CLEARSIDE BIOMEDICAL

Fourth Quarter and Full Year 2024
Financial Results Conference Call
March 27, 2025

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, 2024, filed with the U.S. Securities and Exchange Commission (SEC) on March 27, 2025, 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.

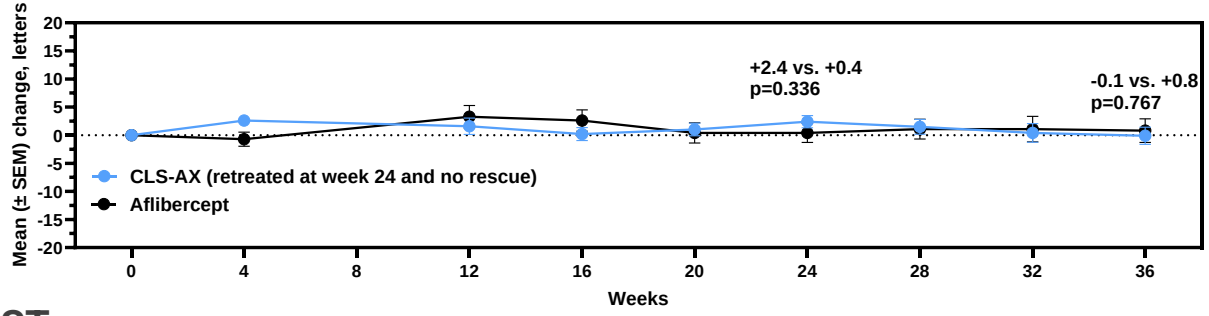
Corporate Update

ODYSSEY Sub-Group Analyses and Insights for Phase 3

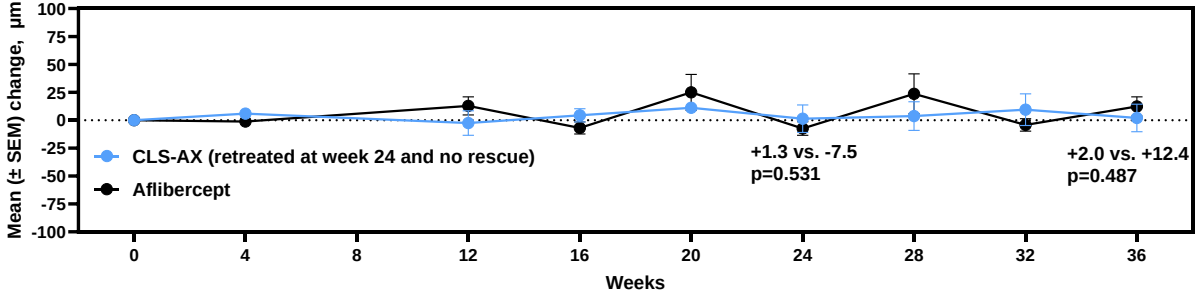
Sub-Group Analysis: Supports Enrolling Treatment Naïve Patients in the Phase 3 Program

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

BCVA



CST



Key Insights for Phase 3

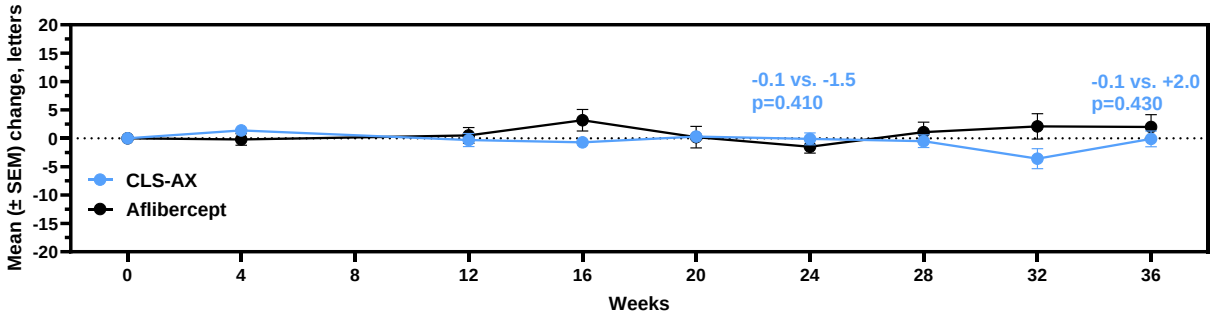
- **ODYSSEY:** 67% of CLS-AX participants did not require rescue or re-dosing until the 6-month mandatory CLS-AX re-dosing in more difficult-to-treat patients.
- **Sub-group:** Stable BCVA and CST in participants who did not require aflibercept rescue or CLS-AX re-dosing prior to Week 24
- **Phase 3:** 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.

