CLEARSIDE BIOMEDICAL

CASIS

OASIS Phase 1/2a Clinical Trial

3-Month Final & 6-Month Interim Results

November 9, 2022

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 forwardlooking 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, 2021, filed with the SEC on March 11, 2022, 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.

OASIS (3 Month) and Extension Study (6 Month, Interim Data) Cohorts 3 and 4: Promising CLS-AX Safety Results, Durability and Biologic Effect

SAFETY RESULTS

- Excellent safety profile at all doses and timepoints
- No Serious Adverse Events
- No dose limiting toxicities
- No Adverse Events from inflammation

DURABILITY

In OASIS, to 3 months:

- ≥73% reduction in treatment burden
- In Extension Study, to 6 months (interim data):
- ≥90% reduction in treatment burden

CASIS

BIOLOGIC EFFECT

- Stable mean Best Corrected Visual Acuity (BCVA)
- Stable mean Central Subfield Thickness (CST)
- On optical coherence tomography (OCT), anatomical signs of tyrosine kinase inhibitor (TKI) biologic effect were observed in anti-VEGF treatment-experienced sub-responders

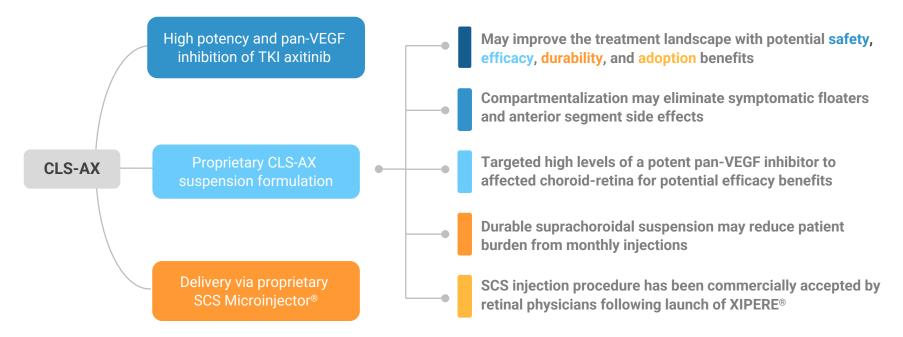
NEXT STEPS

- Follow remaining patients in Extension Study with final data expected in Q1 2023
- Initiate Phase 2 clinical trial in Q1 2023



CLS-AX (axitinib injectable suspension) for Suprachoroidal Use

Leveraging a Highly Potent Pan-VEGF Inhibitor with Suprachoroidal Delivery



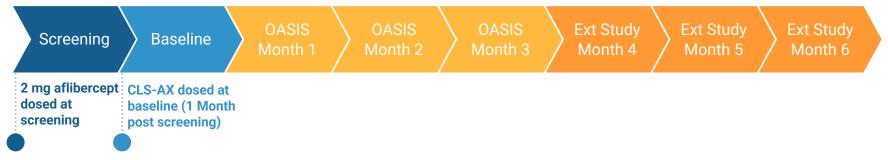


Axitinib is a tyrosine kinase inhibitor (TKI) | XIPERE® (triamcinolone acetonide injectable suspension), for suprachoroidal use has received U.S. FDA Approval. Please see Important Safety Information for XIPERE in the Full Prescribing Information: https://www.bauschhealth.com/Portals/25/Pdf/Pl/XIPERE-Pl.pdf. | Source: Viral S. Kansara, Leroy W. Muya, Thomas A. Ciulla; Evaluation of Long-Lasting Potential of Suprachoroidal Axitinib Suspension Via Ocular and Systemic Disposition in Rabbits. *Trans. Vis. Sci. Tech.* 2021;10(7):19.

OASIS and Extension Study: CLS-AX Phase 1/2a Clinical Trial in Treatment-Experienced Wet AMD Patients with Active Disease at Screening

TRIAL DESIGN AND OBJECTIVES

- Open-label study with a primary endpoint to evaluate safety and tolerability of escalating single doses of CLS-AX administered through suprachoroidal injection following IVT aflibercept
- Wet AMD patients with >2 anti-VEGF treatments in the prior 4 months, reading center confirmation of persistent active disease
- Dose-escalation of CLS-AX (in mg): Cohort 1 at 0.03; Cohort 2 at 0.1; Cohort 3 at 0.5; Cohort 4 at 1.0
- · Secondary endpoints: visual function, ocular anatomy, and need for additional treatment
- Monthly assessment for additional treatment with aflibercept: loss from best measurement of <a>10 letters in BCVA with exudation; increase in CST <a>75 microns; a vision-threatening hemorrhage
- 6-Month follow-up after CLS-AX via a 3-month Extension Study





Note: aflibercept is dosed via intravitreal injection (IVT); CLS-AX is dosed via suprachoroidal injection | clinicaltrials.gov NCT# 04626128

Active Disease definition: Active subfoveal choroidal neovascularization (CNV) secondary to AMD in the study eye confirmed by an independent reading center as leakage from a subfoveal CNV on fluorescein angiography and intra-retinal or sub-retinal fluid on OCT central subfield)

OASIS Enrolled Heavily anti-VEGF Treatment-Experienced Wet AMD Patients

Patients were sub-responders with active disease at screening confirmed by reading center

Why target this patient population instead of treatment naïve or patients with controlled disease?

