UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 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): June 15, 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, GA 30005
(Address of principal executive offices, including zip code)

(678) 270-3631
(Registrant's telephone number, including area code)

N/A
(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 June 15, 2021, Clearside Biomedical, Inc. (the "***Company***") updated its corporate presentation for use in meetings with investors, analysts and others. The presentation is available through the Company's website and a copy 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 June 15, 2021, the Company issued a press release entitled "Clearside Biomedical Announces Positive Safety Results from Cohort 1 of 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	Corporate Presentation
99.2	Press Release, dated June 15, 2021
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

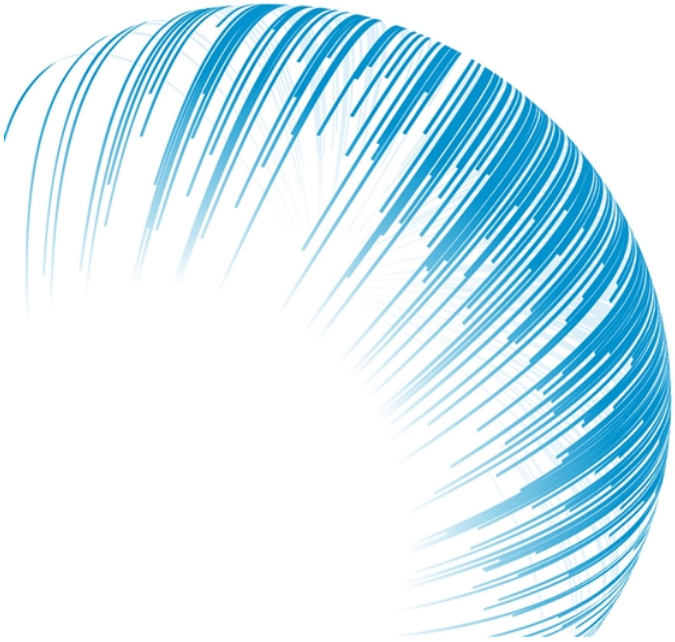
SIGNATURES

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 hereunto duly authorized.

Date: June 15, 2021

CLEARSIDE BIOMEDICAL, INC.

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



CLEARSIDE® BIOMEDICAL

Corporate Presentation | June 2021

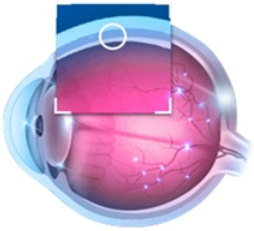
Forward-Looking Statements

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.

Developing and Delivering Treatments that Restore and Preserve Vision for People with Serious Back of the Eye Diseases

Versatile Therapeutic Platform

SCS Microinjector® with proprietary drug formulations target the Suprachoroidal Space



- Proprietary Access to the Suprachoroidal Space (SCS®)
- Utilization Across Small Molecules and Gene Therapy
- Ability to Target Multiple Ocular Diseases
- Internal Research & Development Pipeline
- External Collaborations for Pipeline Expansion

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Core Advantages of Treating Via the Suprachoroidal Space

TARGETED

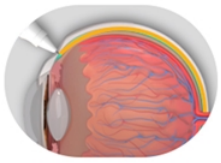
The back of the eye is the location of many irreversible and debilitating visual impairments

for efficacy

COMPARTMENTALIZED

Drug is compartmentalized in the suprachoroidal space, which helps keep it away from non-diseased tissues and entirely behind the visual field

for safety



BIOAVAILABLE & PROLONGED DRUG LEVELS

Fluid spreads circumferentially and posteriorly when injected within the suprachoroidal space, bathing the choroid and adjacent areas with drug

for durability

Sources: Rai UDJ, Young SA, Thrimawithana TR, et al. The suprachoroidal pathway: a new drug delivery route to the back of the eye. Drug Discov Today. 2015;20(4):491-495. | Moisseiev E, Loewenstein A, Yiu G. The suprachoroidal space: from potential space to a space with potential. Clin Ophthalmol. 2016;10:173-178. | Chiang B, Jung JH, Prausnitz MR. The suprachoroidal space as a route of administration to the posterior segment of the eye. Adv Drug Deliv Rev. 2018;126:58-66.

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Pioneers in the Suprachoroidal Space (SCS®) with Patented Technology

Key Intellectual Property Components

1. Comprehensive IP portfolio that includes protection of: SCS delivery technology, proprietary SCS Microinjector, treatment of various conditions with SCS administration of therapeutic products
2. 24 U.S. and >50 European and International issued patents with multiple pending patent applications
3. Granted patents provide exclusivity for our delivery technology and product candidates to mid-2030s with pending applications potentially extending exclusivity beyond 2040

DEVICE PATENTS

SCS Microinjector features

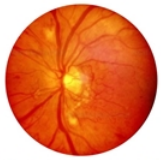
Methods of using SCS Microinjector for drug delivery

Device using an adjustable needle

DRUG PATENTS

Administration of any drug to the suprachoroidal space by microinjection

Administration of any drug to the eye by inserting a microinjector into the sclera



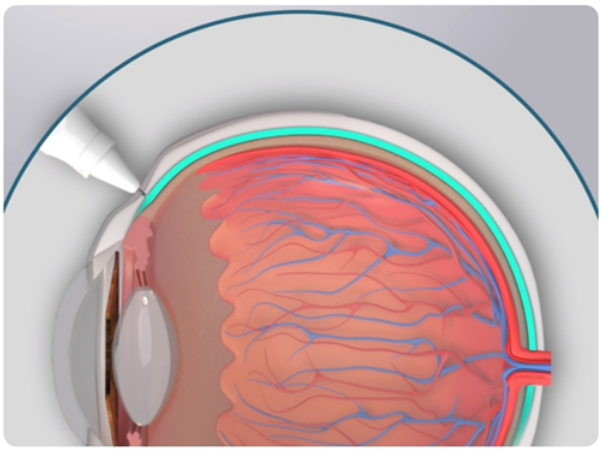
DISEASE PATENTS

Methods of treating posterior ocular disorders by SCS administration

Clearside's SCS Microinjector®: The Only Clinically Tested Injection Device for Suprachoroidal Drug Delivery

- Clinically tested in >1200 suprachoroidal Injections
  - 8 clinical trials completed
  - Injections performed across multiple retinal disorders
- Safety profile comparable to intravitreal injections[1]
  - No Serious Adverse Events (SAEs) involving lens injury, suprachoroidal hemorrhage, or endophthalmitis have been observed
- 4 clinical trials ongoing including partner programs

SUPRACHOROIDAL SPACE INJECTION



Novel SCS Microinjector® allows for precise delivery into the suprachoroidal space

Sources: Clearside data on file | [1]Kurup, et. al, Macula Society 2021 *Safety of the Suprachoroidal Injection Procedure Utilizing SCS Microinjector® across Three Retinal Disorders*

