

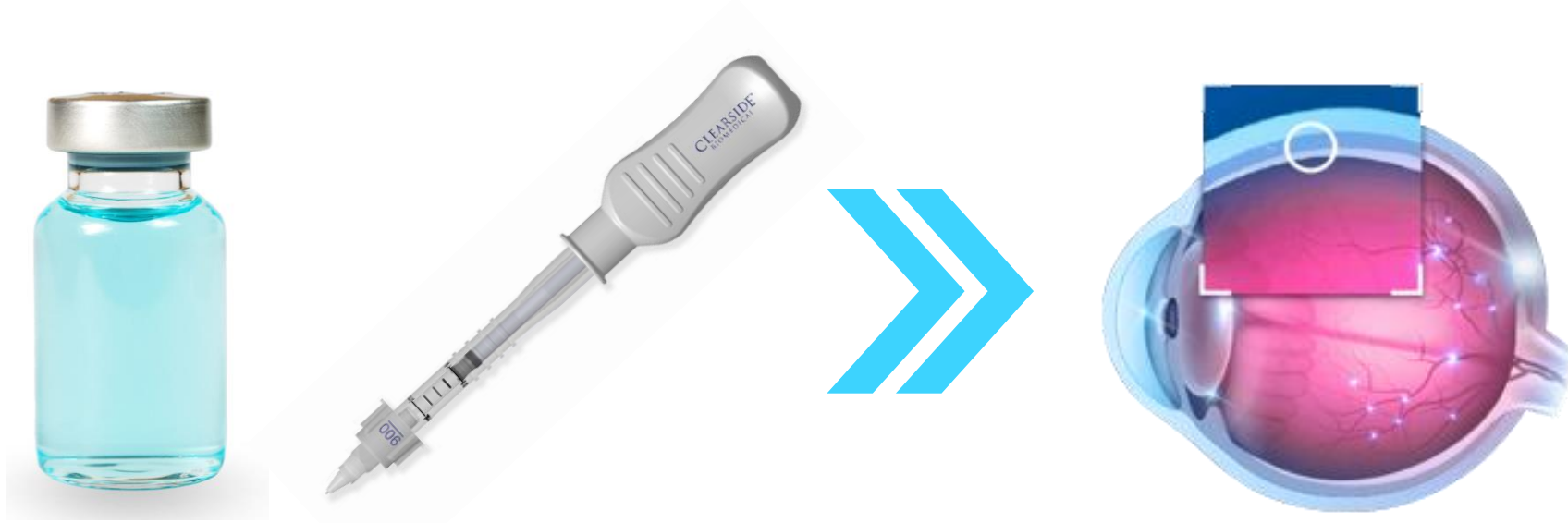
CLEARSIDE<sup>®</sup>  
BIOMEDICAL

Corporate Presentation | November 2019

# Forward-Looking Statements

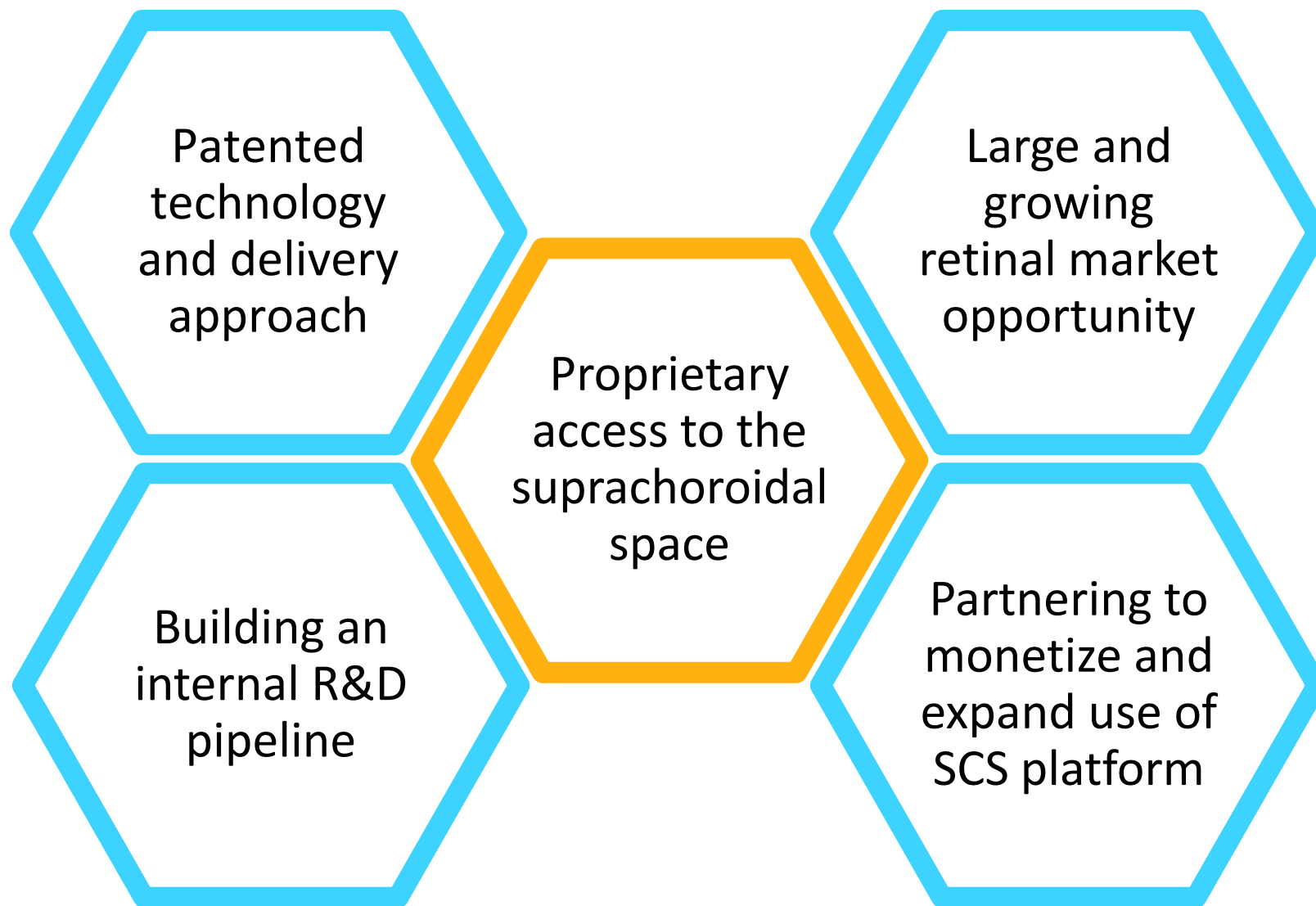
This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. The words “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “target” 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, 2018, filed with the SEC on March 15, 2019, Clearside’s Quarterly Report on Form 10-Q, filed with the SEC on November 8, 2019, 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.

# Dedicated to Developing Treatments that Restore and Preserve Vision for People with Serious Eye Diseases

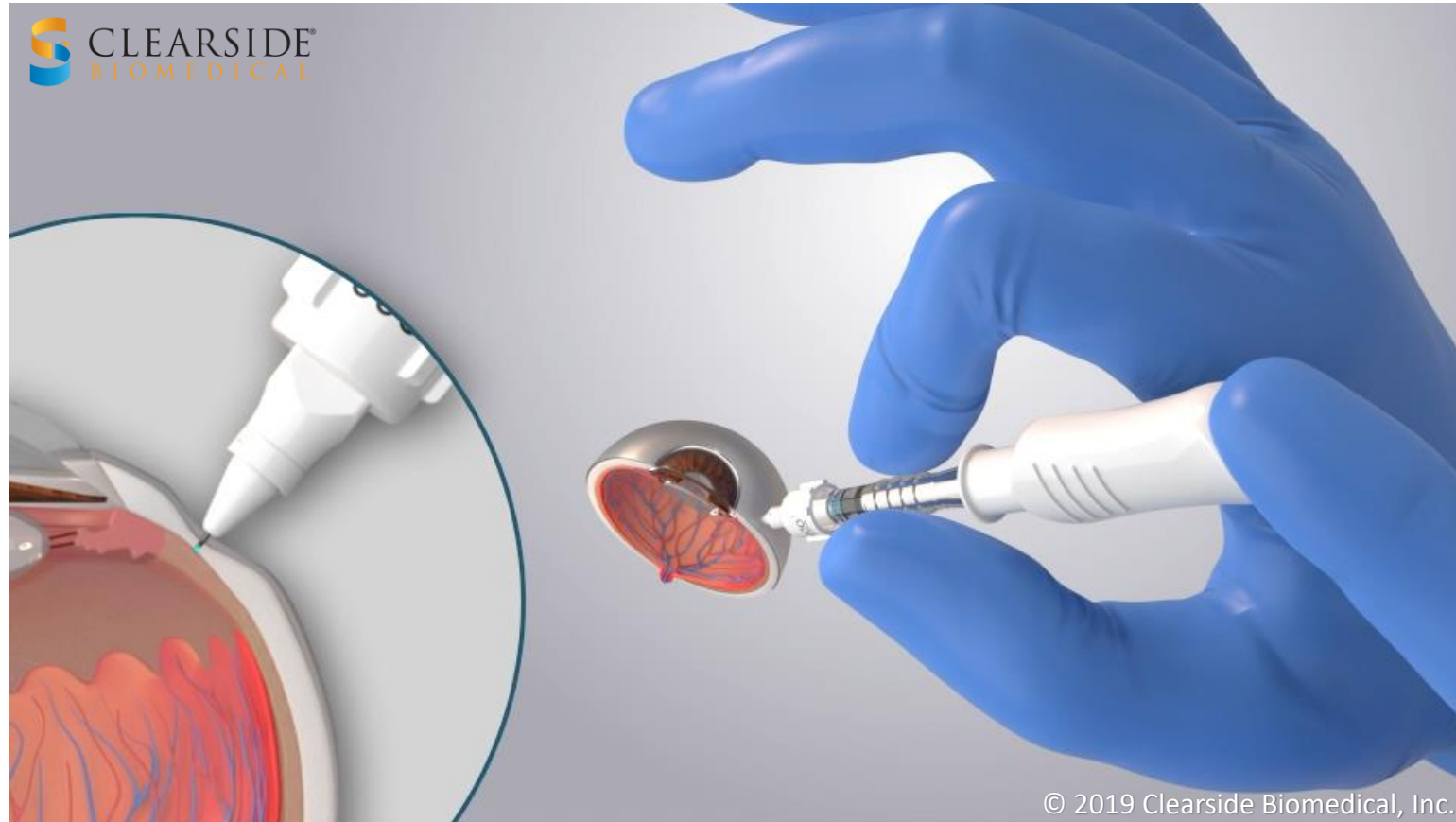


Novel, therapeutic platform combines patented SCS Microinjector™ for Suprachoroidal Injection with proprietary drug formulations

