CLEARSIDE BIOMEDICAL

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CMO, EVP, Head of R&D

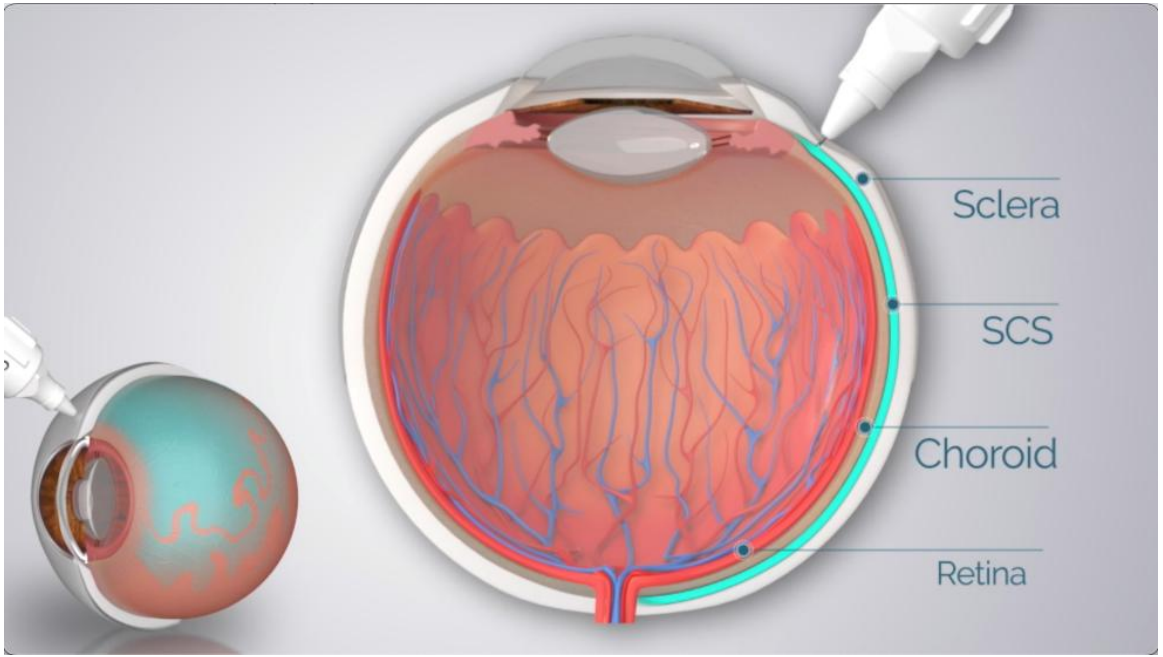
Forward-Looking Statements

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” or the negative of these terms and other similar words or 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. These forward-looking statements include statements regarding Clearside's plans or intentions relating to product candidates, estimates of market size, the clinical development of CLS-AX, the trial design features and timing of Clearside's planned Phase 3 trial and its anticipated benefits and impacts, and the commercial potential and addressable market of CLS-AX, if approved. Although Clearside believes that the expectations reflected in the forward-looking statements are reasonable, new risks and uncertainties may emerge from time to time, and 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; adverse differences between preliminary or interim data and final data; 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; Clearside's ability to expand its pipeline; developments and projections relating to Clearside's competitors and its industry; the impact of government laws and regulations; the timing, design and anticipated results of Clearside's preclinical studies and clinical trials and the risk that the results of Clearside's preclinical studies and clinical trials may not be predictive of future results in connection with future studies or clinical trials and may not support further development and marketing approval; findings from investigational review boards at clinical trial sites and publication review bodies; Clearside's estimates regarding future revenue, expenses, capital requirements and need for additional financing, and Clearside's ability to raise additional capital; 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, 2023, filed with the U.S. Securities and Exchange Commission (SEC) on March 12, 2024, Clearside’s Quarterly Report on Form 10-Q filed with the SEC on November 12, 2024, and Clearside's subsequent filings 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.

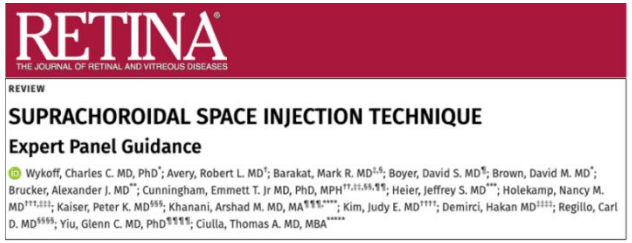
Suprachoroidal Delivery via SCS Microinjector®

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



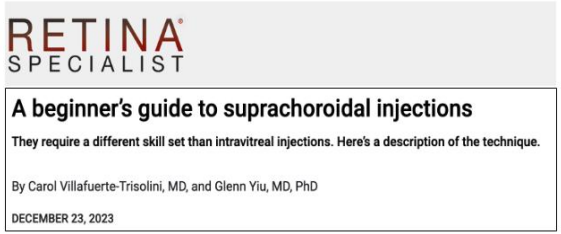
RETINA
THE JOURNAL OF RETINAL AND VITREOUS DISEASES

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*****



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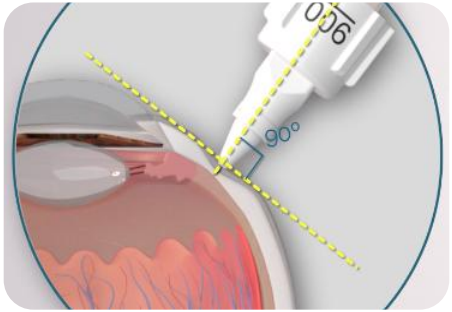
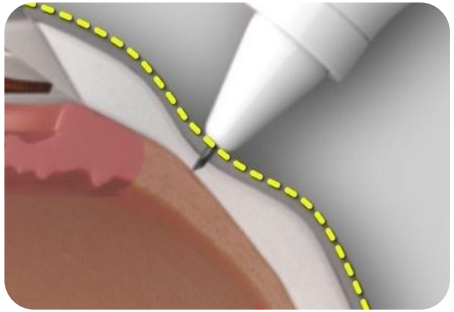
A beginner's guide to suprachoroidal injections

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

Benefits for Patients and Physicians Using SCS Microinjector® Delivery

Enhanced Safety

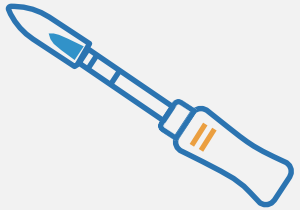
Much lower risk of endophthalmitis as direct contact to immune system vs intravitreal injection

Injectate Flows to Back of the Eye

Reduced risk of floaters, snow globe effect, or other visual disturbances

No Implants or Devices in the Vitreous

Can be easily re-dosed for potentially longer durability



Injection Similar to Intravitreal

Advanced technology requires only a few seconds longer for each injection

Clearside Suprachoroidal Product Development Pipeline Targeting Global Markets

Clearside Research and Clinical Development Programs

THERAPEUTIC	MECHANISM	INDICATION	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	APPROVAL	PARTNER
CLS-AX (axitinib)	Tyrosine Kinase Inhibitor	Wet AMD*			*FDA End-of-Phase 2 Meeting Completed*			
Undisclosed	Improve choroidal perfusion	Geographic Atrophy (GA)						
Undisclosed	Modulate pro-inflammatory cells	Geographic Atrophy (GA)						

Commercial Asset: XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use

THERAPEUTIC	LOCATION	INDICATION	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	APPROVAL	PARTNER
XIPERE®	United States	Uveitic Macular Edema[1]						B+L BAUSCH+LOMB
XIPERE® / ARCATUS™	Australia and Singapore	Uveitic Macular Edema[2]						arctic VISION
XIPERE® / ARCATUS™	China	Uveitic Macular Edema[2]				*NDA Under Review*		arctic VISION Santen
XIPERE® / ARCATUS™	Asia Pacific ex-Japan	Diabetic Macular Edema[2]						arctic VISION

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[1]XIPERE® (triamcinolone acetonide injectable suspension), for suprachoroidal use has received U.S. FDA Approval and is being commercialized by Bausch + Lomb.
[2]In licensed territories, Arctic Vision is responsible for clinical development of ARCATUS™ (triamcinolone acetonide injectable suspension), also known as ARVN001, and known as XIPERE® in the U.S.
*Phase 3 plans are in process.

CLS-AX

(axitinib injectable suspension)

New mechanism of action with potential for longer duration of effect for the treatment of wet AMD

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®

Axitinib is a Highly Potent, Highly Selective Pan-VEGF Inhibitor

Inhibits ALL VEGF Receptors (VEGFR-1, VEGFR-2, VEGFR-3)

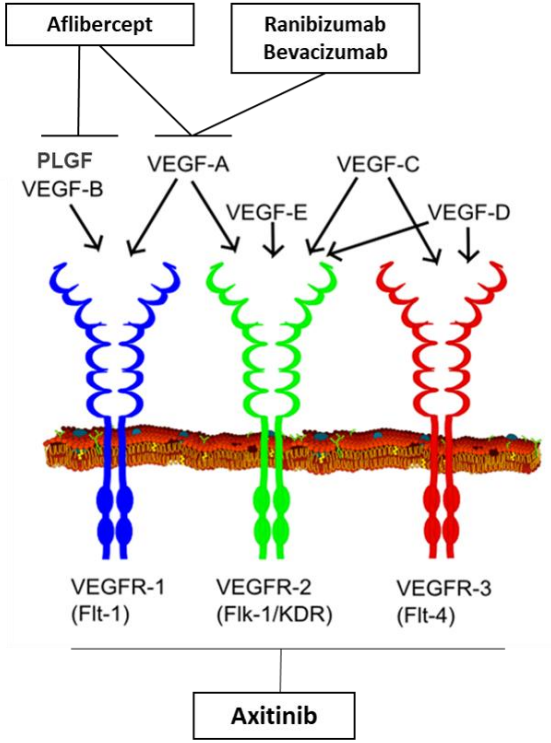
- Intrinsic pan-VEGF inhibition through receptor blockade
- More active than anti-VEGF-A in *in-vitro* angiogenesis model[1-2]
- Approved AMD treatments are focused VEGF-A inhibitors

Tyrosine kinase inhibitor (TKI) with the highest potency

- >10x more potent than other TKIs in in-vitro studies[3]
- Better ocular cell biocompatibility than other TKIs[4]
- More active than other TKIs for experimental corneal neovascularization in preclinical models

Small molecule formulated into suspension for SCS delivery

- Preclinical data showed regression of angiogenesis
- FDA-approved renal oncology treatment with established mechanism of action



VEGF Receptor-2 primarily mediates 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. Gross-Goupil et al. Axitinib: A Review of its Safety and Efficacy in the Treatment of Adults with Advanced Renal Cell Carcinoma. Clinical Medicine Insights: Oncology 2013:7. | 4. Thiele 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/wim/2014.008. ISSN 2002-4436. Public Domain.

