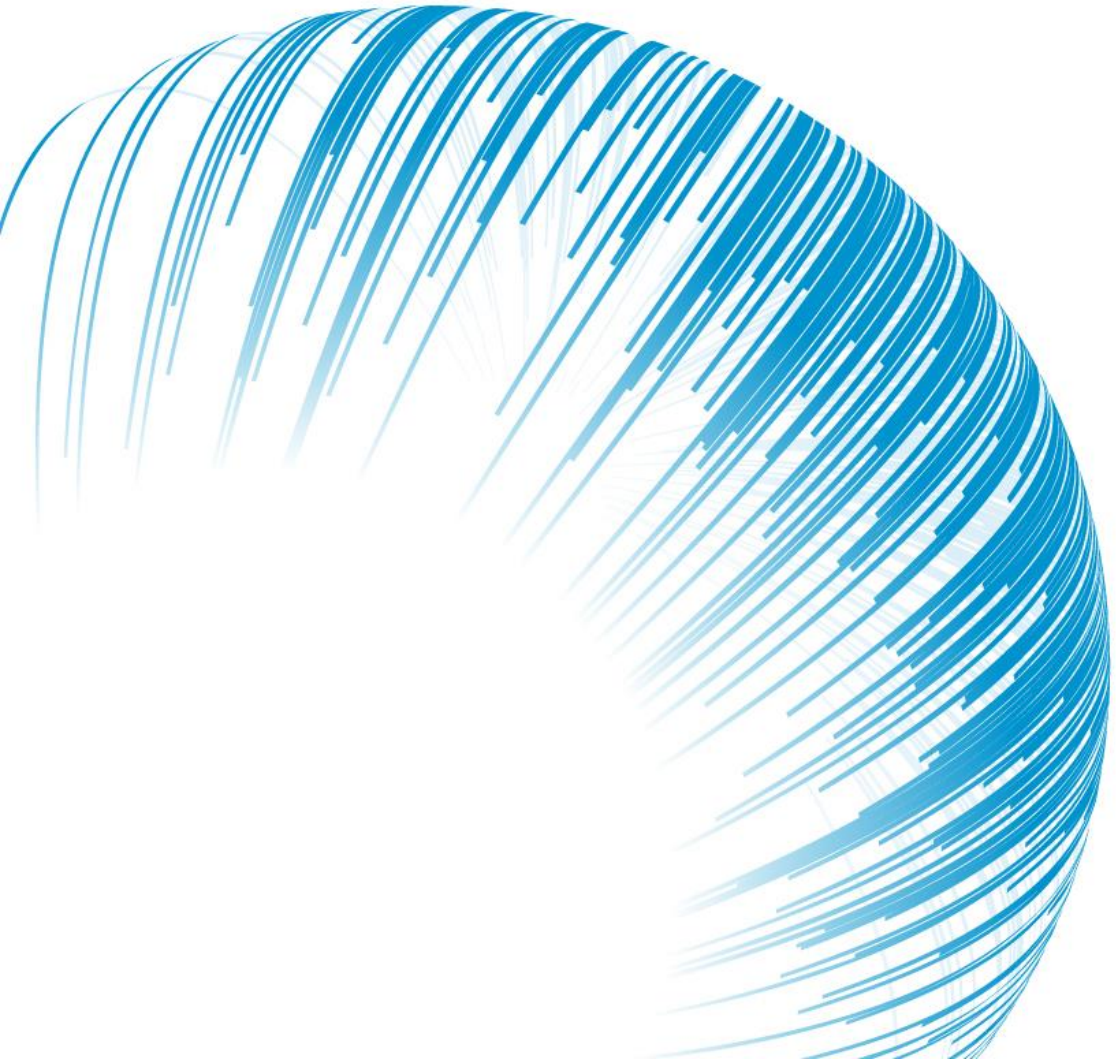

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JMP Securities Life Sciences Conference
June 16, 2021

