BCVA 78, CST 277



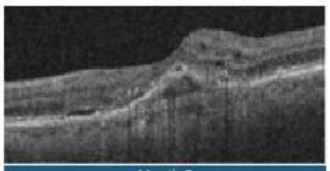
Month 2
BCVA 78, CST 253



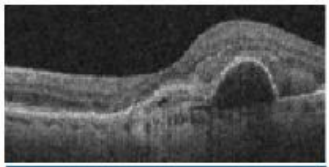

Month 3
BCVA 75, CST 221




Month 4
BCVA 74, CST 182



Month 5
BCVA 75, CST 223



Month 6: Additional therapy administered
BCVA 60, CST 224

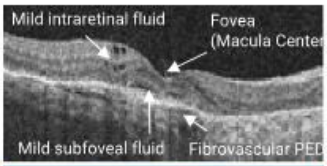


Source: Clearside data on file. | Extension Study interim data as of October 27, 2022.

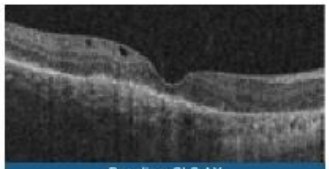
# 5 Month Case Study:
# Durable Stability After CLS-AX

Cohort 3, Subject 3: 66 prior anti-VEGF injections with mild subfoveal and intraretinal fluid at screen

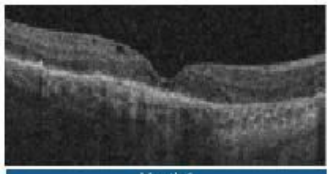
Stable anatomy, BCVA and CST for 5 months after CLS-AX with no additional therapy (Month 6 visit pending)



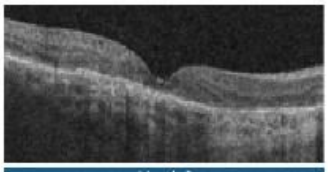

Screening: Aflibercept
BCVA 37, CST 228



Baseline: CLS-AX
BCVA 37, CST 181



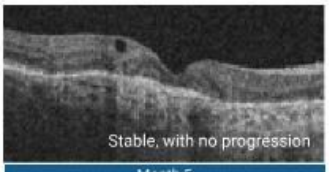
Month 1
BCVA 39, CST 175



Month 2
BCVA 35, CST 175

Month 3
BCVA 36, CST 205

Month 4
BCVA 40, CST 190



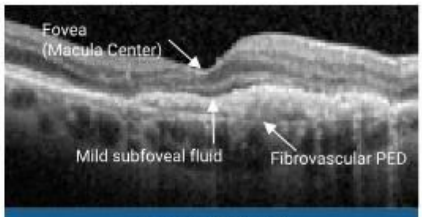

Month 5
BCVA 38 , CST 200



Source: Clearside data on file. | Extension Study interim data as of October 27, 2022.

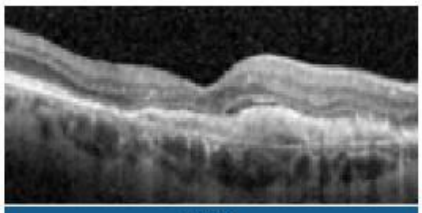
# 6 Month Case Study:
# Durable Stability After CLS-AX

Cohort 3, Subject 4: 15 prior anti-VEGF injections with mild subfoveal fluid at screen
Stable anatomy, BCVA and CST for 6 months after CLS-AX with no additional therapy

