CLS-AX

(axitinib injectable suspension)

for Suprachoroidal Injection

OASIS Cohort 1 Clinical Data

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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 treatment: 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)
- **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

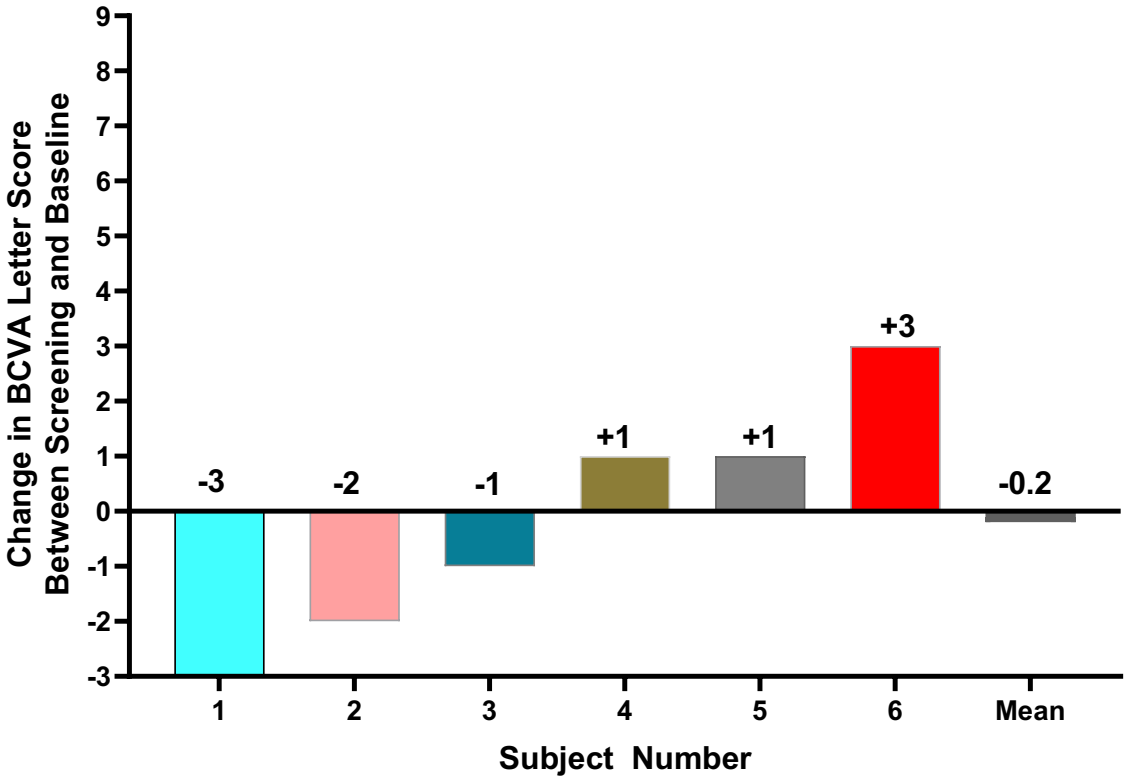
BCVA AND ANATOMIC RESULTS

- **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

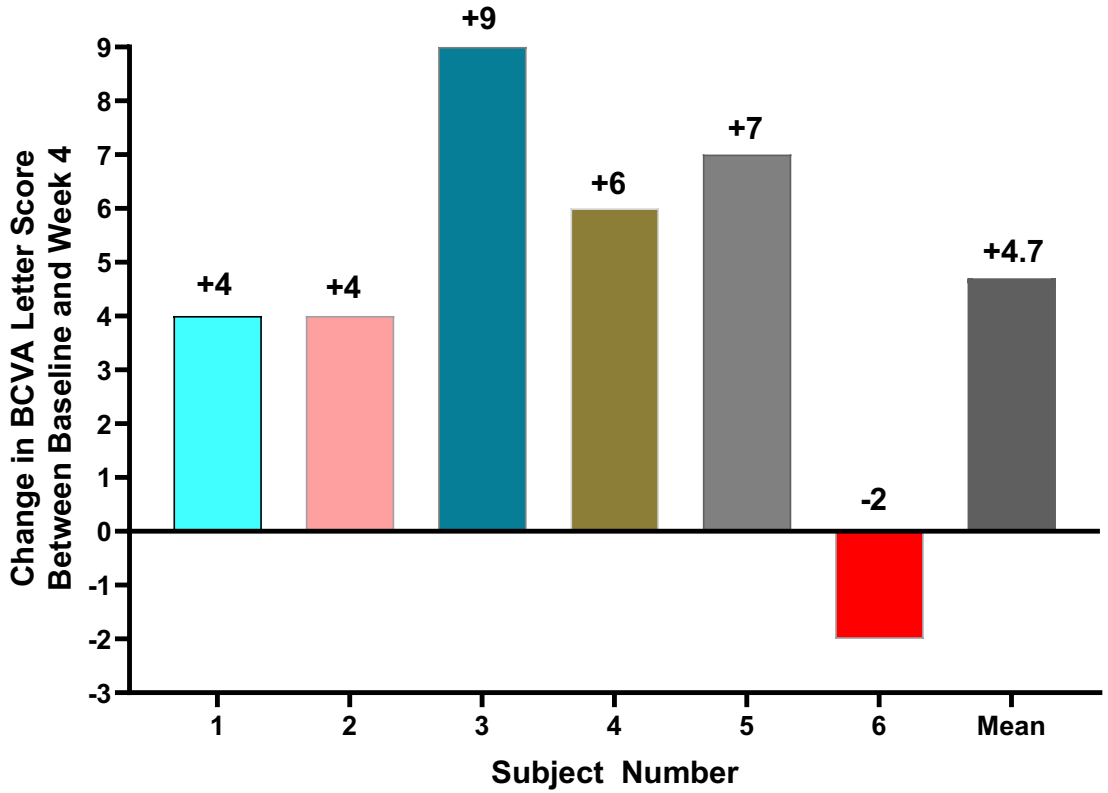
Best Corrected Visual Acuity
One Month Response Following Aflibercept 2 mg vs CLS-AX 0.03 mg