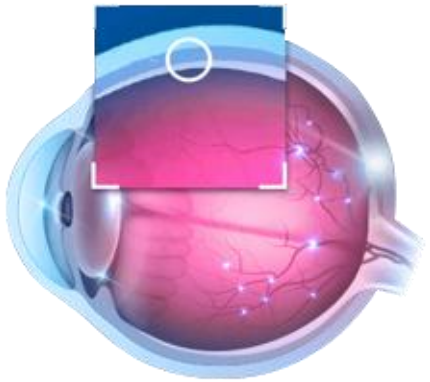
# Forward-Looking Statements

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

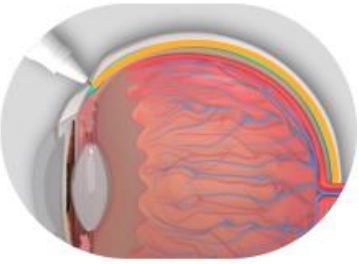
The back of the eye is the location of many irreversible and debilitating visual impairments

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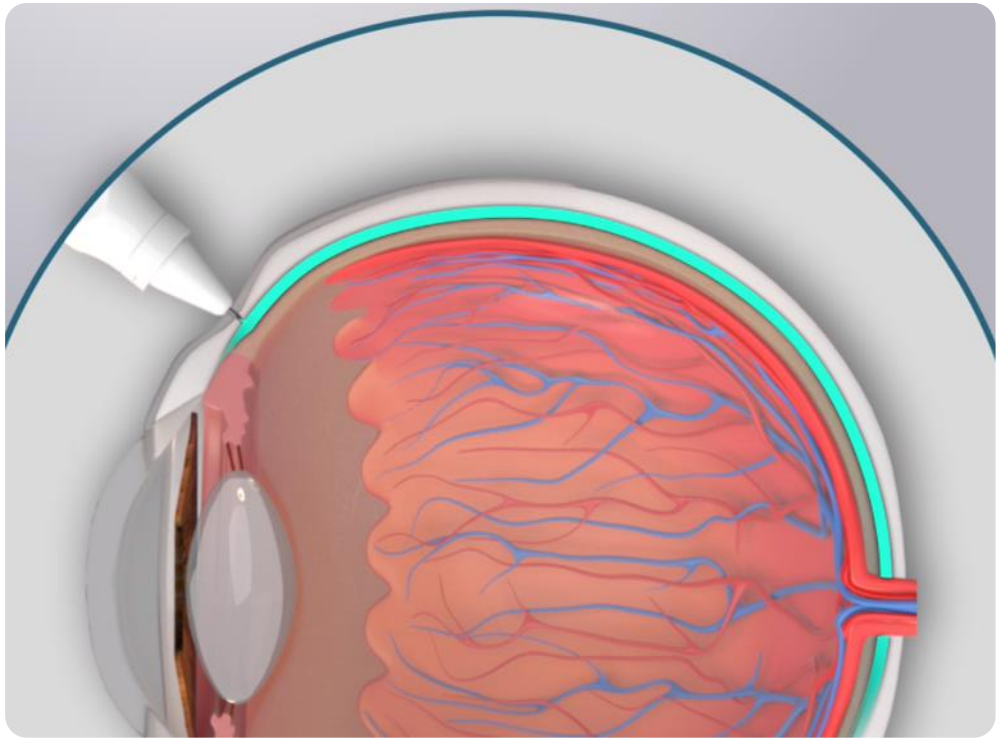
# Clearside's SCS Microinjector®: The Only Clinically Tested Injection Device for Suprachoroidal Drug Delivery

- 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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# 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 | | | | |

