



CLEARSIDE BIOMEDICAL

Corporate Presentation

HC Wainwright Ophthalmology Day

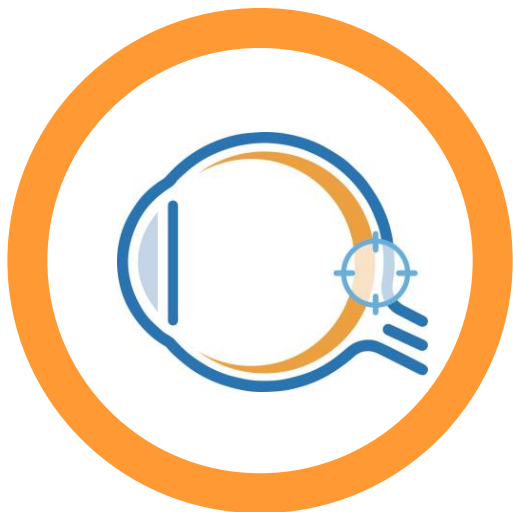
August 2022



Forward-Looking Statements

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



Versatile Therapeutic Platform

SCS Microinjector® with proprietary drug formulations target the suprachoroidal space

First FDA Approved Product: XIPERE™

Proprietary Access to the Suprachoroidal Space (SCS®)

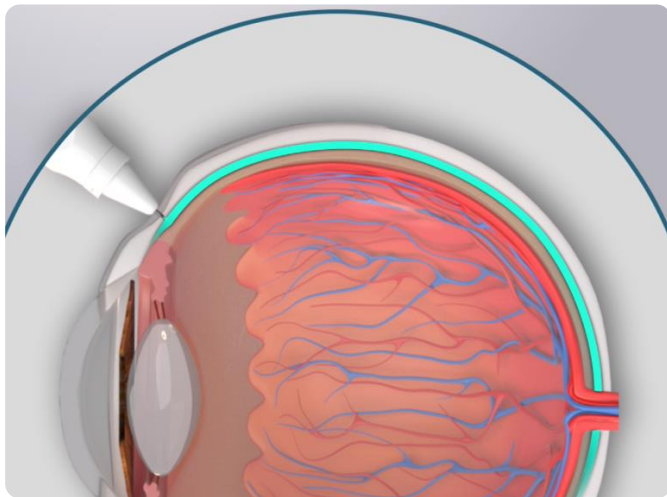
Utilization Across Small Molecules and Gene Therapy

Ability to Target Multiple Ocular Diseases

Internal Research & Development Pipeline

External Collaborations for Pipeline Expansion

Clearside's SCS Microinjector®: The Only Clinically Tested Injection Device for Suprachoroidal Drug Delivery



SUPRACHOROIDAL SPACE INJECTION

Novel SCS Microinjector® allows for precise delivery into the suprachoroidal space

- ✓ **Clinically tested in >1200 suprachoroidal injections**
 - 8 clinical trials completed
 - Injections performed across multiple retinal disorders
- ✓ **Safety profile comparable to intravitreal injections¹**
 - No Serious Adverse Events (SAEs) involving lens injury, suprachoroidal hemorrhage, or endophthalmitis have been observed
- ✓ **6 clinical trials ongoing including partner programs**

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. **24 U.S. and >50 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**



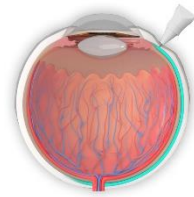
DEVICE PATENTS

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



DRUG PATENTS

- Administration of any drug to the suprachoroidal space by microinjection
- Administration of any drug to the eye by inserting a microinjector into the sclera




DISEASE PATENTS

- Methods of treating posterior ocular disorders by SCS administration

Suprachoroidal Space (SCS®) Injection Platform

Internal Development Pipeline

PROGRAM	THERAPEUTIC ENTITY	INDICATION	RESEARCH	PRECLINICAL	PHASE 1/2	PHASE 3
CLS-AX (axitinib)	Small Molecule	Wet AMD	Fully Enrolled			
CLS-301 (integrin inhibitor)	Small Molecule	Diabetic Macular Edema (DME)				
GENE THERAPY	Non-Viral & Viral Vectors	Open to Partnering				

SCS Microinjector® Partner Programs

PARTNER	THERAPEUTIC ENTITY	LICENSED INDICATION	IND-Enabling	PHASE 2	PHASE 3	APPROVAL
REGENXBIO	AAV-based Gene Therapy	Wet AMD (AAVIATE)				
REGENXBIO	AAV-based Gene Therapy	Diabetic Retinopathy (ALTITUDE)				
AURA BIOSCIENCES	Viral-like Drug Conjugate	Ocular Oncology/Choroidal Melanoma				

XIPERE® Commercial Partners

PARTNER	INDICATION	LICENSED TERRITORY	PRE-CLINICAL	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™				

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
- NDA approved on October 22, 2021;
Launched in Q1 2022 by Bausch + Lomb
 - J-Code obtained in June 2022
- Commercialization and development partnerships to enhance value and expand patient access



First approved therapeutic delivered into the suprachoroidal space

First therapy for macular edema associated with uveitis

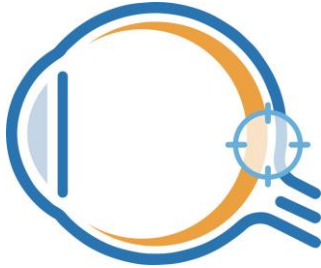
First commercial product developed by Clearside

First trial for uveitic macular edema using visual acuity change as a primary endpoint*

Suprachoroidal Delivery via SCS Microinjector[®]



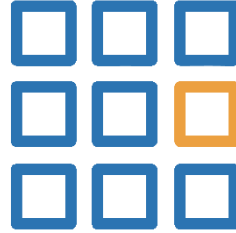
Core Advantages of Treating Via the Suprachoroidal Space (SCS®)



