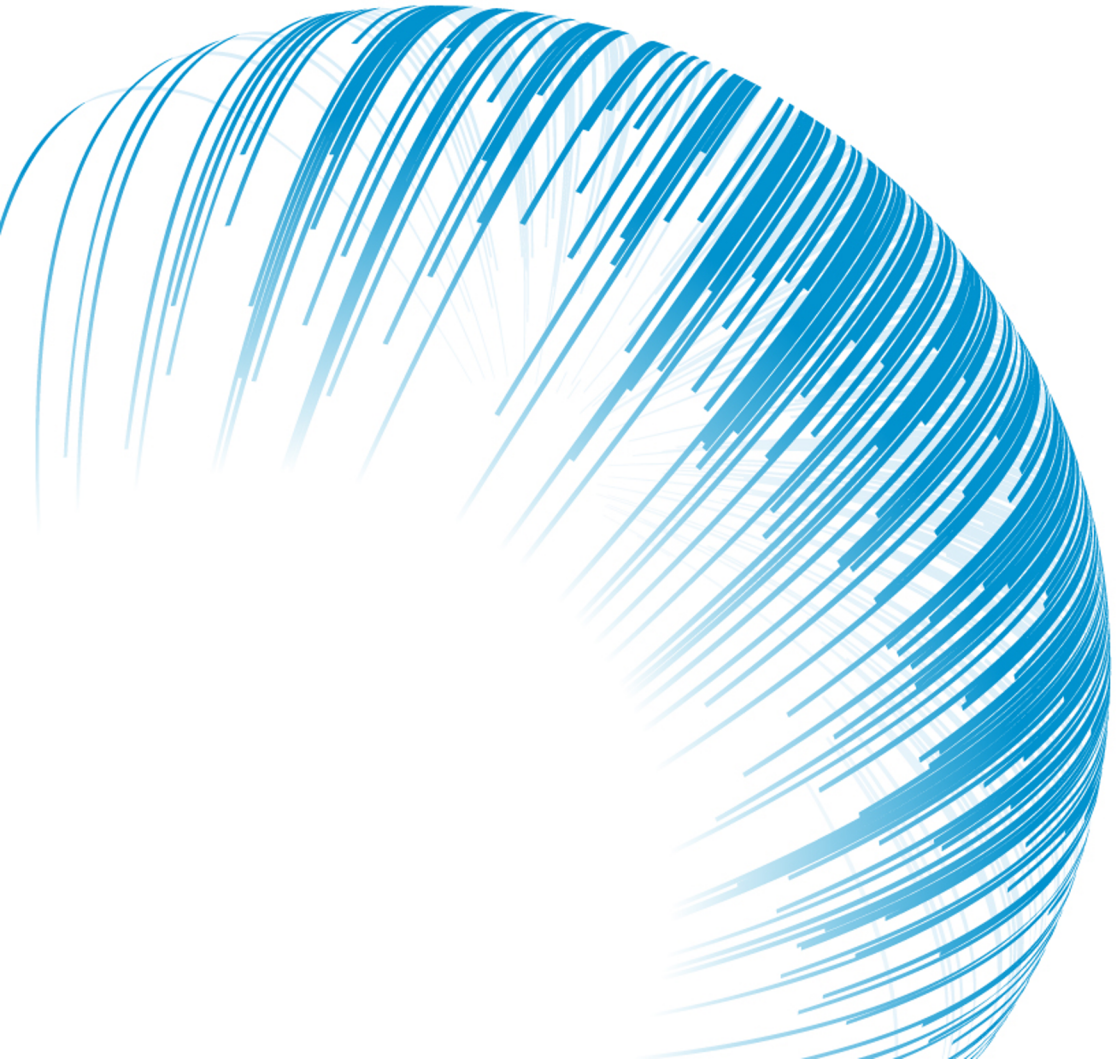


CLEARSIDE® BIOMEDICAL

Corporate Presentation | January 2021

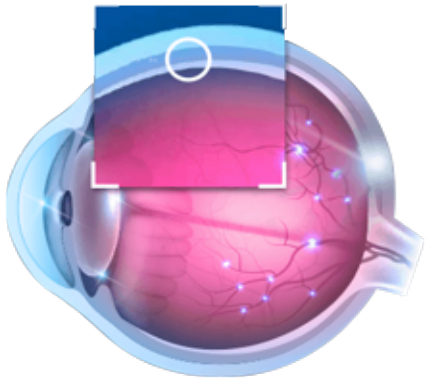
Forward-Looking Statements

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, 2019, filed with the SEC on March 13, 2020, 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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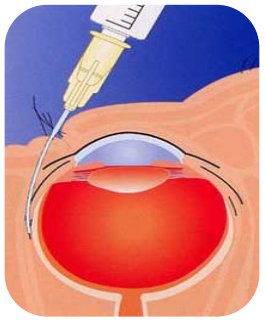
Evolution of Injection Procedures to Reach the Back of the Eye

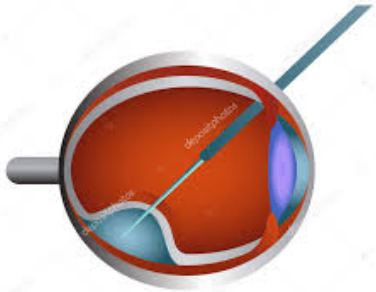


Periocular Injection

Highly variable drug diffusion across the sclera into the eye

Intravitreal Injection

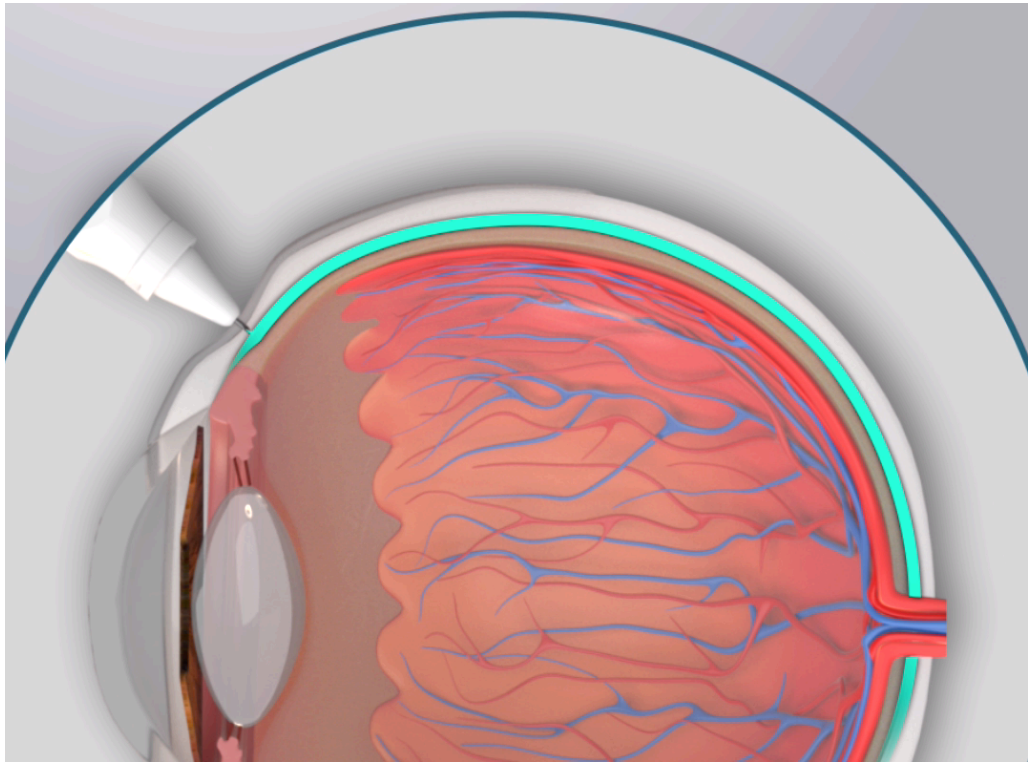
Broad diffusion to all areas of the eye including the anterior chamber and lens



