CLEARSIDE® BIOMEDICAL

Raymond James Human Health Innovation Conference
June 23, 2021

Forward-Looking Statements

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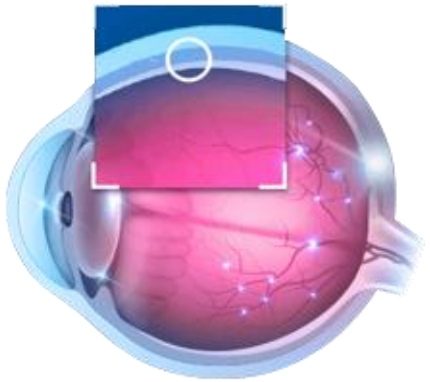
Developing and Delivering Treatments that Restore and Preserve Vision for People with Serious Back of the Eye Diseases

Versatile Therapeutic Platform

SCS Microinjector® with proprietary drug formulations target the Suprachoroidal Space



- 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

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Core Advantages of Treating Via the Suprachoroidal Space

TARGETED

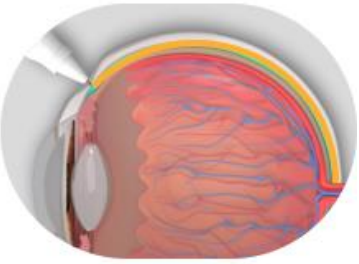
The back of the eye is the location of many irreversible and debilitating visual impairments

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

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

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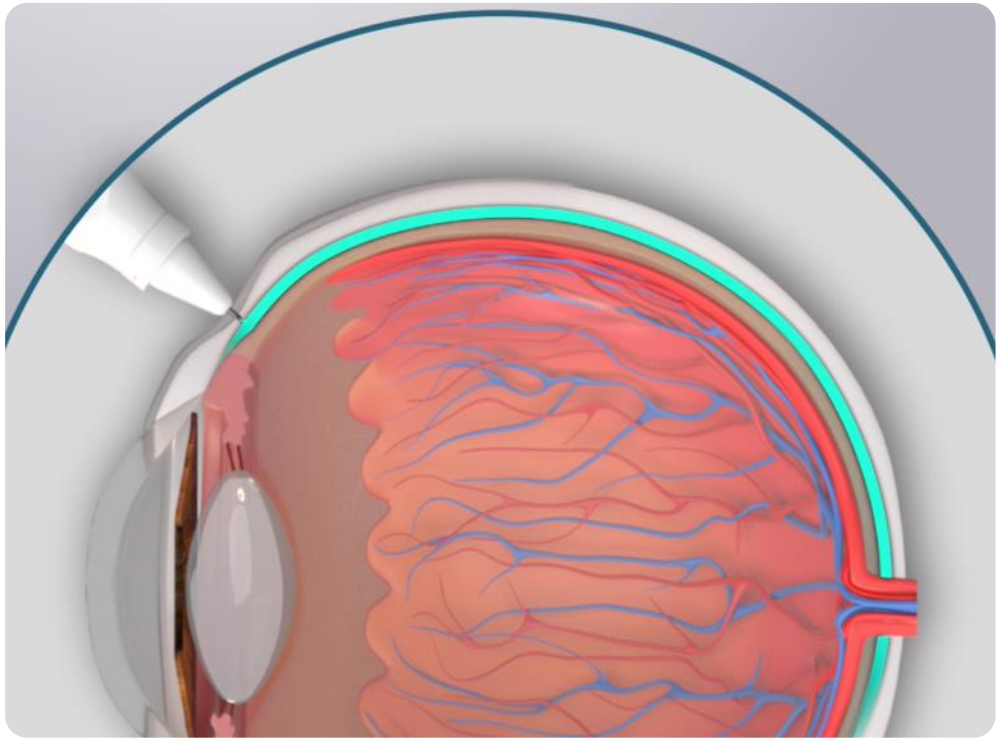
Clearside's SCS Microinjector®: The Only Clinically Tested Injection Device for Suprachoroidal Drug Delivery

- Clinically tested in >1200 suprachoroidal Injections
  - 8 clinical trials completed
  - Injections performed across multiple retinal disorders
- Safety profile comparable to intravitreal injections[1]
  - 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

Sources: Clearside data on file | [1]Kurup, et. al, Macula Society 2021 *Safety of the Suprachoroidal Injection Procedure Utilizing SCS Microinjector® across Three Retinal Disorders*

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Suprachoroidal Space (SCS®) Injection Platform