- Patients have a high need for effective therapy with lower treatment burden
- Minimizes the risk of false signals of biologic effect
- Facilitates assessment for biological effect in a difficult-to-treat nAMD patient population
- Facilitates assessment of an appropriate dose, not only based on both safety but also on biologic effect
- Represents a significant number of patients in clinical practice, with >30% sub-responders
- De-risks future clinical studies

Desired outcomes in this heavily treated patient population:

- · Demonstrate safety and tolerability of CLS-AX
- · Maintain stability of visual acuity and central subfield thickness with lower treatment burden

Enrolling difficult to treat anti-VEGF sub-responders allowed observation of possible signs of biologic effect while minimizing false signals



Core et at. Predominantly Persistent Intraretinal Fluid in the Comparison of Age-related Macular Degeneration Treatments Trials. Ophthalmol Retina. 2022 Sep;6(9):771-785. | Waldstein et al. Morphology and visual acuity in aflibercept and ranibizumab therapy for neovascular age-related macular degeneration in the VIEW trials. Ophthalmology 2016;123:1521-1529. Active Disease definition: Active subfoveal choroidal neovascularization (CNV) secondary to AMD in the study eye confirmed by an independent reading center as leakage from a subfoveal CNV on fluorescein angiography and intra-retinal or sub-retinal fluid on OCT central subfield)

Enrolled Patients All with Active Disease at Screening and Confirmed by Independent Reading Center

Demographics and Wet AMD History

Wet AMD Disease Characteristics	COHORT 1: 0.03 mg	COHORT 2: 0.1 mg	COHORT 3: 0.5 mg	COHORT 4: 1.0 mg
No. of participants	6	5	8	8
Mean age (range), years	81.8 (66-93)	78.2 (65-90)	86.3 (75-97)	76.5 (66-83)
Mean baseline best corrected visual acuity (range), letters	59.0 (29-74)	65.6 (52-75)	58.5 (37-74)	65.8 (50-74)
Mean baseline central subfield retinal thickness (range), μm	231.2 (208-294)	209.4 (184-227)	202.0 (175-238)	218.8 (152-295)
Mean duration of wAMD diagnosis (range), months	50.13 (12.4-110.3)	49.78 (24.7-81.3)	66.64 (6.8-102.1)	48.21 (4.5-132.8)
Number of anti-VEGF injections reported prior to CLS-AX administration on Day 1, mean (range)	26.8 (7-41)	24.2 (12-39)	37.0 (6-90)	28.8 (5-89)
Annualized number of anti-VEGF injections prior to CLS-AX administration on Day 1, mean (range)	9.36 (6.3-12.7)	9.54 (5.4-12.2)	8.47 (4.9-11.8)	11.96 (8.9-13.6)



Safety Results

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CLS-AX Demonstrated a Positive Safety Profile in All Four Cohorts

3-Month Final Data & 6-Month Interim Data

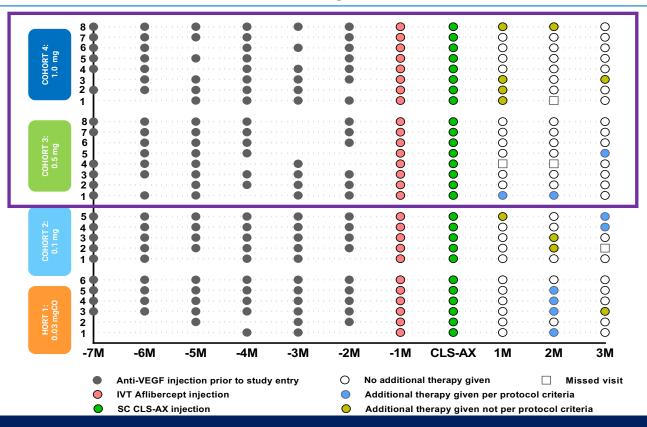
SAFETY RESULTS

Excellent Safety Profile at all doses and timepoints

- No serious adverse events (SAEs)
- No treatment emergent adverse events (TEAEs) related to study treatment
- No dose limiting toxicities
- No adverse events related to inflammation, vasculitis or vascular occlusion
- No vitreous "floaters" or dispersion of CLS-AX into the vitreous
- No retinal detachment
- No endophthalmitis
- No adverse events related to intraocular pressure

Durability

OASIS (3 Month): Prior Anti-VEGF Therapies and <u>All Additional Therapies</u>

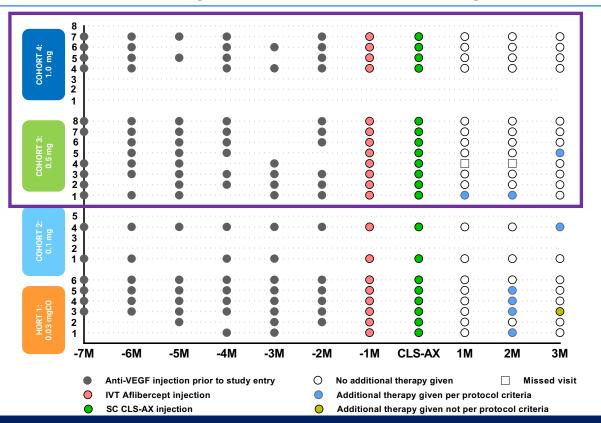


DURABILITY

Cohorts 3 & 4:

11/16 (69%) of patients did not receive additional therapy to 3 months

OASIS (3 Month): Prior Anti-VEGF Therapies and <u>Additional Therapies Per Protocol Criteria</u>





Cohorts 3 & 4:

11/12 (92%) of patients did not receive additional therapy to 3 months



OASIS (3 Month): CLS-AX Reduced Treatment Burden Across All Cohorts

Reduction in Treatment Burden All Therapies

Reduction in Treatment Burden Therapies Per Protocol Criteria

Cohort	Number of Participants	Avg Monthly Injections Before CLS-AX Administration	Avg Monthly Injections After CLS-AX Administration	% Reduction	Cohort	Number of Participants	Avg Monthly Injections Before CLS-AX Administration	Avg Monthly Injections After CLS-AX Administration	% Reduction
4	8	0.88	0.25	72.9	4	4	0.83	0	100
3	8	0.75	0.13	79.2	3	8	0.75	0.13	79.2
2	5	0.93	0.37	63.3	2	2	0.83	0.17	83.3
1	6	0.94	0.28	69.4	1	6	0.94	0.28	69.4

