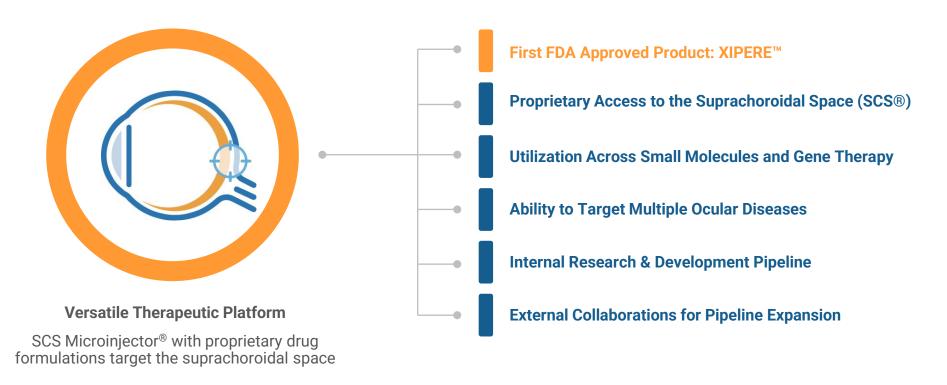


Forward-Looking Statements

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.

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





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





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



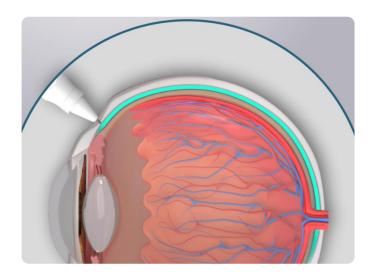
BIOAVAILABLE & PROLONGED DRUG LEVELS

for durability

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



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



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



- 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 First commercial product developed by Clearside First trial for uveitic macular edema using visual

acuity change as a primary endpoint*



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





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



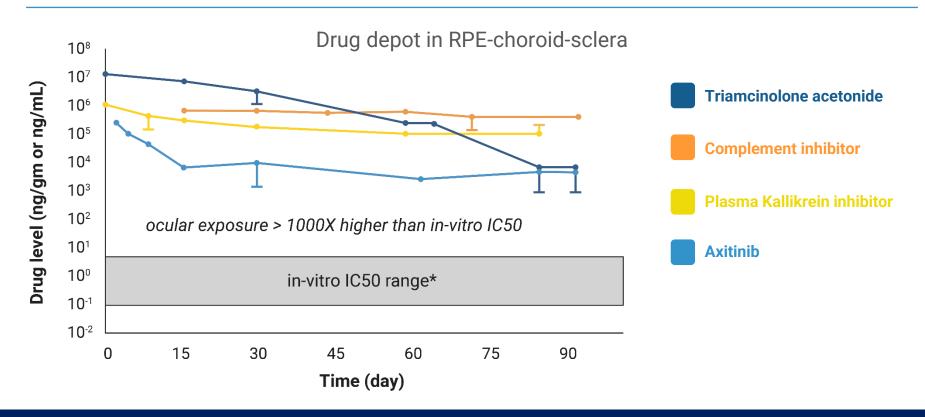


CLS-AX Delivered with SCS Microinjector® for Wet AMD





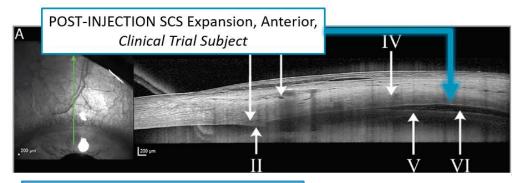
Preclinical Data Supports Durability Potential of Small Molecule Suspensions Delivered into the Suprachoroidal Space

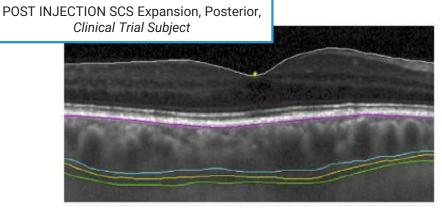




SCS Microinjector Expands the SCS Circumferentially and Posteriorly to Deliver Drugs to the Macula

- 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



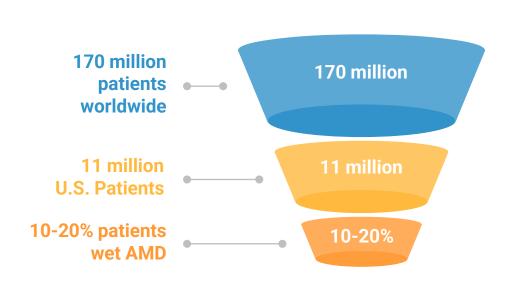






Age-Related Macular Degeneration (AMD)