Internal Development Pipeline

PROGRAM	THERAPEUTC ENTITY	INDICATION	RESEARCH	PRECLINICAL	PHASE 1/2	PHASE 3
CLS-AX (axitinib injectable suspension)	Small Molecule	Wet AMD			OASIS	
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	THERAPEUTC 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	THERAPEUTC ENTITY	TERRITORY	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	NDA
BAUSCH HEALTH	Small Molecule	U.S. & Canada; options ex-North America					PDUFA 10/30/21
ARCTIC VISION	Small Molecule	Greater China & South Korea					

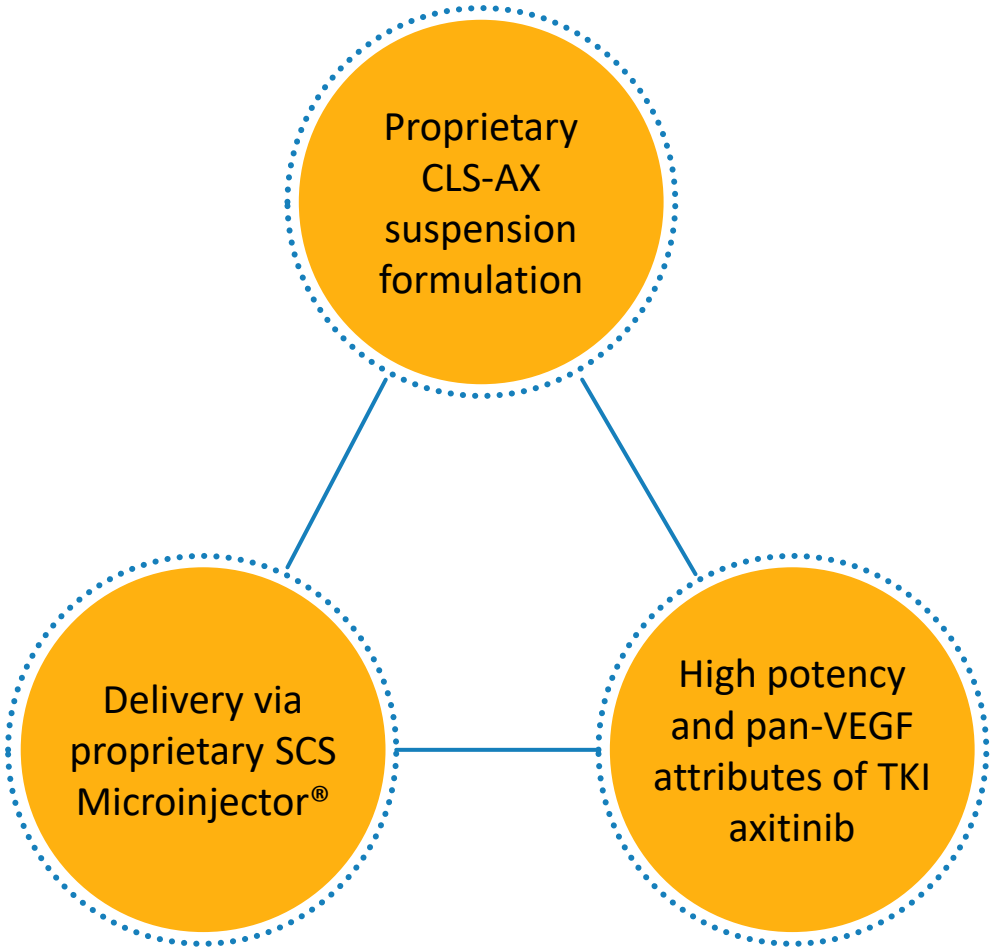
XIPERE™ (triamcinolone acetonide suprachoroidal injectable suspension) is an investigational product

CLS-AX

(axitinib injectable suspension)

