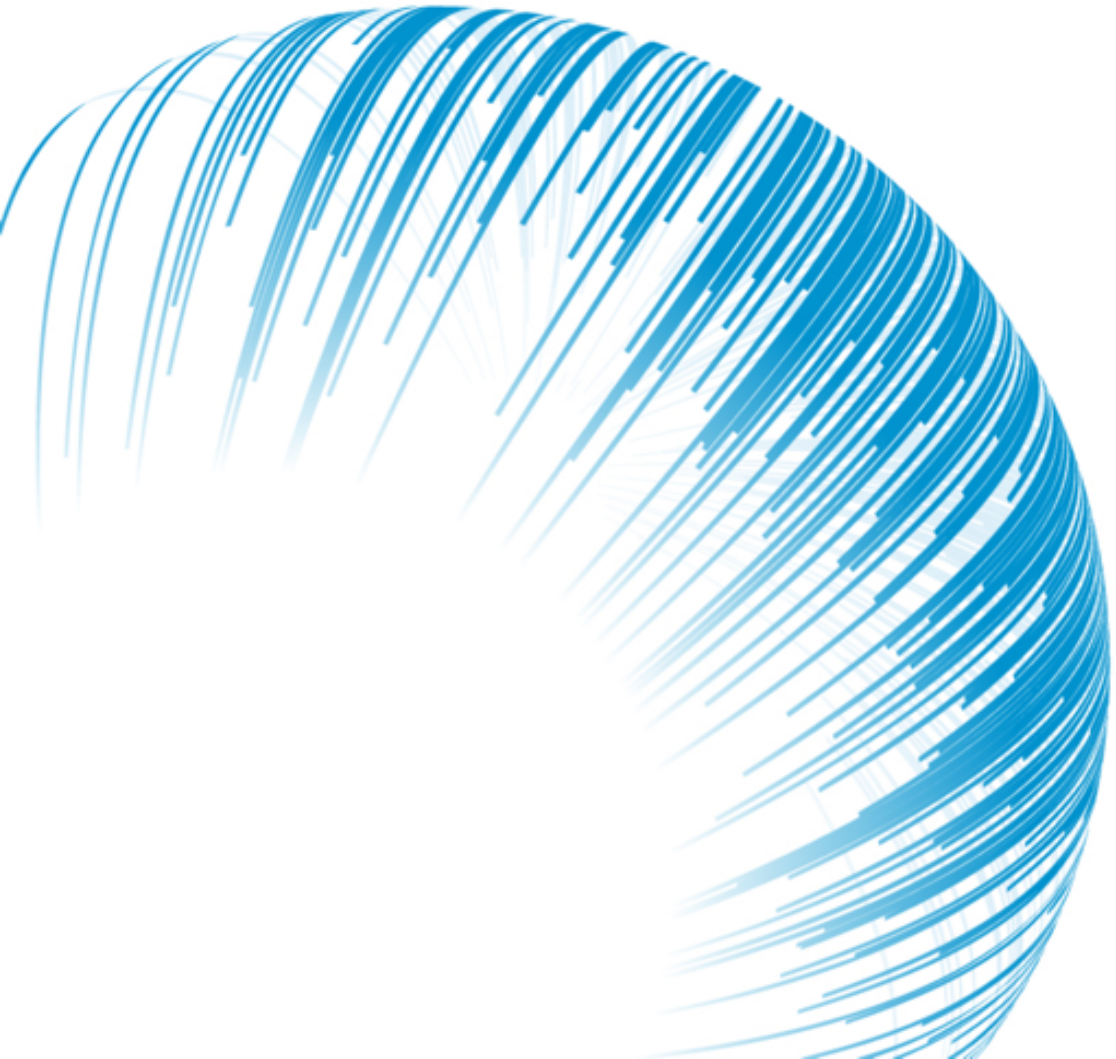


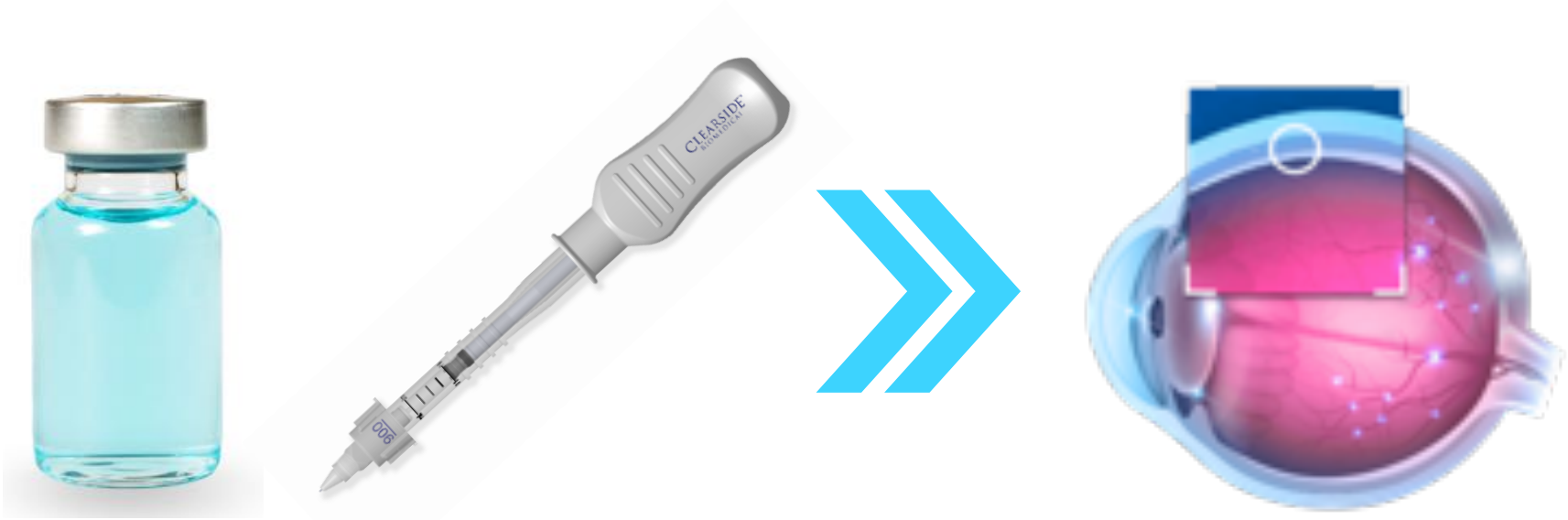
# CLEARSIDE® BIOMEDICAL

Corporate Presentation | September 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 August 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



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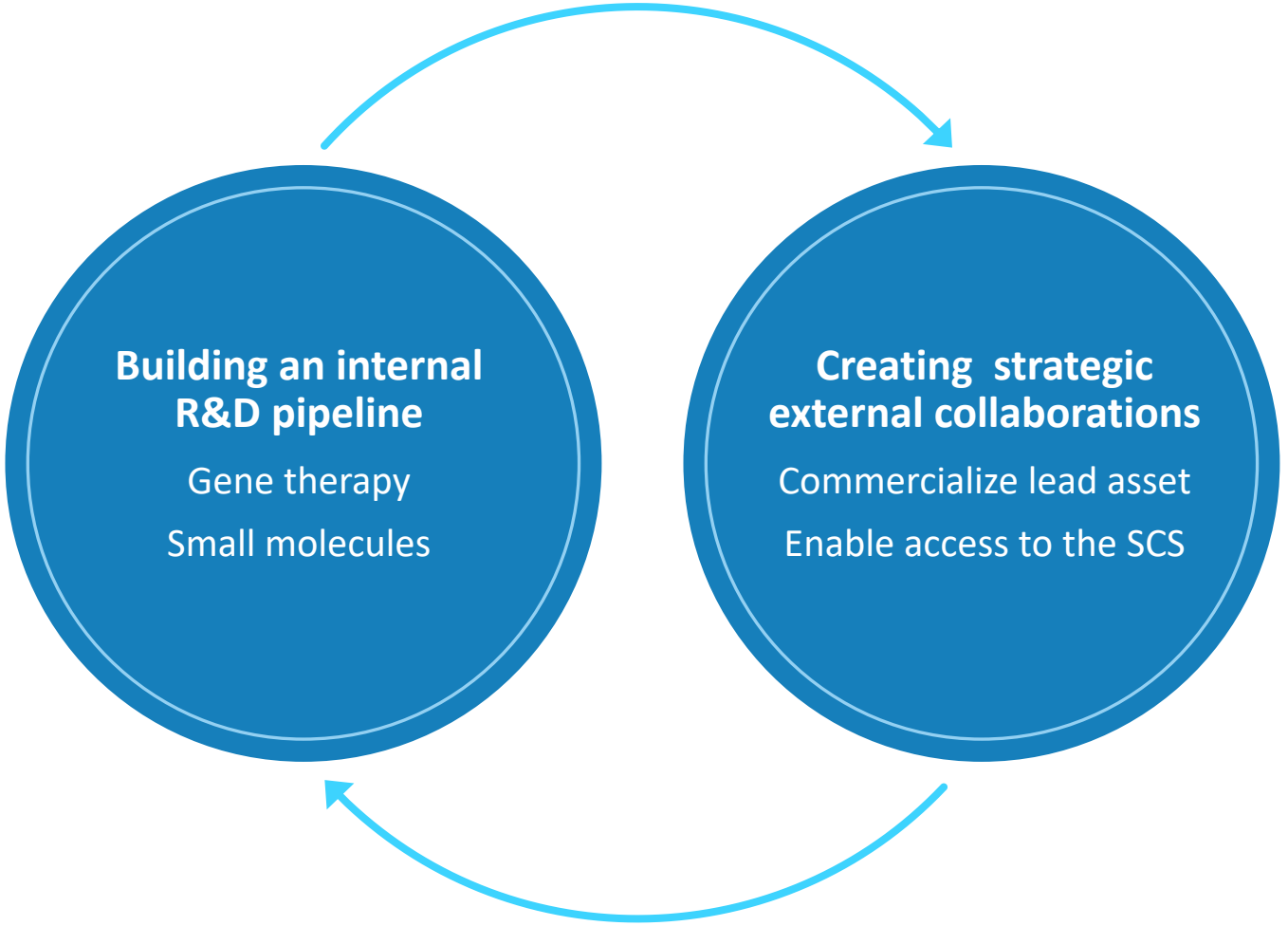
# Two-Prong Corporate Strategy Leveraging Clearside's Proprietary Suprachoroidal Space (SCS) Injection Platform

