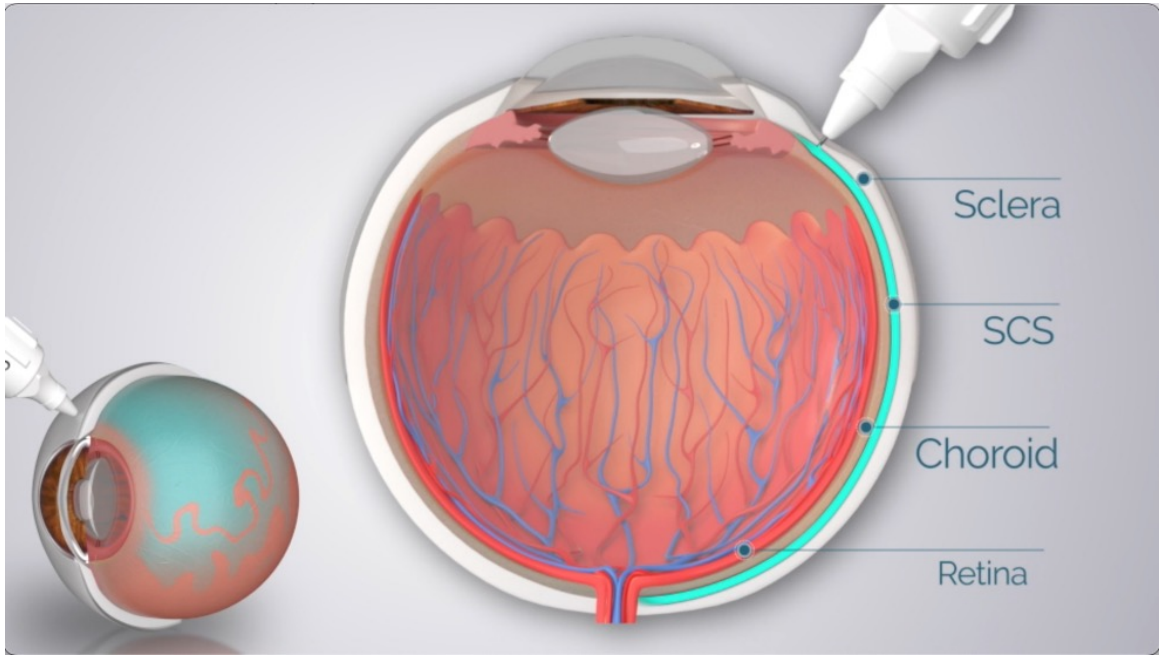
CLEARSIDE BIOMEDICAL

# Suprachoroidal CLS-AX : Program Update

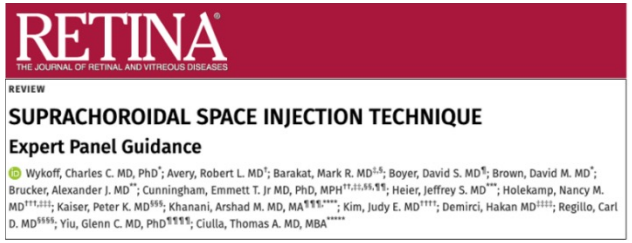

Sobha Sivaprasad, FRCOphth

# Delivering on the Potential of the Suprachoroidal Space (SCS®): A Novel Approach to Drug Delivery for Retinal Diseases

Injectate Flows to the Back of the Eye and Diffuses into the Retina



# Straightforward Suprachoroidal Injection Technique



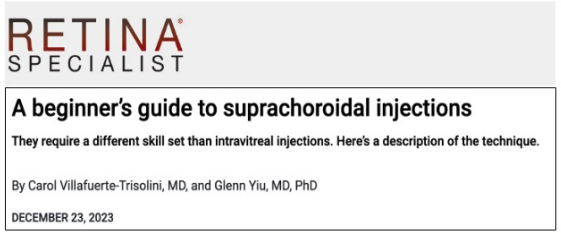
RETINA
THE JOURNAL OF RETINAL AND VITREOUS DISEASES

REVIEW

**SUPRACHOROIDAL SPACE INJECTION TECHNIQUE**

**Expert Panel Guidance**

Wykoff, Charles C. MD, PhD*; Avery, Robert L. MD†; Barakat, Mark R. MD‡,§; Boyer, David S. MD¶; Brown, David M. MD*; Brucker, Alexander J. MD**; Cunningham, Emmett T. Jr MD, PhD, MPH††,‡‡,§§,¶¶; Heier, Jeffrey S. MD***; Holekamp, Nancy M. MD†††,‡‡‡; Kaiser, Peter K. MD§§§; Khanani, Arshad M. MD, MA¶¶¶,****; Kim, Judy E. MD††††; Demirci, Hakan MD‡‡‡‡; Regillo, Carl D. MD§§§§; Yiu, Glenn C. MD, PhD¶¶¶¶; Ciulla, Thomas A. MD, MBA*****



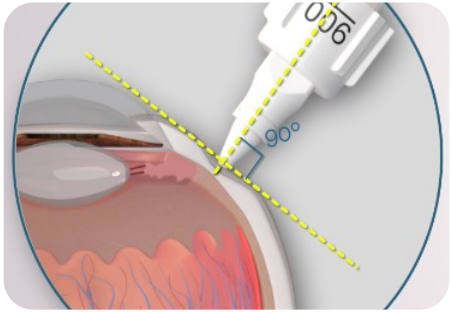
RETINA SPECIALIST

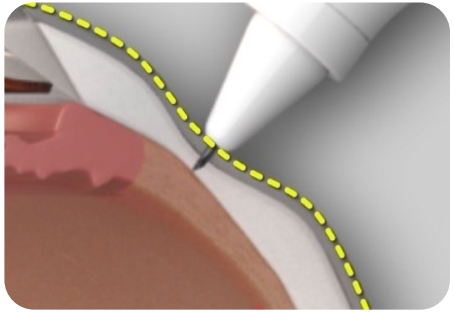
**A beginner's guide to suprachoroidal injections**

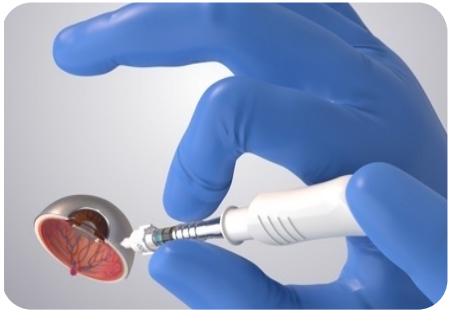
They require a different skill set than intravitreal injections. Here's a description of the technique.

