



CLEARSIDE BIOMEDICAL

Corporate Presentation

April 2024



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. 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 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 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, 2022, filed with the SEC on March 14, 2023, 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.

Revolutionizing Ophthalmic Drug Delivery for Serious Back of the Eye Diseases



Targeting the Suprachoroidal Space (SCS®)

SCS Microinjector® with Proprietary Drug Formulations

Proprietary Suprachoroidal Space Injection Technology

Delivers Small Molecules and Gene Therapy Behind the Visual Field Targeting Multiple Retinal Diseases

First and Only FDA Approved SCS Product: XIPERE®

External Validating SCS Delivery Collaborations

Early-Stage Internal Research & Development Pipeline

Suprachoroidal Delivery via SCS Microinjector[®]



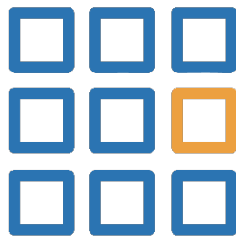
Core Advantages of Treating Via the Suprachoroidal Space (SCS®)



TARGETED

for efficacy¹

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



COMPARTMENTALIZED

for safety²

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



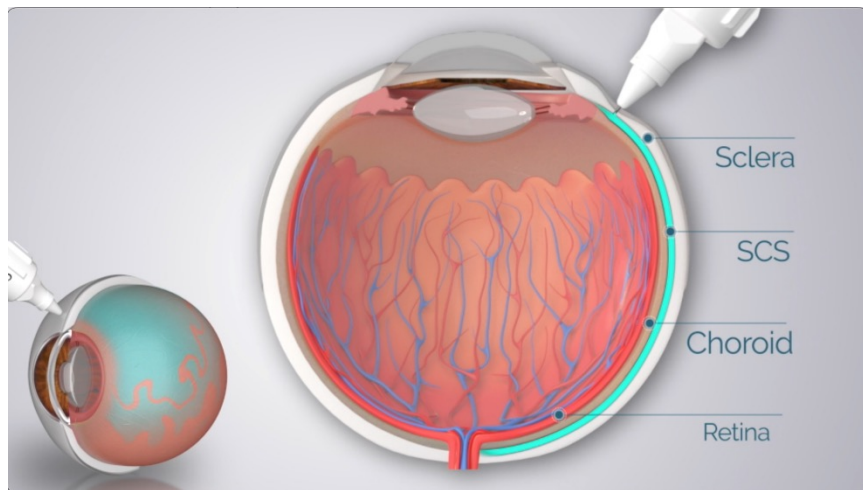
BIOAVAILABLE & PROLONGED DRUG LEVELS

for durability³

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

Clearside's SCS Microinjector®:

Only Commercially-Available Approach for Suprachoroidal Drug Delivery



SUPRACHOROIDAL SPACE INJECTION

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



Versatile: 6 SCS clinical trials in 5 indications delivering 4 potential therapies

- Thousands of injections performed with SCS Microinjector



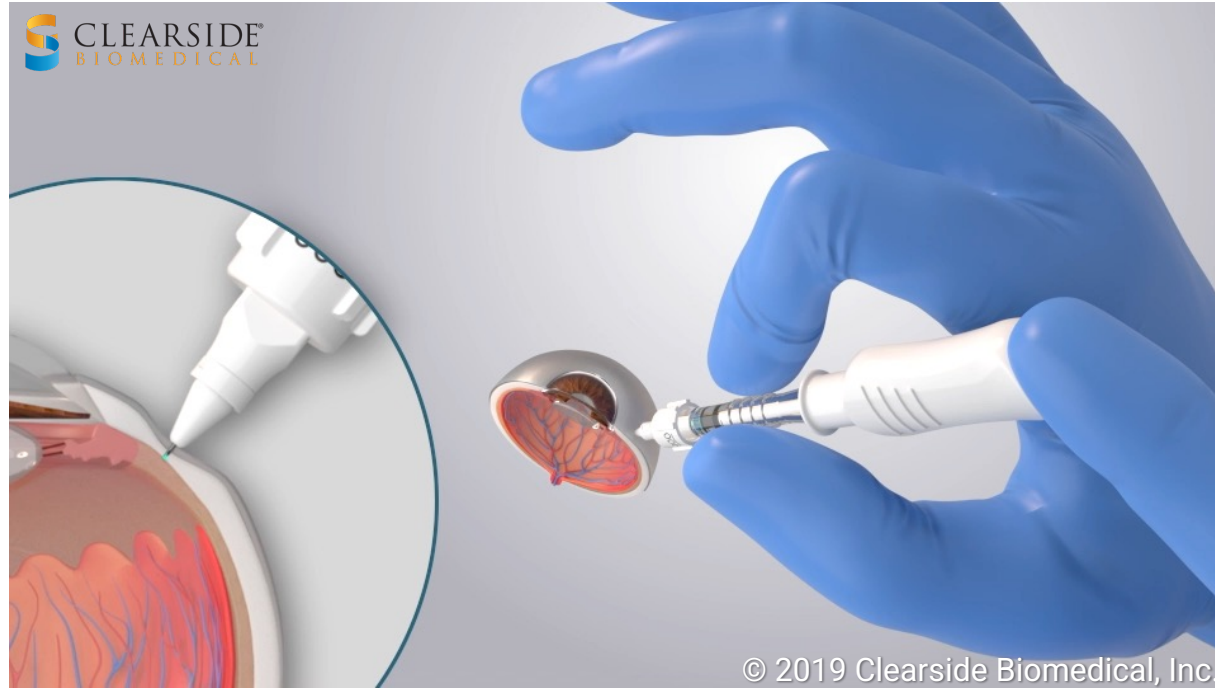
Safety profile of SCS Microinjector comparable to intravitreal injections¹