TARGETED

for efficacy

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



COMPARTMENTALIZED

for safety

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

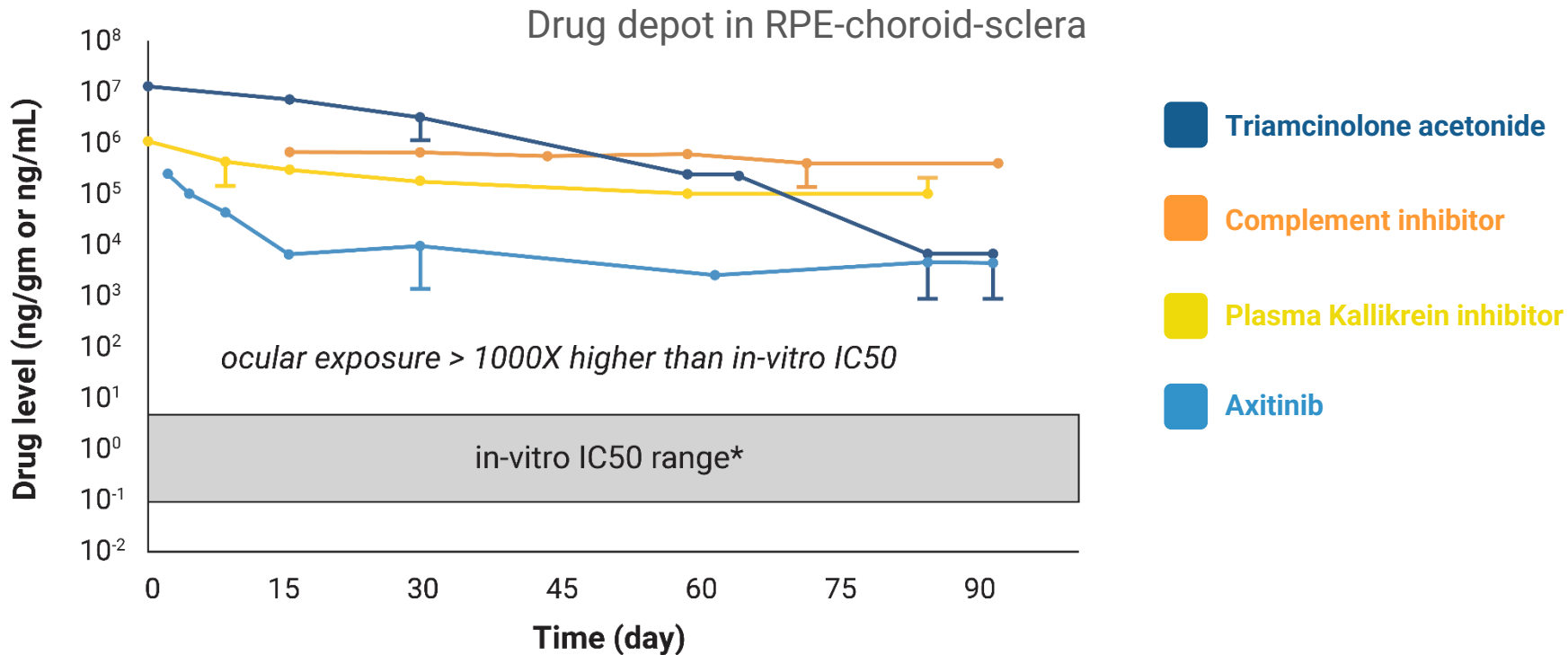


BIOAVAILABLE & PROLONGED DRUG LEVELS

for durability

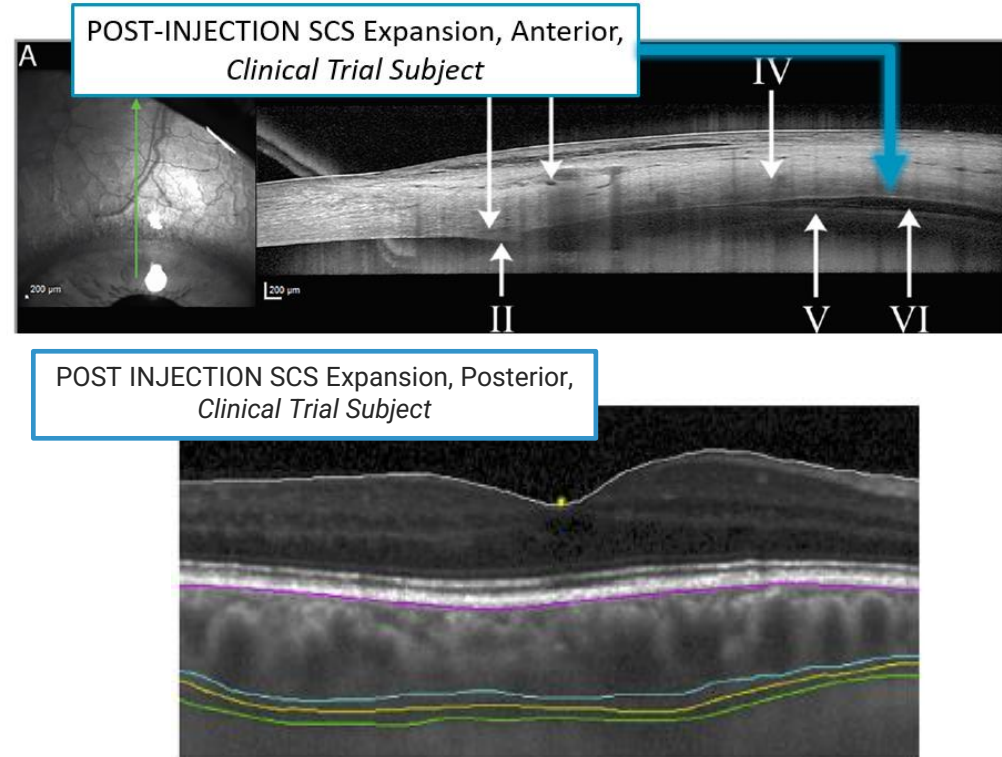
Fluid spreads circumferentially and posteriorly when injected within the suprachoroidal space, bathing the choroid and adjacent areas with drug

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



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

- A natural pressure gradient exists such that $IOP > \text{Anterior SCS Pressure} > \text{Posterior SCS Pressure}$
 - 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



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; I 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 Suprachoroidal Injection of Triamcinolone Acetonide in Eyes With Macular Edema Secondary to Retinal Vein Occlusion, *American Journal of Ophthalmology*, Feb 2018.