By Carol Villafuerte-Trisolini, MD, and Glenn Yiu, MD, PhD

DECEMBER 23, 2023





**Perpendicular**

Hold the microinjector **perpendicular** to the ocular surface

**Dimple**

Ensure firm contact with sclera by maintaining a **dimple** throughout injection

**Slow**

Inject **slowly** over 5 – 10 seconds

# CLS-AX

(axitinib injectable suspension)

*New mechanism of action with potential for longer duration of effect for retinal diseases*

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


**01**

## Axitinib

High potency TKI with pan-VEGF receptor inhibition

**02**

## Proprietary CLS-AX Small Molecule Suspension Formulation

Clearside formulation expertise

**03**

## Delivery via SCS Microinjector®

Utilizes the same administration device as FDA-approved product XIPERE®

# ODYSSEY Phase 2b Clinical Trial Overview

**Trial Objectives:**
Evaluated safety, efficacy & duration of CLS-AX in participants with wet AMD

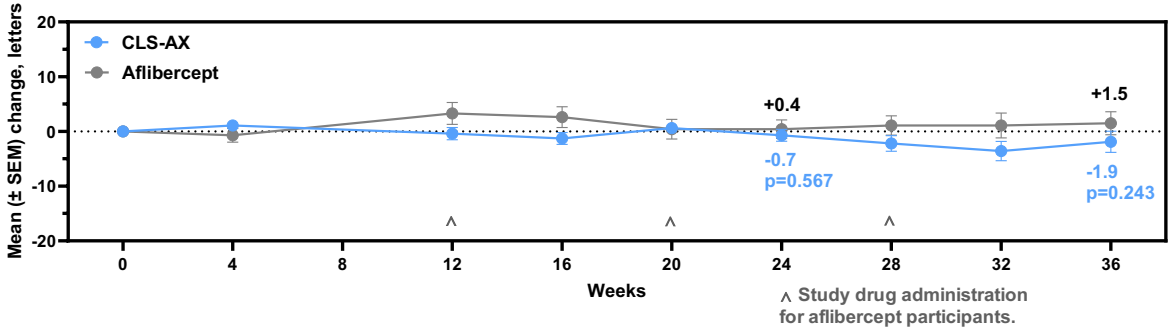
- Primary Outcomes: Mean change in BCVA from Baseline to **Week 36**; Safety & tolerability
- Secondary Outcomes: Other changes in visual function and retinal imaging, including CST; Need for supplemental treatment; Treatment burden as measured by total injections