Well accepted by retinal physicians following launch of XIPERE®

- More than 1,200 physicians trained

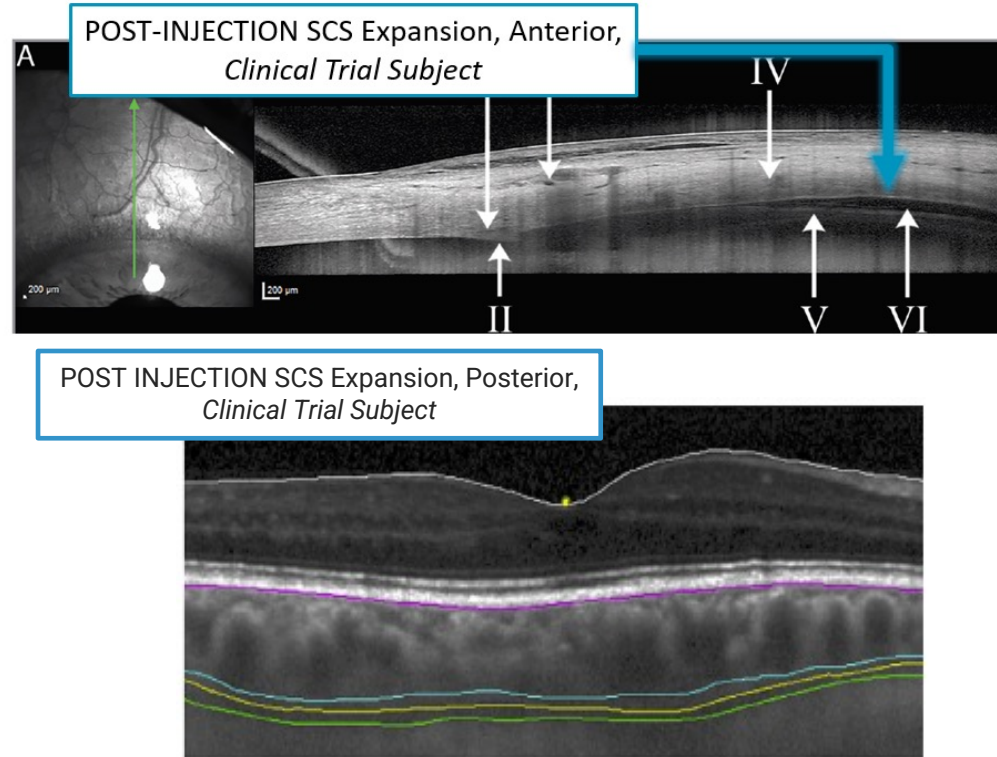
Exclusive Access to the Back of the Eye Using Clearside's Proprietary SCS Microinjector®



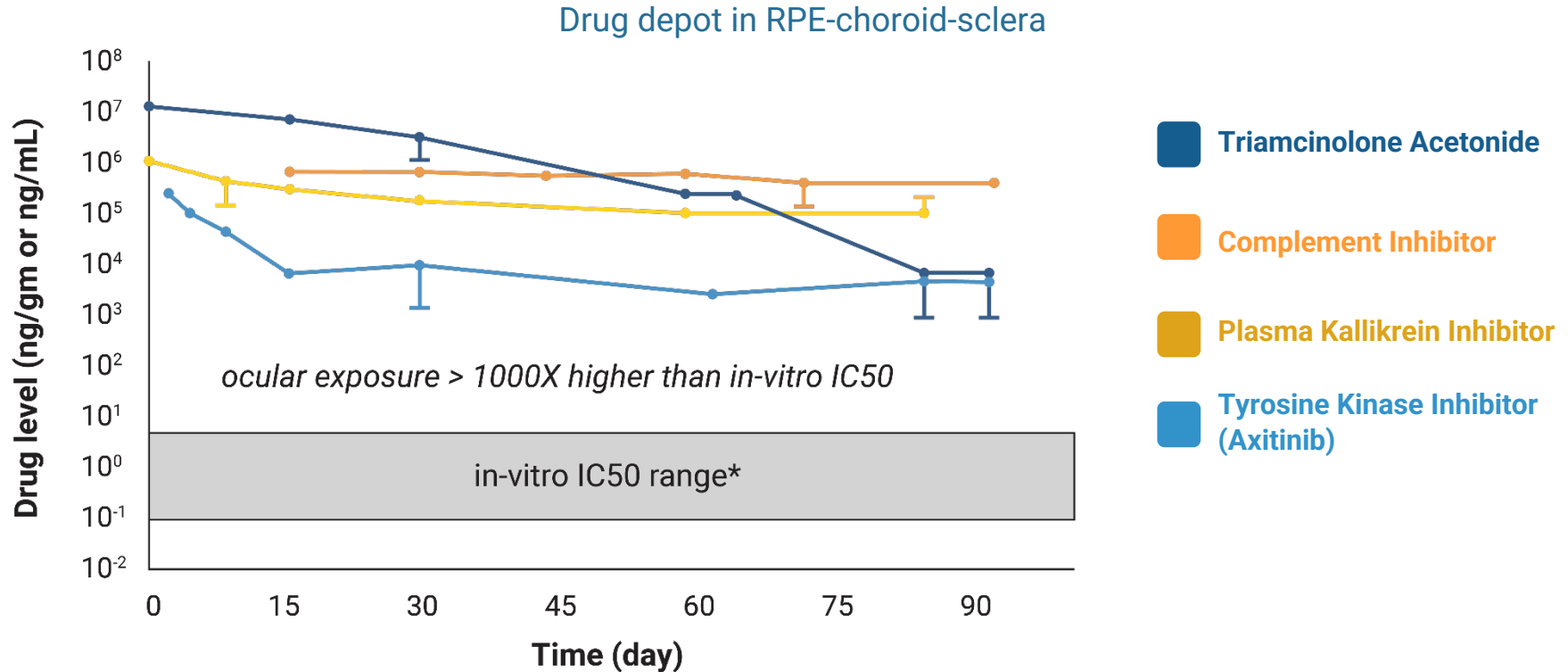
SCS Microinjector®:

