

CLEARSIDE®
BIOMEDICAL

Corporate Presentation | August 2021

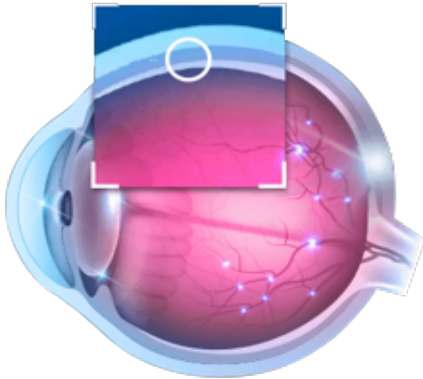
Forward-Looking Statements

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 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, 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, 2020, filed with the SEC on March 15, 2021, 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

Versatile Therapeutic Platform

SCS Microinjector® with proprietary drug formulations target the Suprachoroidal Space



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

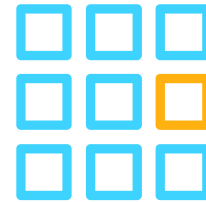
Core Advantages of Treating Via the Suprachoroidal Space



TARGETED

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

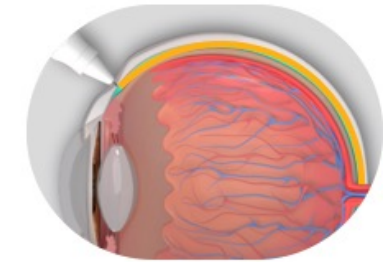
for efficacy



COMPARTMENTALIZED

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

for safety



BIOAVAILABLE & PROLONGED DRUG LEVELS

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

for durability

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



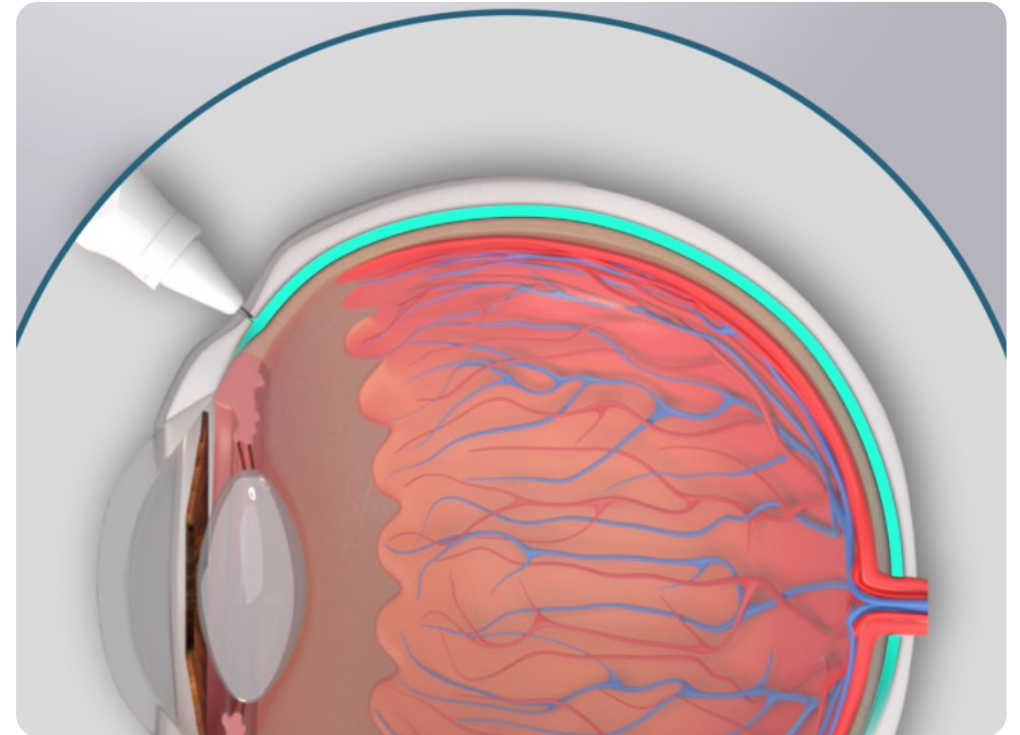
DISEASE PATENTS

Methods of treating posterior ocular disorders by SCS administration

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

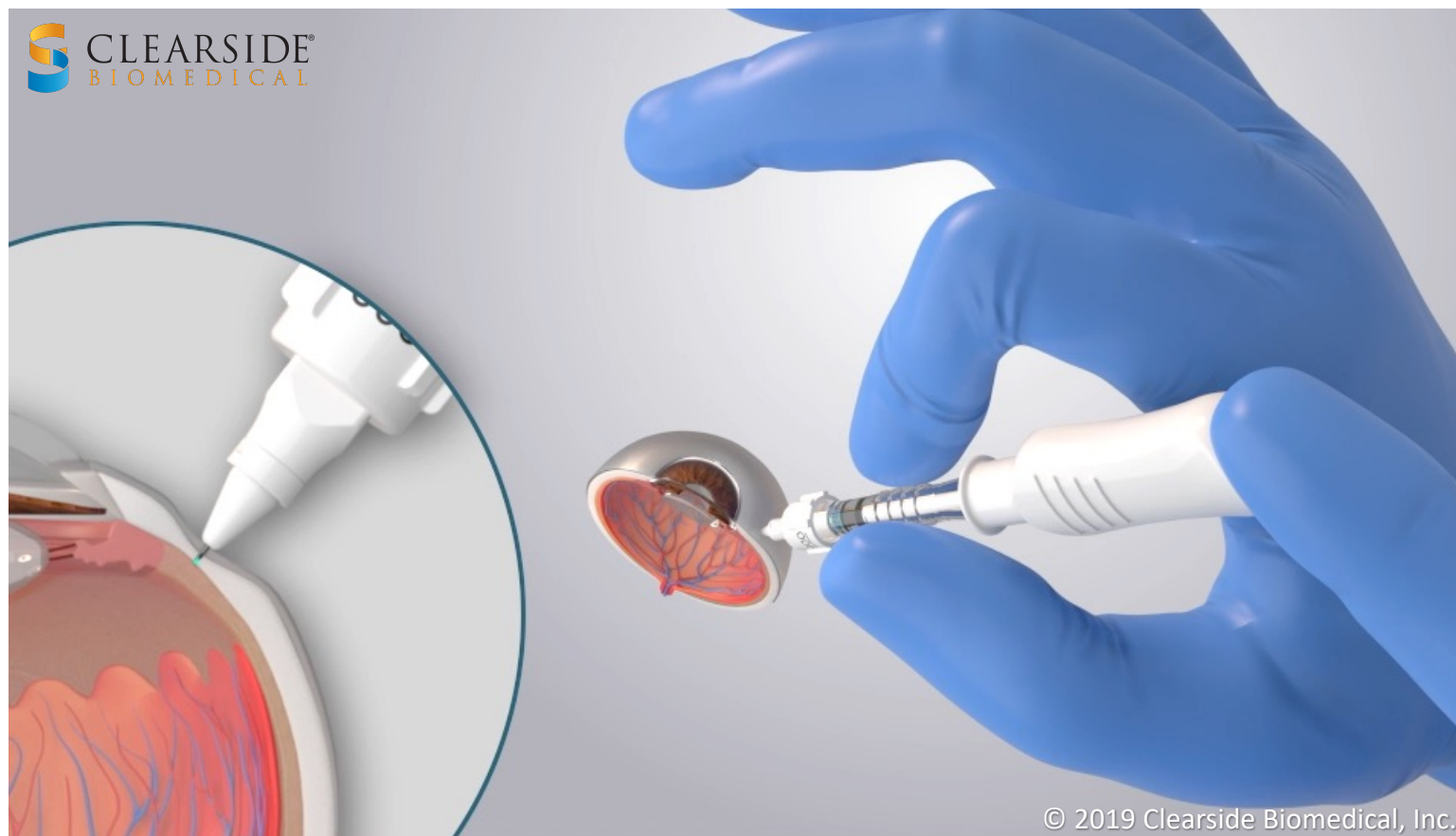
- Clinically tested in >1200 suprachoroidal injections
 - 8 clinical trials completed
 - Injections performed across multiple retinal disorders
- Safety profile comparable to intravitreal injections¹
 - No Serious Adverse Events (SAEs) involving lens injury, suprachoroidal hemorrhage, or endophthalmitis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

SUPRACHOROIDAL SPACE INJECTION



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

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






CLS-AX Delivered with SCS Microinjector® for Wet AMD






Suprachoroidal Space (SCS®) Injection Platform

Internal Development Pipeline



PROGRAM	THERAPEUTIC ENTITY	INDICATION	RESEARCH	PRECLINICAL	PHASE 1/2	PHASE 3
CLS-AX (axitinib injectable suspension)	Small Molecule	Wet AMD				
Integrin Inhibitor (Injectable suspension)	Small Molecule	Diabetic Macular Edema (DME)				
Gene Therapy	Non-Viral Vectors	"Therapeutic Biofactory" / Inherited Retinal Disease				