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



CLS-AX Delivered with SCS Microinjector® for Wet AMD



CLS-AX

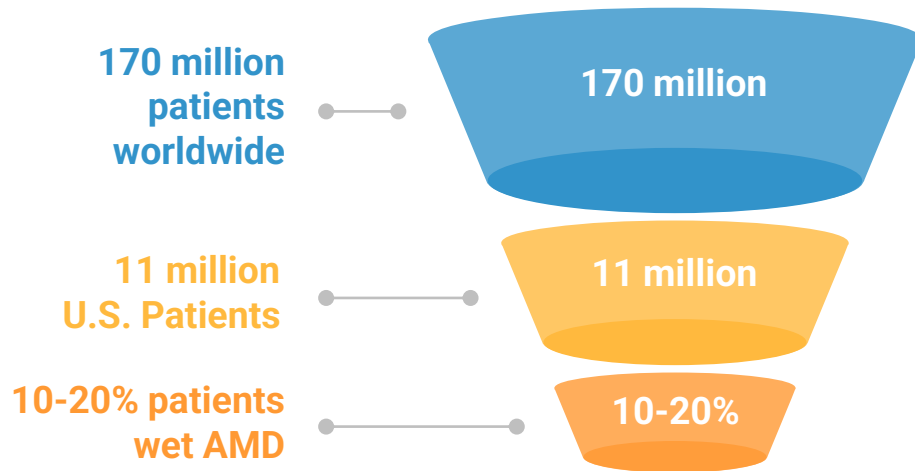
(axitinib injectable suspension)

for Suprachoroidal Injection



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 55
 - Neovascular or Wet AMD accounts for the majority of blindness
- ✓ U.S. prevalence expected to increase to 22 million by the year 2050
- ✓ Global prevalence expected to increase to 288 million by the year 2040
- ✓ Current treatments require frequent injections causing reduced compliance
 - Under-treatment contributes to limited outcomes

Current Wet AMD Therapies Lead to Under-Treatment and Limited “Real-World” Clinical Outcomes

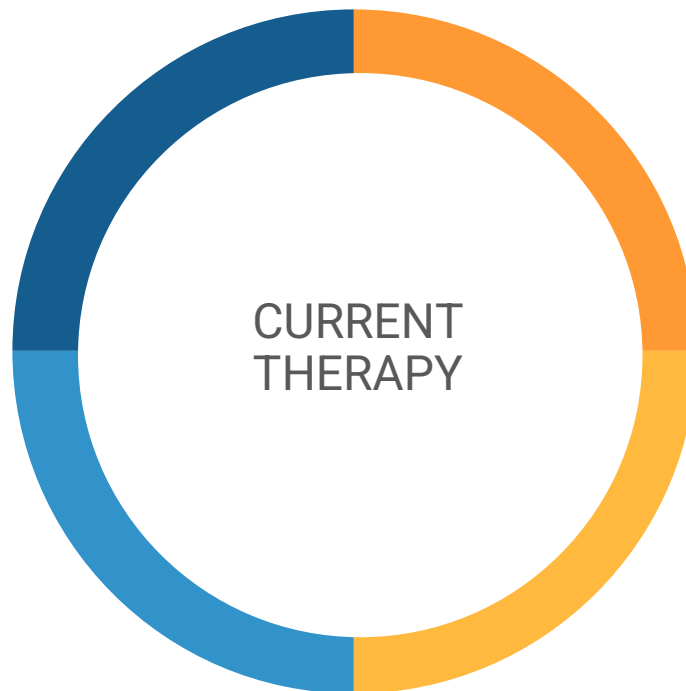
LIMITED OUTCOMES WITH CURRENT REGIMENS

With on-label anti-VEGF dosing, at 1 year¹⁻³:

- ~1/5 of patients lose BCVA
- ~1/2 do not achieve $\geq 20/40$
- ~2/3 do not gain ≥ 3 lines BCVA

CEILING OF EFFICACY

In clinical trials, more intensive anti-VEGF regimens or dosage yield no additional BCVA benefit^{1,6,7}



TREATMENT BURDEN

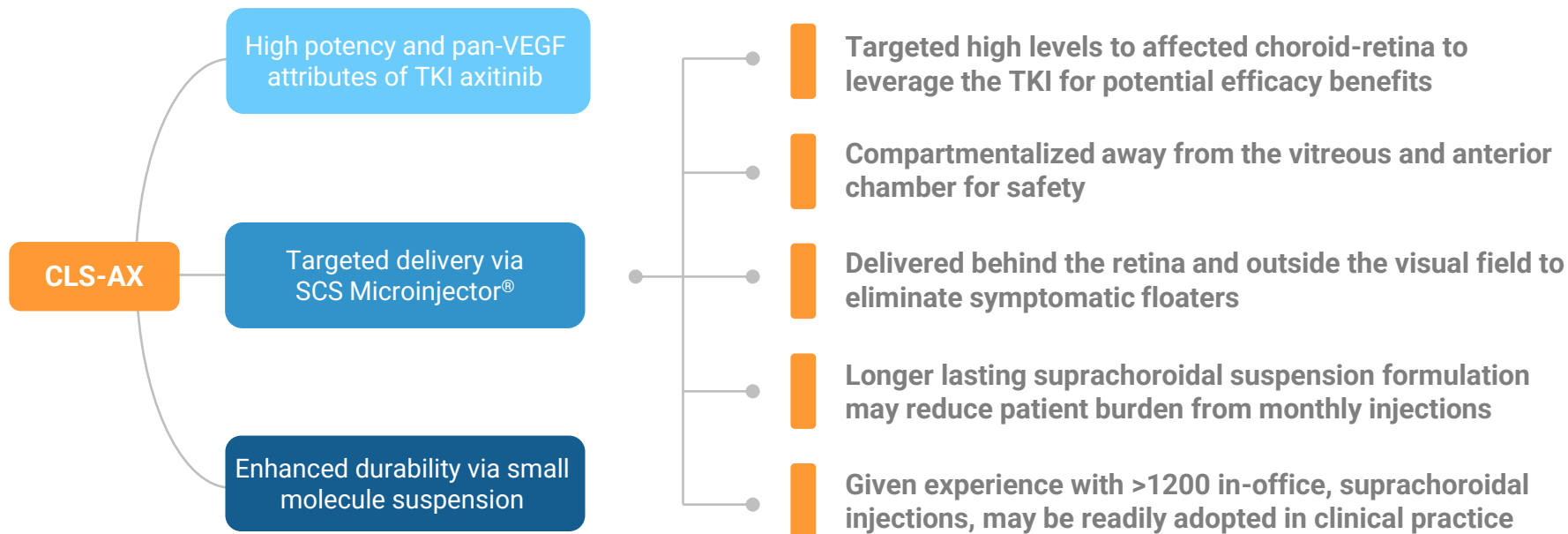
On-label dosing involves fixed frequent injections

