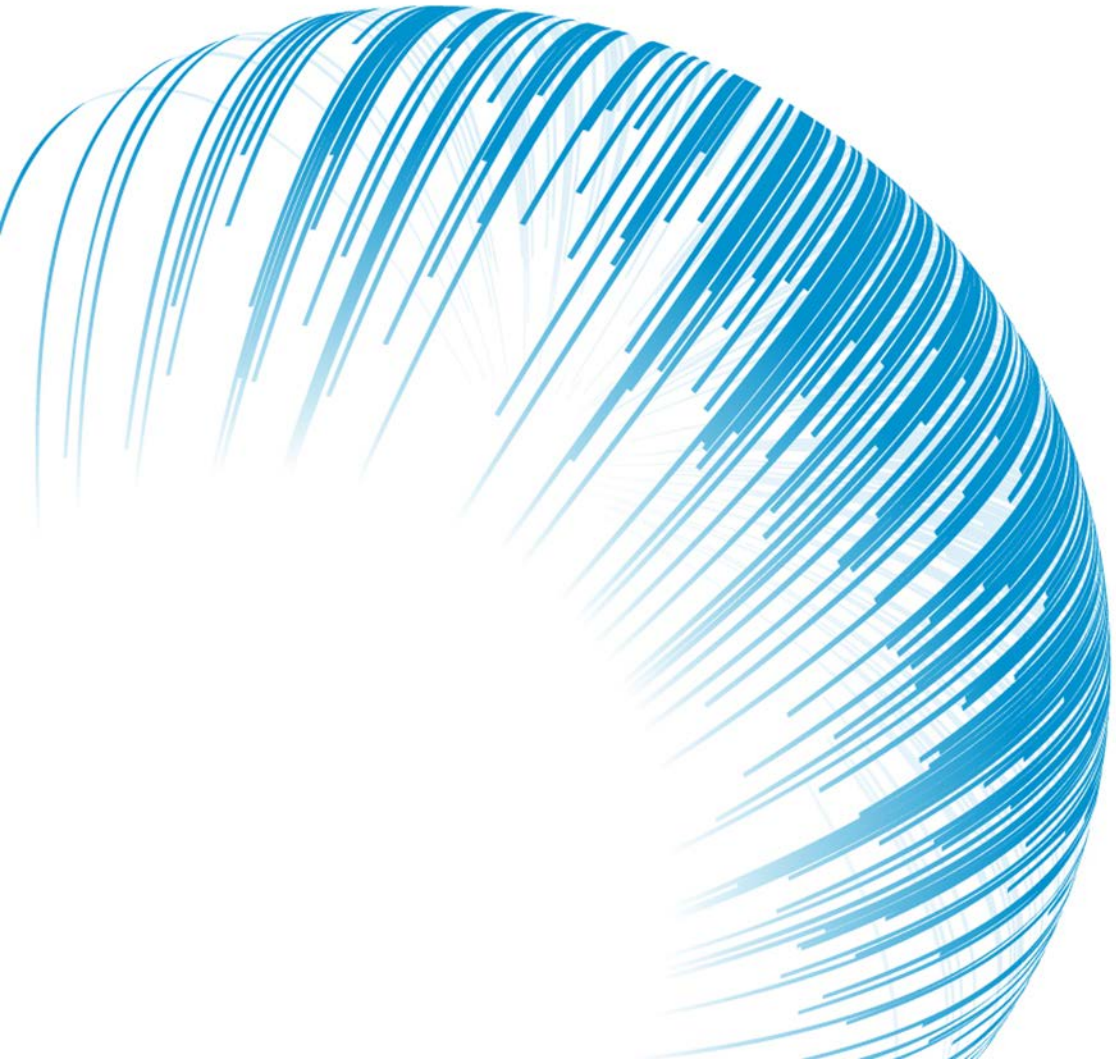


CLEARSIDE® BIOMEDICAL

Corporate Presentation | April 2021

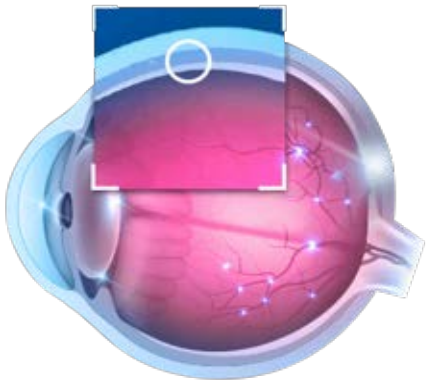
Forward-Looking Statements

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, Clearside's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, filed with the SEC on November 10, 2020, 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

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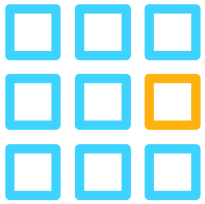
Core Advantages of Treating Via the Suprachoroidal Space

TARGETED

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

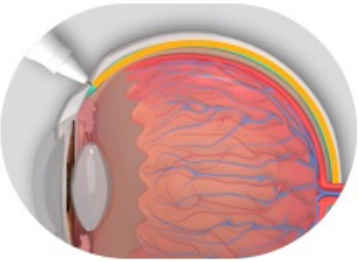
for efficacy



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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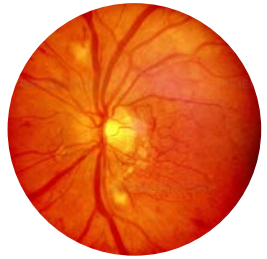
Pioneers in the Suprachoroidal Space (SCS®) with Patented Technology

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. 23 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