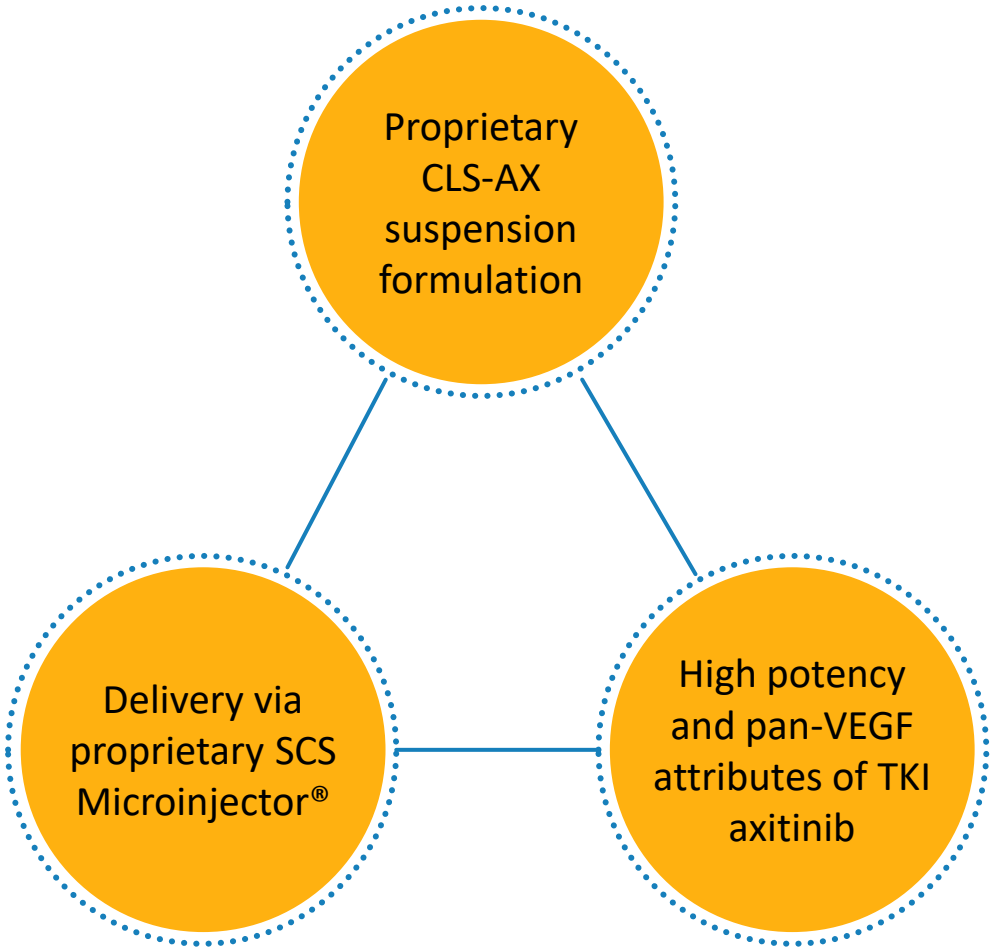
## XIPERE™ Commercial Partners

| 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

# 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)

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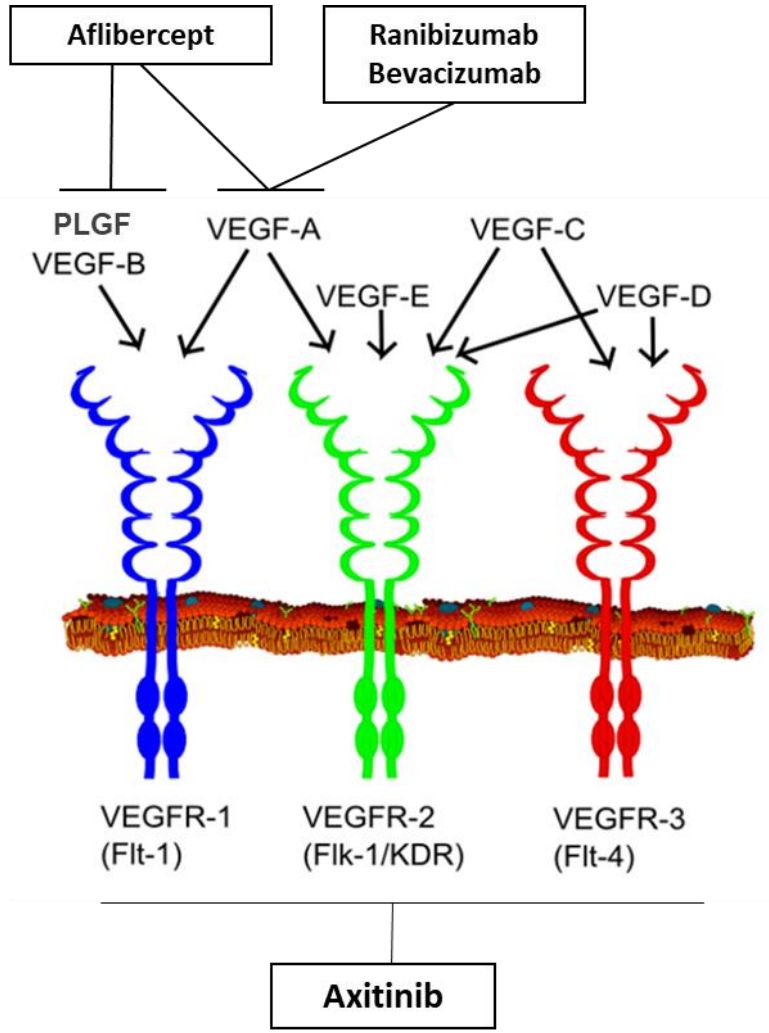
# Axitinib: a Highly Potent, pan-VEGF TKI to Treat Wet AMD