# Clearside Biomedical: Five Key Investment Themes



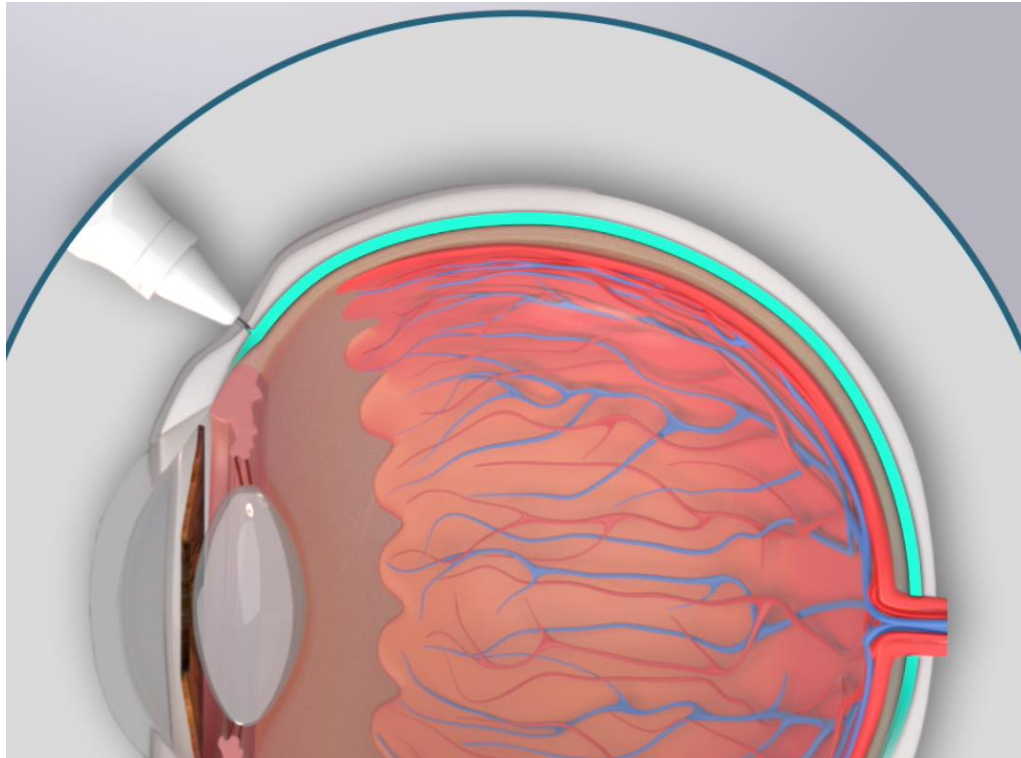
# Exclusive Access to the Back of the Eye Using Clearside's Proprietary SCS Microinjector™





# Ocular Delivery Methods to Reach the Back of the Eye

## Suprachoroidal Space Injection

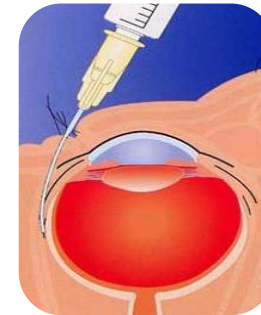


Specially-designed SCS Microinjector™ allows for precise delivery into the suprachoroidal space



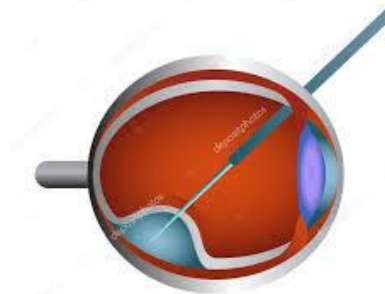
## Intravitreal Injection

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



## Periocular Injection

Highly variable drug diffusion across the sclera into the eye



## Subretinal Injection

Invasive surgery with variable results

# Strong Intellectual Property Coverage of SCS Platform

16

U.S. Patents Total  
Expiring between  
2027 - 2037

2

Methods using  
loss-of-  
resistance  
technology

DEVICE PATENTS

3

Apparatus using  
loss-of-resistance  
technology

3

Apparatus having /  
methods using an  
adjustable puncture  
member

1

Administration of any  
anti-inflammatory  
drug to the  
suprachoroidal space  
by microinjection

DRUG PATENTS

3

Administration of  
any drug to the  
suprachoroidal  
space by  
microinjection

1

Administration  
of any drug to  
the eye by  
inserting a  
microinjector  
into the sclera

3

Methods of  
treating posterior  
ocular disorders  
including macular  
edema or uveitis

DISEASE  
PATENTS

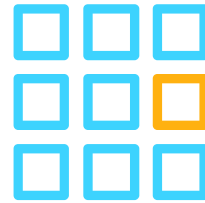
# Core Advantages of Treating Via the Suprachoroidal Space



## TARGETED

The back of the eye is the location of many irreversible and debilitating visual impairments<sup>1</sup>

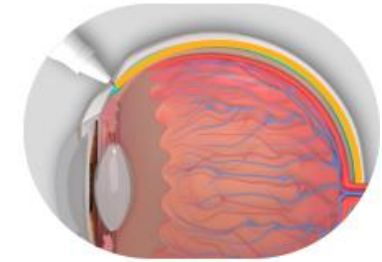
*for efficacy*



## COMPARTMENTALIZED

Drug is compartmentalized in the suprachoroidal space, which helps keep it away from non-diseased tissues<sup>2</sup>

*for safety*



## BIOAVAILABLE PROLONGED PK

Fluid spreads circumferentially and posteriorly when injected within the suprachoroidal space, bathing the choroid and adjacent areas with drug<sup>2</sup>

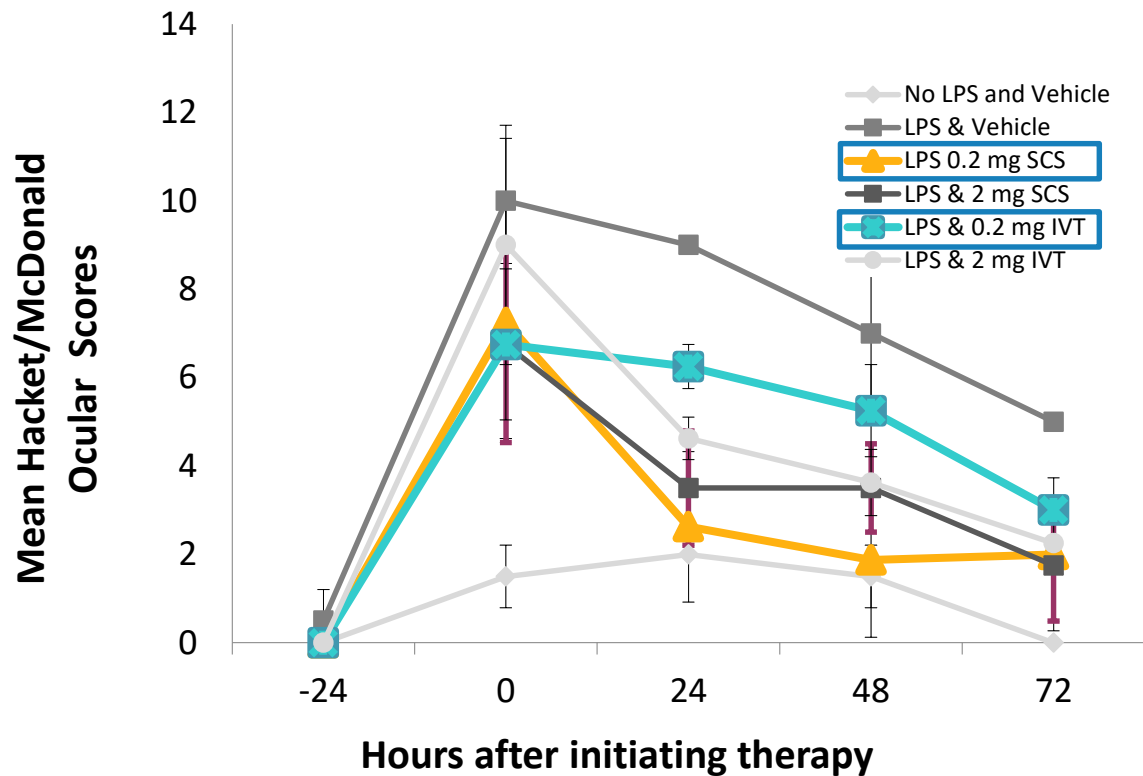
*for durability*



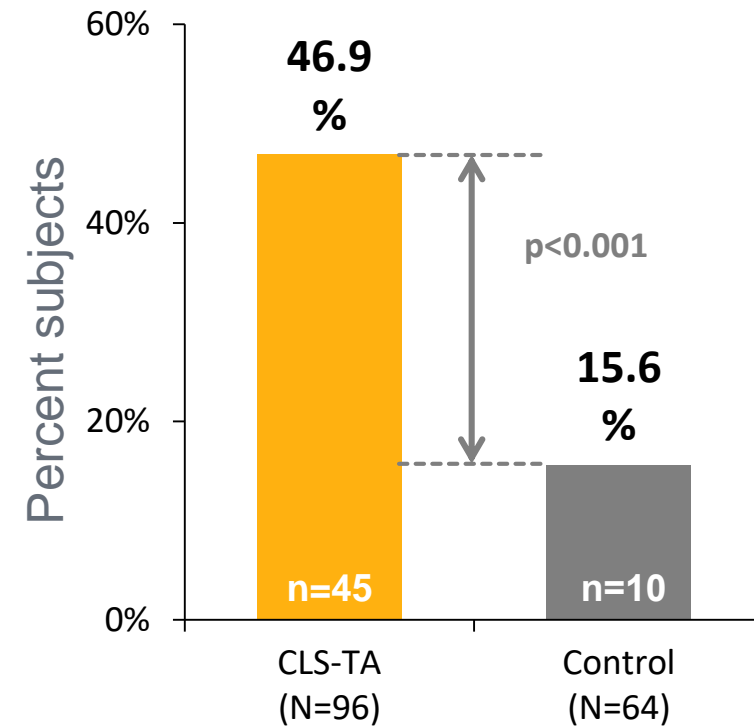
# The Suprachoroidal Space & Triamcinolone Acetonide *targeted for efficacy*