SCS Microinjector® Partner Programs

PARTNER	THERAPEUTIC ENTITY	INDICATION	IND-Enabling	PHASE 2	PHASE 3	NDA
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	THERAPEUTIC ENTITY	TERRITORY	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	NDA
BAUSCH HEALTH	Small Molecule	U.S. & Canada; options ex-North America					
ARCTIC VISION	Small Molecule	Greater China & South Korea					

PDUFA 10/30/21

XIPERE™: Potential Suprachoroidal Approach to Treating Uveitic Macular Edema

- Macular edema is the leading cause of vision loss in patients with non-infectious uveitis
- NDA was resubmitted and accepted for review with PDUFA goal date of October 30, 2021
- Commercialization and development partnerships to enhance value and expand patient access

XIPERE™
(triamcinolone acetonide suprachoroidal
injectable suspension) 40 mg/mL

If approved, XIPERE would represent the

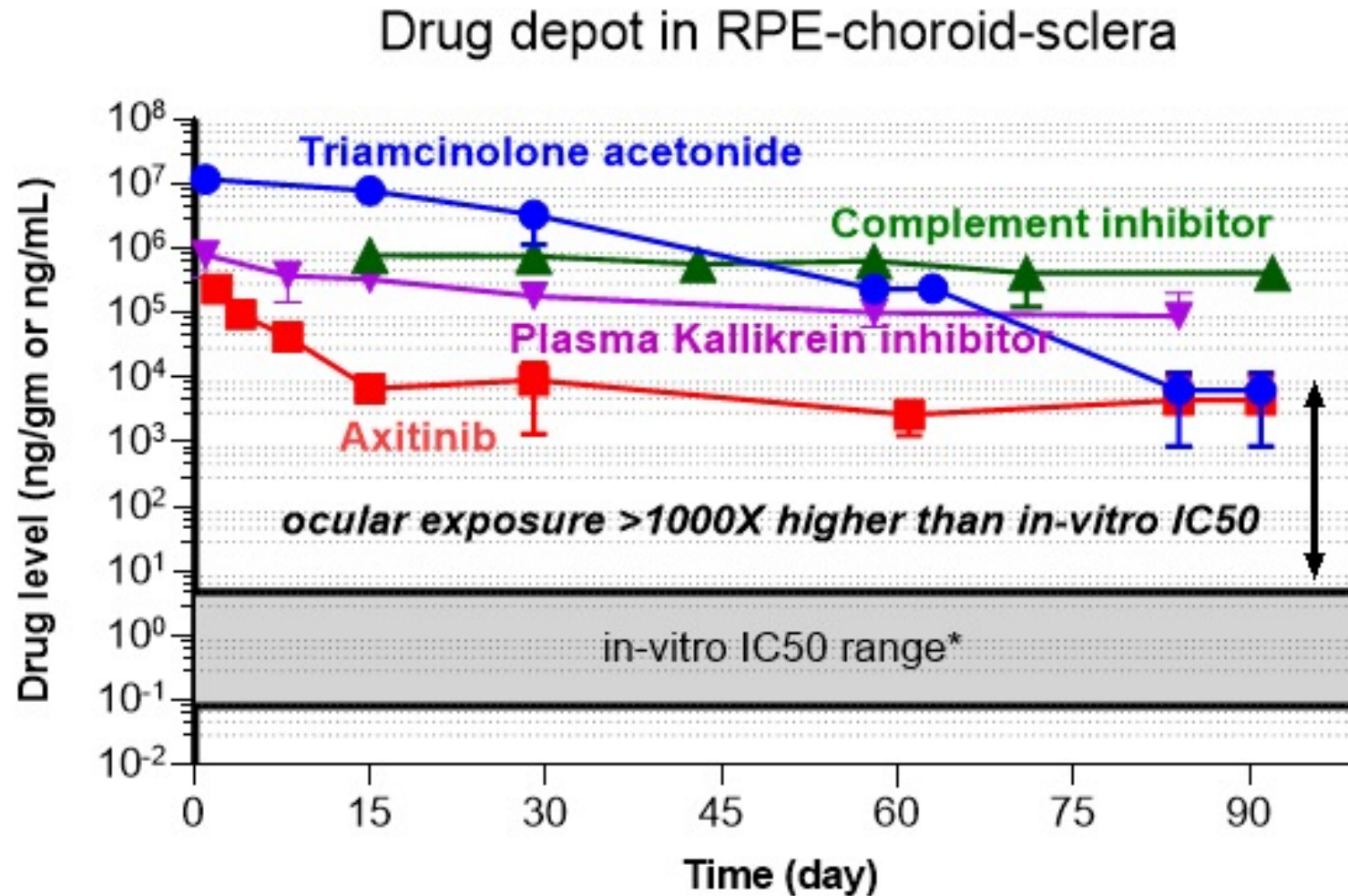
FIRST therapy for macular edema
associated with uveitis

FIRST uveitis trial **using visual acuity change**
as a primary endpoint (Phase 3 PEACHTREE)