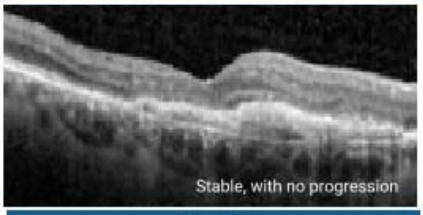



Screening: Aflibercept
BCVA 42, CST 194

Baseline: CLS-AX
BCVA 45, CST 175



Month 3
BCVA 45, CST 196



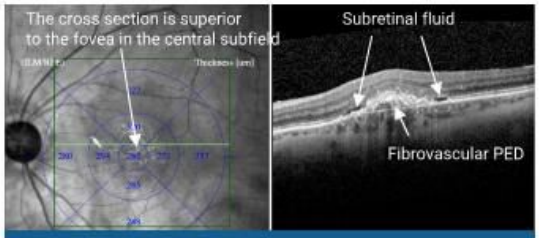

Month 6:
BCVA 46 CST 194



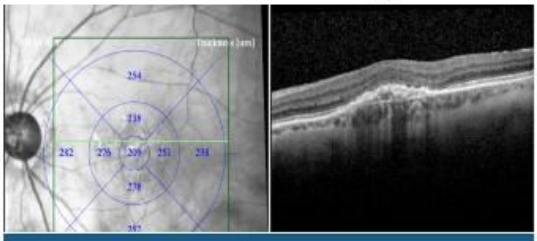
Source: Clearside data on file. | Extension Study interim data as of October 27, 2022.

# 6 Month Case Study:
# Durable Stability After CLS-AX

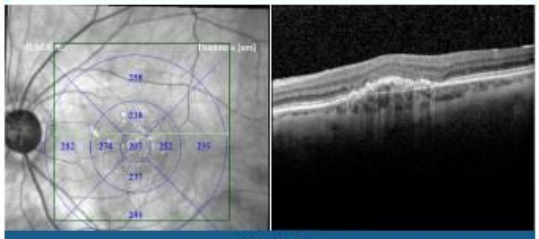
Cohort 3, Subject 6: 50 prior anti-VEGF injections with persistent subretinal fluid in superior central subfield
Stable anatomy, BCVA and CST for 6 months after CLS-AX with no additional therapy



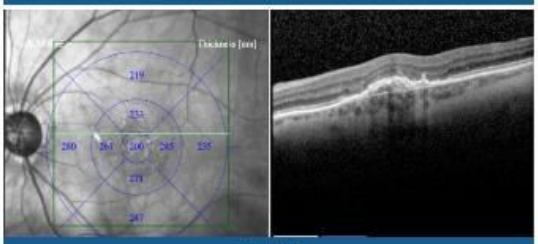

Screening: Aflibercept
BCVA 72, CST 262



Baseline: CLS-AX
BCVA 71, CST 209



Month 3
BCVA 71, CST 207



Month 6
BCVA 69, CST 200



Source: Clearside data on file. | Extension Study interim data as of October 27, 2022.


Summary and
Next Steps

# CLS-AX in Suprachoroidal Space Demonstrates Promising Safety Results, Durability and Biologic Effect in Anti-VEGF Treatment Experienced Sub-responders

| | OASIS Results | Competitive Advantages |
|---|---|---|
| **Safety** (All Cohorts) | **Excellent Safety Profile at all doses and timepoints**<br>• No SAEs, No TEAEs related to study treatment<br>• No dose limiting toxicities<br>• No AEs related to inflammation, vasculitis or vascular occlusion<br>• No vitreous "floaters" or dispersion of CLS-AX into the vitreous<br>• No retinal detachments or endophthalmitis<br>• No AEs related to intraocular pressure | • As a well-characterized small molecule, less risk for inflammation than a novel biologic agent<br>• No need for an operating room setting<br>• No risk of implant migration and very low risk of vitreous "floaters" or haze<br>• SCS injection procedure commercially accepted by retinal physicians following launch of XIPERE ® |
| **Durability** (Cohorts 3&4) | **In OASIS, to 3-month timepoint (N=16):**<br>• **69%** of patients did not receive additional therapy<br>• **92%** of patients did not receive additional therapy per protocol<br>• **≥73%** reduction in treatment burden<br><br>**In Extension Study interim data (N=12):**<br>• **To Month 5: 88% (7/8)** of patients did not receive addl therapy<br>• **To Month 6: 75% (3/4)** of patients did not receive addl therapy<br>• **≥90%** reduction in treatment burden | • CLS-AX showed preliminary signs of durability favorably comparing to other current and investigational intravitreally injected biologic agents<br>• Based on interim extension data at higher doses, CLS-AX suprachoroidal suspension demonstrated it may have durability of effect that favorably compares to other extended release TKI formulations |
| **Biologic Effect** (Cohorts 3&4) | **CLS-AX showed signs of biologic effect:**<br>• Stable mean BCVA<br>• Stable mean CST<br>• On OCT, anatomical signs of TKI biologic effect were observed in anti-VEGF treatment-experienced sub-responders | • The most potent TKI in nAMD trials, differentiated from focused VEGF-A blockade<br>• Targeted high levels to affected choroid-retina may further leverage efficacy, particularly in anti-VEGF sub-responders |