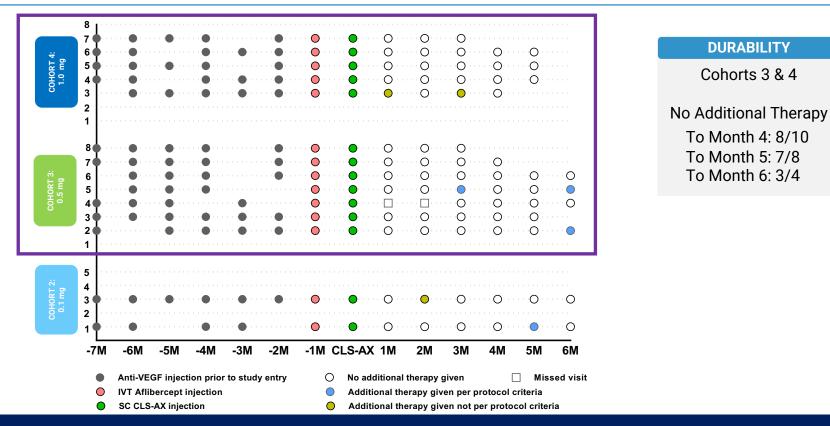
73 – 100% Reduction in Treatment Burden in Cohorts 3 and 4



Note: Average Monthly Injections Before CLS-AX Administration = # treatments three months prior / 3. Average Monthly Injections After CLS-AX Administration = # treatments / # months of follow-up. % Reduction = Average of individual reductions calculated as (after – before) / before × 100%. Source: Clearside data on file.

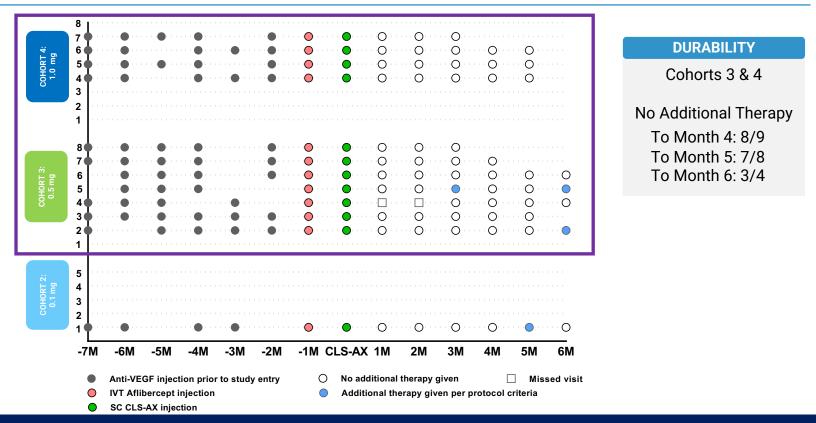
Interim Data

Extension Study (6 Month, Interim Data): Prior Anti-VEGF Therapies and <u>All Additional Therapies</u>





Extension Study (6 Month, Interim Data): Interim Data Prior Anti-VEGF Therapies and <u>Additional Therapies Per Protocol Criteria</u>



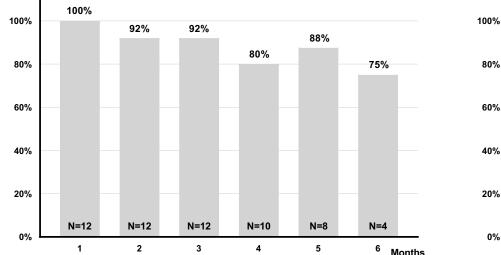


Extension Study (6 Month, Interim Data): Interim Data Supplemental Anti-VEGF Injection-Free Rate up to Each Visit in Cohorts 3 and 4

Extension Study Interim Data: 75% of Patients with No Additional Therapy to Month 6

1

2



All Therapies

100% 100% 100% 89% 88% 80% 75% 60% 40% 20% N=11 N=11 N=11 N=9 N=8 N=4

3

4

5

6

Months

Therapies Per Protocol Criteria



Interim Data

Extension Study (6 Month, Interim Data): CLS-AX Reduced Treatment Burden Across Cohorts

Reduction in Treatment Burden All Therapies

Reduction in Treatment Burden Therapies Per Protocol Criteria

Cohort	Number of Participants	Avg Monthly Injections Before CLS-AX Administration	Avg Monthly Injections After CLS-AX Administration	% Reduction	Cohort	Number of Participants	Avg Monthly Injections Before CLS-AX Administration	Avg Monthly Injections After CLS-AX Administration	% Reduction
4	5	0.87	0.10	90.0	4	4	0.83	0	100
3	7	0.81	0.07	90.0	3	7	0.81	0.07	90.0
2	2	0.83	0.17	79.2	2	1	0.67	0.17	75.0

90 - 100% Reduction in Treatment Burden in Cohorts 3 and 4

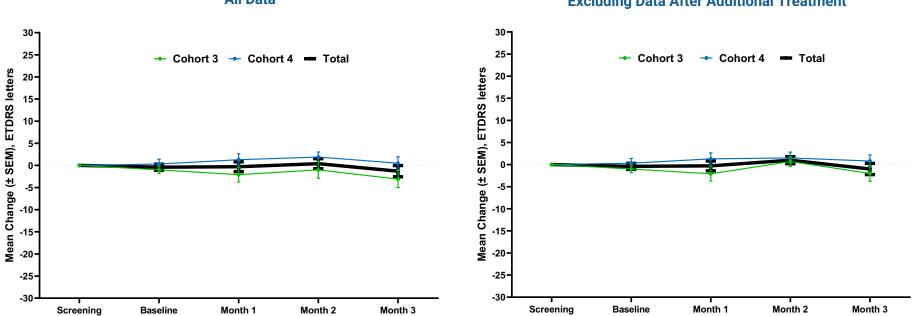


Note: Average Monthly Injections Before CLS-AX Administration = # treatments six months prior/ 6. Average Monthly Injections After CLS-AX Administration = # treatments / # months of follow-up. % Reduction = Average of individual reductions calculated as (after – before) / before × 100%. Source: Clearside data on file. | Extension Study interim data as of October 27, 2022.