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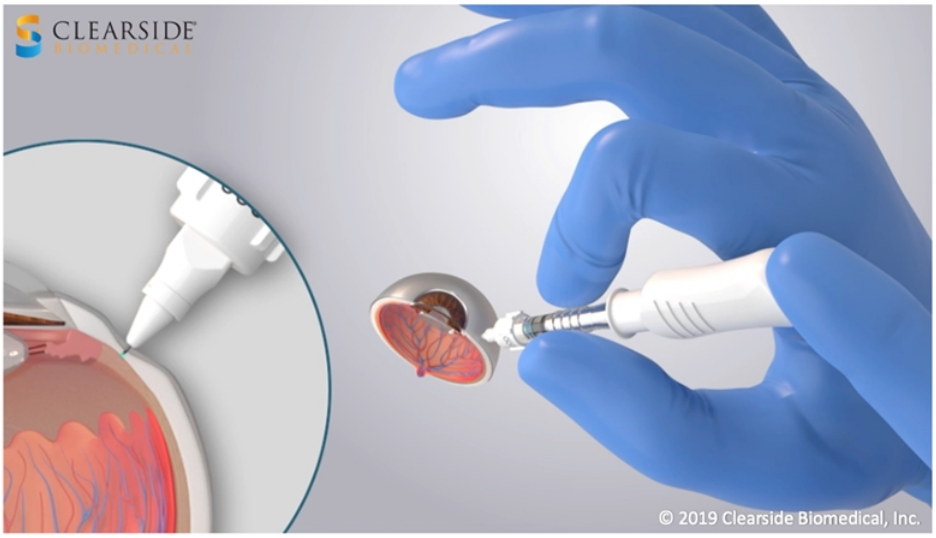
Exclusive Access to the Back of the Eye Using Clearside's Proprietary SCS Microinjector®



CLS-AX Delivered with SCS Microinjector® for Wet AMD

Suprachoroidal Space (SCS®) Injection Platform

Internal Development Pipeline

PROGRAM	THERAPEUTC ENTITY	INDICATION	RESEARCH	PRECLINICAL	PHASE 1/2	PHASE 3
CLS-AX (axitinib injectable suspension)	Small Molecule	Wet AMD				OASIS
Integrin Inhibitor (Injectable suspension)	Small Molecule	Diabetic Macular Edema (DME)				
Gene Therapy	Non-Viral Vectors	"Therapeutic Biofactory" / Inherited Retinal Disease				

SCS Microinjector® Partner Programs

PARTNER	THERAPEUTC ENTITY	INDICATION	IND-Enabling	PHASE 2	PHASE 3	NDA
REGENXBIO	AAV-based Gene Therapy	Wet AMD (AAVIATE)				
REGENXBIO	AAV-based Gene Therapy	Diabetic Retinopathy (ALTITUDE)				
AURA BIOSCIENCES	Viral-like Drug Conjugate	Ocular Oncology/Choroidal Melanoma				

XIPERE™ Commercial Partners

PARTNER	THERAPEUTC ENTITY	TERRITORY	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	NDA
BAUSCH HEALTH	Small Molecule	U.S. & Canada; options ex-North America					PDUFA 10/30/21
ARCTIC VISION	Small Molecule	Greater China & South Korea					

XIPERE™ (triamcinolone acetonide suprachoroidal injectable suspension) is an investigational product

XIPERE™: Potential Suprachoroidal Approach to Treating Uveitic Macular Edema

- Macular edema is the leading cause of vision loss in patients with non-infectious uveitis
- NDA was resubmitted and accepted for review with PDUFA goal date of October 30, 2021
- Commercialization and development partnerships to enhance value and expand patient access

XIPERE™
(triamcinolone acetonide suprachoroidal injectable suspension) 40 mg/mL

If approved, XIPERE would represent the

FIRST therapy for macular edema associated with uveitis

FIRST uveitis trial using visual acuity change as a primary endpoint (Phase 3 PEACHTREE)

FIRST approved therapeutic delivered into the suprachoroidal space

FIRST commercial product for Clearside

XIPERE™ is an investigational product

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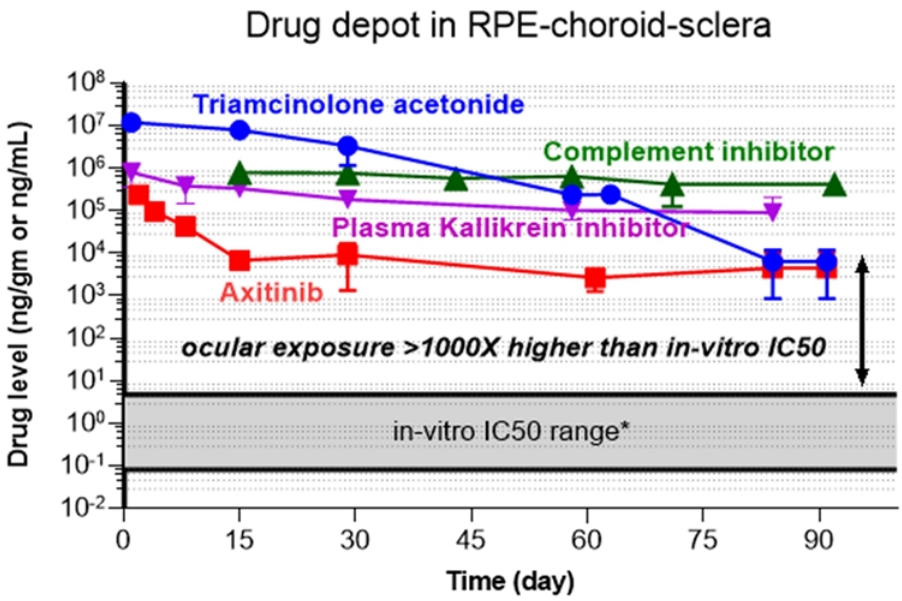
Preclinical Data Supports Durability Potential of Small Molecule Suspensions Delivered into the Suprachoroidal Space



Sources for in-vitro IC50 range: Stellato et al. *J Allergy Clin Immol.* 1999 volume 104, number 3, part 1 | Yuan et al. *Haematologica* 2017 Mar, 102(3) 466-475 | Inlyta, EMA 2012 May; CHMP assessment report | 2014 R13 HAE conference, Che, Wilson, Babu, Preclinical Characterization of BCX4161, an oral plasma kallikrein inhibitor, for the treatment of Hereditary Angioedema.