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Source: Clearside data on file. | Extension Study interim data as of October 27, 2022 | XIPERE® (triamcinolone acetonide injectable suspension), for suprachoroidal use received U.S. FDA Approval in October 2021. Please see Important Safety Information for XIPERE in the Full Prescribing Information, 2022: https://www.bauschhealth.com/Portals/25/Pdf/PI/XIPERE-PI.pdf.

# Plans for Continued Progress with CLS-AX

# Arshad M. Khanani, MD, MA, FASRS

**Sierra Eye Associates**

Managing Partner

Director of Clinical Research

Director of Fellowship

**University of Nevada, Reno School of Medicine**

Clinical Associate Professor


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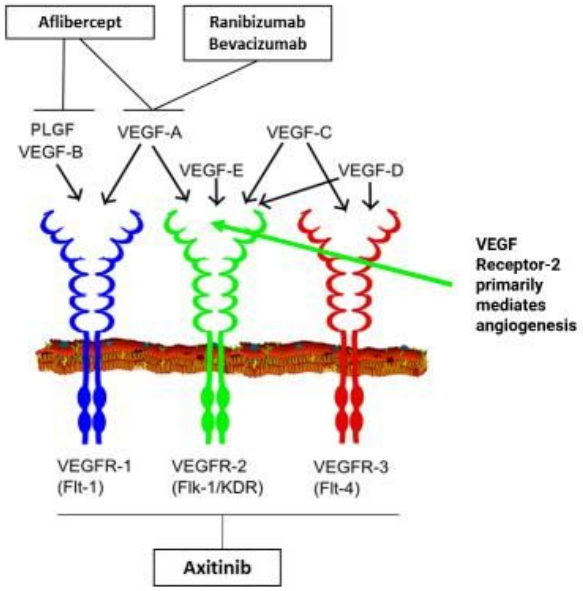
™

# Appendix

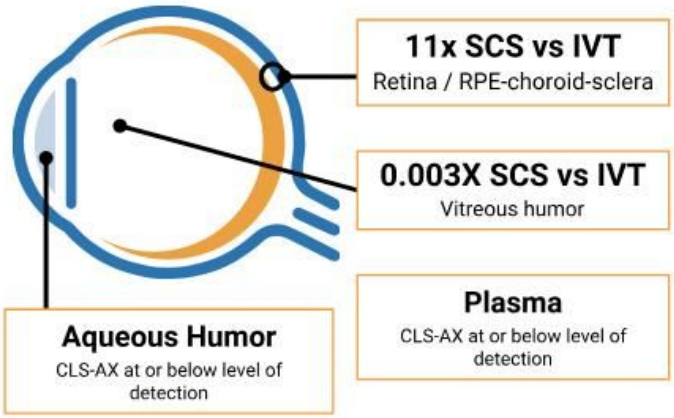
# Axitinib: a Highly Potent, Pan-VEGF TKI to Treat Wet AMD

- Axitinib's intrinsic pan-VEGF inhibition through receptor blockade
  - Approved treatments are focused VEGF-A inhibitors
- Inhibits **VEGFR-1**, **VEGFR-2**, **VEGFR-3** receptors
  - More active than anti-VEGF-A in *in-vitro* angiogenesis model[1-2]
- Highly potent tyrosine kinase inhibitor (TKI)
  - >10x more potent than other TKIs in preclinical studies
  - Better ocular cell biocompatibility than other TKIs[3]
  - More active than other TKIs for experimental corneal neovascularization in preclinical models
- Preclinical data showed axitinib inhibition and regression of angiogenesis




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. Theile 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.

