CLEARSIDE BIOMEDICAL

Corporate Presentation

May 2023

Forward-Looking Statements

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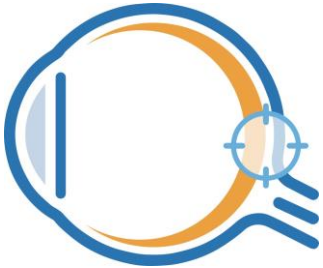
Developing and Delivering Treatments that Restore and Preserve Vision for Serious Back of the Eye Diseases

Versatile Therapeutic Platform

SCS Microinjector® with proprietary drug formulations target the suprachoroidal space

- **Proprietary Access to the Suprachoroidal Space (SCS®)**
- **First FDA Approved Product: XIPERE®**
- **Proprietary CLS-AX Phase 1/2 data in Wet AMD showed significant reduction in treatment burden and an excellent safety profile (OASIS)**
- **Phase 2b Wet AMD Clinical Trial to be initiated in Q2 2023 (ODYSSEY)**
- **External Collaborations for Pipeline Expansion**

Core Advantages of Treating Via the Suprachoroidal Space (SCS®)



TARGETED

for efficacy[1]

The back of the eye is the location of many irreversible and debilitating visual impairments

COMPARTMENTALIZED

for safety[2]

Drug is compartmentalized in the suprachoroidal space, which helps keep it away from non-diseased tissues and entirely behind the visual field

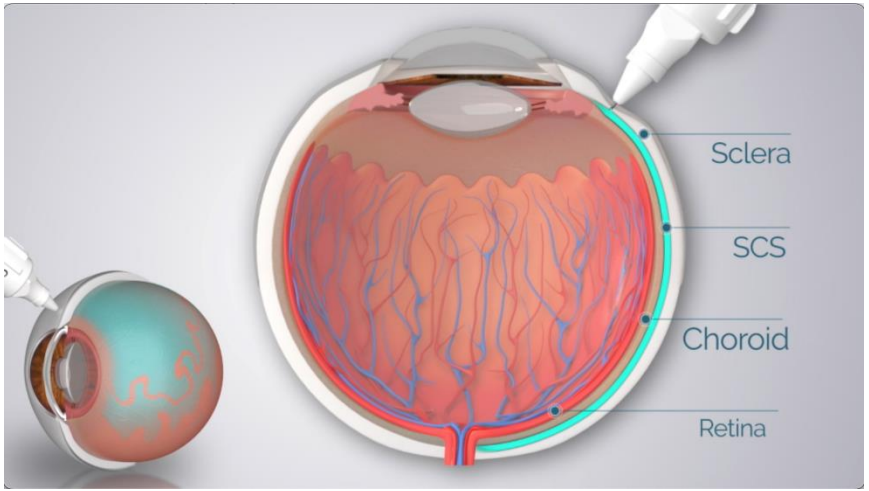
BIOAVAILABLE & PROLONGED DRUG LEVELS

for durability[3]

Fluid spreads circumferentially and posteriorly when injected within the suprachoroidal space, bathing the choroid and adjacent areas with drug

Source: 1. Rai UDJ, Young SA, Thrimawithana TR, et al. The suprachoroidal pathway: a new drug delivery route to the back of the eye. Drug Discov Today. 2015;20(4):491-495. ; 2. Chiang B, Jung JH, Prausnitz MR. The suprachoroidal space as a route of administration to the posterior segment of the eye. Adv Drug Deliv Rev. 2018;126:58-66. ; 3. Moisseiev E, Loewenstein A, Yiu G. The suprachoroidal space: from potential space to a space with potential. Clin Ophthalmol. 2016;10:173-178.

Clearside's SCS Microinjector®: The Only Commercially-Accepted Approach for Suprachoroidal Drug Delivery



SUPRACHOROIDAL SPACE INJECTION

Novel SCS Microinjector® shows a demonstrated ability for precise delivery into the suprachoroidal space

- **SCS injection procedure commercially accepted by retinal physicians following launch of XIPERE®**
  - Thousands of SCS injections performed
- **Safety profile comparable to intravitreal injections[1]**
  - No Serious Adverse Events (SAEs) involving lens injury, suprachoroidal hemorrhage, or endophthalmitis have been observed
- **6 clinical trials ongoing including partner programs**

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.*

XIPERE®: First FDA Approved Suprachoroidal Therapy Establishes Foundation for Small Molecule Suspension Pipeline

XIPERE®
(triamcinolone acetonide injectable suspension) 40 mg/mL

- Macular edema is the leading cause of vision loss in patients with non-infectious uveitis
- Commercialization and development partnerships With Bausch + Lomb and Arctic Vision to enhance value and expand patient access
- NDA approved on October 22, 2021
- Launched Q1 2022 in US by Bausch + Lomb

- First approved therapeutic delivered into the suprachoroidal space
- First therapy for macular edema associated with uveitis
- First commercial product developed by Clearside
- First trial for uveitic macular edema using visual acuity change as a primary endpoint*

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/PI/XIPERE-PI.pdf. | *Clearside's Phase 3 PEACHTREE Trial

Pioneers in the Suprachoroidal Space (SCS®) with Patented Technology

KEY INTELLECTUAL PROPERTY COMPONENTS

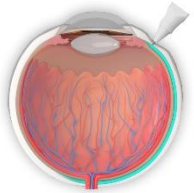
1. Comprehensive IP portfolio that includes protection of: SCS delivery technology, proprietary SCS Microinjector®, treatment of various conditions with SCS administration of therapeutic products
2. 26 U.S. and >70 European and International issued patents with multiple pending patent applications
3. Granted patents provide exclusivity for our delivery technology and product candidates to mid-2030s with pending applications potentially extending exclusivity beyond 2040

DEVICE PATENTS

- SCS Microinjector® features
- Methods of using SCS Microinjector® for drug delivery
- Device using an adjustable needle

DRUG PATENTS

- Administration of a variety of drugs to the suprachoroidal space by microinjection
- Administration of a variety of drugs to the eye by inserting a microinjector into the sclera