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*

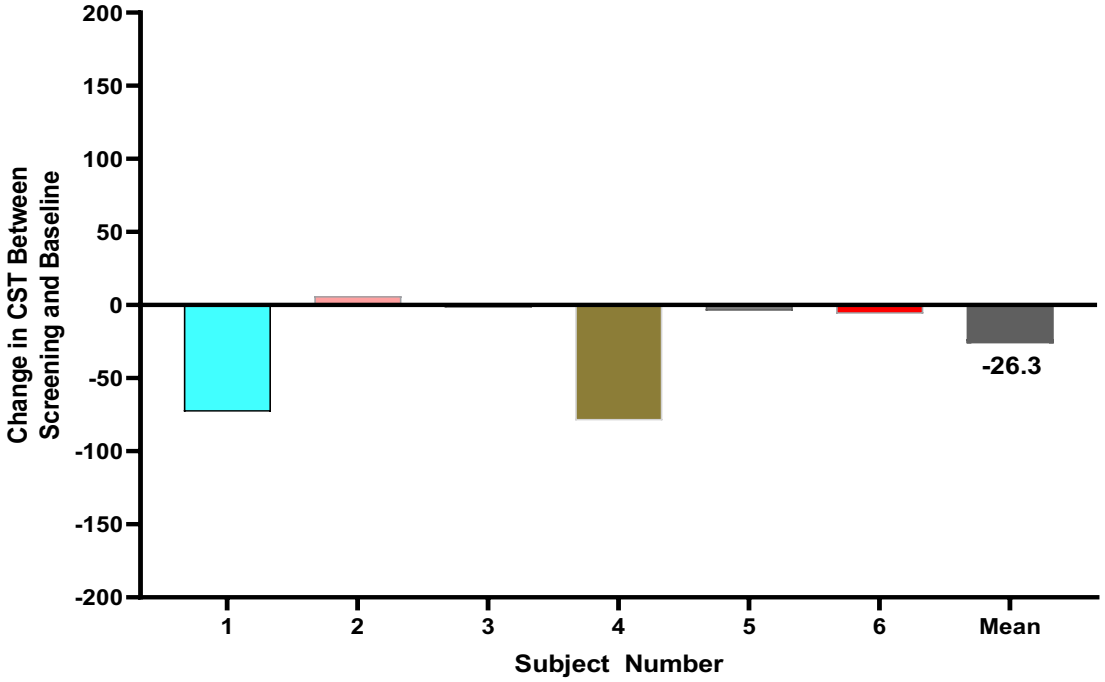


Mean BCVA at baseline (prior to CLS-AX) = 59.0

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

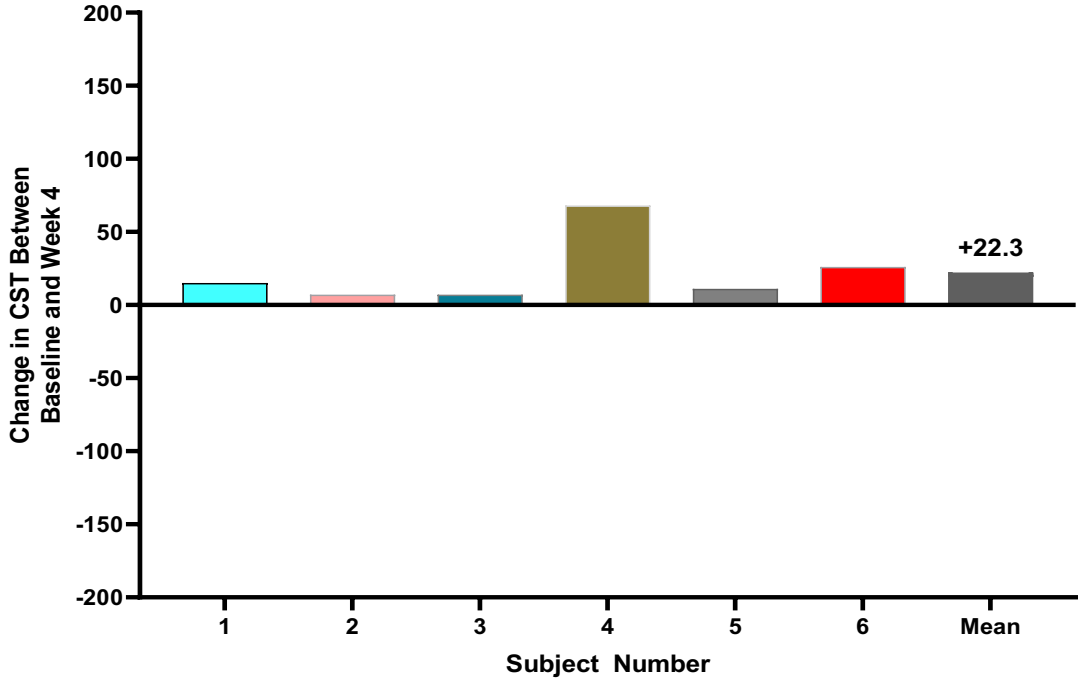
Central Subfield Thickness
Mean CST Stable within 50 *µm* at One Month

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)