Delivers Drugs Circumferentially and Posteriorly to the Macula

- SCS is a potential space that expands after injection, including the macula SCS
- Natural pressure gradient drives injectate toward lower pressured posterior SCS
- Suprachoroidally injected drug levels are similar peripherally and centrally in the retina and SCS in a preclinical model



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



Drug Delivery Using Clearside's Proprietary SCS Microinjector[®]



*Footage courtesy of Dr. Allen Hu
Cumberland Valley Retina Consultants*

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. **28 U.S. and >80 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**



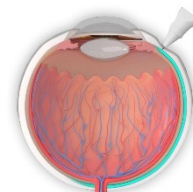
DEVICE PATENTS

- 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

Clearside Biomedical Suprachoroidal Injection Platform

Clearside Developed Programs

Therapeutic	Type	Indication	Ind-Enabling	Phase 1	Phase 2	Phase 3	Approval	Partner
CLS-AX (axitinib):	Tyrosine Kinase Inhibitor	Wet AMD	Phase 2b			ODYSSEY		
XIPERE®	Corticosteroid (Triamcinolone Acetonide)	Uveitic Macular Edema ¹ (U.S. & Canada)						B+L BAUSCH + LOMB
XIPERE® / ARCATUS™	Corticosteroid (Triamcinolone Acetonide)	Uveitic Macular Edema ² Diabetic Macular Edema ²	UME					arctic VISION
XIPERE® / ARCATUS™	Corticosteroid (Triamcinolone Acetonide)	(Asia Pacific ex-Japan)	DME					

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
ABBV-RGX-314	AAV Gene Therapy	Diabetic Retinopathy	ALTITUDE					REGENXBIO abbvie
ABBV-RGX-314	AAV Gene Therapy	Wet AMD	AAVIATE					REGENXBIO abbvie
Avoralstat	Plasma Kallikrein Inhibitor	Diabetic Macular Edema						bio cryst*

SCS Lead Program: CLS-AX

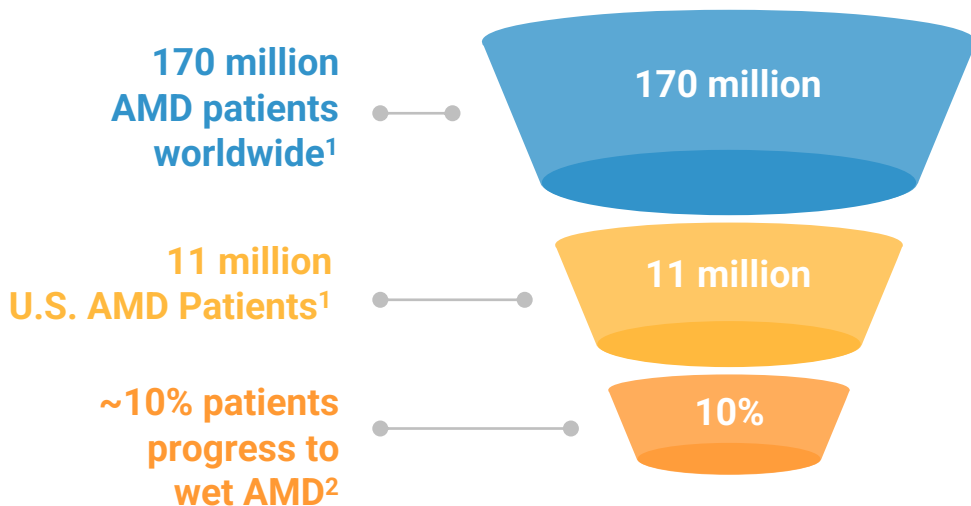
(axitinib injectable suspension)

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



Age-Related Macular Degeneration (AMD)

A large and growing market opportunity



- ✓ AMD causes a progressive loss of central vision and is the most common cause of blindness in individuals over age 55¹
 - Majority of blindness in individuals with AMD is caused by the advanced neovascular stage of the disease (wet AMD)¹
- ✓ U.S. prevalence expected to increase to 22 million by the year 2050¹
- ✓ Global prevalence expected to increase to 288 million by the year 2040¹
- ✓ Current treatments require frequent injections and subset of patients with disappointing visual outcomes²
- ✓ **Opportunity for treatments that may have longer duration of action and may address sub-responders to current anti-VEGF-A treatments**