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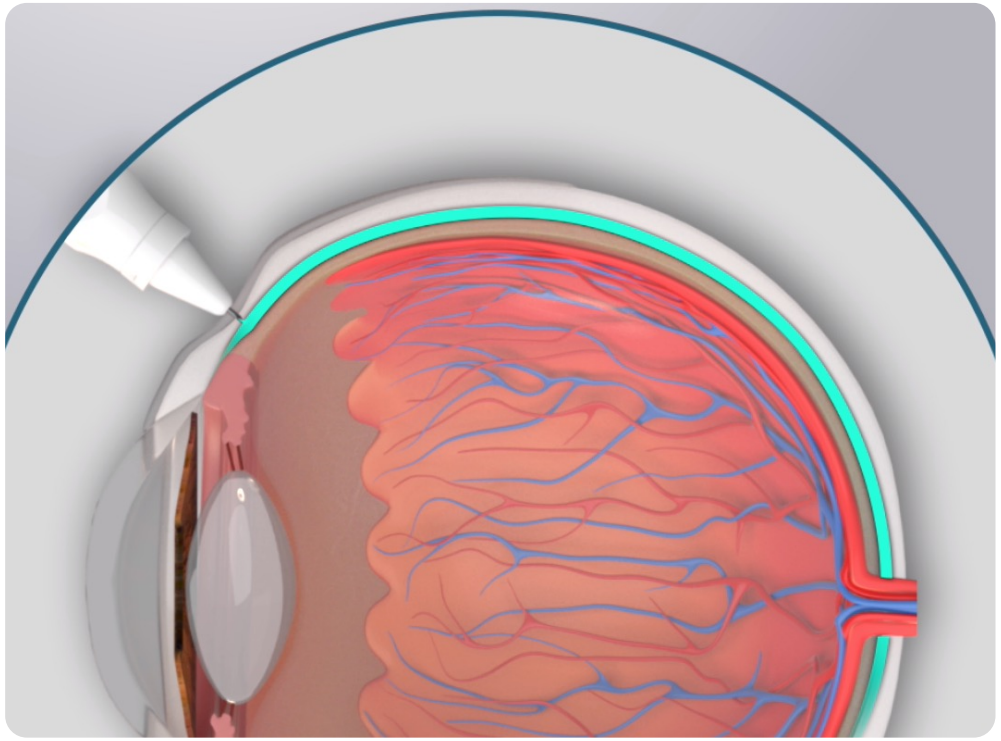
Clearside's SCS Microinjector®: The Only Clinically Tested Injection Device for Suprachoroidal Drug Delivery

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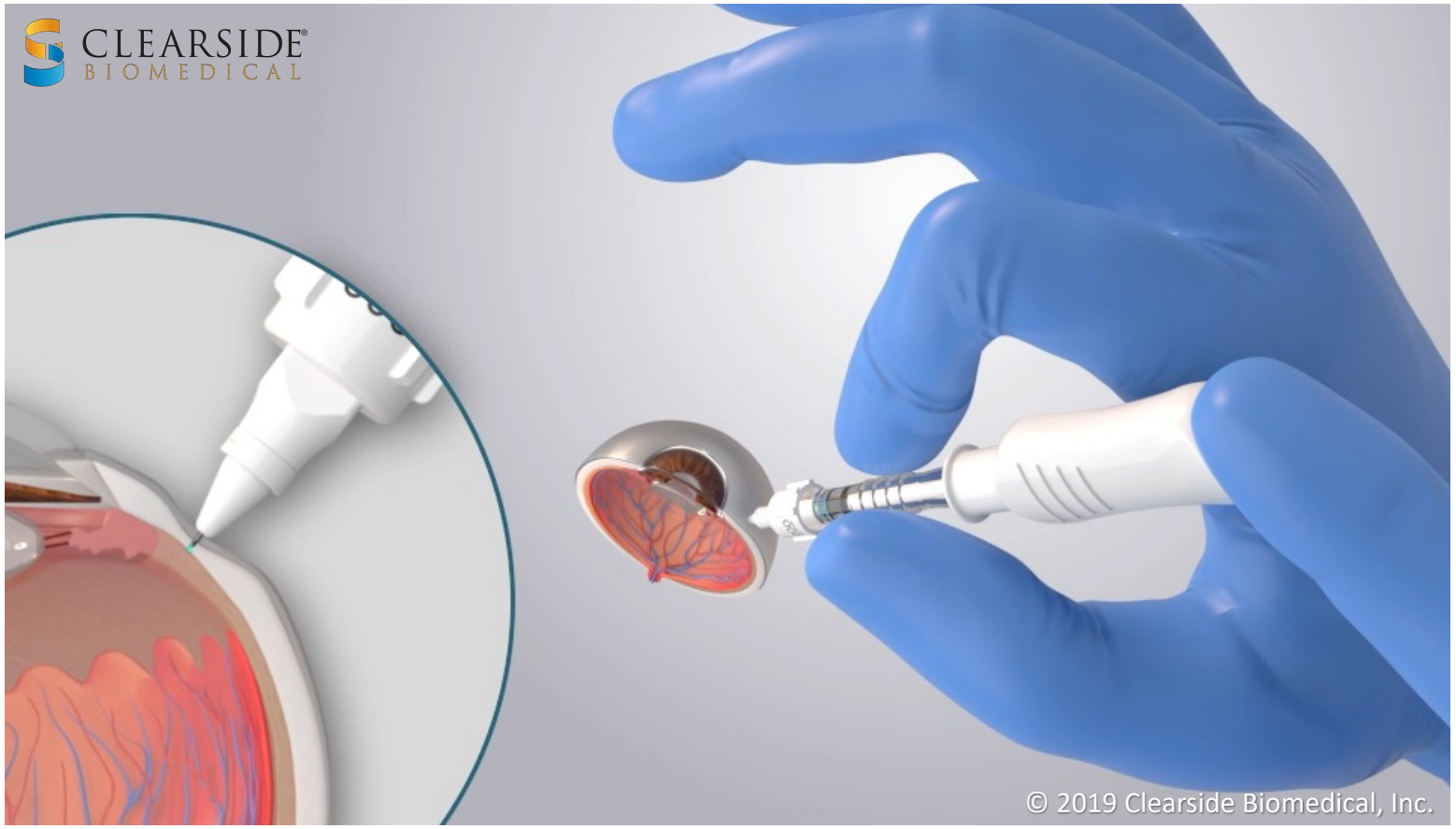
Exclusive Access to the Back of the Eye Using Clearside's Proprietary SCS Microinjector®



CLEARSIDE BIOMEDICAL

CLS-AX Delivered with SCS Microinjector® for Wet AMD

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					
ARCTIC VISION	Small Molecule	Greater China & South Korea					