FIRST approved therapeutic delivered
into the **suprachoroidal space**

FIRST commercial product for Clearside

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

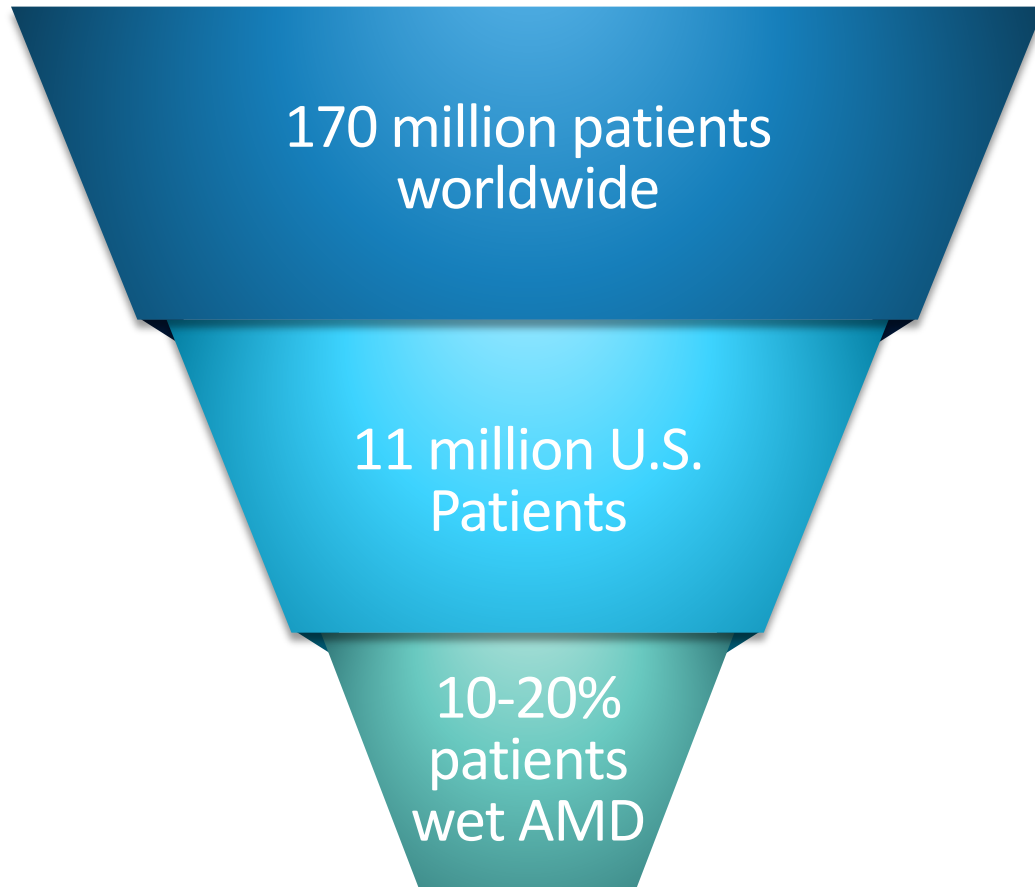


CLS-AX

(axitinib injectable suspension)
for Suprachoroidal Injection

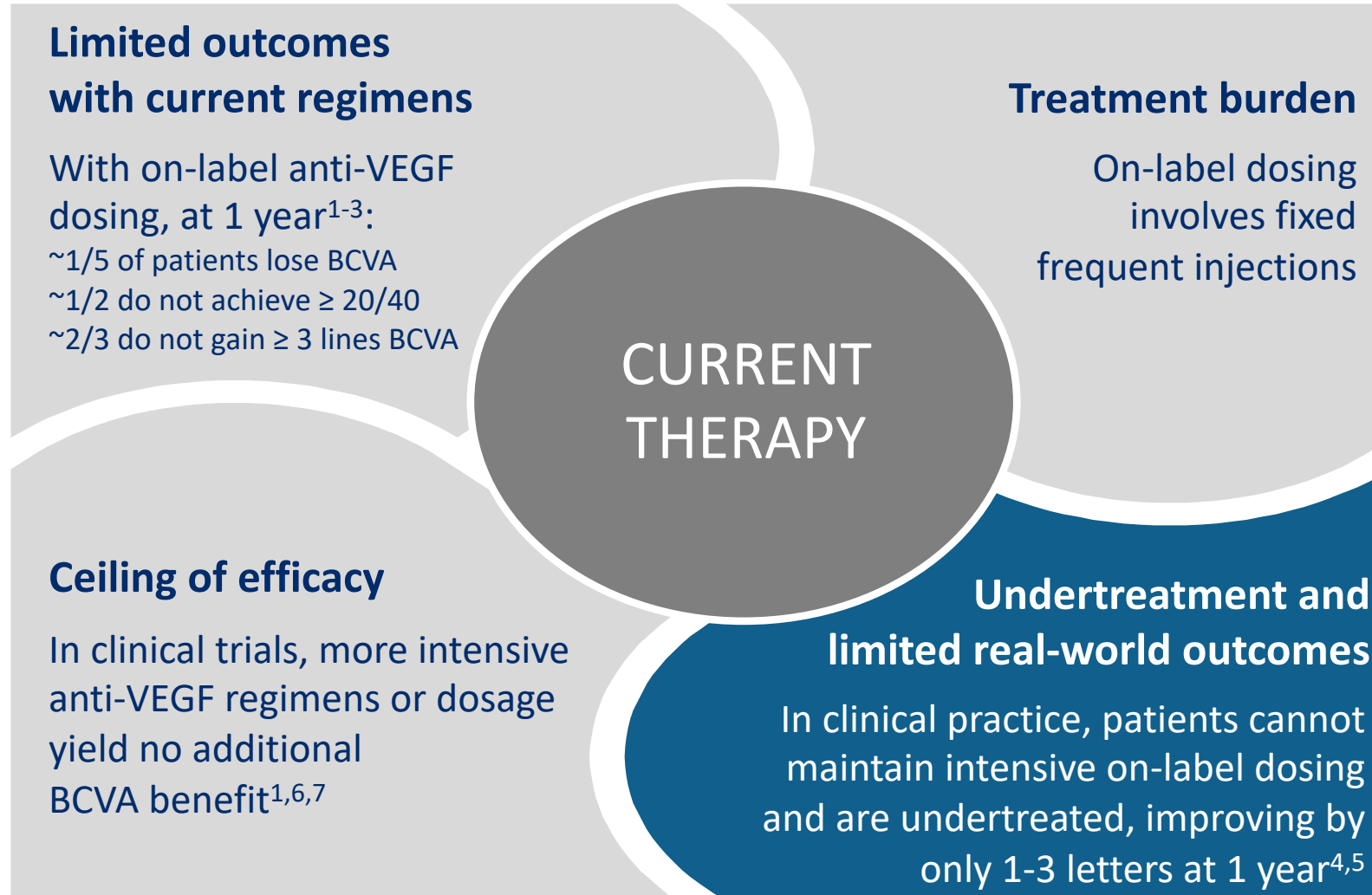
Age-Related Macular Degeneration (AMD)

A large and growing market opportunity

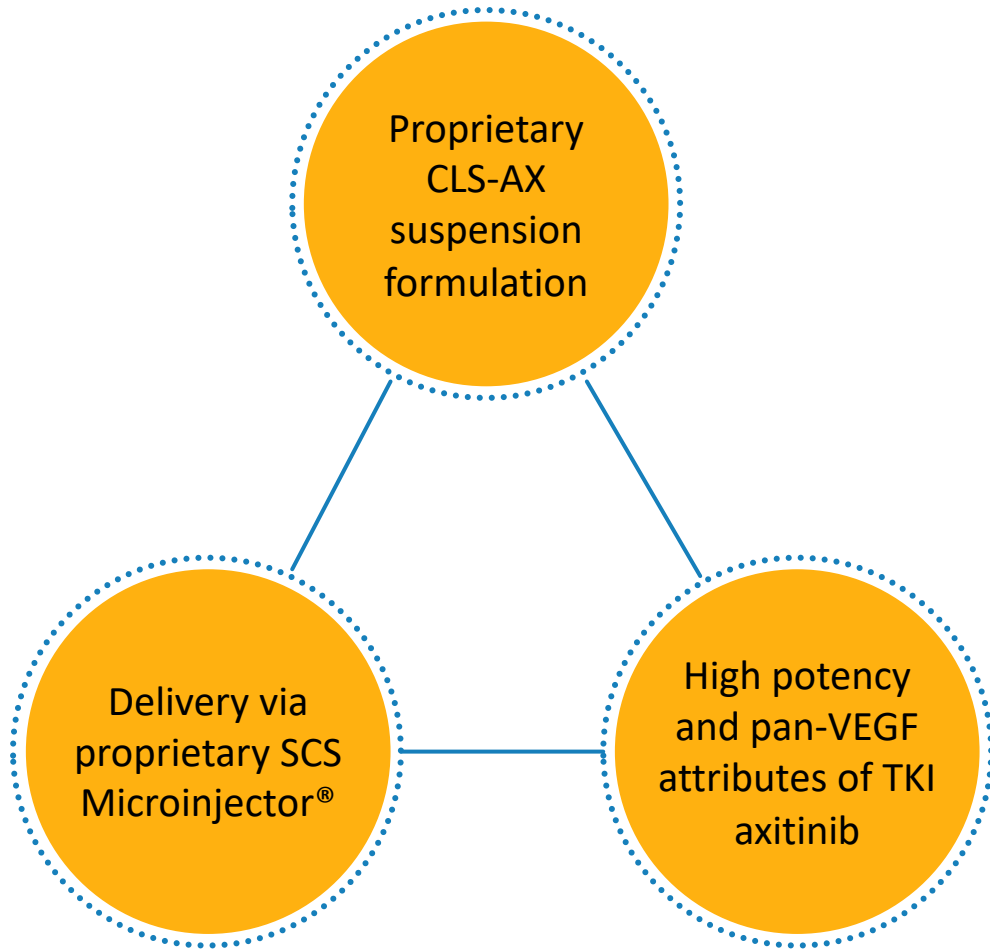


- AMD causes a progressive loss of central vision and is the most common cause of blindness in individuals over age 55
 - Neovascular or Wet AMD accounts for the majority of blindness
- U.S. prevalence expected to increase to 22 million by the year 2050
- Global prevalence expected to increase to 288 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



CLS-AX (axitinib injectable suspension) for Suprachoroidal Injection in wet AMD



Potential to **improve the treatment landscape** for wet AMD patients

Longer lasting treatment may reduce patient burden from monthly injections

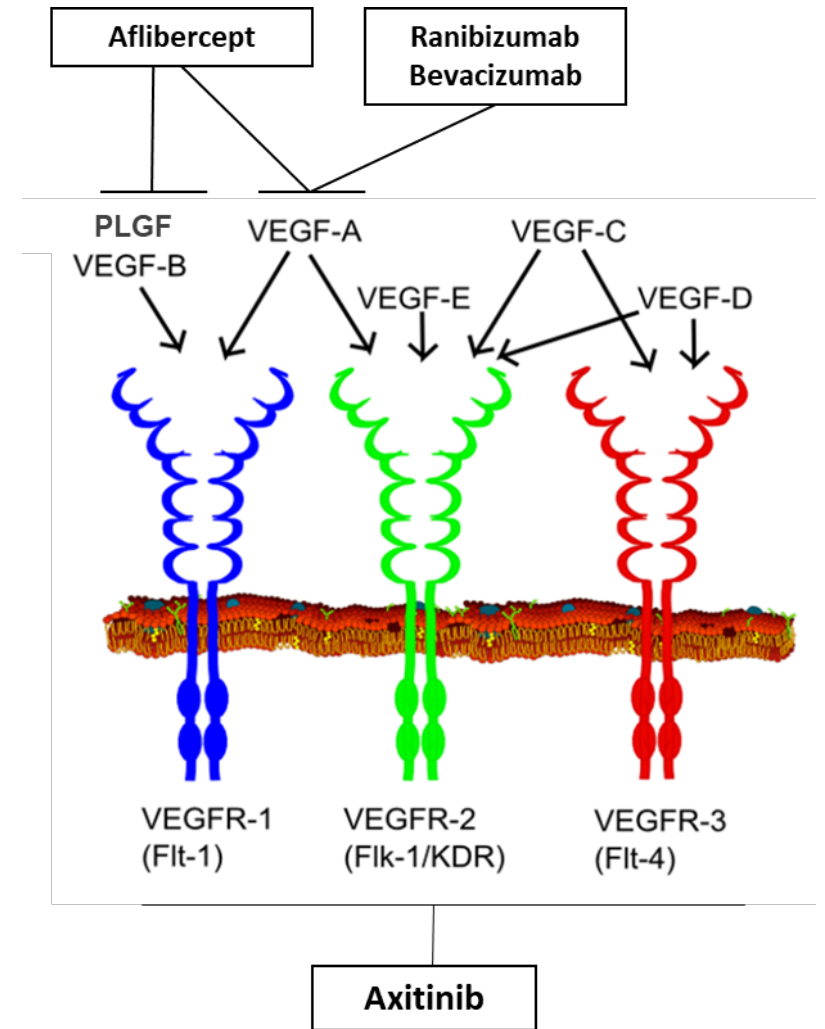
Protecting the vitreous and anterior chamber may **eliminate symptomatic floaters and other side effects**