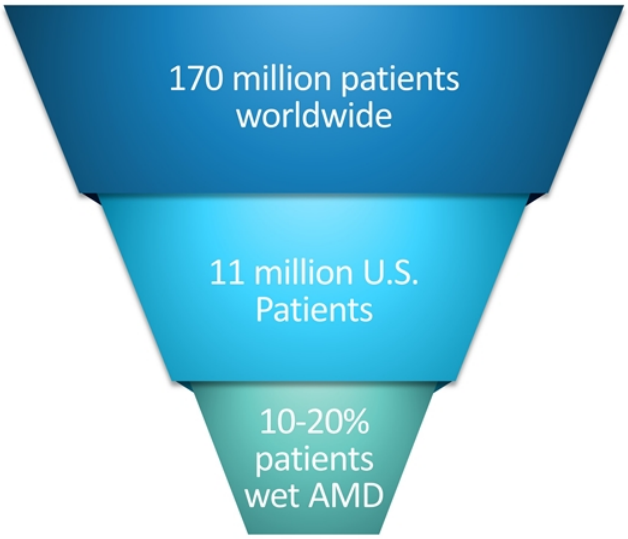
CLS-AX

(axitinib injectable suspension)

for Suprachoroidal Injection

Age-Related Macular Degeneration (AMD)

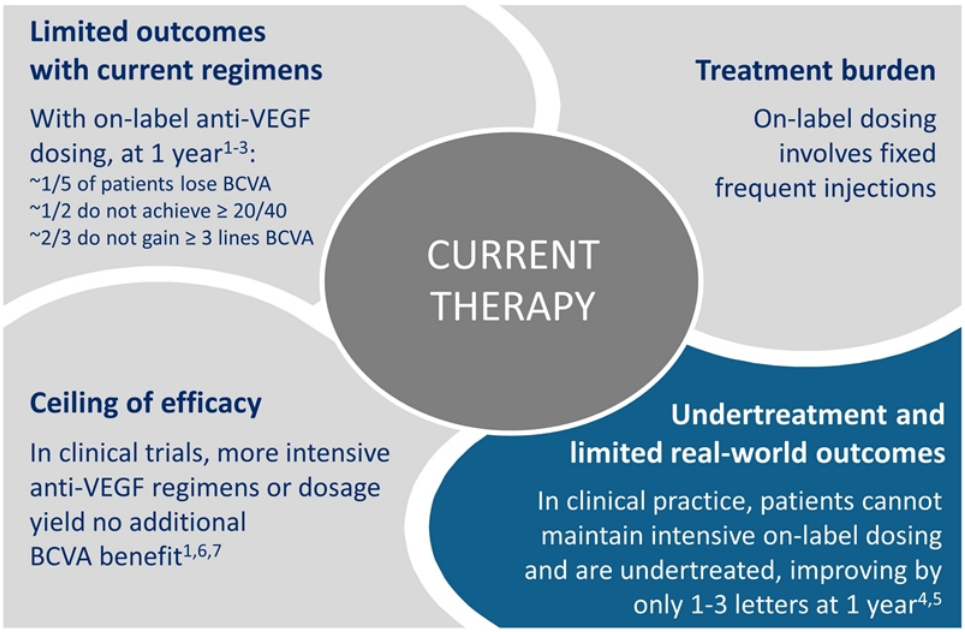
A large and growing market opportunity



- AMD causes a progressive loss of central vision and is the most common cause of blindness in individuals over age 55
  - Neovascular or Wet AMD accounts for the majority of blindness
- U.S. prevalence expected to increase to 22 million by the year 2050
- Global prevalence expected to increase to 288 million by the year 2040
- **Current treatments require frequent injections causing reduced compliance**
  - Under-treatment contributes to limited outcomes

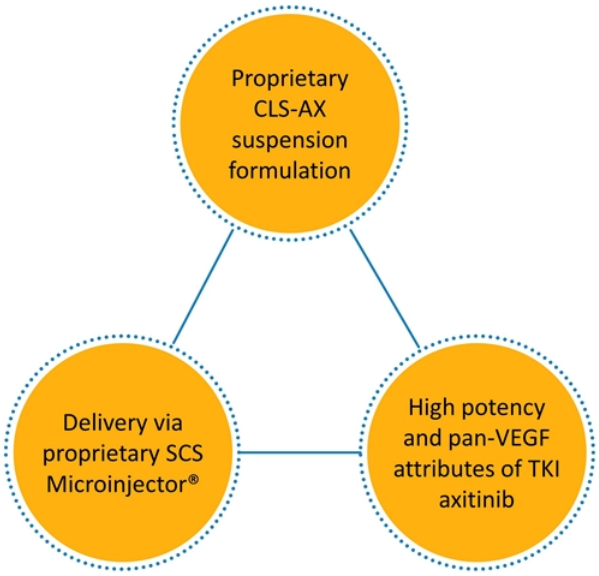
Sources: Medscape: F Ryan Prall, MD, et al Assistant Professor of Ophthalmology, Indiana University School of Medicine | Pennington, Katie L and DeAngelis, Margaret M *Eye and Vision*, Epidemiology of age-related macular degeneration (AMD): associations with cardiovascular disease phenotypes and lipid factors , Dec 22, 2016.

Current Wet AMD Therapies Lead to Under-Treatment and Limited "Real-World" Clinical Outcomes



Sources: 1. Heier JS et al. *Ophthalmology.* 2012;119:2537-2548. | 2. Brown DM et al. Ophthalmology. 2009;116:57-65.e5. | 3. Rosenfeld PJ et al. N Engl J Med. 2006;355:1419-1431. | 4. Ciulla TA et al. Ophthalmology Retina. 2019 May 25. pii: S2468-6530(19)30280-5. | 5. Rao P, Lum F, Wood K, et al. Ophthalmology. 2018;125:522e528. | 6. Busbee BG et al. Ophthalmology. 2013;120:1046-1056. | 7. Schmidt-Erfurth U et al. Ophthalmology. 2014;121:193-201.

CLS-AX (axitinib injectable suspension) for Suprachoroidal Injection in wet AMD

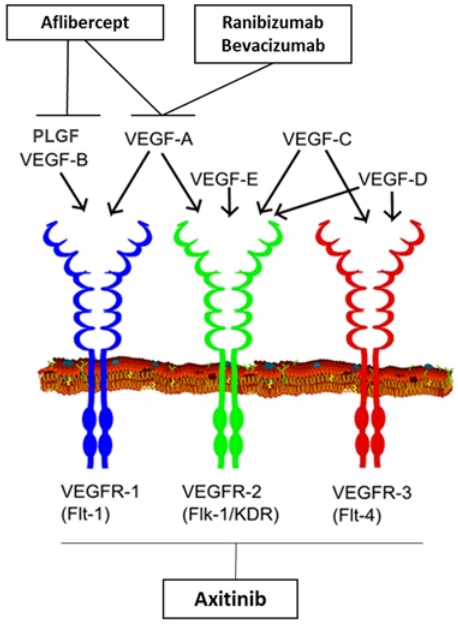


- Potential to **improve the treatment landscape** for wet AMD patients
- **Longer lasting treatment** may reduce patient burden from monthly injections
- Protecting the vitreous and anterior chamber **may eliminate symptomatic floaters and other side effects**
- **Targeted high levels** to affected choriod-retina for potential efficacy benefits
- Given experience with **>1200 injections**, may be **easily adopted** in current clinical practice

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.