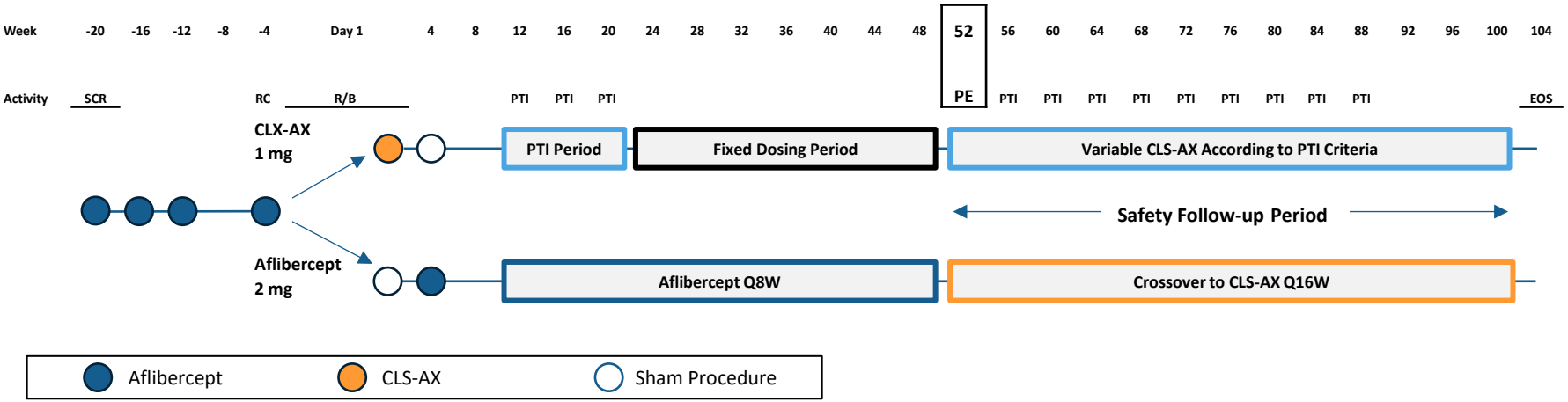
CLS-AX Phase 3 Program Current Plans

Phase 3 plans are in development and subject to change

CLS-AX Phase 3 To Feature the Flexible Dosing of a Biologic with the Duration of a TKI

- Two pivotal, non-inferiority trials in treatment naïve participants
- Similar to Phase 3 trial design of EYLEA HD and VABYSMO in maintenance phase
- Employ more “real world” clinical practice re-dosing criteria for CLS-AX
- CLS-AX flexible dosing is an important differentiation vs other TKI programs
- Successful End-of-Phase 2 FDA Meeting confirms Phase 3 program
- Preparations for Phase 3 program ongoing

