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): December 21, 2021

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 December 21, 2021, Clearside Biomedical, Inc. (the "***Company***") will give a presentation describing its positive safety results from OASIS, the Company's ongoing Phase 1/2a 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 in this Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1, 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 8.01 Other Events.

On December 21, 2021, the Company issued a press release entitled "Clearside Biomedical Announces Positive Safety Results from OASIS Phase 1/2a Clinical Trial of CLS-AX (axitinib injectable suspension) for the Treatment of Wet AMD." 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	Presentation
99.2	Press Release, dated December 21, 2021
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

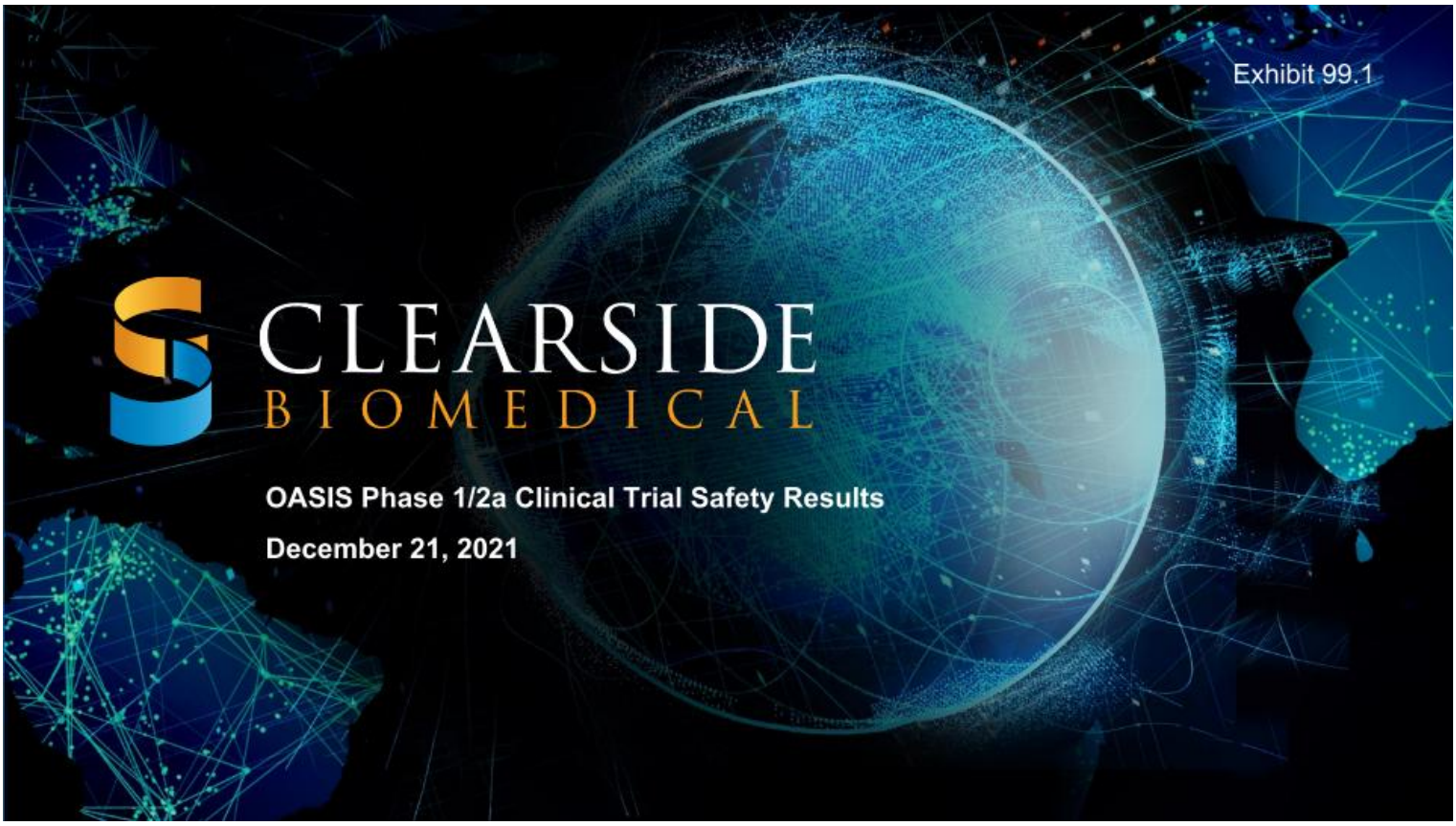
Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Date: December 21, 2021

CLEARSIDE BIOMEDICAL, INC.