Targeted high levels to affected choroid-retina for potential efficacy benefits

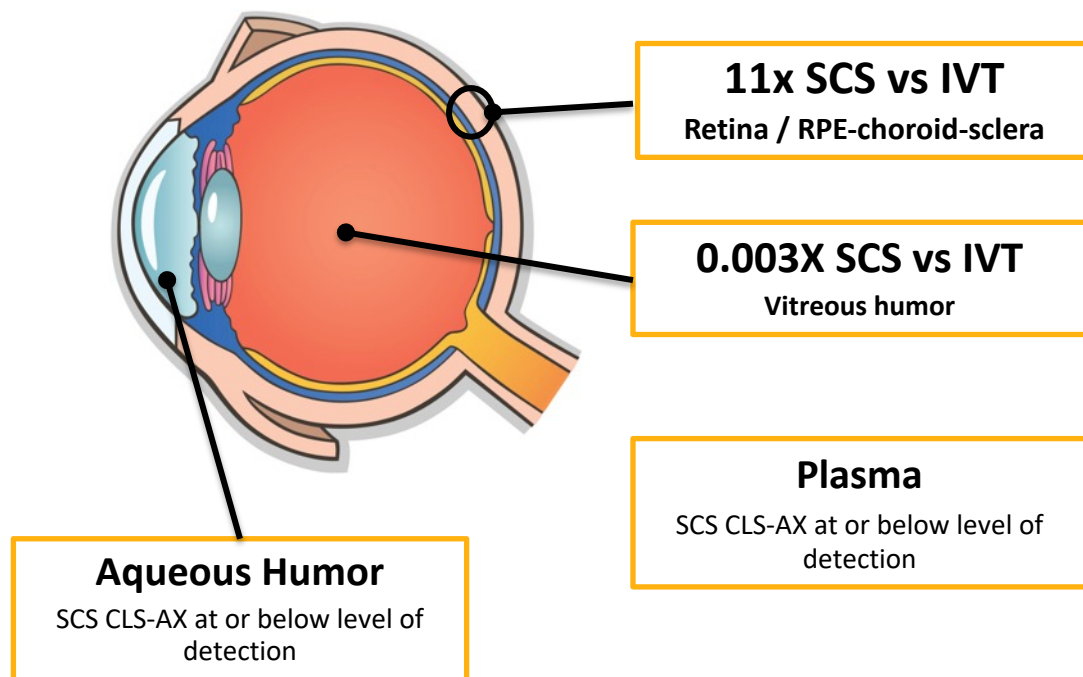
Given experience with **>1200 injections**, may be **easily adopted** in current clinical practice

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

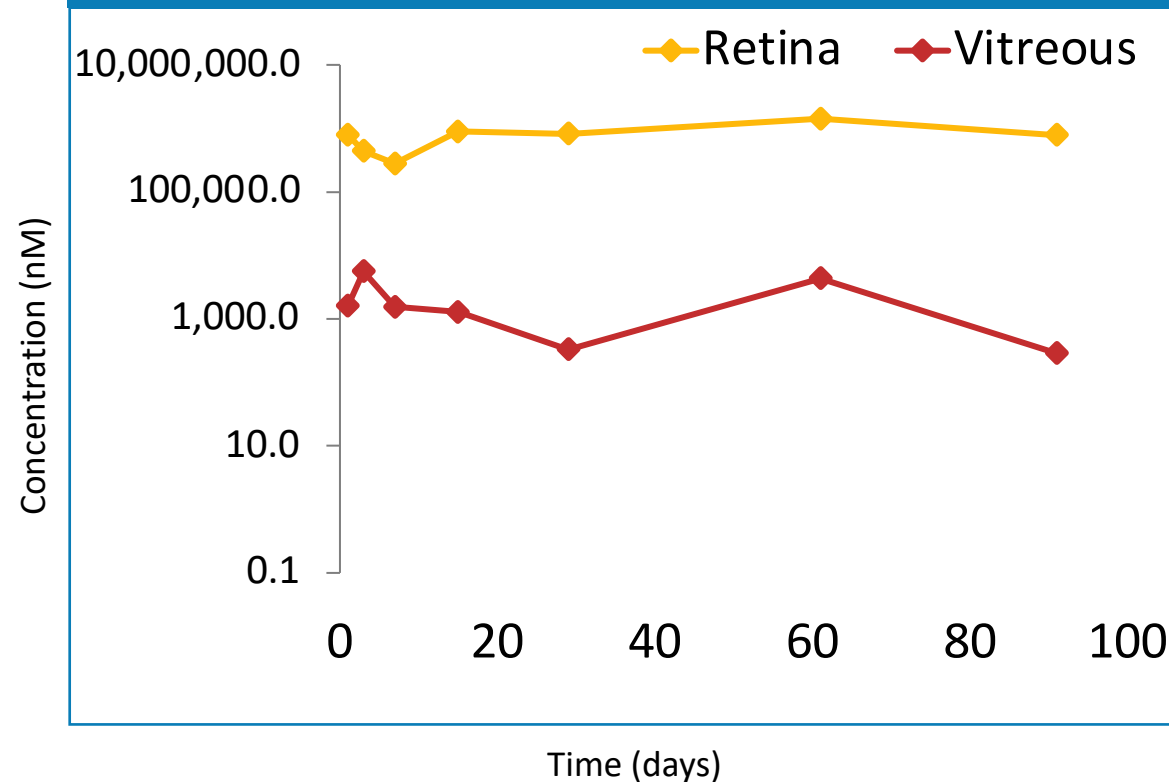
Values: area under the curve ratios, SCS / IVT

SCS : 1 mg/eye, 100 μ L. | IVT: 1 mg/eye, 25 μ L

Single bilateral injection, 1-wk rabbit PK studies

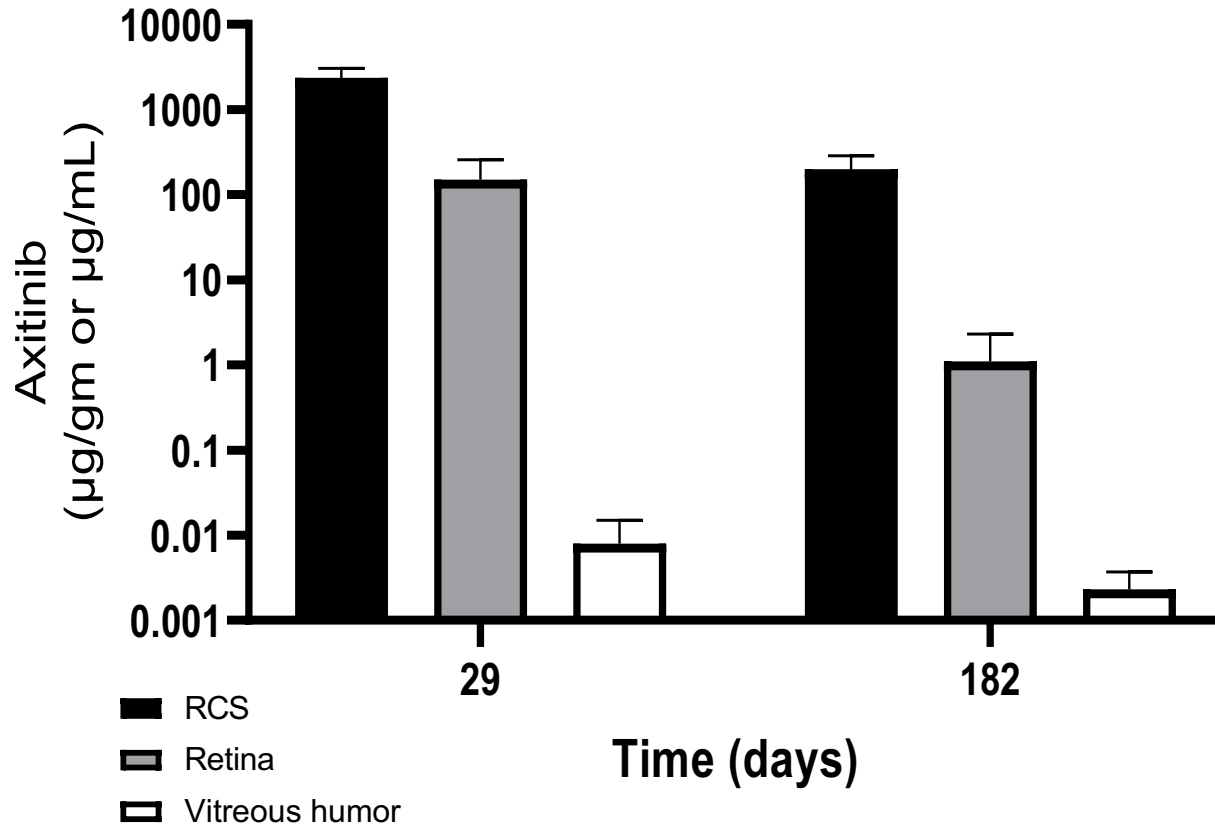
CLS-AX: High, Sustained Drug Levels in the Retina after SCS Administration

- ❖ 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 SC 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.