**Participant Profile:**
60 total with 2:1 randomization (40 in CLS-AX arm & 20 in aflibercept arm)

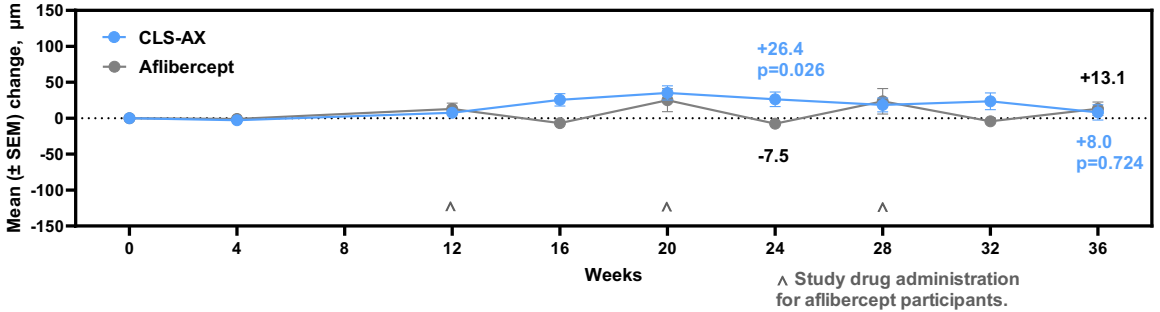
- Treatment experienced participants with reading center confirmation of **persistent active disease**
- Protocol required **re-dosing with CLS-AX** in study arm
  - Participants received at least 2 doses of CLS-AX
  - Provided important data to plan Phase 3 in chronic disease