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

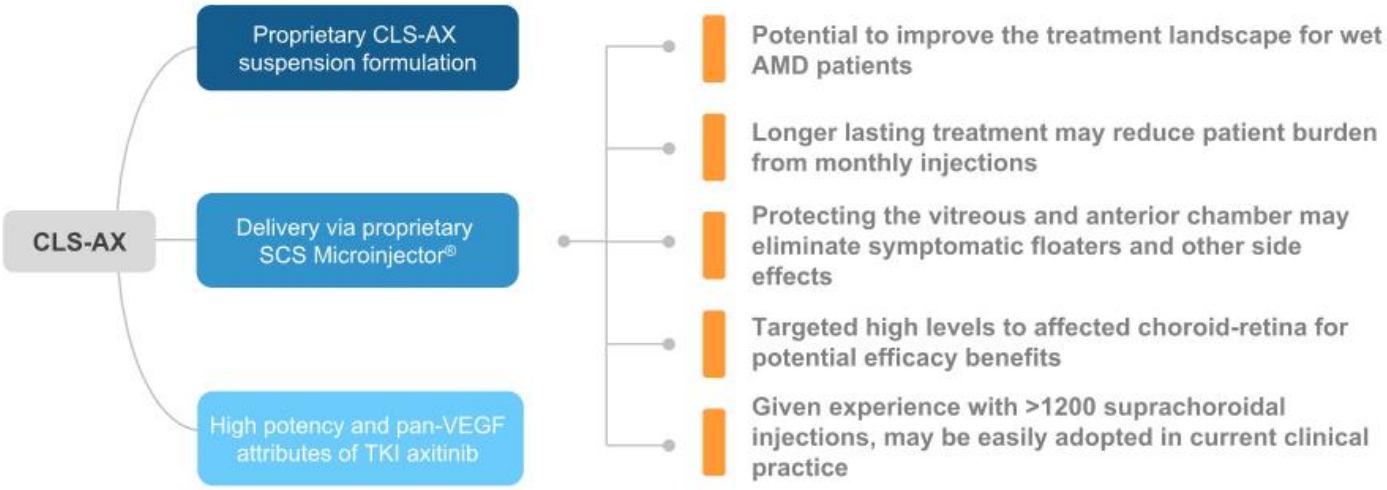
Exhibit 99.1


CLEARSIDE
BIOMEDICAL
OASIS Phase 1/2a Clinical Trial Safety Results
December 21, 2021

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, 2020, filed with the SEC on March 15, 2021, 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.

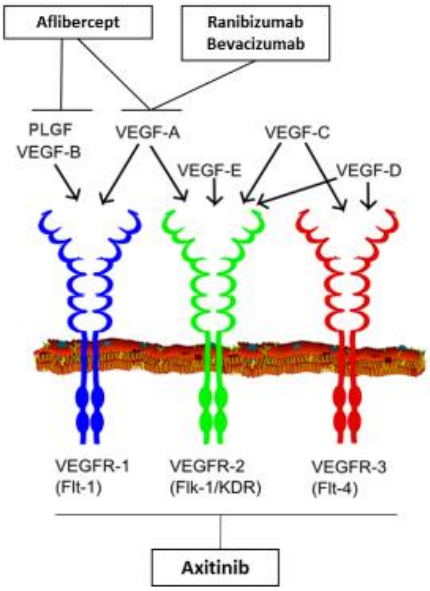
CLS-AX (axitinib injectable suspension) for Suprachoroidal Use



Axitinib is a tyrosine kinase inhibitor (TKI)

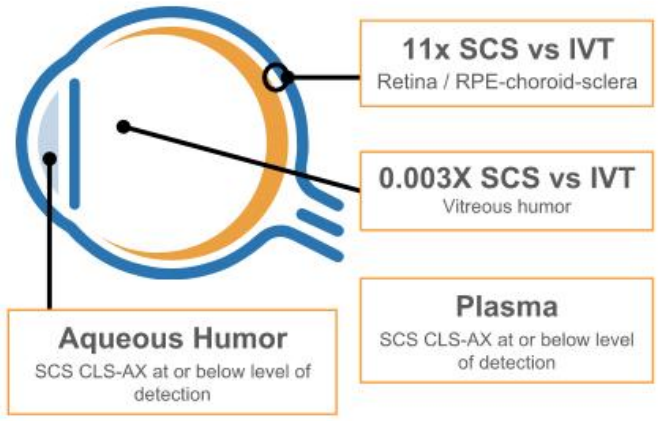
Axitinib: a Highly Potent, Pan-VEGF TKI to Treat Wet AMD

- 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 effective 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 effective 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.

Suprachoroidal CLS-AX Demonstrated Targeted Delivery in Preclinical Models



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

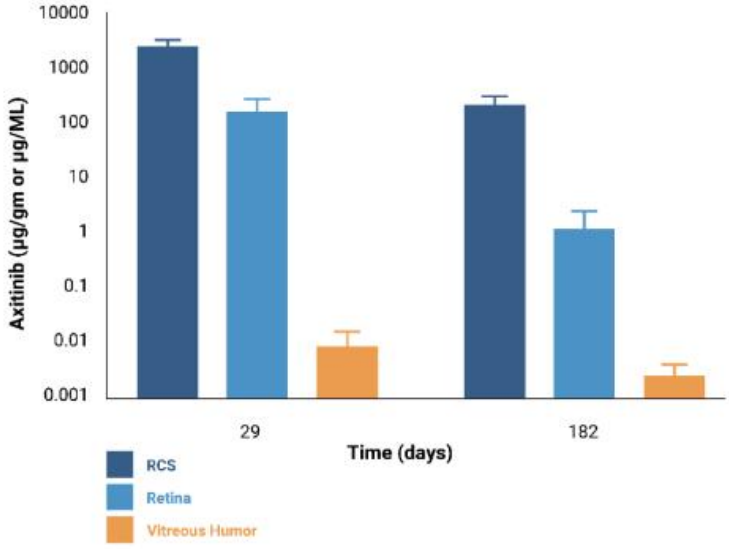
1-wk rabbit PK studies

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. doi:

Abbreviations: SCS: Suprachoroidal Space | IVT: Intravitreal Injection | PK: Pharmacokinetic | RPE: Retinal pigment epithelium

CLS-AX has Potential for Meaningful Durability

Therapeutic Levels > IC50 for 6 months after 1.05 mg/eye SCS Injection in Rabbits



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

- On day 182, mean axitinib levels in the RPE-choroid-sclera (199 µg/gm) and in the retina (1.1 µg/gm) were 3-5 log orders higher than the in-vitro IC50 value (0.2 ng/mL, VEGFR2 autophosphorylation inhibition assay).
- Based on this IC50 value, therapeutic levels were achieved in the RPE-choroid-sclera and retina for 6 months after a single suprachoroidal injection of axitinib in rabbits.