Preclinical

Clinical Trial



**PEACHTREE Met its Primary Endpoint: Efficacy Data**  
Subjects gaining  $\geq 15$  BCVA letters from baseline, %

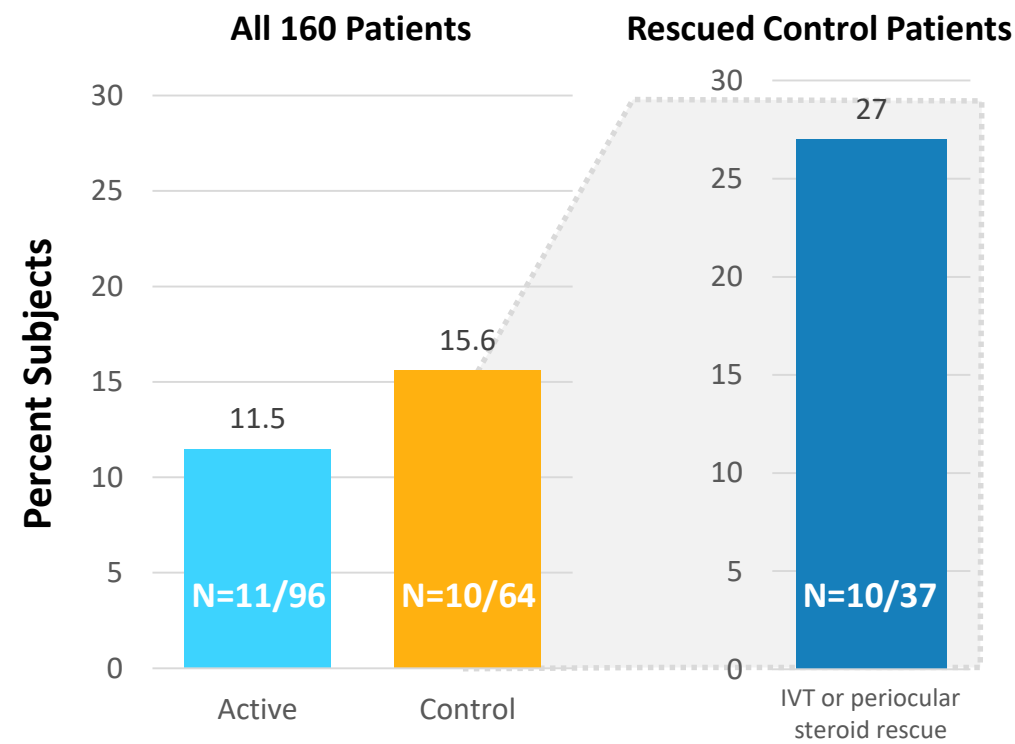
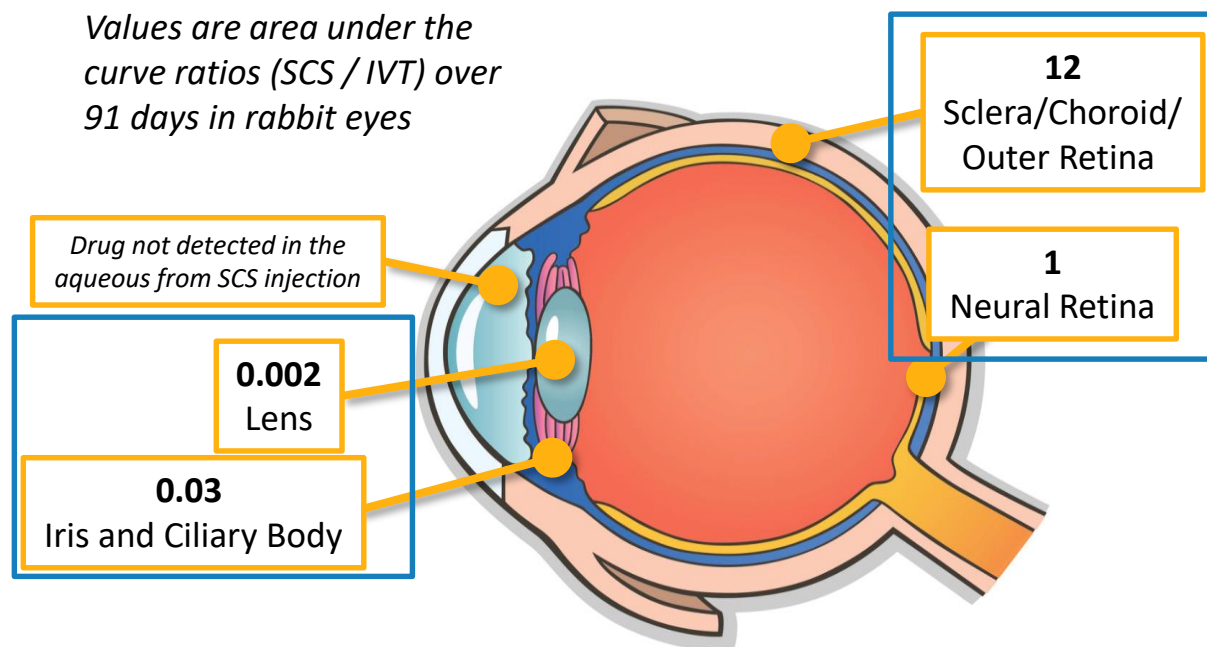


# The Suprachoroidal Space & Triamcinolone Acetonide *compartmentalized for safety*

Preclinical

Clinical Trial

## PEACHTREE IOP AE Rates: Safety Data

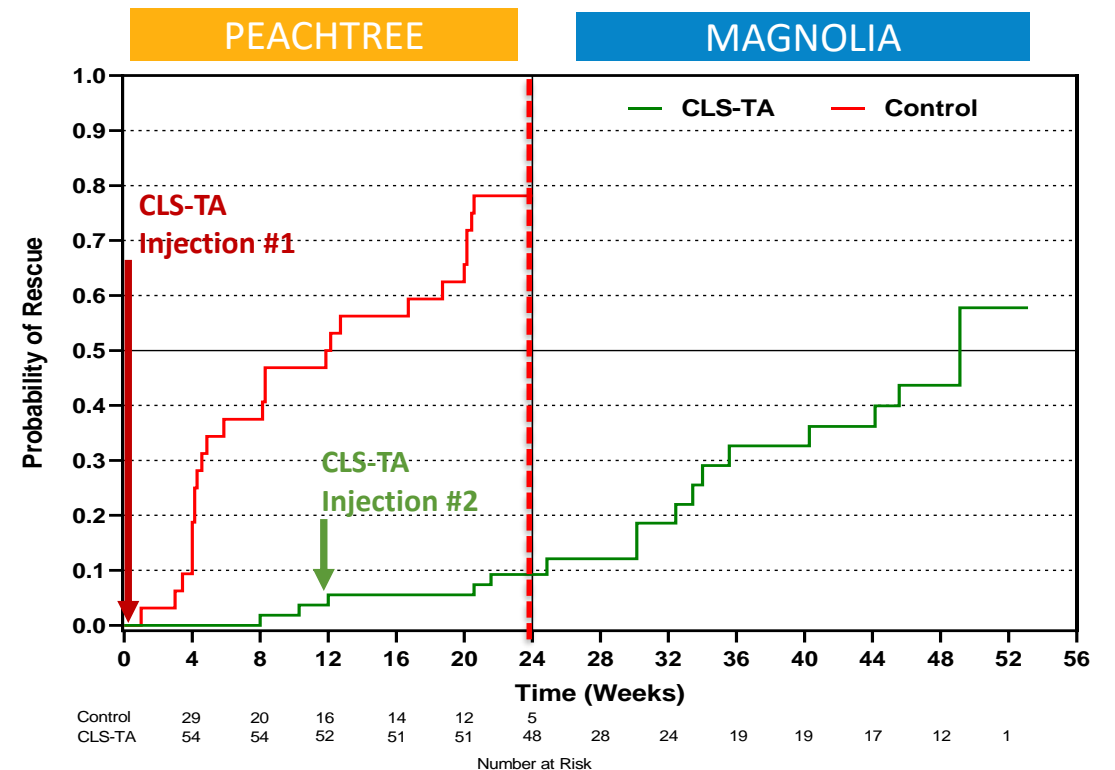
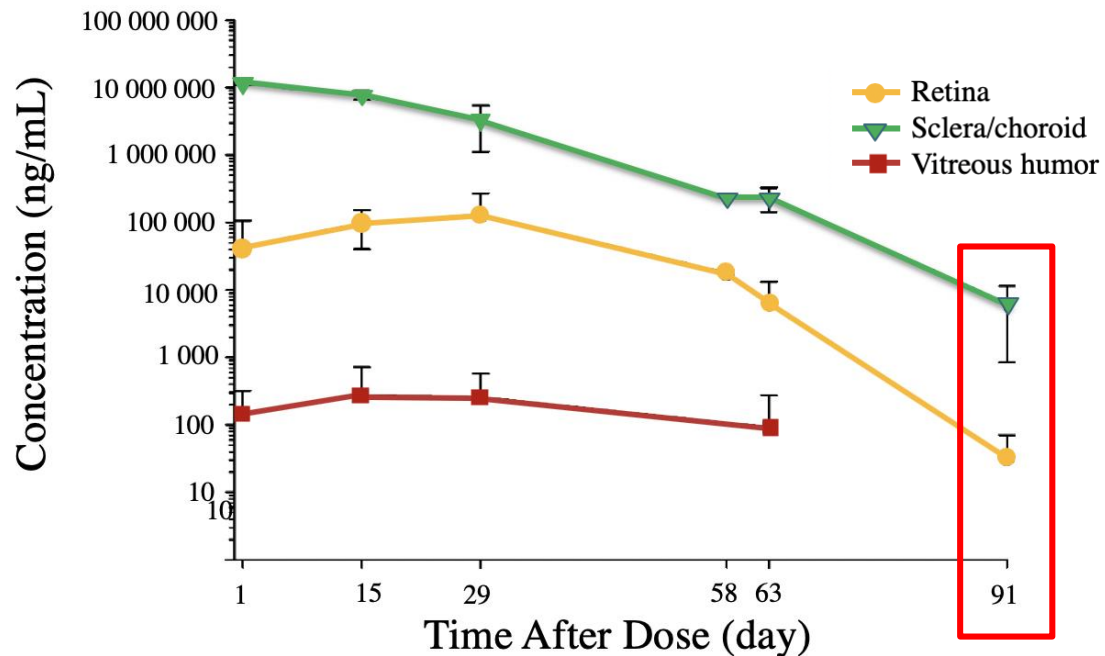