- 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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# 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

| Screening | Baseline | Week 4 | Week 8 | Week 12 |
|---|---|---|---|---|
| *2 mg aflibercept dosed at screening* | *CLS-AX dosed at baseline (30 days post screening)* | *Assessment for additional therapy* | *Assessment for additional therapy* | *Assessment for additional therapy* |



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)
- **Highly treatment-experienced (at screening prior to aflibercept administration)**
  - 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
- **Demographics & disease characteristics (at baseline prior to CLS-AX administration)**
  - Average age: 82 years
  - Mean central subfield thickness (CST) of the macula was 231 µm (range 208 - 294 µm)
  - Mean best corrected visual acuity (BCVA) score was 59.0 (range 29 - 74)
- **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

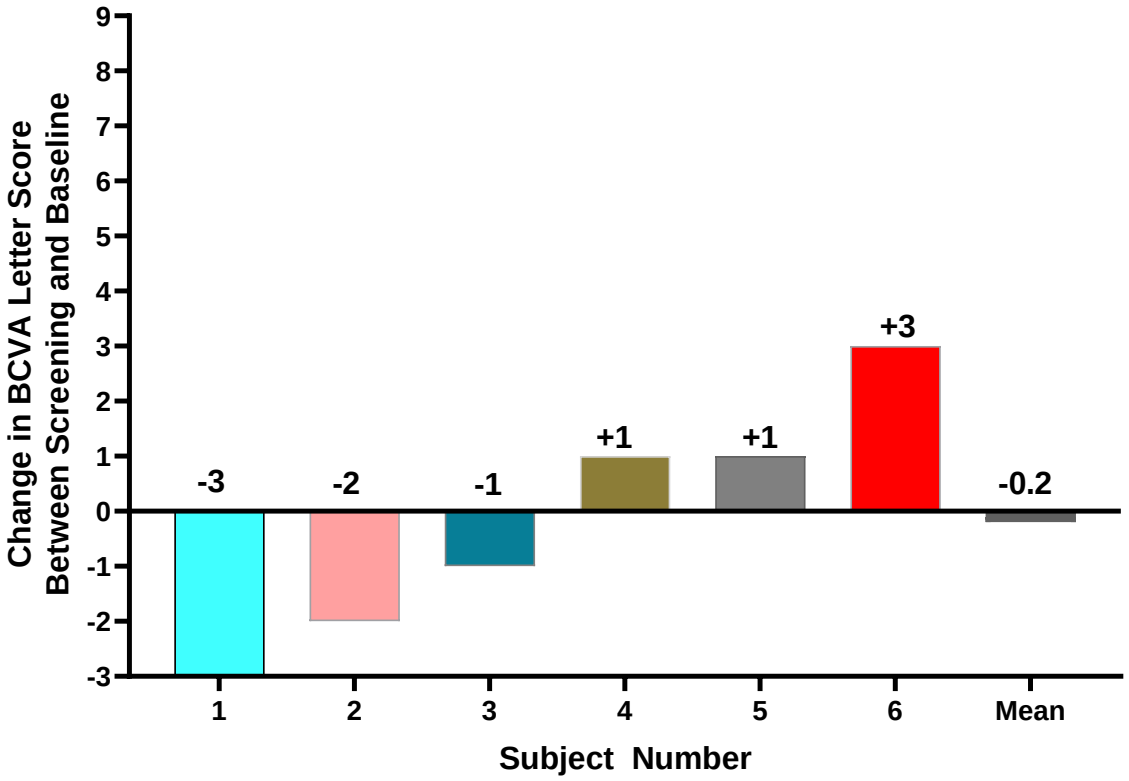
- **1-month visual acuity improvement of 1 line post CLS-AX** vs no change for aflibercept, at this initial low dose
  - Aflibercept: 1-month BCVA change -0.2 ETDRS letters (p=0.862*)
  - CLS-AX 0.03 mg: 1-month BCVA change +4.7 ETDRS letters (p=0.029*) with 5/6 patients improving by 4 or more letters
- **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