UNDERTREATMENT AND LIMITED REAL-WORLD OUTCOMES

In clinical practice, patients cannot maintain intensive on-label dosing and are undertreated, improving by only 1-3 letters at 1 year^{4,5}

CLS-AX (axitinib injectable suspension) for Suprachoroidal Use

Potential to improve the treatment landscape for wet AMD patients



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 effective than anti-VEGF-A in *in-vitro* angiogenesis model¹⁻²

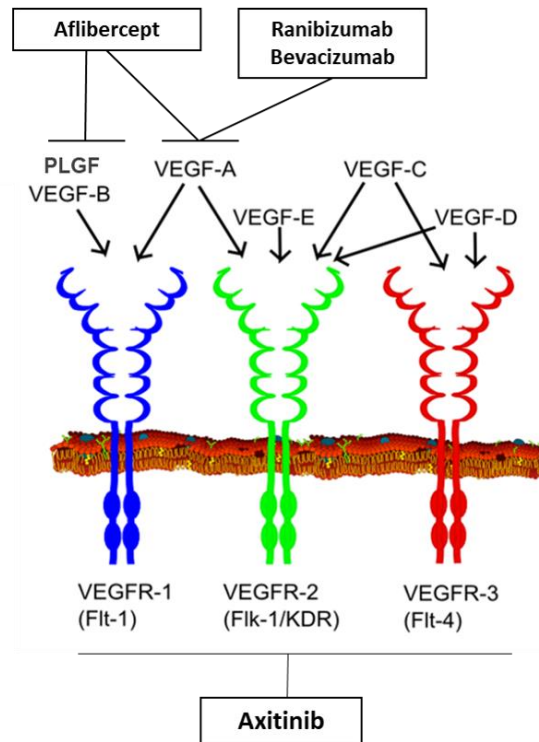


Highly potent tyrosine kinase inhibitor (TKI)

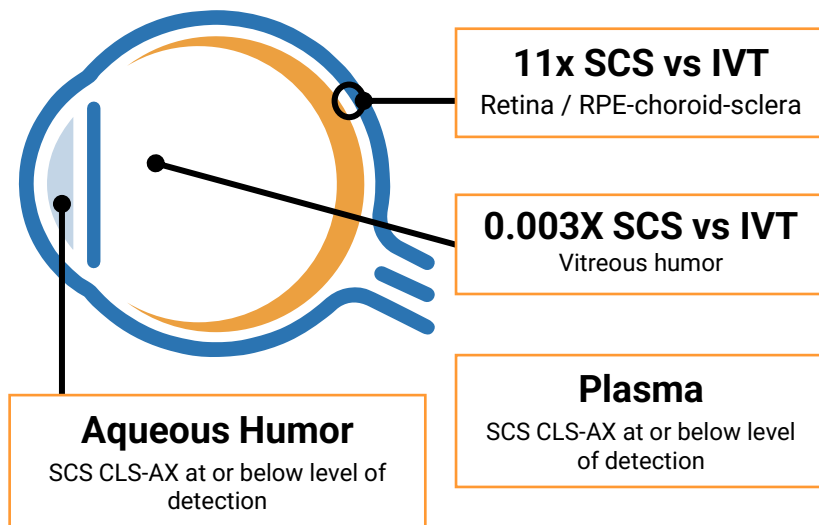
- >10x more potent than other TKIs in preclinical studies
- Better ocular cell biocompatibility than other TKIs³
- More effective than other TKIs for experimental corneal neovascularization in preclinical models



Preclinical data showed axitinib inhibition and regression of angiogenesis



Suprachoroidal Injection of CLS-AX Provides Targeted Delivery Relative to Intravitreal Injection at Same Dose

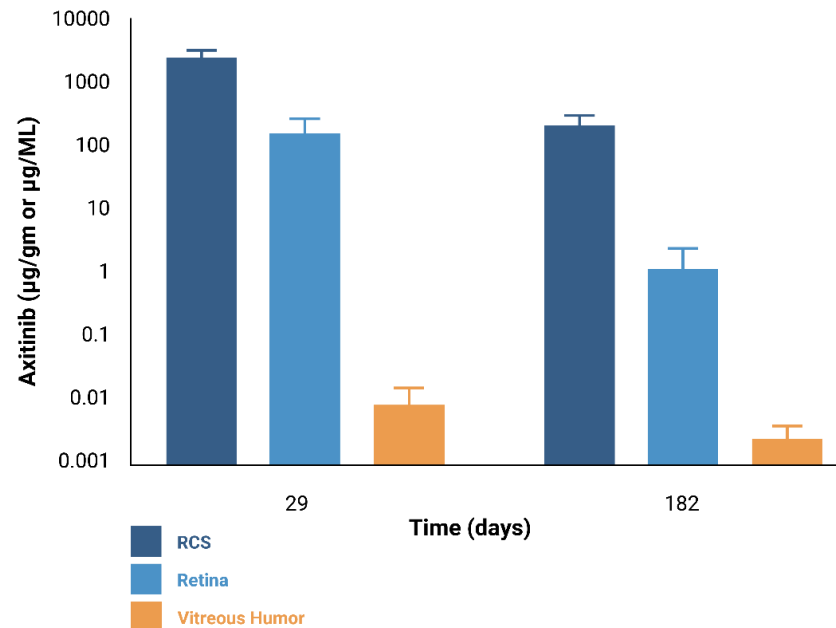


Rabbit Model

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

Therapeutic Levels > IC₅₀ for 6 months after single bilateral 1.05 mg/eye SCS injection in rabbits