# The Suprachoroidal Space & Triamcinolone Acetonide *prolonged PK for durability*

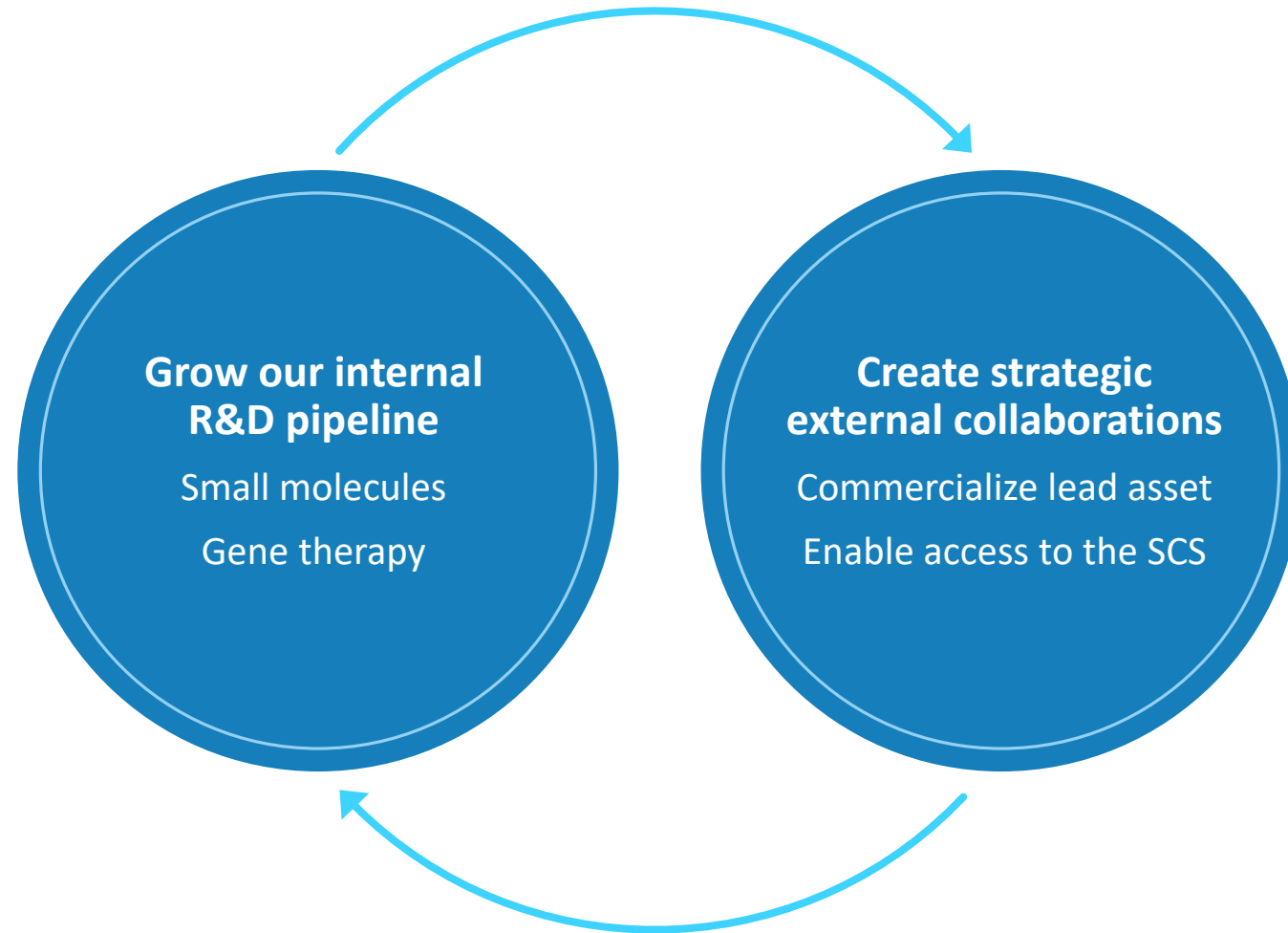
Preclinical

Clinical Trial

## MAGNOLIA: Durability Data


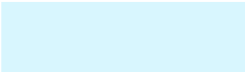
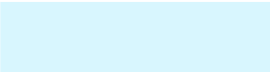
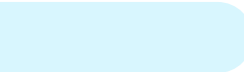

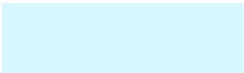
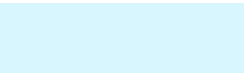
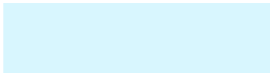
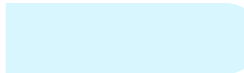


# Two-Prong Corporate Strategy Leveraging Clearside's Proprietary Suprachoroidal Space (SCS) Injection Platform






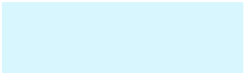
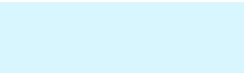
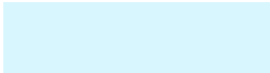
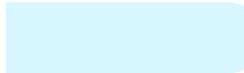

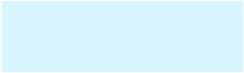
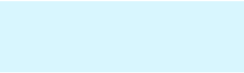
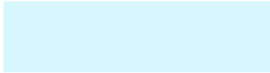
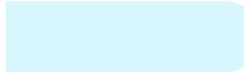




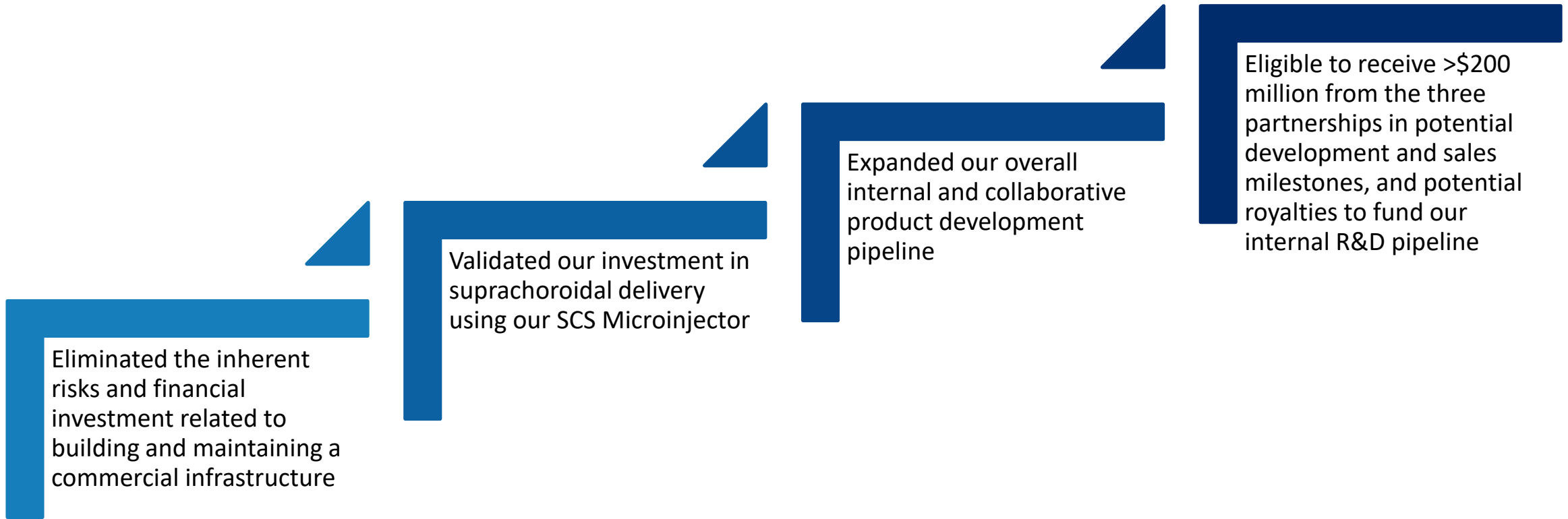
# Pipeline of SCS Treatments with Broad Applicability