CLS-AX (axitinib): Pan-VEGF TKI in Development for Wet AMD



Intrinsic pan-VEGF inhibition through receptor blockade

- Approved AMD 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

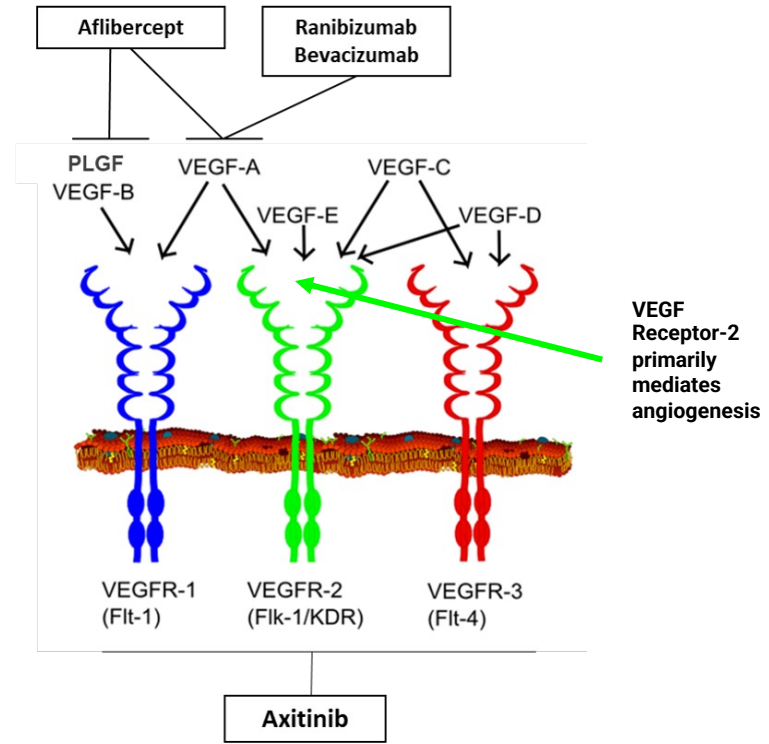


Highly potent tyrosine kinase inhibitor (TKI)

- **>10x more potent than other TKIs** in in-vitro studies³
- Better ocular cell biocompatibility than other TKIs⁴
- More active than other TKIs for experimental corneal neovascularization in preclinical models

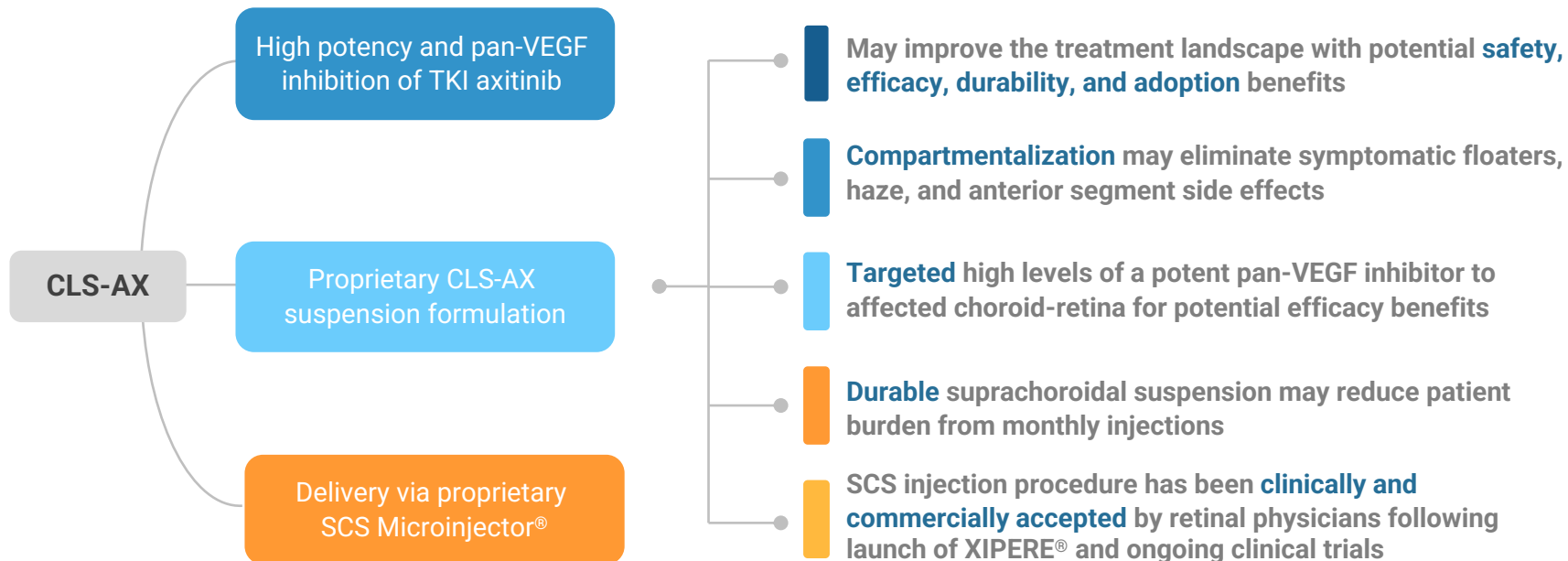


Preclinical data showed axitinib inhibition and regression of angiogenesis



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. 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 Intracocular 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.