for Suprachoroidal Injection

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

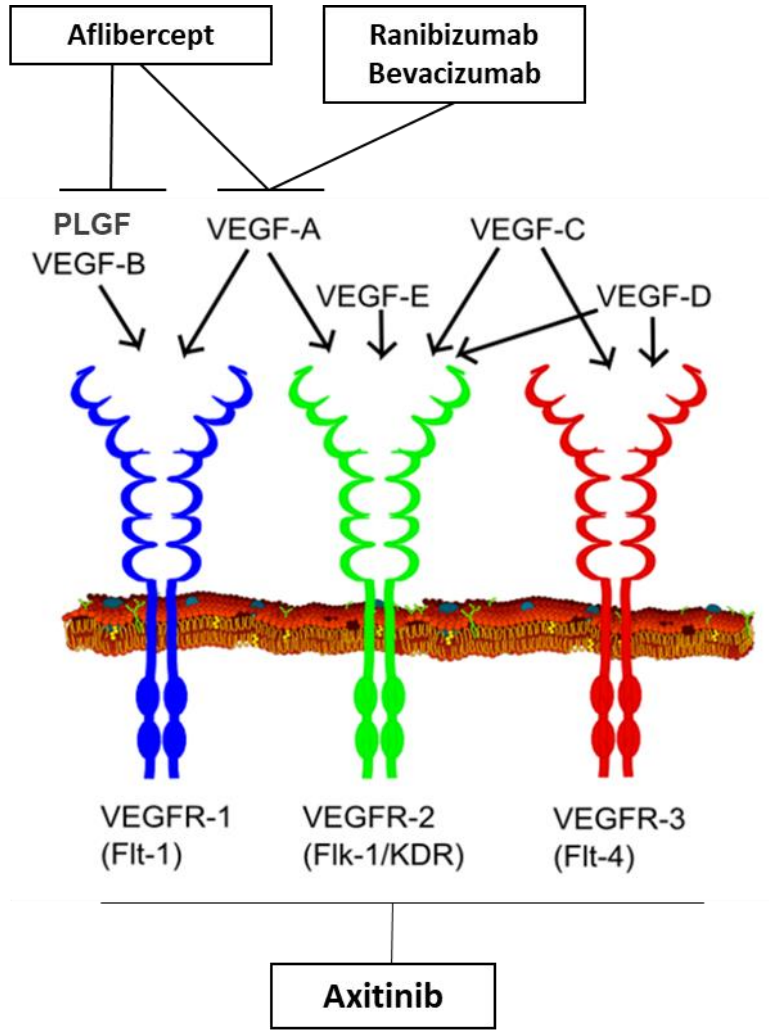


- Potential to **improve the treatment landscape** for wet AMD patients
- **Longer lasting treatment** may reduce patient burden from monthly injections
- Protecting the vitreous and anterior chamber **may eliminate symptomatic floaters and other side effects**
- **Targeted high levels** to affected choriod-retina for potential efficacy benefits
- Given experience with **>1200 injections**, may be **easily adopted** in current clinical practice

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 model[1-2]
- Highly potent tyrosine kinase inhibitor (TKI)
  - >10x more potent than other TKIs in preclinical studies
  - Better ocular cell biocompatibility than other TKIs[3]
  - More effective 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. Theile et al. Multikinase Inhibitors as a New Approach in Neovascular Age-Related Macular Degeneration (AMD) Treatment: In Vitro Safety Evaluations of Axitinib, Pazopanib and Sorafenib for Intraocular Use. Klin Monatsbl Augenheilkd 2013; 230: 247-254. | Image by Mikael Häggström, used with permission. Häggström, Mikael (2014). "Medical gallery of Mikael Häggström 2014". WikiJournal of Medicine 1 (2). DOI:10.15347/wjm/2014.008. ISSN 2002-4436. Public Domain.

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

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

Cohort Enrollment and Treatment

Screening	Baseline	Week 4	Week 8	Week 12
2 mg aflibercept dosed at screening	*CLS-AX dosed at baseline (30 days post screening)*	*Assessment for additional therapy*	*Assessment for additional therapy*	*Assessment for additional therapy*

Note: aflibercept is dosed via intravitreal injection (IVT); CLS-AX is dosed via suprachoroidal injection | clinicaltrials.gov NCT# 04626128

OASIS Cohort 1: Encouraging Results Support 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 supports progression to Cohort 2**

Source: Clearside data on file.