OASIS: CLS-AX Phase 1/2a Clinical Trial in Wet AMD

TRIAL DESIGN AND OBJECTIVES

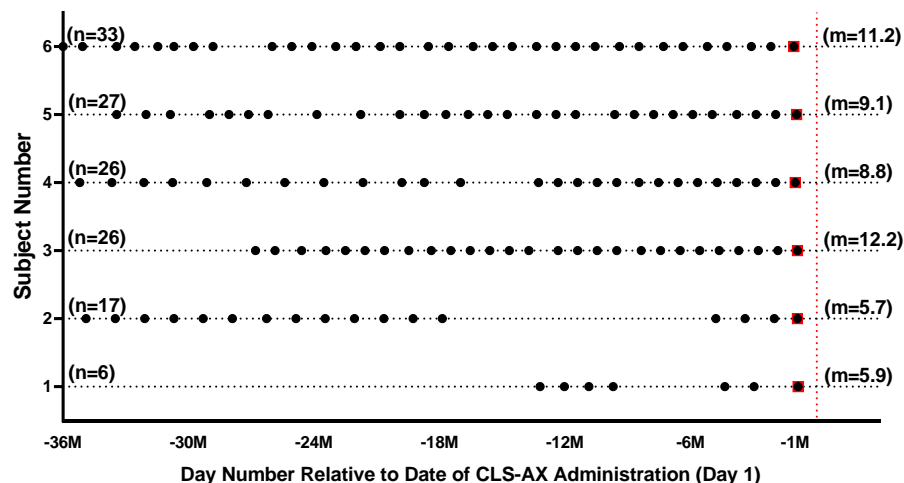
- Open-label study with a primary endpoint to evaluate safety and tolerability of escalating single doses of CLS-AX administered through suprachoroidal injection following IVT aflibercept
- 4 Cohorts with a total of 27 patients
- Dose-escalation of CLS-AX (in mg): Cohort 1 at 0.03; Cohort 2 at 0.10; Cohort 3 at 0.50; Cohort 4 at 1.0
- Secondary endpoints: visual function, ocular anatomy, and need for additional treatment
- 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



Anti-VEGF Treatments up to 3 Years Prior to Screening

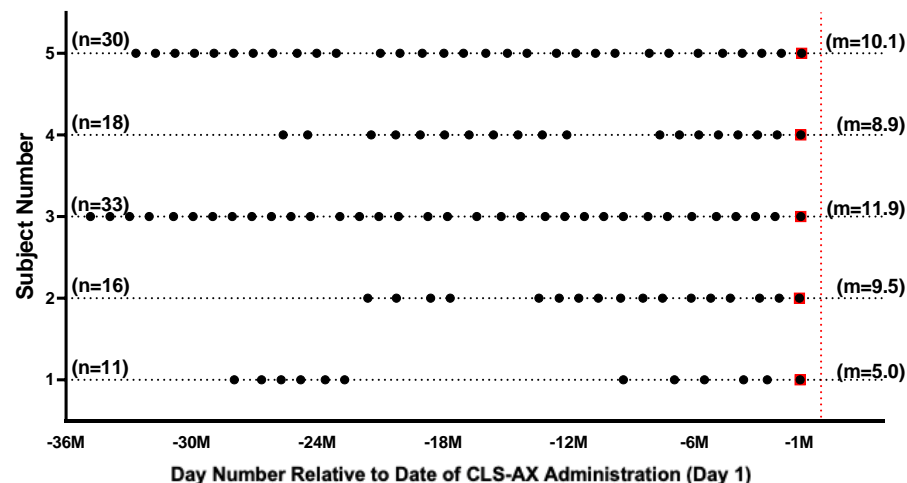
Highly treatment experienced, chronic patients enrolled in Cohorts 1 & 2

COHORT 1: 0.03 mg



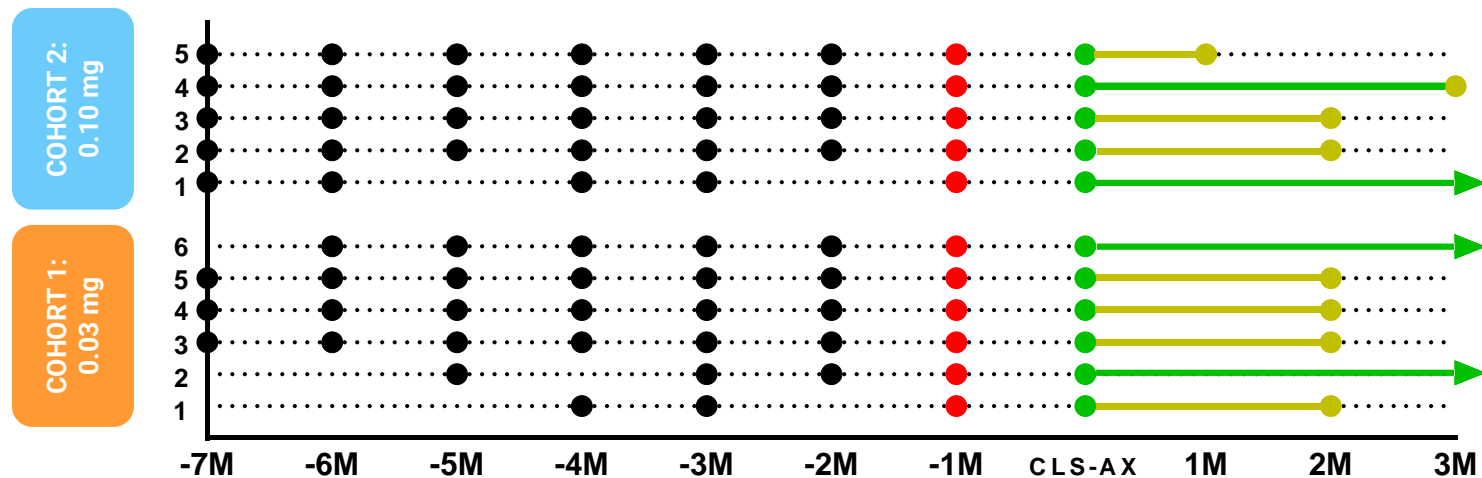
● Prior wAMD Treatment ■ IVT Aflibercept (Screening, Visit 1)
(n=) Total number of wAMD treatments prior to Screening
(m=) Mean number of wAMD treatments prior to Screening per year

COHORT 2: 0.10 mg



● Prior wAMD Treatment ■ IVT Aflibercept (Screening, Visit 1)
(n=) Total number of wAMD treatments prior to Screening
(m=) Mean number of wAMD treatments prior to Screening per year

6 Month Prior Anti-VEGF Therapies and Time to Additional Therapy



- SC CLS-AX injection
- IVT Aflibercept injection
- Anti-VEGF injection prior to study entry
- Additional IVT anti-VEGF injection