CLS-AX Has the Potential to Improve Current Wet AMD Treatment

SCS Delivery May Synergistically Enhance Pan-VEGF Effect

	SAFETY	EFFICACY	TREATMENT BURDEN
AXITINIB	<ul style="list-style-type: none">• Well characterized small molecule• Potential for less immune response & inflammation vs biological products• Better compatibility with retinal pigment epithelial cells vs other TKIs	<ul style="list-style-type: none">• Shows pan-VEGF inhibition• Pan-VEGF inhibition shows greater effect preclinically & clinically• Regresses neovascularization preclinically• >10x the in-vitro potency vs. other TKIs• Current anti-VEGF agents only target VEGF-A	
SUPRACHOROIDAL DELIVERY	<ul style="list-style-type: none">• Compartmentalized SCS drug delivery potentially results in few anterior AEs• Favorable tolerability profile of SCS Microinjector in >1200 patient injections• Use of SCS Microinjector is well accepted by physician-investigators	<ul style="list-style-type: none">• Targets drug to the diseased chorioretinal tissue in wAMD• Shows up to 11x higher drug levels vs intravitreal administration	<ul style="list-style-type: none">• Shown prolonged duration in preclinical studies• Potential to have less frequent dosing compared to current anti-VEGF products which may:<ul style="list-style-type: none">• Limit undertreatment by facilitating better compliance• Further enhance clinical outcomes

Trial Design and Objectives

- Open-label study to evaluate safety and tolerability of escalating single doses of CLS-AX administered through suprachoroidal injection following IVT aflibercept
- 3 Cohorts of 5 patients each: n=15
- Dose-escalation of CLS-AX (in mg): Cohort 1 at 0.03; Cohort 2 at 0.10; Cohort 3 currently planned at 0.30
- Evaluate visual function, ocular anatomy, and need for additional treatment
- Assessment for additional treatment: loss from best measurement of ≥ 10 letters in BCVA with exudation; increase in CST > 75 microns; a vision-threatening hemorrhage

Cohort Enrollment and Treatment



Cohort 1: Encouraging Results Supported Progression to Cohort 2

- **Cohort 1 Objective:** To establish a floor of safety in this first-in-human trial with low dose CLS-AX (0.03 mg dose)
- **Highly treatment-experienced (at screening prior to aflibercept administration)**
 - Total number prior anti-VEGF treatments: mean = 25.8, median = 28.0
 - Total number prior anti-VEGF treatments within the last 12 months: mean = 9.0, median = 11.0
- **Demographics & disease characteristics (at baseline prior to CLS-AX administration)**
 - Average age: 82 years
 - Mean central subfield thickness (CST) of the macula was 231 μm (range 208 - 294 μm)
 - Mean best corrected visual acuity (BCVA) score was 59.0 (range 29 - 74)
- **Conclusion**
 - **Cohort 1 supported progression to Cohort 2**

SAFETY: CLS-AX WELL TOLERATED

- **No study suspension or stopping rules were met**
- **No SAEs have been reported**
- No signs of inflammation, vitreous haze, IOP safety signals, vasculitis, or intravitreal dispersion of investigational product
- 2 TEAEs assessed as unrelated to CLS-AX by the investigators

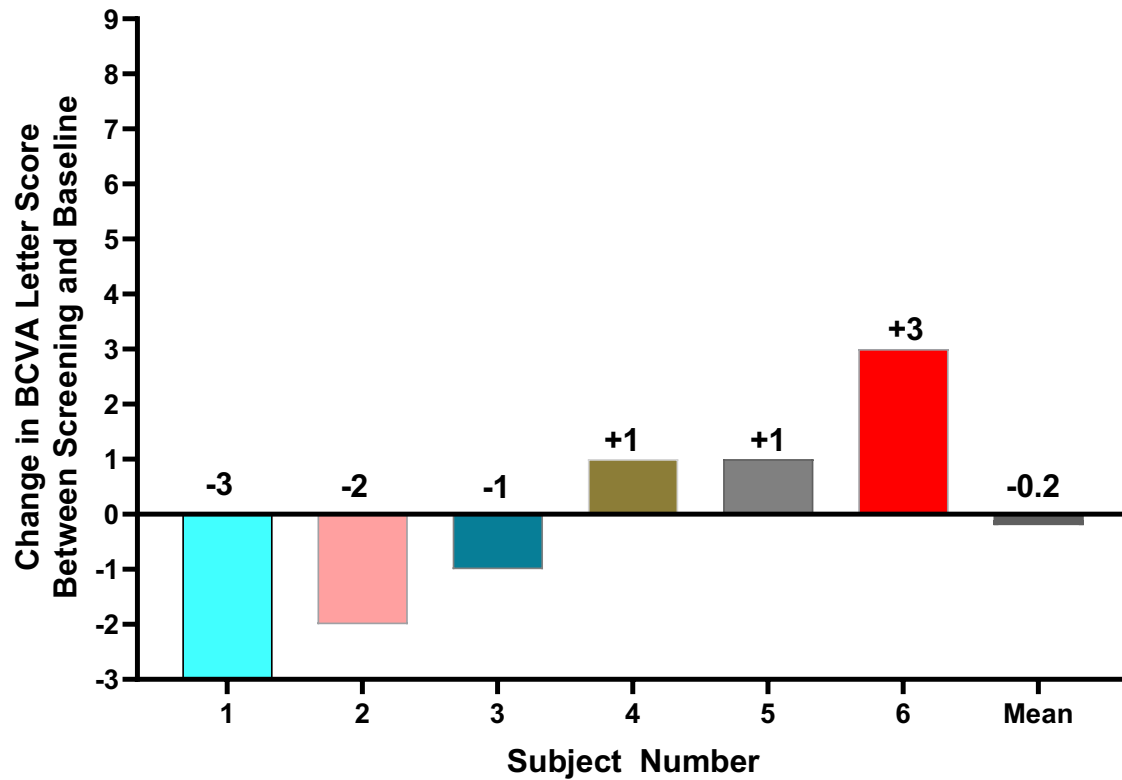
BCVA AND ANATOMIC RESULTS

- **1-month visual acuity improvement of 1 line post CLS-AX vs no change for aflibercept, at this initial low dose**
 - Aflibercept: 1-month BCVA change -0.2 ETDRS letters (p=0.862*)
 - CLS-AX 0.03 mg: 1-month BCVA change +4.7 ETDRS letters (p=0.029*) with 5/6 patients improving by 4 or more letters
- **Mean CST stable within 50 μ m at one month post 2 mg aflibercept and at one month post 0.03 mg CLS-AX**
 - In these treatment-experienced patients, the normal screening baseline CST imposes a floor effect, limiting improvement in CST