Subretinal Injection

Invasive surgery with variable results

Suprachoroidal Space Injection



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

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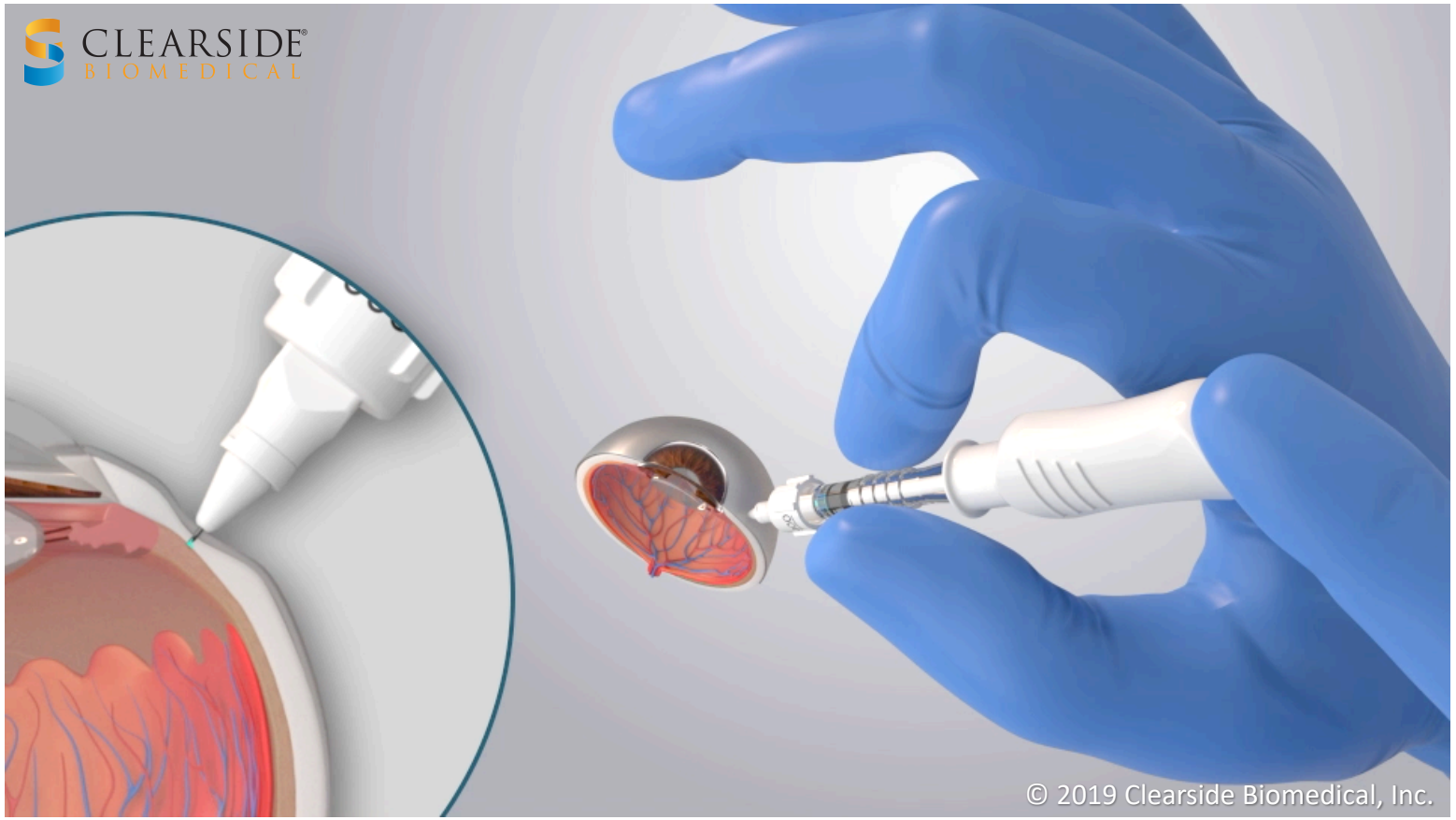
Exclusive Access to the Back of the Eye Using Clearside's Proprietary SCS Microinjector®



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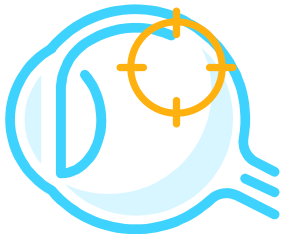
Core Advantages of Treating Via the Suprachoroidal Space



TARGETED

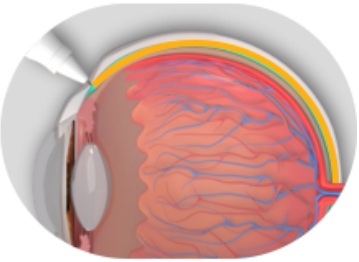
The back of the eye is the location of many irreversible and debilitating visual impairments

for efficacy

COMPARTMENTALIZED

Drug is compartmentalized in the suprachoroidal space, which helps keep it away from non-diseased tissues

for safety



BIOAVAILABLE PROLONGED PK

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

for durability

PK = pharmacokinetic | 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.

CLEARSIDE BIOMEDICAL

Strong Intellectual Property Coverage of SCS Platform

21 U.S. Patents Total Expiring between 2027 - 2037

Plus >20 European and International Patents

2	5	4	1	1	4	1	3
Methods using loss-of-resistance technology	Apparatus using loss-of-resistance technology	Apparatus having / methods using an adjustable puncture member	Ocular injection apparatus packaging	Administration of any anti-inflammatory drug to the suprachoroidal space by microinjection	Administration of any drug to the suprachoroidal space by microinjection	Administration of any drug to the eye by inserting a microinjector into the sclera	Methods of treating posterior ocular disorders including macular edema or uveitis
DEVICE PATENTS				**DRUG PATENTS**			**DISEASE PATENTS**

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Partnered Suprachoroidal Pipeline

Development and Commercial Programs using SCS Microinjector®

PARTNER	INDICATION	IND-Enabling	PHASE 2	PHASE 3	NDA
REGENXBIO	Wet AMD (AAVIATE)				
REGENXBIO	Diabetic Retinopathy (ALTITUDE)				
AURA BIOSCIENCES	Ocular Oncology / Choroidal Melanoma				

XIPERE™ Commercial Licenses

PARTNER	TERRITORY	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	NDA
BAUSCH HEALTH	U.S. & Canada; options outside North America					
ARCTIC VISION	Greater China & South Korea					

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

Suprachoroidal Internal Development Pipeline

STUDY DRUG	INDICATION	RESEARCH	PRECLINICAL	PHASE 1/2	PHASE 3	NDA
CLS-AX (axitinib injectable suspension)	Wet AMD					
Integrin Inhibitor (Injectable suspension)	Diabetic Macular Edema (DME)					
Gene Therapy: Extracellular protein	"Therapeutic Biofactory"					
Gene Therapy: Intracellular protein	Inherited Retinal Disease					

CLS-AX
(axitinib injectable suspension)

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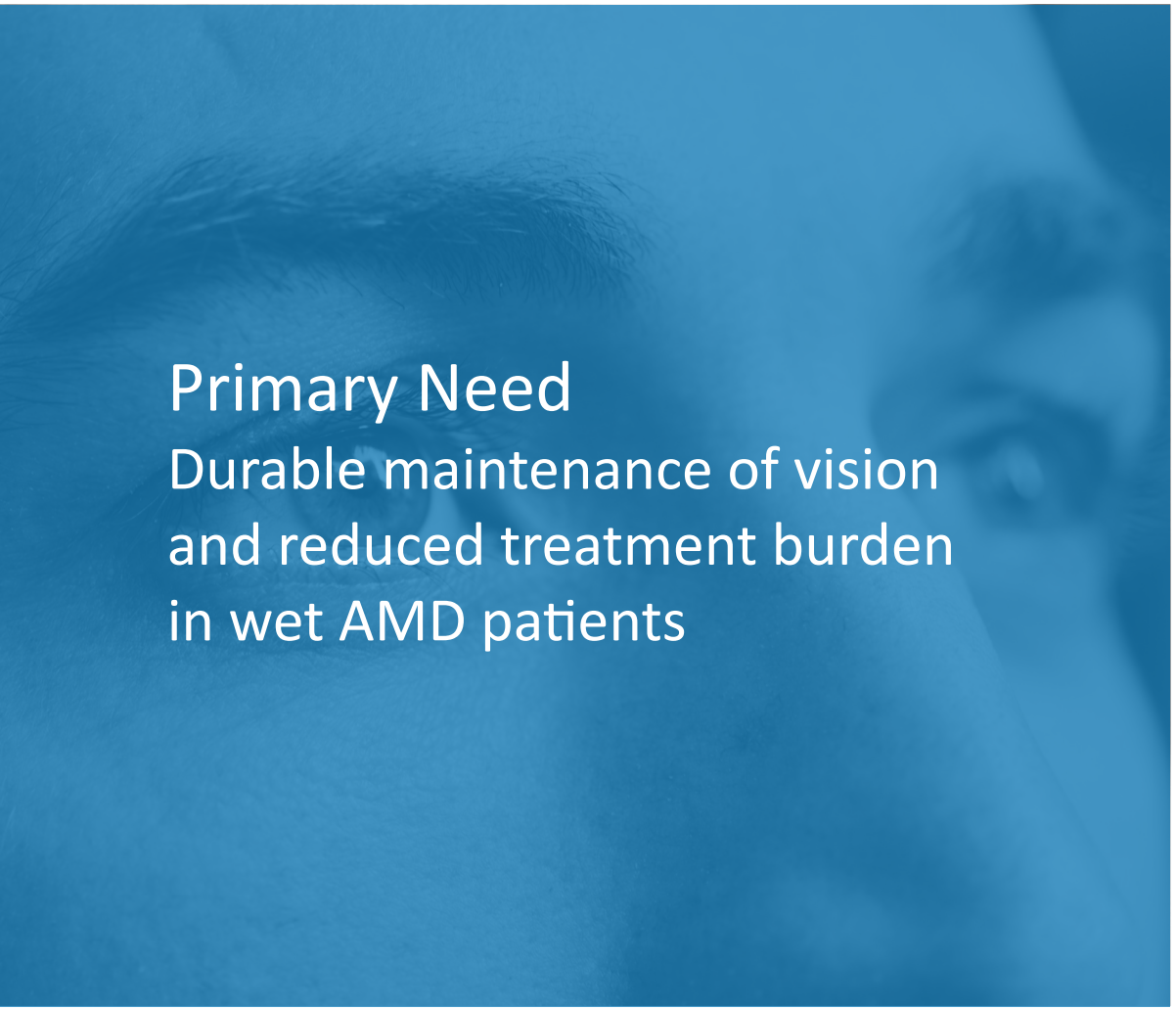
CLS-AX (axitinib injectable suspension): A Potential Solution for Treatment Burden