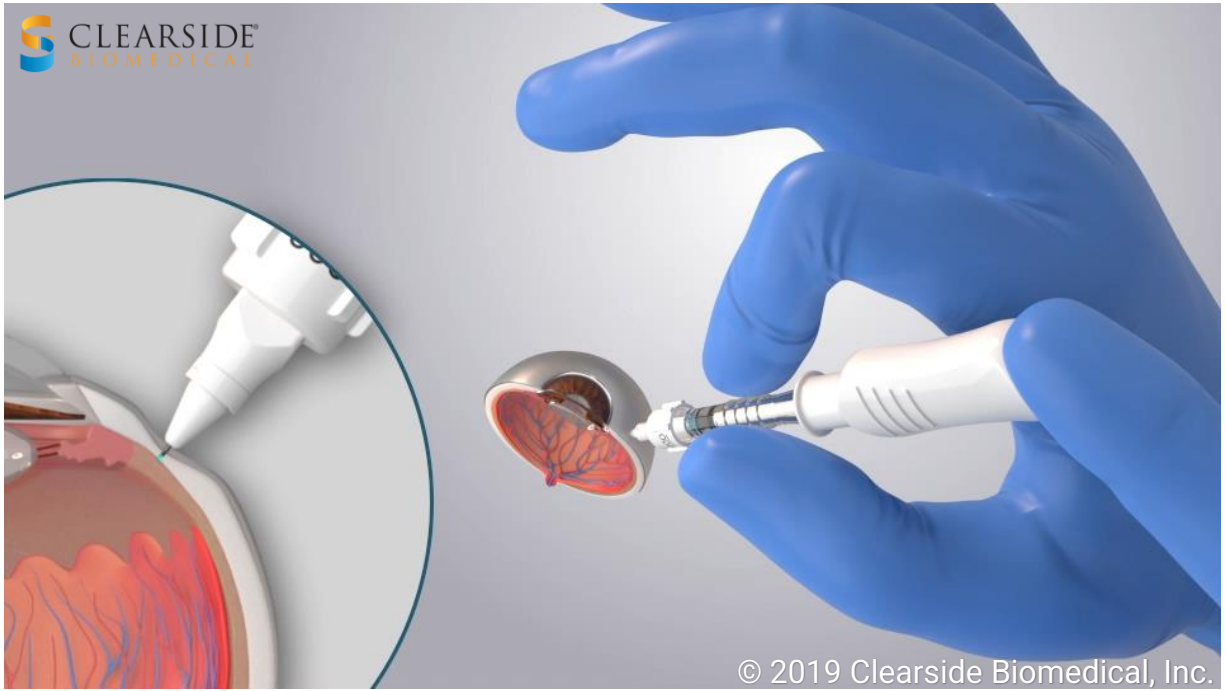


DISEASE PATENTS

- Methods of treating posterior ocular disorders by SCS administration

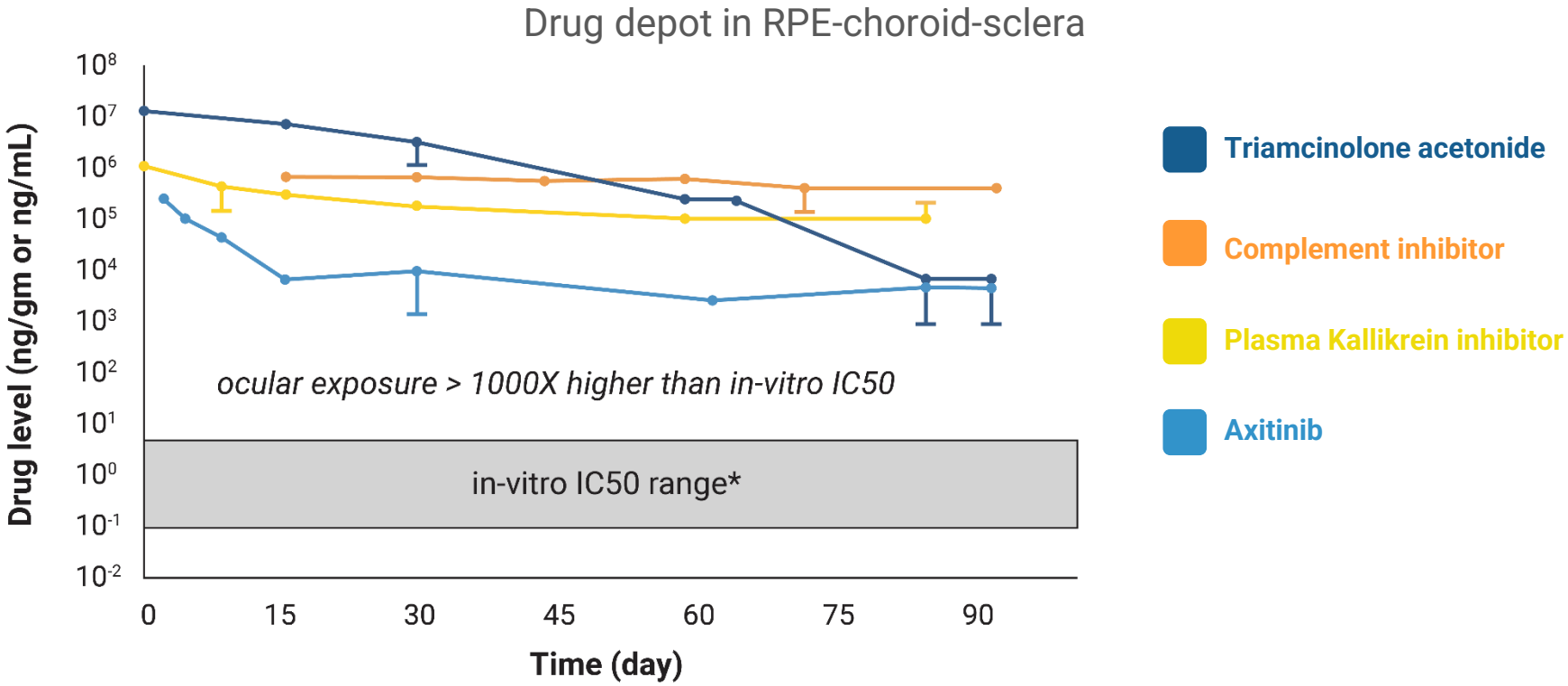
Suprachoroidal Delivery via SCS Microinjector®

Exclusive Access to the Back of the Eye Using Clearside's Proprietary SCS Microinjector®



CLS-AX Delivered with SCS Microinjector® for Wet AMD

Preclinical Data Supports Durability Potential of Small Molecule Suspensions Delivered into the Suprachoroidal Space

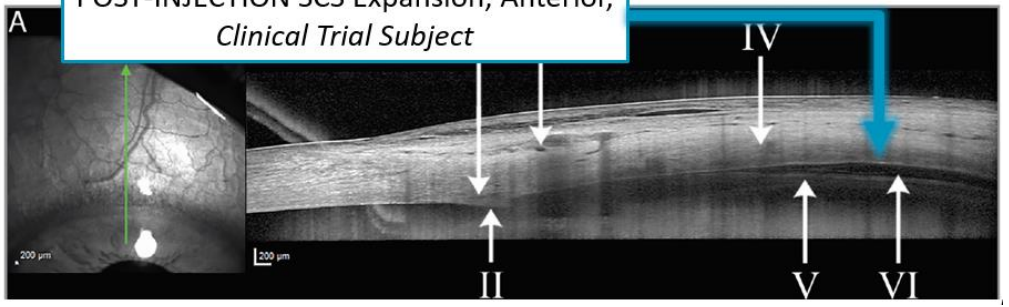


Sources for in-vitro IC50 range*: Stellato et al. *J Allergy Clin Immol.* 1999 volume 104, number 3, part 1 | Yuan et al. *Haematologica* 2017 Mar, 102(3) 466-475 | Inlyta, EMA 2012 May; CHMP assessment report | 2014 R13 HAE conference, Che, Wilson, Babu, Preclinical Characterization of BCX4161, an oral plasma kallikrein inhibitor, for the treatment of Hereditary Angioedema.