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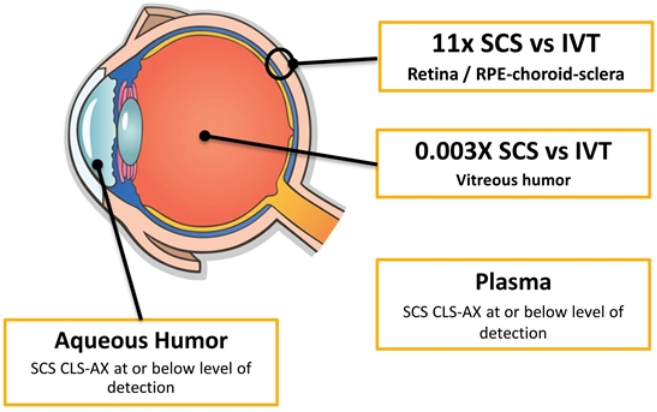
Suprachoroidal Injection of CLS-AX Provides Targeted Delivery Relative to Intravitreal Injection at Same Dose



Rabbit Model

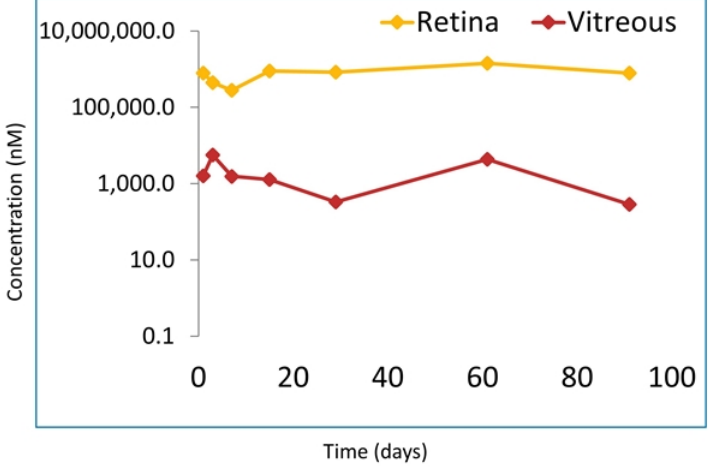
Values: area under the curve ratios, SCS / IVT

SCS : 1 mg/eye, 100 µL. | IVT: 1 mg/eye, 25 µL

Single bilateral injection, 1-wk rabbit PK studies

CLS-AX: High, Sustained Drug Levels in the Retina after SCS Administration

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

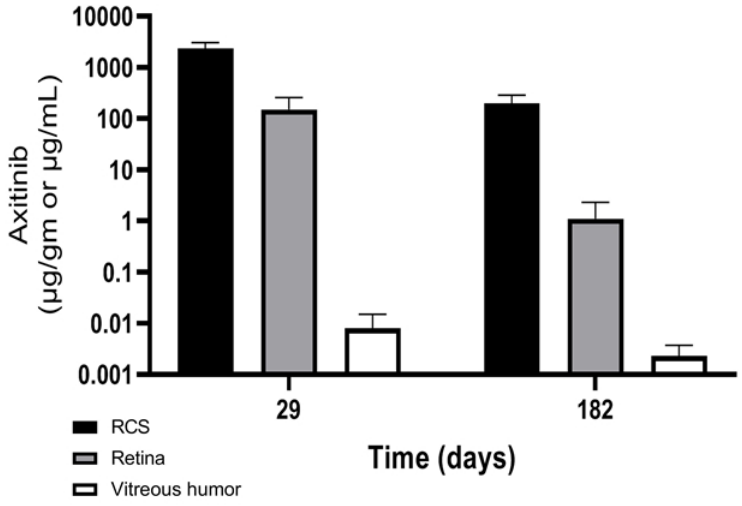


Source: Based on Clearside Biomedical preclinical data

Abbreviations: SCS: Suprachoroidal Space | IVT: Intravitreal Injection | PK: Pharmacokinetic | LLOQ: lower limit of quantification, 0.15 mg/mL | RPE: Retinal pigment epithelium

CLS-AX has Potential for Meaningful Durability

Therapeutic Levels > IC50 for 6 months after 1.05 mg/eye SC 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.

Source: *Translational Vision Science & Technology*, 2021, in press.

CLS-AX Has the Potential to Improve Current Wet AMD Treatment

SCS Delivery May Synergistically Enhance Pan-VEGF Effect

	SAFETY	EFFICACY	TREATMENT BURDEN
AXITINIB	• Well characterized small molecule • Potential for less immune response & inflammation vs biological products • Better compatibility with retinal pigment epithelial cells vs other TKIs	• Shows pan-VEGF inhibition • Pan-VEGF inhibition shows greater effect preclinically & clinically • Regresses neovascularization preclinically • >10x the in-vitro potency vs. other TKIs • Current anti-VEGF agents only target VEGF-A	

SUPRACHOROIDAL DELIVERY	• Compartmentalized SCS drug delivery potentially results in few anterior AEs
	• Favorable tolerability profile of SCS Microinjector in >1200 patient injections
	• Use of SCS Microinjector is well accepted by physician-investigators
		• Targets drug to the diseased chorioretinal tissue in wAMD
		• Shows up to 11x higher drug levels vs intravitreal administration
			• Shown prolonged duration in preclinical studies
			• Potential to have less frequent dosing compared to current anti-VEGF products which may:
			  ◦ Limit undertreatment by facilitating better compliance
			  ◦ Further enhance clinical outcomes

Sources: Clearside Biomedical preclinical and clinical studies | 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. | Lieu et al. The Association of Alternate VEGF Ligands with Resistance to Anti-VEGF Therapy in Metastatic Colorectal Cancer. PLoS ONE 8(10): e77117. | 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.

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

Trial Design and Objectives

- Open-label study 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 currently planned at 0.30
- Evaluate visual function, ocular anatomy, and need for additional treatment
- Assessment for additional therapy: loss from best measurement of ≥10 letters in BCVA with exudation; increase in CST >75 microns; a vision-threatening hemorrhage

Cohort Enrollment and Treatment

Note: aflibercept is dosed via intravitreal injection (IVT); CLS-AX is dosed via suprachoroidal injection | clinicaltrials.gov NCT# 04626128

OASIS Cohort 1: Encouraging Results Support Progression to Cohort 2

- **Cohort 1 Objective:** To establish a floor of safety in this first-in-human trial with low dose CLS-AX (0.03 mg dose)
- **Patients:** Highly treatment-experienced
  - Total number prior anti-VEGF treatments: mean = 25.8, median = 28.0
  - Total number prior anti-VEGF treatments within the last 12 months: mean = 9.0, median = 11.0
- **Conclusion**
  - **Cohort 1 supports progression to Cohort 2**

Source: Clearside data on file.