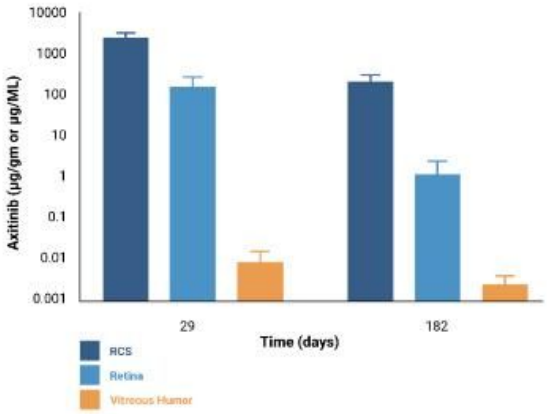
## CLS-AX Injected Suprachoroidally Provides Targeted Delivery Relative to Intravitreal Injection at Same Dose




**Rabbit Model Values: area under the curve ratios, SCS / IVT**
SCS : 1 mg/eye, 100 µL. | IVT: 1 mg/eye, 25 µL
Single bilateral injection, 1-wk rabbit PK studies

## CLS-AX has Potential for Meaningful Durability CLS-AX Levels to 6 Months

High Retina Levels: Sufficient to block VEGF pathway
Low Plasma Levels: <1 ng/mL




**Rabbit toxicology study** with single bilateral suprachoroidal injection of axitinib, 1.05 mg/eye (n=4 eyes/ timepoint)

CLEARSIDE BIOMEDICAL

Sources: Viral S. Kansara, Leroy W. Muya, Thomas A. Ciulla; Evaluation of Long-Lasting Potential of Suprachoroidal Axitinib Suspension Via Ocular and Systemic Disposition in Rabbits. *Trans. Vis. Sci. Tech.* 2021;10(7):19.
Abbreviations: SCS: Suprachoroidal Space | IVT: Intravitreal Injection | PK: Pharmacokinetic | RPE: Retinal pigment epithelium | RCS: RPE, Choroid, Sclera

# Enrolled Patients All with Active Disease at Screening and Confirmed by Independent Reading Center

Demographics and Wet AMD History

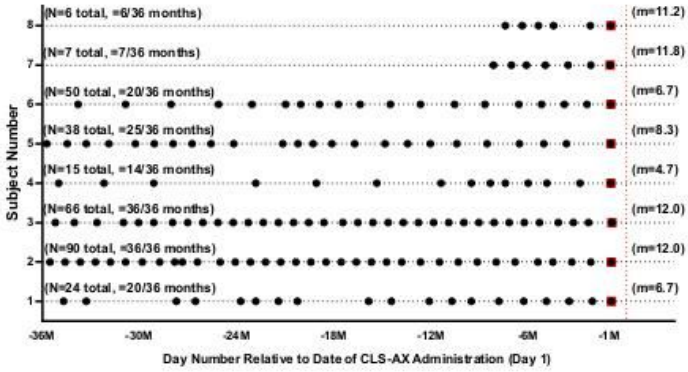
| Wet AMD Disease Characteristics | COHORT 1: 0.03 mg | COHORT 2: 0.1 mg | COHORT 3: 0.5 mg | COHORT 4: 1.0 mg | All Cohorts |
|---|---|---|---|---|---|
| No. of participants | 6 | 5 | 8 | 8 | 27 |
| Mean age (range), years | 81.8 (66-93) | 78.2 (65-90) | 86.3 (75-97) | 76.5 (66-83) | 80.9 (65-97) |
| Mean baseline best corrected visual acuity (range), letters | 59.0 (29-74) | 65.6 (52-75) | 58.5 (37-74) | 65.8 (50-74) | 62.1 (29-75) |
| Mean baseline central subfield retinal thickness (range), µm | 231.2 (208-294) | 209.4 (184-227) | 202.0 (175-238) | 218.8 (152-295) | 214.8 (152-295) |
| **Mean duration of wAMD diagnosis (range), months** | **50.13 (12.4-110.3)** | **49.78 (24.7-81.3)** | **66.64 (6.8-102.1)** | **48.21 (4.5-132.8)** | **54.39 (4.5-132.8)** |
| **Number of anti-VEGF injections reported prior to CLS-AX administration on Day 1, mean (range)** | **26.8 (7-41)** | **24.2 (12-39)** | **37.0 (6-90)** | **28.8 (5-89)** | **29.9 (5-90)** |
| **Annualized number of anti-VEGF injections prior to CLS-AX administration on Day 1, mean (range)** | **9.36 (6.3-12.7)** | **9.54 (5.4-12.2)** | **8.47 (4.9-11.8)** | **11.96 (8.9-13.6)** | **9.90 (4.9-13.6)** |



Source: Clearside data on file.