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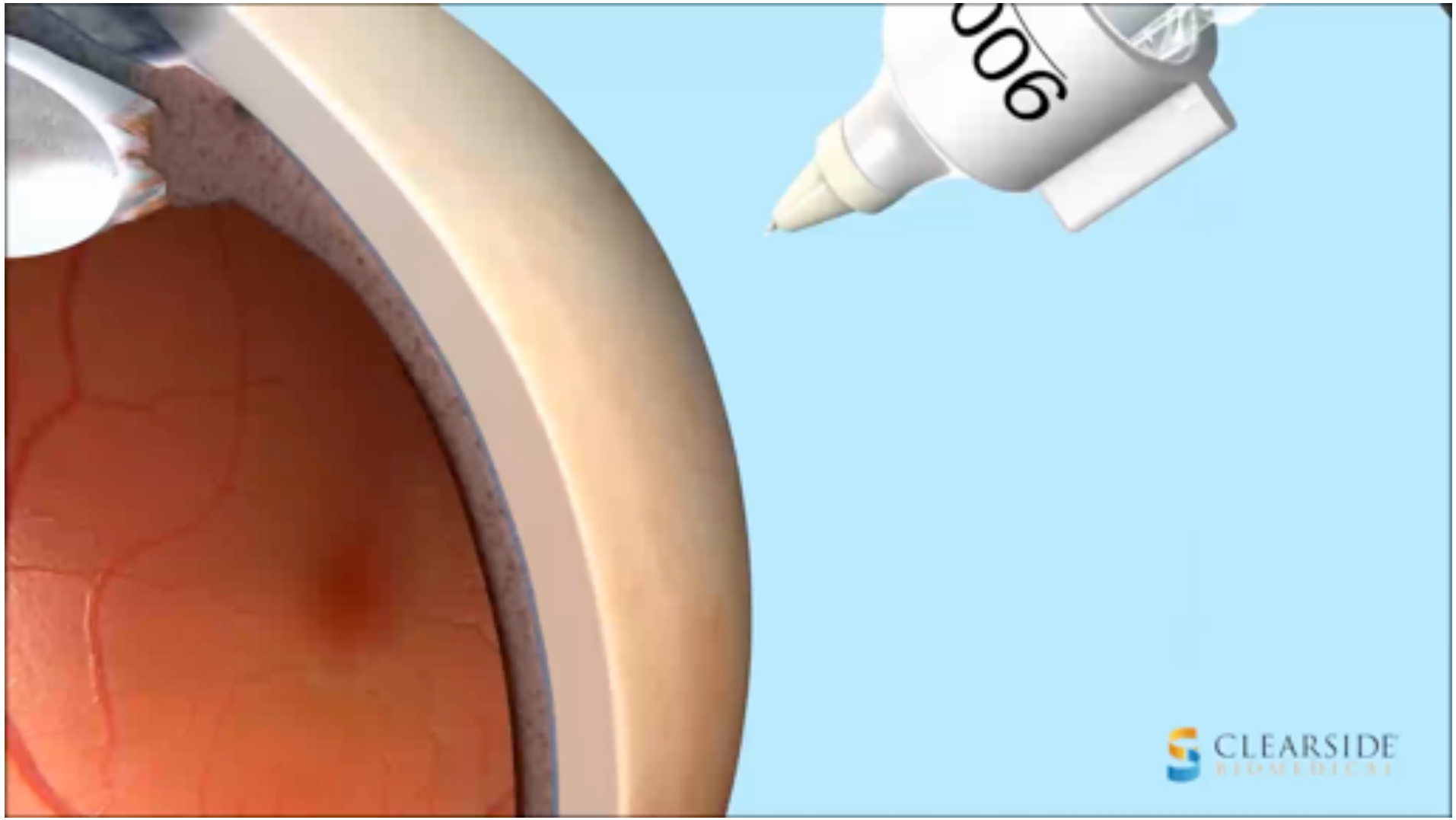
# Exclusive and Proprietary Access to the Back of the Eye

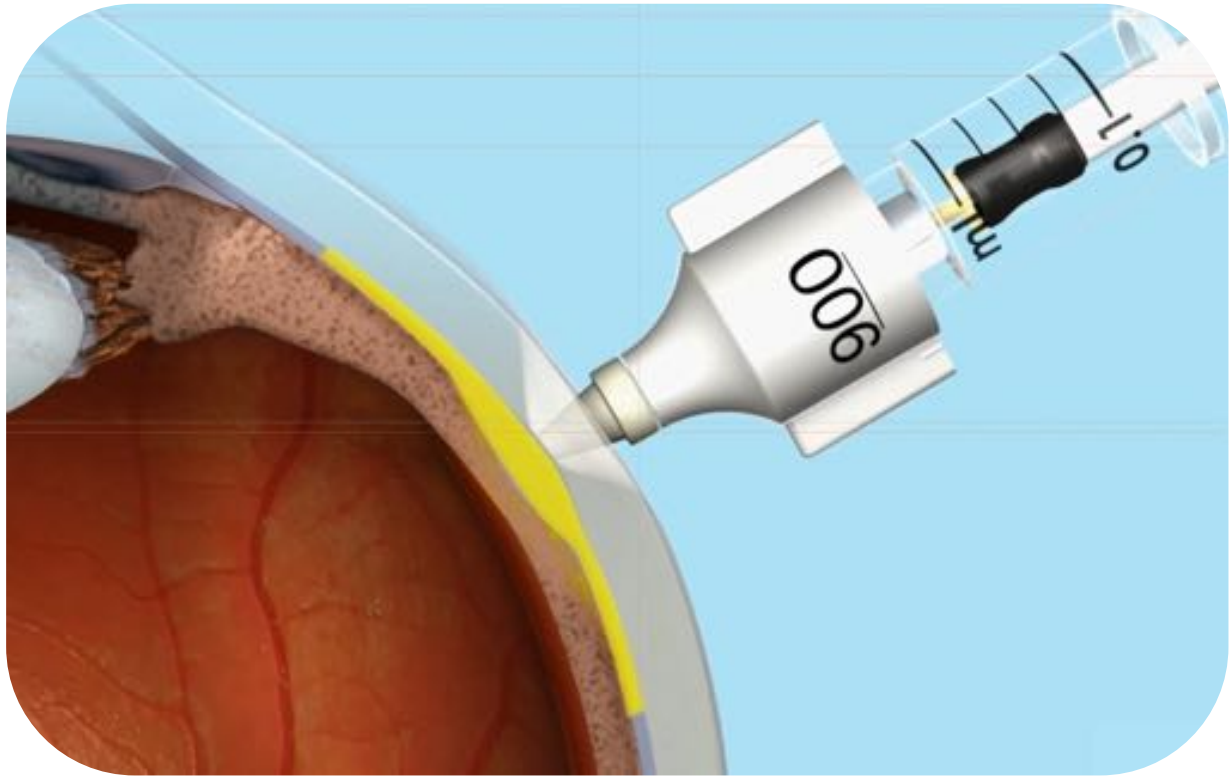





CLEARSIDE BIOMEDICAL

# Ocular Delivery Methods to Reach the Back of the Eye

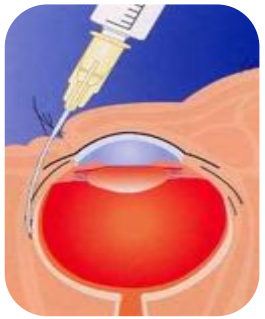
## Suprachoroidal Space (SCS) Injection




Specially-designed SCS Microinjector allows for consistent injection 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