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



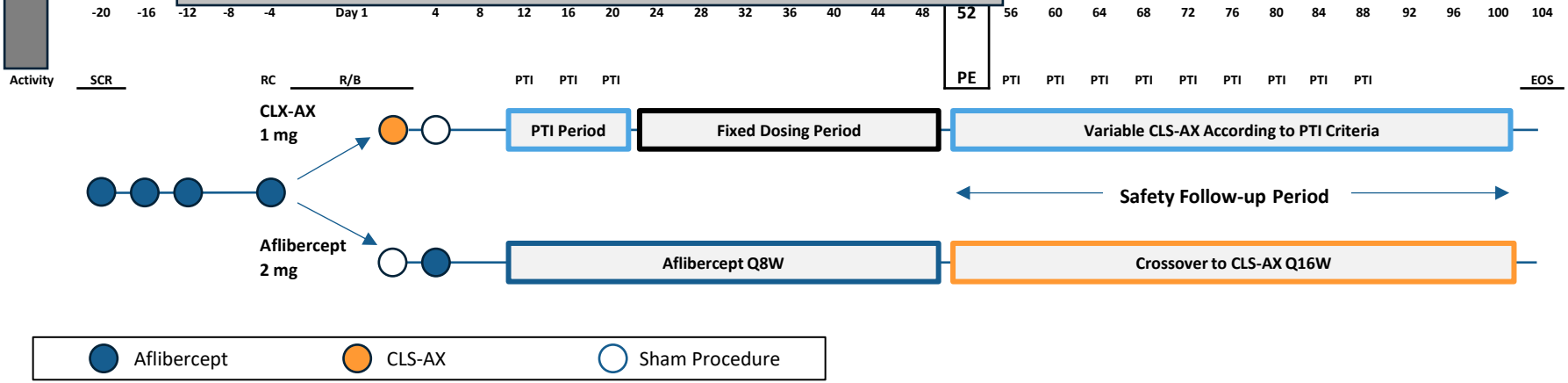
- Participants will be randomized 1:1 to CLS-AX 1 mg or aflibercept 2 mg on Day 1.
- Personalized Treatment Interval (PTI) Assessment: At Weeks 12, 16, and 20, participants will undergo an assessment of disease activity based on PTI criteria. If the criteria were not met, the participants will be given 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 2 Program Designed to Potentially Reduce Regulatory Risk and ... in Wet AMD

Target Patient Population:
- **Treatment naïve**

Designed to increase commercial value



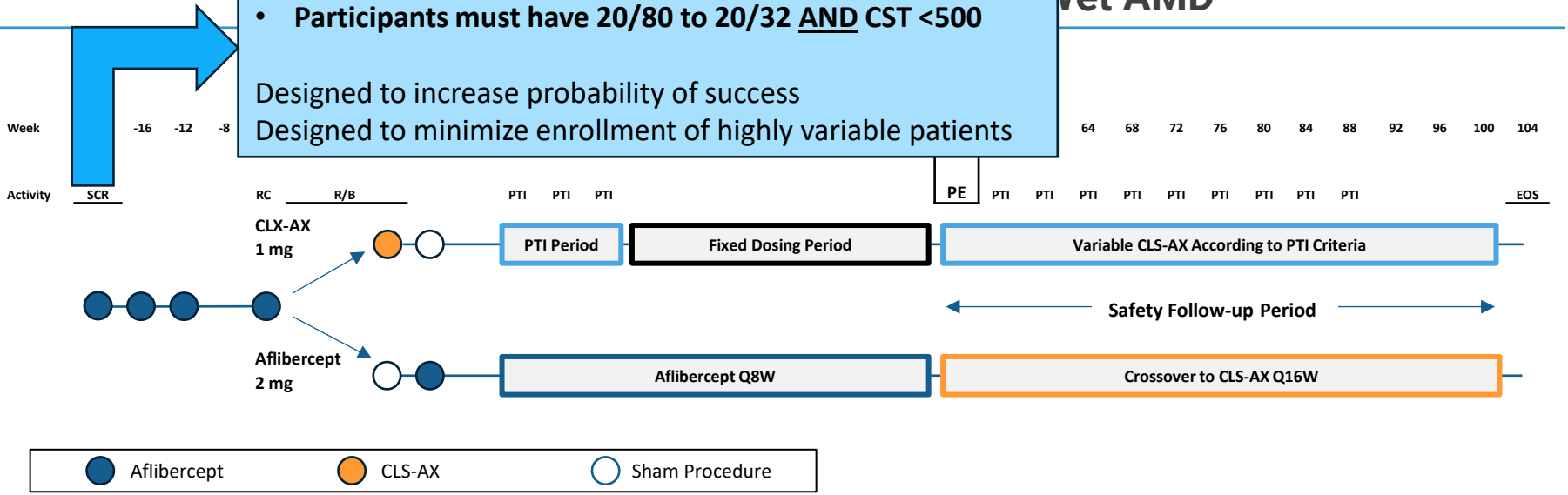
- Participants will be randomized 1:1 to CLS-AX 1 mg or aflibercept 2 mg on Day 1.
- Personalized Treatment Interval (PTI) Assessment: At Weeks 12, 16, and 20, participants will undergo an assessment of disease activity based on PTI criteria. If the criteria were not met, the participants will be given 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 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