Cohort 1: Summary of Primary and Secondary Measures

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

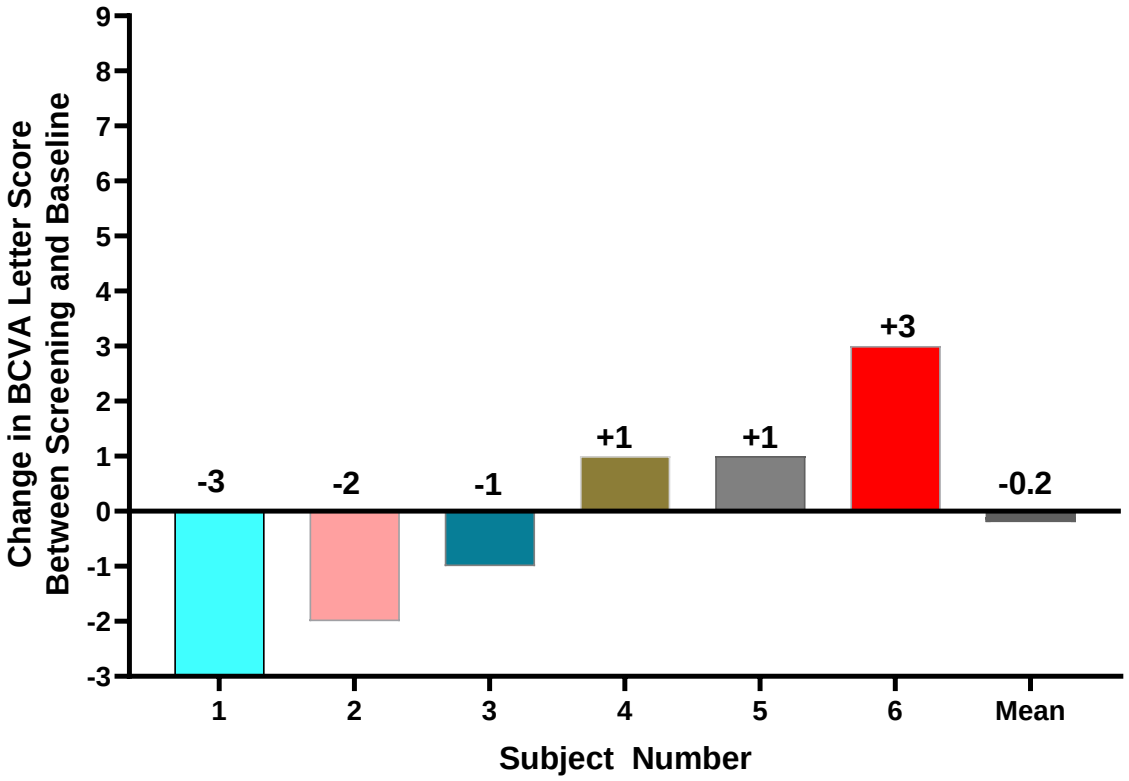
BCVA AND ANATOMIC RESULTS

- **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 *µm* 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

Source: Clearside data on file. |. *Post hoc, unadjusted

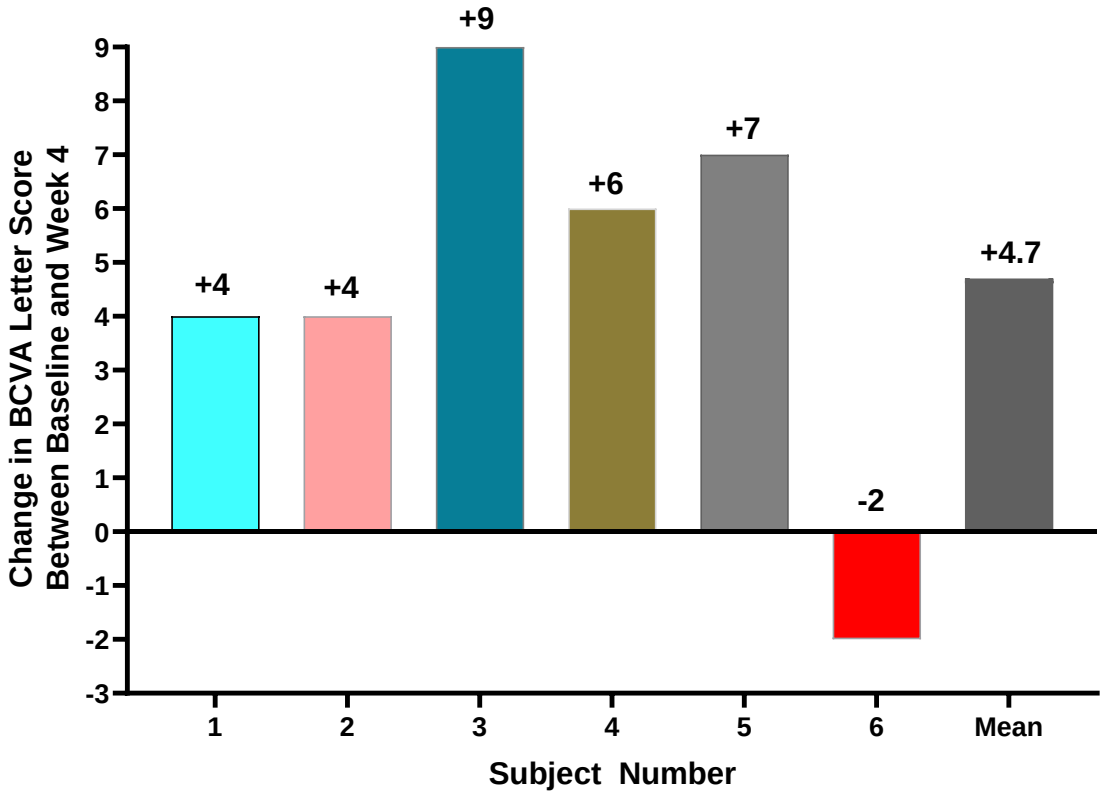
Best Corrected Visual Acuity
One Month Response Following Aflibercept 2 mg vs CLS-AX 0.03 mg