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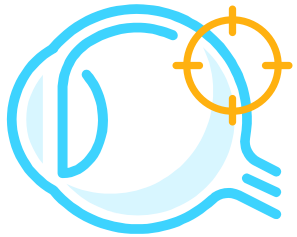
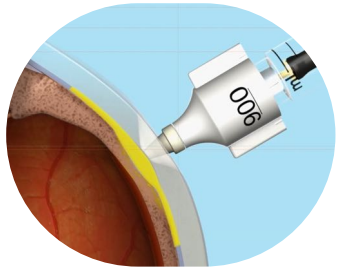
# Core Advantages of Treating Via the Suprachoroidal Space



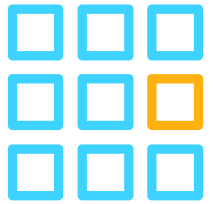
## TARGETED

The back of the eye is the location of many irreversible and debilitating visual impairments[1]




## BIOAVAILABLE

Fluid spreads circumferentially and posteriorly when injected within the suprachoroidal space, bathing the choroid and adjacent areas with drug[2]



## COMPARTMENTALIZED

Drug is compartmentalized in the suprachoroidal space, which helps keep it away from non-diseased tissues[2]



References: 1. 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. 3. Moisseiev E, Loewenstein A, Yiu G. The suprachoroidal space: from potential space to a space with potential. Clin Ophthalmol. 2016;10:173-178. 2. 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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# Pipeline of SCS Treatments with Broad Applicability

| INDICATION | STUDY DRUG | CURRENT STATUS | | | | |
|---|---|---|---|---|---|---|
| | | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 | NDA |
| Uveitis (macular edema associated with uveitis) | XIPERE™ (triamcinolone acetonide suprachoroidal injectable suspension) 40 mg/mL | | | | | |
| DME (diabetic macular edema) | XIPERE™ (triamcinolone acetonide suprachoroidal injectable suspension) 40 mg/mL | | | | | |
| Inherited Retinal Diseases | Gene Therapy | | | | | |
| Retinal Neovascular Diseases | Small Molecules | | | | | |
| **PARTNER PROGRAMS using SCS Microinjector™** | | | | | | |
| Ocular Oncology / Choroidal Melanoma | Aura Biosciences | | | | | |
| Wet AMD, Diabetic Retinopathy | REGENXBIO (RGX-314) | | | | | |



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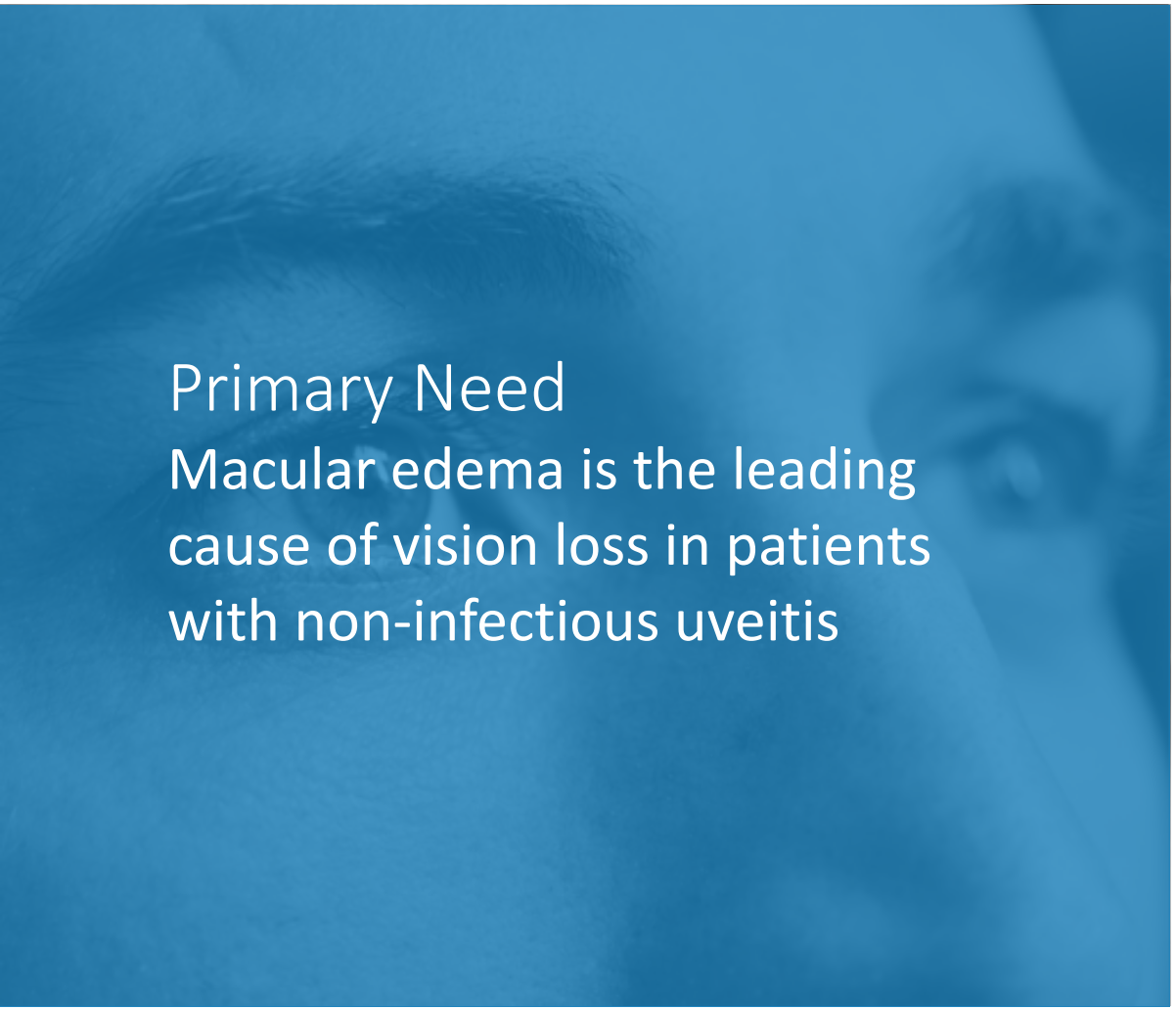
# Macular Edema Associated with Uveitis



## Primary Need

Macular edema is the leading cause of vision loss in patients with non-infectious uveitis