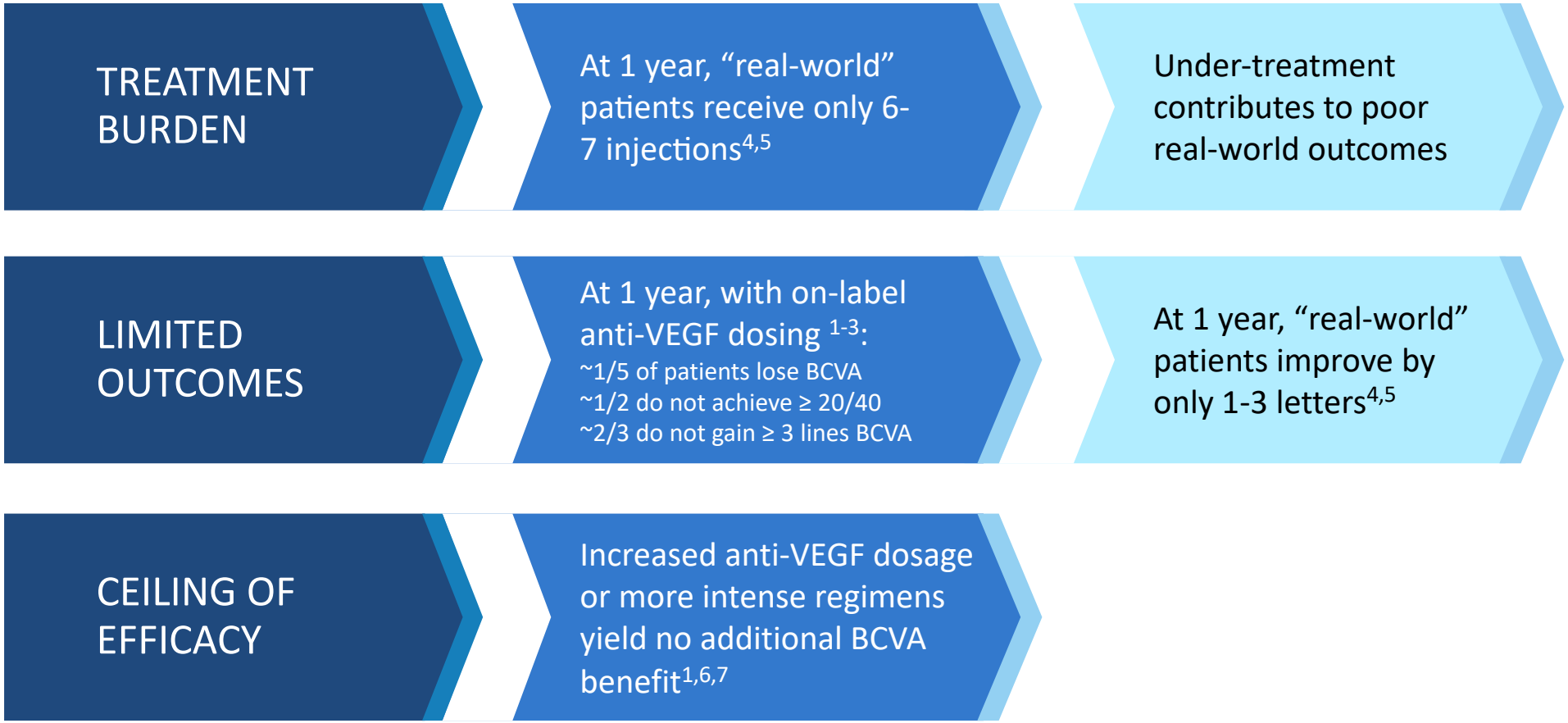


The Opportunity

- Reduce patient burden from monthly injections to every six months or longer
- Pan-VEGF inhibition potentially more efficacious than current approaches
- Improve long-term, real-world visual outcomes for patients
- Provide physicians with ability to titrate dose based on patient need
- Protect the anterior chamber from toxic exposure to TKIs

TKIs = Tyrosine Kinase Inhibitors

CLS-AX via SCS May Address Unmet Needs in wet AMD



Sources: 1. Heier JS et al. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. Ophthalmology. 2012;119:2537-2548. | 2. Brown DM et al. Ranibizumab versus verteporfin photodynamic therapy for neovascular age-related macular degeneration: two-year results of the ANCHOR study. Ophthalmology. 2009;116:57-65.e5. | 3. Rosenfeld PJ et al. Ranibizumab for neovascular age-related macular degeneration. N Engl J Med. 2006;355:1419-1431. | 4. Ciulla TA et al. Visual Acuity Outcomes and Anti-Vascular Endothelial Growth Factor Therapy Intensity in Neovascular Age-Related Macular Degeneration Patients: A Real-World Analysis of 49,485 Eyes. Ophthalmol Retina. 2019 May 25. pii: S2468-6530(19)30280-5. | 5. Rao P, Lum F, Wood K, et al. Real-world vision in age-related macular degeneration patients treated with single anti-VEGF drug type for 1 year in the IRIS Registry. Ophthalmology. 2018;125:522e528. | 6. Busbee BG et al. Twelve-month efficacy and safety of 0.5 mg or 2.0 mg ranibizumab in patients with subfoveal neovascular age-related macular degeneration. Ophthalmology. 2013;120:1046-1056. | 7. Schmidt-Erfurth U et al. Intravitreal aflibercept injection for neovascular age-related macular degeneration: ninety-six-week results of the VIEW studies. Ophthalmology. 2014;121:193-201.

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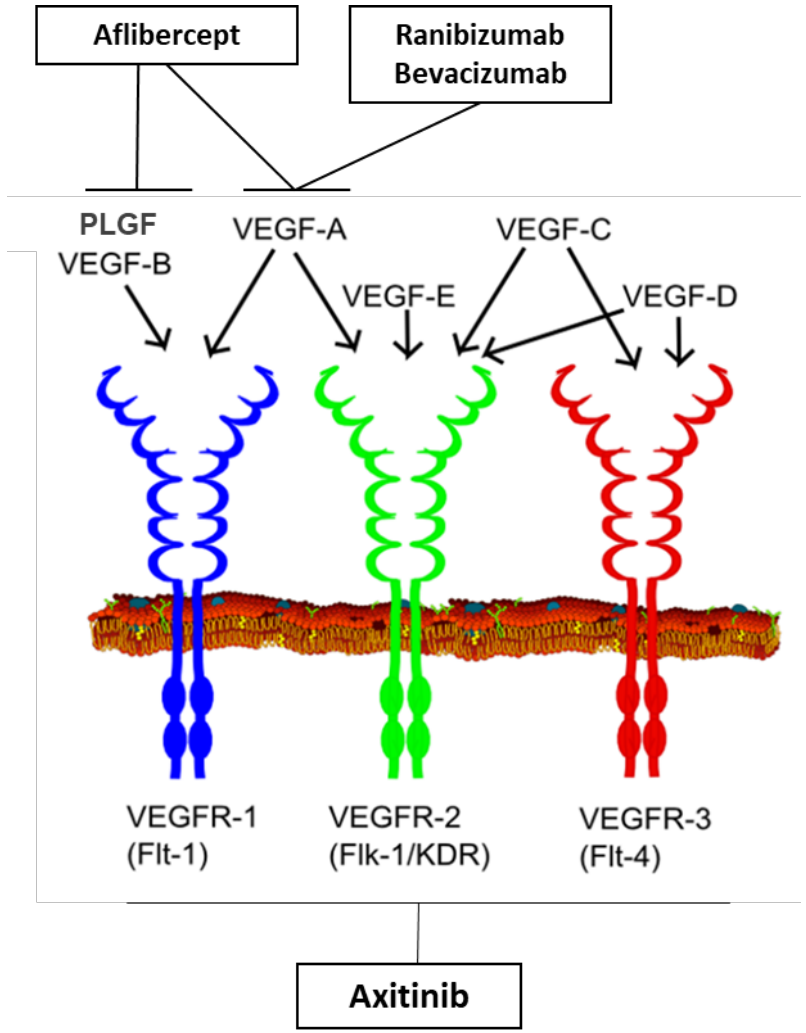
AMD Vascular Endothelial Growth Factor Treatment Approaches