Time to Additional Therapy	Number (%) of Participants
≥ 3 months	4 (36.4%)
2 months	6 (54.5%)
1 month	1 (9.1%)

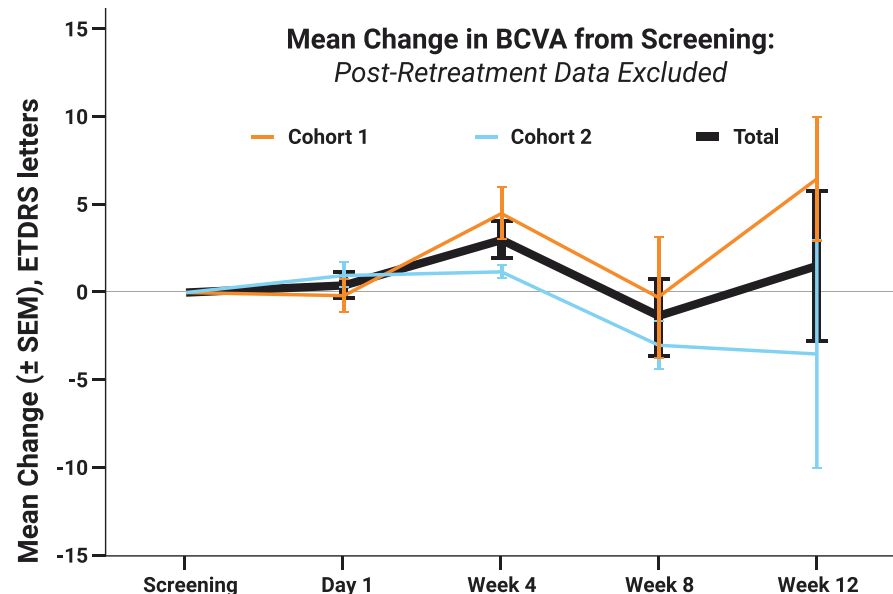
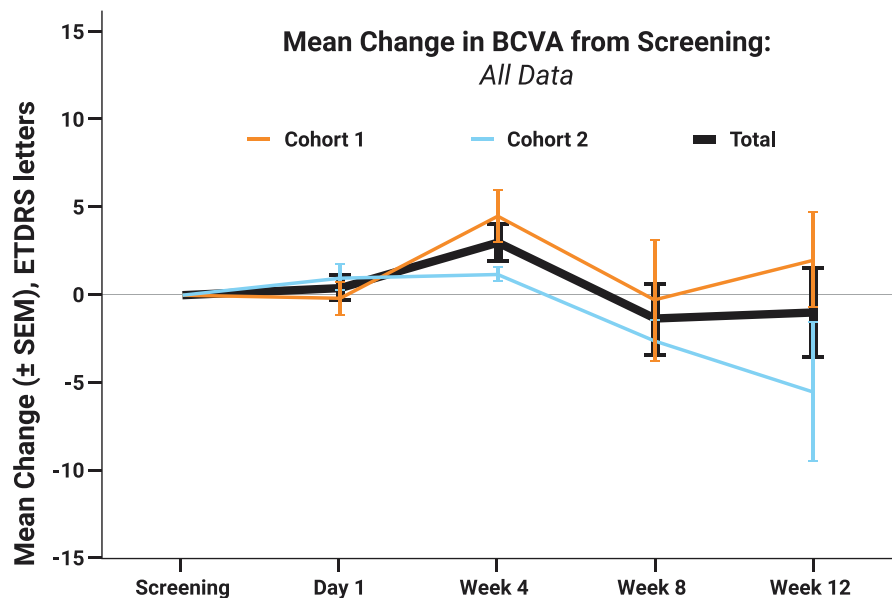
Reason for Retreatment

COHORT	SUBJECT	RETREATMENT VISIT	REASON FOR RETREATMENT
COHORT 1: 0.03 mg (N=6)	5	2 months post CLS-AX	BCVA
	4	2 months post CLS-AX	CST
	3	2 months post CLS-AX	CST
	1	2 months post CLS-AX	BCVA
COHORT 2: 0.10 mg (N=5)	5	1 month post CLS-AX	CST – retreatment criteria <u>not met</u> according to independent reading center
	4	3 months post CLS-AX	BCVA
	3	2 months post CLS-AX	Hemorrhage – no hemorrhage observed by the independent reading center; retreatment criteria <u>not met</u>
	2	2 months post CLS-AX	CST – retreatment criteria <u>not met</u> according to independent reading center

Protocol based Assessment for additional aflibercept treatment:

- loss from best measurement of ≥ 10 letters in BCVA with exudation
- increase in CST >75 microns
- a vision-threatening hemorrhage

Mean Best Corrected Visual Acuity Letter Score, Change from Screening

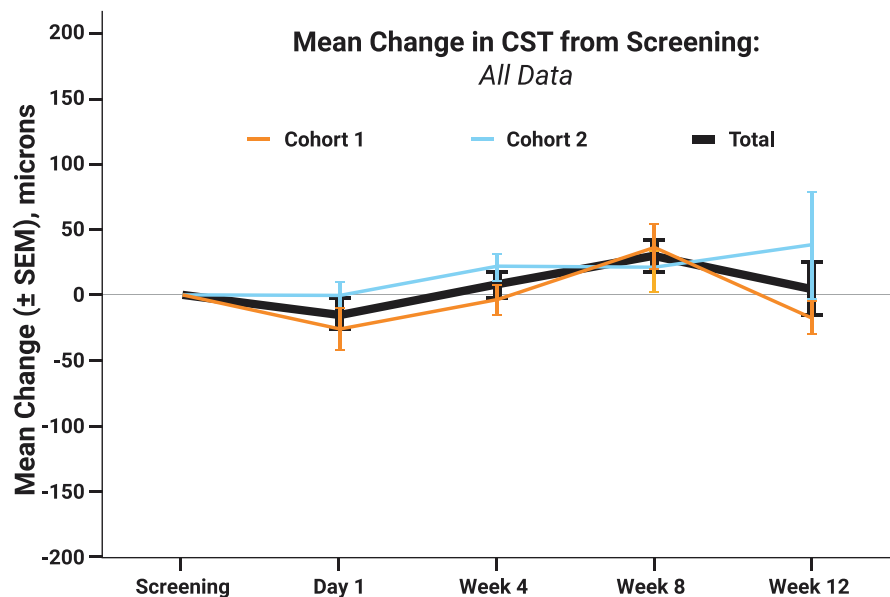


Cohort	Screening	Baseline	Week 4	Week 8	Week 12
Cohort 1, n	6	6	6	6	6
Cohort 2, n	5	5	5	5	4*