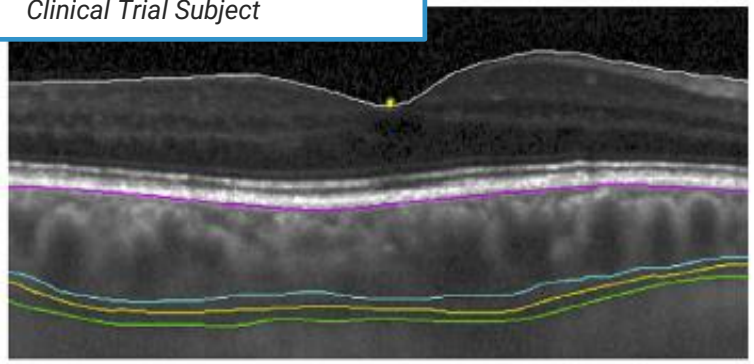
SCS Microinjector® Expands the SCS Circumferentially and Posteriorly to Deliver Drugs to the Macula

- A natural pressure gradient exists such that IOP > Anterior SCS Pressure > Posterior SCS Pressure
  - This gradient drives injectate towards the lower pressured posterior SCS
- OCT images demonstrate expansion of the SCS after injection, including the macula SCS in humans
- Suprachoroidally injected drug levels are similar peripherally and centrally in the retina and SCS in a preclinical model

POST-INJECTION SCS Expansion, Anterior, *Clinical Trial Subject*



POST INJECTION SCS Expansion, Posterior, *Clinical Trial Subject*



Sources: Lampen SIR, Khurana RN, Noronha G, Brown DM, Wykoff CC. Suprachoroidal Space Alterations Following Delivery of Triamcinolone Acetonide: Post-Hoc Analysis of the Phase 1/2 HULK Study of Patients With Diabetic Macular Edema. Ophthalmic Surg Lasers Imaging Retina. 2018;49(9):692-697. doi:10.3928/23258160-20180831-07,| Kansara VS, Cooper M, Sesenoglu-Laird O, Muya L, Moen R, Ciulla TA. Suprachoroidally Delivered DNA Nanoparticles Transfect Retina and Retinal Pigment Epithelium/Choroid in Rabbits. Transl Vis Sci Technol. 2020;9(13):21. Published 2020 Dec 15. doi:10.1167/tvst.9.13.21 | Leroy Muya, Viral Kansara, Thomas Ciulla; Pharmacokinetics and Ocular Tolerability of Suprachoroidal CLS-AX (axitinib injectable suspension) in rabbits. Invest. Ophthalmol. Vis. Sci. 2020;61(7):4925 | Emi K, Pederson JE, Toris CB. Hydrostatic pressure of the suprachoroidal space. Invest Ophthalmol Vis Sci. 1989;30(2):233-238. Willoughby et al., Choroidal Changes After SuprachoroidalInjection of Triamcinolone Acetonide in EyesWith Macular Edema Secondary to Retinal VeinOcclusion, American Journal of Ophthalmology, Feb 2018.

CLS-AX

(axitinib injectable suspension)

for Suprachoroidal Injection

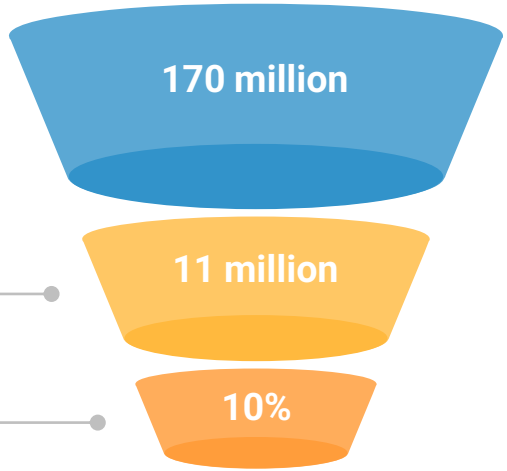
Age-Related Macular Degeneration (AMD)

A large and growing market opportunity

170 million AMD patients worldwide[1]

11 million U.S. AMD Patients[1]

~10% patients progress to wet AMD[2]

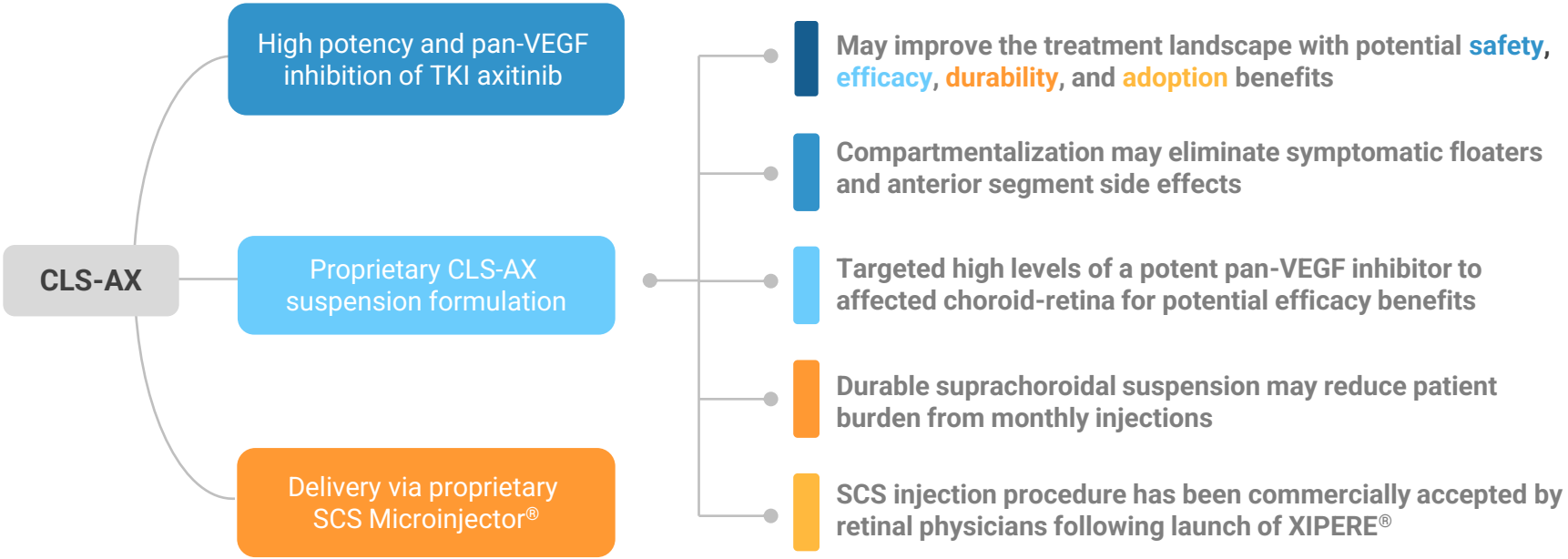


- AMD causes a progressive loss of central vision and is the most common cause of blindness in individuals over age 55[1]
  - Neovascular or Wet AMD accounts for the majority of blindness[1]
- U.S. prevalence expected to increase to 22 million by the year 2050[1]
- Global prevalence expected to increase to 288 million by the year 2040[1]
- Current treatments require frequent injections
  - Subset of patients with disappointing visual outcomes[2]

Sources: [1] Pennington, Katie L and DeAngelis, Margaret M, Eye and Vision, Epidemiology of age-related macular degeneration (AMD): associations with cardiovascular disease phenotypes and lipid factors, Dec 22, 2016.
[2] Prall, F Ryan and Ciulla, Thomas A, Medscape: Exudative (Wet) Age-Related Macular Degeneration (AMD), June 16, 2022.