Current AMD Therapies Predominantly Focus on Binding VEGF-A

- Anti-VEGF-A increases expression of VEGF-C [1] VEGF-D[2]
- Broad VEGF receptor blockade may improve outcomes
- A Phase 2 study yielded better AMD outcomes with anti-VEGF-A,C,D vs anti-VEGF-A



Axitinib Injected Suprachoroidally May Improve Outcomes with Its Broad VEGF Receptor Blockade

- Inhibits VEGFR-1, VEGFR-2, VEGFR-3 receptors
- Inhibited corneal, retinal, and choroidal angiogenesis in animal models[3-7]
- More effective than other TKIs for experimental corneal neovascularization in animal models
- Better ocular cell biocompatibility than other TKIs[8]

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. Riquelme et al. Topical axitinib is a potent inhibitor of corneal neovascularization. Clinical and Experimental Ophthalmology 2018; 46: 1063–1074 | 4. Yuan et al. Ocular Drug Delivery Nanowafer with Enhanced Therapeutic Efficacy. ACS Nano. 2015 Feb 24;9(2):1749-58. | 5. Giddabasappa et al. Axitinib inhibits retinal and choroidal neovascularization in in-vitro and in-vivo models. Exp Eye Res. 2016, 145: 373-379. | 6. Nakano et al. Short-term treatment with VEGF receptor inhibitors induces retinopathy of prematurity-like abnormal vascular growth in neonatal Rats. Exp Eye Res. 2016. 143: 120-131. | 7. Kang et al. Antiangiogenic Effects of Axitinib, an Inhibitor of Vascular Endothelial Growth Factor Receptor Tyrosine Kinase, on Laser-Induced Choroidal Neovascularization in Mice. Curr Eye Res. 2012. 38: 119-127. | 8. 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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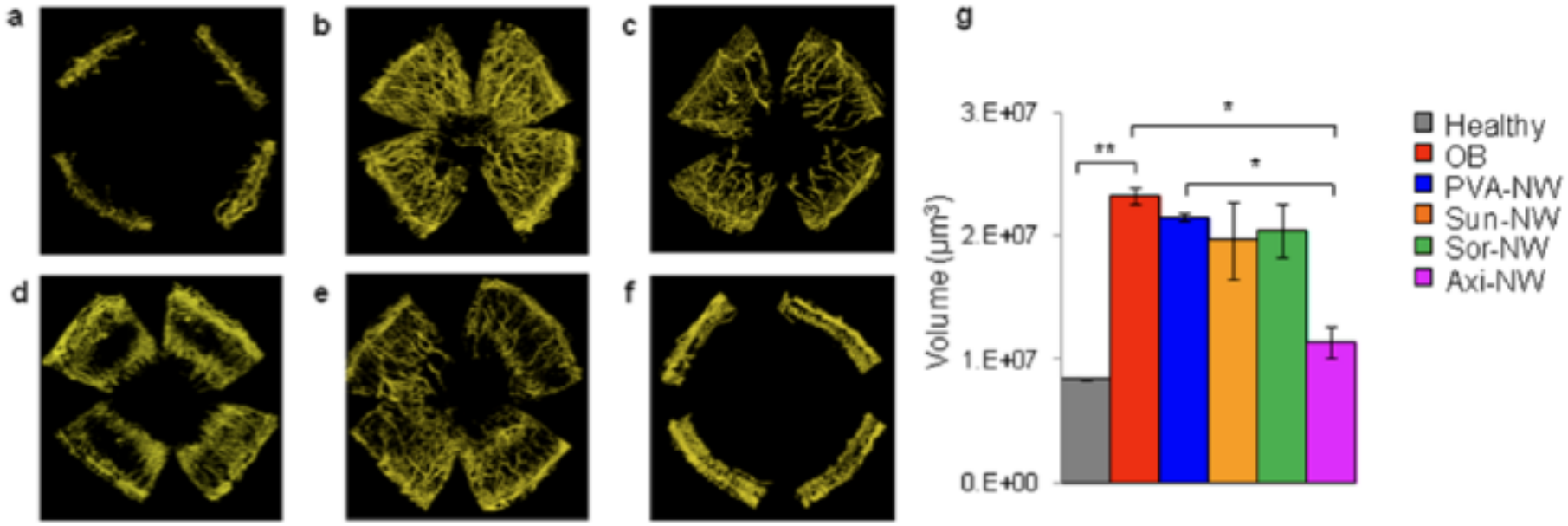
Topical Axitinib More Effectively Inhibited Experimental Murine Corneal Neovascularization than Sunitinib and Sorafenib (same dose)

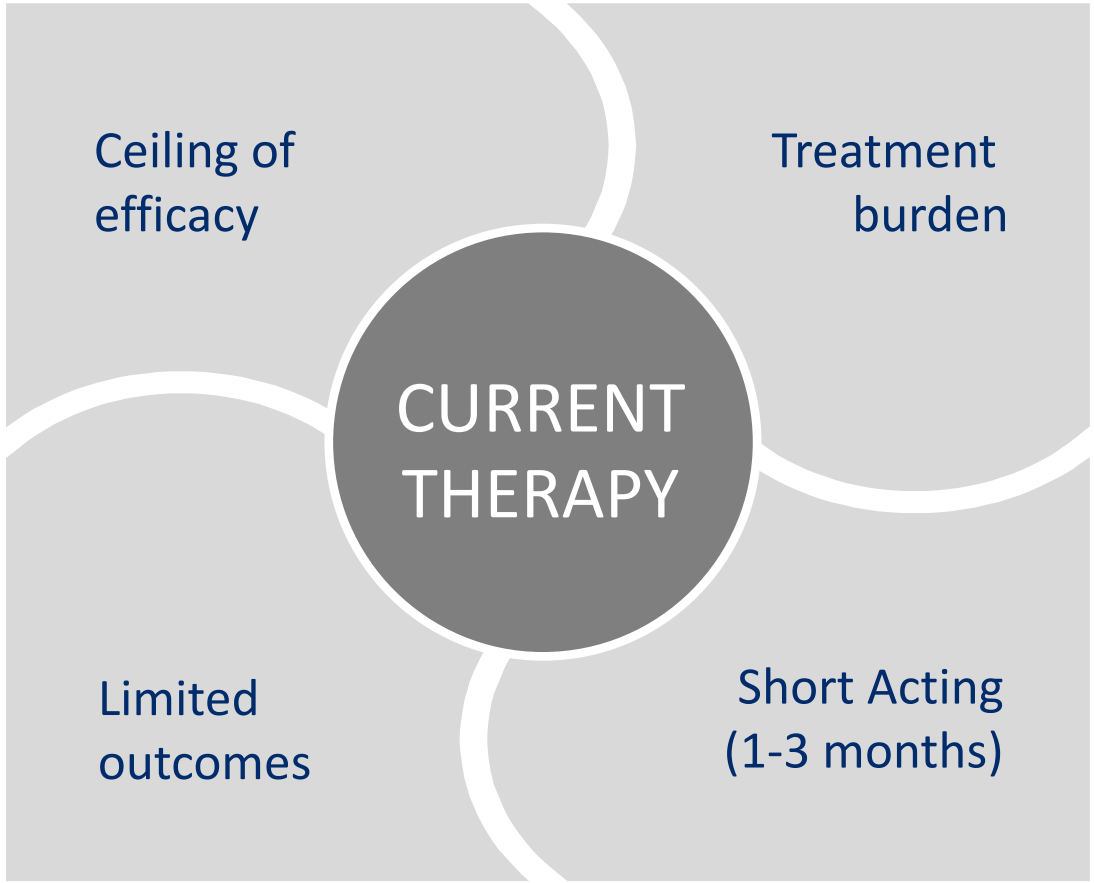


Screening of tyrosine kinase inhibitor drugs loaded nanowafers for their relative therapeutic efficacy in inhibiting corneal neovascularization after 10 days of treatment. Representative 3D reconstructed corneal images of fluorescence confocal microscopy: (a) healthy cornea (control); (b) untreated ocular 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.