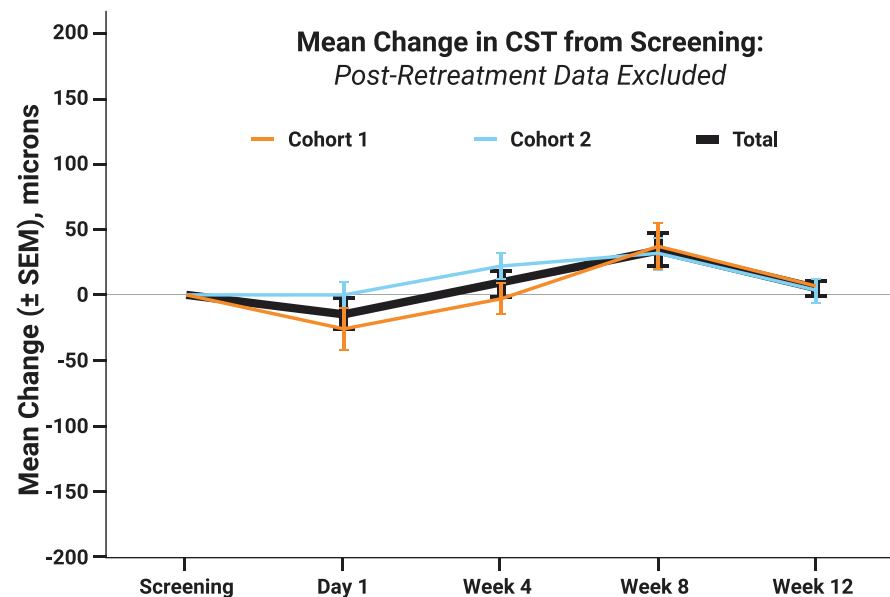
Cohort	Screening	Baseline	Week 4	Week 8	Week 12
Cohort 1, n	6	6	6	6	2
Cohort 2, n	5	5	5	4	2

*Cohort 2 subject 2 discontinued after receiving additional therapy | Source: Clearside data on file.

Mean Change Central Subfield Thickness, Change from Screening



Cohort	Screening	Baseline	Week 4	Week 8	Week 12
Cohort 1, n	6	6	6	6	6
Cohort 2, n	5	5	5	5	4*



Cohort	Screening	Baseline	Week 4	Week 8	Week 12
Cohort 1, n	6	6	6	6	2
Cohort 2, n	5	5	5	4	2

OASIS Cohorts 1 & 2 Results Supported Advancing to Higher Dosing

SAFETY

- CLS-AX well tolerated with no dose limiting toxicities
- No dispersion of investigational product into the vitreous
- No adverse events related to intraocular pressure (IOP), inflammation, or vasculitis

ANATOMIC EFFECTS

- Stable disease activity (based on CST), on average, over three months even after excluding patients who were retreated

VISUAL ACUITY

- Stable visual acuity, on average, over three months even after excluding patients who were retreated

DURABILITY

Post CLS-AX in Heavily Pre-Treated Patients

- 4/11 (36%) of patients did not require additional therapy for ≥ 3 months
- 6/11 (55%) of patients did not require additional therapy for 2 months
- 1/11 (9%) patient was retreated at 1 month

OASIS CURRENT STATUS

✓ Total enrollment of n=27 patients

- Cohort 3 enrolled with n=8 patients at a dose of 0.50 mg CLS-AX
- Cohort 4 enrolled with n=8 patients at a dose of 1.0 mg CLS-AX

✓ Endpoints

- **Primary endpoints:** safety and tolerability of escalating single doses of CLS-AX administered through suprachoroidal injection following IVT aflibercept
- **Secondary endpoints:** visual function, ocular anatomy, and need for retreatment per protocol

✓ Full OASIS Data Set Expected in November 2022

Corporate Partnerships & Milestones





THE OPPORTUNITY: GENE THERAPY

- Exclusive worldwide rights to our SCS Microinjector for delivery of adeno-associated virus (AAV)-based therapeutics to the suprachoroidal space to treat wet AMD, diabetic retinopathy and certain other conditions for which anti-VEGF treatment is the standard of care
- Delivery of gene therapy through the SCS may provide a targeted, in-office, non-surgical treatment approach option
- Two 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**

THE TERMS

- Up to an additional \$34M in development milestones across multiple indications
- Up to \$102M in sales milestones
- Mid single digit royalties on net sales of products using SCS Microinjector

**AAVIATE: RGX-314 in wet AMD**

- Cohorts 1-3: Suprachoroidal delivery well tolerated in 50 patients with no drug-related SAEs
- **Cohort 1: Positive interim efficacy data (Q4 2021)**
- **Cohort 2: Positive interim efficacy data (Q4 2021)**
 - Treatment effect observed with stable visual acuity and retinal thickness
 - Demonstrated meaningful reduction (>70%) in anti-VEGF treatment burden; 40% of patients were anti-VEGF injection-free
- Cohort 3 & Cohort 5: neutralizing antibody (NAb) positive patients
- Cohorts 4 and 5 at a higher dose
- No prophylactic immune suppressive corticosteroid therapy

ALTITUDE: RGX-314 in Diabetic Retinopathy

- **Enrollment Completed**
- **Cohort 1: Positive Interim data (Q1 2022)**
 - Suprachoroidal delivery well tolerated in 15 patients in Cohort 1 with no drug-related SAEs at 6 months
 - No intraocular inflammation observed
 - 47% of patients demonstrated a ≥ 2 step improvement from baseline on the ETDRS-DRSS at six months, compared to 0% of patients in observational control; increase from 33% of patients at three months
 - Stable mean change in BCVA of +0.3 letters compared to baseline at 6 months
- Cohort 3 enrolled NAb positive patients
- No prophylactic immune suppressive corticosteroid therapy