- 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.

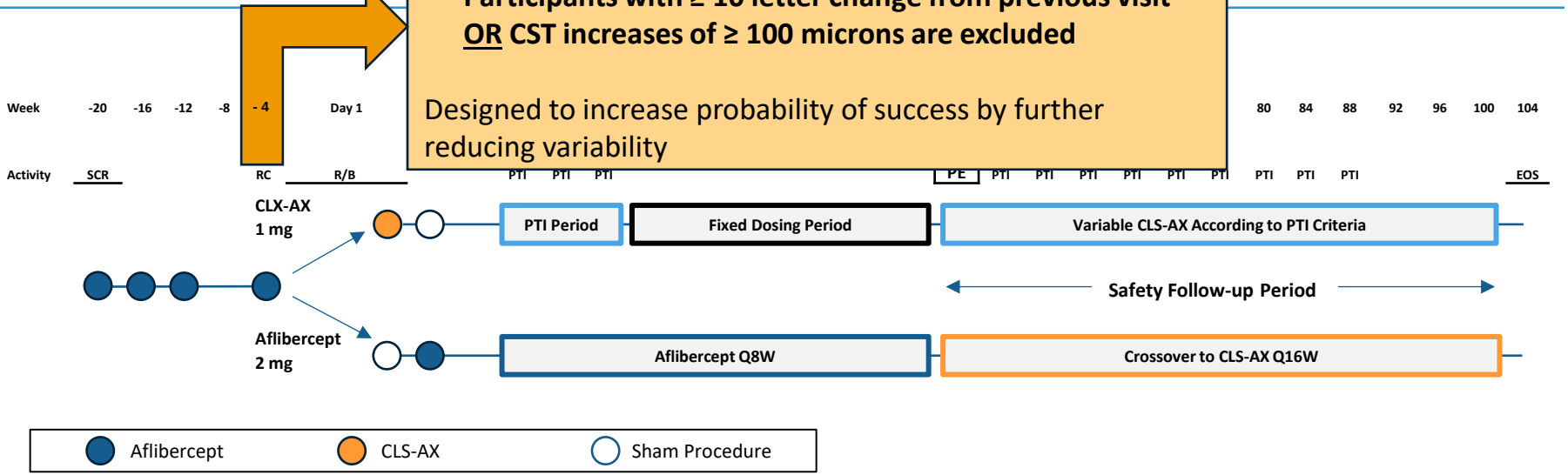
Abbreviations: SCR = Screening Visit; RC = Randomization Criteria; R/B = Randomization/Baseline; PE = Primary Endpoint;