Cohort 1: Summary of Primary and Secondary Measures

SAFETY: CLS-AX WELL TOLERATED

- **No study suspension or stopping rules were met**
- **No SAEs have been reported**
- No signs of inflammation, vitreous haze, IOP safety signals, vasculitis, or intravitreal dispersion of investigational product
- 2 TEAEs assessed as unrelated to CLS-AX by the investigators

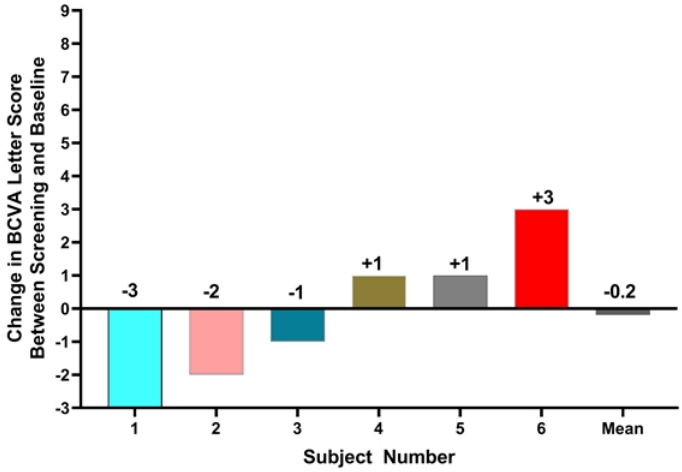
BCVA AND ANATOMIC RESULTS

- **1-month visual acuity improvement of 1 line post CLS-AX** vs no change for aflibercept, at this initial low dose
  - Aflibercept: 1-month BCVA change -0.2 ETDRS letters (p=0.862*)
  - CLS-AX 0.03 mg: 1-month BCVA change +4.7 ETDRS letters (p=0.029*) with 5/6 patients improving by 4 or more letters
- **Mean CST stable within 50 *µm* at one month post 2 mg aflibercept and at one month post 0.03 mg CLS-AX**
  - In these treatment-experienced patients, the normal screening baseline CST imposes a floor effect, limiting improvement in CST

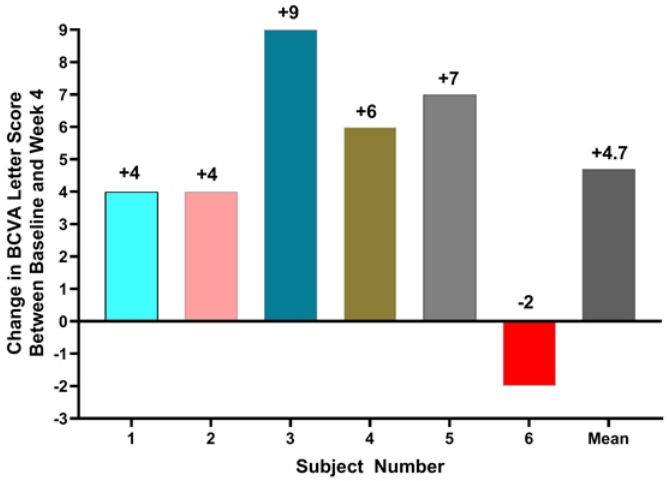
Source: Clearside data on file. |. *Post hoc, unadjusted

Best Corrected Visual Acuity
One Month Response Following Aflibercept 2 mg vs CLS-AX 0.03 mg

1 Mo Change after Aflibercept : -0.2 letters, P=0.862*



1 Mo Change after CLS-AX : +4.7 letters, P=0.029*

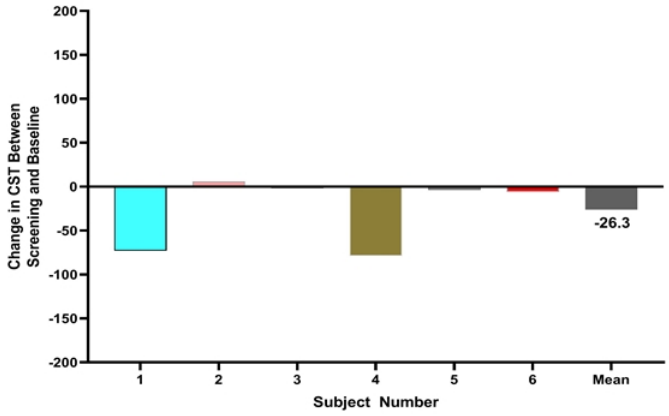


Source: Clearside data on file. |. *Post hoc, unadjusted

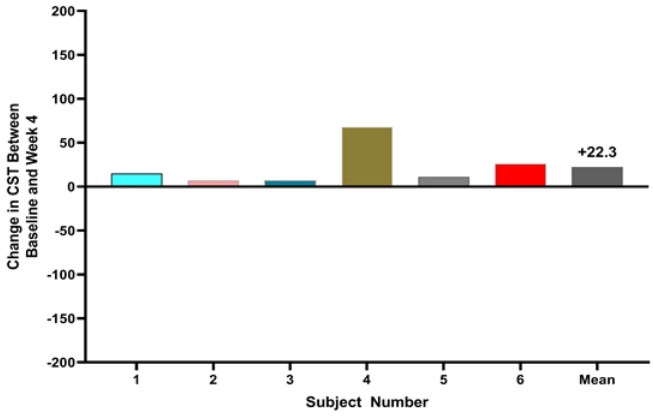
OASIS

Central Subfield Thickness
Mean CST Stable within 50 μm at One Month

1 Mo Change after Aflibercept (2 mg)



1 Mo Change after CLS-AX (0.03 mg)



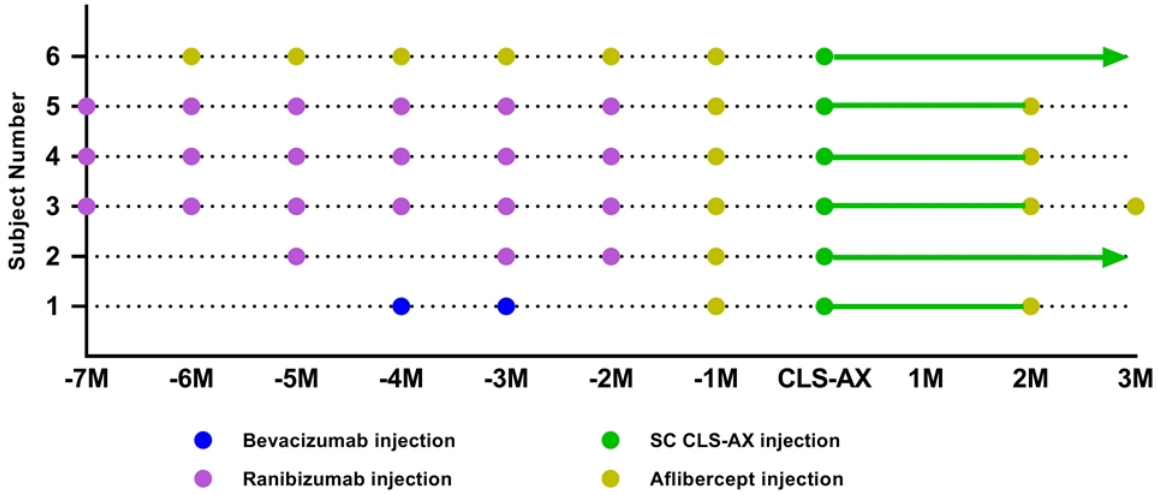
Source: Clearside data on file.