THE OPPORTUNITY: OCULAR ONCOLOGY

- Worldwide licensing agreement for the use of our SCS Microinjector to deliver their proprietary drug candidates into the SCS for the potential treatment of certain ocular cancers, including choroidal melanoma
- Non-surgical alternative to intravitreal delivery of Aura's oncology drug candidates via our SCS Microinjector
- Choroidal melanoma is the most common, primary intraocular tumor in adults
- THE TERMS:
 - Up to \$21M in regulatory and development milestones
 - Low to mid single digit royalties on net sales of products using SCS Microinjector

AU-011 PHASE 2 CLINICAL TRIAL

- Evaluate Safety and Efficacy of AU-011 Via Suprachoroidal Administration in Subjects With Primary Indeterminate Lesions and Small Choroidal Melanoma
- **Preliminary results indicate a positive safety and tolerability profile:** No treatment related SAEs, dose limiting toxicities, or grade 3/4 AEs reported
- Cohorts 1-5: Fully enrolled (n=14)
- Cohort 6: Enrolling

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 \$57M 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 \$33M in additional approvals, development and sales milestones
- Tiered royalties of 10% to 12%

Non-Dilutive Royalty Financing Provides Cash Runway into 2024

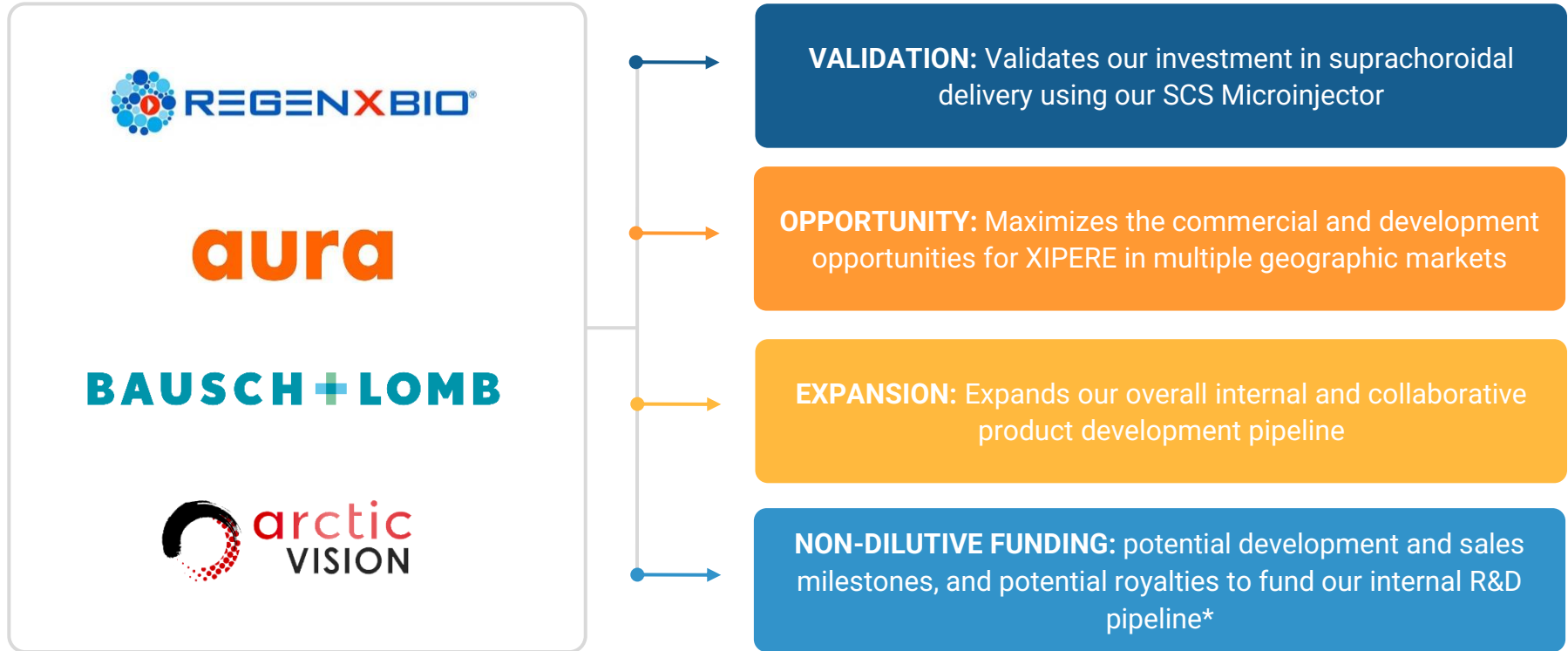
FUNDING

- May receive up to \$65 million dollars
- Upfront cash payment of \$32.5M, less certain expenses
- Additional \$12.5M deposited in an escrow account to be released to CLSD upon attainment of a pre-specified sales milestone for XIPERE by 3/31/24
- Eligible for additional payment of \$20M to CLSD upon attainment of a second, pre-specified 2024 XIPERE sales milestone
- Closing date: August 8, 2022

TERMS

- Funder will receive royalties and milestone payments due to CLSD from XIPERE and certain SCS Microinjector license agreements
- Repayment capped at 2.5 times total payments; cap may be increased under certain circumstances
- Excludes all internally developed assets and programs, including CLS-AX, as well as any future in-licensed assets

Four Validating Partnerships to Drive Growth



Targeted Catalysts in 2022

INTERNAL R&D PIPELINE

CLS-AX OASIS Phase 1/2a Clinical Trial

- ✓ Q2: Cohort 4 initiated
- Q4: Cohorts 3 & 4 data and complete OASIS analysis
- Q4: Cohort 2 data from 6-month extension

CLS-AX Phase 2 Clinical Trial

- YE: Ready for recruitment

YE 2022: Integrin Inhibitor preclinical data

Medical/Scientific meeting presentations

- ✓ Q1 & Q2: Angiogenesis, ARVO, Macula Society
- Q3 & Q4: ASRS, Retina Society, AAO

PARTNER PROGRAMS

BAUSCH + LOMB:

- ✓ XIPERE® launch in U.S. in Q1 2022

ARCTIC VISION: Arcatus™ in China

- ✓ Initiate Phase 1 trial in diabetic macular edema
- Phase 3 trial data in uveitic macular edema

REGENXBIO: RGX-314

- ✓ ALTITUDE trial in DR: Positive interim data
- Additional data from ALTITUDE & AAVIATE trial in wet AMD

AURA BIOSCIENCES: AU-011

- Additional data from Phase 2 trial in choroidal melanoma



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Nasdaq: CLSD