CLS-AX (axitinib injectable suspension) for Suprachoroidal Use

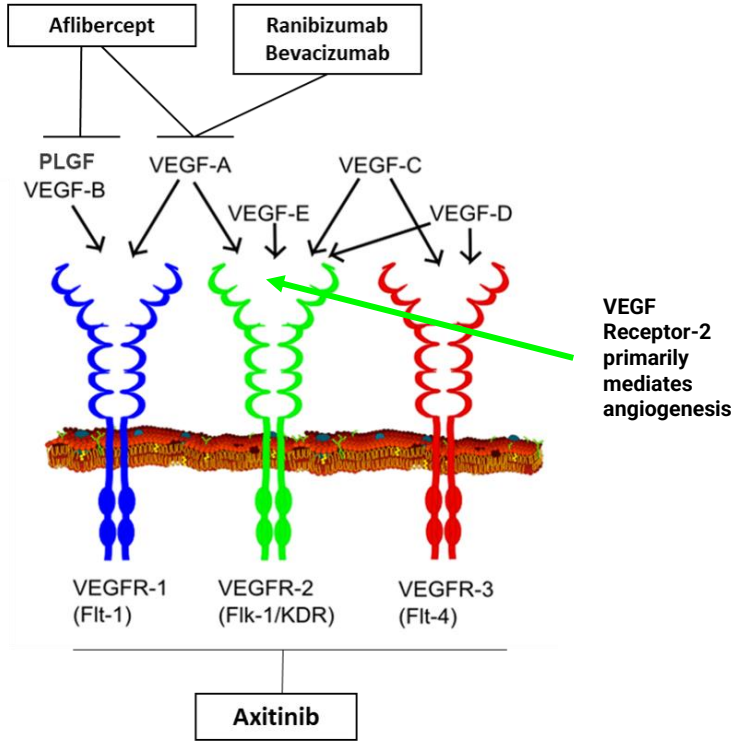
Leveraging a Highly Potent Pan-VEGF Inhibitor with Suprachoroidal Delivery



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/PI/XIPERE-PI.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.

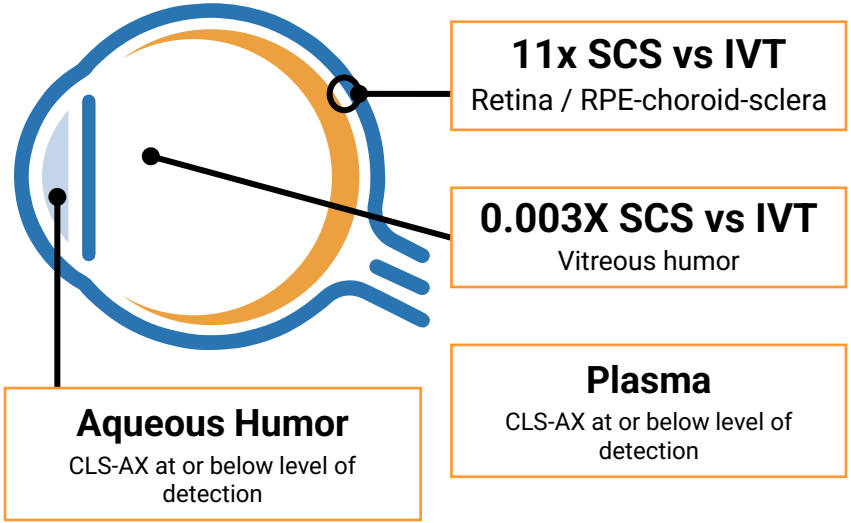
Axitinib: a Highly Potent, Pan-VEGF TKI to Treat Wet AMD

- 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 model[1-2]
- Highly potent tyrosine kinase inhibitor (TKI)
  - >10x more potent than other TKIs in preclinical studies
  - Better ocular cell biocompatibility than other TKIs[3]
  - 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. 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/wjm/2014.008. ISSN 2002-4436. Public Domain.

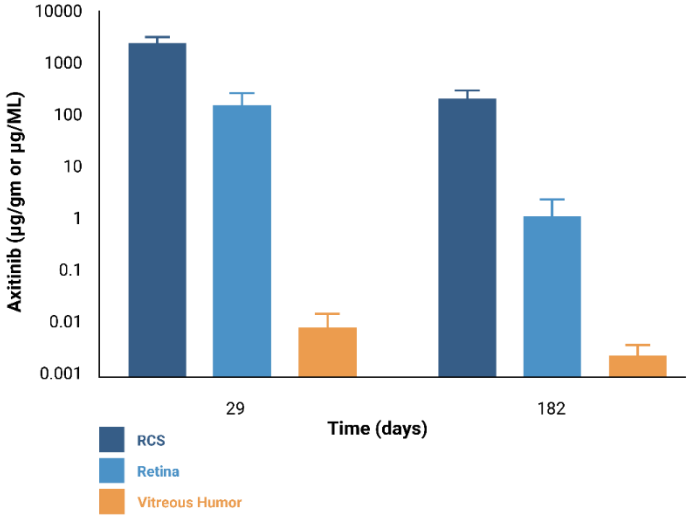
CLS-AX Injected Suprachoroidally Provides Targeted Delivery Relative to Intravitreal Injection at Same Dose



Rabbit Model Values: area under the curve ratios, SCS / IVT
SCS : 1 mg/eye, 100 µL. | IVT: 1 mg/eye, 25 µL
Single bilateral injection, 1-wk rabbit PK studies

CLS-AX has Potential for Meaningful Durability Based on 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)

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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 I RCS: RPE, Choroid, Sclera

OASIS Phase 1/2a Clinical Trial

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 ≥10 letters in BCVA with exudation; increase in CST >75 microns; a vision-threatening hemorrhage
- **Extension study:** A total of 6 months' follow-up for patients in Cohorts 2, 3, & 4 who chose to continue for an additional 3 months

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)
Cohort 1 not offered extension trial

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, based on safety and biologic effect
- Represents a significant number of patients in clinical practice, with >30% sub-responders
- Supports future clinical trials

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)**

Source: Clearside data on file.

OASIS Results: Safety, Durability, & Treatment Burden Reduction

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

SAFETY DATA

- Excellent safety profile at all doses and timepoints
- No Serious Adverse Events
- No dose limiting toxicities
- No Adverse Events (AEs) from inflammation
- No AEs related to intraocular pressure

DURABILITY

- In OASIS, to 3 months:
  - ≥72% reduction in treatment burden
- In Extension Study, to 6 months:
  - ≥77% reduction in treatment burden
  - Patients not requiring additional therapy:
    - ≥ 3 Months: 11/12 (92%)
    - ≥ 4 Months: 10/12 (83%)
    - **≥ 6 Months: 8/12 (67%)**
    - **> 6 Months: 6/12 (50%)**

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

- Expect to initiate Phase 2b clinical trial in Q2 2023 with Topline Results anticipated in Q3 2024

Source: Clearside data on file.