STUDY DRUG	INDICATION	PRECLINICAL	IND-Enabling	PHASE 1/2	PHASE 3	NDA
CLS-AX (suprachoroidal axitinib)	Wet AMD		IND mid-2020			
Gene Therapy	Inherited Retinal Disease					

## PARTNER PROGRAMS using SCS Microinjector™

PARTNER	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NDA
BAUSCH HEALTH	XIPERE™ (macular edema associated with uveitis)					Q2 Resubmission
AURA BIOSCIENCES	Ocular Oncology / Choroidal Melanoma					
REGENXBIO	Wet AMD, Diabetic Retinopathy					

# Three Partnering Deals to Drive Growth



**BAUSCH** Health

**aura**

 **REGENXBIO**<sup>®</sup>

 **CLEARSIDE**<sup>™</sup>  
BIOMEDICAL

# Maximizing Commercial Potential of XIPERE™

## The Opportunity: XIPERE Commercialization & Development

- Exclusive license for XIPERE commercialization and development in the U.S. and Canada
- Right to develop and commercialize XIPERE for additional ophthalmic indications including diabetic macular edema and retinal vein occlusion
- Right to develop and commercialize a specified set of corticosteroids and non-steroidal anti-inflammatory drugs in ophthalmology using our proprietary SCS Microinjector

## The Terms:

- \$5 million upfront
- Up to \$15M in FDA approval and pre-launch milestones
- Up to \$56M in milestone payments
- Tiered royalties on net sales

**BAUSCH** Health

# Novel Approach to Targeting Uveitic Macular Edema

XIPERE™

(triamcinolone acetonide suprachoroidal  
injectable suspension) 40 mg/mL

- Pivotal Phase 3 PEACHTREE trial met its primary endpoint
- MAGNOLIA Phase 3 extension study demonstrated durability
- If approved, XIPERE would be the first therapy for this indication
- Expect to resubmit NDA in Q2 2020 with additional stability data and device use assessment



# Enabling In-office Delivery of Gene Therapy

## 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:

- \$2 million upfront / exercise of option
- Up to \$34M in development milestones across multiple indications
- Up to \$102M in sales milestones
- Royalties on net sales of products using SCS Microinjector



# Optimizing Ocular Oncology Drug Delivery with SCS Microinjector™

## The Opportunity: Ocular Oncology

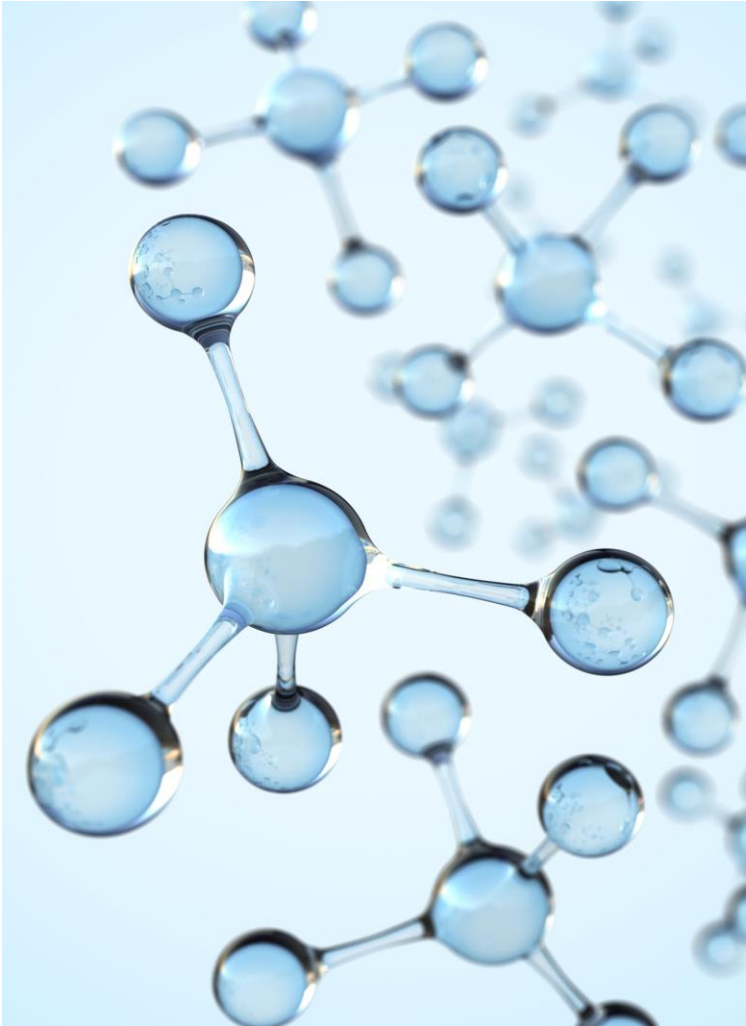
- Non-surgical alternative to intravitreal delivery of Aura's oncology drug candidates via our SCS Microinjector
- Choroidal melanoma is the most common, primary intraocular tumor in adults
- Expect Aura to submit an IND amendment and initiate a clinical trial using our SCS Microinjector in the first half of next year

**aura**

## The Terms:

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

# Broad Applicability of SCS Injection Platform: Small Molecules



## Primary Need

Targeted delivery to the retina with prolonged durability to enhance efficacy and relieve treatment burden

## Opportunity

1. Concentrated distribution
2. Protection of off-target tissues
3. Migration of small molecules into the anterior chamber
4. Extended duration of action

# Axitinib for Suprachoroidal Injection (CLS-AX): A Potential Solution for Treatment Burden

## Primary Need

Durable maintenance of vision  
and reduced treatment burden  
in wet AMD patients

## The Opportunity

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



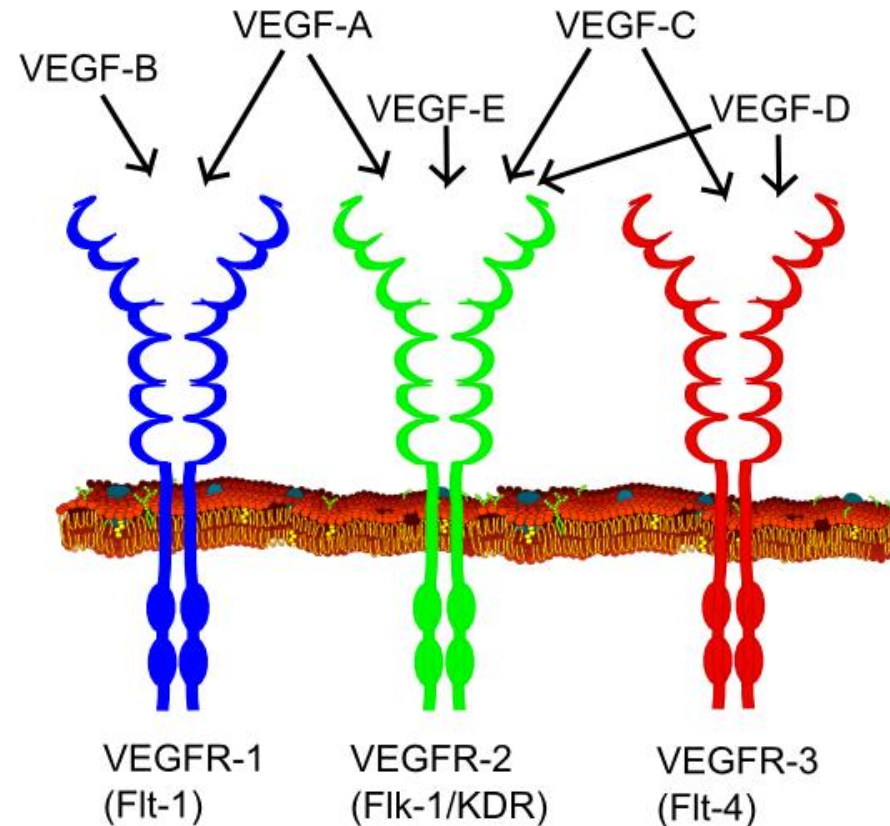
# CLS-AX Overview

Items	Details
Target Patients	For patients receiving frequent intravitreal anti-VEGF injections for neovascular AMD and diabetic macular edema
Agent / Route of Administration	Axitinib suspension for suprachoroidal injection
Mechanism of Action	Broadly inhibits VEGF angiogenesis as a tyrosine kinase inhibitor (TKI) of VEGF receptors VEGFR-1, VEGFR=2, VEGFR-3, c-KIT and PDGFR
Regimen	Twice yearly
Historic development & regulatory history by Pfizer, Inc.	<ul style="list-style-type: none"><li>• INLYTA<sup>®</sup> (axitinib) tablets</li><li>• Approved for renal cell carcinoma from US FDA (2012), EMA (2012), UK MHRA (2012) and Australian TGA (2012)</li></ul>

# AMD Vascular Endothelial Growth Factor Treatment Approaches

## Current AMD Therapies Predominantly Focus on VEGF-A Blockade, not VEGF Receptors

- Anti-VEGF-A increases VEGF-C<sup>1</sup> & VEGF-D<sup>2</sup>
- Broad VEGF blockade may improve outcomes
- A Phase 2 study yielded better AMD outcomes with anti-VEGF-A,C,D vs anti-VEGF-A