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. doi:
Abbreviations: RCS: RPE-choroid-scleral | RPE: Retinal pigment epithelium

CLS-AX Phase 1/2a Clinical Trial in Wet AMD

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
- 3 Cohorts of 5 patients each: n=15
- Dose-escalation of CLS-AX (in mg): Cohort 1 at 0.03; Cohort 2 at 0.10; Cohort 3 planned at 0.50
- Secondary endpoints: visual function, ocular anatomy, and need for additional treatment
- 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

Wet AMD History

Wet AMD Disease Characteristics	COHORT 1: 0.03 mg (N=6)	COHORT 2: 0.10 mg (N=5)
No. of participants	6	5
Bilateral wAMD, n	0	4
Mean duration of wAMD diagnosis (range), months	50.13 (12.4-110.3)	49.78 (24.7-81.3)
Mean duration since first wAMD treatment (range), months	50.08 (12.4-110.3)	49.70 (24.7-81.1)
Total mean number of wAMD treatments prior to screening (range)	25.8 (6-40)	23.2 (11-38)
wAMD treatments administered prior to Screening, n (%) [No. of injections]		
Aflibercept	1 (16.7%) [29]	2 (40.0) [16]
Bevacizumab	1 (16.7%) [6]	2 (40.0) [21]
Ranibizumab	4 (66.7%) [114]	4 (80.0) [79]
Blinded therapy	1 (16.7%) [6]	0
Total number of wAMD treatments prior to Screening (within 3 years), n (%)		
3-6	1 (16.7)	0
7-12	0	1 (20.0)
13-18	1 (16.7)	2 (40.0)
>18	4 (66.7)	2 (40.0)
Mean (range)	22.5 (6-33)	21.6 (11-33)

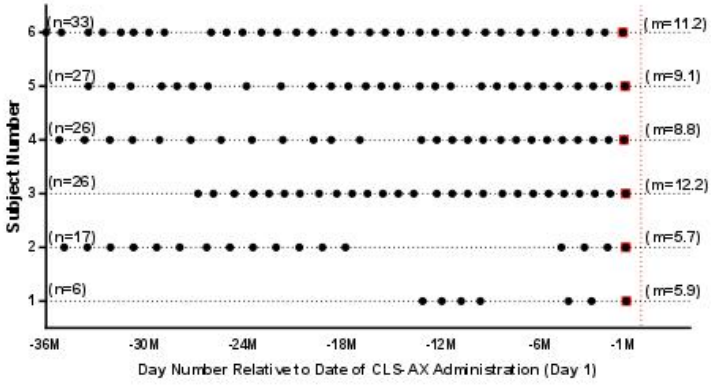
Demographics and Characteristics at Baseline

CHARACTERISTICS	COHORT 1: 0.03mg (N=6)	COHORT 2: 0.10mg (N=5)
No. of participants	6	5
Mean age (range), years	81.8 (66-93)	78.2 (65-90)
Women, no. (%)	2 (33.3)	3 (60.0)
Mean baseline best corrected visual acuity (range), letters	59.0 (29-74)	65.6 (52-75)
Mean central subfield retinal thickness (range), µm	231.2 (208-294)	209.4 (184-227)
Mean total lesion area (range), mm2	6.252 (3.58-9.58)	7.712 (1.06-18.02)

Source: Clearside data on file.

Anti-VEGF Treatments up to 3 Years Prior to Screening

COHORT 1: 0.03 mg

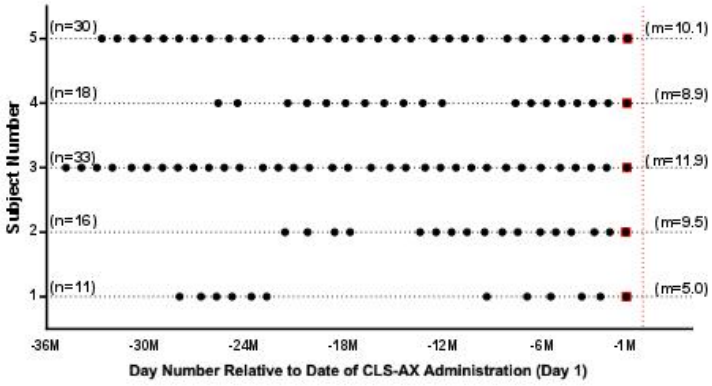


● Prior wAMD Treatment ■ IVT Aflibercept (Screening, Visit 1)