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

3-Month & 6-Month Extension Study Data

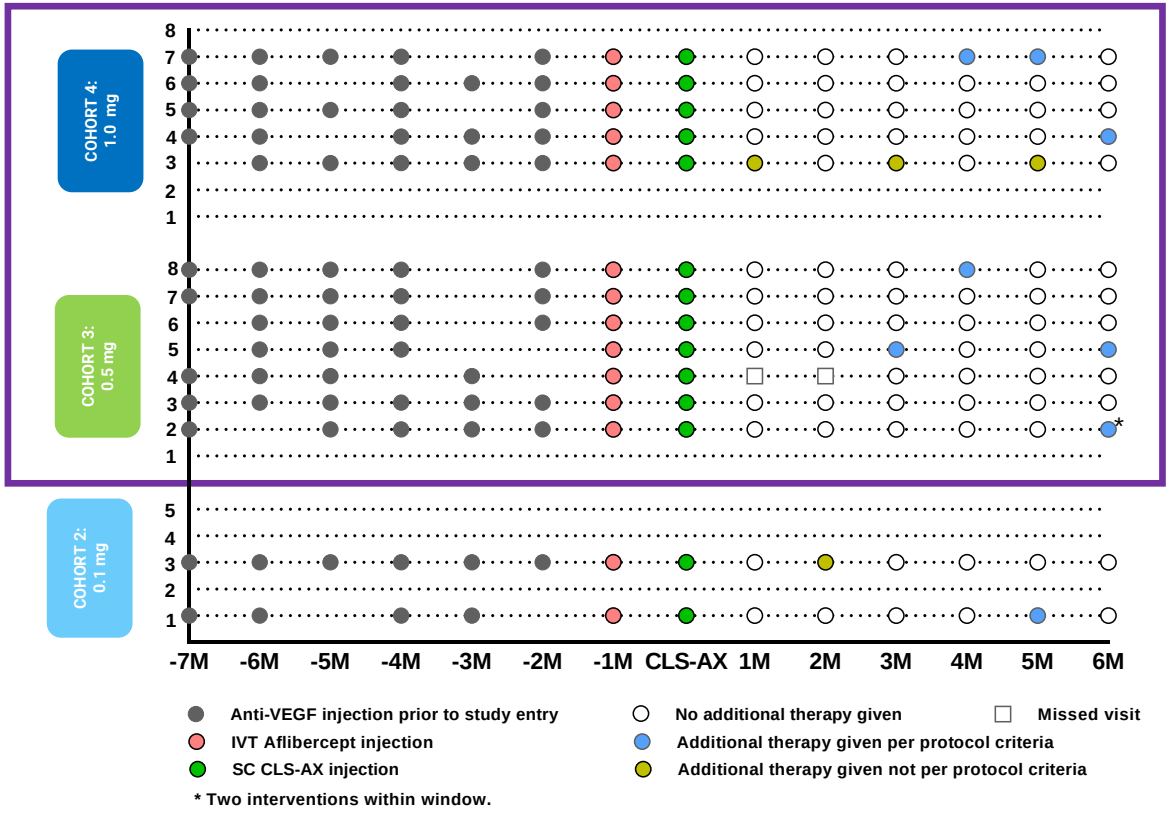
SAFETY DATA

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

Source: Clearside data on file.

Extension Study (6 Month Data): Prior Anti-VEGF Therapies and All Additional Therapies



DURABILITY

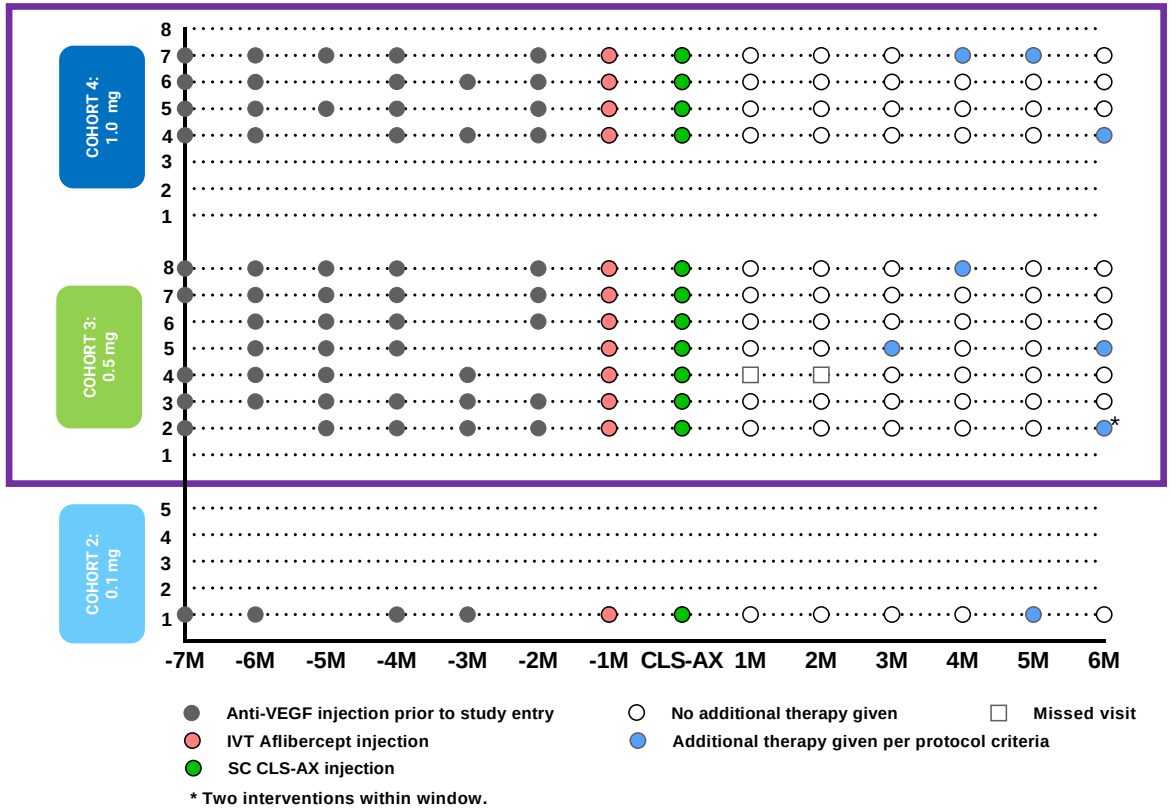
Cohorts 3 & 4

No Additional Therapy

- ≥ 3 Months: 11/12 (92%)
- ≥ 4 Months: 10/12 (83%)
- ≥ 6 Months: 8/12 (67%)
- > 6 Months: 6/12 (50%)

Source: Clearside data on file.

Extension Study (6 Month Data): Prior Anti-VEGF Therapies and Additional Therapies Per Protocol Criteria



DURABILITY

Cohorts 3 & 4

No Additional Therapy

≥ 3 Months: 11/11 (100%)
≥ 4 Months: 10/11 (91%)
≥ 6 Months: 8/11 (73%)
> 6 Months: 6/11 (55%)

Excludes patients whose first additional therapy was not per protocol-defined criteria.
Source: Clearside data on file.