CLEARSIDE BIOMEDICAL

Cohort 1: Preliminary Signs of Potential Durability at Low Dose in Highly Treatment Experienced and Dependent Patients

No subjects required additional treatment at 1 month post CLS-AX
2 of 6 subjects did not require additional treatment for 3 months post CLS-AX

Therapies for nAMD up to 6 Months Prior to Screening



Source: Clearside data on file.

OASIS Cohort 1 Results Support Advancing to Cohort 2

SAFETY
- CLS-AX well tolerated
- No signs of inflammation, vitreous haze, IOP safety signals, vasculitis, or intravitreal dispersion of investigational product

VISUAL ACUITY
- At 1 month, 5 of 6 patients had improved BCVA ≥4 letters (mean +4.7 letters)
- At 3 months, 2/6 no need for additional therapy and BCVA improved by 5 and 7 letters from baseline

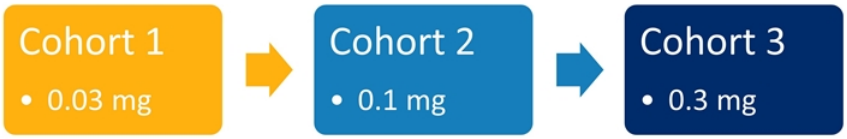
COHORT 1 RESULTS

ANATOMIC EFFECTS
- Mean CST stable within 50 μm at 1 month

DURABILITY POST CLS-AX
- No subjects required additional therapy at 1 month
- 2/6 no need for additional therapy through 3 months
- 4/6 received additional therapy at 2 months

Source: Clearside data on file.

Cohorts 2 and 3 Continue to Escalate Single CLS-AX Dose



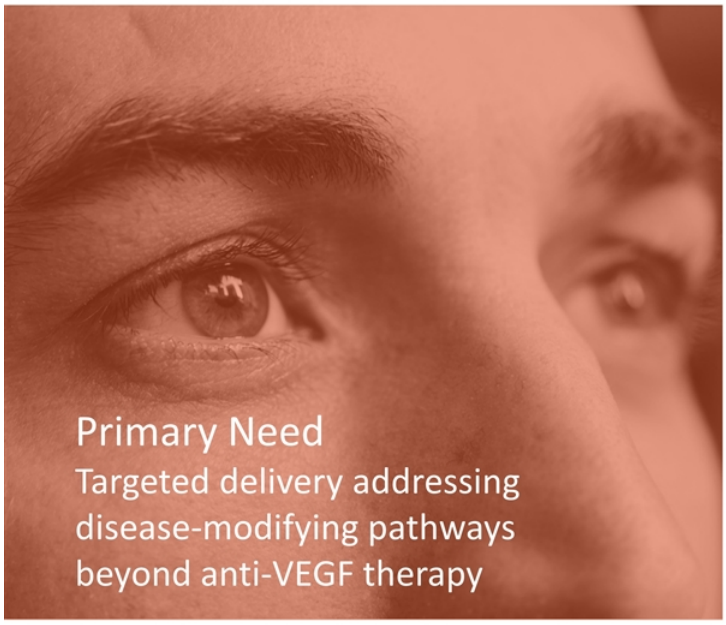
- With 3.3x and 10x dosing in cohorts 2 and 3 respectively:
  - We expect progressively increased durability, based on our preclinical pharmacokinetic studies
  - And potential for better visual acuity outcomes than anti-VEGFA based on pan-VEGF inhibition

- Preclinical pharmacokinetic studies show progressively prolonged tissue levels with increased dosing

Source: Clearside data on file.

Early-Stage Pipeline

SCS Injection Platform and Integrin Inhibition



The Opportunity Beyond the VEGF pathway

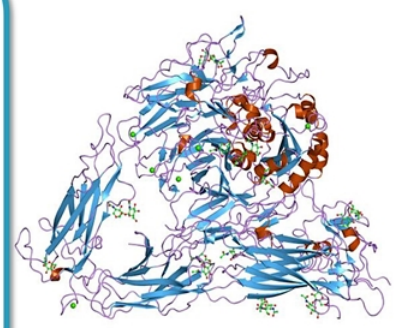
- Novel target
- Early industry validation in DME and AMD
- Advantages of targeted suprachoroidal administration with potential for:
  - Improved safety profile, through compartmentalization in SCS
  - Enhanced efficacy, through drug levels at affected tissues
  - Extended durability
- Limited potential competition in the non-VEGF approach to treatment

CLEARSIDE BIOMEDICAL

Integrin Small Molecule Suspension for SCS administration

Multi-functional cell-adhesion molecules, heterodimeric receptors with α and β subunits

- Connect extracellular matrix (ECM) to actin cytoskeleton in the cell cortex
- Regulate cellular adhesion, migration, proliferation, invasion, survival, and apoptosis
- Also play a role in inflammation, angiogenesis and fibrosis



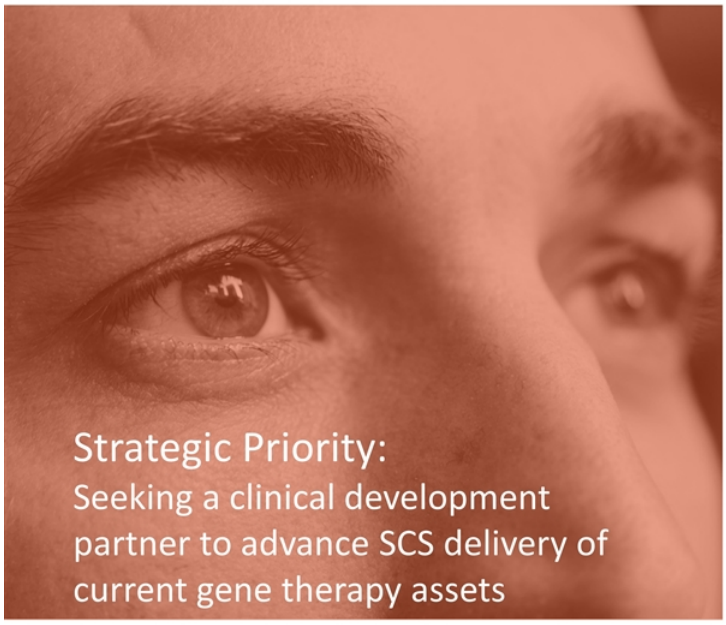
Targets integrins avβ3, avβ5 and a5β1 implicated in DME, DR & AMD

Given unique MOA, could serve as:

- Primary therapy
- Adjunctive therapy to anti-VEGF
- Secondary therapy in refractory cases

Note: This image of integrin $a_v\beta_3$ extracellular domains has been released for public use by its creator and original copyright holder: http://www.ebi.ac.uk/.