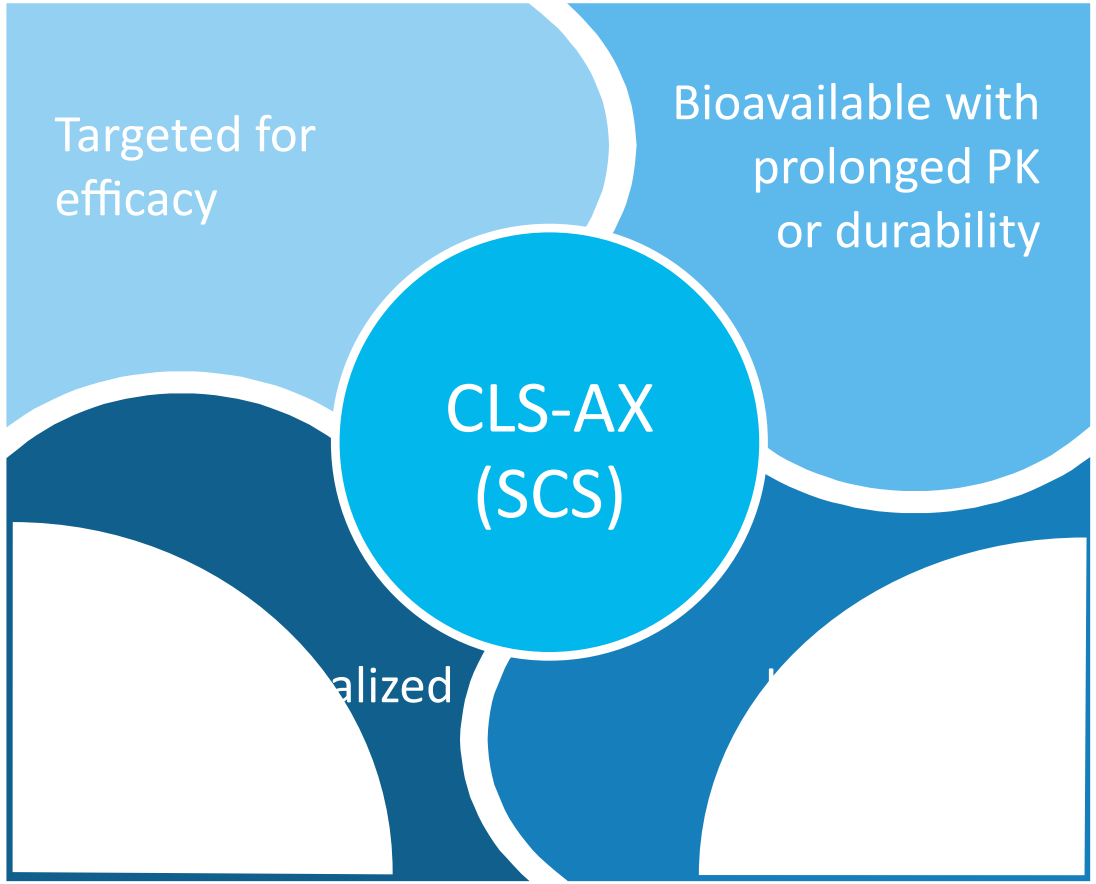
Source: Yuan et al. Ocular Drug Delivery Nanowafer with Enhanced Therapeutic Efficacy. *ACS Nano*. 24 Feb 2015;9(2):1749-58

Potential to Disrupt the AMD Treatment Landscape

Focused VEGF Blockade



Broad VEGF Blockade



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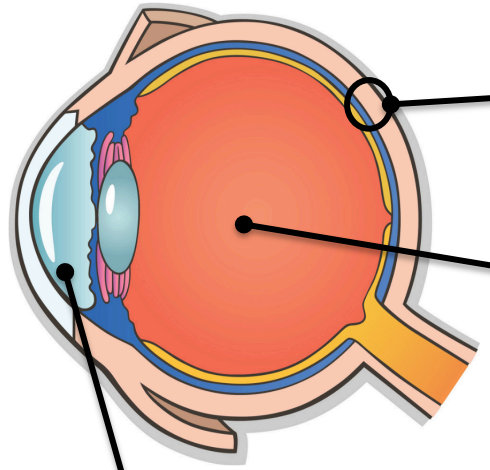
Suprachoroidal Injection of CLS-AX Provides Targeted Delivery Relative to Intravitreal Injection at Same Dose



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

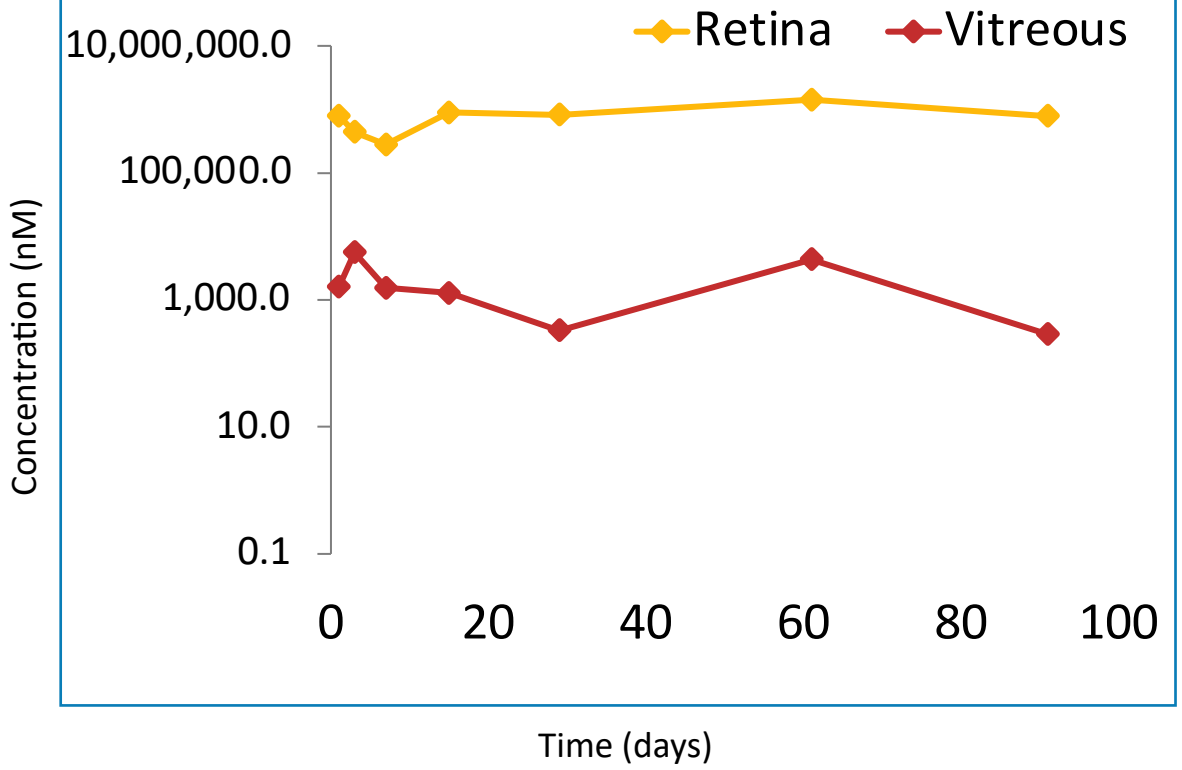
Values: area under the curve ratios, SCS / IVT

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

Single bilateral injection, 1-wk rabbit PK studies

CLS-AX: Durable, High Drug Levels Maintained in the Retina after Suprachoroidal 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 Injection | IVT: Intravitreal Injection | PK: Pharmacokinetic | LLOQ: lower limit of quantification, 0.15 mg/mL | RPE: Retinal pigment epithelium

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

Trial Design

- Open-label study to assess the safety and tolerability of single doses of CLS-AX administered through suprachoroidal injection
- 3 Cohorts of 5 patients each: n=15
- Dose-escalation will begin at 0.03 mg CLS-AX; proceed to next cohort following review by Safety Monitoring Committee

Cohort Enrollment and Treatment

Primary Endpoint:

Evaluate **safety and tolerability** over 3 months of a single dose of CLS-AX given via suprachoroidal injection following IVT aflibercept

Secondary Endpoints:

Evaluate and compare 3 cohorts on **visual function and ocular anatomy, and need for additional treatment** with IVT injected aflibercept; Evaluate **PK**

Note: aflibercept is dosed via intravitreal injection (IVT); CLS-AX is dosed via suprachoroidal injection

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Early Stage Pipeline Opportunities

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Broad Applicability of SCS Injection Platform: Integrin Inhibitor