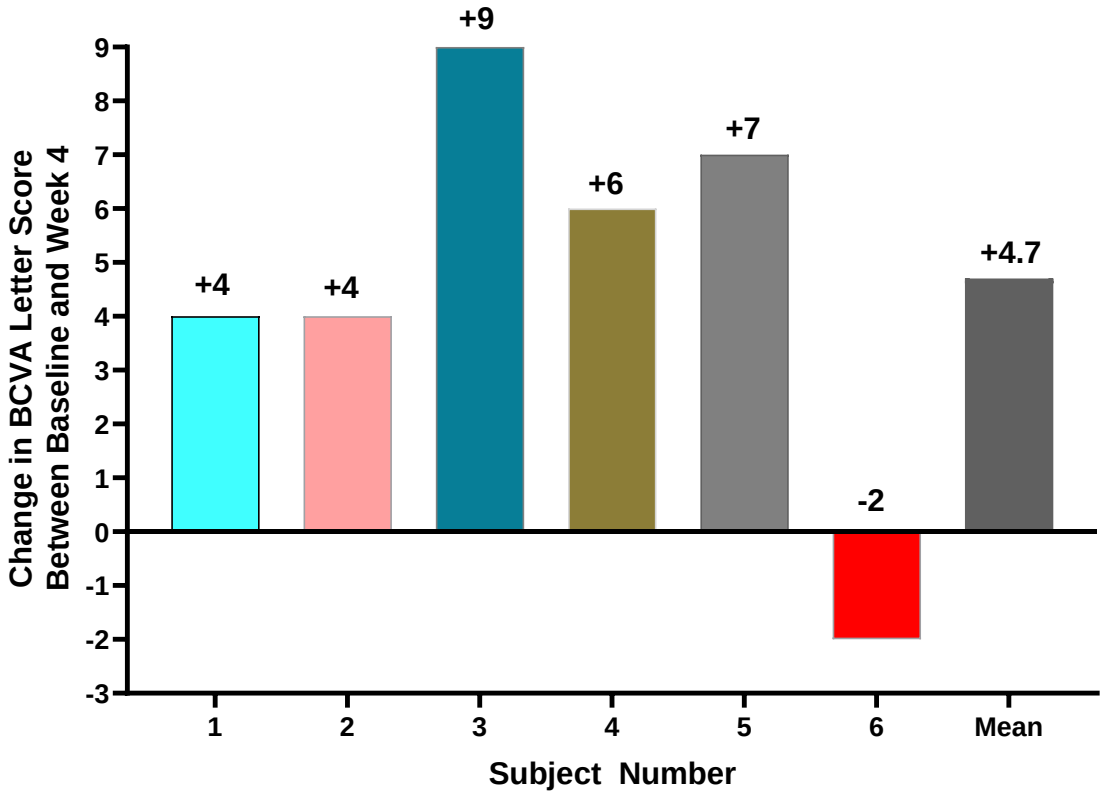
# Best Corrected Visual Acuity
# One Month Response Following Aflibercept 2 mg vs CLS-AX 0.03 mg