# Anti-VEGF Treatments up to 3 Years Prior to Baseline CLS-AX Administration

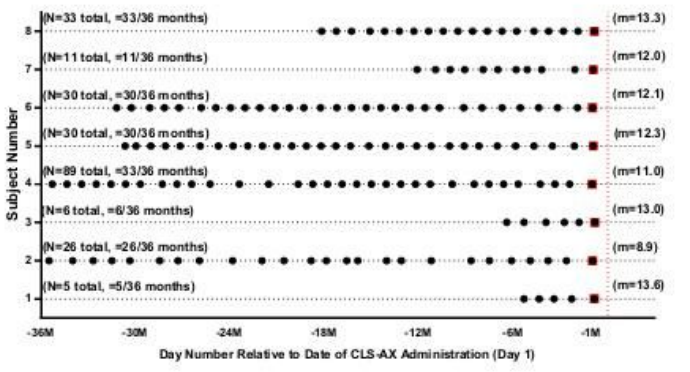
## COHORT 3: 0.5 mg




● Prior nAMD Treatment ■ IVT Aflibercept (Screening, Visit 1)

(N=) Total number of nAMD treatments reported prior to Screening, within 36 months
(m=) Annualized number of injections in the past 36 months defined as (total number of injections in 36 months prior to CLS-AX (Day 1)) / (minimum(3, (duration between first injection and Day 1)/365.25)).

## COHORT 4: 1.0 mg




● Prior nAMD Treatment ■ IVT Aflibercept (Screening, Visit 1)

(N=) Total number of nAMD treatments reported prior to Screening, within 36 months
(m=) Annualized number of injections in the past 36 months defined as (total number of injections in 36 months prior to CLS-AX (Day 1)) / minimum(3, (duration between first injection and Day 1)/365.25)).



Source: Clearside data on file.

# OASIS: Reason for Use of Additional Therapies

| COHORT | SUBJECT # | ADDITIONAL THERAPY VISIT | REASON FOR ADDITIONAL THERAPY |
|---|---|---|---|
| COHORT 1: 0.03 mg (N=6) | 1 | 2 months post CLS-AX | BCVA with exudation |
| | 3 | 2 months post CLS-AX | CST |
| | | 3 months post CLS-AX | BCVA with exudation (not verified by reading center) |
| | 4 | 2 months post CLS-AX | CST |
| | 5 | 2 months post CLS-AX | BCVA with exudation |
| COHORT 2: 0.1 mg (N=5) | 2 | 2 months post CLS-AX | CST (not verified by reading center) |
| | 3 | 2 months post CLS-AX | Macular hemorrhage (not verified by reading center) |
| | 4 | 3 months post CLS-AX | BCVA with exudation |
| | 5 | 1 month post CLS-AX | CST (not verified by reading center) |
| | | 3 months post CLS-AX | BCVA with exudation |
| COHORT 3: 0.5 mg (N=8) | 1 | 1 month post CLS-AX | BCVA with exudation |
| | | 2 months post CLS-AX | BCVA with exudation |
| | 5 | 3 months post CLS-AX | CST |
| COHORT 4: 1.0 mg (N=8) | 1 | 1 month post CLS-AX | CST (not verified by reading center) |
| | 2 | 1 month post CLS-AX | CST (not verified by reading center) |
| | 3 | 1 month and 3 month post CLS-AX | CST (not verified by reading center both times) |
| | 8 | 1 month and 2 months post CLS-AX | Investigator discretion both times |

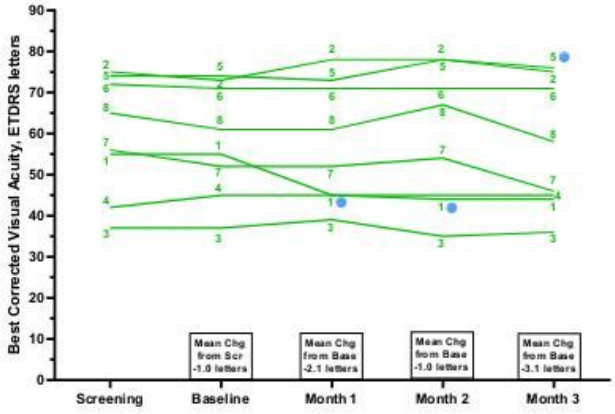
*Red = not treated per protocol defined criteria*