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



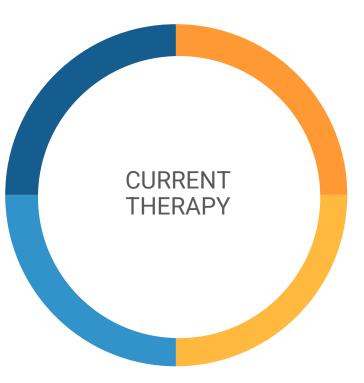
Current Wet AMD Therapies Lead to Under-Treatment and Limited "Real-World" Clinical Outcomes

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 ≥ 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

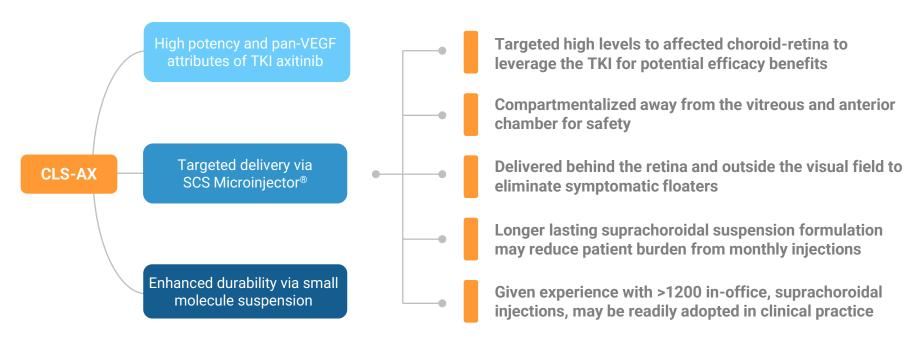
UNDERTREATMENT AND LIMITED REAL-WORLD OUTCOMES

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 is a tyrosine kinase inhibitor (TKI)

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

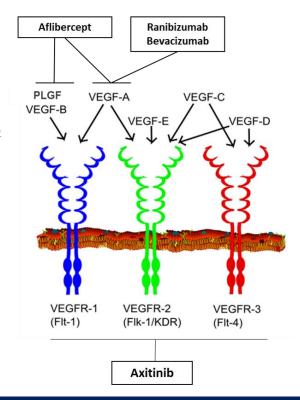


Highly potent tyrosine kinase inhibitor (TKI)

- >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

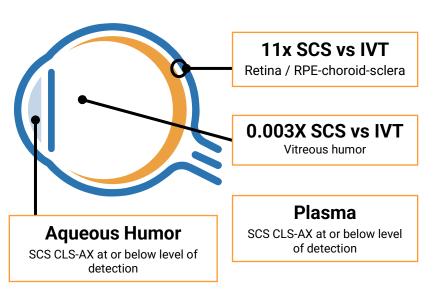


Preclinical data showed axitinib inhibition and regression of angiogenesis





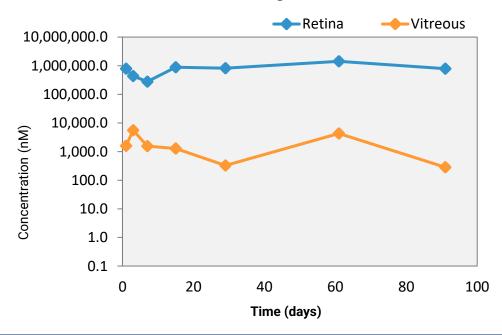
Suprachoroidal Injection of CLS-AX Provides Targeted Delivery Relative to Intravitreal Injection at Same Dose



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: High, Sustained Drug Levels in the Retina after SCS Administration

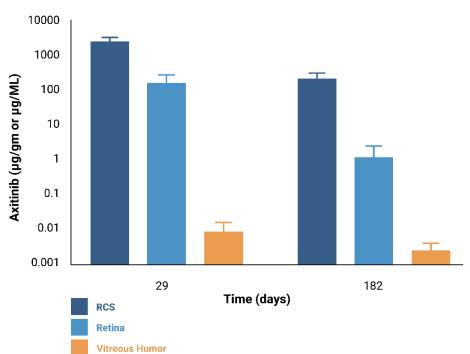
High Retina Levels: Sufficient to block VEGF pathway Low Plasma Levels: <1 ng/mL





CLS-AX has Potential for Meaningful Durability

Therapeutic Levels > IC50 for 6 months after 1.05 mg/eye SCS Injection in Rabbits



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

- On day 182, mean axitinib levels in the RPE-choroid-sclera (199 μg/gm) and in the retina (1.1 μg/gm) were 3-5 log orders higher than the in-vitro IC50 value (0.2 ng/mL, VEGFR2 autophosphorylation inhibition assay).
- Based on this IC50 value, therapeutic levels were achieved in the RPE-choroid-sclera and retina for 6 months after a single suprachoroidal injection of axitinib in rabbits.