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




Mean BCVA at screening (prior to aflibercept) = 59.2

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



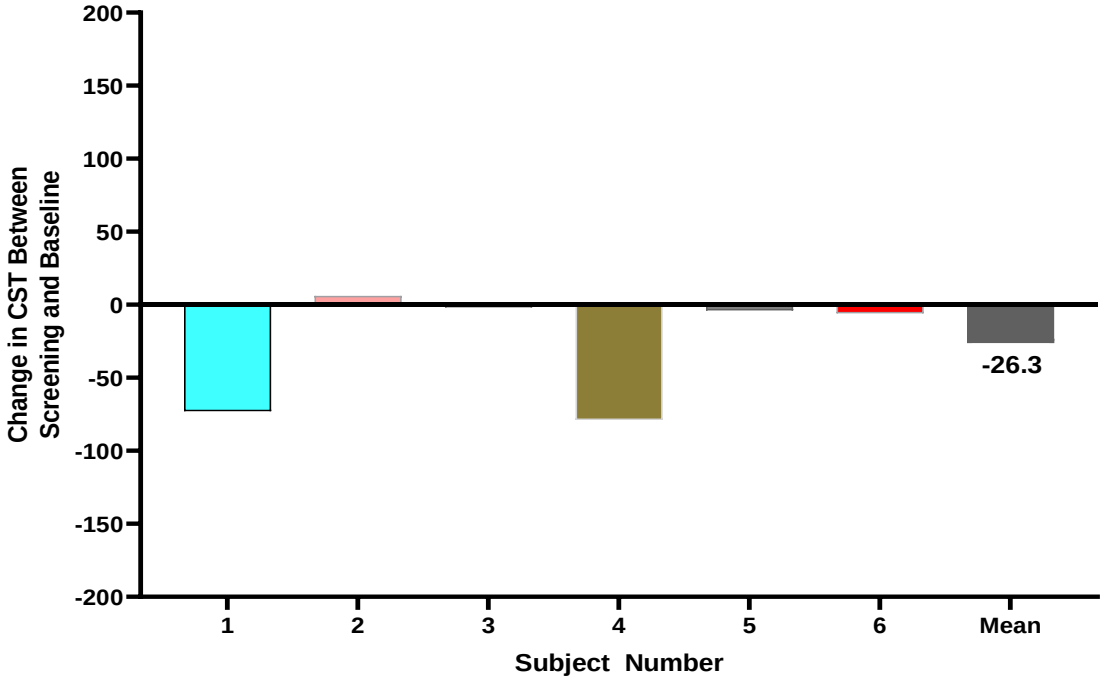

Mean BCVA at baseline (prior to CLS-AX ) = 59.0



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

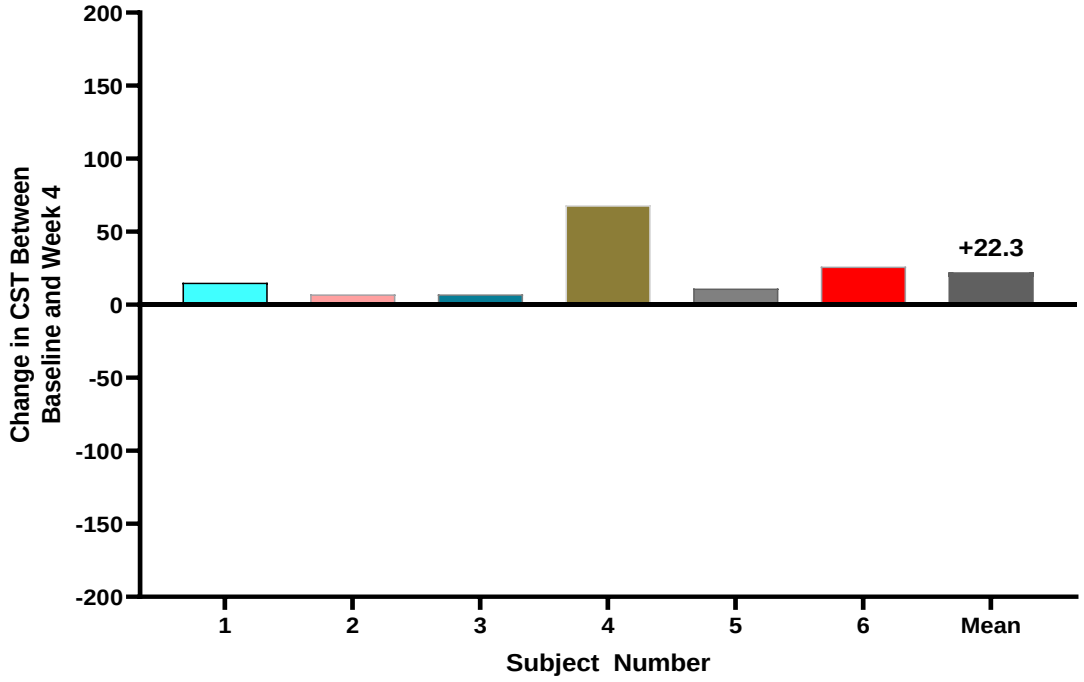
# Central Subfield Thickness
# Mean CST Stable within 50 *µm* at One Month