Assessment for additional treatment with aflibercept:
Decrease from best measurement of ≥10 letters in BCVA with exudation; Increase in CST >75 microns; A vision-threatening hemorrhage

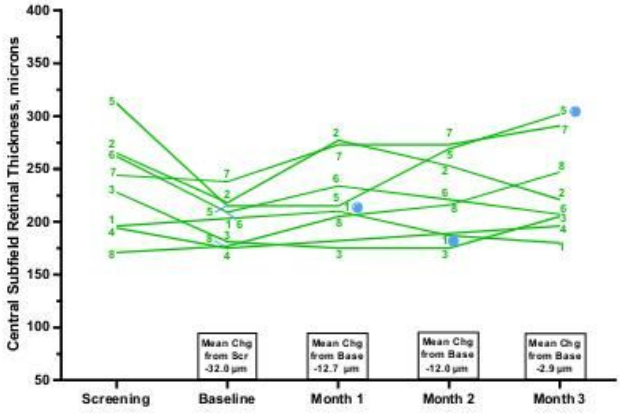

Source: Clearside data on file.

# Cohort 3:
# Stable Best Corrected Visual Acuity and Central Subfield Thickness to 3 Months

**COHORT 3 (0.5 mg): BCVA**




**COHORT 3 (0.5 mg): CST**



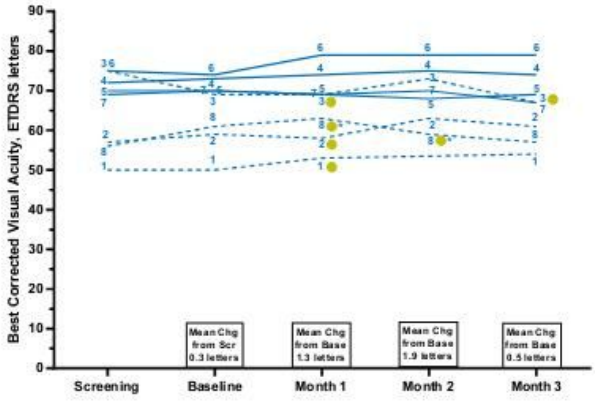

● Additional Therapy (reading center verified) ● Additional Therapy (not reading center verified) ● Additional Therapy (reading center verified) ● Additional Therapy (not reading center verified)

CLEARSIDE BIOMEDICAL

Source: Clearside data on file.

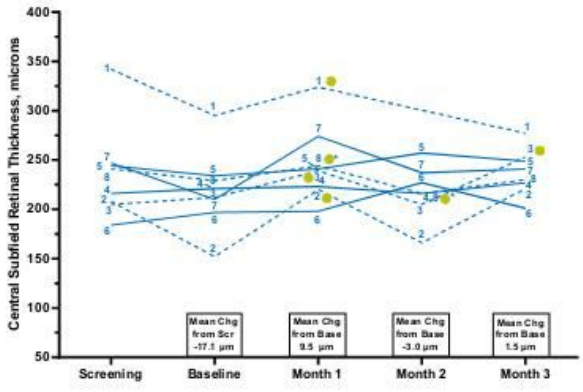
# Cohort 4:
# Stable Best Corrected Visual Acuity and Central Subfield Thickness to 3 Months

**COHORT 4 (1.0 mg): BCVA**




● Additional Therapy (reading center verified) ● Additional Therapy (not reading center verified or * physician discretion)

**COHORT 4 (1.0 mg): CST**




● Additional Therapy (Investigator discretion) ● Additional Therapy (not reading center verified or * physician discretion)

*Dotted line = patient received additional therapy not per protocol (not reading center verified or physician discretion)*

CLEARSIDE BIOMEDICAL

Source: Clearside data on file.