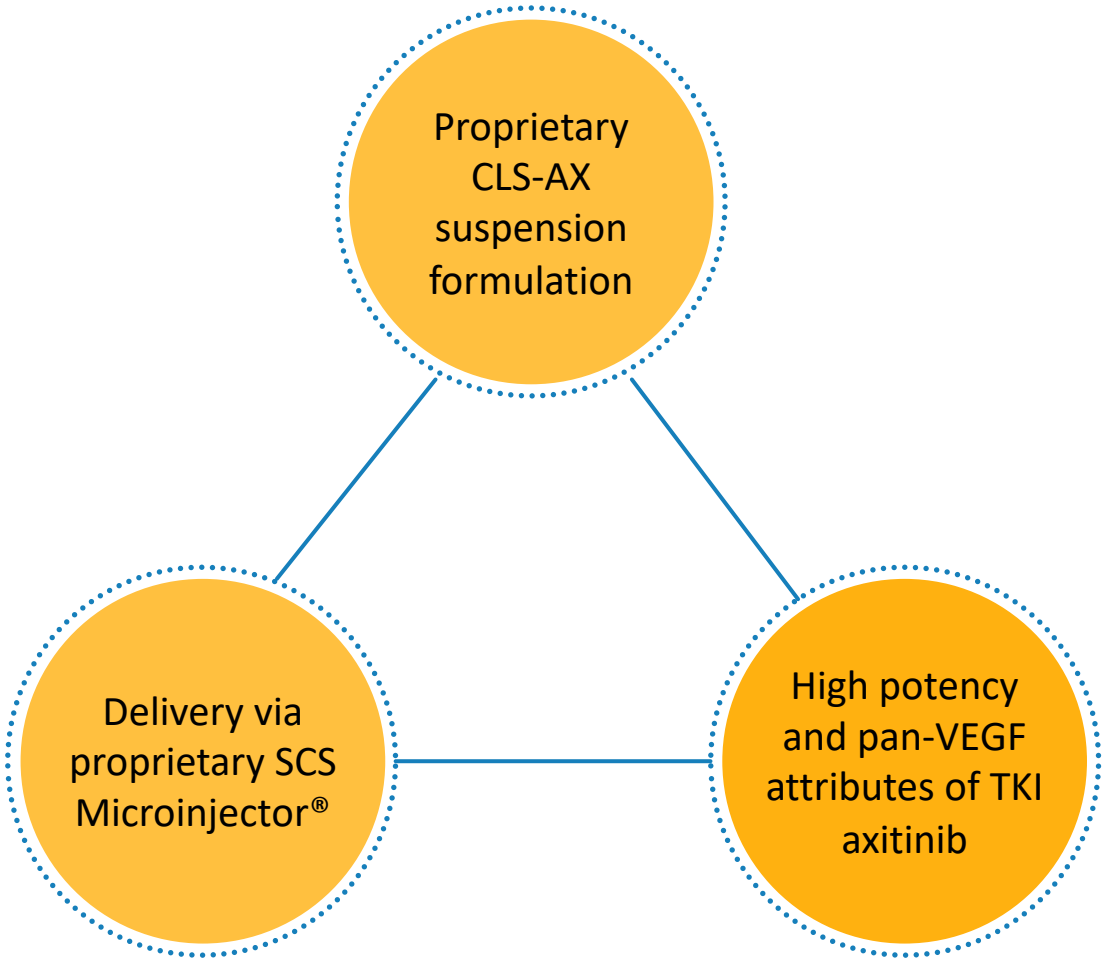
XIPERE™ (triamcinolone acetonide suprachoroidal injectable suspension) is an investigational product

CLS-AX

(axitinib injectable suspension)

for Suprachoroidal Injection

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

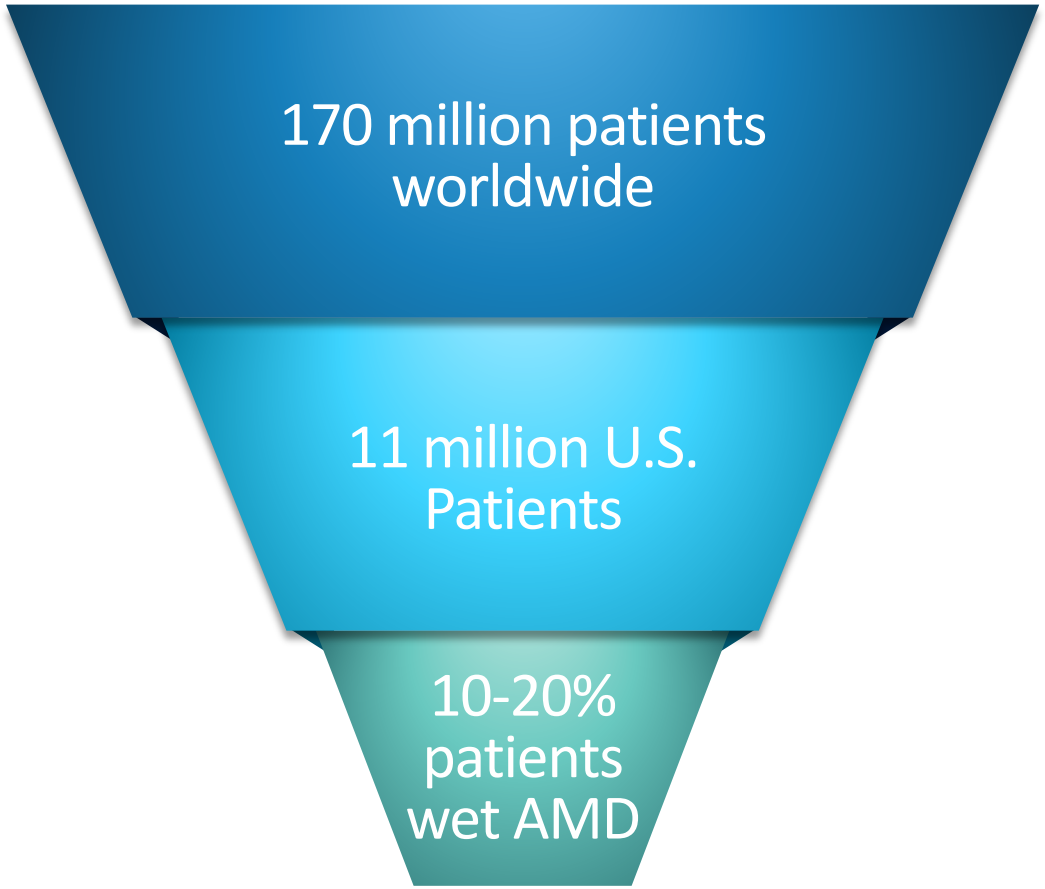


- Potential to **improve the treatment landscape** for wet AMD patients
- **Longer lasting treatment** may reduce patient burden from monthly injections
- Protecting the vitreous and anterior chamber **may eliminate symptomatic floaters and other side effects**
- **Targeted high levels** to affected chorio-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)