(n=) Total number of wAMD treatments prior to Screening

(m=) Mean number of wAMD treatments prior to Screening per year

COHORT 2: 0.10 mg



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

(n=) Total number of wAMD treatments prior to Screening

(m=) Mean number of wAMD treatments prior to Screening per year

Injection Procedure Questionnaire Responses

INJECTING PHYSICIAN QUESTION	COHORT 1: 0.03 mg (N=6)	Cohort 2: 0.10 mg (N=5)
Were you able to inject all contents of the syringe? **YES, n (%)**	6 (100)	5 (100)
Needle length used to perform procedure: 900 µm needle, **n (%)**	6 (100)	5 (100)
IF 900 µm NEEDLE WAS USED: Were adjustments in the syringe positioning/alignment required during this procedure? **NO, n (%)**	6 (100)	5 (100)
Did you have to remove the needle and reinsert that same needle into a new location during this procedure? **NO, n (%)**	6 (100)	5 (100)
Did you feel adequately prepared to give an injection based on the training you received? **YES, n (%)**	6 (100)	5 (100)
How do you rate the force necessary to complete the injection? **ACCEPTABLE, n (%)**	6 (100)	5 (100)
Were you able to perform the injection based on the training you received? **YES, n (%)**	6 (100)	5 (100)

Safety Overview

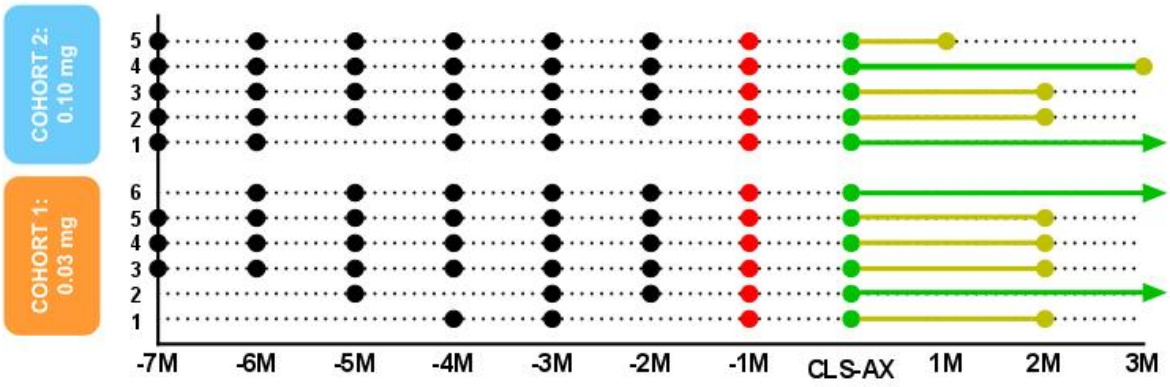
COHORT 1: 0.03 mg

- **No study suspension or stopping rules were met**
- **No Serious Adverse Events (SAEs)**
- No treatment emergent adverse events (TEAEs) related to aflibercept, CLS-AX or suprachoroidal injection procedure
- No dispersion of investigational product into the vitreous
- No adverse events related to intraocular pressure (IOP), inflammation, or vasculitis

COHORT 2: 0.10 mg

- **No study suspension or stopping rules were met**
- **No Serious Adverse Events (SAEs)**
- No treatment emergent adverse events (TEAEs) related to aflibercept, CLS-AX or suprachoroidal injection procedure
- No dispersion of investigational product into the vitreous
- No adverse events related to intraocular pressure (IOP), inflammation, or vasculitis

6 Month Prior Anti-VEGF Therapies and Time to Additional Therapy



- SC CLS-AX injection
- IVT Aflibercept injection
- Anti-VEGF injection prior to study entry
- Additional IVT anti-VEGF injection

Time to Additional Therapy	Number (%) of Participants
≥ 3 months	4 (36.4%)
2 months	6 (54.5%)
1 month	1 (9.1%)

Source: ADLS (CLSD ADaM), ADPTRT (CLSD ADaM), ADRM (CLSD ADaM)

Reason for Retreatment

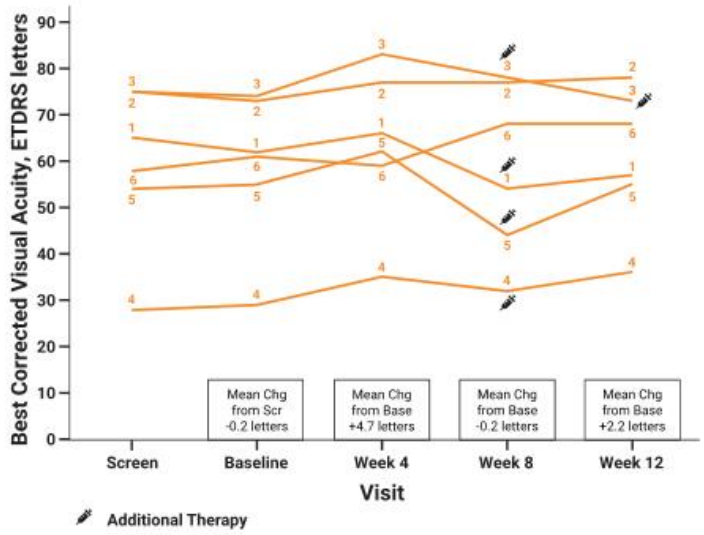
COHORT	SUBJECT	RETREATMENT VISIT	REASON FOR RETREATMENT
COHORT 1: 0.03 mg (N=6)	5	2 months post CLS-AX	BCVA
	4	2 months post CLS-AX	CST
	3	2 months post CLS-AX	CST
	1	2 months post CLS-AX	BCVA
COHORT 2: 0.10 mg (N=5)	5	1 month post CLS-AX	CST – retreatment criteria not met according to independent reading center
	4	3 months post CLS-AX	BCVA
	3	2 months post CLS-AX	Hemorrhage – no hemorrhage observed by the independent reading center; retreatment criteria not met
	2	2 months post CLS-AX	CST – retreatment criteria not met according to independent reading center