Biologic Effect in Cohorts 3 & 4

OASIS (3 Months): **Stable Visual Acuity**

Mean Best Corrected Visual Acuity Letter Score, Change from Screening



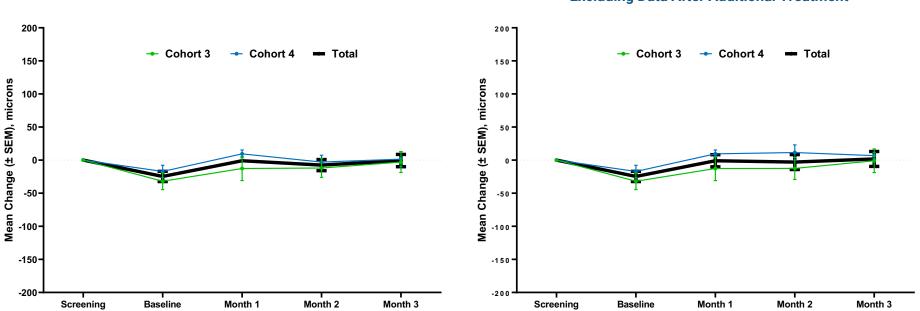
All Data

Source: Clearside data on file

Excluding Data After Additional Treatment

OASIS (3 Months): Stable Central Subfield Thickness

Mean Central Subfield Thickness, Change from Screening



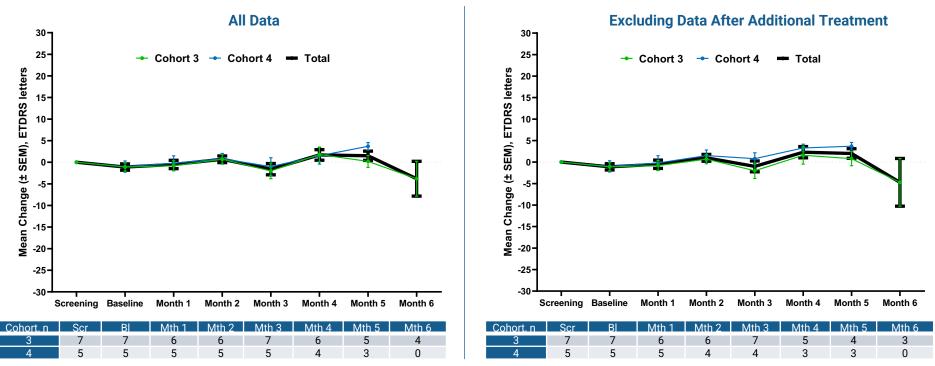
Excluding Data After Additional Treatment

All Data

Interim Data

Extension Study (6 Month, Interim Data): Stable Visual Acuity

Mean Best Corrected Visual Acuity Letter Score, Change from Screening

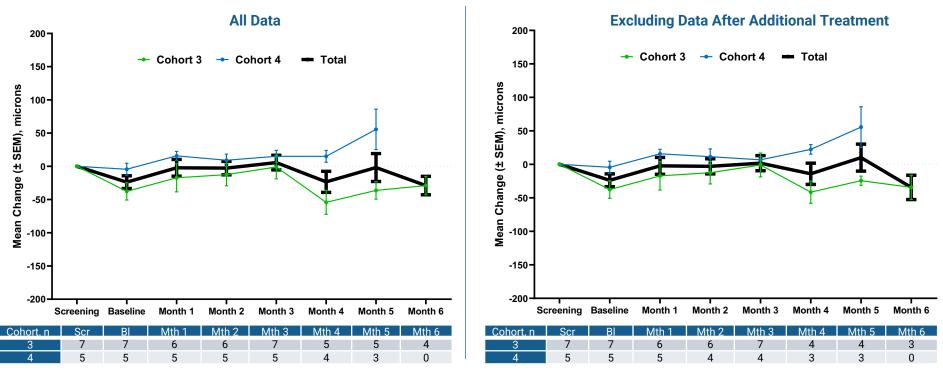




Interim Data

Extension Study (6 Month, Interim Data): Stable Central Subfield Thickness

Mean Central Subfield Thickness, Change from Screening



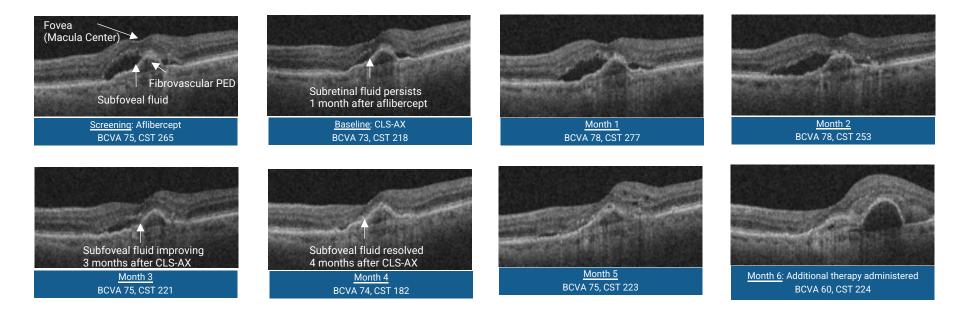


Case Studies

an farmer and a survey

6 Month Case Study: CLS-AX Demonstrated Biologic Effect in anti-VEGF Sub-responder

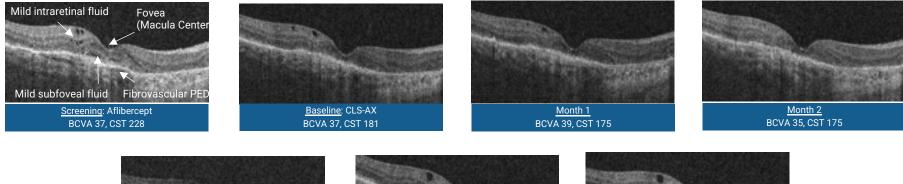
Cohort 3, Subject 2: 89 prior anti-VEGF injections with persistent subfoveal fluid 1 month after aflibercept at screen Subretinal fluid gradually resolves through 4 months after CLS-AX with stable BCVA and improved CST