1 Mo Change after Aflibercept (2 mg)




Mean CST at screening (prior to aflibercept) = 257.5 µm

1 Mo Change after CLS-AX (0.03 mg)




Mean CST at baseline (prior to CLS-AX ) = 231.2 µm

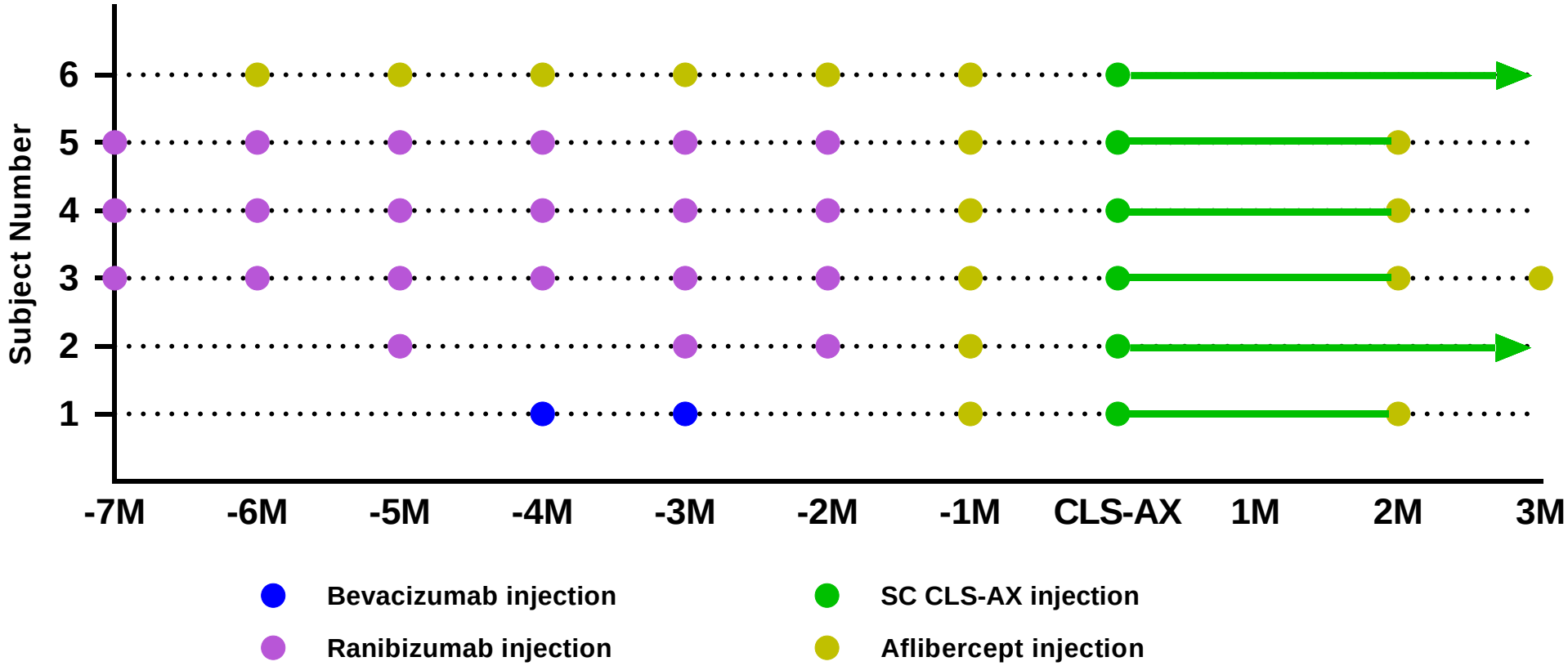


Source: Clearside data on file.

# 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**




Assessment for additional therapy: loss from best measurement of ≥10 letters in BCVA with exudation; increase in CST >75 microns; a vision-threatening hemorrhage

Source: Clearside data on file.

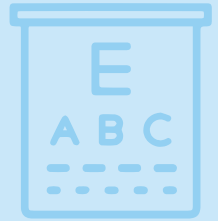
# OASIS Cohort 1 Results Support Advancing to Cohort 2

## 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

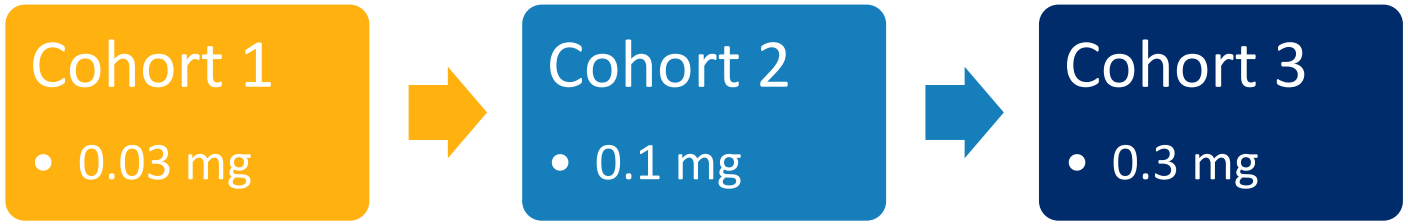
## DURABILITY POST CLS-AX

- 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.