Positioning CLS-AX for Real-World Success in the $12 Billion Dollar Wet AMD Market[1]

Maintain Vision & Reduce Office Visits

- Objective is to maintain visual acuity and reduce the number of injections; therefore, reducing the number of office visits
- Reduced treatment burden benefits patients, caregivers and payors with improved outcomes

Ability to Re-dose

- Wet AMD is a chronic disease requiring ongoing treatment
- Goal is a label that allows re-dosing comparable to VABYSMO® and EYLEA HD® in the real-world setting

Extend Duration Over Currently Approved Drugs

2x - 4x/year maintenance dosing anticipated for CLS-AX compared to approved drugs on label[2]:

- LUCENTIS®: 12x/year
- VABYSMO®: 3x - 12x/year
- EYLEA®: 6x - 12x/year
- EYLEA HD®: 3x - 6x/year

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[1]Annual financial reports from Regeneron Pharmaceuticals, Inc. and Genentech/Roche
[2]Dosing regimens are per respective product labels

PHASE 2 TOPLINE DATA SUMMARY

ODYSSEY Phase 2b Clinical Trial Overview

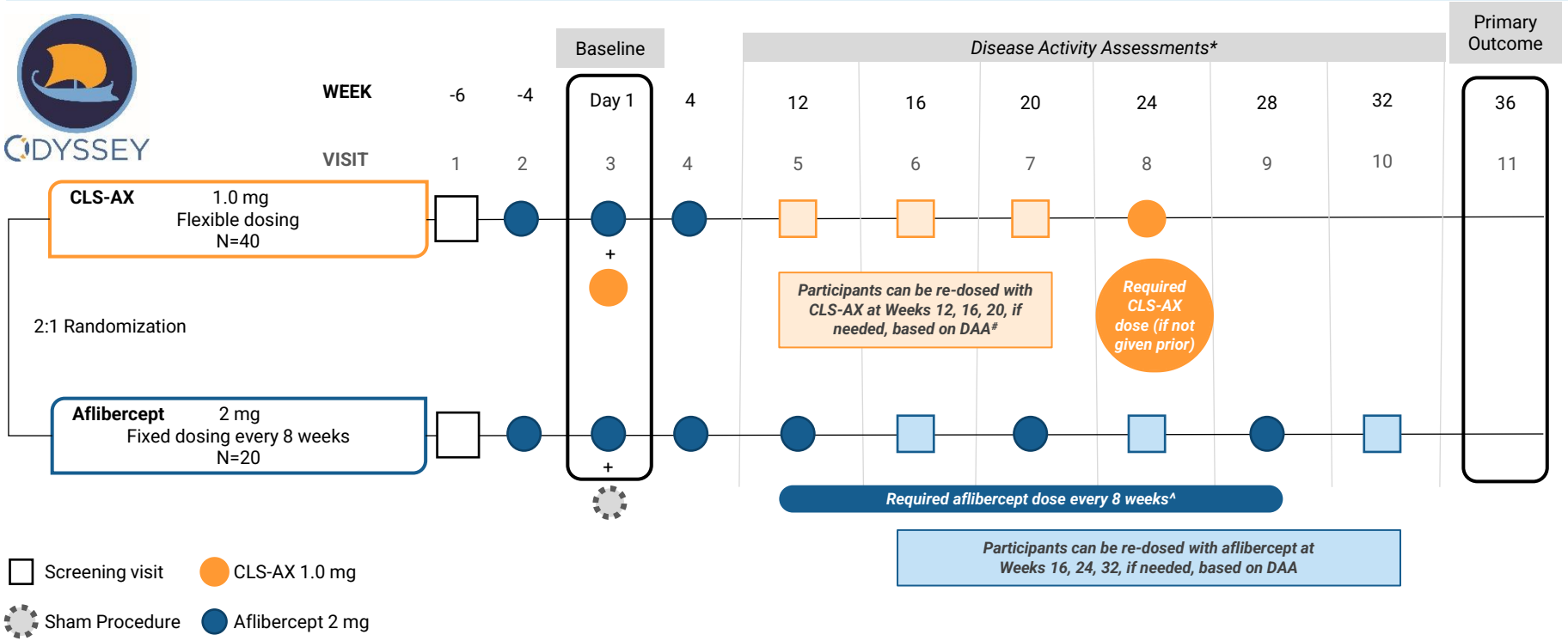
Trial Objectives:
Evaluated safety, efficacy & duration of CLS-AX in participants with wet AMD

- 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

ODYSSEY Trial Design

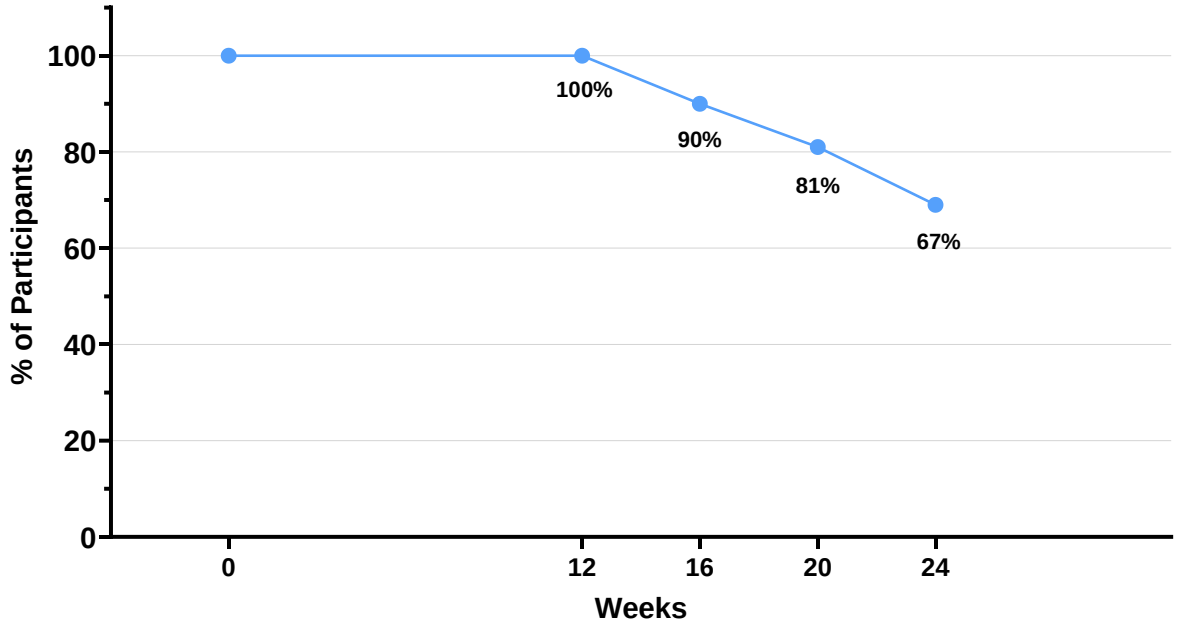


#Participants can be re-dosed with CLS-AX up to every 12 weeks; All arms are sham controlled

* Disease Activity Assessments (DAA): Conducted at Week 12 through 32 to determine need for supplemental treatment.
\# In CLS-AX arm, following 3 loading doses of aflibercept and initial dose of CLS-AX at Baseline, participants will receive CLS-AX at least every 24 weeks unless more frequently required based on DAA;
if disease is active and participant is <12 weeks since last CLS-AX injection, participant receives dose of aflibercept;
if disease is active and participant is >12 weeks since last CLS-AX injection, participant receives dose of CLS-AX.
^ In aflibercept arm, following 3 loading doses of aflibercept, participants will receive aflibercept on fixed dosing regimen every 8 weeks unless more frequently required based on DAA;
if disease is active, participant receives dose of aflibercept.

Two-Thirds of Participants Dosed with CLS-AX Reached Six Months Without Additional Treatment

Intervention–Free Rates By Week Up to Each Visit



Week 12: 40/40 (100%)
Week 16: 35/39 (89.7%)
Week 20: 30/37 (81.1%)
Week 24: 26/39 (66.7%)

Calculation accounts for missed treatments; time of initial administration of study drug shown as month 0 on figure.
Intervention-free rate calculation: if participant received intervention at a study visit, those were reflected in the count at the following study visit.

CLS-AX Consistently Reduced the Frequency of Injections

Comparison of Wet AMD Treatments Pre- and Post- Randomization

24 Weeks Before and After

Average number of treatments
24 Weeks prior to Screening Visit:
2.95 injections

Average number of treatments
up to 24 Weeks after Baseline Visit:
0.475 injections

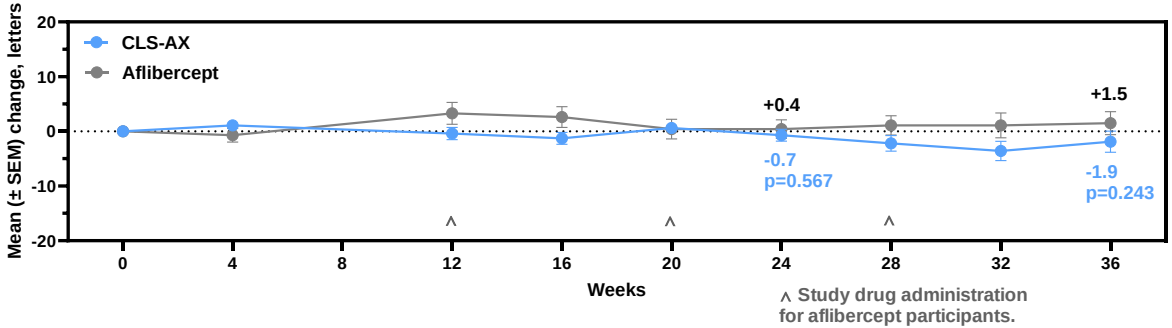
Reduced injection frequency by

84%

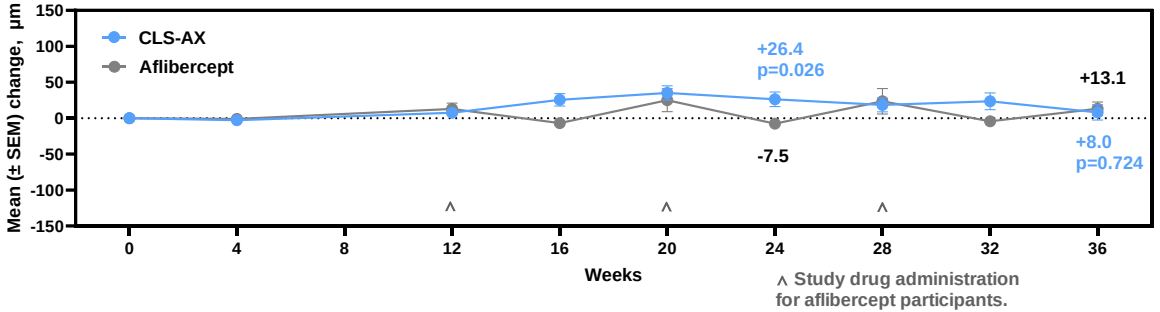
Injection post Baseline includes re-dosing with CLS-AX and/or supplementary treatment with aflibercept.
Injection frequency reduction calculated by the average number of treatments 24 Weeks prior to Screening Visit as compared to average number of treatments up to 24 Weeks after Baseline Visit.