Best Corrected Visual Acuity

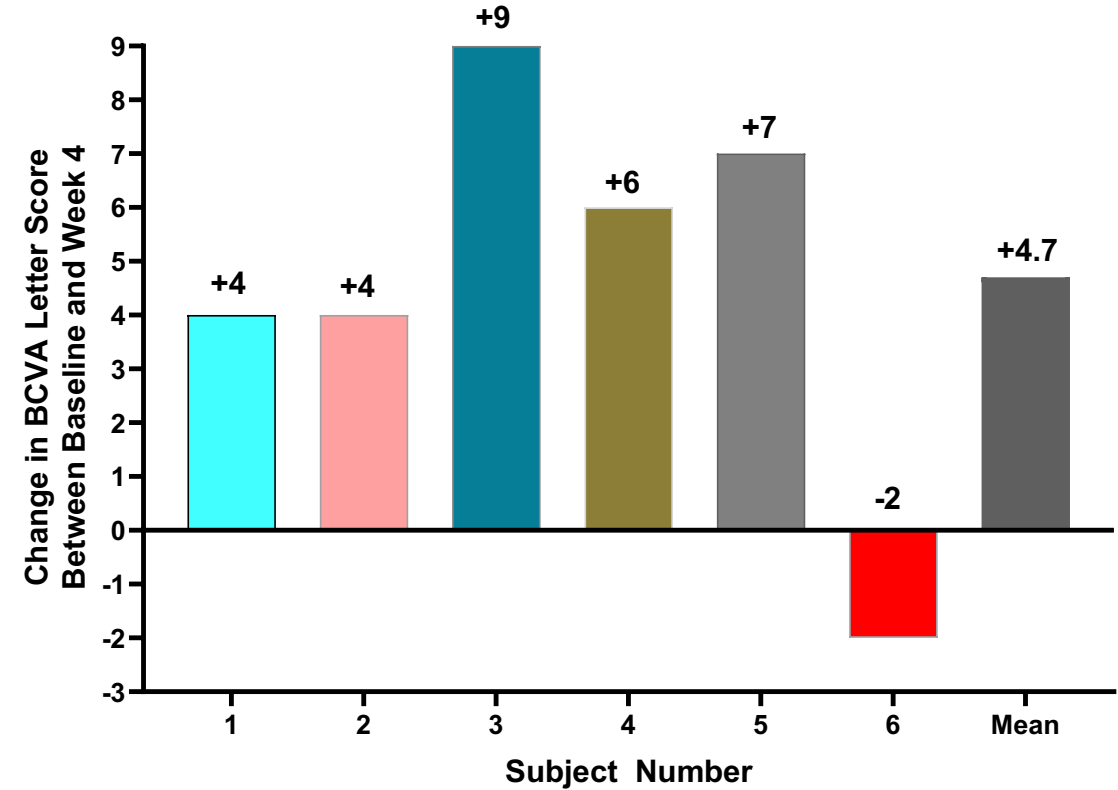
One Month Response Following Aflibercept 2 mg vs CLS-AX 0.03 mg

1 Mo Change after Aflibercept : -0.2 letters, P=0.862*



Mean BCVA at screening (prior to aflibercept) = 59.2

1 Mo Change after CLS-AX : +4.7 letters, P=0.029*

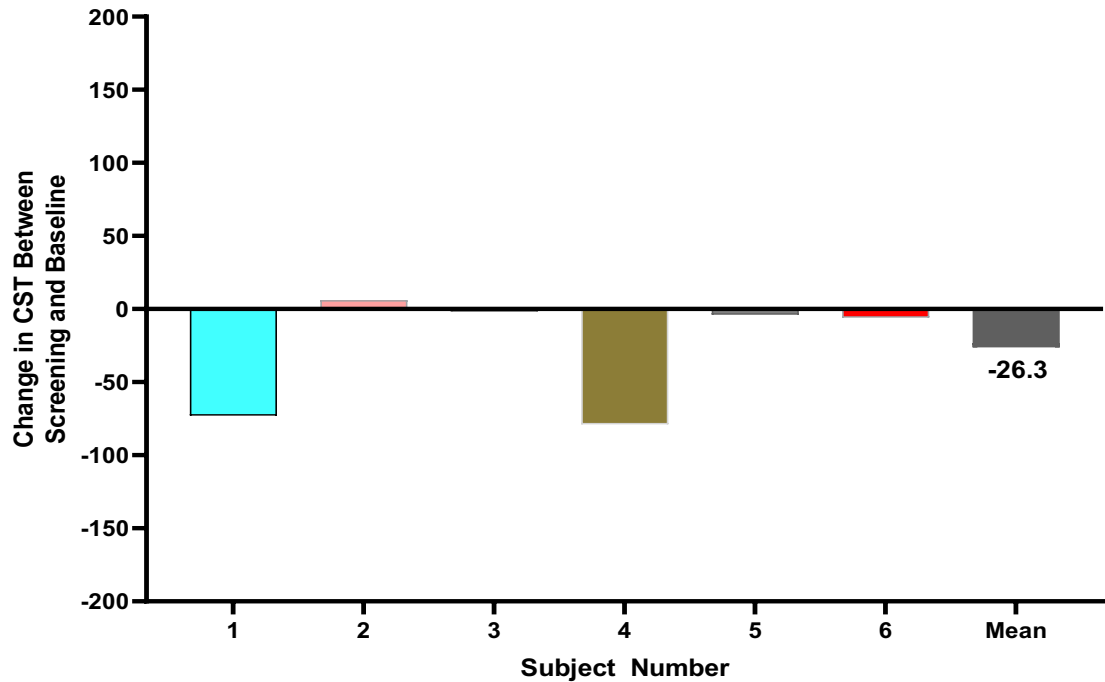


Mean BCVA at baseline (prior to CLS-AX) = 59.0

Central Subfield Thickness

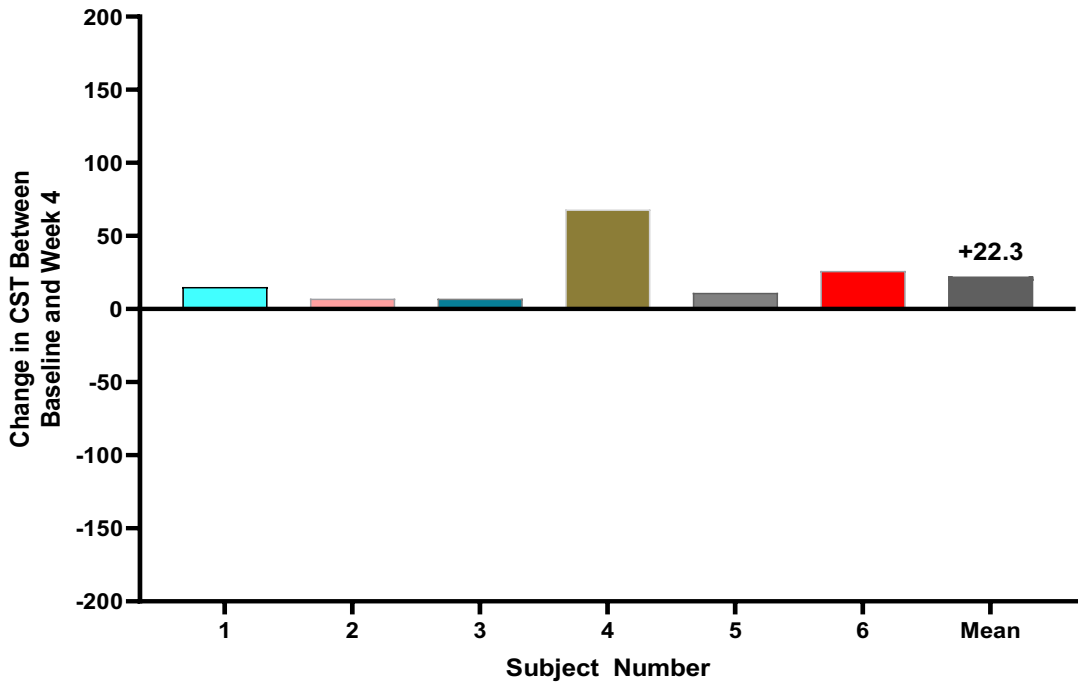
Mean CST Stable within 50 μm at One Month