Leveraging a Highly Potent Pan-VEGF Inhibitor with Suprachoroidal Delivery



OASIS

CLS-AX

Phase 1/2a
Clinical Trial

*Observed Positive Safety Profile,
Durability, & Treatment Burden Reduction*

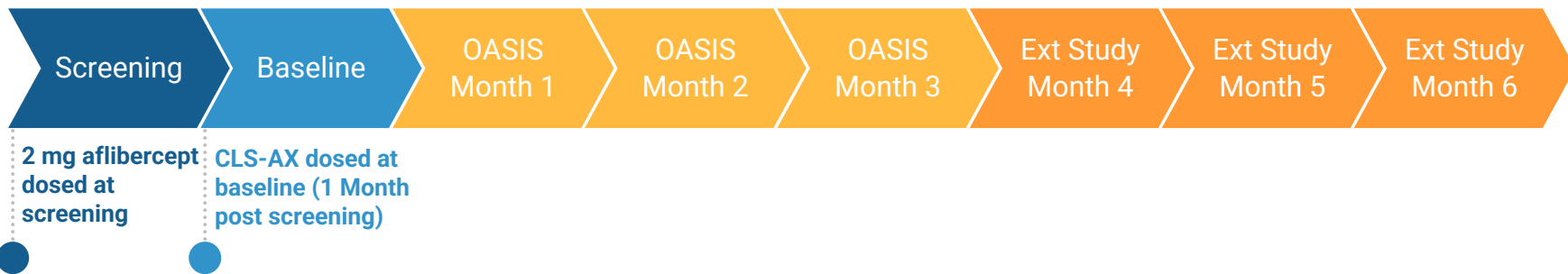


TM

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 3-month 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:** Total of 6 months' follow-up for patients in Cohorts 2, 3, & 4 who chose to continue for an additional 3 months



CLS-AX OASIS Extension Trial: Demonstrated Excellent Safety Profile and Promising 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

- 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

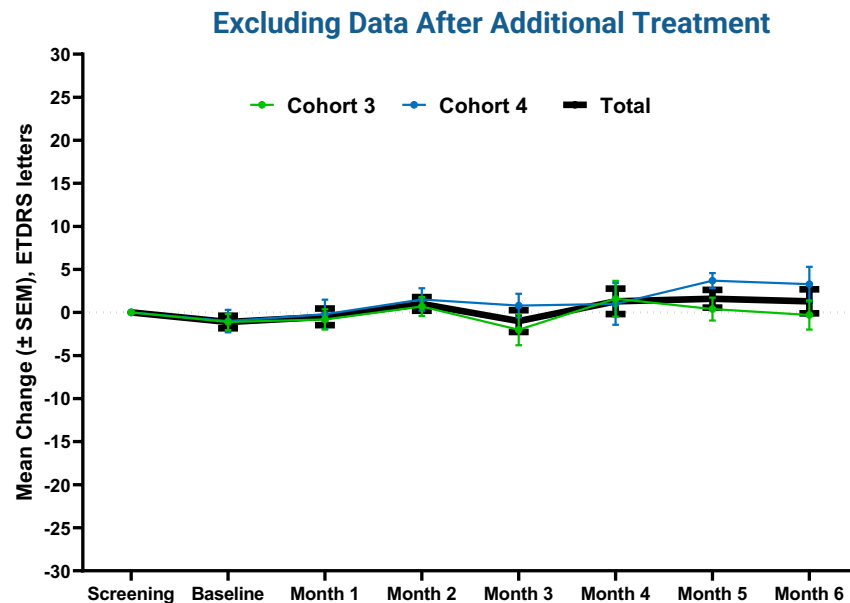
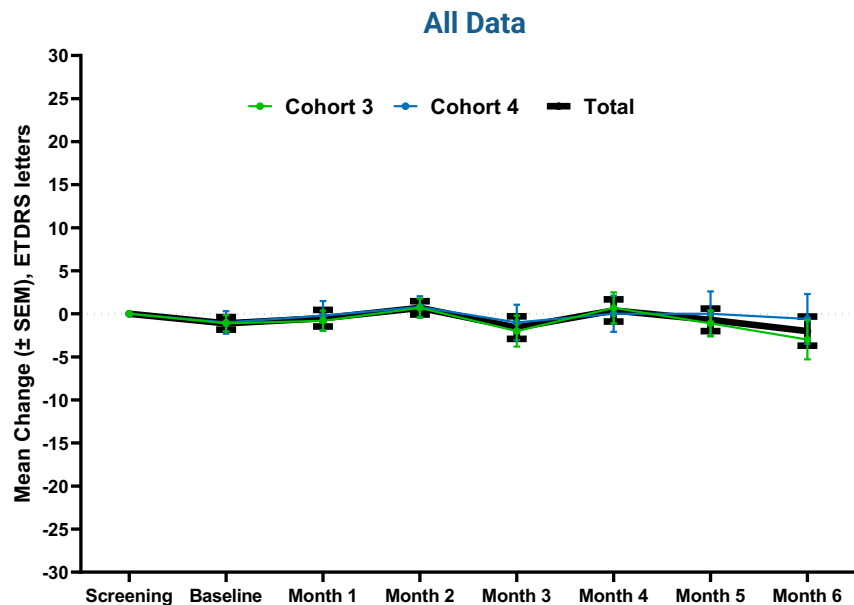
- Stable mean Best Corrected Visual Acuity (BCVA)
- Stable mean Central Subfield Thickness (CST)
- On OCT, anatomical signs of TKI biologic effect observed in anti-VEGF treatment-experienced sub-responders

REDUCED TREATMENT BURDEN

- $\geq 72\%$ reduction in treatment burden In OASIS, to 3 months:
- **77% to 85% reduction in treatment burden in Extension Study, to 6 months**