Suprachoroidal Injection of Gene Therapy May Offer Potential for Safe and Efficient Delivery



The Opportunity

- Convert gene therapy into an office-based procedure
  - Avoid risks of vitrectomy (surgery)
  - Avoid risks of retinotomy, subretinal injection, and macular detachment
  - Enhance patient access
- Equivalent expression for subretinal and suprachoroidal administration preclinically
- Potential for broader retinal coverage & repeat dosing of suprachoroidal vs subretinal injection
- Delivery of viral and non-viral vectors
  - Preclinical studies with AAV show transfection of photoreceptors

Sources: Clearside data on file. | Campochiaro, P. A. (2019). AAV8-vectored suprachoroidal gene transfer produces widespread ocular transgene expression. *Journal of Clinical Investigation*. doi: 10.1172/jci129085

Corporate Partnerships & Milestones

Enabling SCS Delivery of AAV Gene Therapy for Retinal Disease

The Opportunity: Gene Therapy

- Exclusive worldwide rights to our SCS Microinjector for delivery of adeno-associated virus (AAV)-based therapeutics to the suprachoroidal space to treat wet AMD, diabetic retinopathy and other conditions for which anti-VEGF treatment is the standard of care
- Delivery of gene therapy through the SCS may provide a targeted, in-office, non-surgical treatment approach option
- Encouraging preclinical results delivering RGX-314 into the SCS
- SCS delivery of AAV gene therapy well tolerated to date

The Terms:

- Up to an additional $34M in development milestones across multiple indications
- Up to $102M in sales milestones
- Mid single digit royalties on net sales of products using SCS Microinjector

REGENXBIO: Two Phase 2 Trials Using SCS Microinjector®

- Two multi-center, open-label, randomized, controlled, dose-escalation studies evaluating the efficacy, safety and tolerability of suprachoroidal delivery of RGX-314
- RGX-314 for Treatment of Wet Age-Related Macular Degeneration (wet AMD)
  - Phase 2 AAVIATE trial of suprachoroidal delivery of RGX-314 using SCS Microinjector **is ongoing**
  - Patient population: severe wet AMD patients who are responsive to anti-VEGF treatment
  - Interim efficacy data from Cohort 1 expected in **Q3 2021**
  - Interim data from Cohort 2 expected in **H2 2021**
  - Enrolling Cohort 3 in patients who are positive for neutralizing antibodies
- RGX-314 for Treatment of Diabetic Retinopathy (DR)
  - Phase 2 ALTITUDE trial of suprachoroidal delivery of RGX-314 using SCS Microinjector **is ongoing**
  - Initial data expected **in 2021**

CLEARSIDE BIOMEDICAL

Aura Bioscience: Phase 2 Ocular Oncology trial using SCS Microinjector®

The Opportunity: Ocular Oncology

- Worldwide licensing agreement for the use of our SCS Microinjector to deliver their proprietary drug candidates into the SCS for the potential treatment of certain ocular cancers, including choroidal melanoma
- Non-surgical alternative to intravitreal delivery of Aura's oncology drug candidates via our SCS Microinjector
- Choroidal melanoma is the most common, primary intraocular tumor in adults
- Aura's Phase 2 clinical trial is **ongoing** using SCS Microinjector
- SCS delivery clinically well tolerated to date

The Terms:

- Potential future financial upside for Clearside from pre-specified development and sales milestones
- Royalties on net sales of products using SCS Microinjector

aura

XIPERE: Two Global Commercialization & Development Partners

XIPERE™
(triamcinolone acetonide suprachoroidal injectable suspension) 40 mg/mL

BAUSCH Health

- License for the U.S. and Canada; options for other territories
- Received $5M upfront payment
- Up to $15M in FDA approval and pre-launch milestones
- Up to $57.3M in milestone payments; tiered royalties from the high-teens to 20%

arctic VISION

- License for Greater China & South Korea
- Received $4M upfront payment
- $4M at U.S. approval
- Up to $31.5M in approval, development and sales milestones
- Tiered royalties of 10% to 12%

XIPERE™ is an investigational product

CLEARSIDE BIOMEDICAL

Four Validating Partnerships to Drive Growth

REGENXBIO aura BAUSCH+ Health arctic VISION

Validates our investment in suprachoroidal delivery using our SCS Microinjector

Expands our overall internal and collaborative product development pipeline

Maximizes the commercial and development opportunities for XIPERE in multiple geographic markets

Eligible to receive >$230M from the four partnerships in potential development and sales milestones, and potential royalties to fund our internal R&D pipeline

CLEARSIDE BIOMEDICAL

2021 Research and Development Investment Highlights

Versatile therapeutic platform with proprietary access to the suprachoroidal space

Patented technology & delivery approach

XIPERE

- ✓**Q2:** NDA Resubmission
- **October 2021:** PDUFA Date
- **Q4:** Arctic Vision initiates Phase 3 trial in China in uveitic macular edema (**ARVN001**)

Scientific presentations and publications

- ✓**Q1:** Angiogenesis, Macula Society
- ✓**Q2:** ARVO
- **Q3:** ASRS, Retina Society
- **Q4:** AAO

Building an internal R&D pipeline

CLS-AX Phase 1/2a OASIS

- ✓**Q1:** Complete Cohort 1 Enrollment
- ✓**Mid 2021:** Cohort 1 Safety Data
- **June 2021:** Initiate Cohort 2 Screening
- **YE:** Cohort 2 Completion

2021: Integrin Inhibitor preclinical data

Exploratory preclinical SC non-viral vector delivery studies ongoing

Partnering to expand use of SCS platform*

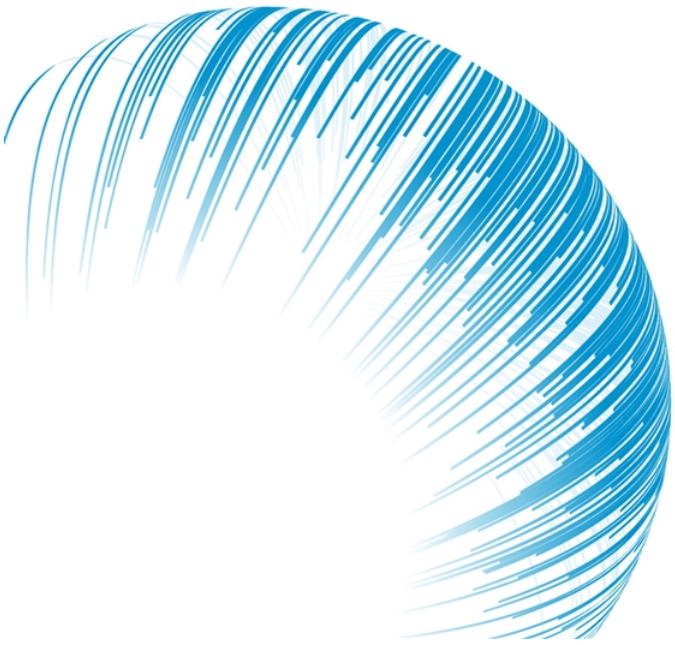
REGENXBIO: RGX-314

- ✓**Q1:** Initiate Cohort 2 Phase 2 AAVIATE trial in wet AMD
- **Q3:** Interim Cohort 1 Phase 2 AAVIATE trial data in wet AMD
- **2021:** Initial Data Phase 2 ALTITUDE Trial in DR

AURA BIOSCIENCES: AU-011

- **2021**: Phase 2 trial in choroidal melanoma ongoing

*REGENXBIO (RGNX) trials involve suprachoroidal delivery of RGX-314 using the SCS Microinjector; Aura Biosciences trials involve suprachoroidal delivery of AU-011 using the SCS Microinjector; Arctic Vision program involves suprachoroidal delivery of ARVN001 (triamcinolone acetonide suprachoroidal injectable suspension) using the SCS Microinjector.