# CLS-AX Demonstrated Stable BCVA and CST Over 36 Weeks

## BCVA Within 2 Letters From Baseline at Both Week 24 and Week 36 in CLS-AX Arm



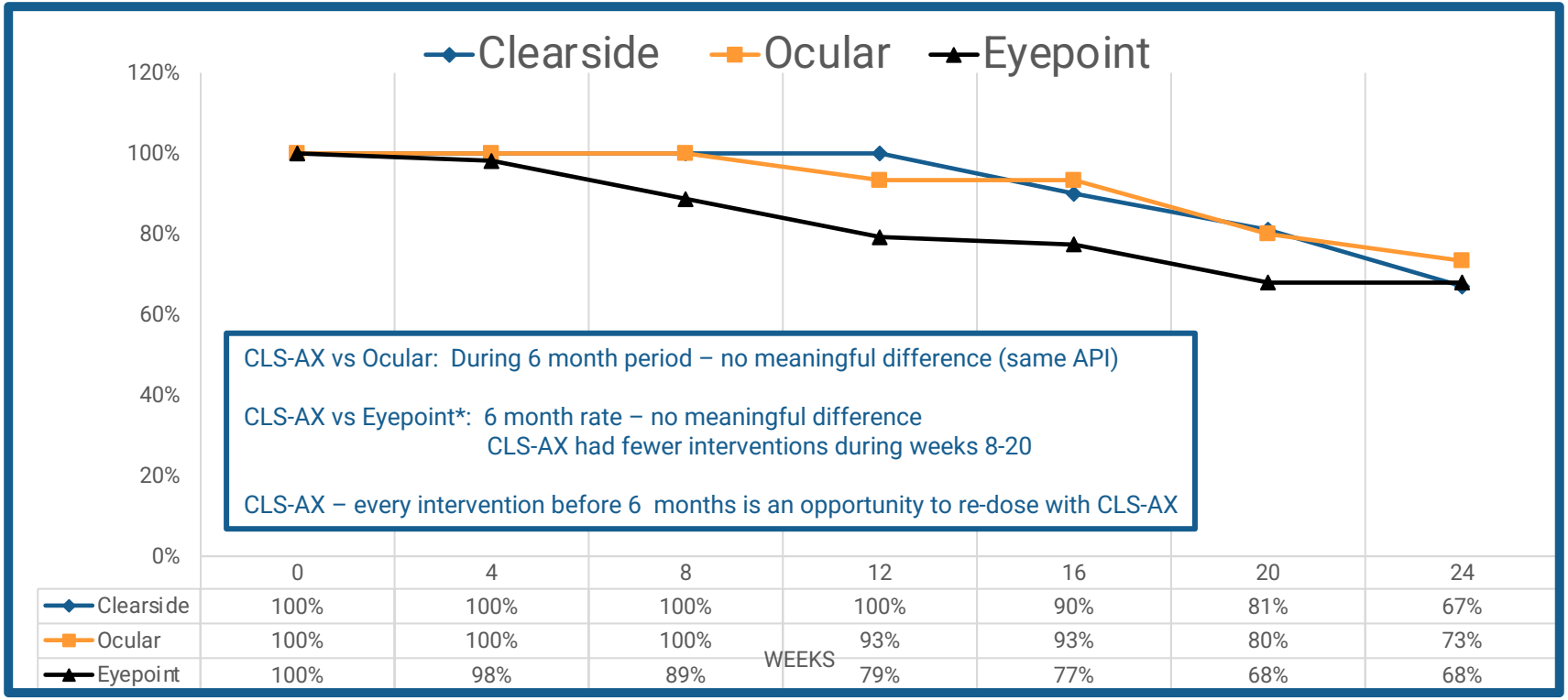

## CLS-AX Demonstrates Stable Anatomical Control and Reduces Fluctuation




*CLS-AX results do not include supplemental therapy with aflibercept*

^Study drug administration for aflibercept participants given at Weeks 12, 20 and 28.
Abbreviations: BCVA = best corrected visual acuity; CST = central subfield thickness as reported by the reading center; SEM = standard error of the mean
P-value based on a 2-sample t-test between treatment groups .

# Comparative TKI Intervention Free Rate Over 6 months




| | 0 | 4 | 8 | 12 | 16 | 20 | 24 |
|---|---|---|---|---|---|---|---|
| Clearside | 100% | 100% | 100% | 100% | 90% | 81% | 67% |
| Ocular | 100% | 100% | 100% | 93% | 93% | 80% | 73% |
| Eyepoint | 100% | 98% | 89% | 79% | 77% | 68% | 68% |

Clearside Biomedical is developing CLS-AX. Ocular Therapeutix is developing OTX-TKI. EyePoint Pharmaceuticals is developing EYP-1901.
Results based on publicly available information provided by each company as of February 2025.
Data presented above is not based on head-to-head studies and may not be directly comparable. EYP-1901 is pooled 2mg and 3mg.

# CLS-AX

(axitinib injectable suspension)

## *Program Update*

*Phase 2 for non-proliferative diabetic retinopathy*

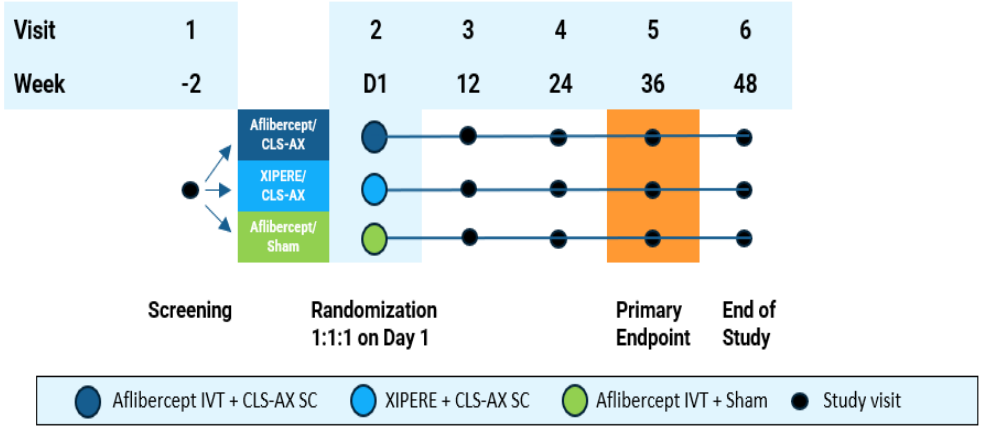
*Phase 3 for wet age-related macular degeneration*