Age-Related Macular Degeneration (AMD)

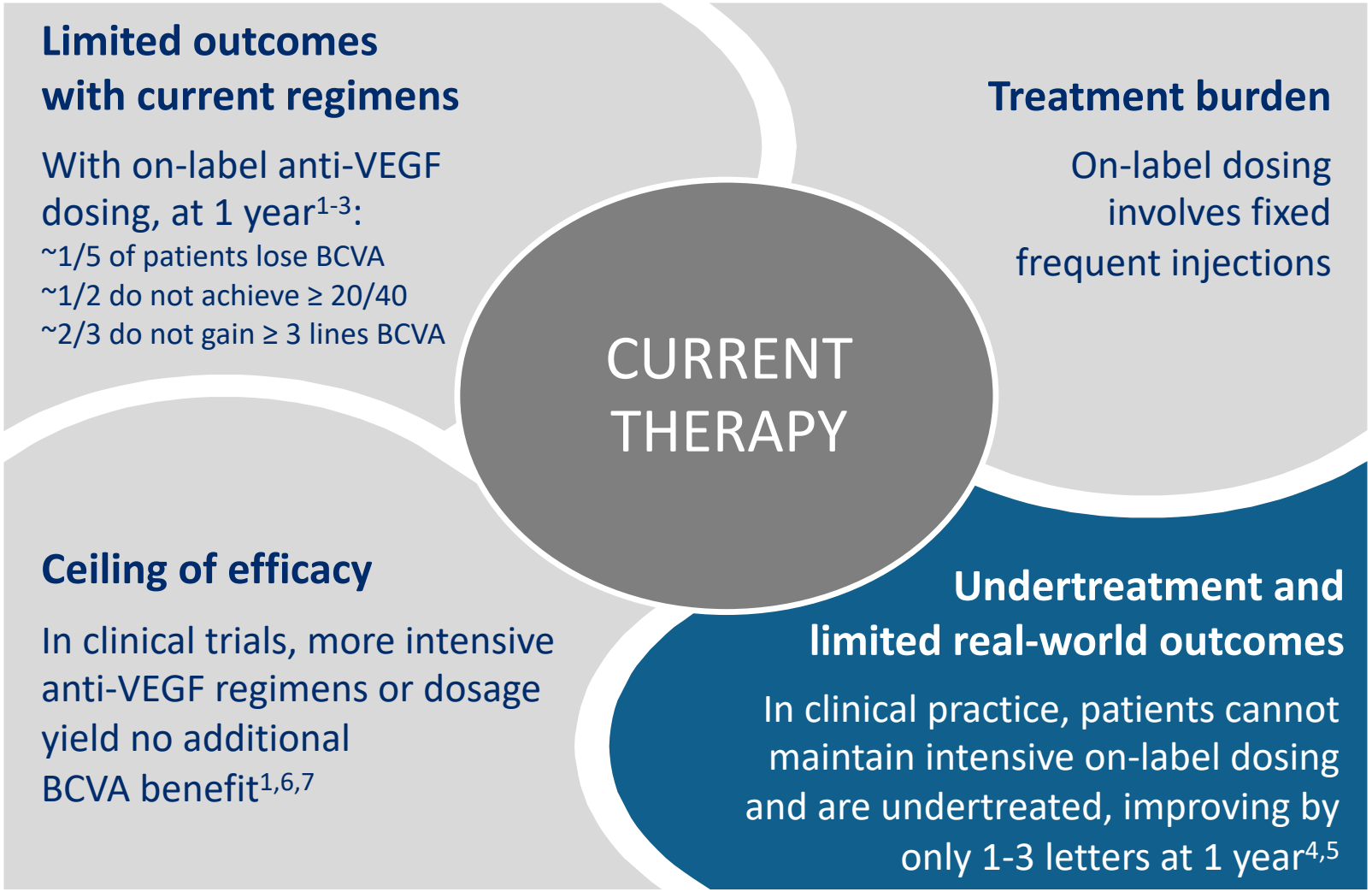
A large and growing market opportunity



- 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

Sources: Medscape: F Ryan Prall, MD, et al Assistant Professor of Ophthalmology, Indiana University School of Medicine | Pennington, Katie L and DeAngelis, Margaret M *Eye and Vision*, Epidemiology of age-related macular degeneration (AMD): associations with cardiovascular disease phenotypes and lipid factors , Dec 22, 2016.

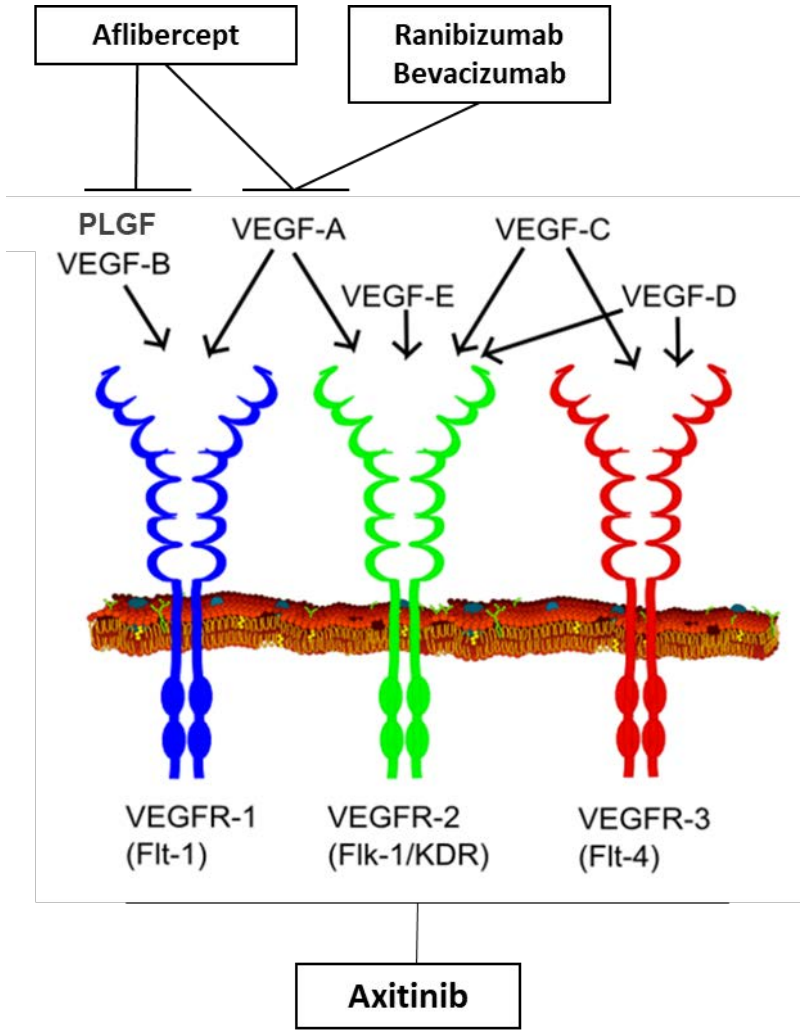
Current Wet AMD Therapies Lead to Under-Treatment and Limited "Real-World" Clinical Outcomes