Protocol based Assessment for additional aflibercept treatment:

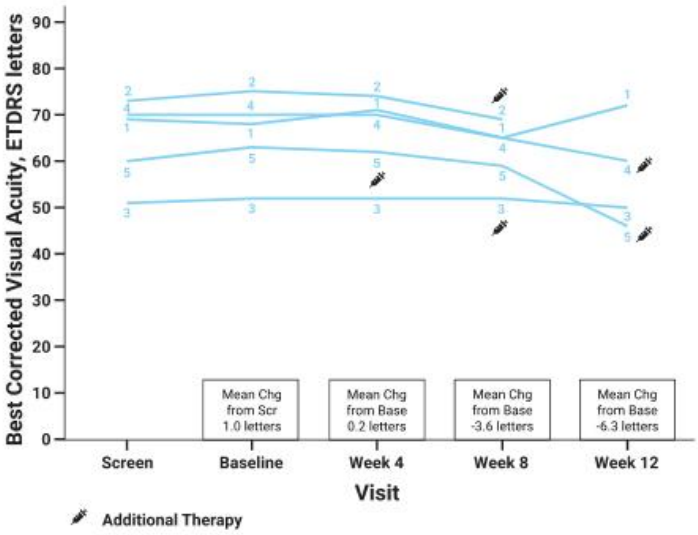
- loss from best measurement of ≥10 letters in BCVA with exudation
- increase in CST >75 microns
- a vision-threatening hemorrhage

Individual Best Corrected Visual Acuity Letter Score, by Visit

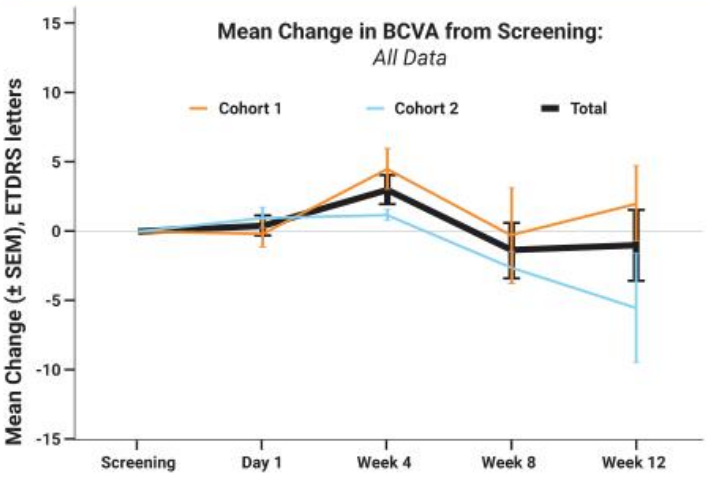
COHORT 1: 0.03 mg



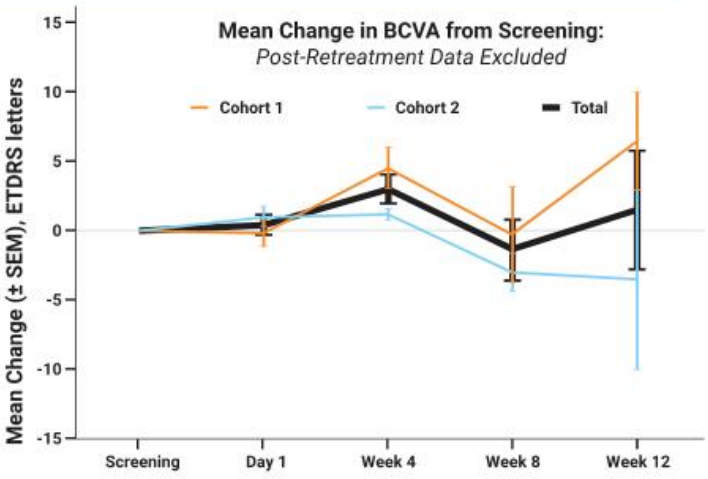
COHORT 2: 0.10 mg



Mean Best Corrected Visual Acuity Letter Score, Change from Screening



Cohort	Screening	Baseline	Week 4	Week 8	Week 12
Cohort 1, n	6	6	6	6	6
Cohort 2, n	5	5	5	5	4*

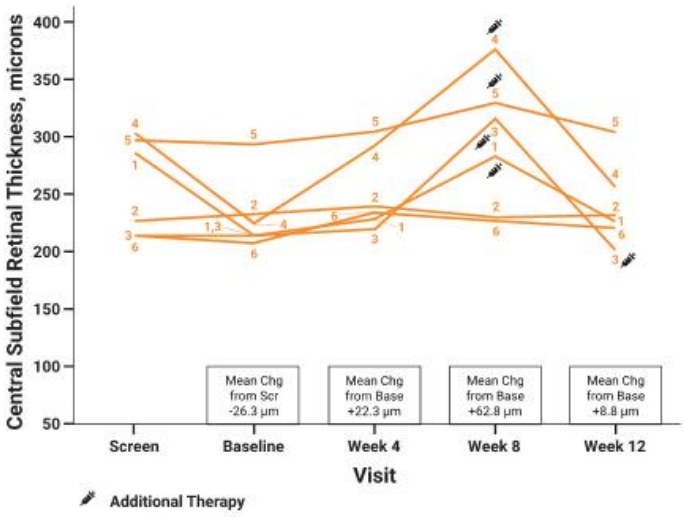


Cohort	Screening	Baseline	Week 4	Week 8	Week 12
Cohort 1, n	6	6	6	6	2
Cohort 2, n	5	5	5	4	2