CLS-AX Phase 3 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**

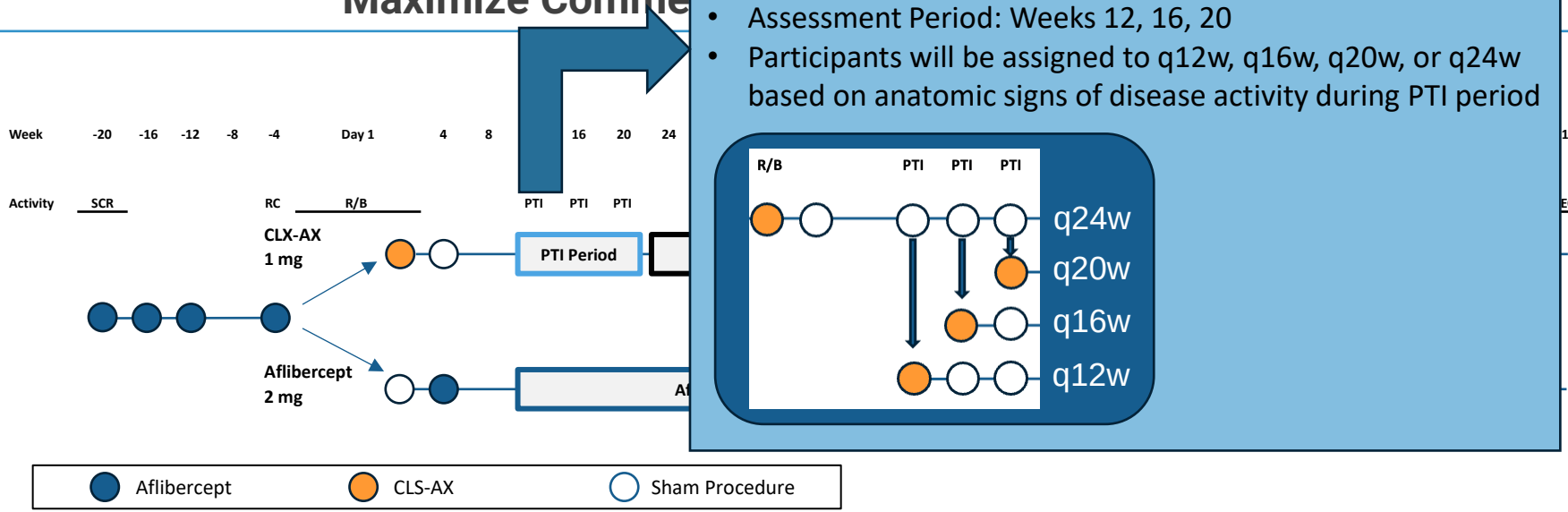
Designed to increase probability of success by further reducing variability



- 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;

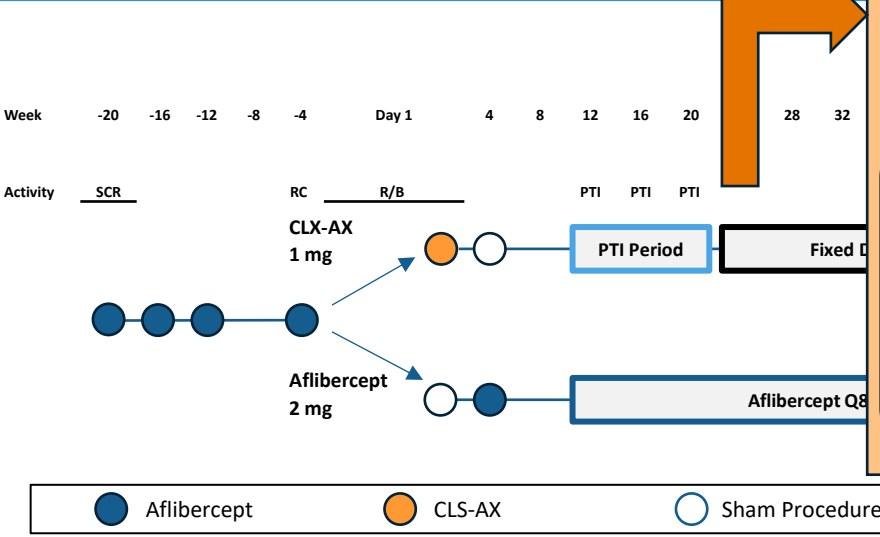
CLS-AX Phase 3 Program Designed to Potentially Reduce Regulatory Risk and Maximize Comme



- 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.