Sources: 1. Heier JS et al. *Ophthalmology.* 2012;119:2537-2548. | 2. Brown DM et al. Ophthalmology. 2009;116:57-65.e5. | 3. Rosenfeld PJ et al. N Engl J Med. 2006;355:1419-1431. | 4. Ciulla TA et al. Ophthalmology Retina. 2019 May 25. pii: S2468-6530(19)30280-5. | 5. Rao P, Lum F, Wood K, et al. Ophthalmology. 2018;125:522e528. | 6. Busbee BG et al. Ophthalmology. 2013;120:1046-1056. | 7. Schmidt-Erfurth U et al. Ophthalmology. 2014;121:193-201.

Axitinib: a Highly Potent, pan-VEGF TKI to Treat Wet AMD

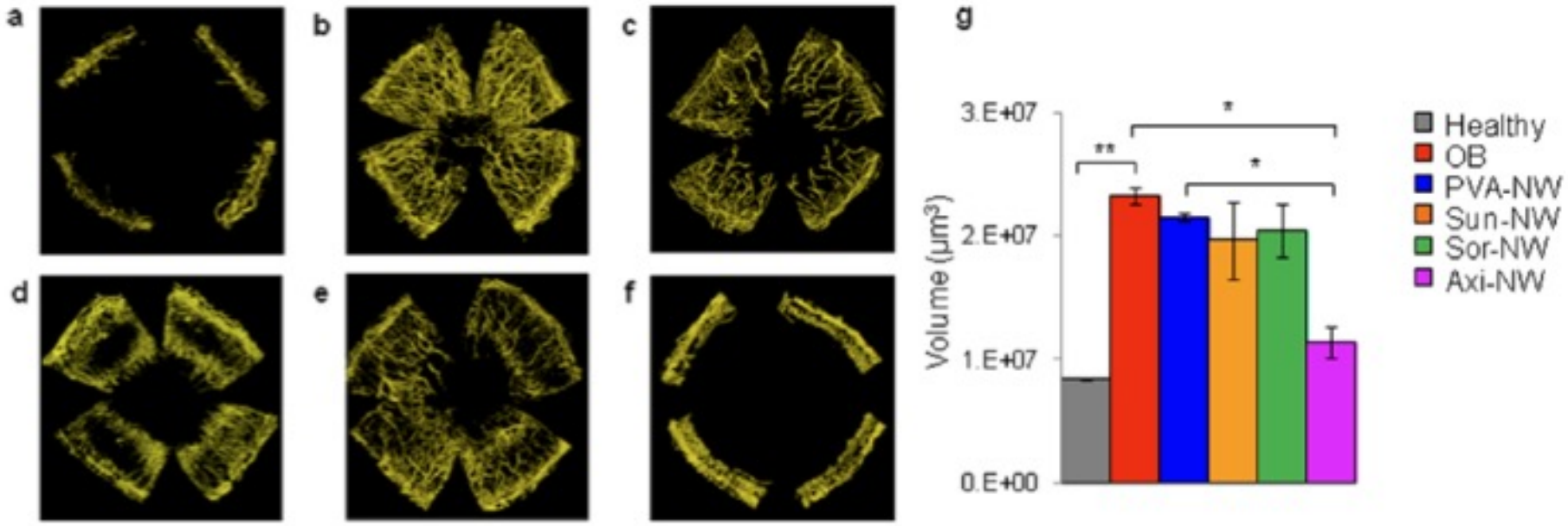
- Axitinib's intrinsic pan-VEGF inhibition through receptor blockade
  - Approved treatments are focused VEGF-A inhibitors
- Inhibits VEGFR-1, VEGFR-2, VEGFR-3 receptors
  - More effective than anti-VEGF-A in *in-vitro* angiogenesis model[1-2]
- Highly potent tyrosine kinase inhibitor (TKI)
  - >10x 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.

Topical Axitinib Demonstrated Superior Potency (same dose) as other TKIs Including Sunitinib

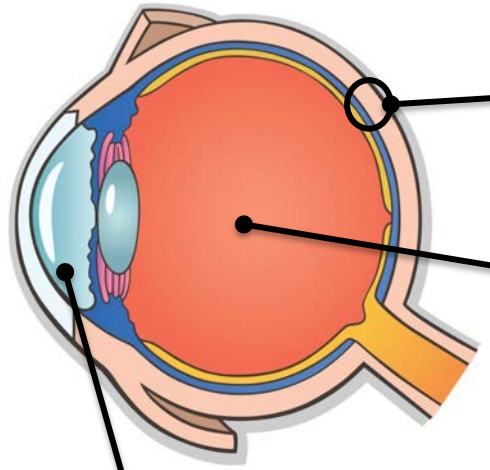
Inhibited Experimental Murine Corneal Neovascularization



Screening of tyrosine kinase inhibitor drugs loaded nanowafers for their relative therapeutic efficacy in inhibiting corneal neovascularization after 10 days of treatment. Representative 3D reconstructed corneal images of fluorescence confocal microscopy: (a) healthy cornea (control); (b) untreated ocular burn (control); (c) blank PVA-NW; (d) Sora-NW; (e) Suni-NW; (f) Axi-NW. (g) Quantification of corneal neovascularization volume. n=3 animals, *P<0.05 vs OB control and P<0.05 vs PVA-NW, **P<0.01. All error bars represent standard deviation from the mean.