The Opportunity

- 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

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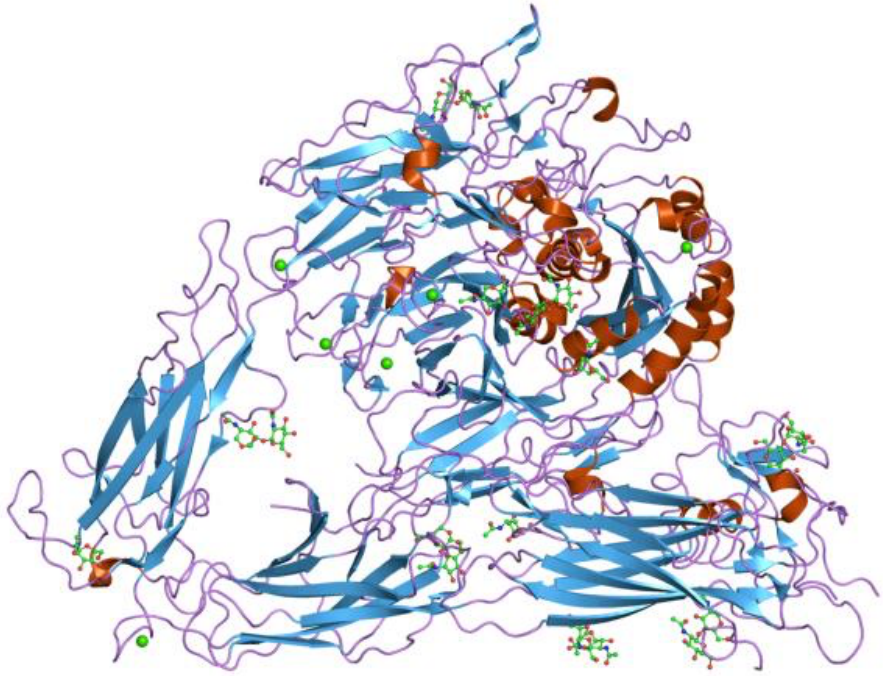
Integrin Inhibitors

- 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

- Integrins $\alpha_v\beta_3$ and $\alpha_v\beta_5$ implicated in DR and AMD
  - Given unique MOA, could serve as:
    - Primary therapy
    - Adjunctive therapy to anti-VEGF
    - Secondary therapy in refractory cases

- Clearside anti-integrin therapy
  - Formulated as a suprachoroidal suspension with extended duration potential
  - Initiating preclinical studies



Broad Applicability of SCS Injection Platform: Ocular Gene Therapy

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
- Potential for broader retinal coverage facilitated by suprachoroidal injection
- Delivery of viral and non-viral vectors

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Preclinical Studies Demonstrate Suprachoroidal Injections of DNA nanoparticles (DNPs) May Offer the Potential for a Safe and Efficient Delivery Method

Potential Advantages

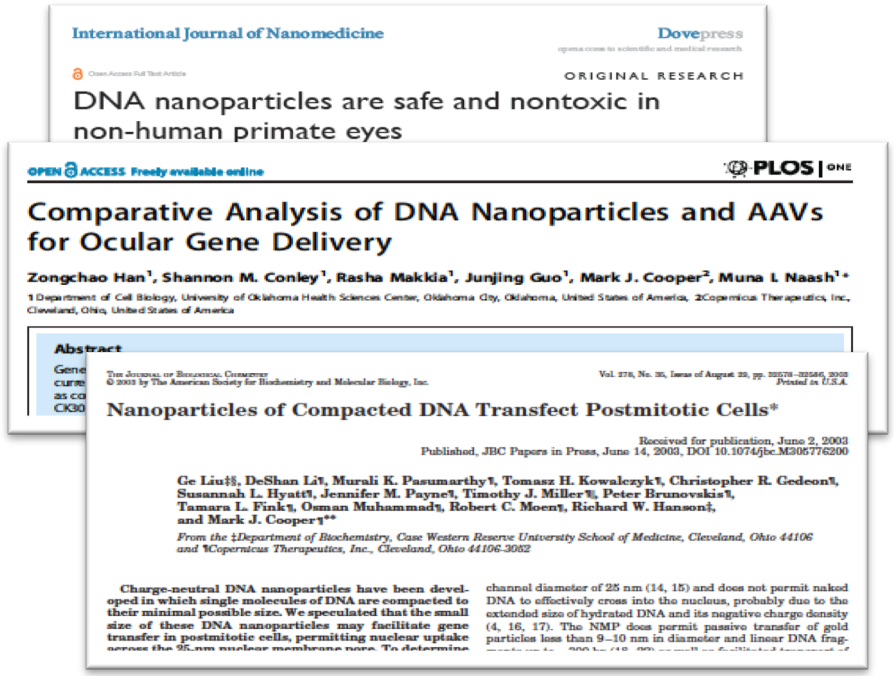
Efficacy: demonstrated in numerous ocular animal models

- Transfer large genes (up to ~20 kb)

Safety: Non-immunogenic, without viral capsid proteins or pre-existing immunity.

- Potential for repeat dosing facilitated by suprachoroidal injection
- Higher doses possible to enhance transfection

Well established literature on DNA nanoparticle gene therapy



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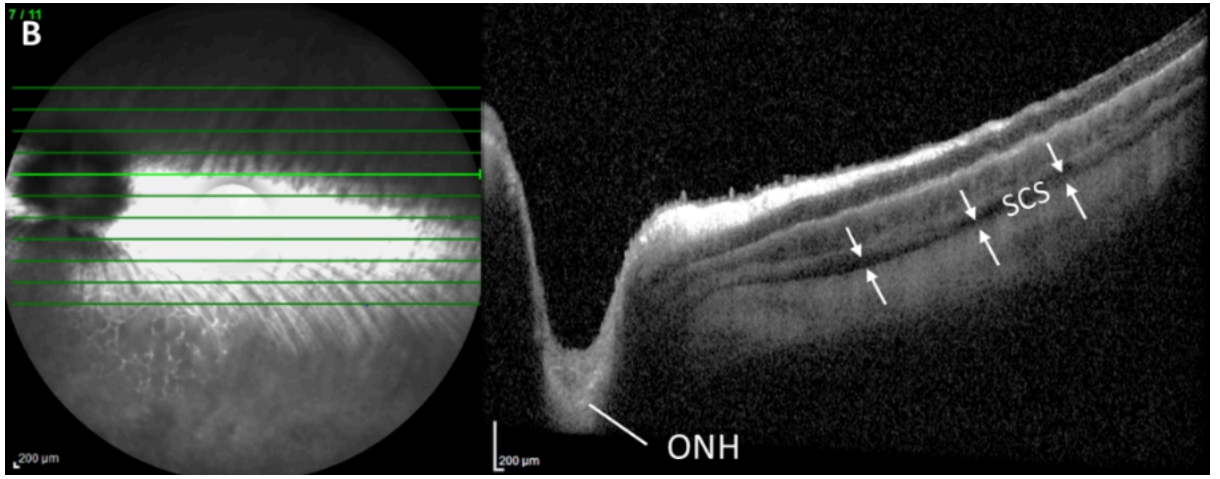
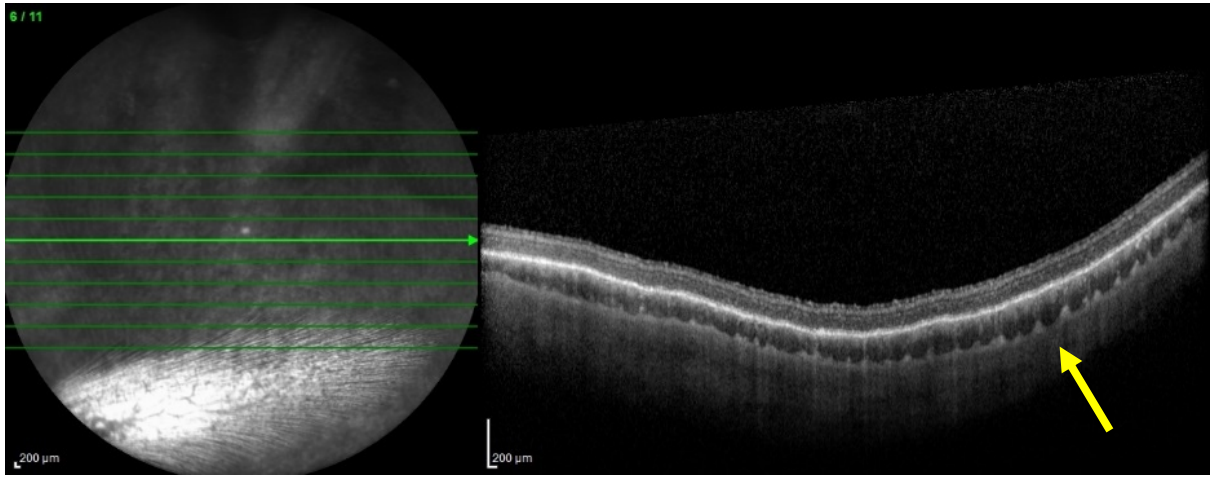
The Suprachoroidal Space Reversibly Opens Posteriorly and Circumferentially Following DNA Nanoparticle Administration in Rabbits