5 Month Case Study: Durable Stability After CLS-AX

Cohort 3, Subject 3: 66 prior anti-VEGF injections with mild subfoveal and intraretinal fluid at screen Stable anatomy, BCVA and CST for 5 months after CLS-AX with no additional therapy (Month 6 visit pending)

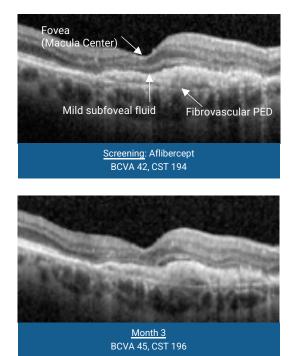


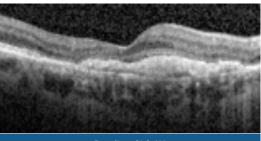




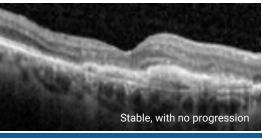
6 Month Case Study: Durable Stability After CLS-AX

Cohort 3, Subject 4: 15 prior anti-VEGF injections with mild subfoveal fluid at screen Stable anatomy, BCVA and CST for 6 months after CLS-AX with no additional therapy





<u>Baseline</u>: CLS-AX BCVA 45, CST 175

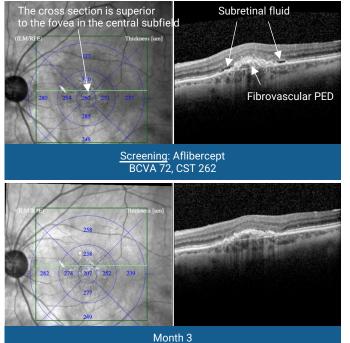


Month 6: BCVA 46 CST 194

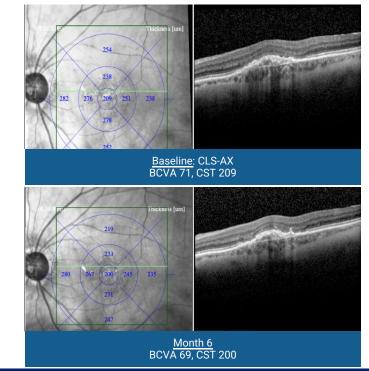


6 Month Case Study: Durable Stability After CLS-AX

Cohort 3, Subject 6: 50 prior anti-VEGF injections with persistent subretinal fluid in superior central subfield Stable anatomy, BCVA and CST for 6 months after CLS-AX with no additional therapy



<u>Month 3</u> BCVA 71, CST 207





Summary and Next Steps

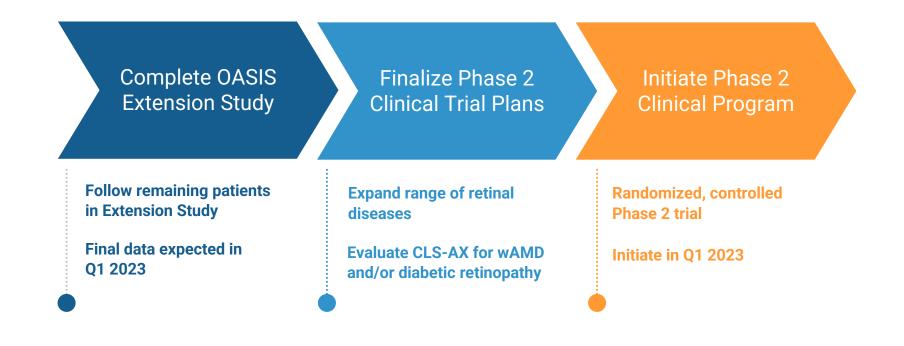
CLS-AX in Suprachoroidal Space Demonstrates Promising Safety Results, Durability and Biologic Effect in Anti-VEGF Treatment Experienced Sub-responders

	OASIS Results	Competitive Advantages
Safety (All Cohorts)	 Excellent Safety Profile at all doses and timepoints No SAEs, No TEAEs related to study treatment No dose limiting toxicities No AEs related to inflammation, vasculitis or vascular occlusion No vitreous "floaters" or dispersion of CLS-AX into the vitreous No retinal detachments or endophthalmitis No AEs related to intraocular pressure 	 As a well-characterized small molecule, less risk for inflammation than a novel biologic agent No need for an operating room setting No risk of implant migration and very low risk of vitreous "floaters" or haze SCS injection procedure commercially accepted by retinal physicians following launch of XIPERE[®]
Durability (Cohorts 3&4)	 In OASIS, to 3-month timepoint (N=16): 69% of patients did not receive additional therapy 92% of patients did not receive additional therapy per protocol ≥73% reduction in treatment burden In Extension Study interim data (N=12): To Month 5: 88% (7/8) of patients did not receive addl therapy To Month 6: 75% (3/4) of patients did not receive addl therapy ≥90% reduction in treatment burden 	 CLS-AX showed preliminary signs of durability favorably comparing to other current and investigational intravitreally injected biologic agents Based on interim extension data at higher doses, CLS-AX suprachoroidal suspension demonstrated it may have durability of effect that favorably compares to other extended release TKI formulations
Biologic Effect (Cohorts 3&4)	 CLS-AX showed signs of biologic effect: Stable mean BCVA Stable mean CST On OCT, anatomical signs of TKI biologic effect were observed in anti-VEGF treatment-experienced sub-responders 	 The most potent TKI in nAMD trials, differentiated from focused VEGF-A blockade Targeted high levels to affected choroid-retina may further leverage efficacy, particularly in anti-VEGF sub-responders



Source: Clearside data on file. | Extension Study interim data as of October 27, 2022 | XIPERE[®] (triamcinolone acetonide injectable suspension), for suprachoroidal use received U.S. FDA Approval in October 2021. Please see Important Safety Information for XIPERE in the Full Prescribing Information, 2022: https://www.bauschhealth.com/Portals/25/Pdf/PI/XIPERE-PI.pdf.