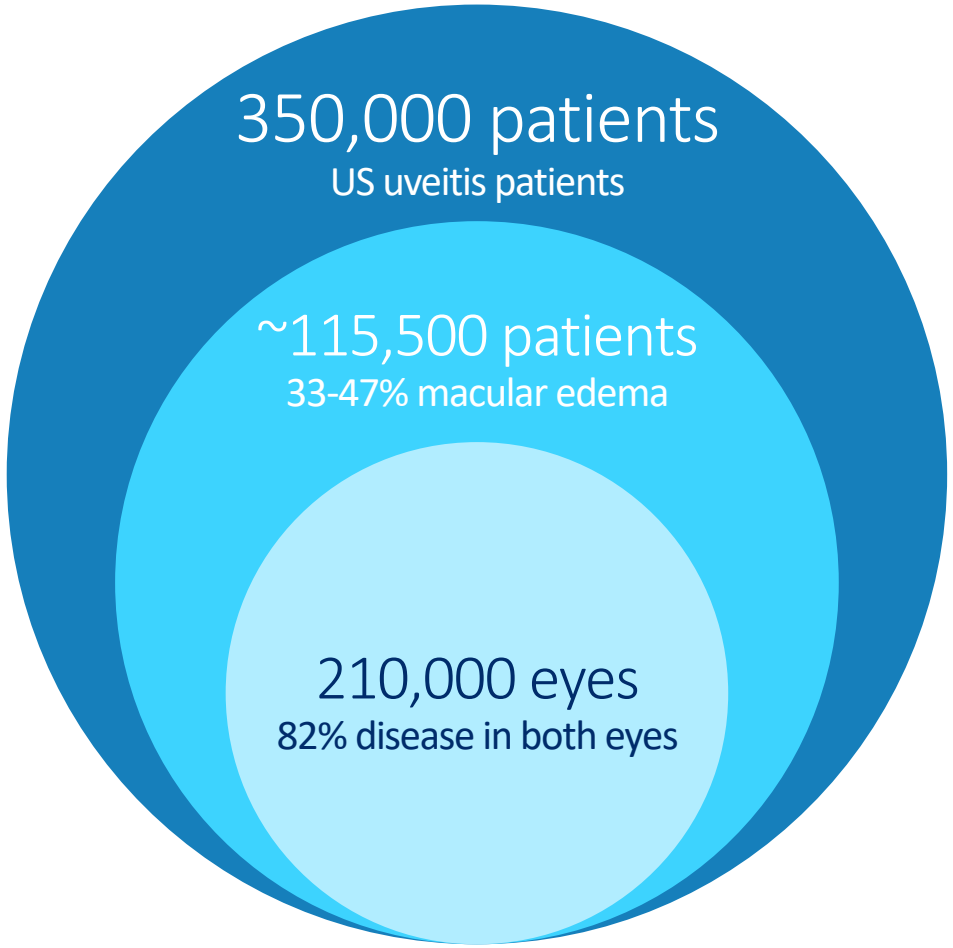
## The Opportunity

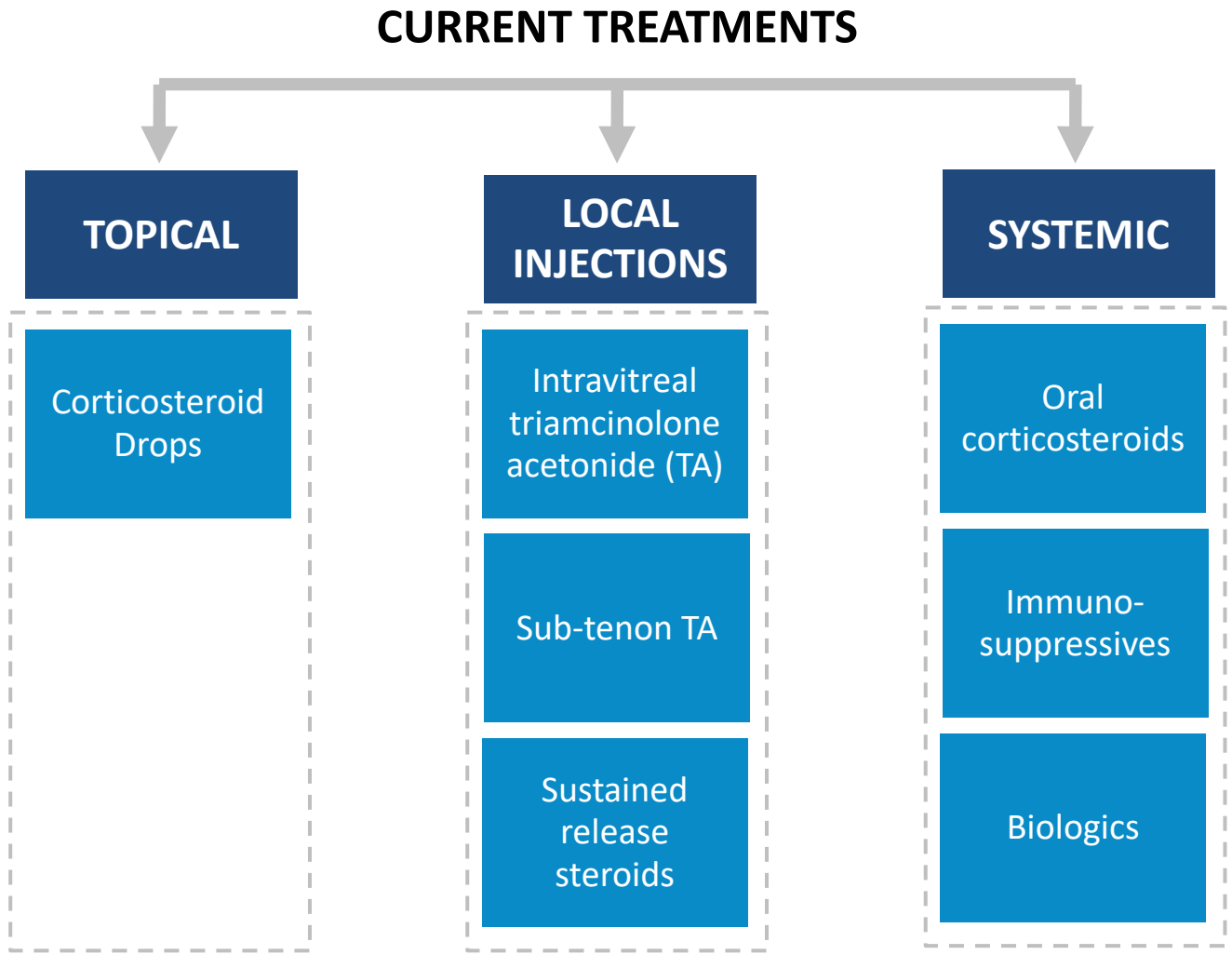
1. ~50% of patients continue to have macular edema, even after a course of treatment for non-infectious uveitis
2. No approved treatment for macular edema associated with uveitis
3. All anatomic locations of uveitis included in Clearside clinical trials



Source: Durrani, 2004

# U.S. Market Size and Current Treatment Paradigm for Uveitis






Sources: 1) Target Ophthalmologist ATU, May 2018; 2) Lardenoye, C. et al. Ophthalmology 113.8 (2006): 1446-1449.

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# Novel Approach to Targeting Uveitic Macular Edema

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

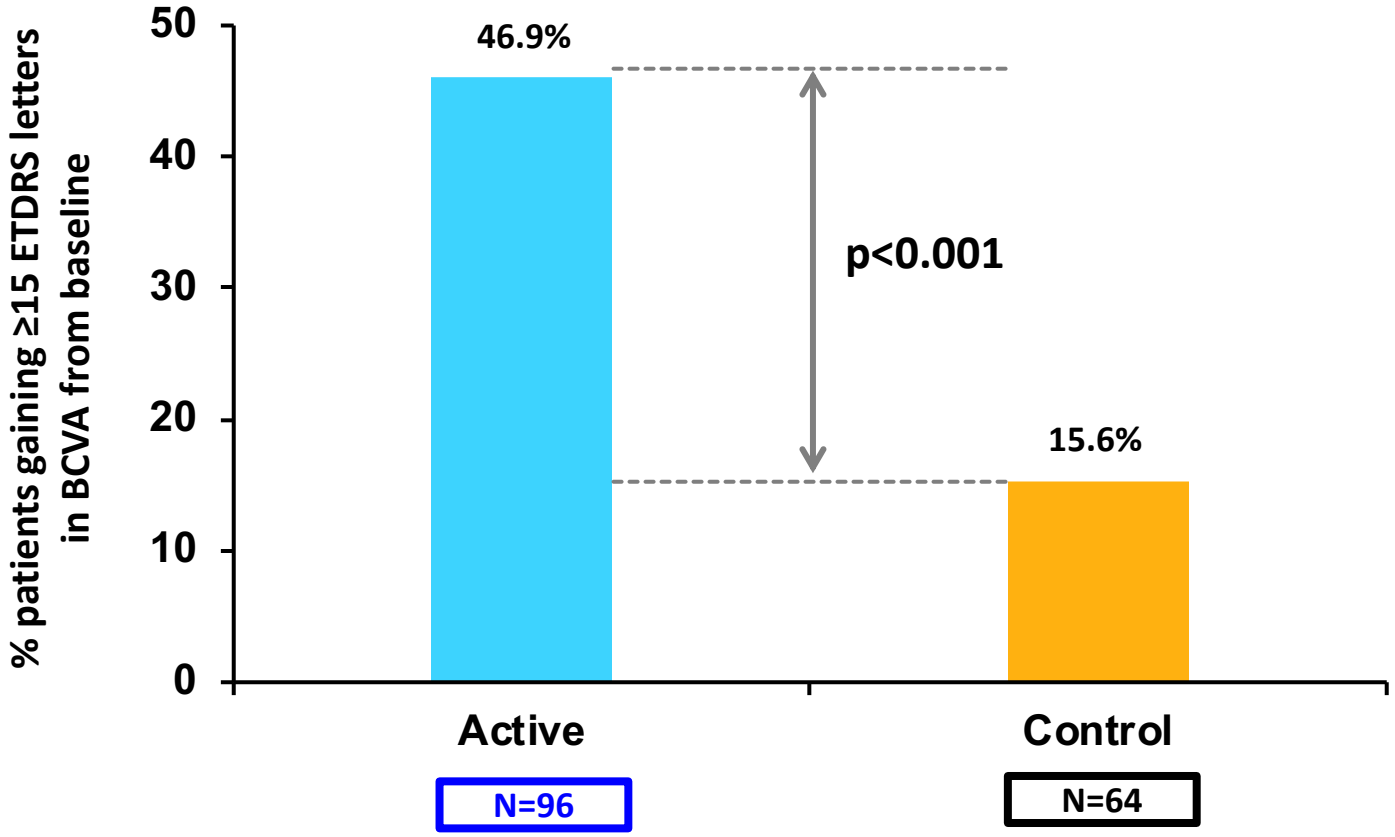
- Pivotal Phase 3 PEACHTREE trial met its primary BCVA endpoint
- MAGNOLIA Phase 3 extension study demonstrated durability
- If approved, XIPERE would be the first therapy for this indication
- Expect to partner commercialization rights including future development
- Expect to resubmit NDA in Q1 2020