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

TRIAL DESIGN AND OBJECTIVES

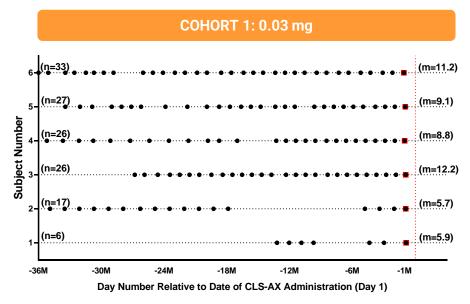
- Open-label study with a primary endpoint to evaluate safety and tolerability of escalating single doses of CLS-AX administered through suprachoroidal injection following IVT aflibercept
- 4 Cohorts with a total of 27 patients
- Dose-escalation of CLS-AX (in mg): Cohort 1 at 0.03; Cohort 2 at 0.10; 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



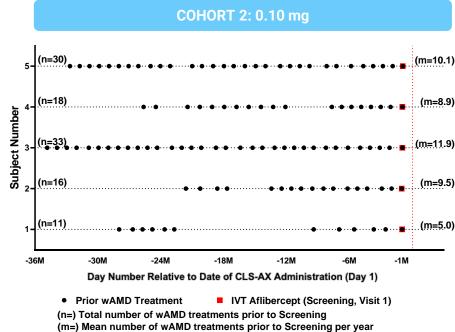


Anti-VEGF Treatments up to 3 Years Prior to Screening

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









Enrolling Anti-VEGF Sub-Responders with Active*, Chronic Disease

Inclusion of difficult-to-treat patients supports dose selection and mitigates risk in Phase 2b

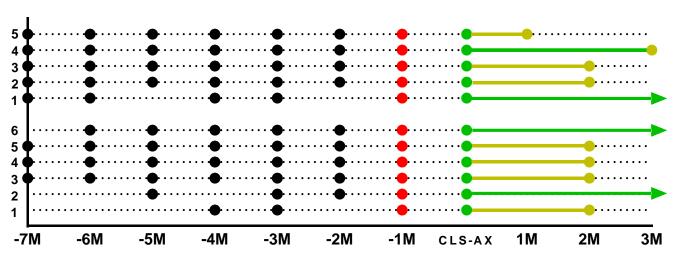
CHARACTERISTICS	COHORT 1: 0.03mg (N=6)	COHORT 2: 0.10mg (N=5)		
No. of participants	6	5		
Mean age (range), years	81.8 (66-93)	78.2 (65-90)		
Women, no. (%)	2 (33.3)	3 (60.0)		
Total mean number of wAMD treatments prior to screening (range)	25.8 (6-40)	23.2 (11-38)		
Mean baseline best corrected visual acuity (range), letters	59.0 (29-74)	65.6 (52-75)		
Mean central subfield retinal thickness (range), μm	231.2 (208-294)	209.4 (184-227)		
Mean total lesion area (range), mm2	6.252 (3.58-9.58)	7.712 (1.06-18.02)		

^{*}Active disease verified by independent reading center



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
	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
COHORT 2: 0.10 mg (N=5)	3	2 months post CLS-AX	Hemorrhage – no hemorrhage observed by the independent reading center; retreatment criteria not met
	2	2 months post CLS-AX	CST – retreatment criteria <u>not met</u> according to independent reading center