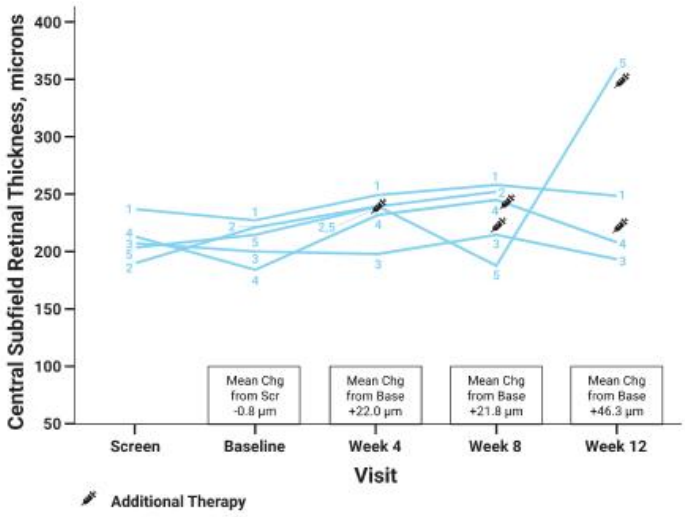
*Cohort 2 subject 2 discontinued after receiving additional therapy | Source: Clearside data on file.

Individual Central Subfield Thickness, by Visit

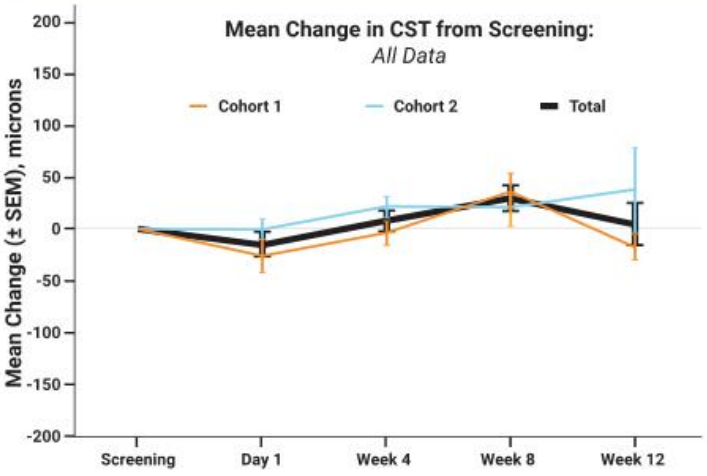
COHORT 1: 0.03 mg



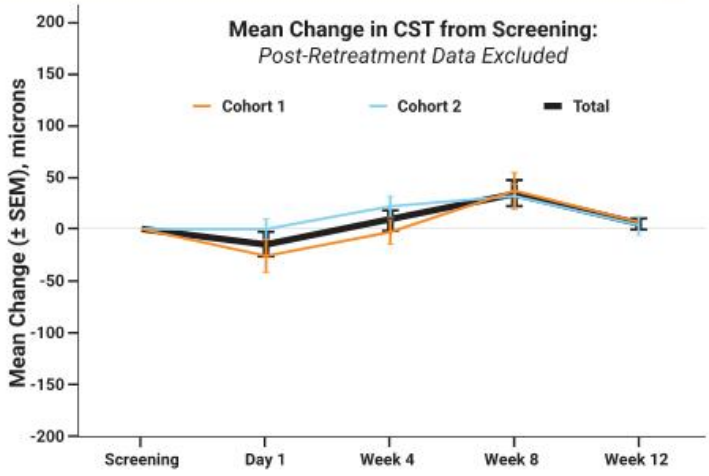
COHORT 2: 0.10 mg



Mean Change Central Subfield Thickness, Change from Screening



Cohort	Screening	Baseline	Week 4	Week 8	Week 12
Cohort 1, n	6	6	6	6	6
Cohort 2, n	5	5	5	5	4*



Cohort	Screening	Baseline	Week 4	Week 8	Week 12
Cohort 1, n	6	6	6	6	2
Cohort 2, n	5	5	5	4	2

*Cohort 2 subject 2 discontinued after receiving additional therapy | Source: Clearside data on file.

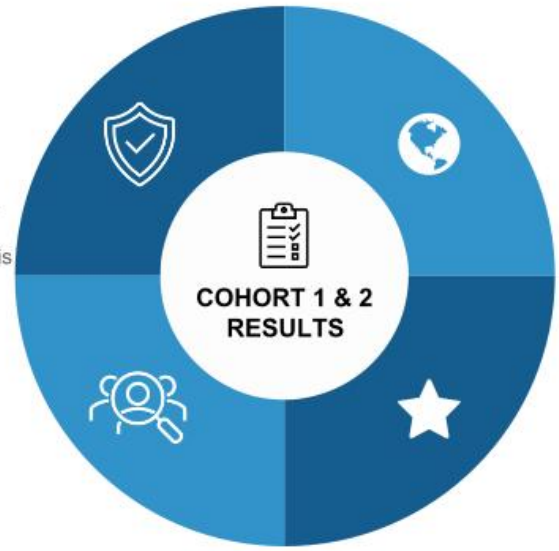
OASIS Cohort 1 & 2 Results Support Advancing to Cohort 3

SAFETY

- CLS-AX well tolerated with no dose limiting toxicities
- No dispersion of investigational product into the vitreous
- No adverse events related to intraocular pressure (IOP), inflammation, or vasculitis