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*

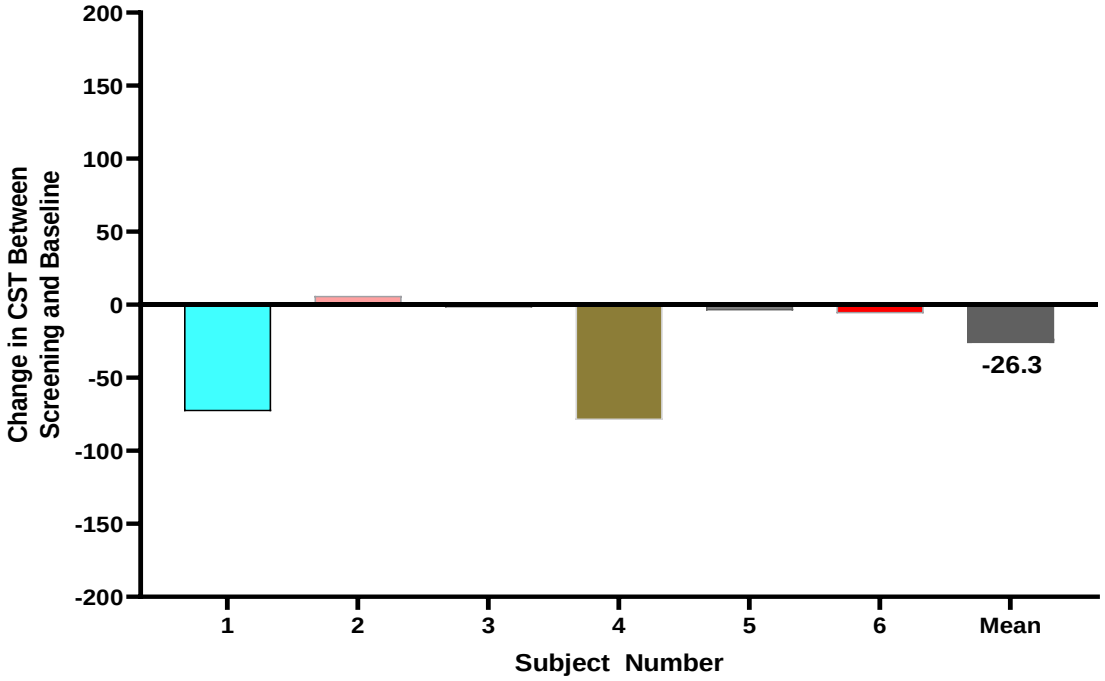


Mean BCVA at baseline (prior to CLS-AX) = 59.0

Source: Clearside data on file. |. *Post hoc, unadjusted

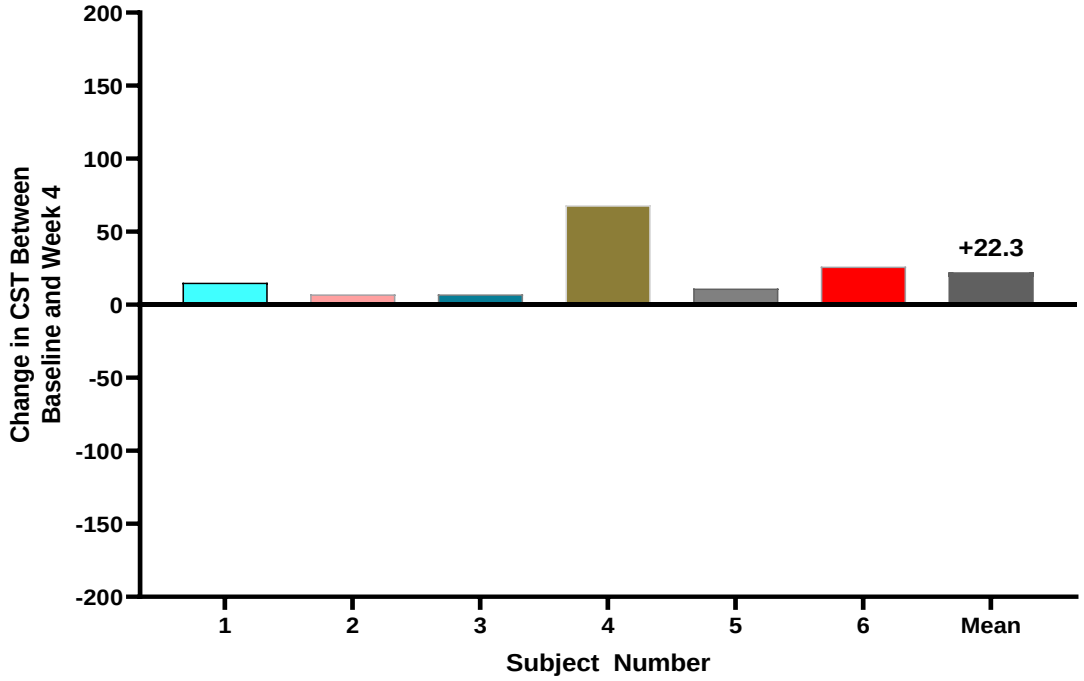
Central Subfield Thickness
Mean CST Stable within 50 *µm* at One Month