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 .

CLS-AX Demonstrated A Positive Safety Profile

Safety Profile

Well-tolerated safety profile through 36 weeks including after mandatory re-dosing of CLS-AX at Week 24

No Serious Adverse Events (SAEs)

No ocular SAEs or treatment-related SAEs:

- No drug or procedure related ocular SAEs
- No reported drug or procedure related systemic SAEs
- No endophthalmitis
- No retinal vasculitis

Positive Adverse Event (AE) Profile

Ocular AEs were considered **clinically mild** in both arms

- Only one reported incident related to mild eye pain out of 84 total CLS-AX injections (1.2%)

Discontinuation Rates

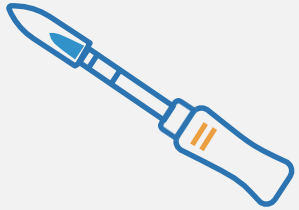
Similar discontinuation rates between treatment and comparator groups

CLS-AX Now Phase 3 Ready Based on Positive ODYSSEY Data in Wet AMD

ODYSSEY

Enrolled Only Difficult-to-Treat Participants with Active Disease

Achieved Primary Outcome Maintaining Stable BCVA with Repeat Dosing



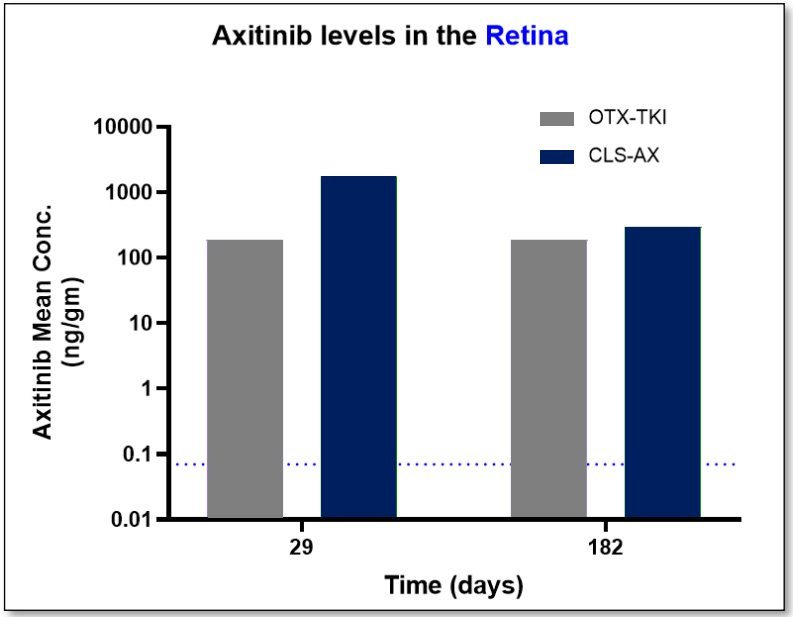
Compelling Intervention-Free Rates

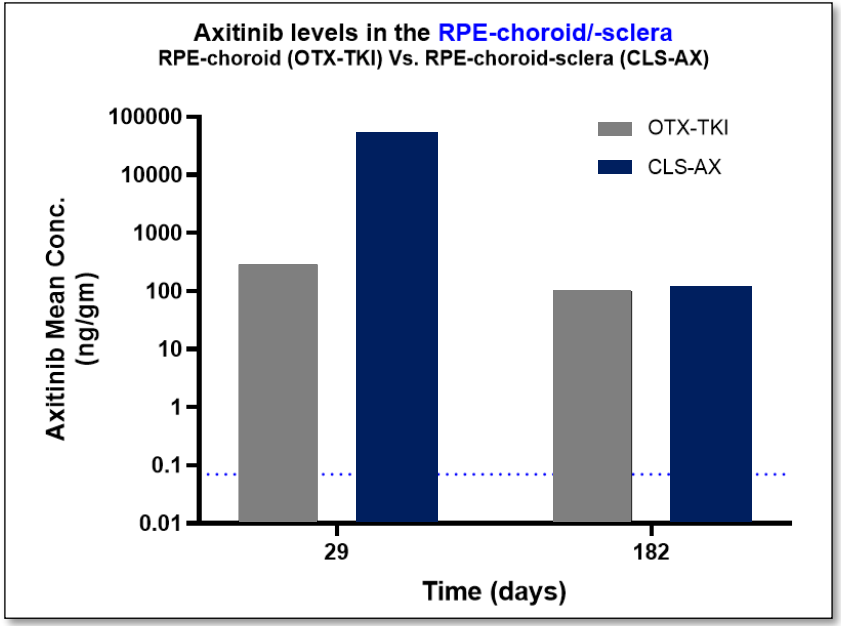
Positive Safety Profile with Repeat Dosing

Abbreviation: Wet AMD = neovascular age-related macular degeneration; BCVA = Best Corrected Visual Acuity

Comparison Between TKIs Currently in Development

CLS-AX Achieved Higher or Similar Chorioretinal Drug Levels Compared to OTX-TKI in Rabbits





- Dutch-Belted Pigmented rabbits | Dose: OTX-TKI, 0.11 mg/eye ; CLS-AX, 0.1 mg/eye
- Blue dotted line represents in-vitro IC50 value, 0.2nM = 0.07ng/gm. Tissue density assumed to be 1 g/mL
- Note: For graphical purpose, the OTX hydrogel data values were estimated from a graph presented at ARVO 2023

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CLS-AX: Rabbit toxicokinetic study in rabbits , CLS-1002-TOX-003
OTX-TKI: May 2023 | OTX presentation 2 ARVO 2023 | Phase 1 wAMD trial, 10-month clinical data

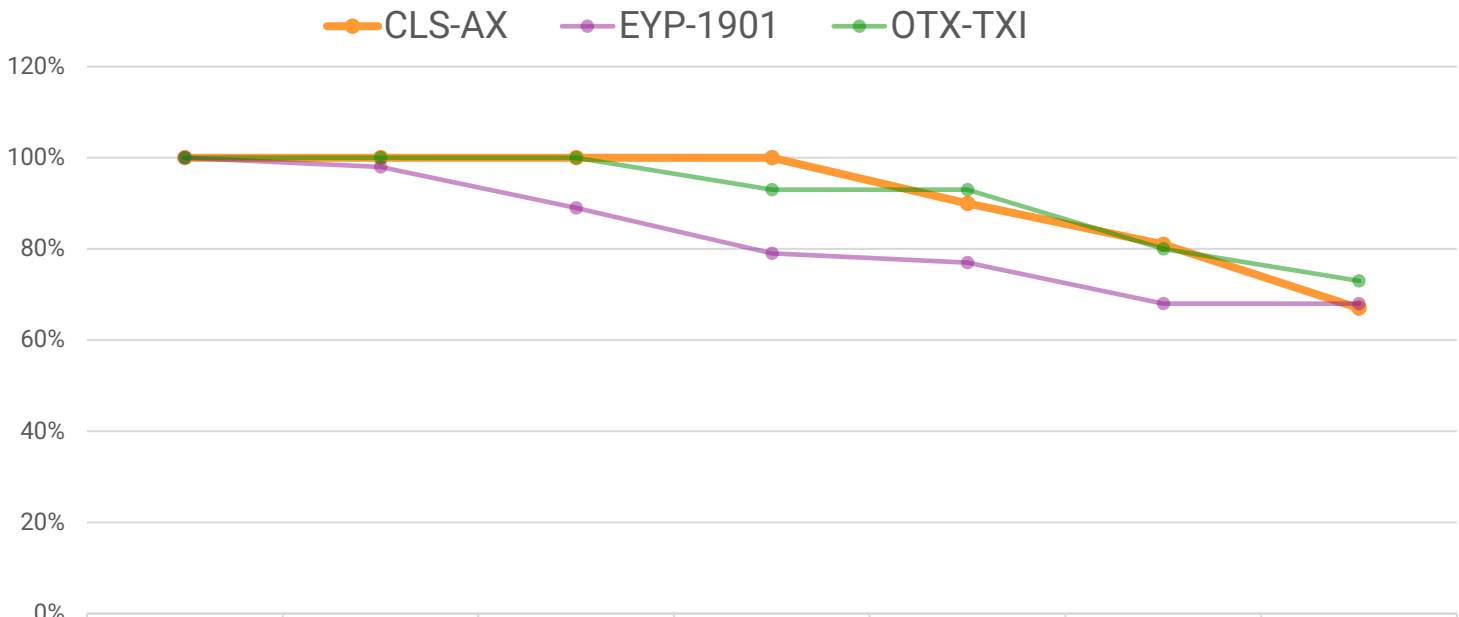
Differences in Rescue Criteria Impact Results

Comparative TKI Mid-Stage Trials

CLS-AX	EYP-1901	OTX-TKI
Increase in CST >100 µm from ***baseline***	***≥***100 µm increase from lowest CST for ***two consecutive measurements***	***No separate CST change criteria***
BCVA reduction of >10 letters from ***baseline*** due to wAMD	Loss of ≥10 letters from ***best*** BCVA	Loss of ≥10 letters from ***best*** BCVA with current BCVA ***worse than baseline***
BCVA reduction of > 5 letters from baseline and increase in CST of >75 µm from ***baseline*** due to wAMD	≥5 letter loss from ***best*** BCVA and ≥75 µm CST increase from ***lowest*** CST	≥5 letter loss from ***best*** BCVA and ≥75 µm CST increase from ***lowest*** CST
New hemorrhage	New hemorrhage	New hemorrhage

Clearside Biomedical is developing CLS-AX. Ocular Therapeutix is developing OTX-TKI. EyePoint Pharmaceuticals is developing EYP-1901.
Based on publicly available information provided by the companies as of February 2025.