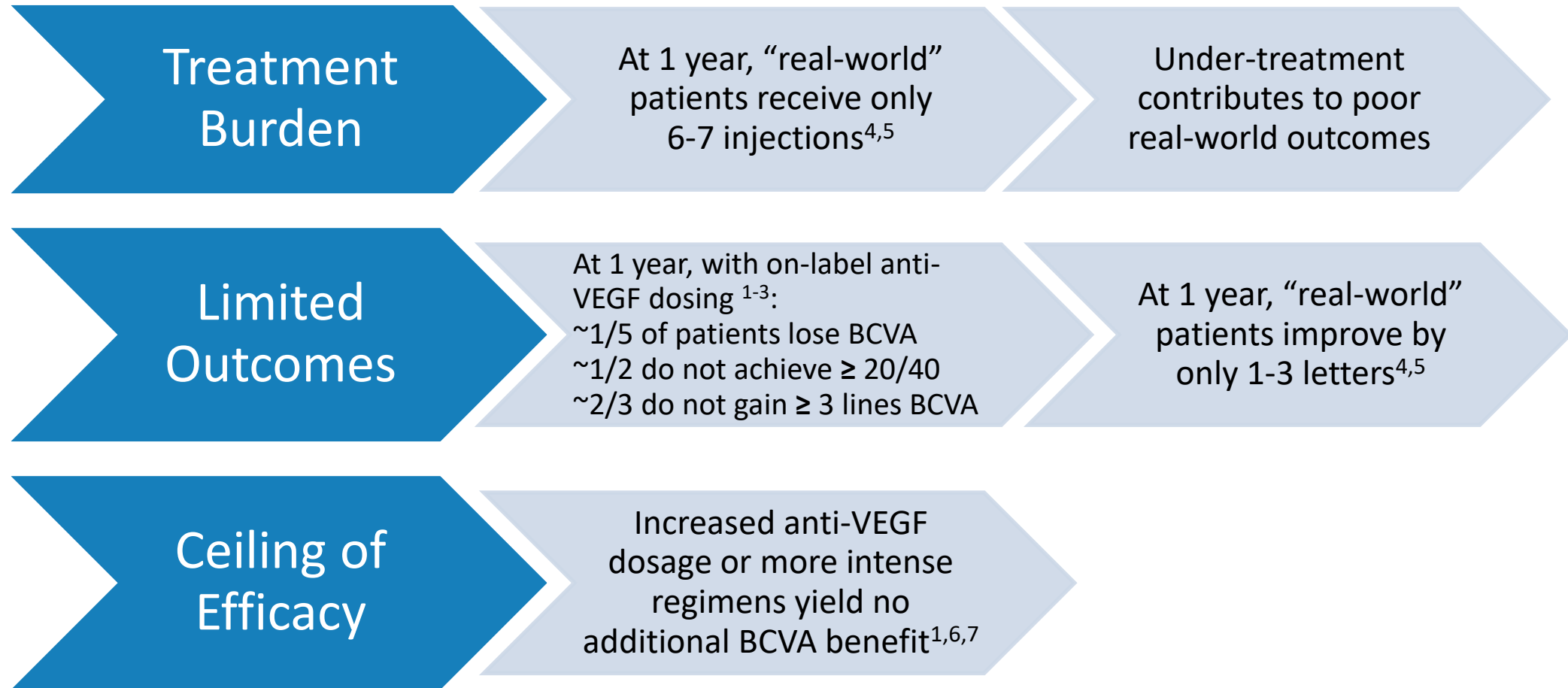


## Suprachoroidal Axitinib May Improve Outcomes with Its Broad VEGF Blockade

- Inhibits **VEGFR-1**, **VEGFR-2**, **VEGFR-3**
- Inhibited corneal, retinal, and choroidal angiogenesis in animal models<sup>3-7</sup>
- More effective than other TKIs for experimental corneal neovascularization in animal models
- Better ocular cell biocompatibility than other TKIs<sup>8</sup>

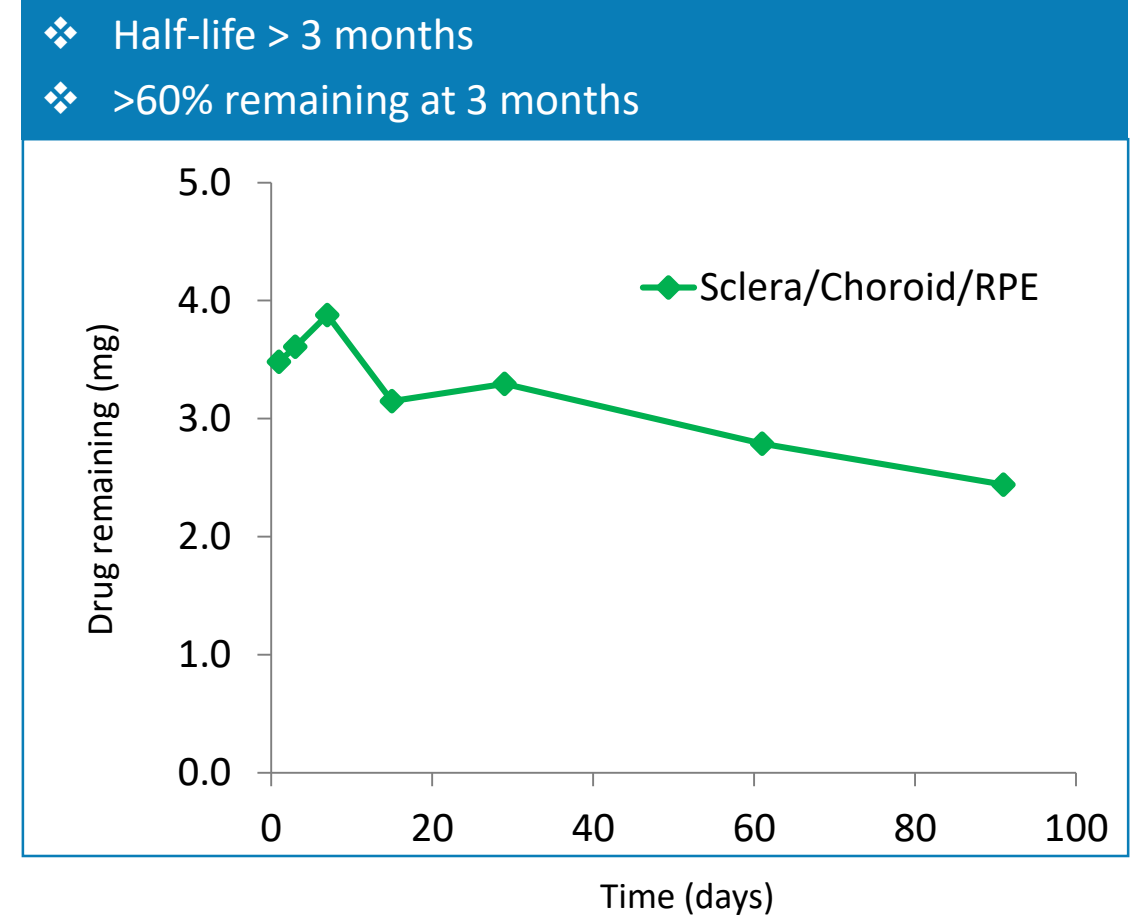
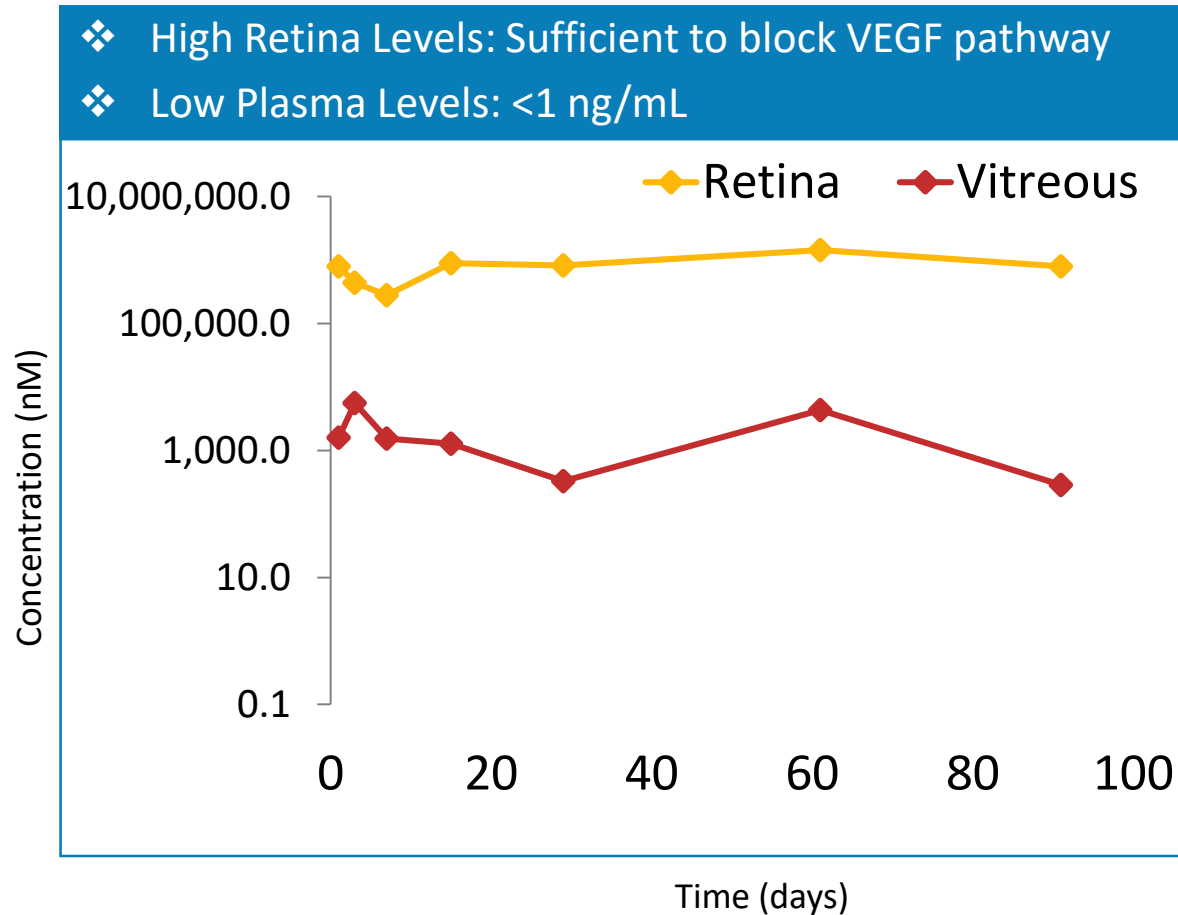
Sources: 1. Cabral T et al. Bevacizumab Injection in Patients with Neovascular Age-Related Macular Degeneration Increases Angiogenic Biomarkers. Ophthalmol Retina. 2018 January ; 2(1): 31–37. doi:10.1016/j.oret.2017.04.004. | 2. Lieu et al. The Association of Alternate VEGF Ligands with Resistance to 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.