ANATOMIC EFFECTS

Stable disease activity (based on CST), on average, over three months even after excluding patients who were retreated



VISUAL ACUITY

Stable visual acuity, on average, over three months even after excluding patients who were retreated

DURABILITY POST CLS-AX IN HEAVILY PRE-TREATED PATIENTS

- 4/11 (36%) of patients did not require additional therapy for ≥ 3 months
- 6/11 (55%) of patients did not require additional therapy for 2 months
- 1/11 (9%) patient was retreated at 1 month

Protocol Dosing Change for Cohort 3

- Given that this is the first time a tyrosine kinase inhibitor has been injected suprachoroidally in humans, we initiated OASIS with a low dose to establish a foundation for safety.
- **The lack of dose limiting toxicities in Cohorts 1 and 2, along with preclinical toxicology studies, support greater dose escalation than previously planned.**

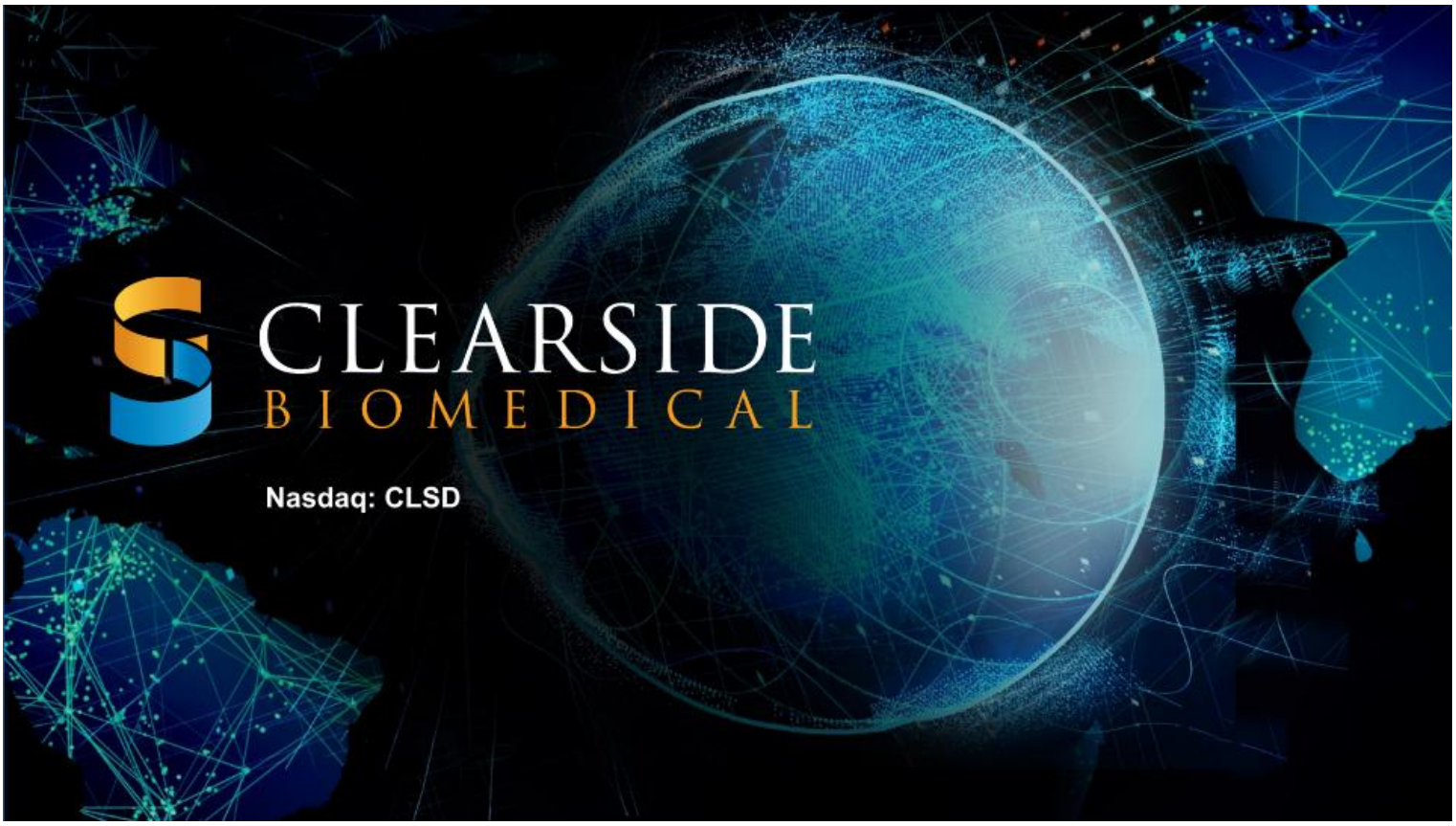

CLEARSIDE
BIOMEDICAL
Nasdaq: CLSD

Exhibit 99.2

Clearside Biomedical Announces Positive Safety Results from OASIS Phase 1/2a Clinical Trial of CLS-AX (axitinib injectable suspension) for the Treatment of Wet AMD

- Suprachoroidal Injection of CLS-AX 0.1 mg Dose Well-Tolerated in Cohort 2 with No Treatment Related Adverse Events –
- Consistent Safety Profile Observed in Cohorts 1 and 2 Supports Advancement to Cohort 3 -
- Webcast and Conference Call Today at 8:30 A.M. ET Hosted by Management and Including Key Opinion Leader, Peter Kaiser, M.D. -

ALPHARETTA, Ga., December 21, 2021 -- 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 safety results from OASIS, its ongoing Phase 1/2a clinical trial of CLS-AX (axitinib injectable suspension) administered by suprachoroidal injection via Clearside's SCS Microinjector®. OASIS is evaluating CLS-AX for the treatment of neovascular age-related macular degeneration (wet AMD).