[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

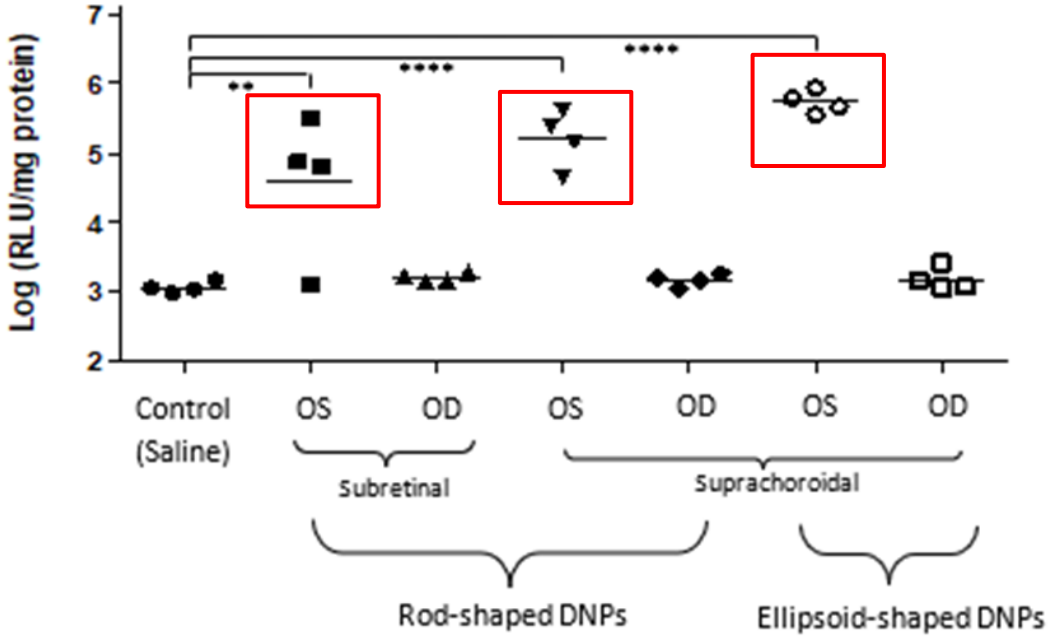


Source: Clearside preclinical studies. Data on file.

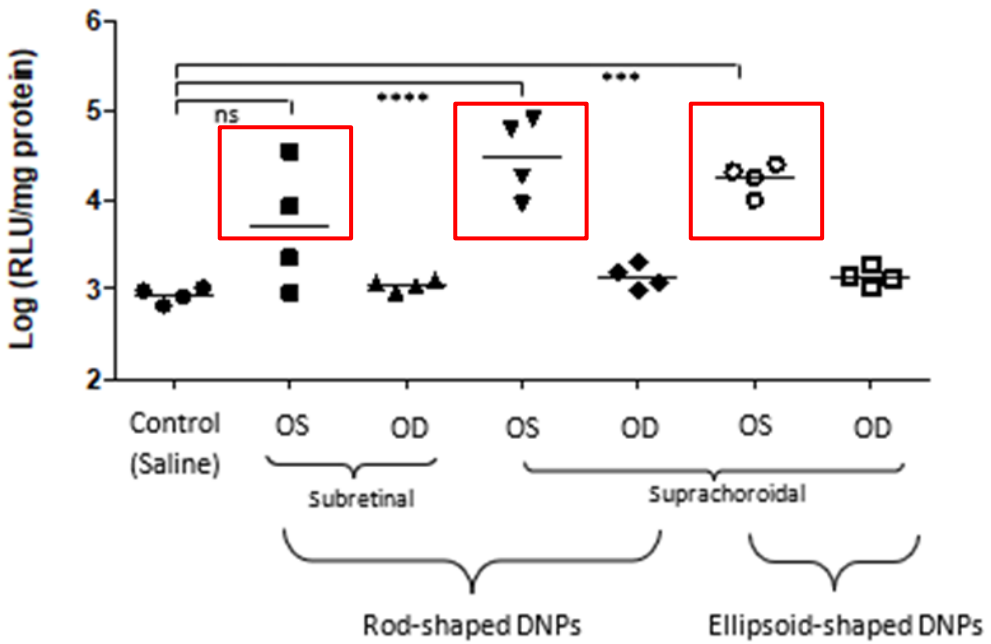
CLEARSIDE BIOMEDICAL

Preclinical Suprachoroidal and Subretinal Injections of DNA Nanoparticles Produced Comparable Luciferase Activity

CHOROID-RPE-Sclera
Non-Viral Luciferase, Rabbit



RETINA
Non-Viral Luciferase, Rabbit



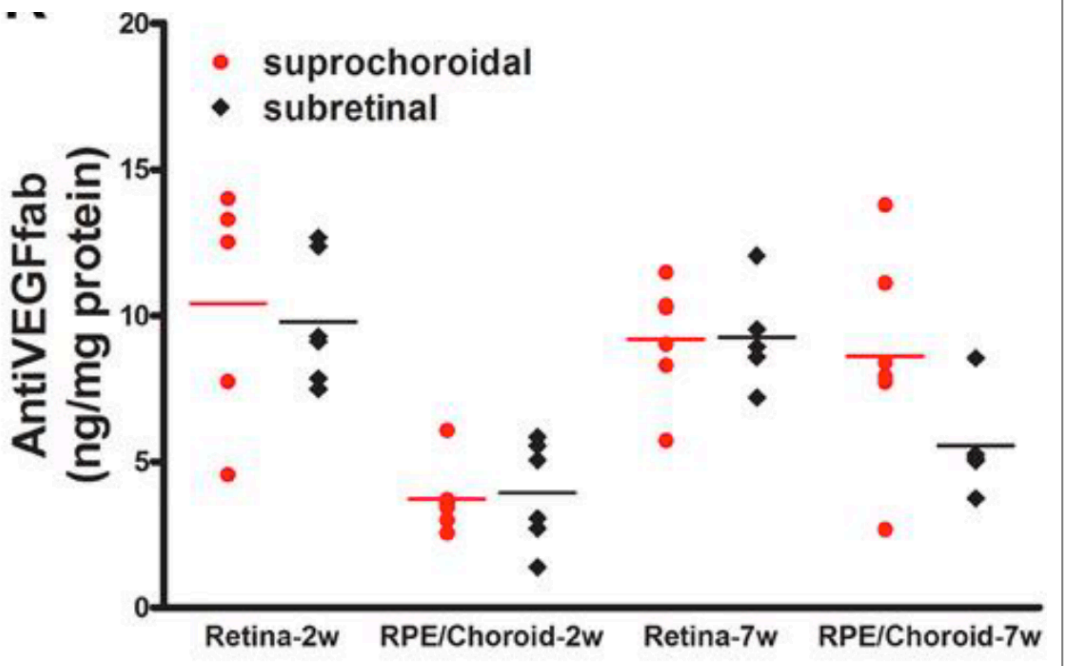
DNA Nanoparticles Transfect Choroid and Retina

Source: Szilárd Kiss, MD, Macula Society Presentation February 2019

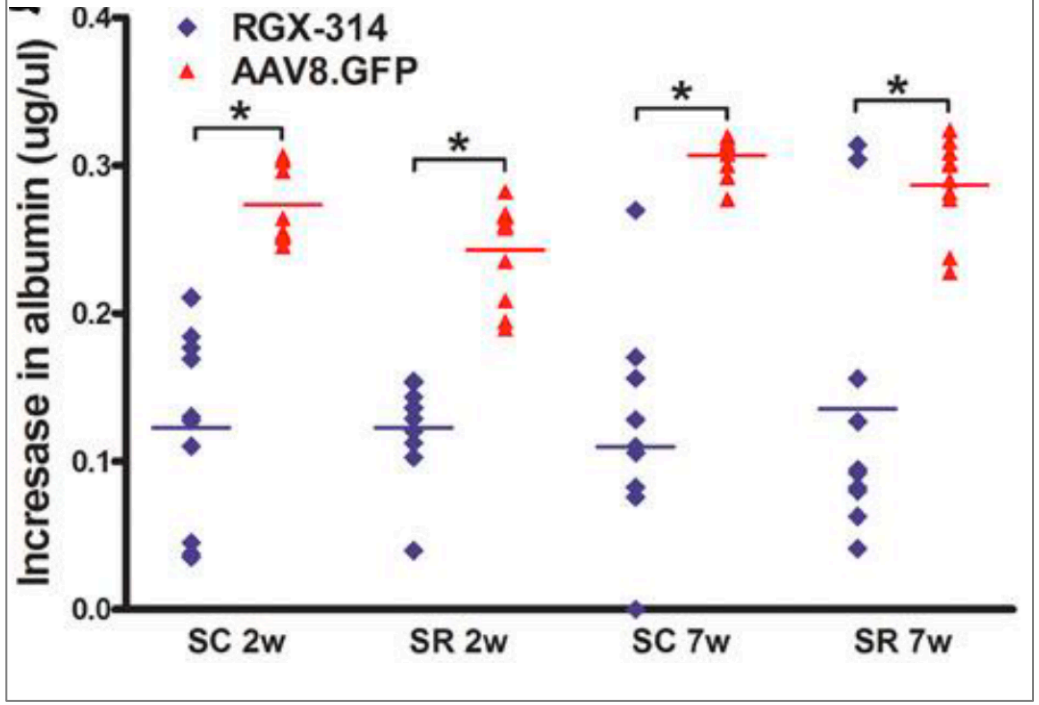
Published Preclinical Data on RGX-314 in SCS