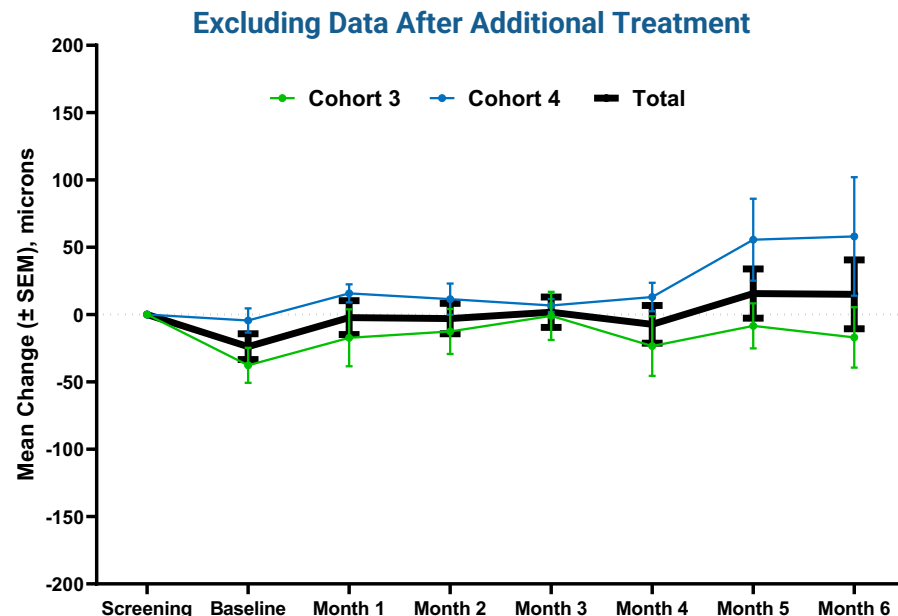
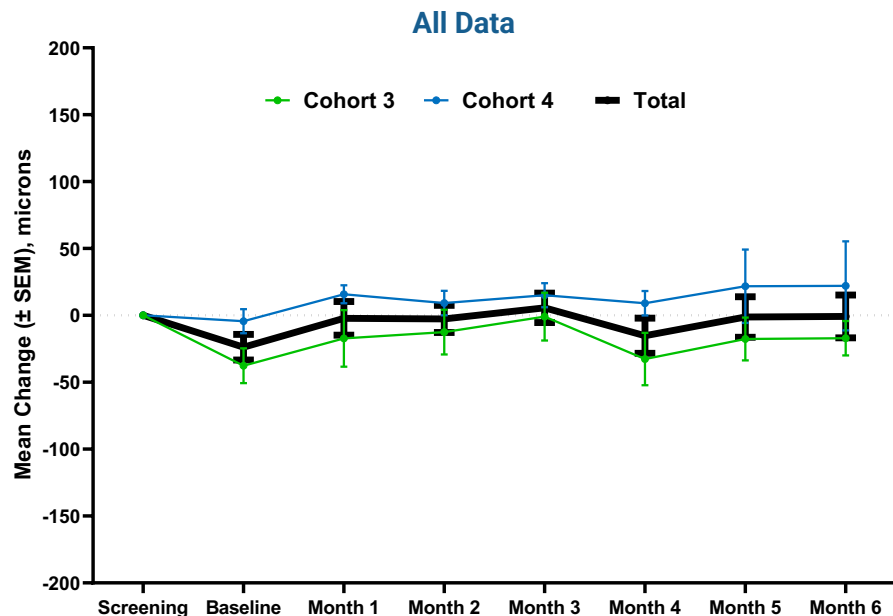
Extension Study (6 Month): Stable Visual Acuity

Mean Best Corrected Visual Acuity Letter Score, Change from Screening

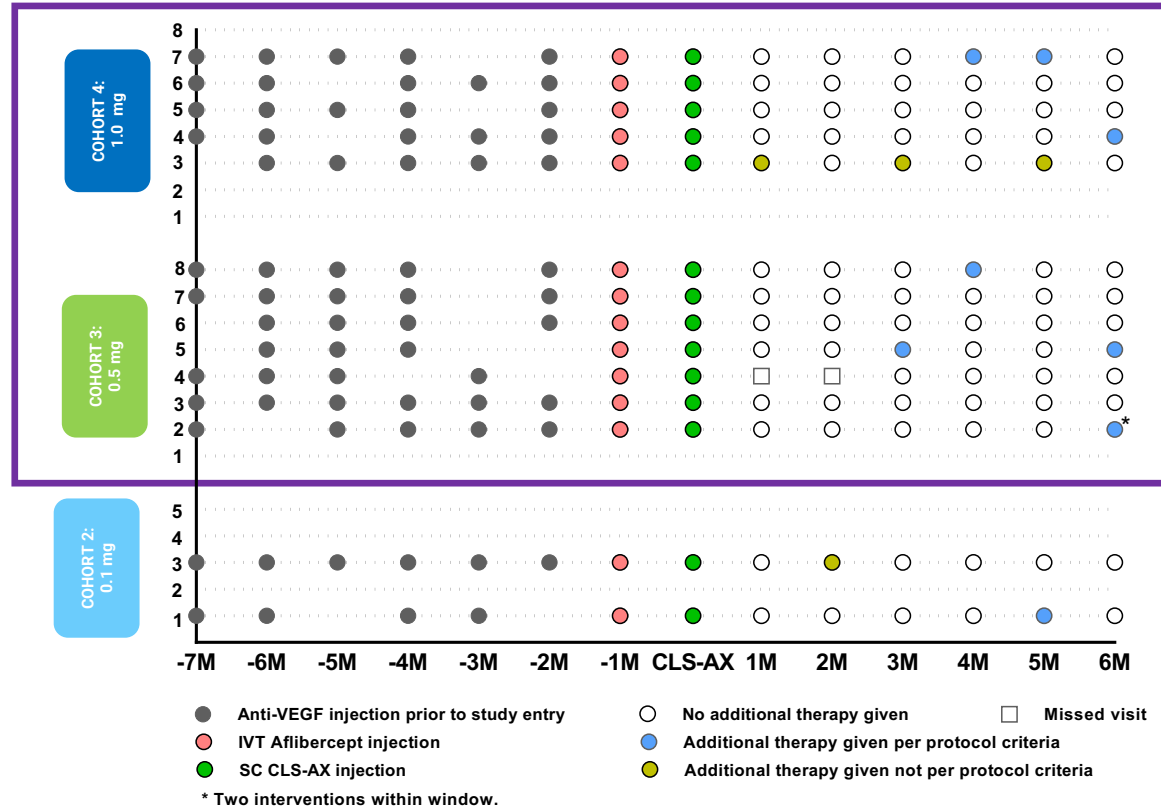


Extension Study (6 Month): Stable Central Subfield Thickness

Mean Central Subfield Thickness, Change from Screening



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%)