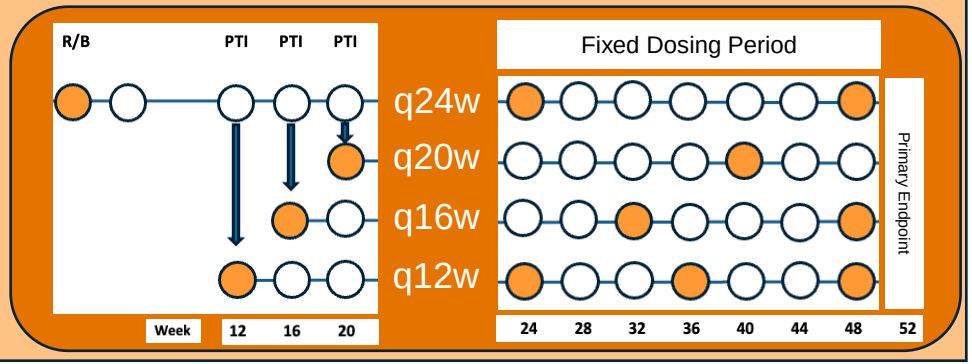
Abbreviations: SCR = Screening Visit; RC = Randomization Criteria; R/B = Randomization/Baseline; PE = Primary Endpoint;

CLS-AX Phase 3 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)



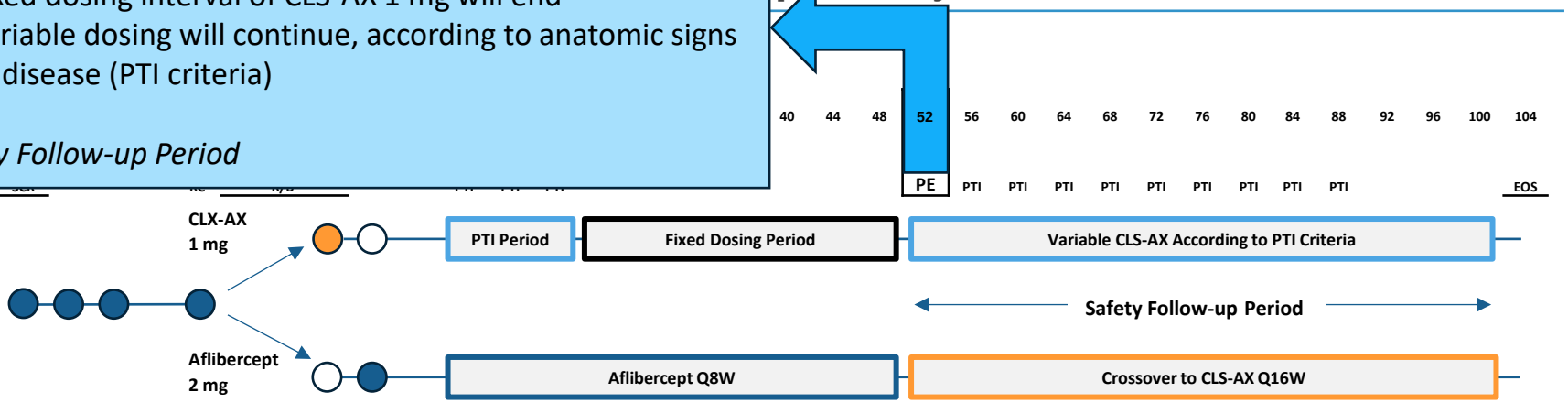
- Participants will be randomized 1:1 to CLS-AX 1 mg or aflibercept 2 mg on Day 1.
- Personalized Treatment Interval (PTI) Assessment: At Weeks 12, 16, and 20, participants will undergo an assessment of disease activity based on PTI criteria. If the criteria were not met, the participants will be given CLS-AX every 24 weeks.
- Fixed Dosing Period: Once the treatment interval is determined in the PTI period, the participant will stay at that interval until week 52 (primary endpoint). For instance, if the participant 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 Program Designed to Potentially Reduce Regulatory Risk and ...pportunity 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.

- 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;

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

Why Flexible Dosing Matters

- Wet AMD is a chronic disease requiring numerous injections to maintain vision and stabilize the disease
- We know from clinical experience that patients require differing frequency of treatment to stabilize their disease
- 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)

Planned 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.

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)

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.

Pipeline Opportunities

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 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

CLEARSIDE BIOMEDICAL

Nasdaq: CLSD