Extension Study (6 Month): CLS-AX Demonstrated Reduction of Treatment Burden Across Cohorts

Observed Reduction in Treatment Burden
All Therapies

Cohort	Number of Participants	Avg Monthly Injections Before CLS-AX Administration	Avg Monthly Injections After CLS-AX Administration	% Reduction
4	5	0.87	0.20	**77.0**
3	7	0.81	0.12	**85.2**
2	2	0.83	0.17	79.5

Observed 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
4	4	0.83	0.13	**84.3**
3	7	0.81	0.12	**85.2**
2	1	0.67	0.17	74.6

77 – 85% Reduction in Treatment Burden in Cohorts 3 and 4

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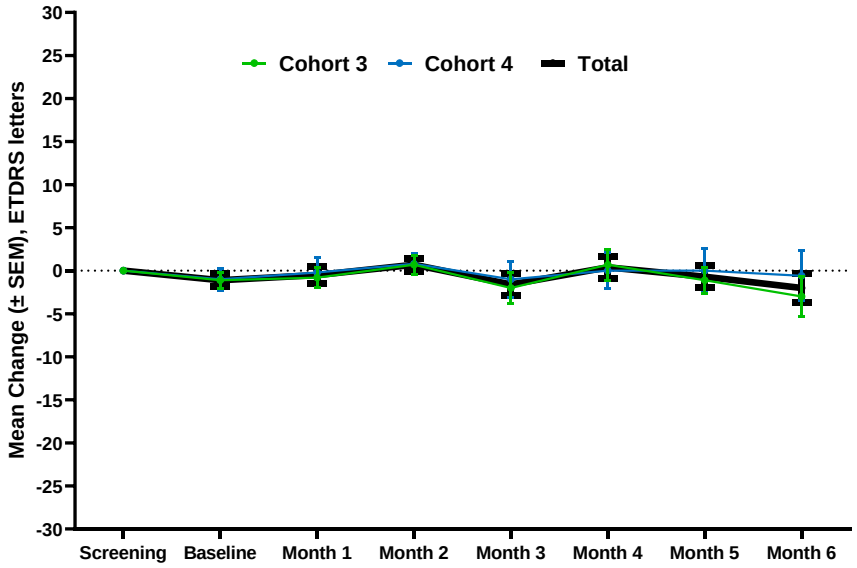
Note: Average Monthly Injections Before CLS-AX Administration = # treatments six months prior/ 6.
Average Monthly Injections After CLS-AX Administration = # treatments / # months of follow-up.
% Reduction = Average of individual reductions calculated as (after – before) / before × 100%.
Source: Clearside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

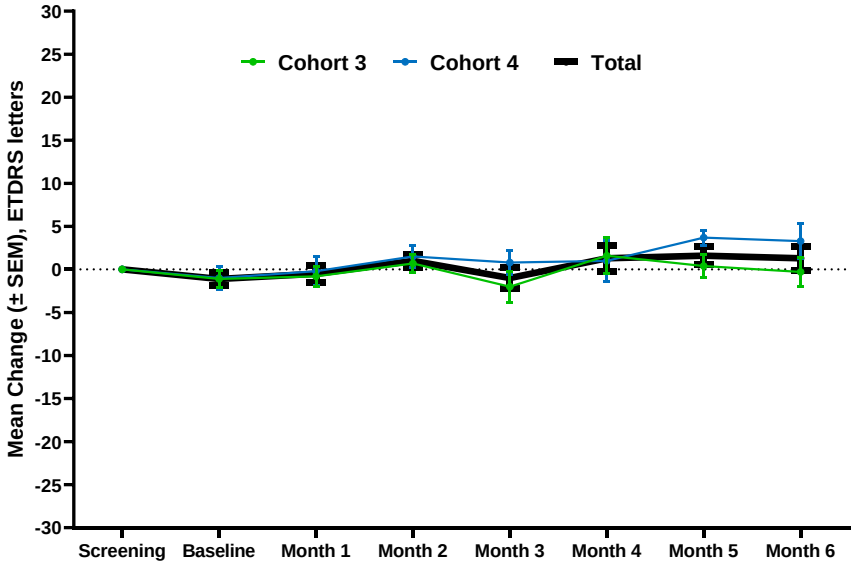
Extension Study (6 Month): Stable Visual Acuity

Mean Best Corrected Visual Acuity Letter Score, Change from Screening

All Data



Excluding Data After Additional Treatment

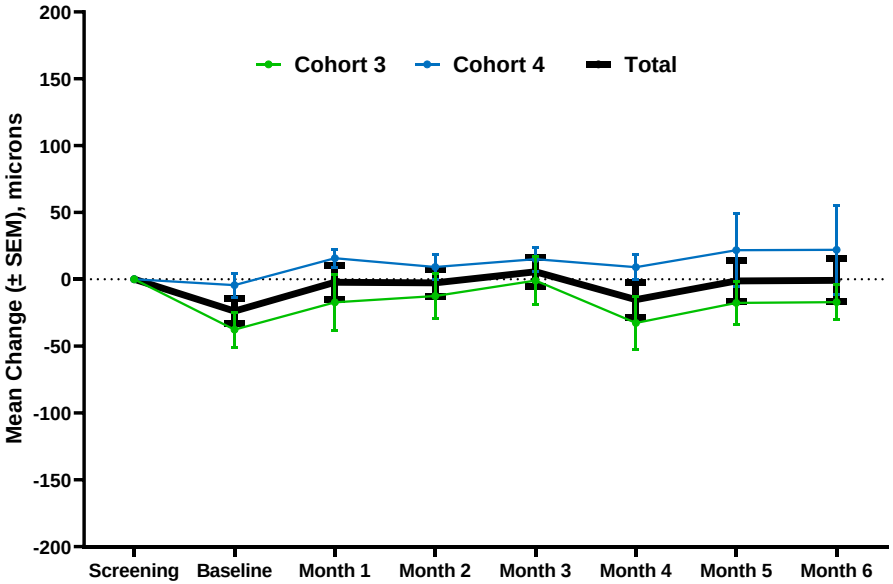


Source: Clearside data on file.

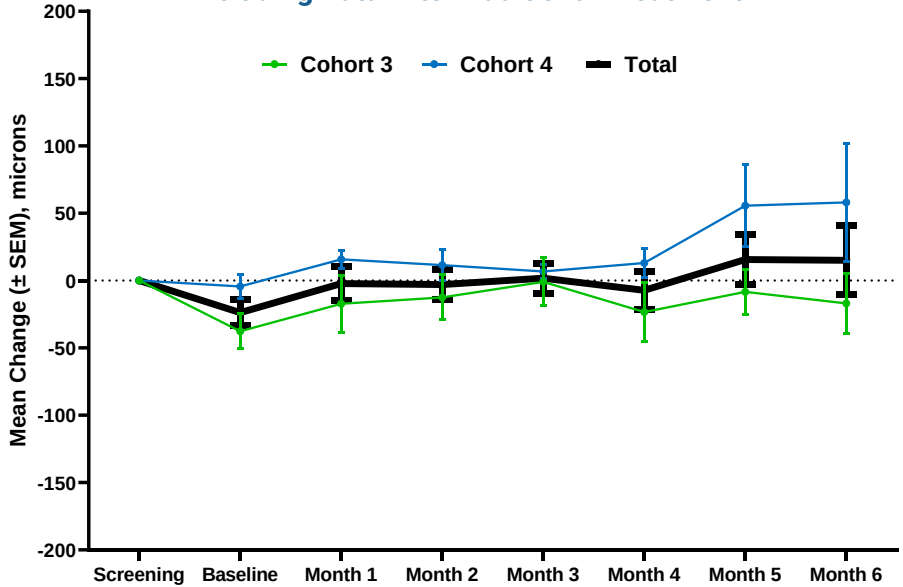
Extension Study (6 Month): Stable Central Subfield Thickness

Mean Central Subfield Thickness, Change from Screening

All Data



Excluding Data After Additional Treatment



Source: Clearside data on file.