1 Mo Change after Aflibercept (2 mg)



Mean CST at screening (prior to aflibercept) = 257.5 μm

1 Mo Change after CLS-AX (0.03 mg)

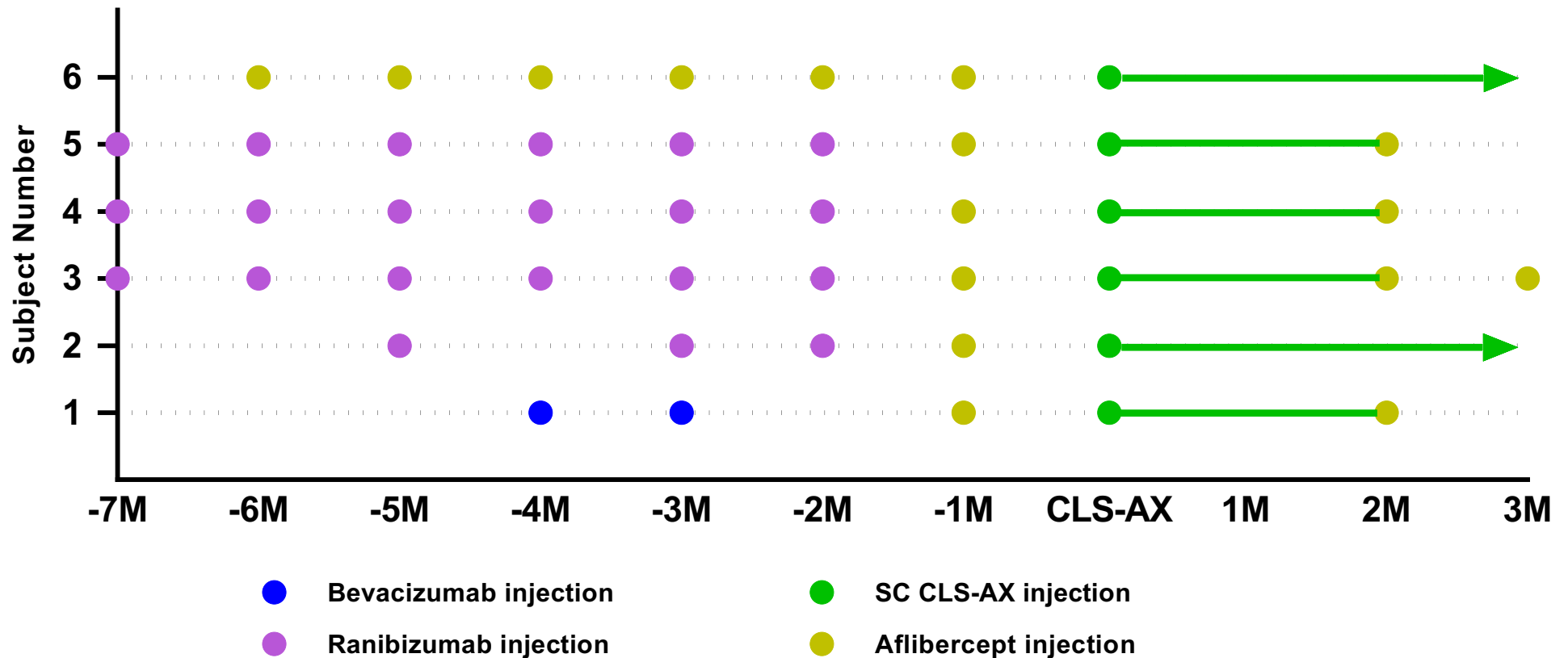


Mean CST at baseline (prior to CLS-AX) = 231.2 μm

Cohort 1: Preliminary Signs of Potential Durability at Low Dose in Highly Treatment Experienced and Dependent Patients

No subjects required additional treatment at 1 month post CLS-AX
2 of 6 subjects did not require additional treatment for 3 months post CLS-AX

Therapies for
nAMD up to
6 Months Prior
to Screening





SAFETY

- CLS-AX well tolerated
- No signs of inflammation, vitreous haze, IOP safety signals, vasculitis, or intravitreal dispersion of investigational product

VISUAL ACUITY

- At 1 month, 5 of 6 patients had improved BCVA ≥ 4 letters (mean +4.7 letters)
- At 3 months, 2/6 no need for additional therapy and BCVA improved by 5 and 7 letters from baseline



COHORT 1 RESULTS

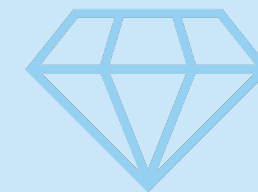
ANATOMIC EFFECTS

- Mean CST stable within 50 μm at 1 month

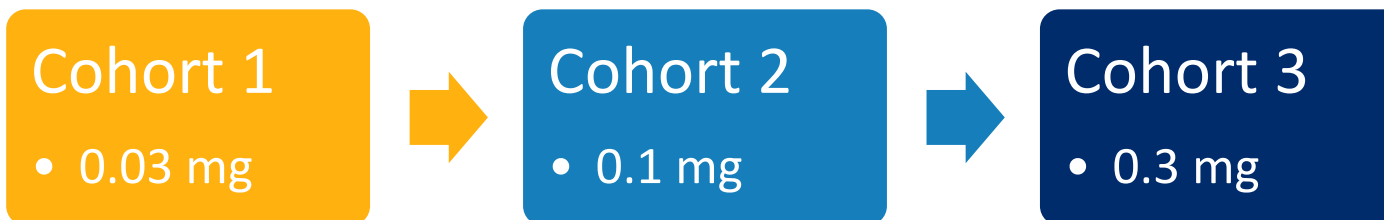


DURABILITY POST CLS-AX

- No subjects required additional therapy at 1 month
- 2/6 no need for additional therapy through 3 months
- 4/6 received additional therapy at 2 months



Cohorts 2 and 3 Continue to Escalate Single CLS-AX Dose



- With 3.3x and 10x dosing in cohorts 2 and 3 respectively:
 - We expect progressively increased durability, based on our preclinical pharmacokinetic studies
 - And potential for better visual acuity outcomes than anti-VEGFA based on pan-VEGF inhibition
- Adding three-month extension study to follow patients in Cohort 2 and Cohort 3
- Preclinical pharmacokinetic studies show progressively prolonged tissue levels with increased dosing
- Cohort 2 recruitment ongoing; expect to complete recruitment in August 2021

Early-Stage Pipeline

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SCS Injection Platform and Integrin Inhibition



Primary Need

Targeted delivery addressing
disease-modifying pathways
beyond anti-VEGF therapy

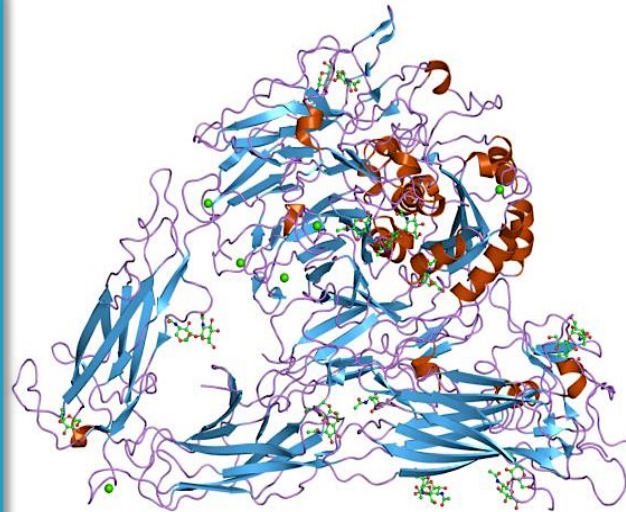
The Opportunity Beyond the VEGF pathway

- Novel target
- Early industry validation in DME and AMD
- Advantages of targeted suprachoroidal administration with potential for:
 - Improved safety profile, through compartmentalization in SCS
 - Enhanced efficacy, through drug levels at affected tissues
 - Extended durability
- Limited potential competition in the non-VEGF approach to treatment

Integrin Small Molecule Suspension for SCS administration

Multi-functional cell-adhesion molecules, heterodimeric receptors with α and β subunits

- Connect extracellular matrix (ECM) to actin cytoskeleton in the cell cortex
- Regulate cellular adhesion, migration, proliferation, invasion, survival, and apoptosis
- Also play a role in inflammation, angiogenesis and fibrosis



Targets integrins $\alpha v\beta 3$, $\alpha v\beta 5$ and $\alpha 5\beta 1$ implicated in DME, DR & AMD

Given unique MOA, could serve as:

- Primary therapy
- Adjunctive therapy to anti-VEGF
- Secondary therapy in refractory cases

Suprachoroidal Injection of Gene Therapy May Offer Potential for Safe and Efficient Delivery



The Opportunity

- Convert gene therapy into an office-based procedure
 - Avoid risks of vitrectomy (surgery)
 - Avoid risks of retinotomy, subretinal injection, and macular detachment
 - Enhance patient access
- Equivalent expression for subretinal and suprachoroidal administration preclinically
- Potential for broader retinal coverage & repeat dosing of suprachoroidal vs subretinal injection
- Delivery of viral and non-viral vectors
 - Preclinical studies with AAV show transfection of photoreceptors

Corporate Partnerships & Milestones

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Enabling SCS Delivery of AAV Gene Therapy for Retinal Disease

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 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
- Encouraging preclinical results delivering RGX-314 into the SCS
- SCS delivery of AAV gene therapy well tolerated to date

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



REGENXBIO: Two Phase 2 Trials Using Clearside's SCS Microinjector®

- Two multi-center, open-label, randomized, controlled, dose-escalation studies evaluating the efficacy, safety and tolerability of suprachoroidal delivery of RGX-314
 - Patients do not receive prophylactic immune suppressive corticosteroid therapy
- AAVIATE: RGX-314 for Treatment of Wet Age-Related Macular Degeneration (wet AMD)
 - Patient population: severe wet AMD patients who are responsive to anti-VEGF treatment
 - Cohort 1: Interim efficacy data expected at **Retina Society Scientific Meeting (Sept 29-Oct 2, 2021)**
 - Cohort 2: Interim data expected in **Q4 2021**
 - Cohort 3: Completed dosing in patients who are positive for neutralizing antibodies
- ALTITUDE: RGX-314 for Treatment of Diabetic Retinopathy (DR)
 - Cohort 1: Enrollment complete with data expected in **Q4 2021**
 - Cohort 2: Enrolling
 - Cohort 3: Enrollment planned in patients who are positive for neutralizing antibodies



Aura Bioscience: Phase 2 Ocular Oncology trial using SCS Microinjector®

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
- Aura's Phase 2 clinical trial is **ongoing** using SCS Microinjector
- SCS delivery clinically well tolerated to date

The Terms:

- Potential future financial upside for Clearside from pre-specified development and sales milestones
- Royalties on net sales of products using SCS Microinjector

The logo for Aura Bioscience, featuring the word "aura" in a bold, orange, lowercase sans-serif font.