# CLS-AX May Address Unmet Needs in Neovascular 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.

# CLS-AX: High Drug Levels Maintained in RPE-Choroid-Sclera





# Topical Axitinib More Effectively Inhibited Experimental Murine Corneal Neovascularization than Sunitinib and Sorafenib (same dose)

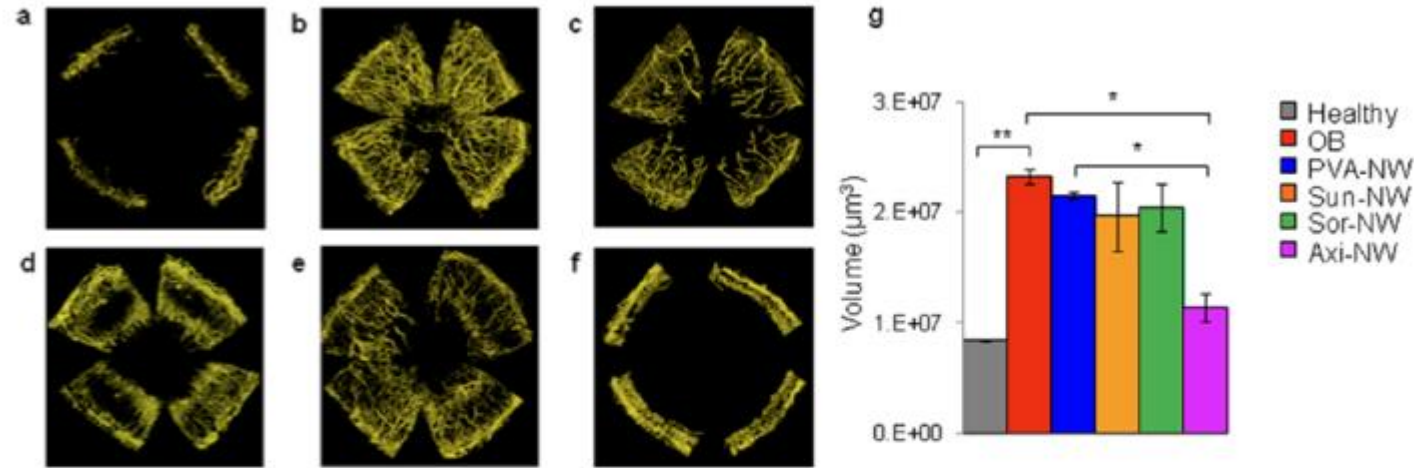
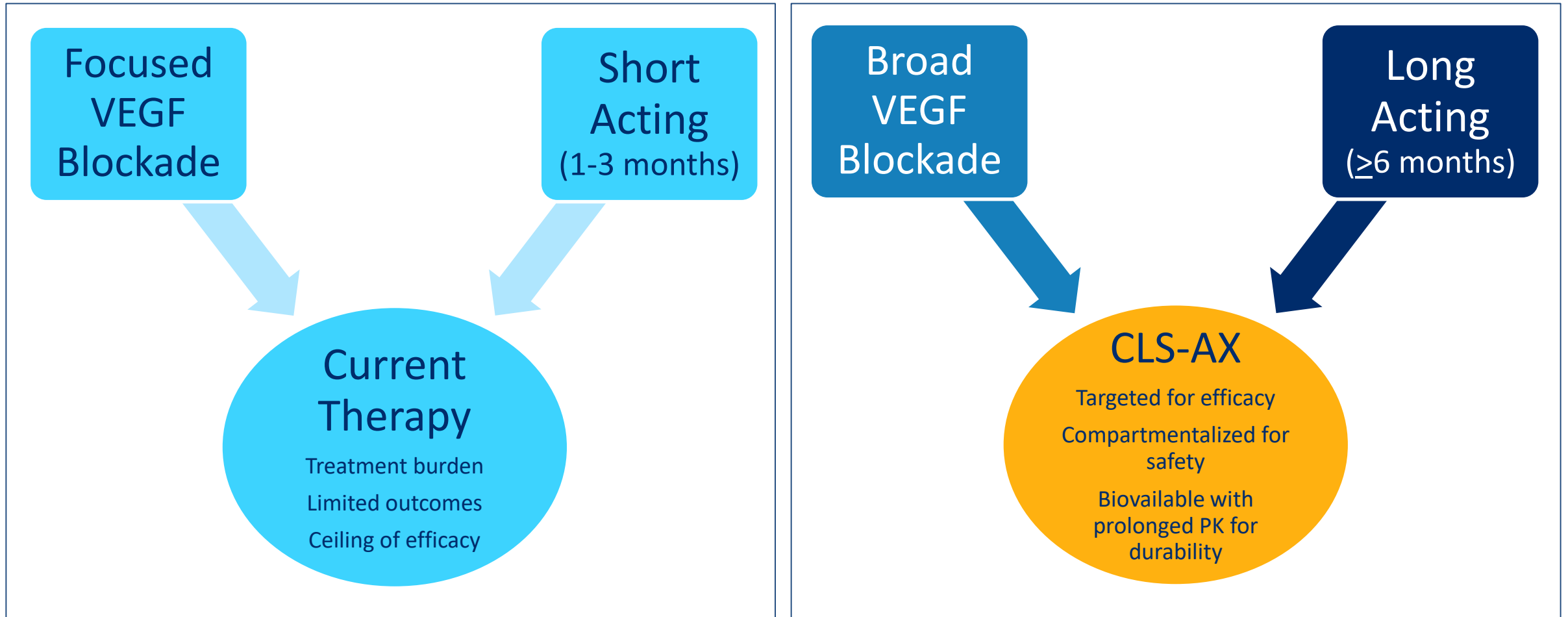


Figure 5. Selection of tyrosine kinase receptor inhibitor drugs. Screening of tyrosine kinase inhibitor drugs loaded nanowafers for their relative therapeutic efficacy in inhibiting corneal neovascularization after 10 days of treatment. Representative 3D reconstructed corneal images of fluorescence confocal 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.

# Potential to Disrupt the AMD Treatment Landscape



# Broad Applicability of SCS Injection Platform: Ocular Gene Therapy



## Primary Need

Targeted delivery of ocular gene therapies in safe, effective, repeatable, and non-surgical manner

## Opportunity

1. Avoid risks of vitrectomy (surgery)
2. Avoid risks of retinotomy, subretinal injection, and macular detachment
3. Potential for broader retinal coverage
4. Enhance patient access
  - Convert gene therapy into an office-based procedure

# DNA Nanoparticle Gene Therapy and the Suprachoroidal Space

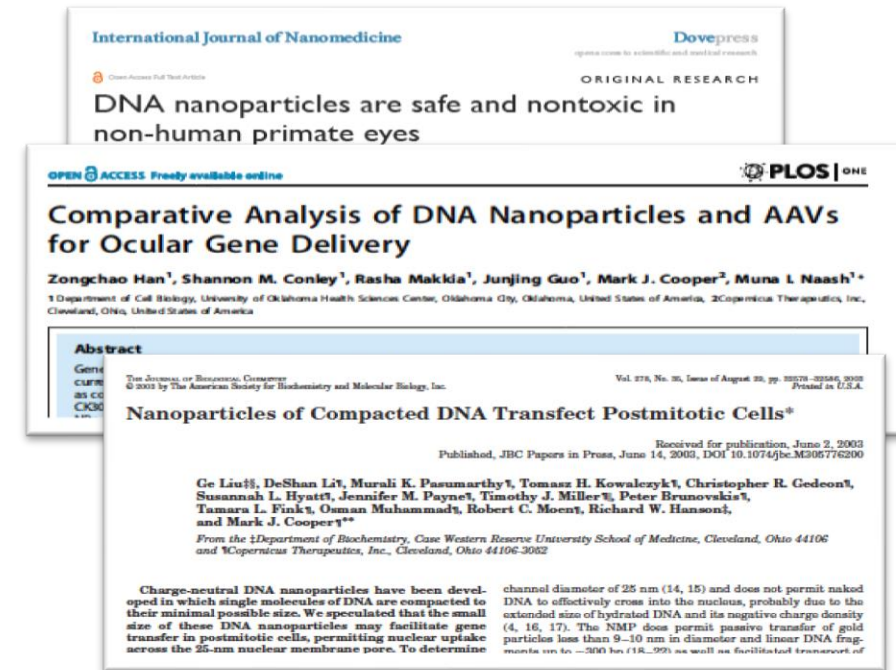
## Potential advantages:

- 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
  - Higher doses possible to enhance transfection

## Potential synergies with suprachoroidal injection:

- In office, repeat dosing as needed
- Targeted circumferential compartmentalized spread to large surface areas
- Potentially ideal distribution for inherited retinal disease treatment or biofactory approach