Source: Yuan et al. Ocular Drug Delivery Nanowafer with Enhanced Therapeutic Efficacy. *ACS Nano*. 24 Feb 2015;9(2):1749-58

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



11x SCS vs IVT
Retina / RPE-choroid-sclera

0.003X SCS vs IVT
Vitreous humor

Plasma
SCS CLS-AX at or below level of detection

Aqueous Humor
SCS CLS-AX at or below level of detection

Rabbit Model

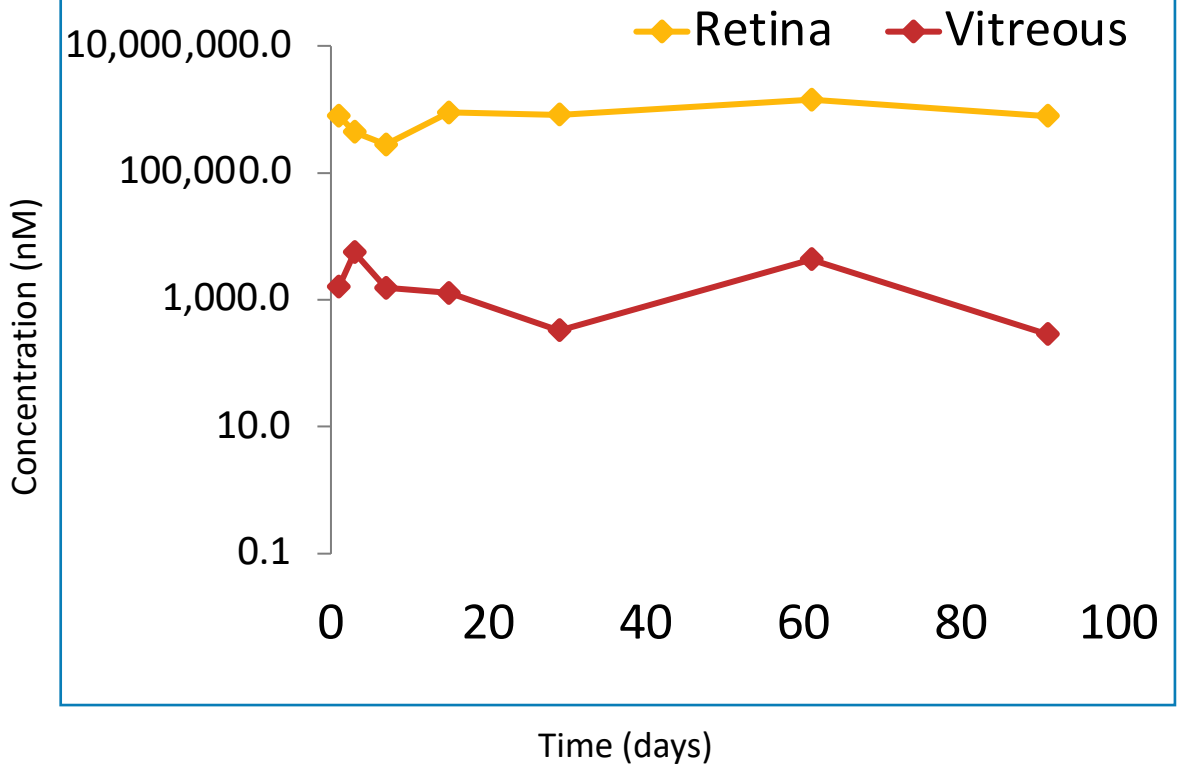
Values: area under the curve ratios, SCS / IVT

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

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



Source: Based on Clearside Biomedical preclinical data

Abbreviations: SCS: Suprachoroidal Space | IVT: Intravitreal Injection | PK: Pharmacokinetic | LLOQ: lower limit of quantification, 0.15 mg/mL | RPE: Retinal pigment epithelium

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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 began at 0.03 mg CLS-AX; proceed to next cohort following review by Safety Monitoring Committee
- Evaluate visual function, ocular anatomy, and need for additional treatment

Cohort Enrollment and Treatment

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

CLS-AX Has the Potential to Improve Wet AMD Treatment

Suprachoroidal Delivery May Synergistically Enhance Pan-VEGF Effect

	SAFETY	EFFICACY	TREATMENT BURDEN
AXITINIB	• **Well characterized** small molecule • **Potential for less immune response & inflammation** compared to some new, contemporary biologic agents • **Better compatibility with retinal pigment epithelial cells** vs other TKIs	• Current anti-VEGF agents target VEGF-A, but **broad VEGF inhibition** has shown greater effect preclinically & clinically • Axitinib shows **pan-VEGF inhibition** via receptor blockade • **>10x the in-vitro potency** & greater inhibition of preclinical angiogenesis vs. other TKIs • **Regresses neovascularization** preclinically	

SUPRACHOROIDAL DELIVERY	• **Compartmentalized delivery** to affected posterior tissues offers **potentially fewer AEs** including vitreous floaters, snow globe effect, corneal & anterior segment exposure
	• **Favorable tolerability profile** of SCS Microinjector in **>1200 injections** across multiple retinal disorders
	• **Well accepted by physician-investigators**
		• Suprachoroidal delivery of CLS-AX **targets the affected chorioretinal tissue** layers for potential efficacy benefits
		• Suprachoroidal CLS-AX has shown **up to 11x higher drug levels** in affected tissues versus intravitreal administration
			• Suprachoroidal CLS-AX has shown **prolonged duration** in preclinical pharmacokinetic studies
			• May **relieve treatment burden of current frequent dosing** with potential to:
			  • Facilitate **better compliance**
			  • **Limit undertreatment**
			  • Further **enhance clinical outcomes**

Sources: Clearside Biomedical preclinical and clinical studies | 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. | Lieu et al. The Association of Alternate VEGF Ligands with Resistance to Anti-VEGF Therapy in Metastatic Colorectal Cancer. PLoS ONE 8(10): e77117. | 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.

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Early-Stage Pipeline

SCS Injection Platform and Integrin Inhibition

The Opportunity Beyond the VEGF pathway

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

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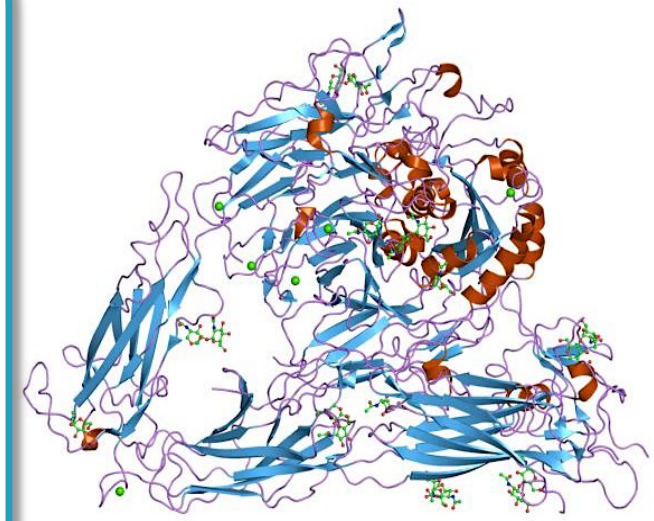
Integrin Small Molecule Suspension for SCS administration

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 avβ3, avβ5 and a5β1 implicated in DME, DR & AMD

Given unique MOA, could serve as:

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

Note: This image of integrin $a_v\beta_3$ extracellular domains has been released for public use by its creator and original copyright holder: http://www.ebi.ac.uk/.