XIPERE: Two Global Commercialization & Development Partners

XIPERE™
(triamcinolone acetonide suprachoroidal
injectable suspension) 40 mg/mL

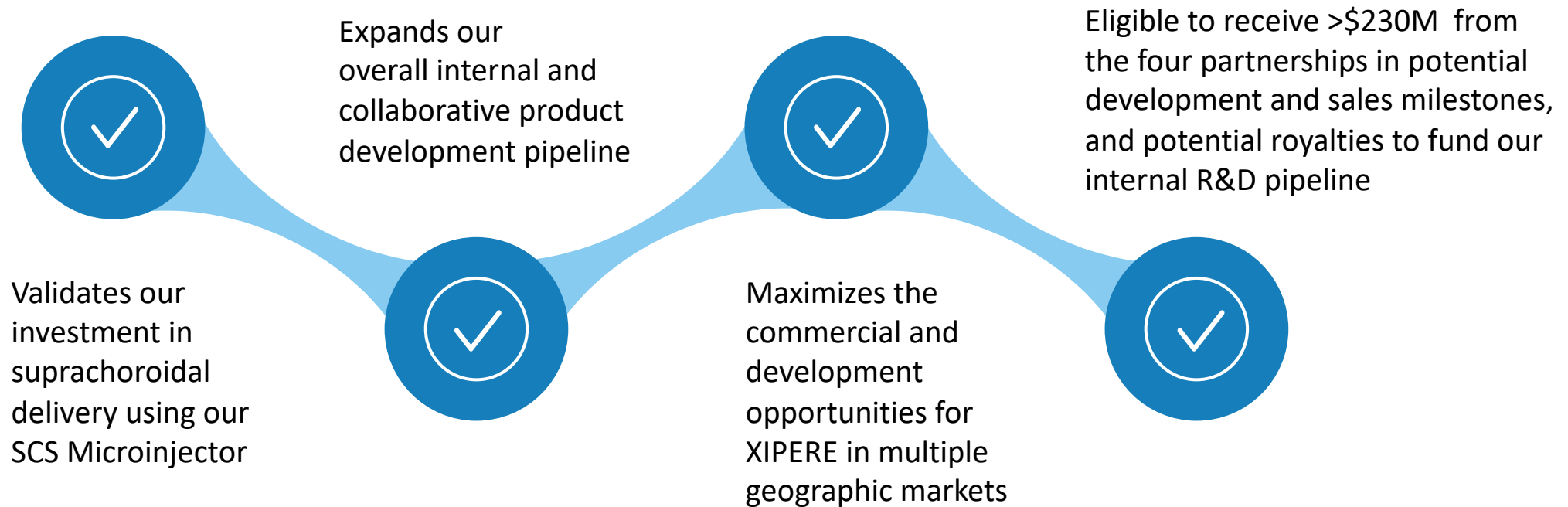
BAUSCH Health

- License for the U.S. and Canada; options for other territories
- Received \$5M upfront payment
- Up to \$15M in FDA approval and pre-launch milestones
- Up to \$57.3M in milestone payments; tiered royalties from the high-teens to 20%



- License for Greater China & South Korea
- Received \$4M upfront payment
- \$4M at U.S. approval
- Up to \$31.5M in approval, development and sales milestones
- Tiered royalties of 10% to 12%

Four Validating Partnerships to Drive Growth



2021 Research and Development Investment Highlights

Versatile therapeutic platform with proprietary access to the suprachoroidal space

Patented technology & delivery approach

XIPERE

- ✓ **Q2:** NDA Resubmission
- **October 2021:** PDUFA Date
- **Q4:** Arctic Vision initiates Phase 3 trial in China in uveitic macular edema (**ARVN001**)

Scientific presentations and publications

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

Building an internal R&D pipeline

CLS-AX Phase 1/2a OASIS

- ✓ **Q1:** Complete Cohort 1 Enrollment
- ✓ **Mid 2021:** Cohort 1 Safety Data
- ✓ **June 2021:** Initiate Cohort 2 Screening
- **YE:** Cohort 2 Data

2021: Integrin Inhibitor preclinical data

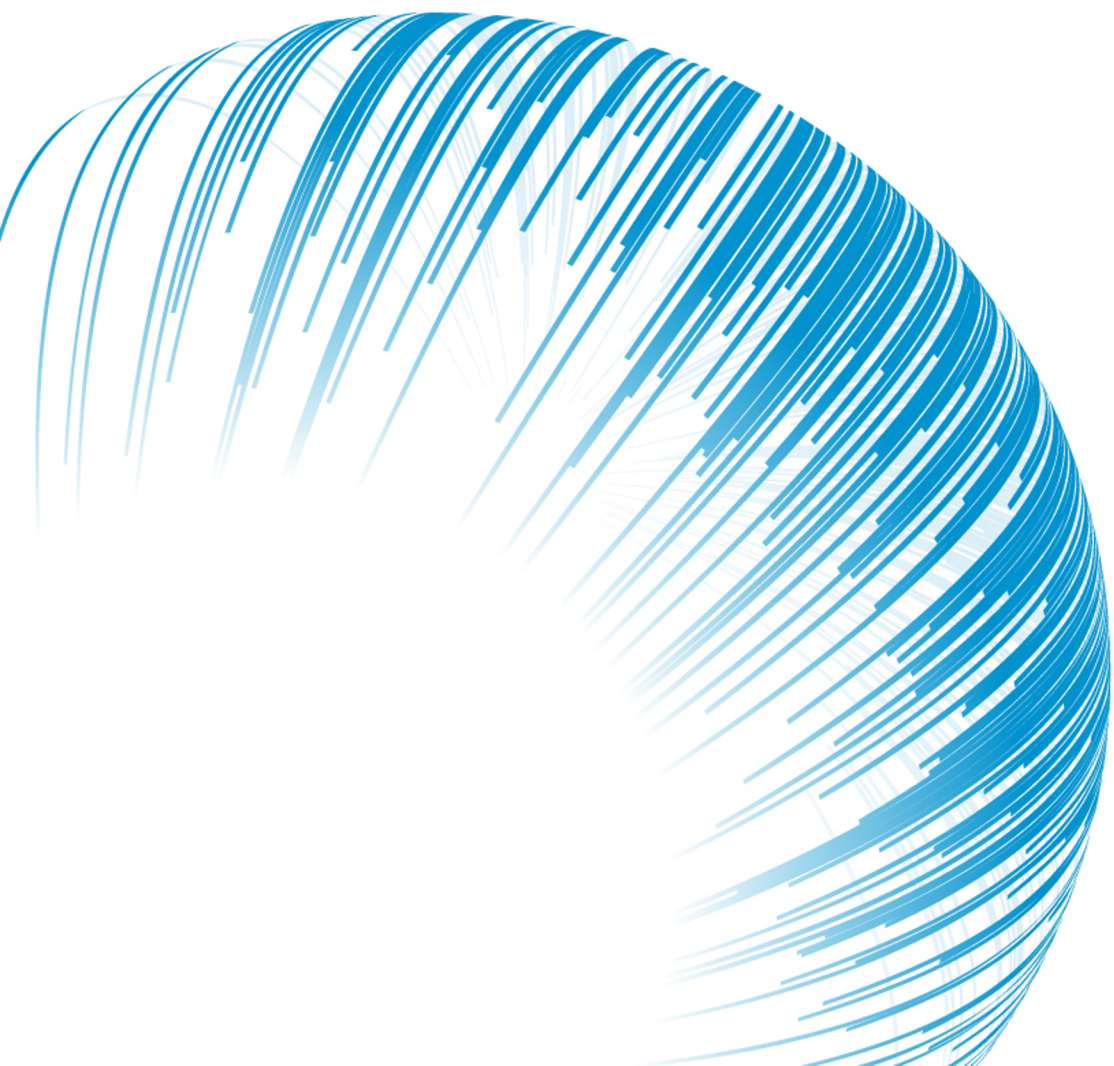
Partnering to expand use of SCS platform*

REGENXBIO: RGX-314

- ✓ **Q1:** Initiate Cohort 2 Phase 2 AAVIATE trial in wet AMD
- **Q3:** Interim Cohort 1 Phase 2 AAVIATE trial data in wet AMD
- **Q4:** Interim Cohort 2 Phase 2 AAVIATE trial data in wet AMD
- **Q4:** Initial Data Phase 2 ALTITUDE Trial in DR

AURA BIOSCIENCES: AU-011

- **2021:** Phase 2 trial in choroidal melanoma ongoing



Nasdaq: CLSD