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

ODYSSEY

CLS-AX

Phase 2b
Clinical Trial

Recruitment Completed



ODYSSEY Phase 2b: Suprachoroidal Delivery Approach in Wet AMD



Trial Objectives:

Evaluate safety, efficacy & duration
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)

- **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
- Intended to guide design of CLS-AX Phase 3 program to conform
with FDA draft guidance for wet AMD drug development
- **Topline results expected in Q3 2024**
- Comparator aflibercept (2 mg) is standard of care for wet AMD
patients
- Large population of treatment-experienced participants to facilitate
trial enrollment
- Minimizes recruitment of anti-VEGF sub- and non-responders

ODYSSEY Trial Design:

Treatment Experienced Participants with Active Disease

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 and response to prior anti-VEGF treatment for wet AMD
- **Reading center confirmation of persistent active disease;** BCVA of 20 to 80 letters#

Dosing Regimen

- **Participants in both arms will receive 3 aflibercept (2 mg) loading doses (2nd dose = Baseline visit)**
- **CLS-AX arm will receive one dose of CLS-AX (1.0 mg) at Baseline visit**
- Unless DAA requires more frequent dosing, **CLS-AX arm dosed at least every 24 weeks** & aflibercept arm dosed every 8 weeks

Disease Activity Assessments (DAA)

- **Monthly DAA: Weeks 12 through 32 in both arms** to determine if there is need for supplemental treatment
- Supplemental treatment criteria^ : Decrease in BCVA, increase in CST, or new or worsening vision-threatening hemorrhage due to wet AMD

Outcome Measures

- **Primary: Mean change in BCVA from Baseline to Week 36; safety & tolerability**
- Secondary: 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

* Aflibercept is dosed via intravitreal injection (IVT); CLS-AX is dosed via suprachoroidal injection.

Using the Early Treatment Diabetic Retinopathy Study (ETDRS) measurement.

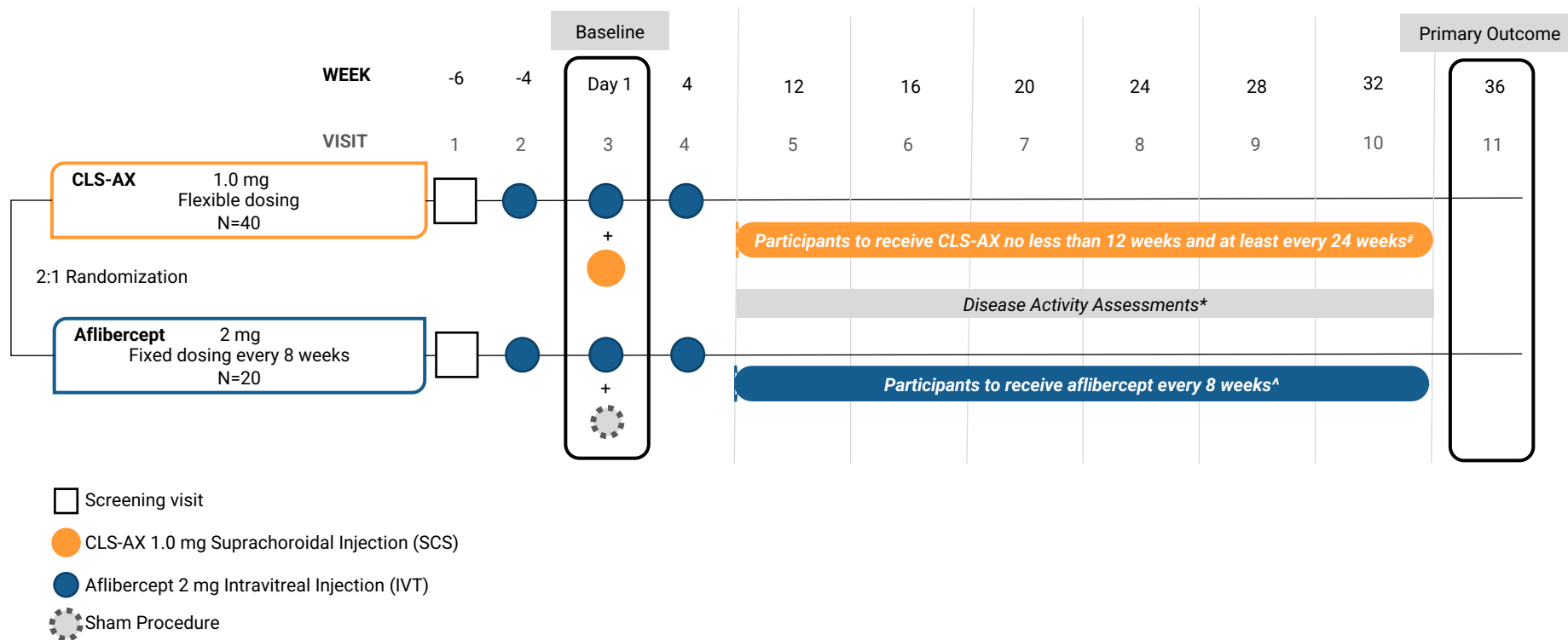
^ - BCVA (Best Corrected Visual Acuity) reduction of >10 letters from Baseline measurement due to wet AMD.