*Clinical development plans are in development and subject to change*

# Phase 2 CLS-AX for Non-proliferative diabetic retinopathy (NPDR)

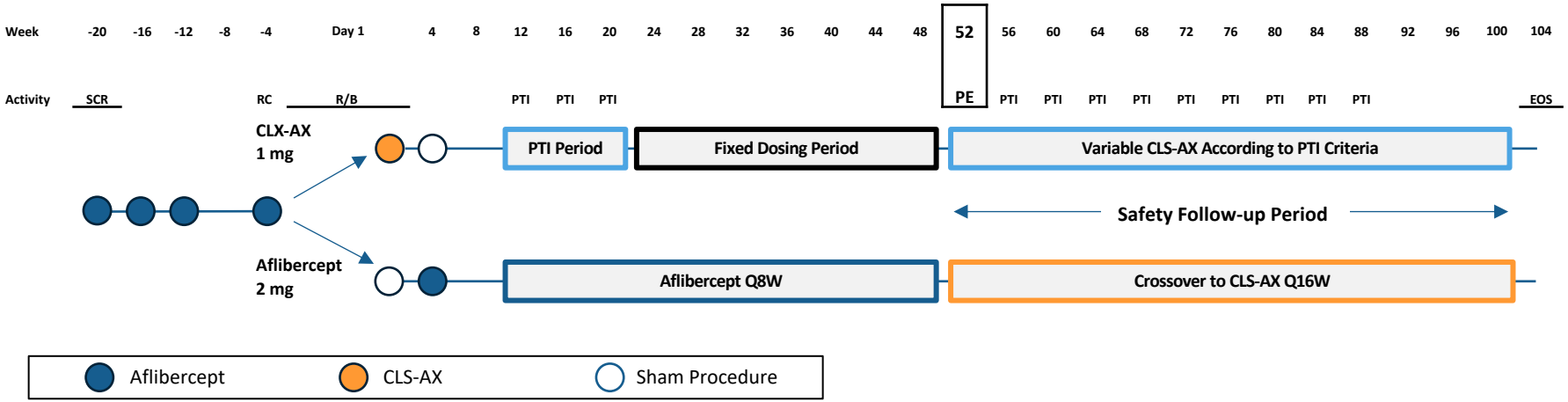
Target population: DRSS 47 to 53 (moderate severe to severe NPDR)

- Anti-VEGF is approved for DR but its usage was low due to treatment burden with no immediate benefit
- Adding CLS-AX may potentially extend the duration of benefit and reduce treatment burden
- Combination of XIPERE® and CLS-AX might provide the same benefit without the risk of endophthalmitis associated with intravitreal injection




Abbreviations: DR = Diabetic Retinopathy; DRSS = Diabetic Retinopathy Severity Score; IVT = Intravitreal ; SC = Suprachoroidal
XIPERE® (triamcinolone acetonide injectable suspension)

# CLS-AX Phase 3 Trial Format




- Participants will be randomized 1:1 to CLS-AX 1 mg or aflibercept 2 mg on Day 1.
- Personalized Treatment Interval (PTI) Assessment: At Weeks 12, 16, and 20, participants will undergo an assessment of disease activity based on PTI criteria. If the criteria were not met, the participants will be given CLS-AX every 24 weeks.
- Fixed Dosing Period: Once the treatment interval is determined in the PTI period, the participants will stay at that interval until week 52 (primary endpoint). For instance, if the participants met the PTI criteria at week 16, they will be given CLS-AX every 16 weeks in the fixed dosing period.
- For participants randomized to CLS-AX on a dosing interval of q24w, q20w, or q16w on or after Week 52, if PTI criteria are met at an active injection visit then the next dosing interval will be reduced by 4 weeks, to a minimum of Q12W.