Comparative TKI Intervention Free Rate Over 6 Months

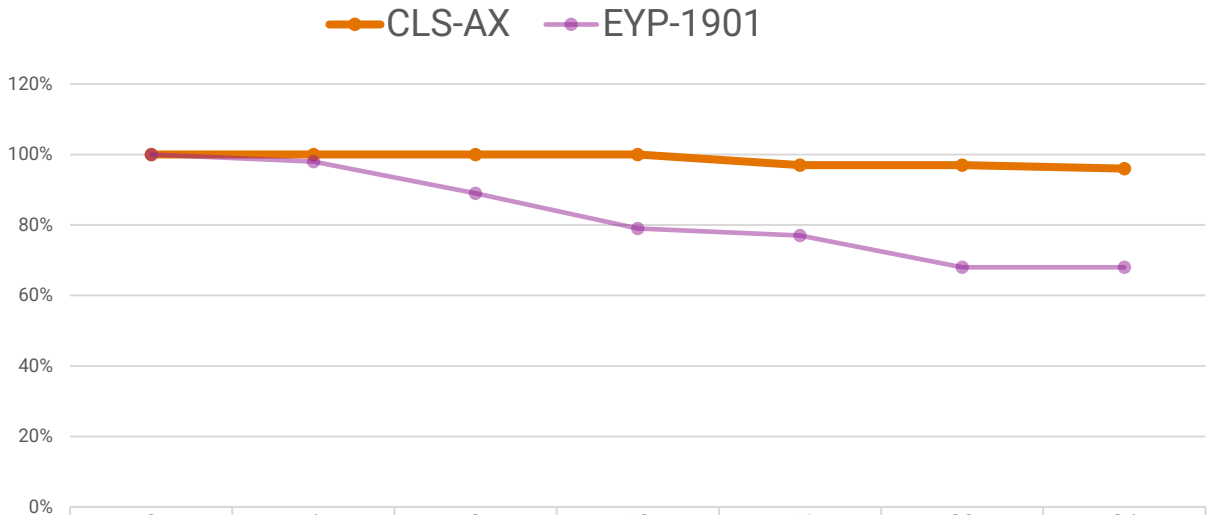


Weeks	0	4	8	12	16	20	24
CLS-AX	100%	100%	100%	100%	90%	81%	67%
EYP-1901	100%	98%	89%	79%	77%	68%	68%
OTX-TXI	100%	100%	100%	93%	93%	80%	73%

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;.

Post-Hoc Analysis: CLSD Intervention Free Rate Even Higher With EYPT Criteria

Comparative Intervention Free Rate for CLS-AX and EYP-1901 Over 6 Months Using EYPT Defined Rescue Criteria



Weeks	0	4	8	12	16	20	24
CLS-AX	100%	100%	100%	100%	97%	97%	96%
EYP-1901	100%	98%	89%	79%	77%	68%	68%

EYPT Rescue Criteria
DAVIO 2

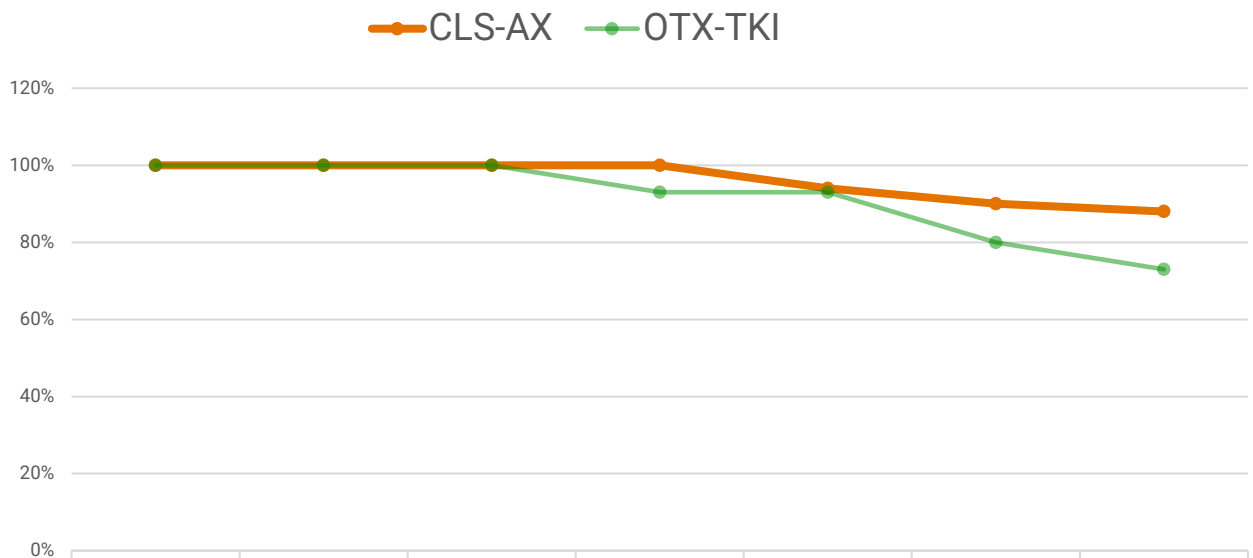
- 5 letter loss with 75 microns of new fluid
- 10 letter loss due to wet AMD
- 100 microns new fluid x2 visits
- New retinal hemorrhage from wet AMD
- Investigator discretion

Calculation accounts for missed treatments; time of initial administration of study drug shown as month 0 on figure. Active disease-free rate calculation: if participant received intervention at a study visit, those were reflected in the count at the following study visit provided the participants attended the next visit.

Results based on publicly available information, including rescue criteria, 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-1901is pooled 2mg and 3mg. Clearside Biomedical is developing CLS-AX. EyePoint Pharmaceuticals is developing EYP-1901.

Post-Hoc Analysis: CLSD Intervention Free Rate Remains Higher with OCUL Criteria

Comparative Intervention Free Rate for CLS-AX and OTX-TKI Over 6 Months Using OCUL Defined Rescue Criteria



Weeks	0	4	8	12	16	20	24
CLS-AX	100%	100%	100%	100%	94%	90%	88%
OTX-TKI	100%	100%	100%	93%	93%	80%	73%

OCUL Rescue Criteria
US Wet AMD Phase 1

- Loss of ≥10 letter from best previous BCVA due to AMD with current BCVA worse than baseline
- Evidence of ≥75 µm CSFT increase from previous best value and ≥5 letters loss from best previous BCVA
- New macular hemorrhage

Calculation accounts for missed treatments; time of initial administration of study drug shown as month 0 on figure. Active disease-free rate calculation: if participant received intervention at a study visit, those were reflected in the count at the following study visit provided the participants attended the next visit.

Results based on publicly available information, including rescue criteria, 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. Clearside Biomedical is developing CLS-AX. Ocular Therapeutix is developing OTX-TKI.

CLS-AX Phase 3 Program Current Plans

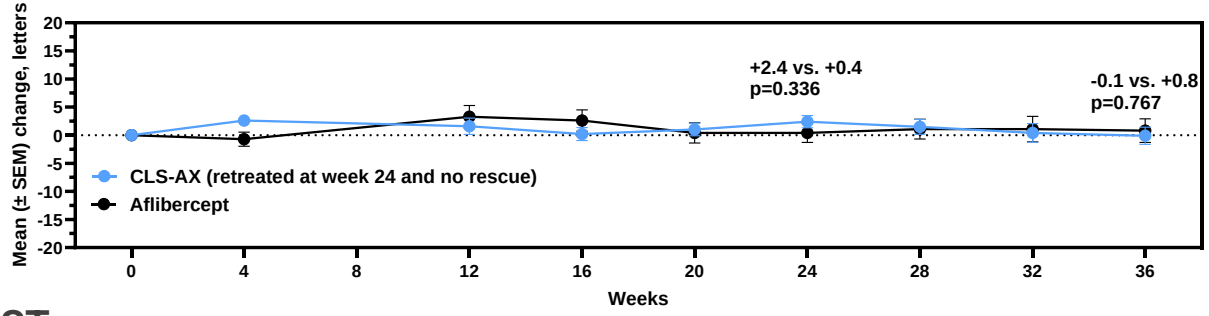
Phase 3 plans are in development and subject to change

ODYSSEY Sub-Group Analyses and Insights for Phase 3

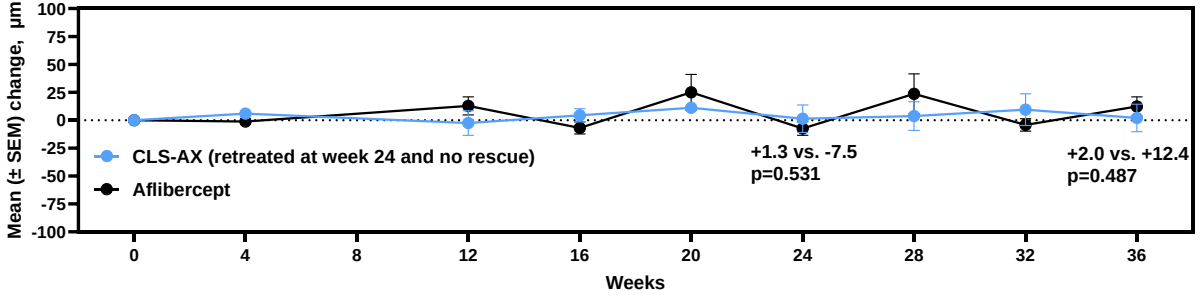
Sub-Group Analysis: Supports Enrolling Treatment Naïve Patients in the Phase 3 Program

Participants Solely Re-Dosed with CLS-AX at Week 24 Without Prior Intervention

BCVA



CST



Key Insights for Phase 3

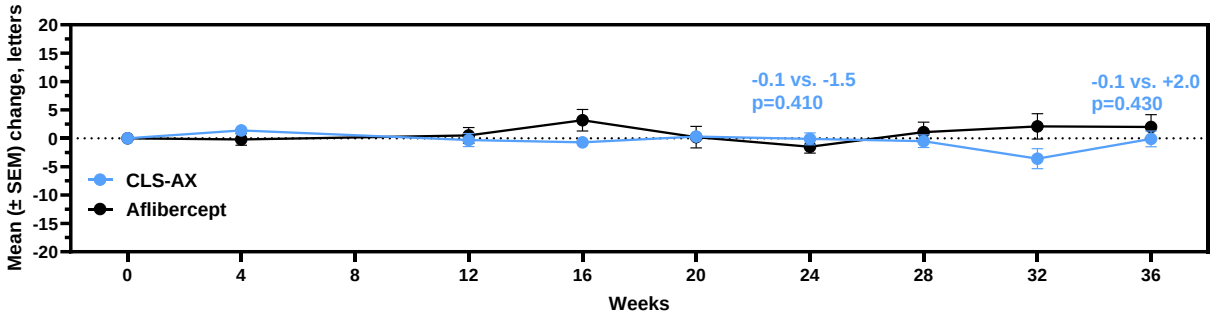
- **ODYSSEY:** 67% of CLS-AX participants did not require rescue or re-dosing until the 6-month mandatory CLS-AX re-dosing in more difficult-to-treat patients.
- **Sub-group:** Stable BCVA and CST in participants who did not require aflibercept rescue or CLS-AX re-dosing prior to Week 24
- **Phase 3:** By targeting treatment naïve there may be an even greater percentage reaching 6-months without the need for any intervention.