Plans for Continued Progress with CLS-AX





Arshad M. Khanani, MD, MA, FASRS

Sierra Eye Associates

Managing Partner Director of Clinical Research Director of Fellowship

University of Nevada, Reno School of Medicine

Clinical Associate Professor





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Appendix /

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



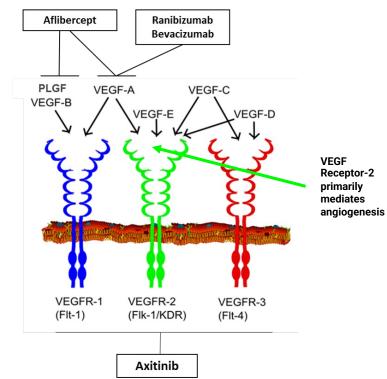
- Axitinib's intrinsic pan-VEGF inhibition through receptor blockade
- Approved treatments are focused VEGF-A inhibitors

Inhibits VEGFR-1, VEGFR-2, VEGFR-3 receptors

- More active than anti-VEGF-A in *in-vitro* angiogenesis model¹⁻²
- Highly potent tyrosine kinase inhibitor (TKI)
 - >10x more potent than other TKIs in preclinical studies
 - Better ocular cell biocompatibility than other TKIs³
 - More active than other TKIs for experimental corneal neovascularization in preclinical models

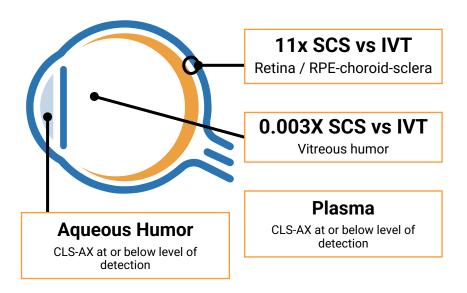


Preclinical data showed axitinib inhibition and regression of angiogenesis





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/wijm/2014.008. ISSN 2002-4436. Public Domain. CLS-AX Injected Suprachoroidally Provides Targeted Delivery Relative to Intravitreal Injection at Same Dose

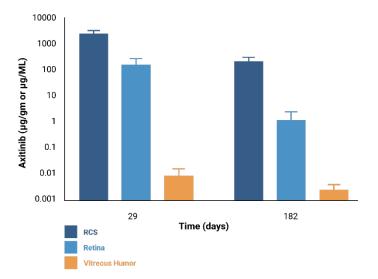


Rabbit Model Values: area under the curve ratios, SCS / IVT SCS : 1 mg/eye, 100 μ L. | IVT: 1 mg/eye, 25 μ L

Single bilateral injection, 1-wk rabbit PK studies

CLS-AX has Potential for Meaningful Durability CLS-AX Levels to 6 Months

High Retina Levels: Sufficient to block VEGF pathway Low Plasma Levels: <1 ng/mL



Rabbit toxicology study with single bilateral suprachoroidal injection of axitinib, 1.05 mg/eye (n=4 eyes/ timepoint)



Sources: Viral S. Kansara, Leroy W. Muya, Thomas A. Ciulla; Evaluation of Long-Lasting Potential of Suprachoroidal Axitinib Suspension Via Ocular and Systemic Disposition in Rabbits. Trans. Vis. Sci. Tech. 2021;10(7):19. Abbreviations: SCS: Suprachoroidal Space | IVT: Intravitreal Injection | PK: Pharmacokinetic | RPE: Retinal pigment epithelium | RCS: RPE, Choroid, Sclera

Enrolled Patients All with Active Disease at Screening and Confirmed by Independent Reading Center

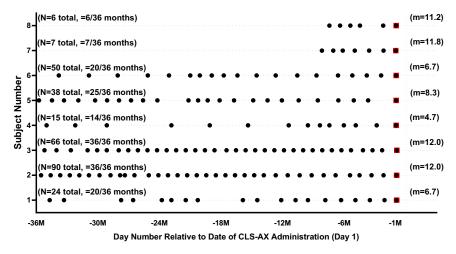
Demographics and Wet AMD History

Wet AMD Disease Characteristics	COHORT 1: 0.03 mg	COHORT 2: 0.1 mg	COHORT 3: 0.5 mg	COHORT 4: 1.0 mg	All Cohorts
No. of participants	6	5	8	8	27
Mean age (range), years	81.8 (66-93)	78.2 (65-90)	86.3 (75-97)	76.5 (66-83)	80.9 (65-97)
Mean baseline best corrected visual acuity (range), letters	59.0 (29-74)	65.6 (52-75)	58.5 (37-74)	65.8 (50-74)	62.1 (29-75)
Mean baseline central subfield retinal thickness (range), µm	231.2 (208-294)	209.4 (184-227)	202.0 (175-238)	218.8 (152-295)	214.8 (152-295)
Mean duration of wAMD diagnosis (range), months	50.13 (12.4-110.3)	49.78 (24.7-81.3)	66.64 (6.8-102.1)	48.21 (4.5-132.8)	54.39 (4.5-132.8)
Number of anti-VEGF injections reported prior to CLS-AX administration on Day 1, mean (range)	26.8 (7-41)	24.2 (12-39)	37.0 (6-90)	28.8 (5-89)	29.9 (5-90)
Annualized number of anti-VEGF injections prior to CLS-AX administration on Day 1, mean (range)	9.36 (6.3-12.7)	9.54 (5.4-12.2)	8.47 (4.9-11.8)	11.96 (8.9-13.6)	9.90 (4.9-13.6)