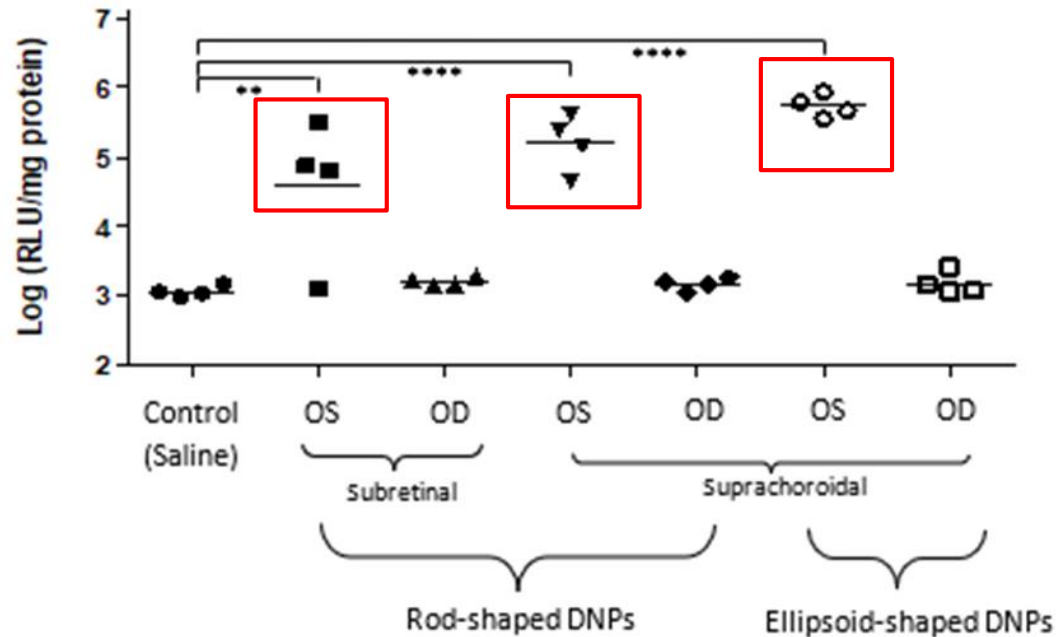
## Well established literature on DNA nanoparticle gene therapy



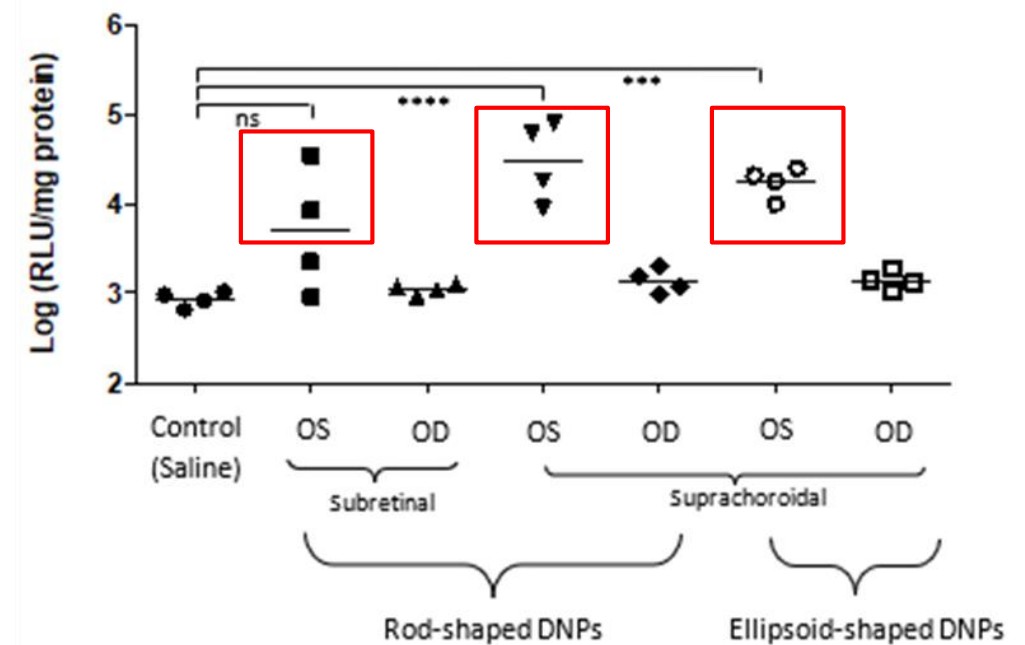
Preclinical studies demonstrate SC injections of DNA nanoparticles (DNPs) may offer the potential for a safe and efficient delivery method

# Preclinical SCS and Subretinal Injections of DNA Nanoparticles Produced Comparable Luciferase Activity

CHOROID-RPE-Sclera  
Non-Viral Luciferase, Rabbit



RETINA  
Non-Viral Luciferase, Rabbit



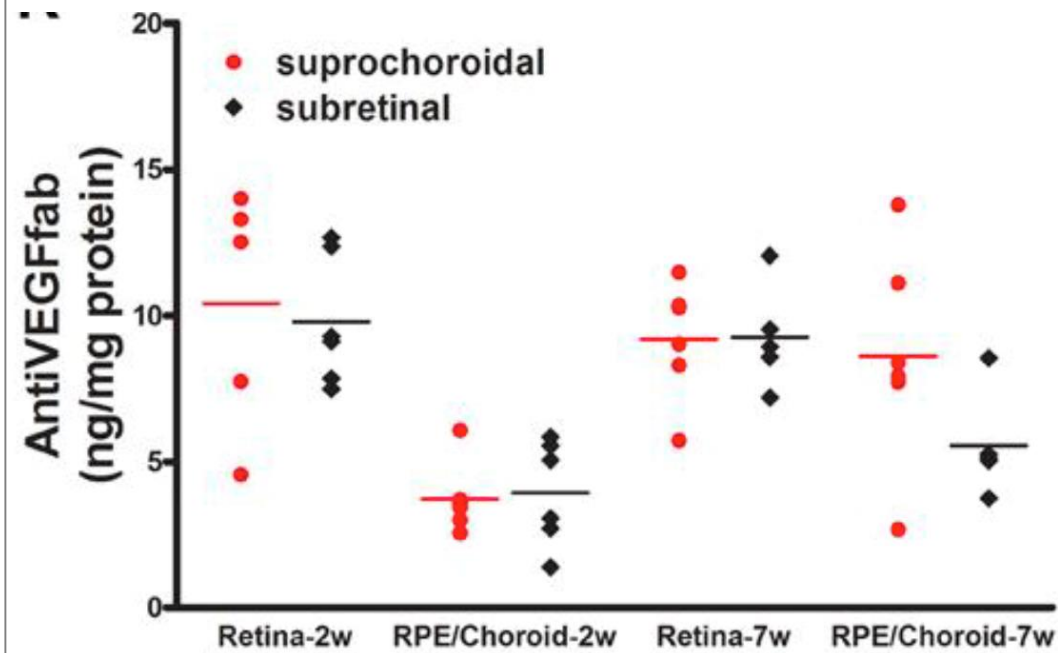
DNA Nanoparticles Transfect Choroid and Retina



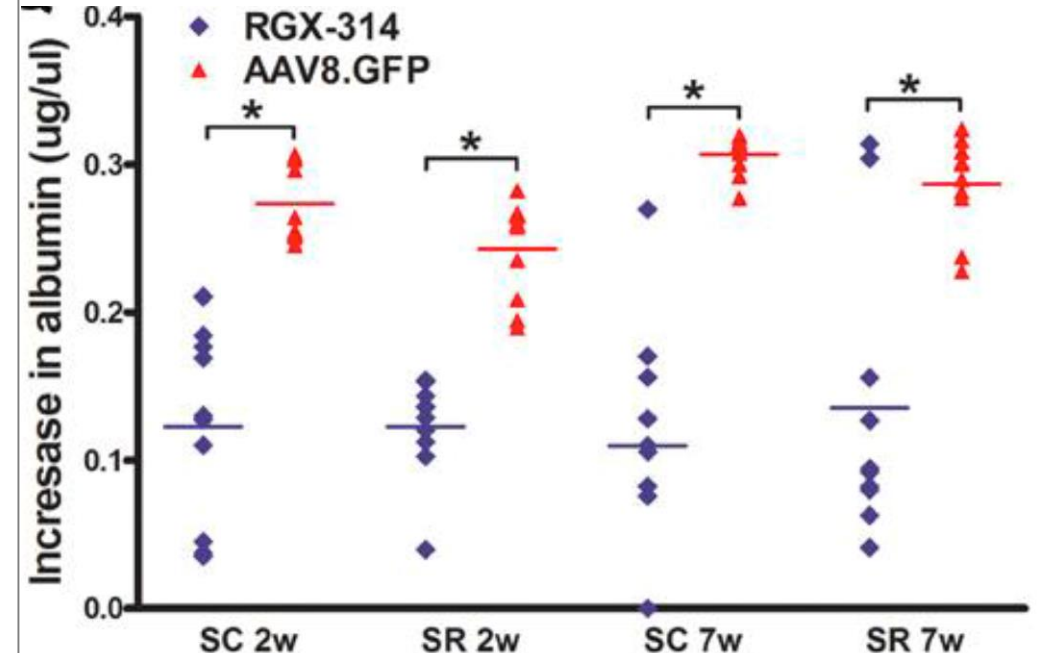
# Partnered Program: Viral Vectors Preclinical Activity

Suprachoroidal delivery of NAV AAV8-based gene therapy may avoid injected drug exposure to the vitreous and anterior segment of eye

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





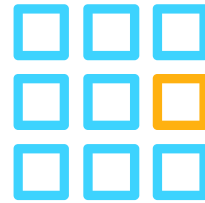
# Core Advantages of Treating Via the Suprachoroidal Space



## TARGETED

The back of the eye is the location of many irreversible and debilitating visual impairments<sup>1</sup>

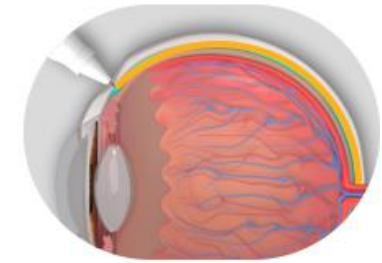
*for efficacy*



## COMPARTMENTALIZED

Drug is compartmentalized in the suprachoroidal space, which helps keep it away from non-diseased tissues<sup>2</sup>

*for safety*



## BIOAVAILABLE PROLONGED PK

Fluid spreads circumferentially and posteriorly when injected within the suprachoroidal space, bathing the choroid and adjacent areas with drug<sup>2</sup>

*for durability*