Analysis includes CLS-AX participants solely re-dosed with CLS-AX at Week 24 who never received rescue therapy vs. aflibercept comparator participants.
Abbreviations: BCVA = best corrected visual acuity; CST = central subfield thickness. P-values are based on a 2-sample t-test.

Sub-Group Analysis: Supports Phase 3 Design that Excludes Participants with Non-Disease Related Changes in Visual Acuity Prior to Randomization

Excluding Observations with ≥10 Letter Change from the Previous Visit in BCVA Without a Corresponding 25 Micron Change in CST

BCVA



Key Insights for Phase 3

- BCVA changes without OCT changes may not be disease related
- **Sub-group:** compelling BCVA results provide evidence that excluding participants with ≥10 letter changes prior to randomization may:
  - Reduce BCVA variability unrelated to Wet AMD activity
  - Better ensure data reflects real world treatment practices

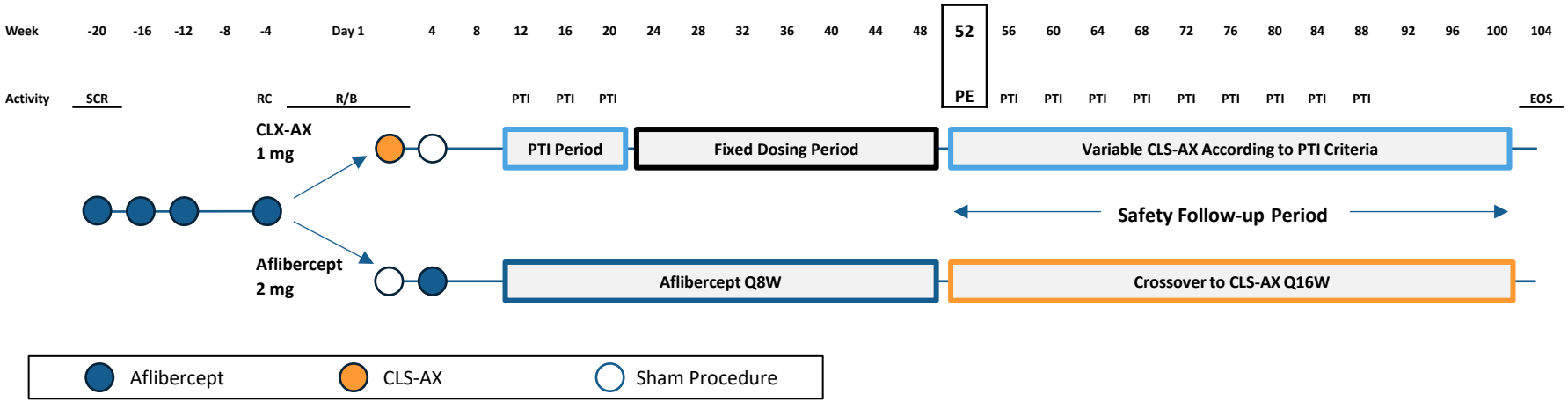
Excluded observations with BCVA changes from the previous visit of 10 letters or more without corresponding CST changes from the previous visit of 25 microns or more suggesting BCVA changes not related to wet AMD

Abbreviations: BCVA = best corrected visual acuity; CST = central subfield thickness. P-values are based on a 2-sample t-test.

Step-By-Step Explanation of CLS-AX Phase 3 Study Design

Phase 3 plans are in development and subject to change

CLS-AX Phase 3 Program Designed to Potentially Reduce Regulatory Risk and Maximize Commercial Opportunity in Wet AMD



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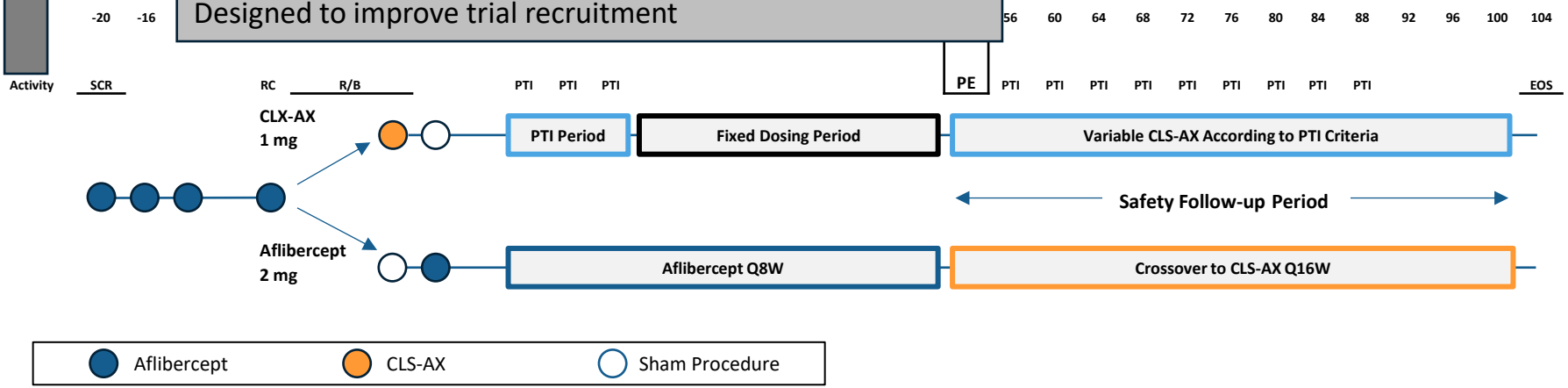
Abbreviations: SCR = Screening Visit; RC = Randomization Criteria; R/B = Randomization/Baseline; PE = Primary Endpoint;

CLS-AX Phase 2 Program Designed to Potentially Reduce Regulatory Risk and ... in Wet AMD

Target Patient Population:
- **Treatment naïve**

Designed to increase commercial value
Designed to improve trial recruitment



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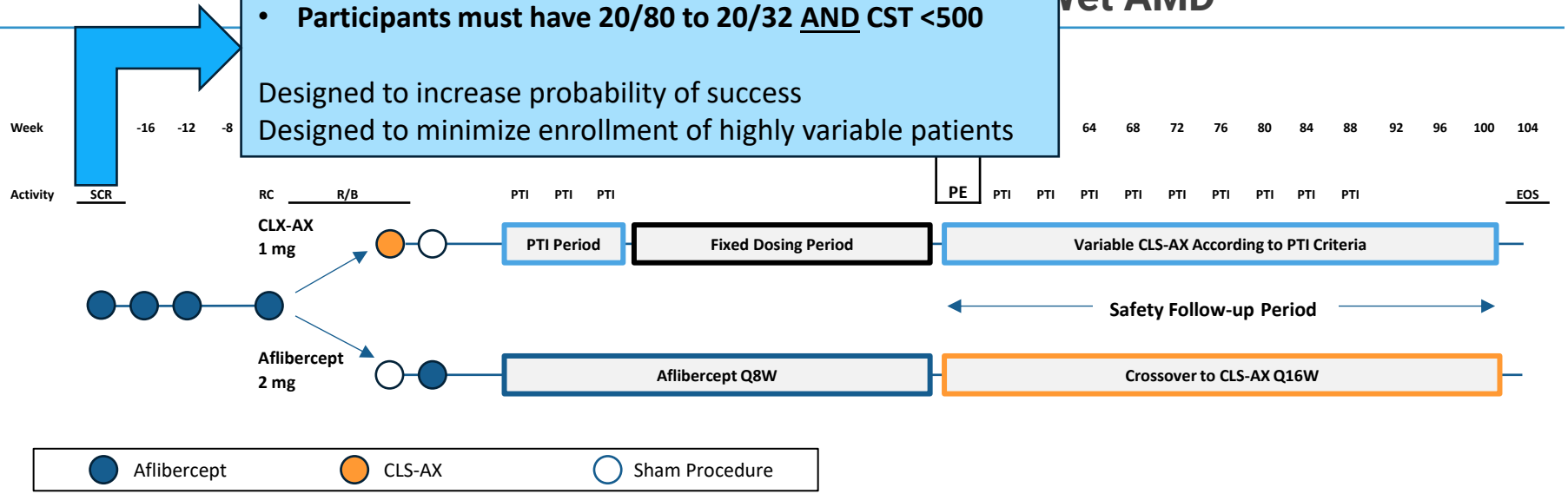
CLS-AX Phase 3 Program Designed to Potentially Reduce Regulatory Risk and Wet AMD

At Screening:
- **Participants must have 20/80 to 20/32 AND CST <500**

Designed to increase probability of success
Designed to minimize enrollment of highly variable patients



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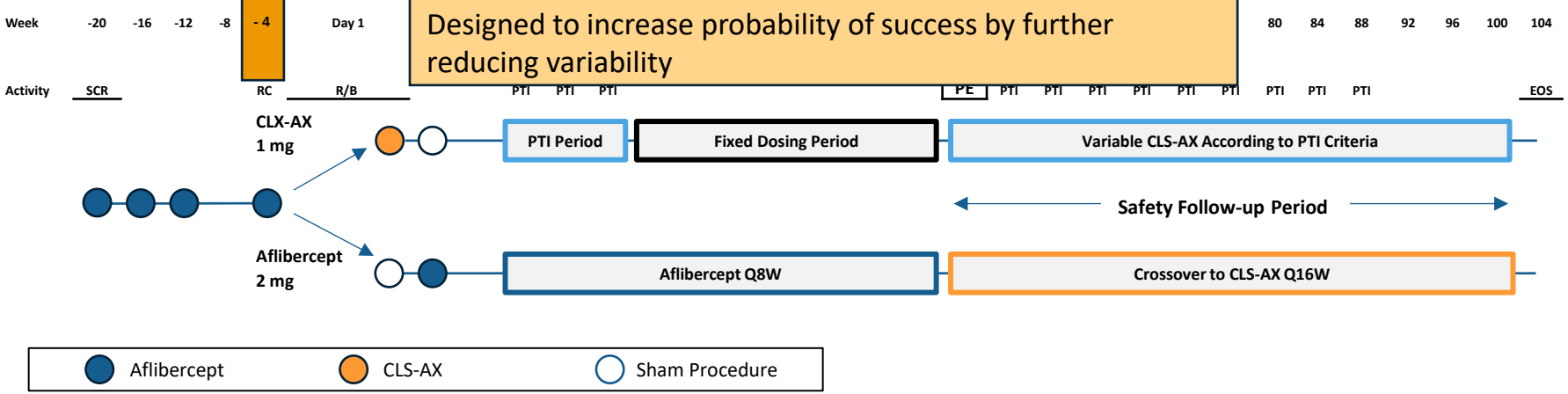
CLS-AX Phase 3 Program Designed to Potentially Reduce Regulatory Risk and Max