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

	OASIS Results	Potential Competitive Advantages*
Safety Data (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 observed incidents of drug migration or vitreous "floaters" or haze in clinical trials, to date • SCS injection procedure commercially accepted by retinal physicians following launch of XIPERE®
Durability (Cohorts 3&4)	**In Extension Study (N=12):** • **≥77%** reduction in treatment burden • Patients not requiring additional therapy: ≥ 3 Months: 11/12 (92%) ≥ 4 Months: 10/12 (83%) **≥ 6 Months: 8/12 (67%)** **> 6 Months: 6/12 (50%)**	• CLS-AX showed preliminary signs of durability favorably comparing to other current and investigational intravitreally injected biologic agents • Based on 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

CLEARSIDE BIOMEDICAL

Source: Clearside data on file. | 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.
*CLS-AX has not been evaluated against other products in head-to-head clinical trials.

ODYSSEY
Phase 2b Trial

ODYSSEY Phase 2b Trial: Treatment Experienced Participants with Active Disease

Randomized, Double-Masked, Parallel-Group, Active-Controlled Multicenter Wet AMD Trial

Trial Objectives:

Evaluate safety & efficacy of CLS-AX in participants with wet AMD

Number of Participants:

60 Total with 2:1 Randomization*
(40 in CLS-AX arm &
20 in aflibercept arm)

- **Key inclusion criteria:**
  - Diagnosed with neovascular AMD (wet AMD) within 36 months of screening
  - History of 2 to 4 anti-VEGF treatments in 6 months before screening
  - History of response to prior anti-VEGF treatment for wet AMD
  - Reading center confirmation of persistent active disease
  - Best corrected visual acuity (BCVA) of 20 to 80 letters#
- **Loading Doses:** Participants in both arms will receive 3 aflibercept (2 mg) loading doses; in CLS-AX arm, participants will receive one dose of CLS-AX (1.0 mg) at same visit as second loading dose of aflibercept (Baseline)
- **Monthly disease activity assessments:** Weeks 12 through 32 in both arms to determine if there is need for supplemental treatment
- **Supplemental treatment criteria^ :** Decrease in BCVA, increase in central subfield thickness (CST), or new or worsening vision-threatening hemorrhage due to wet AMD
- **Primary outcome measures:** Mean change in BCVA from Baseline to Week 36; safety & tolerability
- **Secondary outcome measures:**
  - Other changes in visual function and ocular anatomy, such as CST
  - Need for supplemental treatment
  - Treatment burden as measured by total injections over trial duration

CLEARSIDE BIOMEDICAL

* Aflibercept is dosed via intravitreal injection (IVT); CLS-AX is dosed via suprachoroidal injection.
\# Using the Early Treatment Diabetic Retinopathy Study (ETDRS) measurement.
^ - BCVA reduction of >10 letters from Baseline measurement due to wet AMD.
- Increase in CST of >100 microns on SD-OCT from Baseline measurement due to wet AMD.
- BCVA reduction of > 5 letters from Baseline measurement due to wet AMD AND increase in CST of >75 microns on SD-OCT from Baseline measurement due to wet AMD.
- Presence of new or worsening vision-threatening hemorrhage due to wet AMD.

ODYSSEY Phase 2b Wet AMD Trial Design Rationale

Comparator

- Aflibercept (2 mg) is current standard of care for wet AMD patients
- Intended to position CLS-AX for Phase 3 to conform with FDA draft guidance for wet AMD drug development

Target Participants

- Large population of treatment-experienced participants to facilitate trial enrollment
- Minimizes recruitment of anti-VEGF sub- and non-responders

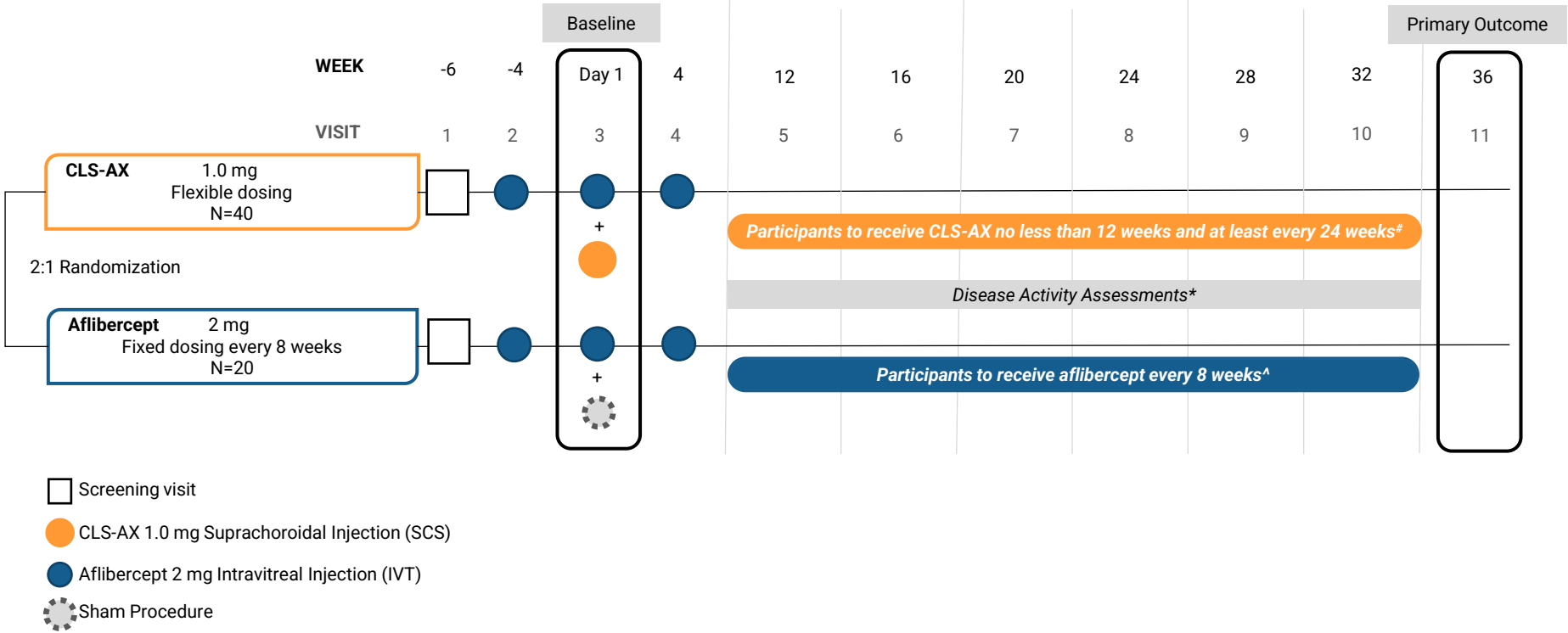
Dosing Regimen

- Designed to evaluate safety, efficacy and duration of CLS-AX in participants with wet AMD
- CLS-AX has potential for 2-3x/year maintenance dosing compared to on-label maintenance dosing for approved drugs: LUCENTIS®: 12x/year, EYLEA®: 6x/year, VABYSMO®: up to 6x/year

Trial Size and Timeline

- Number of participants in line with recent anti-VEGF Phase 2 trials in wet AMD
- 36-week duration to obtain necessary data to design Phase 3 program using FDA draft guidance
- Balanced to meet objectives effectively and efficiently with topline results expected in Q3 2024

ODYSSEY Trial Designed to Provide Data for Phase 3



* 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.