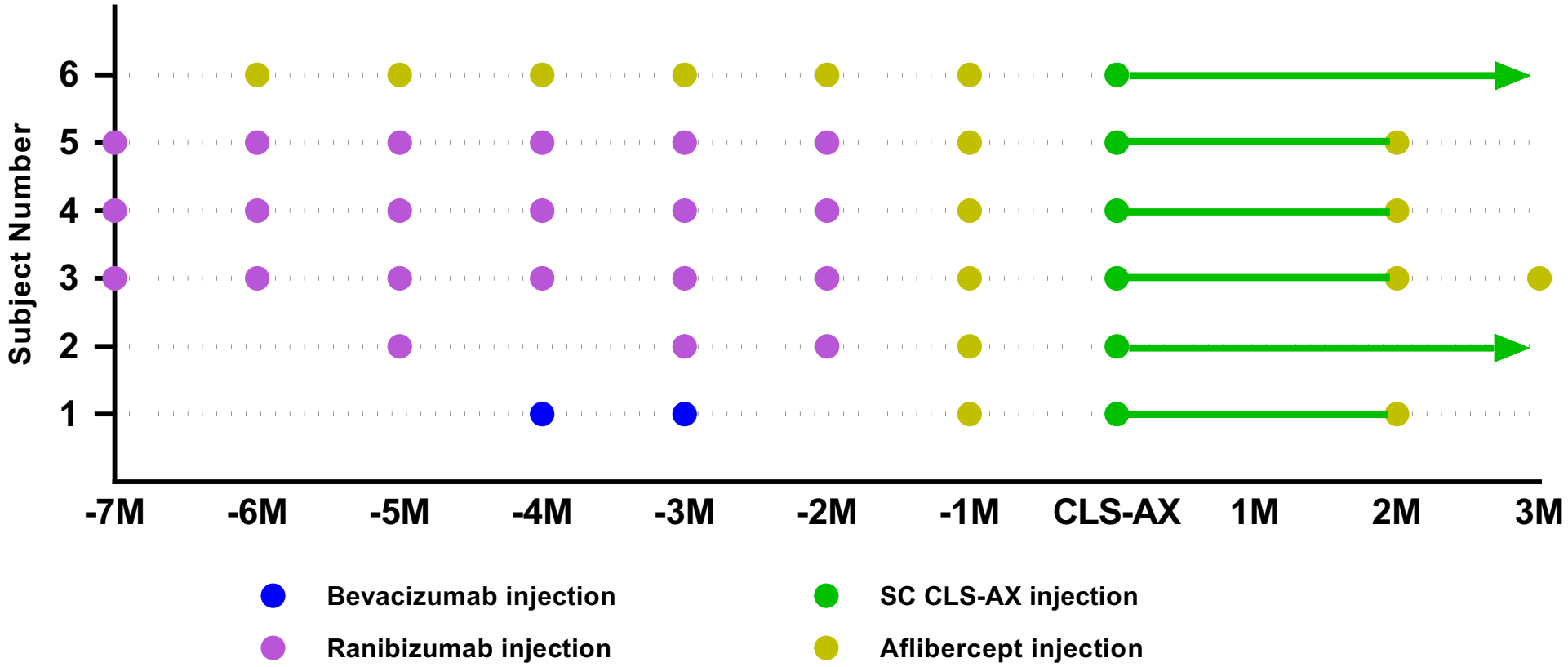
Mean CST at baseline (prior to CLS-AX) = 231.2 µm

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 treatment: 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

COHORT 1 RESULTS

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

ANATOMIC EFFECTS

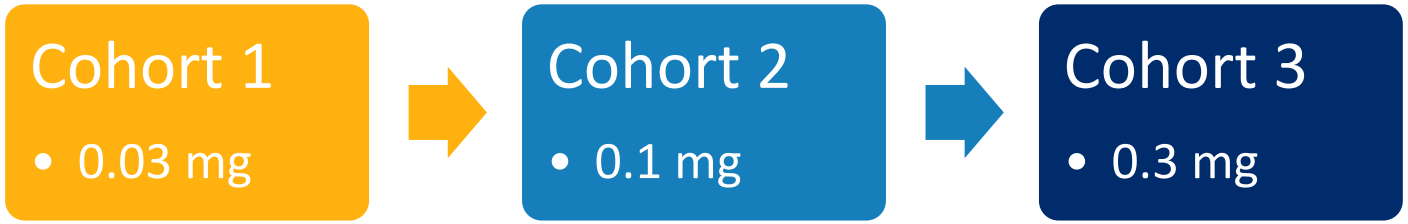
- Mean CST stable within 50 *μm* at 1 month

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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