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)



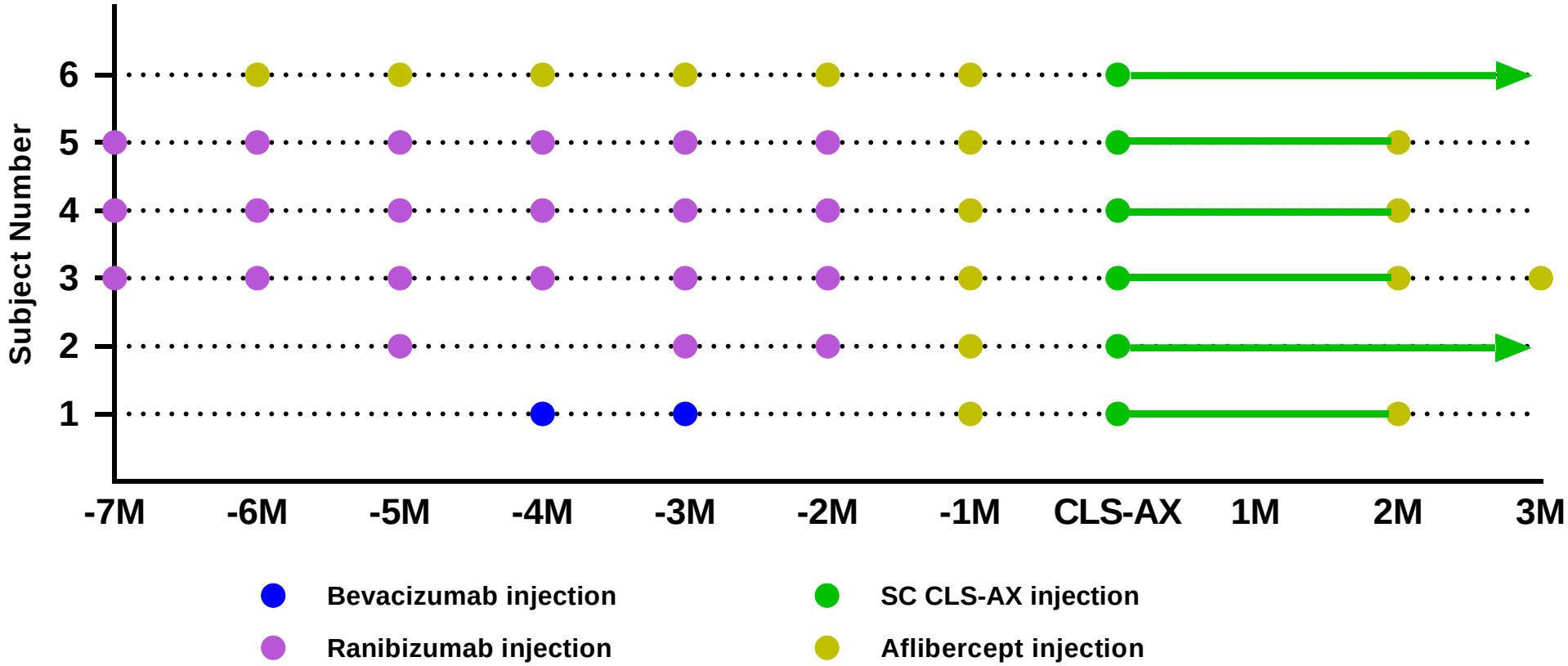
Mean CST at baseline (prior to CLS-AX) = 231.2 µm

Source: Clearside data on file.