Prior to Randomization (Week -4):

- **Participants with ≥ 10 letter change from previous visit <u>OR</u> CST increases of ≥ 100 microns are excluded**

Designed to increase probability of success by further reducing variability



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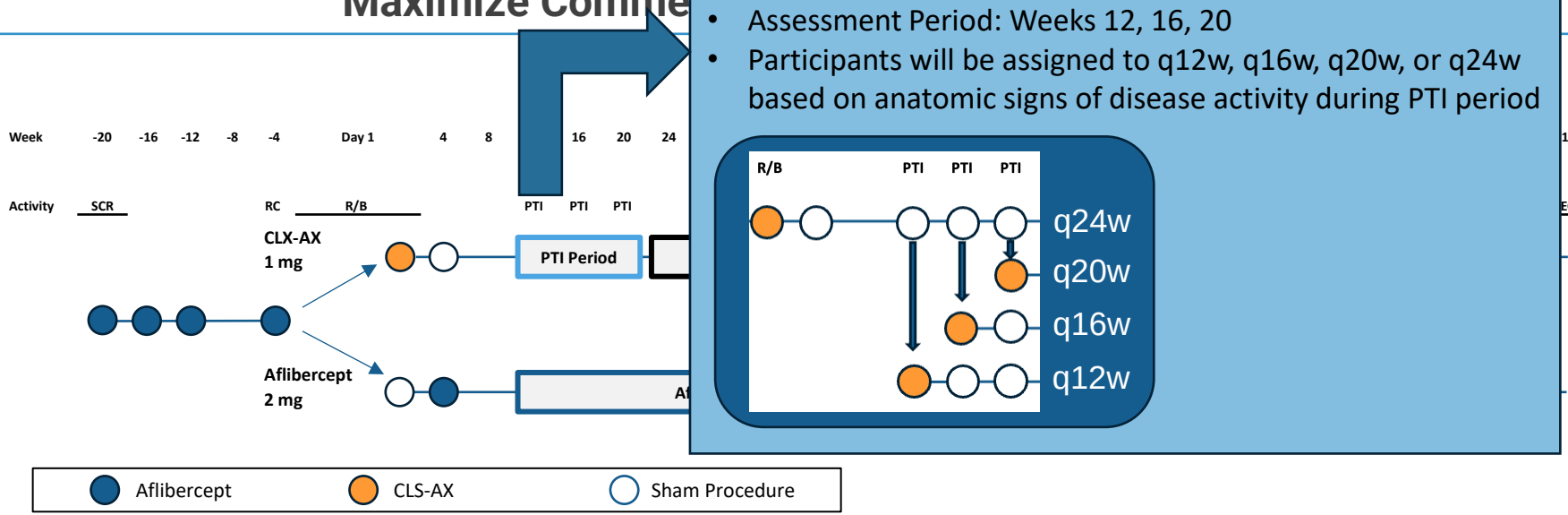
CLS-AX Phase 3 Program Designed to Potentially Reduce Regulatory Risk and Maximize Comme



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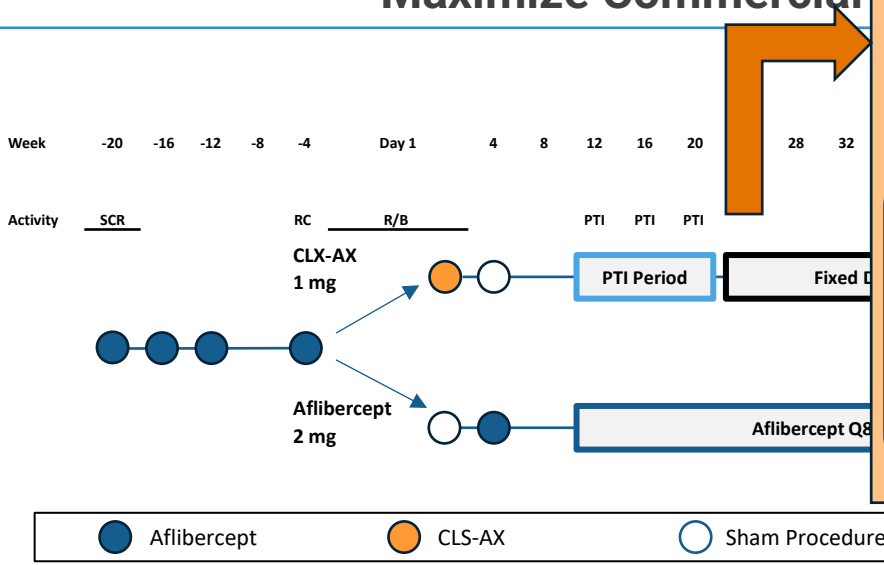
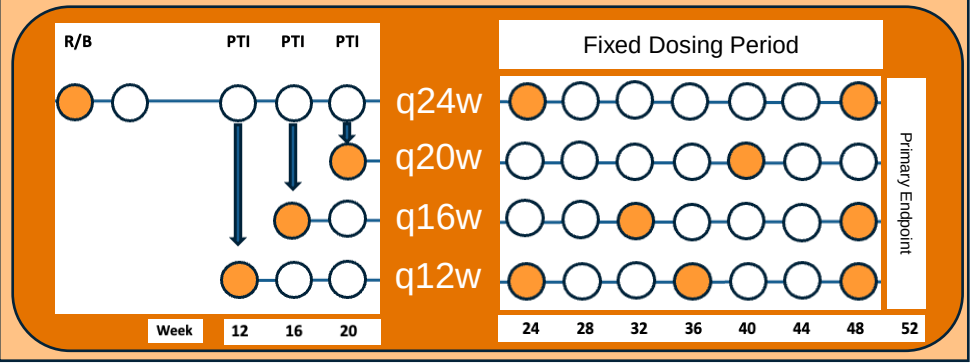
CLS-AX Phase 3 Program Designed to Potentially Reduce Regulatory Risk and Maximize Commercial



Fixed Dosing Period

- Once a dosing interval is established for each participant during the PTI period, it remains the same until the primary endpoint (Week 52)



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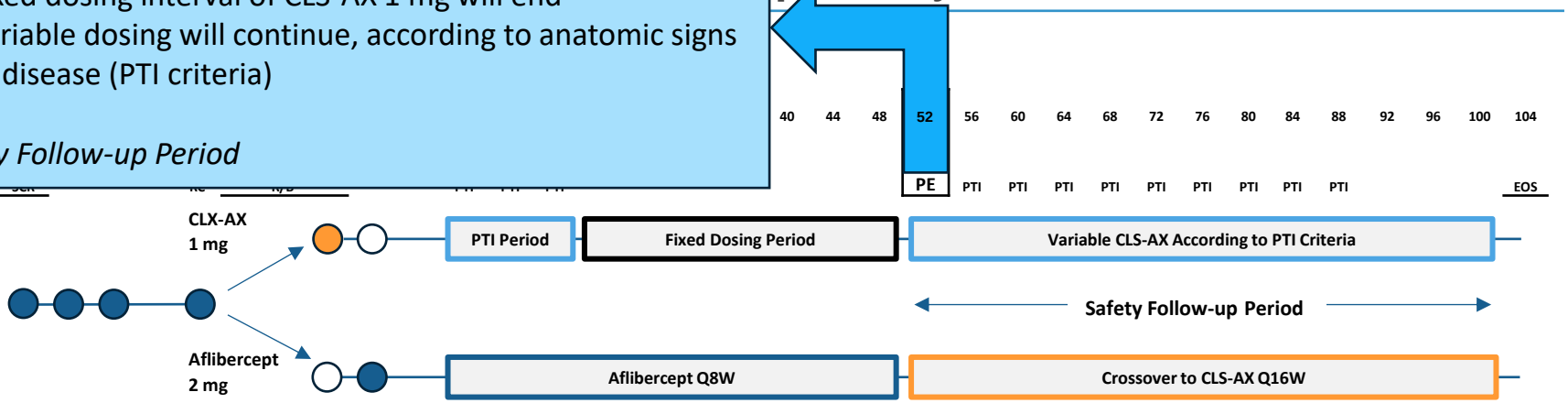
CLS-AX Phase 3 Program Designed to Potentially Reduce Regulatory Risk and Opportunity in Wet AMD

Starting at Primary Endpoint (Week 52):
- Fixed dosing interval of CLS-AX 1 mg will end
- Variable dosing will continue, according to anatomic signs of disease (PTI criteria)

Safety Follow-up Period



Starting at Primary Endpoint (Week 52):
- Patients from Aflibercept 2 mg arm will crossover to receive CLS-AX 1 mg q16w at primary endpoint (Week 52)

Gathers additional safety and efficacy data in anti-VEGF treatment-experienced patient population

ticipants will undergo an assessment of disease activity based on PTI
4 weeks.

the participants will stay at that interval until week 52 (primary endpoint).
CLS-AX every 16 weeks in the fixed dosing period.