Anti-VEGF Treatments up to 3 Years Prior to Baseline CLS-AX Administration

COHORT 3: 0.5 mg

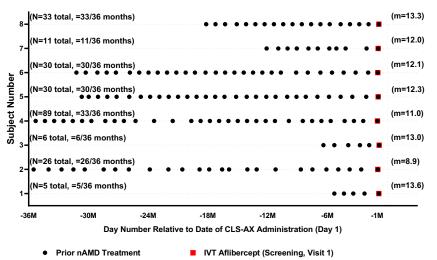


Prior nAMD Treatment
 IVT A

nent IVT Aflibercept (Screening, Visit 1)

(N=) Total number of nAMD treatments reported prior to Screening, within 36 months (m=) Annualized number of injections in the past 36 months defined as (total number of injections in 36 months prior to CLS-AX (Day 1)) / (minimum(3, (duration between first injection and Day 1)/365.25)).

COHORT 4: 1.0 mg



(N=) Total number of nAMD treatments reported prior to Screening, within 36 months (m=) Annualized number of injections in the past 36 months defined as (total number of injections in 36 months prior to CLS-AX (Day 1)) / minimum(3, (duration between first injection and Day 1)/365.25)).

JE Source: Clearside data on file

OASIS: Reason for Use of Additional Therapies

COHORT	SUBJECT #	ADDITIONAL THERAPY VISIT	REASON FOR ADDITIONAL THERAPY
	1	2 months post CLS-AX	BCVA with exudation
	3	2 months post CLS-AX	CST
COHORT 1: 0.03 mg (N=6)	3	3 months post CLS-AX	BCVA with exudation (not verified by reading center)
	4	2 months post CLS-AX	CST
	5	2 months post CLS-AX	BCVA with exudation
	2	2 months post CLS-AX	CST (not verified by reading center)
	3	2 months post CLS-AX	Macular hemorrhage (not verified by reading center)
COHORT 2: 0.1 mg (N=5)	4	3 months post CLS-AX	BCVA with exudation
	-	1 month post CLS-AX	CST (not verified by reading center)
	5	3 months post CLS-AX	BCVA with exudation
	1	1 month post CLS-AX	BCVA with exudation
COHORT 3: 0.5 mg (N=8)		2 months post CLS-AX	BCVA with exudation
	5	3 months post CLS-AX	CST
	1	1 month post CLS-AX	CST (not verified by reading center)
COHORT 4: 1.0 mg (N=8)	2	1 month post CLS-AX	CST (not verified by reading center)
	3	1 month and 3 month post CLS-AX	CST (not verified by reading center both times)
	8	1 month and 2 months post CLS-AX	Investigator discretion both times

Assessment for additional treatment with aflibercept:

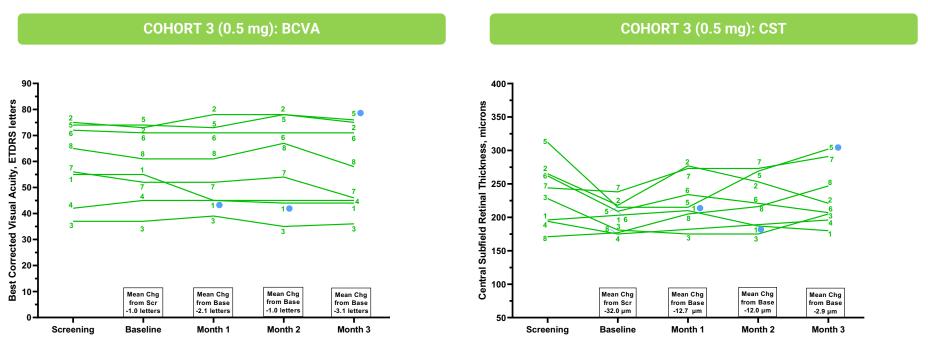
Red = not treated per protocol defined criteria

Decrease from best measurement of >10 letters in BCVA with exudation; Increase in CST >75 microns; A vision-threatening hemorrhage

ARSIDE Source: Clearside data on file.

Cohort 3:

Stable Best Corrected Visual Acuity and Central Subfield Thickness to 3 Months



Additional Therapy (reading center verified)

Additional Therapy (not reading center verified)

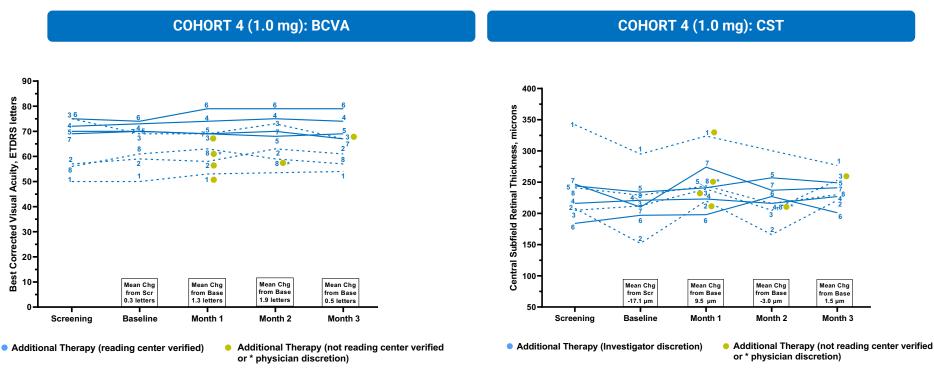
Additional Therapy (reading center verified)

Additional Therapy (not reading center verified)

Source: Clearside data on file

Cohort 4:

Stable Best Corrected Visual Acuity and Central Subfield Thickness to 3 Months



Dotted line = patient received additional therapy not per protocol (not reading center verified or physician discretion)