XIPERE™ is an investigational product under FDA review. | BCVA = Best Corrected Visual Acuity

# PEACHTREE Met Its Primary Endpoint

Proportion of patients in each arm gaining ≥ 15 ETDRS letters in BCVA from baseline at Week 24






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

ETDRS = Early Treatment Diabetic Retinopathy Study | BCVA = Best Corrected Visual Acuity

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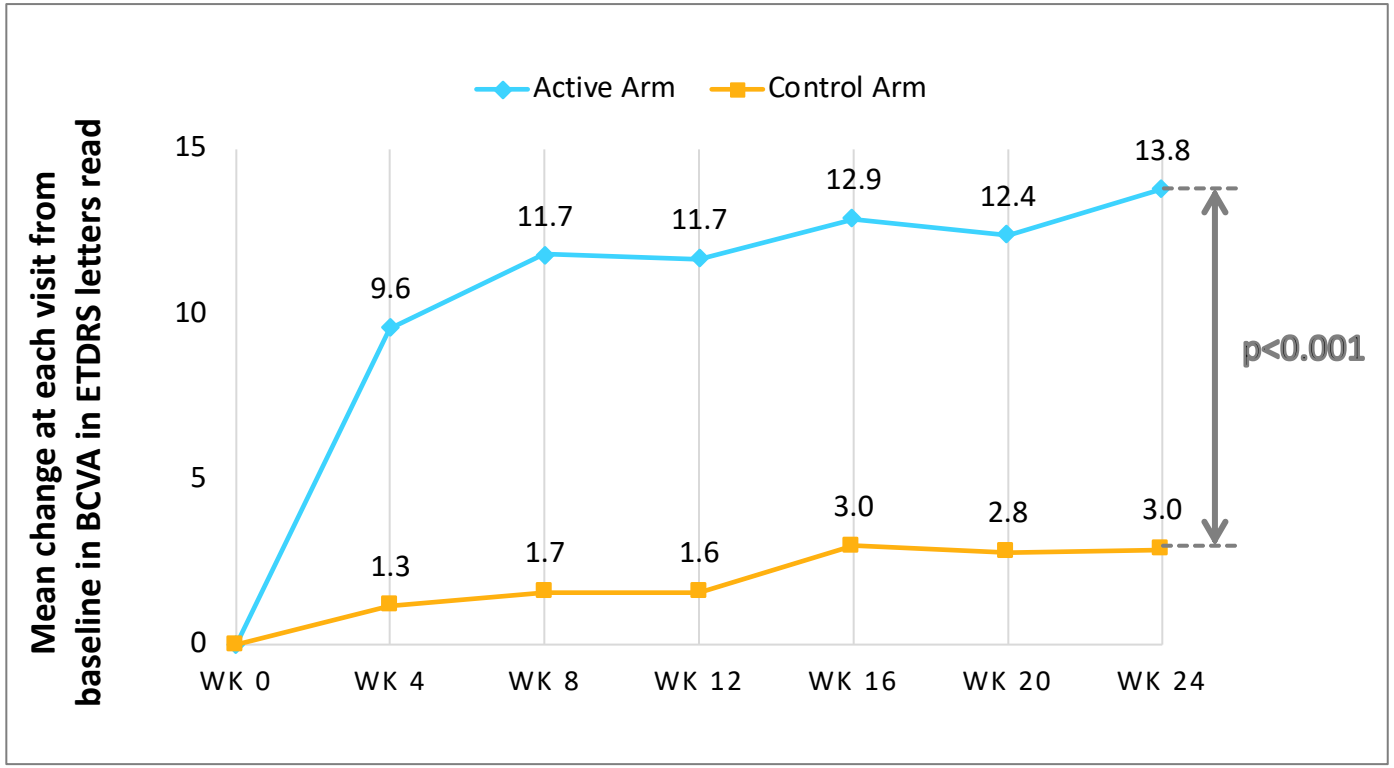
# PEACHTREE Met Secondary Endpoints with Favorable Safety Profile




## Efficacy:

- Mean BCVA increases from baseline were rapid and sustained
- Met Secondary Endpoint at Week 24: Central retinal thickness decreased by 152.6µm (n=96) vs. 17.9µm in control arm (n=64) (p<.001)
- Uveitic inflammation found at baseline resolved in ~70% of those patients

## Safety

- IOP adverse event (AE) rates were favorable (11.5%) compared to all patients (15.6%), and vs those who received rescue local corticosteroid injections (27%)
- Cataract adverse events were balanced between the two arms



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

Source: Phase 3 PEACHTREE data

BCVA = Best Corrected Visual Acuity | ETDRS = Early Treatment Diabetic Retinopathy Study | IOP = Intraocular Pressure

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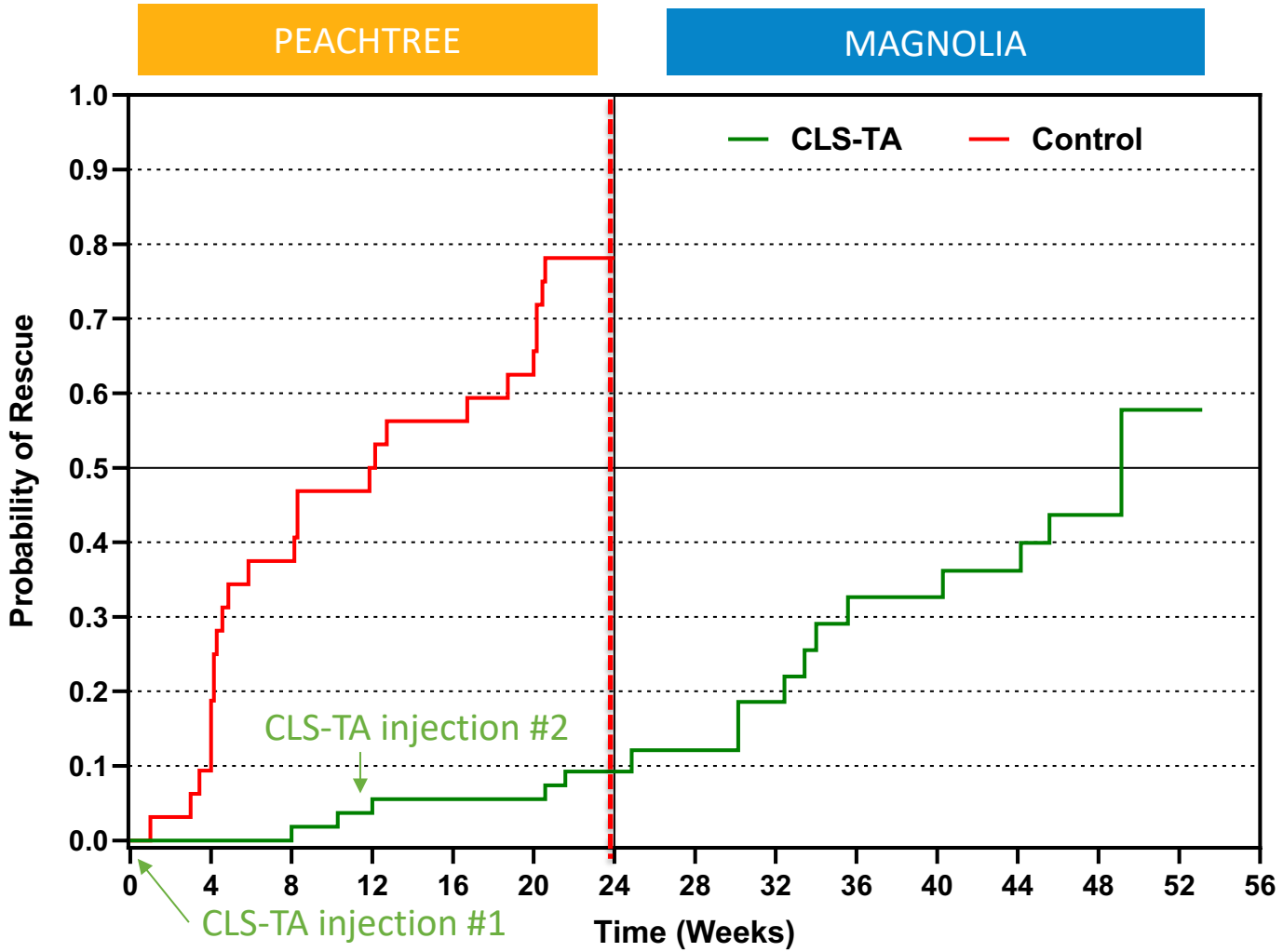
# MAGNOLIA Extension Study Demonstrated Meaningful Durability