CLEARSIDE BIOMEDICAL

Nasdaq: CLSD

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

- CLS-AX 0.03 mg dose delivered via suprachoroidal injection was well-tolerated with no treatment related adverse events -

- Initiating Cohort 2 patient screening for 0.1 mg dose in June 2021-

ALPHARETTA, Ga., June 15, 2021 — Clearside Biomedical, Inc. (NASDAQ:CLSD), a biopharmaceutical company dedicated to developing and delivering treatments that restore and preserve vision for people with serious back of the eye diseases, announced today positive safety results from Cohort 1 of OASIS, its ongoing Phase 1/2a clinical trial of CLS-AX (axitinib injectable suspension) administered by suprachoroidal injection via Clearside's SCS Microinjector® in six patients (n=6) with neovascular age-related macular degeneration (wet AMD).

The primary endpoints were achieved in Cohort 1, as the initial lowest planned dose of 0.03 mg CLS-AX was well tolerated with no serious adverse events and no drug related treatment emergent adverse events observed throughout the study period. There were no signs of inflammation, no vasculitis, no intraocular pressure (IOP) safety signals, no dispersion of drug into the vitreous, or any other drug related adverse events observed in any of the patients. The OASIS Safety Monitoring Committee has reviewed the data and the trial will advance to Cohort 2. Clearside expects to begin Cohort 2 patient screening for a dose of 0.1 mg CLS-AX in June 2021 with completion of this four month study period expected by the end of the year.

"We are very encouraged by the Cohort 1 results of the OASIS trial and we are immediately beginning Cohort 2 enrollment as planned," said Thomas A. Ciulla, M.D., MBA, Chief Medical Officer and Chief Development Officer. "The initial data from Cohort 1 clearly achieved our safety and tolerability endpoints. While still early and recognizing there are a limited number of patients, we believe the Cohort 1 data supports our hypothesis that the combination of targeted and compartmentalized suprachoroidal delivery and the potent pan-VEGF attributes of axitinib may facilitate an effective treatment option for patients suffering from wet AMD."

The average age of the patients in Cohort 1 was 82 years and all 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 prior anti-VEGF treatments within the twelve months and up to the 3 years prior to the start of the trial was 9.0 injections and 22.5 injections, respectively. All enrolled patients underwent diagnostic imaging at screening, followed by masked reading center confirmation of persistent active disease. The mean central subfield thickness (CST) of the macula was 231 µm (range 208 - 294 µm). The mean baseline best corrected visual acuity (BCVA) score as measured by Early Treatment Diabetic Retinopathy Study (ETDRS) letters, at the start of the trial was 59.0 (range 29 - 74).

As part of the trial design, at the initial visit, the six treatment-experienced patients in Cohort 1 received a standard-of-care, single intravitreal injection of 2 mg aflibercept. One month later, the mean ETDRS BCVA score for all patients remained stable, changing only by -0.2 letters, and patients then received a single suprachoroidal dose of 0.03 mg CLS-AX. One month after receiving CLS-AX, five of six patients exhibited improvement in BCVA, each gaining four or more letters, with mean ETDRS BCVA score of all patients increasing by +4.7 letters (p=0.029, post hoc, unadjusted). In Cohort 1: no patients required additional treatment with aflibercept at the one-month visit post CLS-AX; two patients went three months post CLS-AX without additional treatment with aflibercept and BCVA improved by 5 and 7 ETDRS letters for these patients; and four patients received additional treatment with aflibercept at the two month visit post CLS-AX. The mean CST was stable within 50 µm for all Cohort 1 patients both at one month post 2 mg aflibercept and at one month post 0.03 mg CLS-AX.

“CLS-AX was well-tolerated and these initial results in this heavily treatment-experienced group of wet AMD patients are promising. I look forward to the continued clinical advancement of CLS-AX at the planned higher doses to further explore potential benefits in visual acuity, ocular anatomy and durability,” added Mark R. Barakat, M.D., Director of Research, Retinal Consultants of Arizona; Clinical Assistant Professor, University of Arizona College of Medicine, Phoenix.

The current OASIS trial protocol includes a CLS-AX dose of 0.1 mg for Cohort 2 and 0.3 mg for Cohort 3, which equates to 3.3x and 10.0x the Cohort 1 dose of 0.03 mg. The Company expects to add a three-month extension study to follow patients in Cohort 2 and Cohort 3. Combined data from the multiple cohorts of the OASIS trial is planned to be presented at future medical meetings.

Information on Clearside’s pipeline, including the CLS-AX program and Cohort 1 top-line results, are included in the Company’s corporate presentation which may be accessed on the Clearside website under the Investors section: Events and Presentations.

About the OASIS Phase 1/2a Clinical Trial

OASIS is an open-label, single dose-escalation Phase 1/2a trial in wet AMD patients to assess the safety and tolerability of three increasing doses 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 is planned with 3 cohorts of approximately 5 patients each (n=15). Cohort 1 participants received the lowest dose, 0.03 mg of axitinib delivered via suprachoroidal injection, and the trial is proceeding to Cohort 2 with a dose of 0.1 mg of axitinib. Dose escalation to the next Cohort follows review of the safety data by the Safety Monitoring Committee and their recommendation to advance to the next higher dose cohort. Additional information on the Phase 1/2a trial can be found on https://clinicaltrials.gov (NCT04626128).

About CLS-AX (axitinib injectable suspension)

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. Preclinical studies by independent investigators have shown pharmacodynamic effects with reduced growth of experimental neovascularization and decreased fluorescein leakage.

CLS-AX (axitinib injectable suspension) is a proprietary suspension of axitinib for suprachoroidal injection. With suprachoroidal administration of axitinib, there is targeted delivery of this pan-VEGF inhibitor to affected tissue layers for potential efficacy benefits, as well as prolonged chorioretinal tissue levels for potential durability benefits. Suprachoroidal injection of this proprietary suspension of axitinib has demonstrated meaningful potential in preclinical studies in multiple species.

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 dedicated to developing and delivering treatments that restore and preserve vision for people with serious back of the eye diseases. Clearside's proprietary SCS Microinjector® targets the suprachoroidal space (SCS®) and offers unique access to the macula, retina and choroid where sight-threatening disease often occurs. The Company's SCS injection platform is an inherently flexible, in-office, non-surgical procedure, intended to provide targeted delivery to the site of disease and to work with both established and new formulations of medications. 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, including the timing of initiation of Cohort 2 patient screening for the OASIS clinical trial, and the potential benefits of CLS-AX and therapies 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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Source: Clearside Biomedical, Inc.