# Extension Study: Demographics and Wet AMD History

| Wet AMD Disease Characteristics | COHORT 2: 0.10 mg | COHORT 3: 0.50 mg | COHORT 4: 1.0 mg | All Cohorts |
|---|---|---|---|---|
| No. of participants | 2 | 7 | 5 | 14 |
| Mean age (range), years | 74.0 (70-78) | 87.9 (81-97) | 79.6 (74-83) | 82.9 (70-97) |
| Mean baseline best corrected visual acuity (range), letters | 60.0 (52-68) | 59.0 (37-74) | 71.2 (69-74) | 63.5 (37-74) |
| Mean baseline central subfield retinal thickness (range), µm | 213.5 (200-227) | 201.9 (175-238) | 214.8 (197-234) | 208.1 (175-238) |
| **Mean duration of wAMD diagnosis (range), months** | **44.30 (33.9-54.7)** | **67.29 (6.8-102.1)** | **36.42 (6.1-103.4)** | **52.98 (6.1-103.4)** |
| **Number of anti-VEGF injections reported prior to CLS-AX administration on Day 1, mean (range)** | **23.0 (12-34)** | **38.9 (6-90)** | **33.2 (6-89)** | **34.6 (6-90)** |
| **Annualized number of anti-VEGF injections prior to Enrollment, mean (range)** | **8.81 (5.4-12.2)** | **8.84 (4.9-11.9)** | **12.01 (10.5-13.1)** | **9.97 (4.9-13.1)** |



Source: Clearside data on file. | Extension Study interim data as of October 27, 2022.
Cohort 2 data calculated with number of patients with available data. Cohorts 3 & 4 data calculated with number of participants currently enrolled.

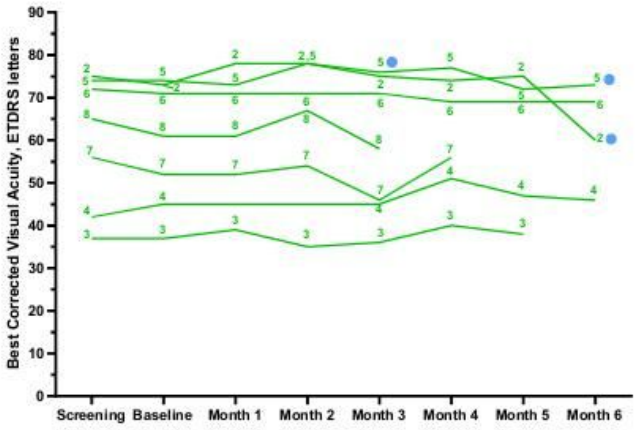
# Extension Study: Reason for Use of Additional Therapies (in Months 4, 5, 6)

| COHORT | SUBJECT | ADDITIONAL THERAPY VISIT | REASON FOR ADDITIONAL THERAPY |
|---|---|---|---|
| COHORT 2: 0.10 mg (N=2) | 1 | 5 months post CLS-AX | Macular hemorrhage |
| COHORT 3: 0.5 mg (N=7) | 2 | 6 months post CLS-AX | BCVA with exudation |
| | 5 | 6 months post CLS-AX | CST |
| COHORT 4: 1.0 mg (N=5) | | No patients treated to Oct 27, 2022 | |

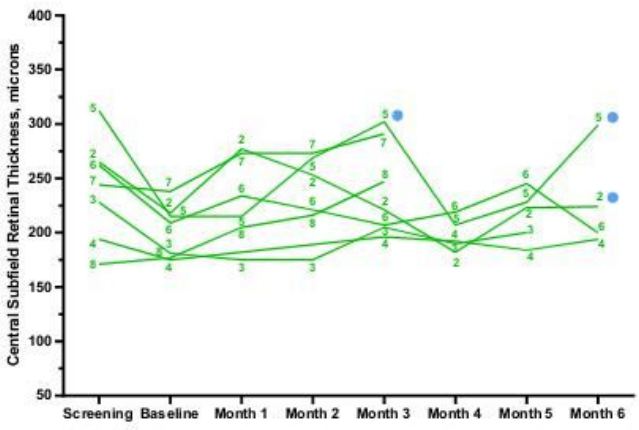
Assessment for additional treatment with aflibercept:
Decrease from best measurement of ≥10 letters in BCVA with exudation; Increase in CST >75 microns; A vision-threatening hemorrhage