## Efficacy and Durability

- 50% of patients did not receive additional medication through week 48
- Results were durable for 36 weeks after last injection of XIPERE
- At Week 48, mean change in BCVA from Baseline was 12.1 letters and mean CST was ~170 microns

## Safety

- There were no Serious AEs related to study medication and AE rates were low
- Elevations in IOP were consistent with those seen in the PEACHTREE trial



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

Source: Phase 3 PEACHTREE data; MAGNOLIA data

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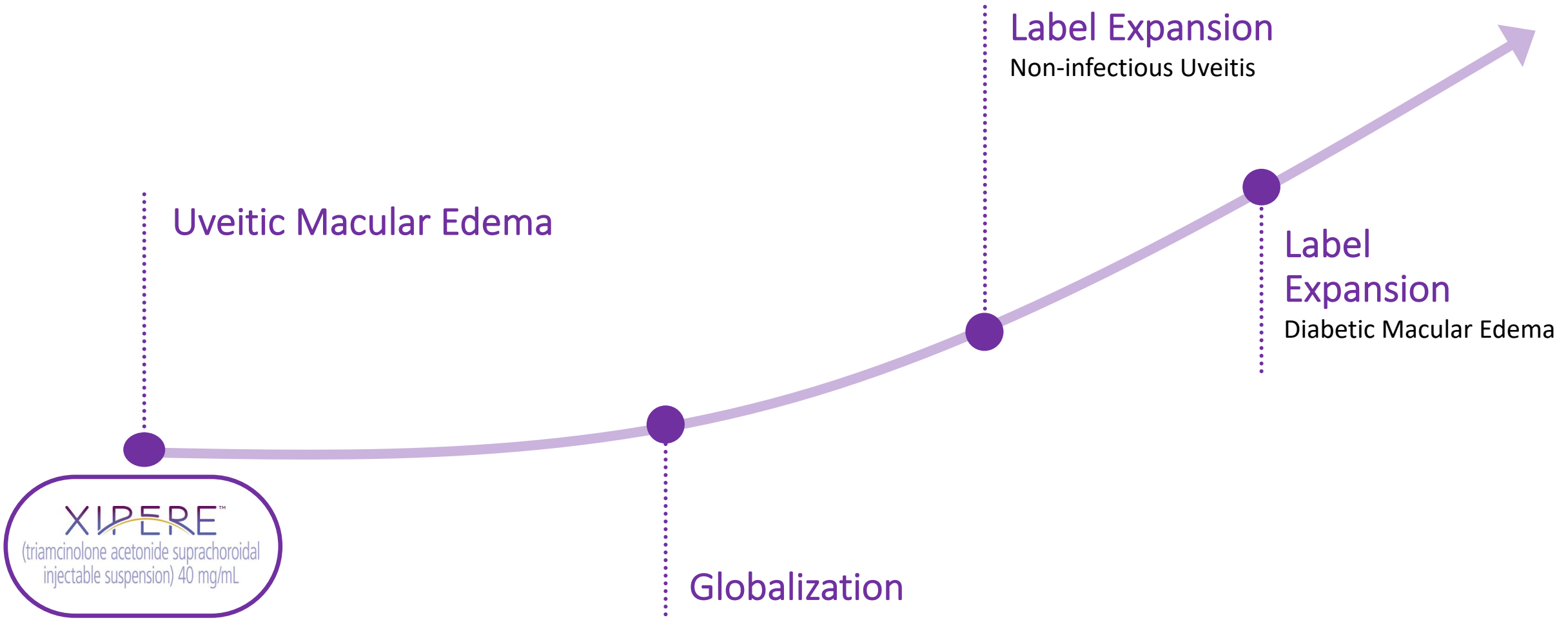
# Opportunities for a Partner to Drive Value With XIPERE






XIPERE™ is an investigational product under FDA review.

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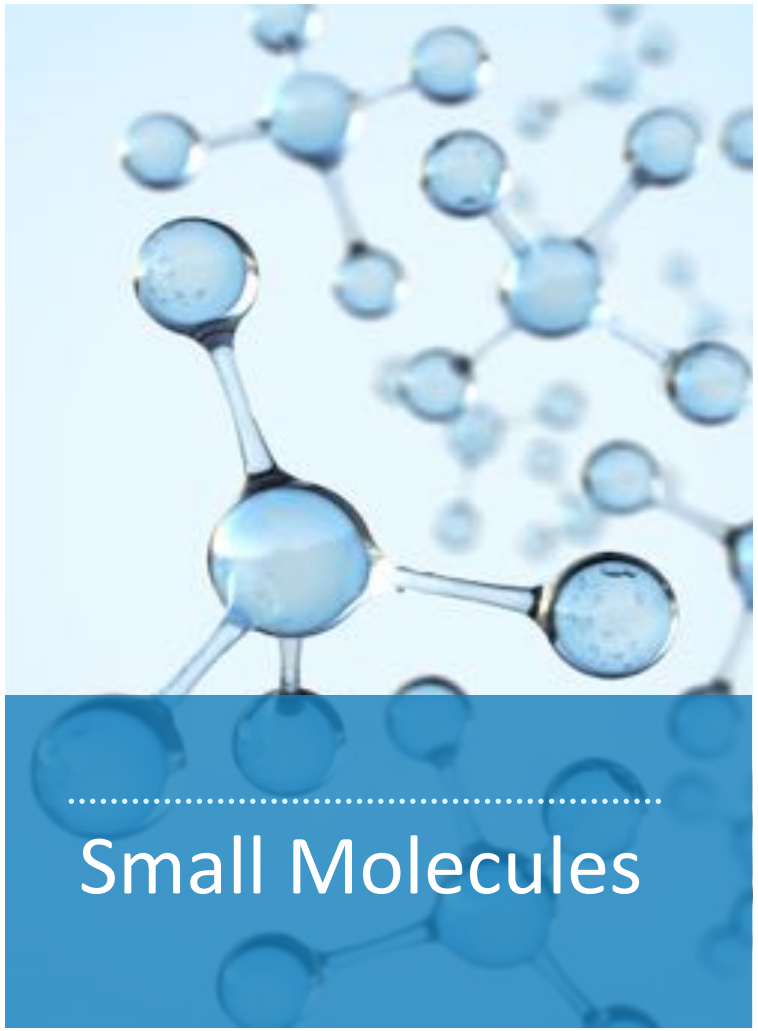
# Broad Applicability of SCS Injection Platform

Gene Therapy



Small Molecules

Partner Programs



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# Strong Intellectual Property Coverage of SCS Platform

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

| 2 | 3 | 3 | 1 | 3 | 1 | 3 |
|---|---|---|---|---|---|---|
| Methods using loss-of-resistance technology | Apparatus using loss-of-resistance technology | Apparatus having / methods using an adjustable puncture member | 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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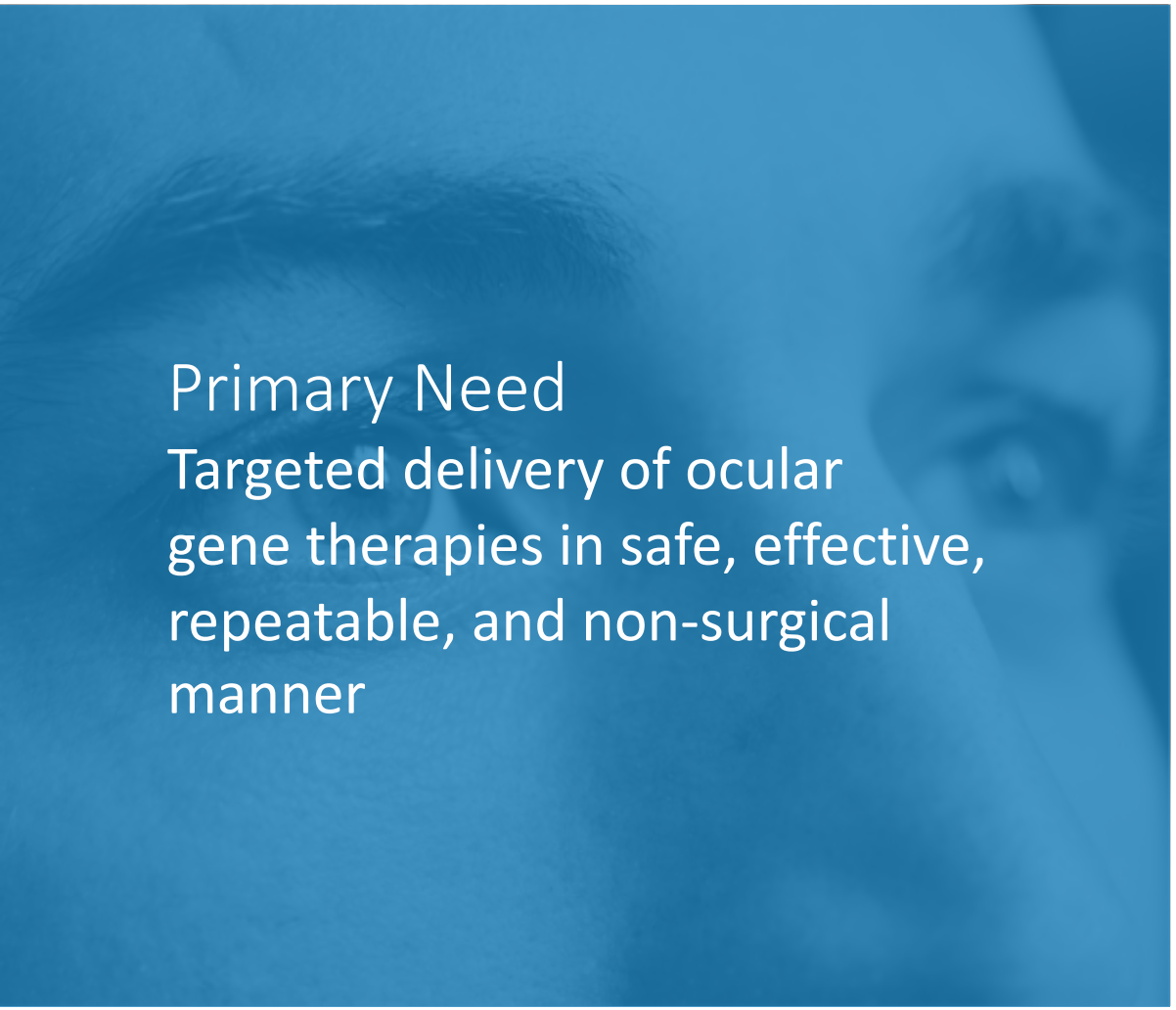
# SCS Platform Expansion: Ocular Gene Therapy