Strategic SCS Collaborations & Catalysts

Clinical Programs Utilizing Clearside's SCS Microinjector®

Clinical Development

PROGRAM	THERAPEUTC ENTITY	INDICATION	PHASE 1	PHASE 2	PHASE 3	APPROVAL
CLS-AX (axitinib): CLEARSIDE	Small Molecule	Wet AMD (ODYSSEY)	*P2b Planned Q2 2023*			

SCS Microinjector® Partner Programs

PARTNER	Therapeutic Entity	LICENSED Indication	IND-Enabling	PHASE 2	PHASE 3	APPROVAL
RGX-314: REGENXBIO	AAV-based Gene Therapy	Wet AMD (AAVIATE)				
RGX-314: REGENXBIO	AAV-based Gene Therapy	Diabetic Retinopathy (ALTITUDE)				
AU-011: AURA BIOSCIENCES	Viral-like Drug Conjugate	Ocular Oncology/Choroidal Melanoma				

XIPERE® Commercial Partners

PARTNER	INDICATION	LICENSED TERRITORY	PHASE 1	PHASE 2	PHASE 3	APPROVAL
BAUSCH + LOMB	Uveitic Macular Edema	U.S. & Canada	U.S.A.			
ARCTIC VISION	Uveitic Macular Edema	Greater China, South Korea, ASEAN Countries, India, Australia, New Zealand	Arcatus™			
	Diabetic Macular Edema		Arcatus™			

CLEARSIDE BIOMEDICAL

XIPERE® (triamcinolone acetonide injectable suspension), for suprachoroidal use has received U.S. FDA Approval | In China, Arctic Vision is developing Arcatus™ (triamcinolone acetonide injectable suspension), formerly referred to as ARVN001, and known as XIPERE® in the U.S.

Four Validating Partnerships to Drive Growth

VALIDATION: Validates our investment in suprachoroidal delivery using our SCS Microinjector

OPPORTUNITY: Maximizes the commercial and development opportunities for XIPERE in multiple geographic markets

EXPANSION: Expands our overall internal and collaborative product development pipeline

NON-DILUTIVE FUNDING: Royalty financing agreement provides the potential for up to $65 million based on development/sales milestones & royalties*

*Subject to royalty financing agreement signed in August 2022 with HealthCare Royalty Management, LLC.

SCS Microinjector®: Two Global Development & Commercialization Partners

GENE THERAPY FOR RETINAL DISEASES

- Exclusive worldwide rights for SCS delivery of adeno-associated virus (AAV) vector gene-based therapy RGX-314 to treat wet AMD, diabetic retinopathy and certain other conditions
- Two ongoing multi-center, open-label, randomized, controlled, dose-escalation studies evaluating the efficacy, safety and tolerability of suprachoroidal delivery of RGX-314
- **First data ever presented utilizing gene therapy delivered into the suprachoroidal space***
- TERMS:
  - Up to $136M in regulatory, development and sales milestones across certain vascular endothelial growth factor ("VEGF") mediated retinal diseases
  - Mid single digit royalties on net sales of SCS Microinjector products

OCULAR ONCOLOGY

- Exclusive worldwide licensing agreement for the SCS delivery of their proprietary drug candidates into the SCS for the potential treatment of certain ocular cancers, including choroidal melanoma (CM)
- **CM is the most common, primary intraocular cancer in adults**
- **Completing Phase 2 trial**
- **Planning to initiate Phase 3 pivotal trial in 2023 using SCS administration**
- TERMS:
  - Up to $21M in regulatory, commercial sales and development milestones
  - Low to mid single digit royalties on net sales of SCS Microinjector® products

* Retina Society 54th Annual Scientific Meeting presentation, Nikolas London, M.D., Oct 2021.
Sources: CLSD, RGNX and AURA company filings.
Note: future royalty and milestone payments related to these partnerships are subject to Clearside's royalty financing agreement signed in August 2022 with HealthCare Royalty Management, LLC.

XIPERE®: Two Global Commercialization & Development Partners

XIPERE®
(triamcinolone acetonide injectable suspension) 40 mg/mL

BAUSCH + LOMB

- License for the U.S. and Canada
- Received $20M in upfront, U.S. approval and pre-launch milestones
- Up to $55M in milestone payments
- Tiered royalties from the high-teens to 20%

arctic VISION

- License for Greater China, South Korea, ASEAN Countries, India, Australia, New Zealand
- Received $11M in upfront and U.S. approval payments
- Up to $22.5M in milestone payments
- Tiered royalties of 10% to 12%

Note: future royalty and milestone payments related to these partnerships are subject to Clearside's royalty financing agreement signed in August 2022 with HealthCare Royalty Management, LLC.
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/PI/XIPERE-PI.pdf. | *Clearside's Phase 3 PEACHTREE Trial

Targeted 2023 Catalysts

CLEARSIDE PROGRAMS

CLS-AX (axitinib injectable suspension)

- ✓ **Q1 2023:** Final OASIS Phase 1/2a data from 6-month extension study
- • **Q2 2023:** ODYSSEY Phase 2b trial initiation
- • **Q3 2024:** ODYSSEY Phase 2b Topline Results

Medical/Scientific meeting presentations

- ✓ **Q1 2023:** Angiogenesis, Macula Society, Next Generation Ophthalmic Drug Delivery Summit - Suprachoroidal Delivery Workshop
- • **Q2/Q3 2023:** ARVO, ASRS
- • **Q4 2023:** AAO, Retina Society

Publications

- • Expert panel practice guidelines on SCS® delivery
- • OASIS Data

PARTNER PROGRAMS

Bausch + Lomb:

- ✓ XIPERE® marketing in North America
- ✓ XIPERE® submitted for regulatory approval in Canada

Arctic Vision: XIPERE® (Arcatus™) development in China

- ✓ Phase 3 UME trial enrolling
- • Phase 1 DME trial data

REGENXBIO: RGX-314 delivered via SCS Microinjector®

- ✓ H1 2023: Complete enrollment in wet AMD & DR trials
- • H2 2023: Report additional interim trial data

Aura Biosciences: AU-011 delivered via SCS Microinjector® in choroidal melanoma

- • H1 2023: Initiate and enroll first patient in Phase 3 trial
- • H2 2023: Report 12-month Phase 2 data

XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use | In China, Arctic Vision is developing Arcatus™ (triamcinolone acetonide injectable suspension), formerly referred to as ARVN001, and known as XIPERE® in the U.S. | REGENXBIO (RGNX) trials involve suprachoroidal delivery of RGX-314 using the SCS Microinjector® | Aura Biosciences trials involve suprachoroidal delivery of AU-011 using the SCS Microinjector®.

CLEARSIDE BIOMEDICAL

Nasdaq: CLSD