Extension Study: Demographics and Wet AMD History

Wet AMD Disease Characteristics	COHORT 2: 0.10 mg	COHORT 3: 0.50 mg	COHORT 4: 1.0 mg	All Cohorts
No. of participants	2	7	5	14
Mean age (range), years	74.0 (70-78)	87.9 (81-97)	79.6 (74-83)	82.9 (70-97)
Mean baseline best corrected visual acuity (range), letters	60.0 (52-68)	59.0 (37-74)	71.2 (69-74)	63.5 (37-74)
Mean baseline central subfield retinal thickness (range), µm	213.5 (200-227)	201.9 (175-238)	214.8 (197-234)	208.1 (175-238)
Mean duration of wAMD diagnosis (range), months	44.30 (33.9-54.7)	67.29 (6.8-102.1)	36.42 (6.1-103.4)	52.98 (6.1-103.4)
Number of anti-VEGF injections reported prior to CLS-AX administration on Day 1, mean (range)	23.0 (12-34)	38.9 (6-90)	33.2 (6-89)	34.6 (6-90)
Annualized number of anti-VEGF injections prior to Enrollment, mean (range)	8.81 (5.4-12.2)	8.84 (4.9-11.9)	12.01 (10.5-13.1)	9.97 (4.9-13.1)



Extension Study: Reason for Use of Additional Therapies (in Months 4, 5, 6)

COHORT	SUBJECT	ADDITIONAL THERAPY VISIT	REASON FOR ADDITIONAL THERAPY
COHORT 2: 0.10 mg (N=2)	1	5 months post CLS-AX	Macular hemorrhage
COHORT 3: 0.5 mg (N=7)	2	6 months post CLS-AX	BCVA with exudation
	5	6 months post CLS-AX	CST
COHORT 4: 1.0 mg (N=5)		No patients treated to Oct 27, 2022	

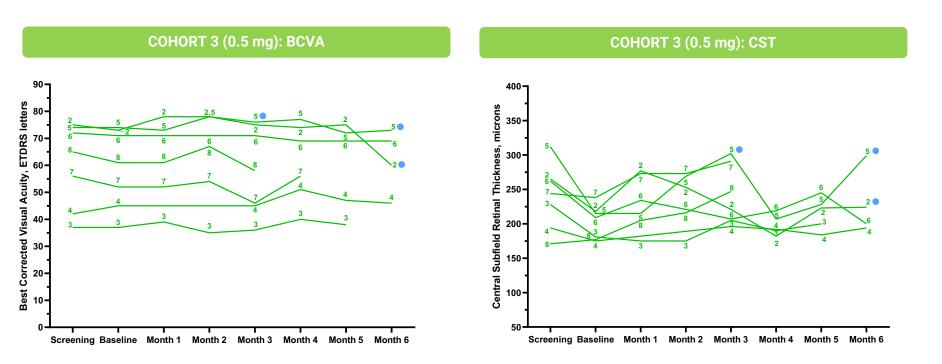
Assessment for additional treatment with aflibercept:

Decrease from best measurement of >10 letters in BCVA with exudation; Increase in CST >75 microns; A vision-threatening hemorrhage



Cohort 3 Interim Extension Study:

Stable Best Corrected Visual Acuity and Central Subfield Thickness Beyond 3 Months

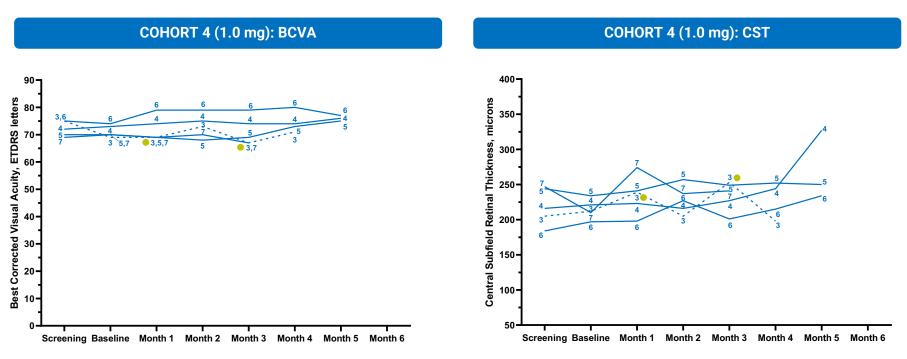


Additional Therapy (reading center verified)
 Additional Therapy (not reading center verified)
 Additional Therapy (reading center verified)
 Additional Therapy (not reading center verified)
 Dotted line = patient received additional therapy not per protocol (not reading center verified or physician discretion)



Cohort 4 Interim Extension Study:

Stable Best Corrected Visual Acuity and Central Subfield Thickness Beyond 3 Months



Additional Therapy (not reading center verified)

Dotted line = patient received additional therapy not per protocol (not reading center verified or physician discretion)

Additional Therapy (not reading center verified)

Arshad M. Khanani, MD, MA, FASRS

Managing Partner, Director of Clinical Research, and Director of Fellowship at Sierra Eye Associates

Clinical Associate Professor at the University of Nevada, Reno School of Medicine

Dr. Khanani founded the clinical research department at Sierra Eye Associates, which is now one of the leading clinical research centers in the country. He has served as a principal investigator for over 100 clinical trials and has been a top enroller in the country for multiple Phase 1-3 trials. In addition, Dr Khanani has been the first one to perform surgical procedures in multiple surgical clinical trials dealing with sustained delivery and gene therapy. He has over 75 scientific publications.

Dr. Khanani also serves as a member of national and international clinical trial steering committees as well as scientific advisory boards with the goal of bringing new treatment options for patients with retinal diseases. Dr. Khanani is frequently invited as a guest speaker at national and international meetings.

Dr. Khanani is an elected member of the Macula Society, Retina Society and has received numerous awards of distinction. In 2019, he received the Nevada Business Magazine Healthcare Heroes Physician of the Year award for his continued dedication to the field of ophthalmology. He has received the Senior Honor Award from the American Society of Retina Specialists (ASRS) and was also awarded the prestigious ASRS Presidents' Young Investigator Award in 2021.