Abbreviations: SCR = Screening Visit; RC = Randomization Criteria; R/B = Randomization/Baseline; PE = Primary Endpoint;

# CLS-AX Phase 3 Designed to Compete with Currently Approved Drugs

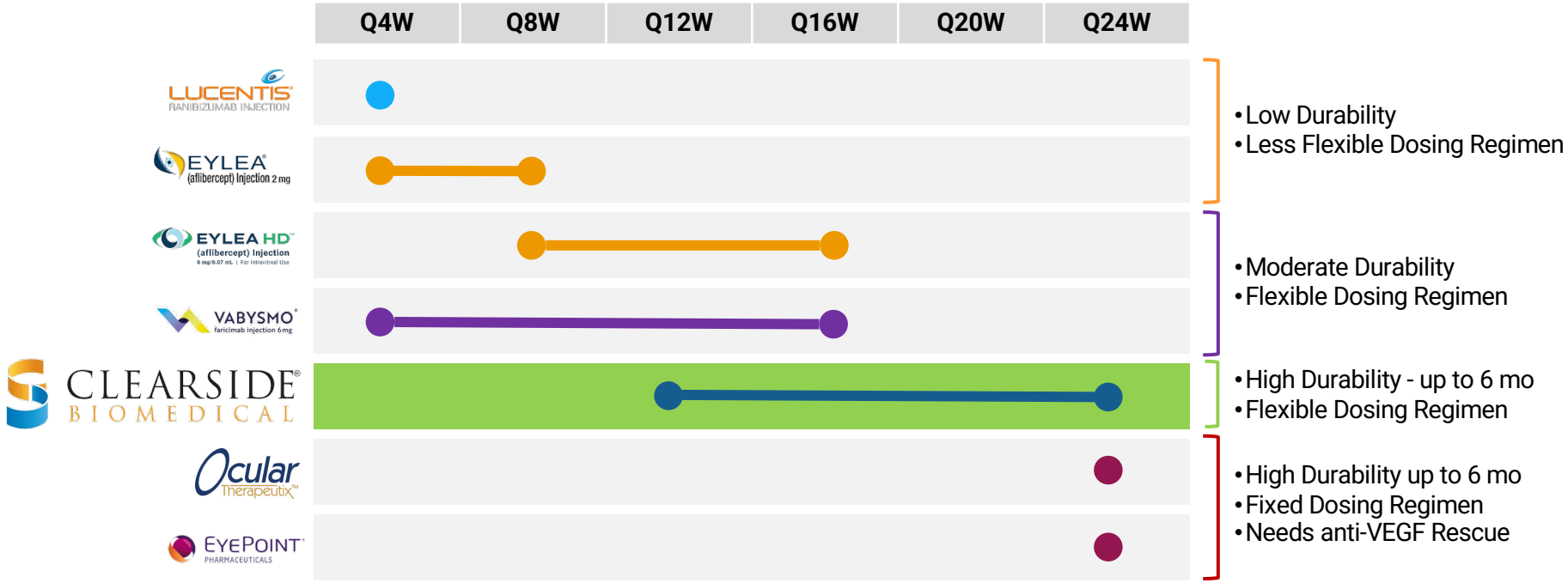
Phase 3 Clinical Trial Design Comparison

| | VABYSMO® | CLS-AX | OTX-TKI | EYP-1901 |
|---|---|---|---|---|
| Non-inferiority | 2 | 2 | 1 | 2 |
| Multiple dosing | 2 | 2 | 1 | 2 |
| Flexible dosing | Y | Y | N | N |
| Tested Interval in Months | 2 to 4 | 3 to 6 | 6 | 6 |
| Rescue / Redosing | Redosing | Redosing | Rescue | Rescue |
| Study population optimization | N | Y | Y | N |

Phase 3 design based on publicly available information provided by the companies as of February 2025.
VABYSMO is a registered trademark of Genentech. CLS-AX is in development by Clearside Biomedical.
OTX-TKI is in development by Ocular Therapeutix. EYP-1901 is in development by EyePoint Pharmaceuticals

# CLS-AX Potentially Versatile Label with Large Total Addressable Market Based on Planned 3-6 Month Dosing Flexibility

## WET AMD Intended Dosing Interval Range (Weeks)




Dosing based on publicly available information provided by each company as of March 2025.
LUCENTIS and VABYSMO are registered trademarks of Genentech. EYLEA and EYLEA HD are registered trademarks of Regeneron Pharmaceuticals.
Clearside Biomedical is developing CLS-AX. Ocular Therapeutix is developing OTX-TKI. EyePoint Pharmaceuticals is developing EYP-1901.

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**Thank You**