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



Assessment for additional treatment: loss from best measurement of ≥10 letters in BCVA with exudation; increase in CST >75 microns; a vision-threatening hemorrhage

Source: Clearside data on file.

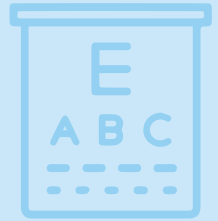
OASIS Cohort 1 Results Support Advancing to Cohort 2

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

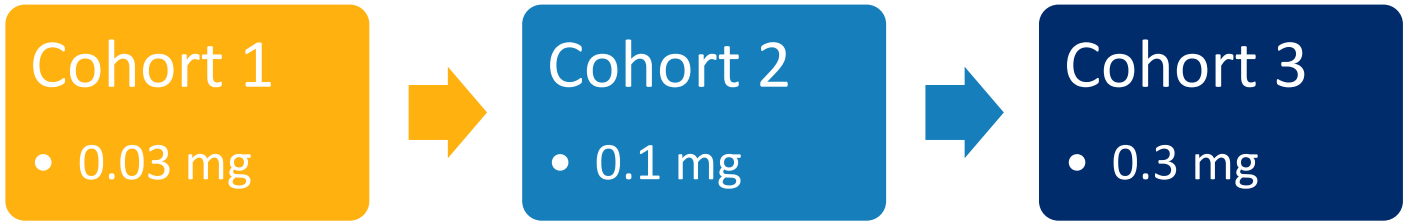
- Mean CST stable within 50 *μm* at 1 month

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

Source: Clearside data on file.

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

Source: Clearside data on file.

Corporate Partnerships & Milestones

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

XIPERE™ is an investigational product

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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%

arctic VISION

- 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%

XIPERE™ is an investigational product

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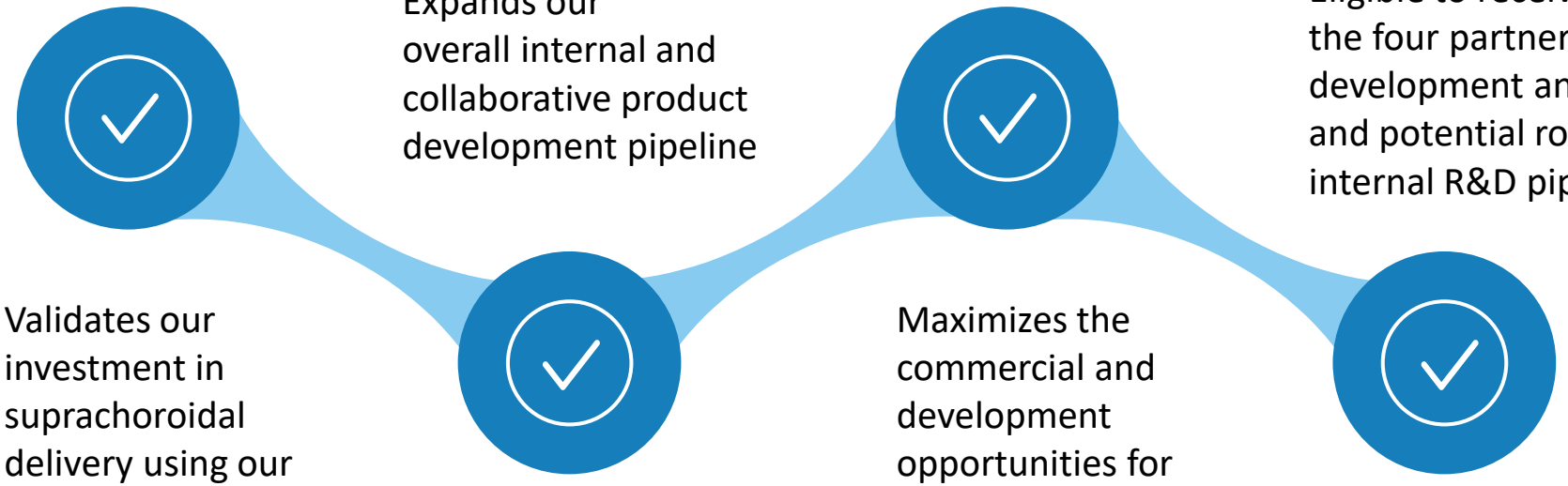
Four Validating Partnerships to Drive Growth

REGENXBIO | aura | BAUSCH+ Health | arctic VISION



Validates our investment in suprachoroidal delivery using our SCS Microinjector

Expands our overall internal and collaborative product development pipeline

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

Eligible to receive >$230M from the four partnerships in potential development and sales milestones, and potential royalties to fund our internal R&D pipeline