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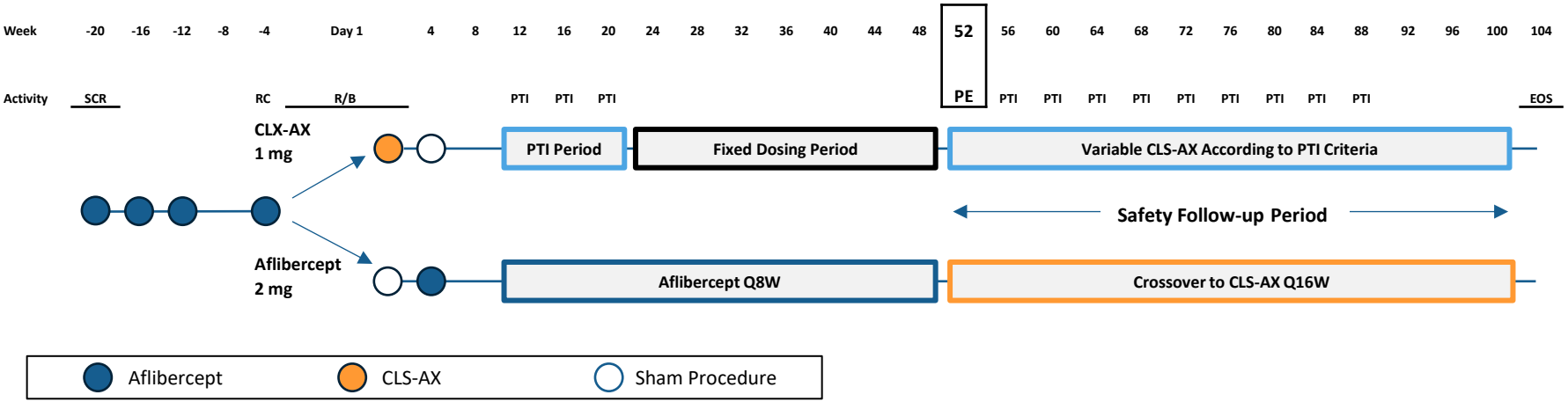
CLS-AX Phase 3 Program Designed to Potentially Reduce Regulatory Risk and Maximize Commercial Opportunity in Wet AMD



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CLS-AX Ability to Re-Dose vs Rescue Supports Regulatory & Commercial Strategy

Why Flexible Dosing Matters

- Retinal physicians prefer to see patients at least every 6 months
  - CLS-AX: 90% demonstrated disease control at 4 months in Phase 2. EYLEA® HD and VABYSMO® cannot make that claim based on Phase 3 data.
- Payer research confirmed reimbursement with a 3 to 6-month label to be on par with competitors
- Other TKIs in development initiated Phase 3 trials without multi-dose data and are only re-dosing at 6 months (”rescues” expected)

Our Phase 3 Approach

- **Personalized Treatment Interval (PTI)** assessment enables physicians to use a “real world” approach with flexible dosing schedule based on participant needs
- **Minimal to No “rescues” expected** due to PTI defined CLS-AX re-dosing every 3 to 6 months
- **Employ in-office OCT biomarkers** (IRF and SRF) determined using AI tool to improve consistency in assessing need for re-dosing

IRF = intraretinal fluid; SRF = subretinal fluid; AI = artificial intelligence
Disease control and dosing based on publicly available information provided by each company as of March 2025.
EYLEA is a registered trademarks of Regeneron Pharmaceuticals. VABYSMO is a registered trademark of Genentech.

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

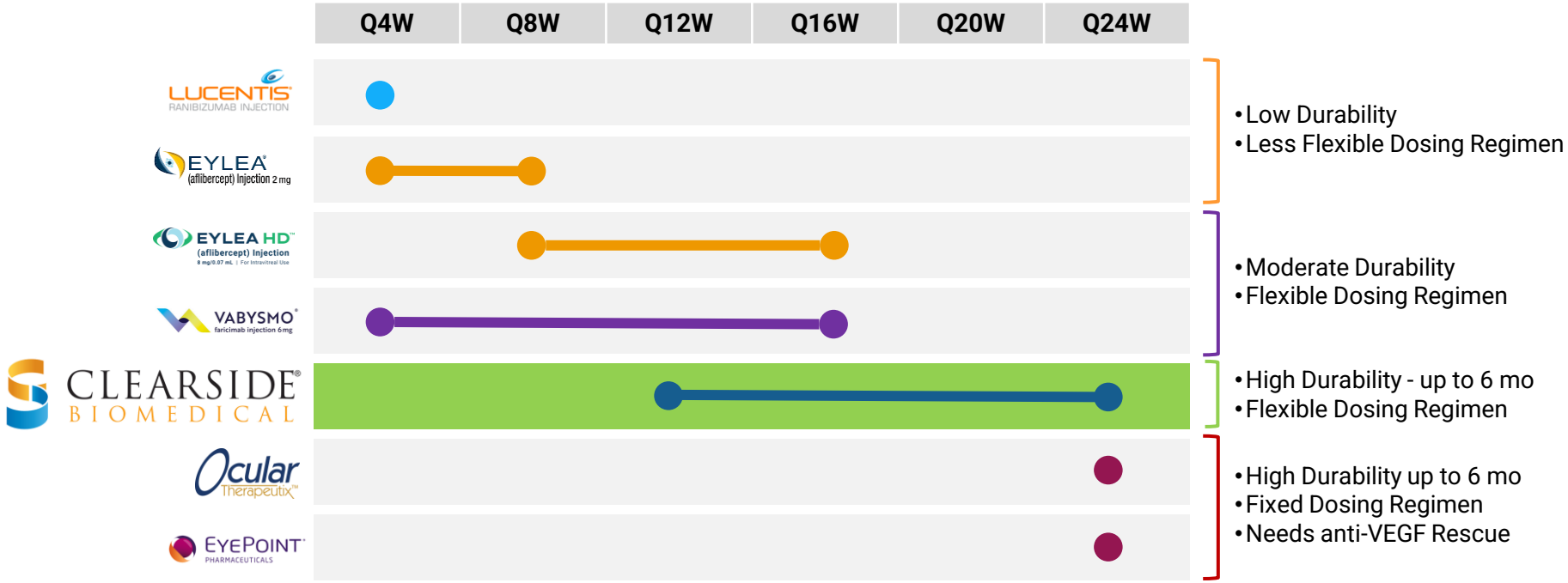
Phase 3 Clinical Trial Design Comparison

	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 and Commercially Appealing Label with Large Total Addressable Market Based on Planned 3-6 Month Dosing Flexibility

WET AMD Intended Dosing Interval Range (Weeks)



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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.

Why We Believe CLS-AX Should Be the “Preferred TKI”

Efficacy Profile vs. Other TKIs

- Equivalent 6-month Duration of Effect as EYPT and OCUL
- Equivalent Intervention Free Rates despite more rigorous intervention criteria
- Equivalent reduction in treatment burden
- More potent API vs EYPT, Same API as OCUL

Potential SCS Safety Advantages

- Very low risk of endophthalmitis since CLS-AX not injected into vitreous
- No implant floating in vitreous
- No evidence TKI implants fully dissolved in vitreous at 6 months
- Same gauge injection needle as EYLEA/VABYSMO; EYPT and OCUL each use larger needle gauges to inject implants

Rigorous Phase 2 Trial Design Should Reduce Phase 3 Risks facing other TKIs

- ODYSSEY enrolled only participants with active disease vs OCUL whose participants had to be inactive (dry)
- ODYSSEY more sensitive re-treatment/rescue criteria yet similar durability of effect to other TKIs
- CLS-AX may have even better results if using same inclusion/re-treatment criteria as other TKIs
- OCUL did not conduct Phase 2 trial (only limited Phase 1 data in 15 active arm participants)

Physician/Commercially Preferred Target Label (3 - 6 months)

- As flexible as VABYSMO and EYLEA HD and as durable as other TKIs – potentially translatable to a larger market share
- EYPT and OCUL must “rescue” with anti-VEGF biologics
- Physicians prefer re-dose with same product for harder to treat patients
- CLS-AX may be re-dosed as often as every 3 months
- CPT code for SCS administration reimburses physicians at a higher rate than IVT

Pipeline Expansion Opportunity in Geographic Atrophy

Clearside Suprachoroidal Product Development Pipeline Targeting Global Markets

Clearside Research and Clinical Development Programs

THERAPEUTIC	MECHANISM	INDICATION	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	APPROVAL	PARTNER
CLS-AX (axitinib)	Tyrosine Kinase Inhibitor	Wet AMD*			*FDA End-of-Phase 2 Meeting Completed*			
Undisclosed	Improve choroidal perfusion	Geographic Atrophy (GA)						
Undisclosed	Modulate pro-inflammatory cells	Geographic Atrophy (GA)						

Commercial Asset: XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use

THERAPEUTIC	LOCATION	INDICATION	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	APPROVAL	PARTNER
XIPERE®	United States	Uveitic Macular Edema[1]						B+L BAUSCH+LOMB
XIPERE®/ ARCATUS™	Australia and Singapore	Uveitic Macular Edema[2]						arctic VISION
XIPERE®/ ARCATUS™	China	Uveitic Macular Edema[2]				*NDA Under Review*		arctic VISION Santen
XIPERE®/ ARCATUS™	Asia Pacific ex-Japan	Diabetic Macular Edema[2]						arctic VISION

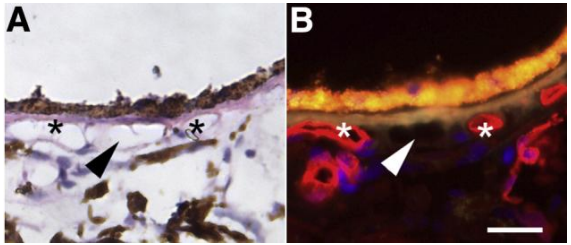
CLEARSIDE BIOMEDICAL

[1]XIPERE® (triamcinolone acetonide injectable suspension), for suprachoroidal use has received U.S. FDA Approval and is being commercialized by Bausch + Lomb.
[2]In licensed territories, Arctic Vision is responsible for clinical development of ARCATUS™ (triamcinolone acetonide injectable suspension), also known as ARVN001, and known as XIPERE® in the U.S.
*Phase 3 plans are in process.