# Cohort 3 Interim Extension Study: Stable Best Corrected Visual Acuity and Central Subfield Thickness Beyond 3 Months

## COHORT 3 (0.5 mg): BCVA




## COHORT 3 (0.5 mg): CST




● Additional Therapy (reading center verified) ● Additional Therapy (not reading center verified) ● Additional Therapy (reading center verified) ● Additional Therapy (not reading center verified)

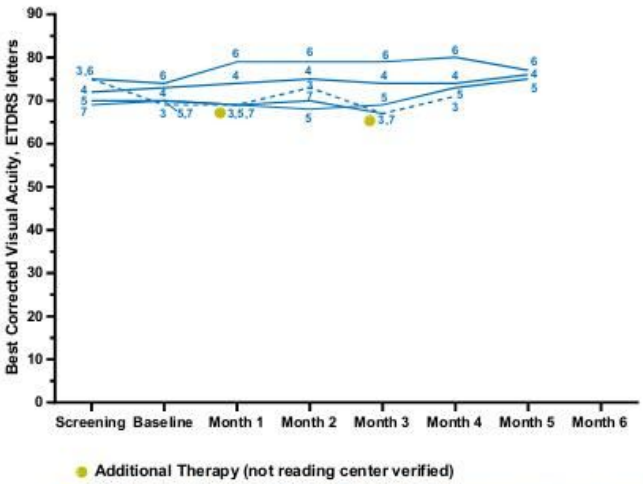
*Dotted line = patient received additional therapy not per protocol (not reading center verified or physician discretion)*



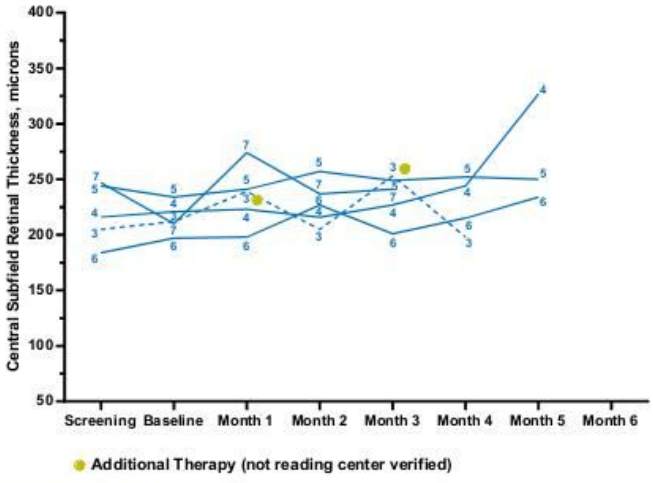
Source: Clearside data on file. | Extension Study interim data as of October 27, 2022.

# Cohort 4 Interim Extension Study: Stable Best Corrected Visual Acuity and Central Subfield Thickness Beyond 3 Months

## COHORT 4 (1.0 mg): BCVA




## COHORT 4 (1.0 mg): CST




*Dotted line = patient received additional therapy not per protocol (not reading center verified or physician discretion)*

# Arshad M. Khanani, MD, MA, FASRS

Managing Partner, Director of Clinical Research, and Director of Fellowship at Sierra Eye Associates

Clinical Associate Professor at the University of Nevada, Reno School of Medicine

Dr. Khanani founded the clinical research department at Sierra Eye Associates, which is now one of the leading clinical research centers in the country. He has served as a principal investigator for over 100 clinical trials and has been a top enroller in the country for multiple Phase 1-3 trials. In addition, Dr Khanani has been the first one to perform surgical procedures in multiple surgical clinical trials dealing with sustained delivery and gene therapy. He has over 75 scientific publications.

Dr. Khanani also serves as a member of national and international clinical trial steering committees as well as scientific advisory boards with the goal of bringing new treatment options for patients with retinal diseases. Dr. Khanani is frequently invited as a guest speaker at national and international meetings.

Dr. Khanani is an elected member of the Macula Society, Retina Society and has received numerous awards of distinction. In 2019, he received the Nevada Business Magazine Healthcare Heroes Physician of the Year award for his continued dedication to the field of ophthalmology. He has received the Senior Honor Award from the American Society of Retina Specialists (ASRS) and was also awarded the prestigious ASRS Presidents' Young Investigator Award in 2021.