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

Sources: Clearside data on file. | Campochiaro, P. A. (2019). AAV8-vectored suprachoroidal gene transfer produces widespread ocular transgene expression. *Journal of Clinical Investigation*. doi: 10.1172/jci129085

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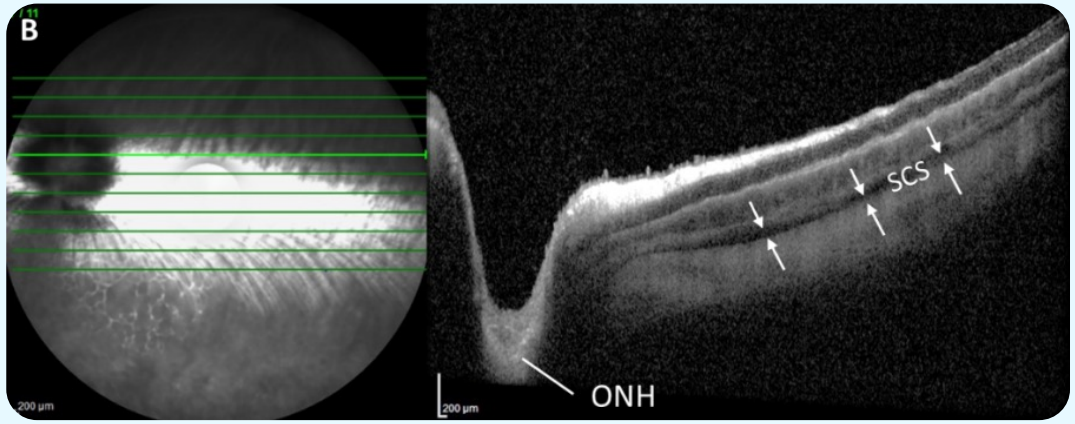
The Suprachoroidal Space Reversibly Opens Posteriorly and Circumferentially Following DNA Nanoparticle Administration in Rabbits

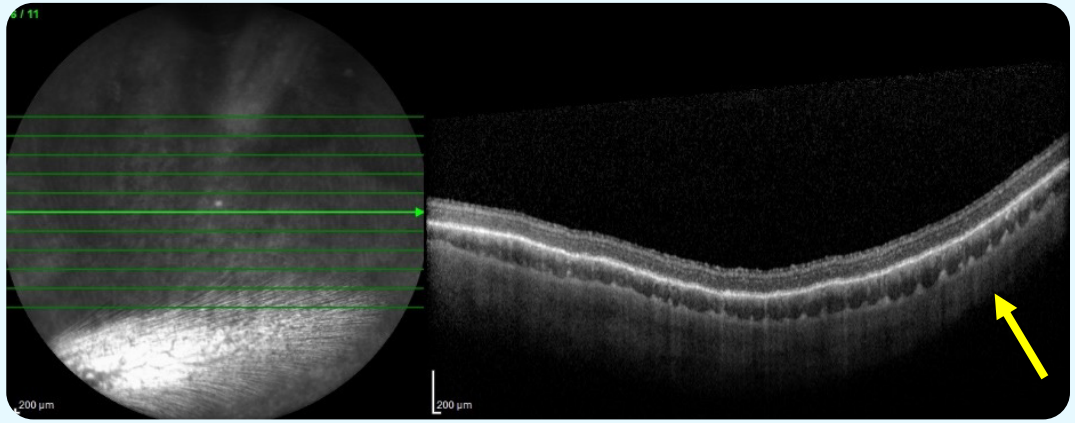
[Day 1]

The suprachoroidal space (SCS) opens posteriorly to the optic nerve head (ONH)



[Day 30]

There is well-tolerated reversible closure of the SCS



Source: Clearside preclinical studies. Data on file.

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Corporate Partnerships & Milestones

Enabling In-office Delivery of 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
- Well tolerated to date in the AAVIATE trial

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®

CLEARSIDE BIOMEDICAL

REGENXBIO: Two Phase 2 Trials Using SCS Microinjector®

- Two multi-center, open-label, randomized, controlled, dose-escalation studies evaluating the efficacy, safety and tolerability of suprachoroidal delivery of RGX-314
- RGX-314 for Treatment of Wet Age-Related Macular Degeneration (wet AMD)
  - Phase 2 AAVIATE trial of suprachoroidal delivery of RGX-314 using SCS Microinjector **is ongoing**.
  - Patient population: severe wet AMD patients who are responsive to anti-VEGF treatment
  - Interim efficacy data from Cohort 1 expected in **Q3 2021**
  - Patient enrollment in Cohort 2 expected to be complete in **Q2 2021**.
- RGX-314 for Treatment of Diabetic Retinopathy (DR)
  - Phase 2 ALTITUDE trial of suprachoroidal delivery of RGX-314 using SCS Microinjector **is ongoing**.
  - Initial data expected **in 2021**.