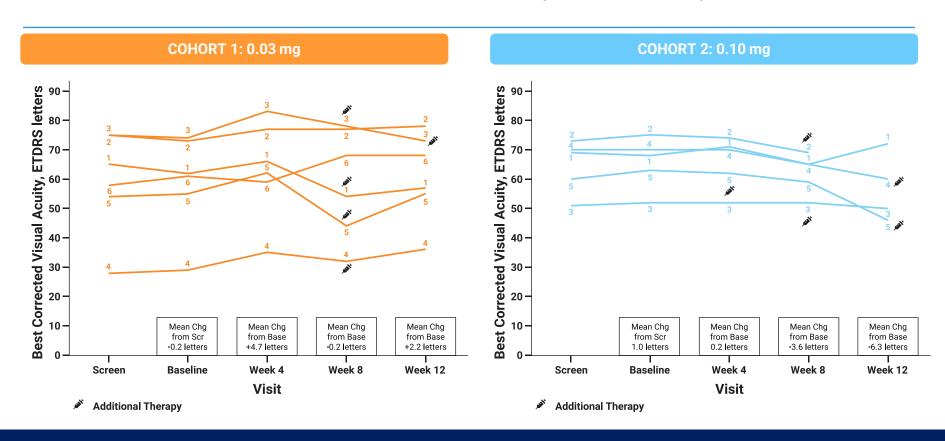
Protocol based Assessment for additional aflibercept treatment:

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



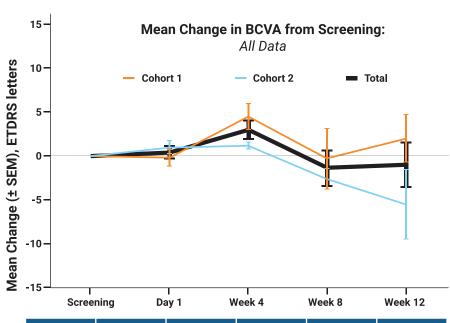


Individual Best Corrected Visual Acuity Letter Score, by Visit

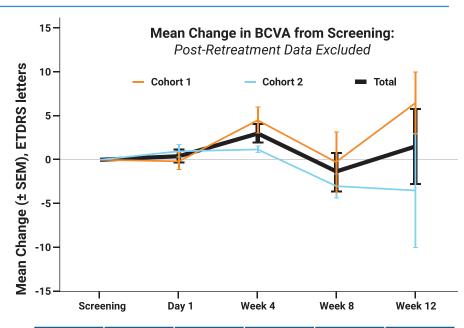




Mean Best Corrected Visual Acuity Letter Score, Change from Screening



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*

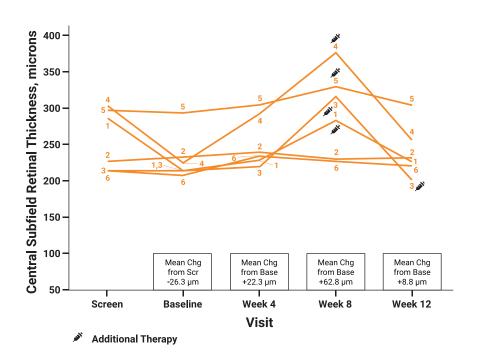


Cohort	Screening	Baseline	Week 4	Week 8	Week 12
Cohort 1, n	6	6	6	6	2
Cohort 2, n	5	5	5	4	2