## 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

# Current Focus Areas for SCS Gene Therapy

## Partnered Program: Viral Vectors

- Delivery of NAV AAV8-based gene therapy through the SCS can potentially:
  - Provide targeted, in-office, non-surgical approach for widespread transgene expression in retina
  - Avoid injected drug exposure to the vitreous and anterior segment of eye
- Potential indications: wet AMD, diabetic retinopathy, other conditions where anti-VEGF treatment is standard of care
- Partnered with REGENXBIO

## Internal Development: DNA Nanoparticles

- Recently published preclinical studies demonstrated SCS injections of DNA nanoparticles (DNPs) may offer the potential for a safe and efficient delivery method
  - Luciferase activity was observed in the retina, retinal pigment epithelial (RPE), and choroid of all eyes
  - In rabbits, SCS injection of luciferase DNPs produced activity comparable to that seen from subretinal injections of luciferase DNPs
  - DNPs can transfer large genes and higher doses may be used to enhance transfection
  - SCS injections of DNPs were generally well-tolerated across both rabbits and non-human primates, and no significant abnormalities were observed on ophthalmic exams
- Potential indications: inherited retinal diseases such as Stargardt Disease and Ushers Syndrome



Source: Szilárd Kiss, MD, Macula Society Presentation February 2019 | Anti-VEGF = anti-vascular endothelial growth factor

# Platform Expansion via Partnership: AAV Vector Gene Therapy

## Primary Need

In-office delivery could allow for treatment of expanded patient populations with wet AMD and DR with one-time gene therapy

REGENXBIO®

## The Opportunity: REGENXBIO

1. A pioneer in the development and manufacturing of AAV vectors for delivery of ophthalmic anti-VEGF antibodies
2. REGENEXBIO to evaluate RGX-314 using Clearside's SCS Microinjector for in-office, non-surgical delivery into the SCS
   - RGX-314 currently in Phase 1/2 development in wet AMD (subretinal)
   - Encouraging preclinical results delivering RGX-314 into the SCS
3. Potential proceeds to Clearside:
   - Fee upon REGENXBIO's 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



wet AMD  = Wet age-related macular degeneration; DR = diabetic retinopathy;
Anti-VEGF = anti-vascular endothelial growth factor

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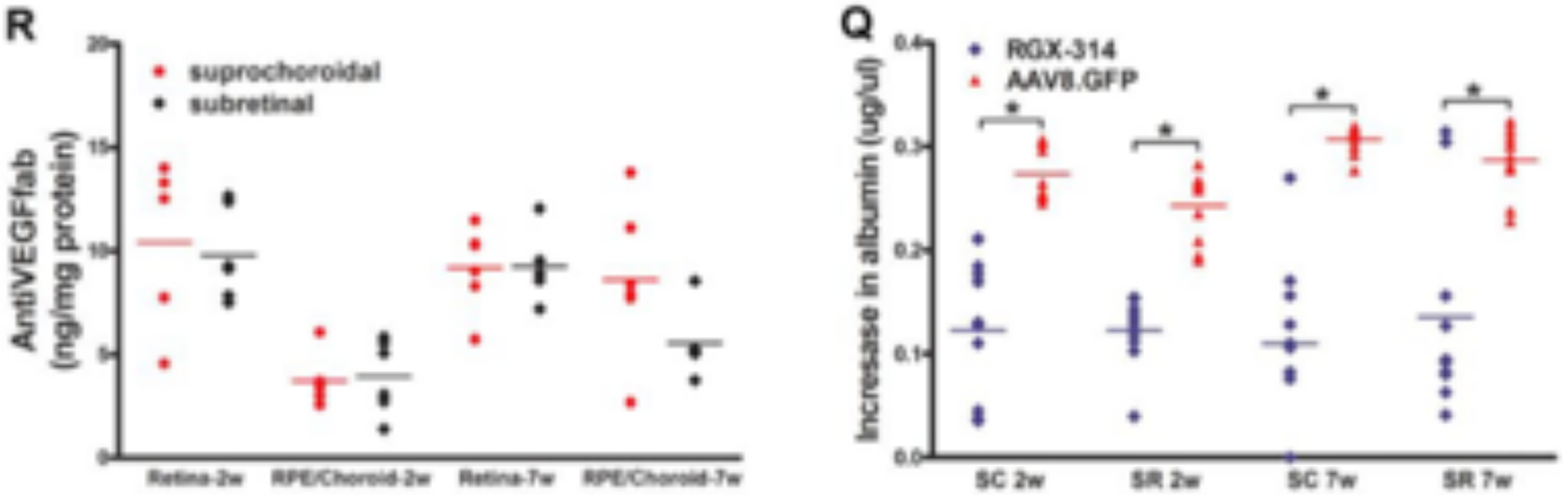
# Encouraging Preclinical Results of SCS Delivery of RGX-314

RGX-314 SCS delivery resulted in similar expression of anti-VEGF Fab and suppression of VEGF-induced vascular leakage as subretinal delivery 2 weeks and 7 weeks after RGX-314 administration