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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 Completion

2021: Integrin Inhibitor preclinical data

Exploratory preclinical SC non-viral vector delivery studies ongoing

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
- **2021:** Initial Data Phase 2 ALTITUDE Trial in DR

AURA BIOSCIENCES: AU-011

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

*REGENXBIO (RGNX) trials involve suprachoroidal delivery of RGX-314 using the SCS Microinjector; Aura Biosciences trials involve suprachoroidal delivery of AU-011 using the SCS Microinjector; Arctic Vision program involves suprachoroidal delivery of ARVN001 (triamcinolone acetonide suprachoroidal injectable suspension) using the SCS Microinjector.

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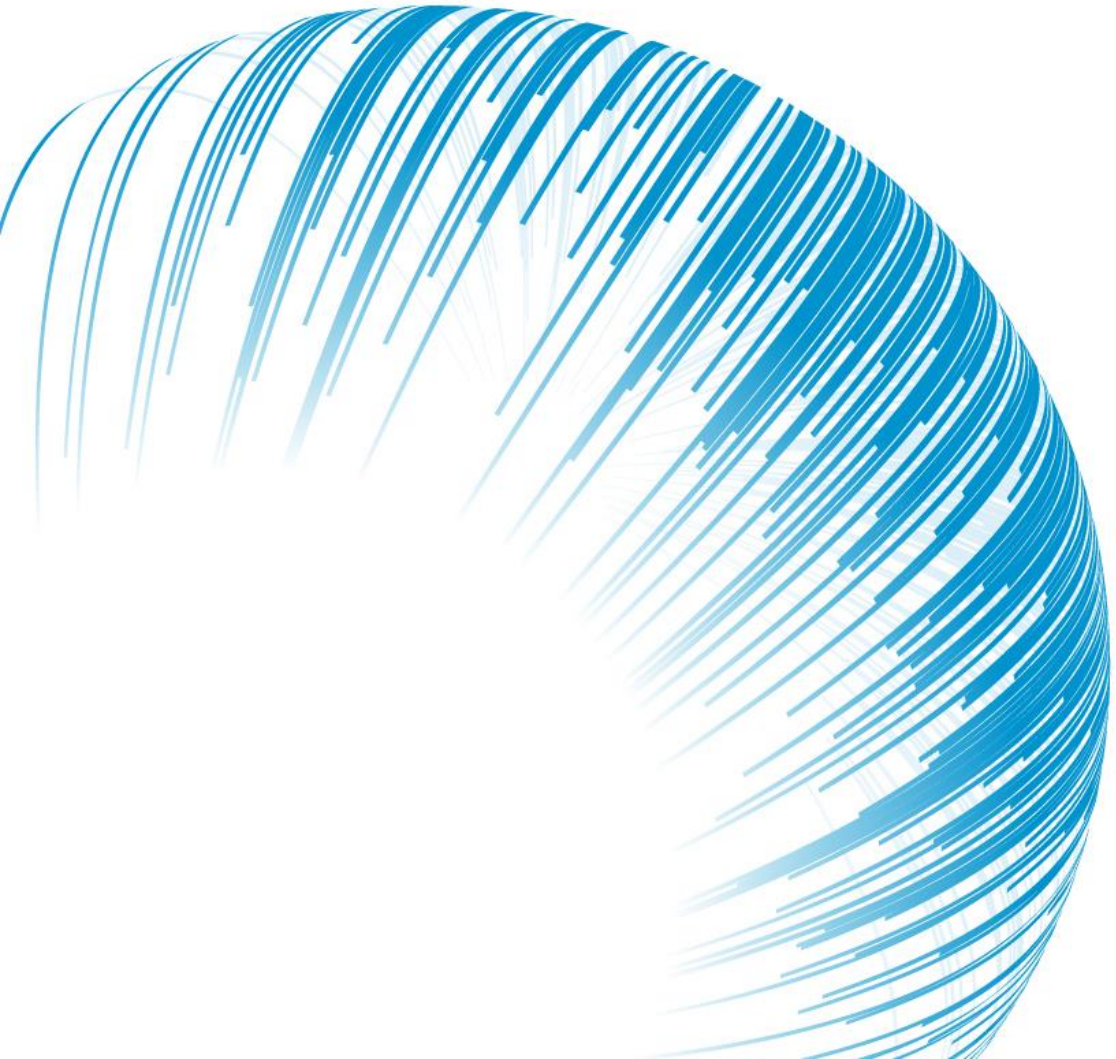

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Nasdaq: CLSD