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

The Terms:

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

aura

XIPERE™: Potential Suprachoroidal Approach to Treating Uveitic Macular Edema

- Macular edema is the leading cause of vision loss in patients with non-infectious uveitis
- If approved, XIPERE would be the first therapy for this indication
- Expect to resubmit NDA with three months additional stability data in Q2 2021
- Commercialization and development partnerships to enhance value and expand patient access

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%

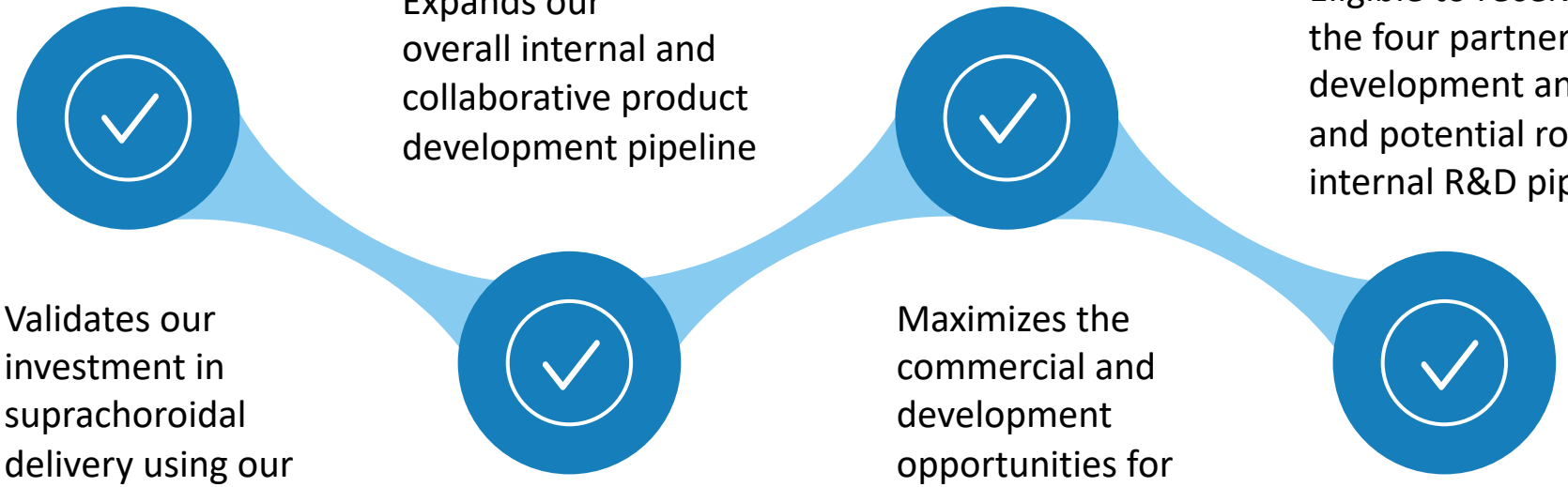
arctic VISION

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

XIPERE™ is an investigational product

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 Planned

YE 2021: Expected NDA Approval

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

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 Data Cohort 1 Phase 2 AAVIATE trial in wet AMD
- **2021:** Initial Data Phase 2 ALTITUDE Trial in DR

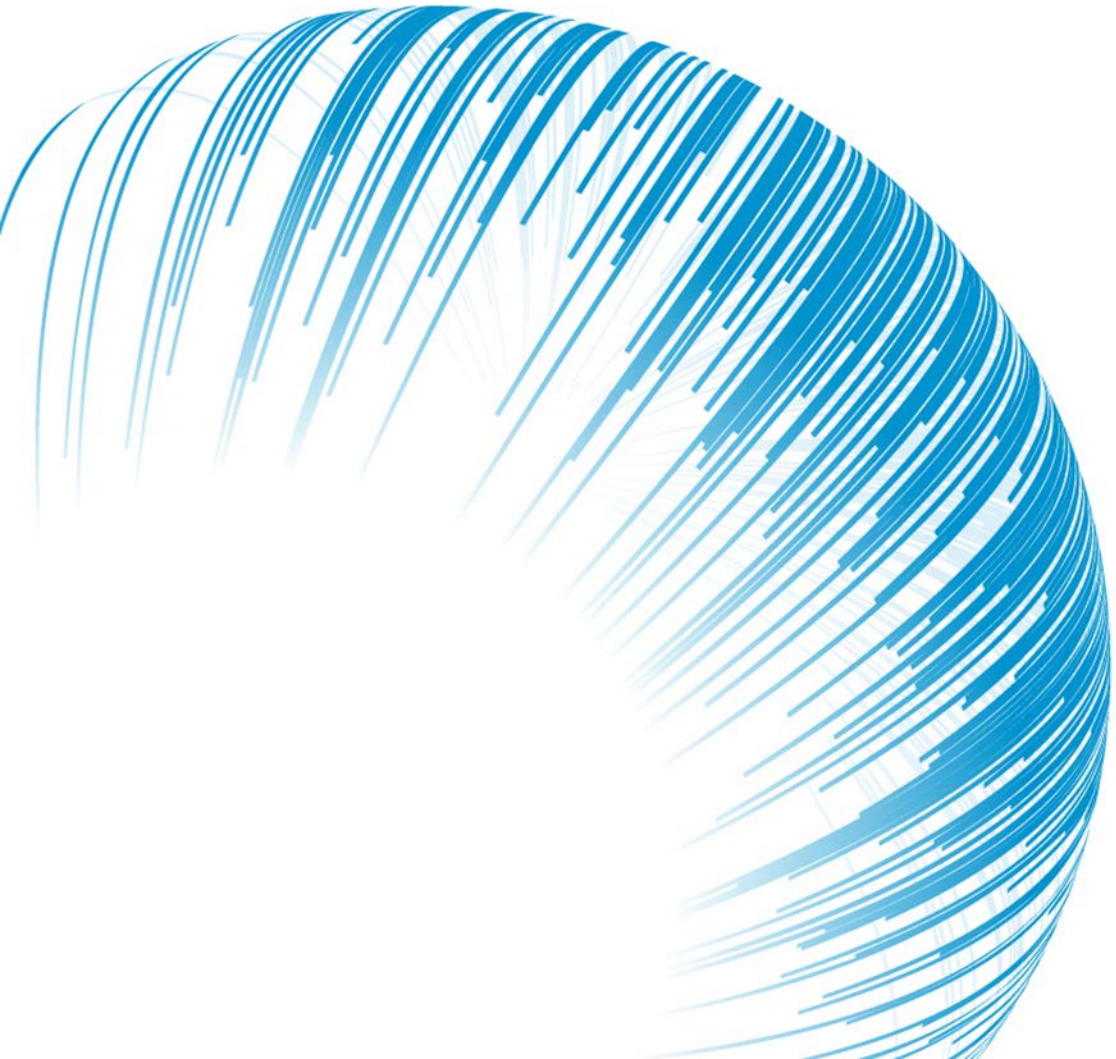
AURA BIOSCIENCES: AU-011

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

ARCTIC VISION: ARVN001

- **2021:** Initiate Phase 3 trial in China in uveitic macula edema

*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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Nasdaq: CLSD