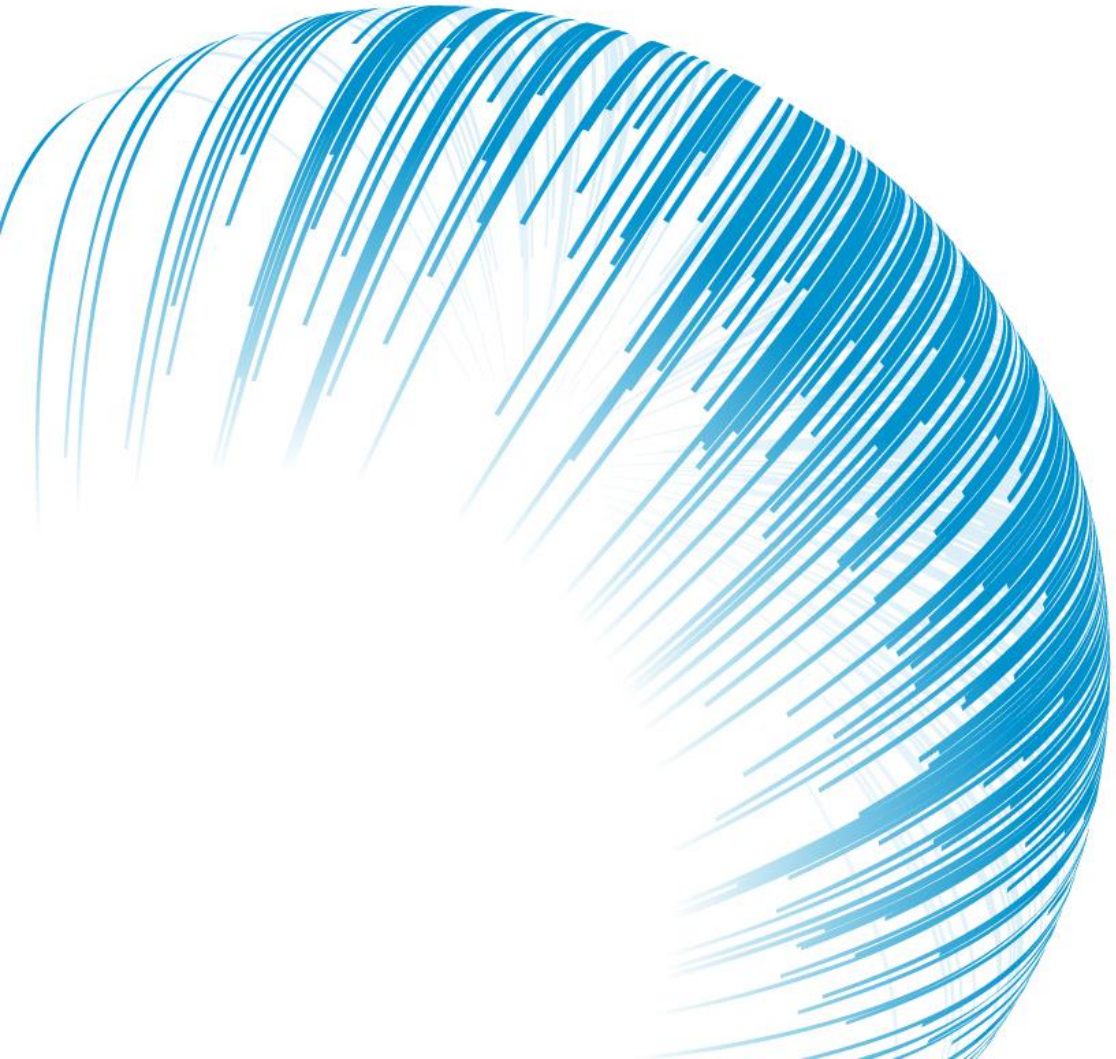
# Cohorts 2 and 3 Continue to Escalate Single CLS-AX Dose




- 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
- Adding three-month extension study to follow patients in Cohort 2 and Cohort 3
- Preclinical pharmacokinetic studies show progressively prolonged tissue levels with increased dosing



Source: Clearside data on file.



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