- Increase in CST (Central Subfield Thickness) 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 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



Multiple Validating Partnerships to Drive Growth

BAUSCH+LOMB



aura



VALIDATION: Highlights the potential for suprachoroidal delivery using our SCS Microinjector®

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

EXPANSION: Enhances our partner product development pipeline to broader uses incl. gene therapy and ocular cancer

NON-DILUTIVE FUNDING: Provides upfront license fees and potential for funding from royalty financing agreement*

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



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

- **First approved therapeutic delivered into the suprachoroidal space**
- FDA Approved for macular edema associated with uveitis
- Clearside received US NDA approval then transferred NDA to B+L
- Launched Q1 2022 in U.S. by Bausch + Lomb
- Arctic Vision completing Phase 3 in China
- Commercialization and development partnerships to enhance value and expand patient access

BAUSCH + LOMB

License for the U.S. and Canada

Received \$20M in payments to date

Up to \$55M in post-approval milestone payments

Tiered royalties from the high-teens to 20%



License for Greater China, South Korea, ASEAN
Countries, India, Australia, New Zealand

Received \$13M in payments to date

Up to \$22.5M in milestone payments;

Tiered royalties of 10% to 12%

SCS Microinjector®: Global Development & Commercialization Partners



GENE THERAPY FOR RETINAL DISEASES

- Exclusive worldwide rights for SCS delivery of adeno-associated virus (AAV) vector gene-based therapy ABBV-RGX-314 to treat wet AMD, diabetic retinopathy (DR) and certain other conditions
- Two ongoing Phase 2 multi-center, open-label, randomized, controlled, dose-escalation studies evaluating the efficacy, safety and tolerability of suprachoroidal delivery of ABBV-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 VEGF mediated retinal diseases
 - Mid single digit royalties



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
- **Choroidal Melanoma is the most common, primary intraocular cancer in adults**
- Completed Phase 2 trial of AU-011
- **Planning to initiate Phase 3 pivotal trial in 2H 2023 using SCS administration exclusively**
- TERMS:
 - Up to \$21M in regulatory, development, and sales milestones
 - Low to mid single digit royalties

New Partnership Expands the Utilization of SCS Microinjector®



PLASMA KALLIKREIN INHIBITOR FOR DIABETIC MACULA EDEMA

- Exclusive, worldwide license to Clearside's SCS Microinjector for the **delivery of BioCryst Pharmaceuticals' proprietary plasma kallikrein inhibitor, avoralstat**, for the treatment and prevention of diabetic macular edema (DME)
- **Avoralstat has high potency and low solubility**, characteristics that are ideal for suprachoroidal administration and important to achieving potential efficacy with reduced dosing frequency in the eye for DME patients
 - Delivering avoralstat directly into the suprachoroidal space could allow avoralstat to inhibit plasma kallikrein at the sites of edema formation in DME disease, the retinal and choroidal vascular endothelium
- Collaboration provides **CLSD pipeline expansion** with BioCryst advancing development of avoralstat into a proof-of-concept trial
- **TERMS:**
 - Clearside is eligible to receive \$82.5 million in total payments from BioCryst. This includes:
 - \$5 million upfront license fee
 - Up to \$30 million in clinical and regulatory milestone payments
 - Up to \$47.5 million in a series of post-approval sales-based milestone payments as annual global net sales progress to \$2B
 - Tiered mid-single digit royalties on annual global net product sales, including a top tier of greater than \$1.5B

Upcoming Clearside Catalysts

CLEARSIDE PROGRAMS

CLS-AX (axitinib injectable suspension)

- **Q3 2024: ODYSSEY Phase 2b Topline Results**

Medical/Scientific meeting presentations

- ✓ **Q1 2024:** Macula Society, Next Generation Ophthalmic Drug Delivery Summit
- **Q4 2024:** AAO

Publications

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

SUPRACHOROIDAL PARTNER PROGRAMS

Arctic Vision: XIPERE® (ARCATUS™) in Asia-Pacific

- **2024:** Results from Phase 3 UME trial in China
- **2024:** NDA submissions in various APAC territories

Aura Biosciences: AU-011 in choroidal melanoma

- **2024:** Ongoing patient enrollment in Phase 3 trial

Bausch + Lomb: XIPERE® in North America

- ✓ **Q1 2024:** New permanent CPT code in U.S.

BioCryst Pharmaceuticals: Avoralstat in DME

- **2024:** Conduct formulation and nonclinical work
- **2025:** Begin clinical trials

REGENXBIO: ABBV-RGX-314 in wet AMD & DR

- ✓ **Q1 2024:** Present Phase 2 wet AMD data
- **2024:** Ongoing progress in AAVIATE® & ALTITUDE®

Clearside Biomedical: Leader in the Suprachoroidal Space

Pioneered Retinal Drug Delivery Behind the Visual Field

- **SCS® Microinjector:** provides in-office, non-surgical drug delivery to the Suprachoroidal Space (SCS®)
- **Robust safety profile:** thousands of SCS injections performed
- **Versatile:** 6 ongoing SCS trials* with 4 potential therapies in 5 indications including wet AMD, DR, DME and choroidal melanoma
- **XIPERE®:** the first and only FDA-approved SCS product
- **CLS-AX: Large market opportunity in wet AMD**
 - New mechanism of action – Pan VEGF inhibition
 - Unique mode of delivery – SCS Microinjector®
 - Potential for:
 - longer duration of effect and
 - meaningful treatment burden reduction





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Nasdaq: CLSD