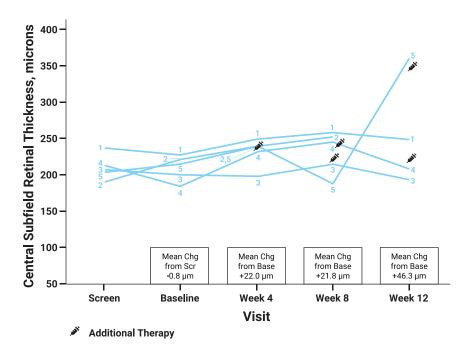


Individual Central Subfield Thickness, by Visit



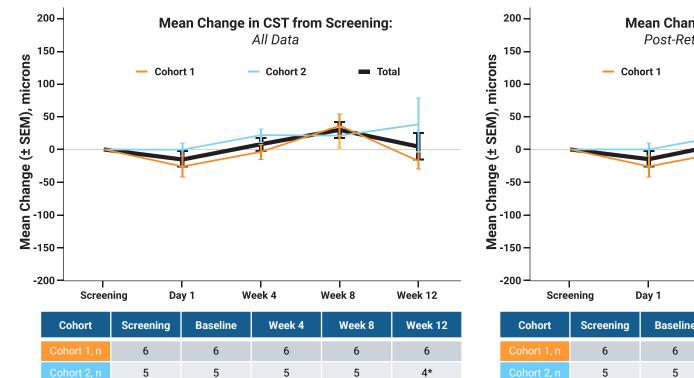


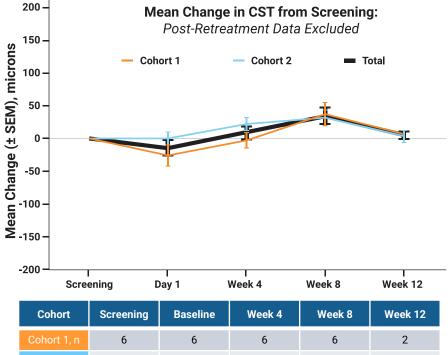
COHORT 2: 0.10 mg





Mean Change Central Subfield Thickness, Change from Screening





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







Suprachoroidal Space (SCS®) Injection Platform

		Internal Developmen	t Pipeline				
PROGRAM	THERAPEUTC ENTITY	INDICATION	RESEARCH	PRECLINICAL	. PH	ASE 1/2	PHASE 3
CLS-AX (axitinib)	Small Molecule	Wet AMD	Fully Enrolled QAS				
CLS-301 (integrin inhibitor)	Small Molecule	Diabetic Macular Edema (DME)					
GENE THERAPY	Non-Viral & Viral Vectors	Open to Partnering					
		SCS Microinjector® Parti	ner Programs				
PARTNER	THERAPEUTC ENTITY	LICENSED INDICATION	IND-Enabling	PHASE 2	Pl	HASE 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® Commercia	l Partners				
PARTNER	INDICATION	LICENSED TERRITORY	PRE- CLINICAL	PHASE 1 P	HASE 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			Ar	catus™	
	Diabetic Macular Edema	Countries, India, Australia, New Zealand	Aı	rcatus™			





Enabling SCS Delivery of AAV Gene Therapy for Retinal Disease

THE OPPORTUNITY: GENE THERAPY FOR RETINAL DISEASES

- 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
- Two ongoing multi-center, open-label, randomized, controlled, dose-escalation studies evaluating the efficacy, safety and tolerability of suprachoroidal delivery of RGX-314
- Delivery of gene therapy through the SCS may provide a targeted, in-office, non-surgical treatment approach option
- First data ever presented utilizing gene therapy delivered into the suprachoroidal space
- THE TERMS:
 - Up to \$136M in regulatory, development and sales milestones across certain VEGF mediated retinal diseases
 - Mid single digit royalties on net sales of SCS Microinjector products





Two Phase 2 Trials Using Clearside's 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





Enabling SCS Drug Delivery for Ocular Oncology

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 SCS Microinjector products

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



BAUSCH+LOMB

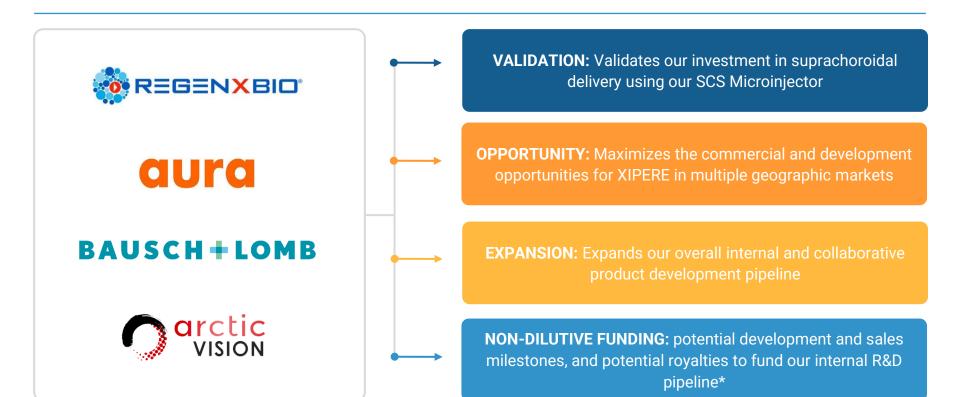
- License for the U.S. and Canada
- Received \$20M in upfront, U.S. approval and pre-launch milestones
- Up to \$57M in milestone payments
- Tiered royalties from the high-teens to 20%



- 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%



Four Validating Partnerships to Drive Growth







Non-Dilutive Royalty Financing Provides Cash Runway into 2024

FUNDING

- Upfront cash payment of \$32.5M, less certain expenses
- May receive up to \$65 million dollars
 - Additional \$12.5M deposited in an escrow account to be released to CLSD upon attainment of a prespecified 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
- Provides funding into 2024

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 received by CLSD. Then CLSD will keep any future royalty and milestone payments from these agreements
- Cap may be increased under certain circumstances after 2024
- Excludes all internally developed assets and programs, including CLS-AX, as well as any future in-licensed assets



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