Data reported today includes results from Cohort 2 as well as combined data from Cohorts 1 and 2. The primary endpoints were achieved in Cohort 2 (n=5), as the 0.1 mg dose of CLS-AX was well tolerated with no serious adverse events; there were no treatment emergent adverse events related to aflibercept, CLS-AX or the suprachoroidal injection procedure; and there was no dispersion of drug into the vitreous. In addition, there were no adverse events related to intraocular pressure (IOP), inflammation, or vasculitis. The OASIS Safety Monitoring Committee has reviewed the data and approved advancing to Cohort 3 with a dose of 0.5 mg of CLS-AX.

Thomas A. Ciulla, M.D., MBA, Chief Medical Officer and Chief Development Officer, commented, "Our OASIS trial continues to demonstrate positive safety results as we escalate the dose. Given that this trial represents the first time a tyrosine kinase inhibitor has been injected suprachoroidally in humans, we started OASIS with low dose levels to

establish a foundation for safety. We believe the absence of any dose limiting toxicities in the first two cohorts of the OASIS trial, combined with our pre-clinical toxicology data, supports our plan to escalate to the higher CLS-AX dose of 0.5 mg in Cohort 3 rather than the previous 0.3 mg dose. We have initiated patient screening for Cohort 3, with target completion of this cohort planned for mid-year 2022. We look forward to gathering more data on the potential benefits of combining targeted and compartmentalized suprachoroidal delivery with the broad pan-VEGF attributes of axitinib for patients suffering from wet AMD."

Data Summary

In Cohort 2, five patients were enrolled with an average age of 78 years. All patients were anti-VEGF treatment-experienced, having undergone numerous injections of standard-of-care anti-VEGF treatments prior to entering the OASIS trial. The mean number of anti-VEGF treatments prior to the start of the trial was 9.2 injections within twelve months and 21.6 injections within 3 years. In Cohort 2, at three months post CLS-AX dose, one patient did not require any retreatment and one other patient was retreated per protocol defined retreatment criteria. Two patients were retreated at month two and one patient was retreated at month one, although based on independent reading center assessment, the protocol defined retreatment criteria were not met in these three patients.

In the combined Cohorts 1 and 2, eleven patients were enrolled with an average age of 80 years. The mean number of anti-VEGF treatments prior to the start of the trial was 9.1 injections within twelve months and 22.1 injections within 3 years. In the combined cohorts: four patients (36% of the total) went at least three months post CLS-AX dosing without retreatment; six patients (55% of the total) went two months without retreatment; and one patient (9% of the total) was retreated at one month. The mean best corrected visual acuity (BCVA) score as measured by Early Treatment Diabetic Retinopathy Study (ETDRS) letters and the mean change in central subfield thickness (CST) of the macula were stable in the combined first two cohorts of the OASIS study.

"The suprachoroidal injection procedure has been easy to perform, reliable and well tolerated by patients during this study. The consistent safety data from Cohorts 1 and 2 support escalation to higher dosing, which we anticipate will provide further insights related to safety, visual acuity, ocular anatomy and durability," added Mark R. Barakat, M.D., Director of Research, Retinal Consultants of Arizona, and Clinical Assistant Professor, University of Arizona College of Medicine, Phoenix, and an investigator in the OASIS clinical trial.

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, Peter Kaiser, M.D., Chaney Family Endowed Chair for Ophthalmology Research and a Professor of Ophthalmology at the Cleveland Clinic Lerner College of Medicine, and a member of Clearside's Scientific Advisory Board. 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 844-263-8310 (domestic) or 213-358-0959 (international) and entering conference code: 7369695.

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 are those who demonstrate stable visual acuity following two or more previous injections with an intravitreal anti-VEGF agent. All enrolled patients undergo diagnostic imaging on screening, followed by masked reading center confirmation of persistent active disease.

Enrolled patients initially receive 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 will assess the safety and tolerability of CLS-AX for the three months following the administration of CLS-AX, and secondary endpoints will evaluate the pharmacokinetics, visual function, ocular anatomy, and the need for additional treatment with intravitreal aflibercept during the three-month period.

The study design includes 3 cohorts of approximately 5 patients each (n=15). Cohorts 1 and 2 are complete. Cohort 1 and Cohort 2 participants received 0.03 mg and 0.1 mg of axitinib, respectively. Cohort 3 is currently enrolling participants for a planned dose of 0.5 mg of axitinib delivered via suprachoroidal injection. There is also a three-month extension study to follow patients in Cohorts 2 and 3. Additional information on the Phase 1/2a trial can be found on https://clinicaltrials.gov (NCT04626128).

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. Preclinical results from Clearside and independent investigators have shown pharmacodynamic effects with reduced growth of experimental neovascularization and decreased fluorescein leakage. 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 wet AMD.

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

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 injection platform with companies utilizing other ophthalmic therapeutic innovations. Clearside's first product, XIPERE™ (triamcinolone acetonide injectable suspension) for suprachoroidal use, was approved by the U.S. Food and Drug Administration in October 2021. 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 and the potential benefits of CLS-AX and product candidates using 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, 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, 2020, filed with the U.S. Securities and Exchange Commission (SEC) on March 15, 2021, 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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