Suprachoroidal delivery of AAV8-based RGX-314 gene therapy produced similar protein expression and suppression of vascular leakage

SC RGX-314 resulted in similar expression of anti-VEGF Fab



- SC RGX-314 resulted in similar activity of anti-VEGF Fab with suppression of VEGF-induced vascular leakage as subretinal delivery



Source: Ding, K., Shen, J., Hafiz, Z., Hackett, S. F., Silva, R. L. E., Khan, M., ... 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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Corporate Collaborations

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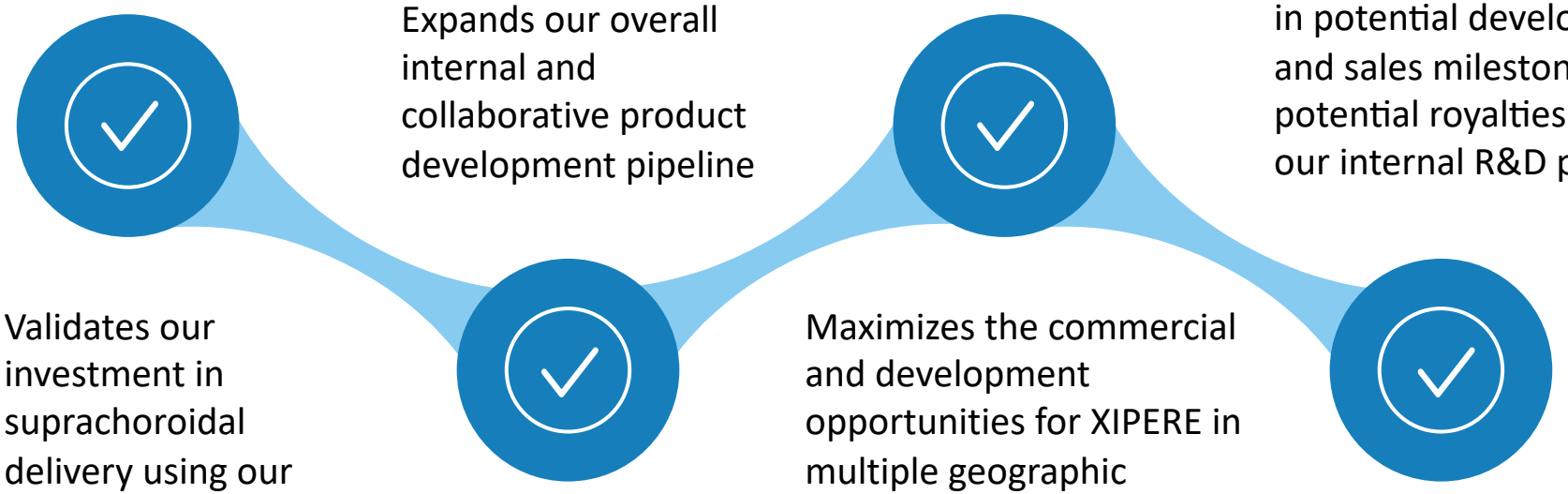
Four Partnering Deals to Drive Growth

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

CLEARSIDE BIOMEDICAL

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

The Terms:

- $2M upfront / exercise of option
- Up to $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

CLEARSIDE BIOMEDICAL

REGENXBIO Initiating 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 Data from Cohort 1 expected in **Q3 2021**; Patient enrollment in Cohort 2 expected in **Q1, 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**.

REGENXBIO®

CLEARSIDE BIOMEDICAL

Optimizing Ocular Oncology Drug Delivery with 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™: Novel Approach Targeting 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 no later than 1H, 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

CLEARSIDE BIOMEDICAL

Research and Development Investment Highlights

Versatile therapeutic platform with proprietary access to the suprachoroidal space

Patented technology & delivery approach

XIPERE

No later than 1H 2021: NDA Resubmission

YE 2021: Expected NDA Approval

Scientific presentations and publications

- **1Q 2021:** Angiogenesis, Macula Society
- **2Q 2021:** ARVO
- **3Q 2021:** ASRS, Retina Society
- **4Q 2021:** AAO

Building an internal R&D pipeline

Mid 2021: Interim Data Cohort 1 Phase 1/2a OASIS trial for CLS-AX

2021: Integrin Inhibitor preclinical data

Exploratory preclinical SC non-viral vector delivery studies ongoing

Partnering to expand use of SCS platform*

REGENXBIO: RGX-314

- **1Q 2021:** Initiate Cohort 2 Phase 2 AAVIATE trial in wet AMD
- **3Q 2021:** Interim Data Cohort 1 Phase 2 AAVIATE trial in wet AMD
- **2021:** Initial Data Phase 2 ALTITUDE Trial in DR

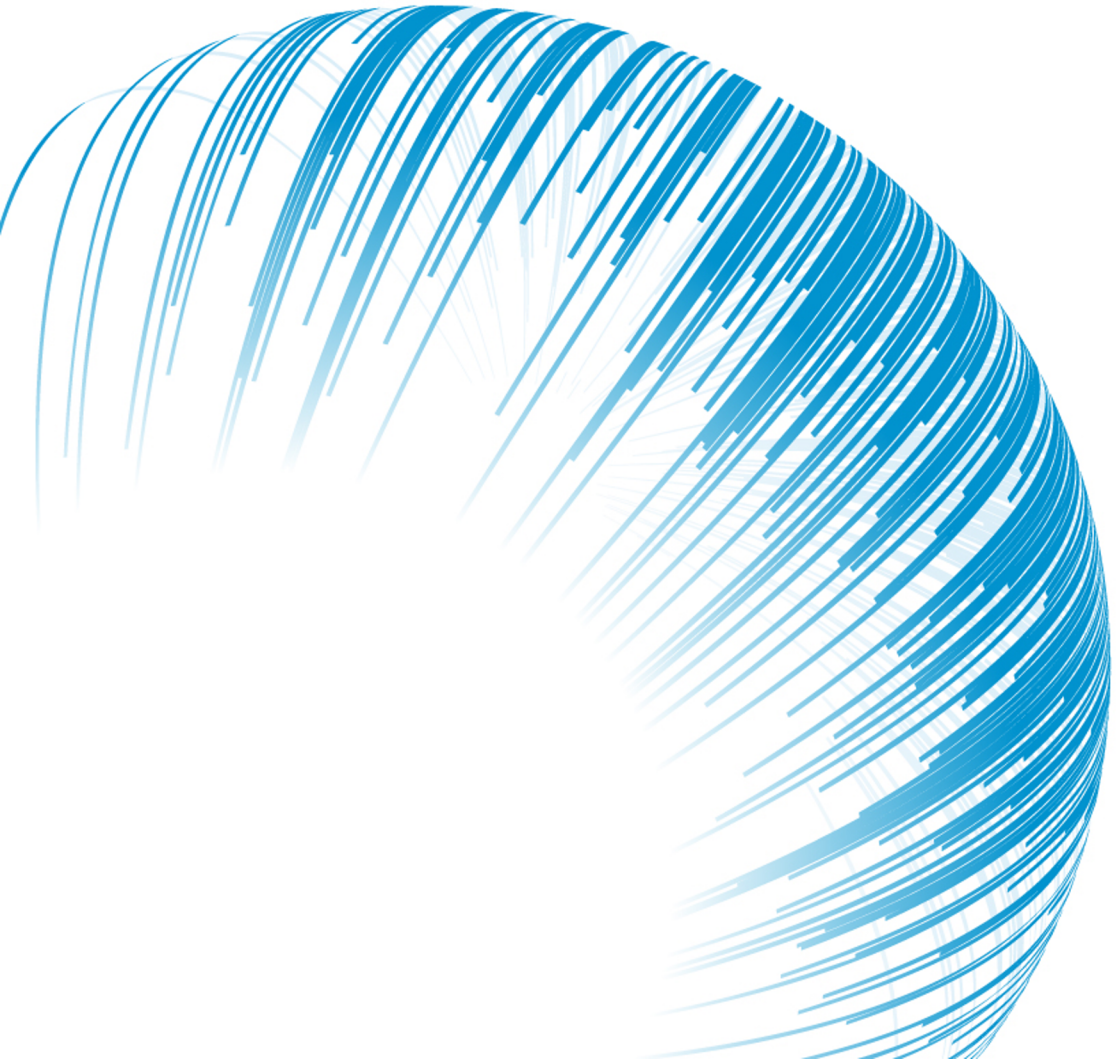
AURA BIOSCIENCES: AU-011

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

ARCTIC VISION: ARVN001

- Planning 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.



CLEARSIDE® BIOMEDICAL

Nasdaq: CLSD