Geographic Atrophy is a Choroidal Disease and an Advanced Form of Age-Related Macular Degeneration (AMD)

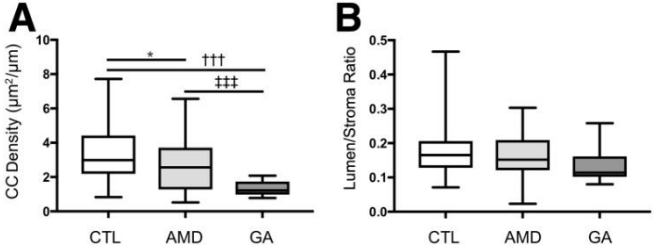
Choroidal Hypoxia Theory and Choriocapillaris are Damaged First

1



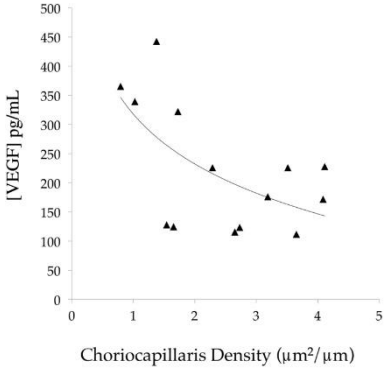
Choriocapillaris endothelial cells damage with ghost vessels before any significant RPE changes

2



- Choriocapillaris (CC) vascular density is significantly lower in GA donor
- No meaningful differences in vascular lumen area / stroma area

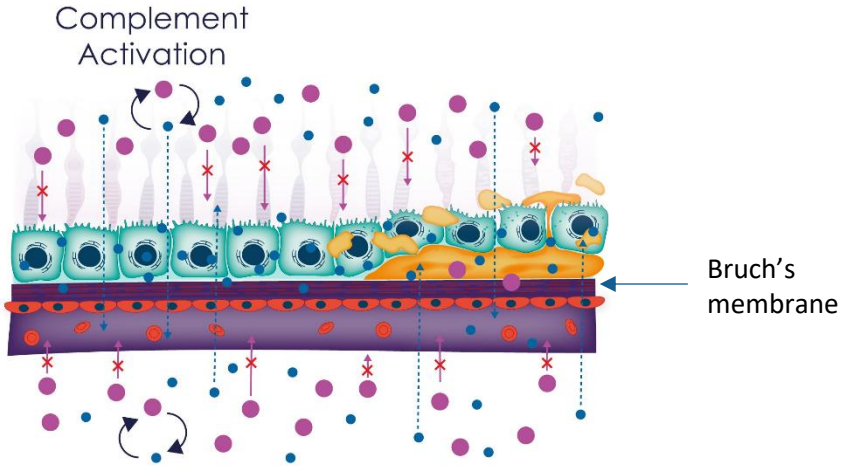
3

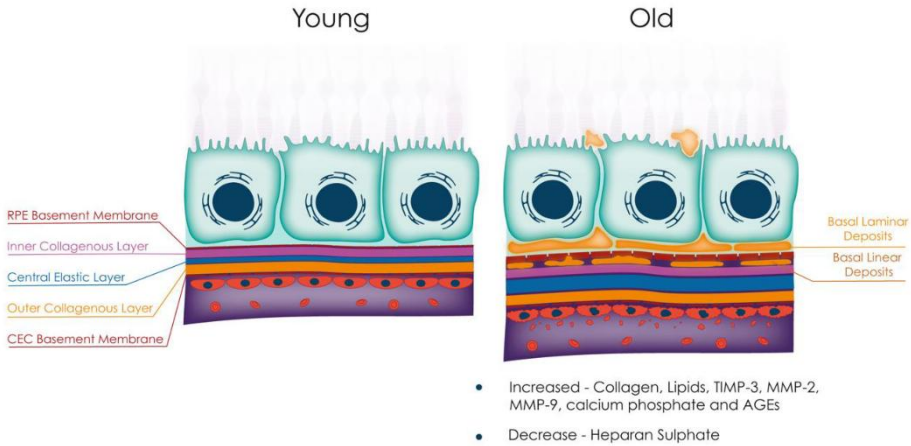


VEGF level increased with low vascular density support the choroidal hypoxia theory

RPE = Retinal Pigment Epithelium
Images modified from Sohn EH et al., Am J Path 2019: 189: 1473-80

Small Molecule Can Access the Diseased Area of the RPE and Choroid





Larger molecules cannot get through Bruch's membrane. Therefore, if given intravitreally, it can only treat the RPE side.

Aging intensifies disease actions and even peptides might not be able to get through.

Images modified from Hammadi et al JCM 2023, 12 (8), 2870

Potential Advantages of Suprachoroidal Delivery in Geographic Atrophy

- Able to reach the choroid first
- Small molecules may have better efficacy than current therapies
- In-office procedure
- Targeted delivery compartmentalized to the posterior segment
- SCS may be ideal delivery for gene therapy as subretinal is too invasive and intravitreal delivery lacks efficacy with a high risk of inflammation

Near-Term Geographic Atrophy Program Focused on Small Molecule Suspensions

Evaluating Two Mechanisms That Could Potentially Be Used as Add On to Complement-Based Therapies

Small Molecule Suspensions

- Can treat both sides of the Bruch's membrane (Retina, RPE and Choroid)
- Higher concentration of drug in the choroid

1. Improve choroidal perfusion

Blood flow improvement can improve retinal function directly and slow progression

2. Modulate pro-inflammatory cells

Inflammatory cells manipulation can reduce the root cause of complement activation

Multiple Validating Partnerships Expand Utilization of SCS Microinjector® Technology

SCS Microinjector® Partner Clinical Development Programs

THERAPEUTIC	TYPE	INDICATION	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	APPROVAL	PARTNER
Bel-Sar	Viral-like Drug Conjugate	Choroidal Melanoma	CoMpass					aura
Sura-vec	AAV Gene Therapy	Diabetic Retinopathy (DR)*	ALTITUDE					REGENXBIO abbvie
Sura-vec	AAV Gene Therapy	Wet AMD	AAVIATE					REGENXBIO abbvie
Avoralstat	Plasma Kallikrein Inhibitor	Diabetic Macular Edema						bio cryst

aura

Ocular Oncology

- Actively enrolling Phase 3

REGENXBIO

Gene Therapy

- DR: Initiate global pivotal trial in H1 2025
- ALTITUDE: enrolling a DME cohort at dose level 4
- AAVIATE: Enrolling new cohort in Wet AMD at dose level 4

bio cryst

Plasma Kallikrein Inhibitor

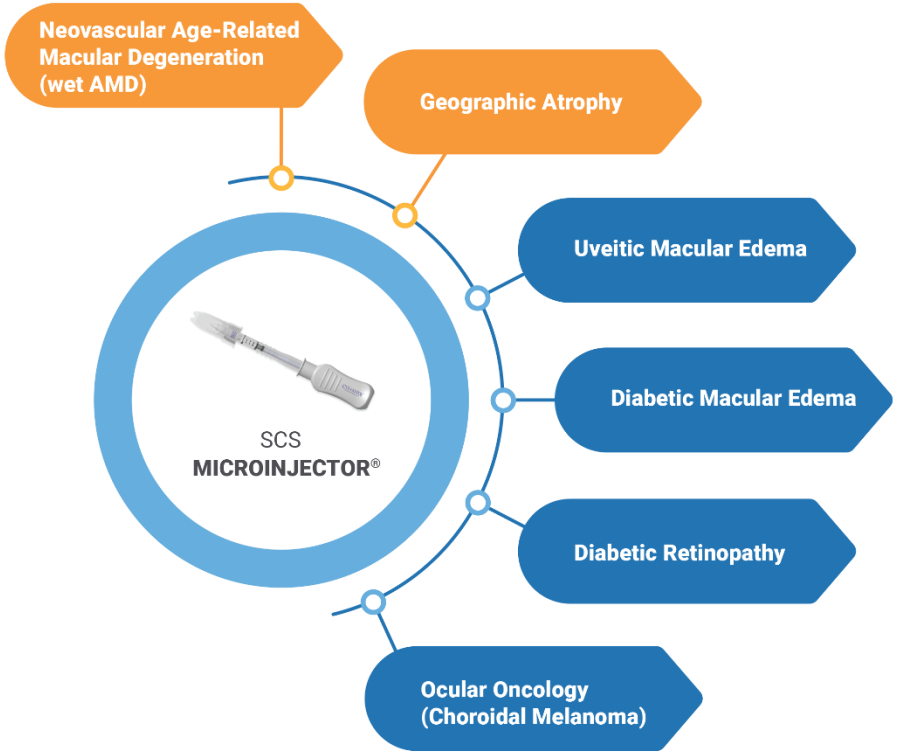
- Conducting formulation and nonclinical work
- Begin clinical trial in 2025

Surabgene lomparvovec (sura-vec, ABBV-RGX-314); *Phase 3 plans are in process by partner.

Summary

SCS Microinjector®: Drug/Device Combination with Proven Versatility

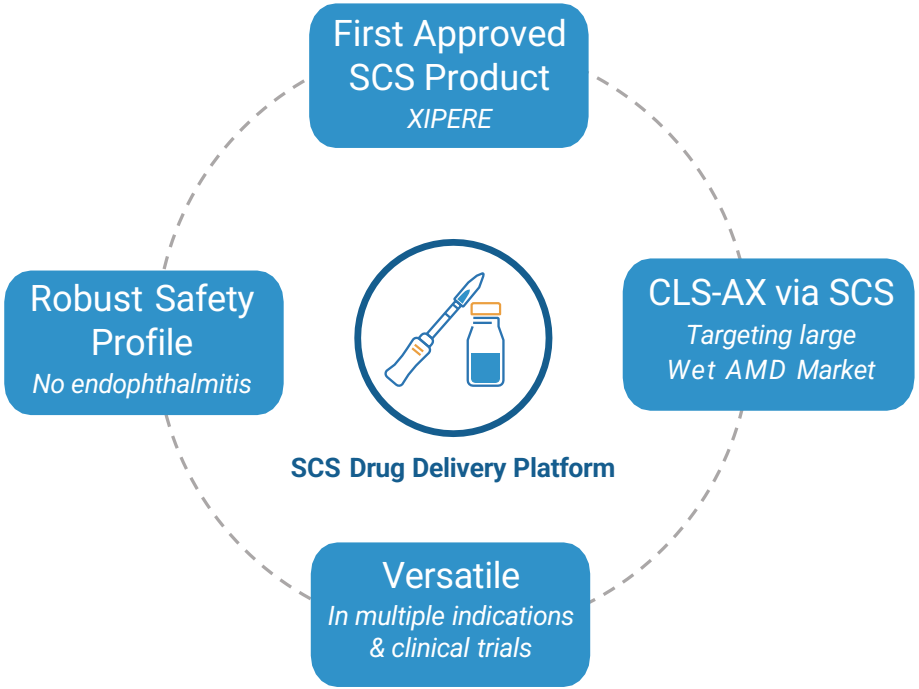
- **Demonstrated ability for precise delivery into the suprachoroidal space**
- **First and Only FDA-approved SCS product**
- **Safety profile of SCS Microinjector comparable to intravitreal injections[1]**
- **Well-accepted by retinal physicians with thousands of injections performed**



Abbreviations: UME = uveitic macular edema; DME = diabetic macular edema; DR = diabetic retinopathy;
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.*

Innovative and Experienced Leader in Suprachoroidal Drug Delivery

- Differentiated ophthalmology company with a platform of assets
- Patented SCS Microinjector® delivers agents directly to the back of the eye
- Validated technology with multiple partners
- Aligned with the FDA on the Phase 3 program designed to support a commercially appealing label
- Potential pipeline expansion in geographic atrophy, diabetic retinopathy, and the combination of CLS-AX and a steroid (CLS-TA) for DME



CLS-TA is also known by brand name XIPERE® (triamcinolone acetonide injectable suspension)

CLEARSIDE BIOMEDICAL

Thank You