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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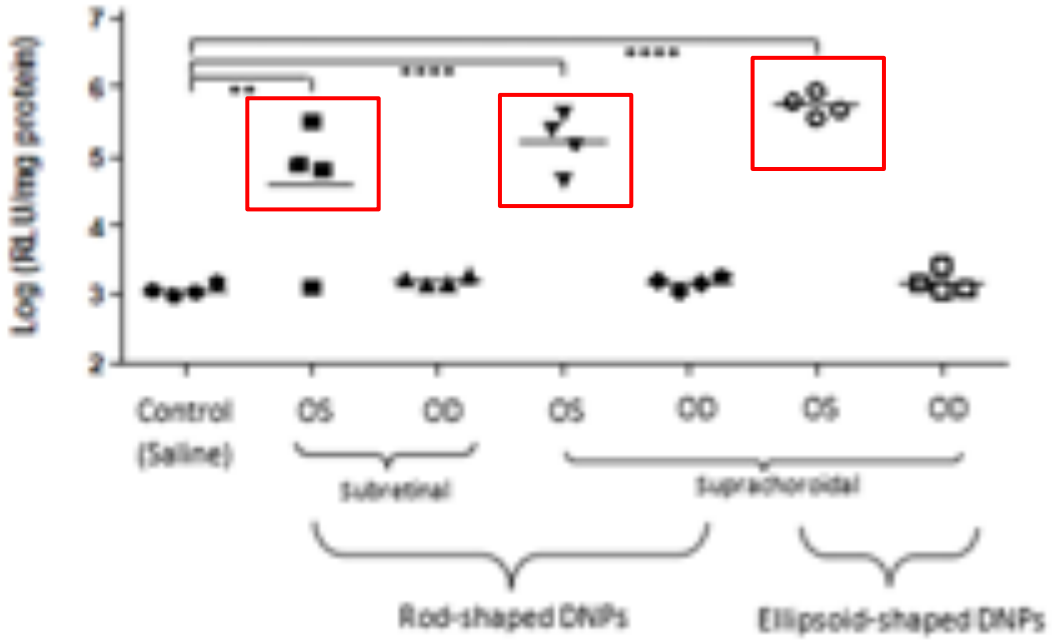
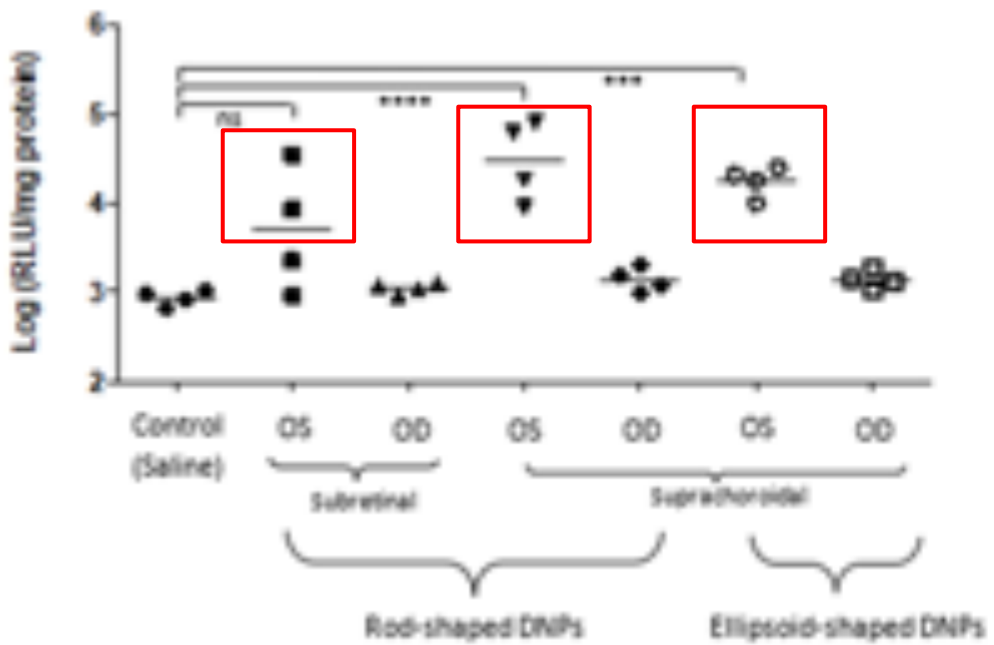
# Similar pre-clinical evidence using DNA Nanoparticle Subretinal and Suprachoroidal Delivery

Non Viral-Luciferase, Rabbit
CHOROID




| | |
|---|---|
| OS: Dosed<br>OD: Undosed | Bonferroni's multiple comparison test: ** p<0.01, *** p<0.001, **** p<0.0001<br>ns, non-significant |

Non Viral-Luciferase, Rabbit
RETINA




| | |
|---|---|
| OS: Dosed<br>OD: Undosed | Bonferroni's multiple comparison test: *** p<0.001, **** p<0.0001<br>ns, non-significant |



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

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# SCS Platform Expansion: Small Molecules

## Primary Need

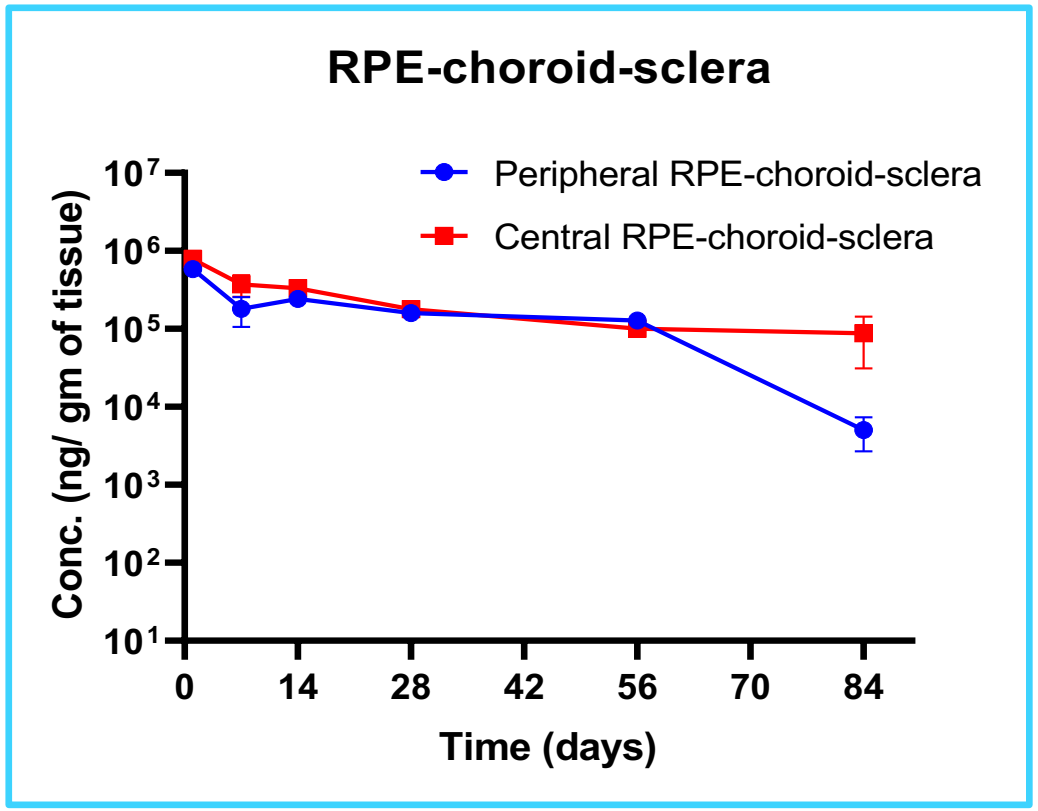
Targeted delivery to retina with prolonged durability to enhance efficacy and relieve treatment burden respectively

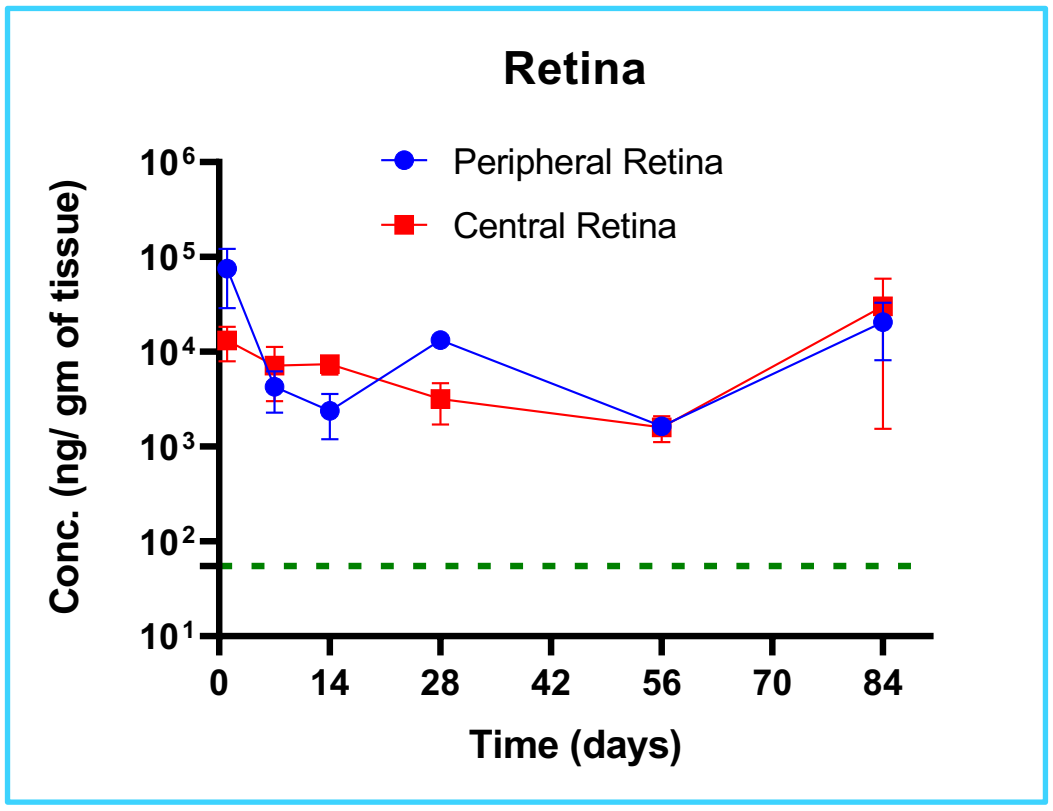
## The Opportunity

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

# SCS Platform May Offer Unique Distribution and Better Duration

High drug levels achieved in retina and choroid-RPE-sclera



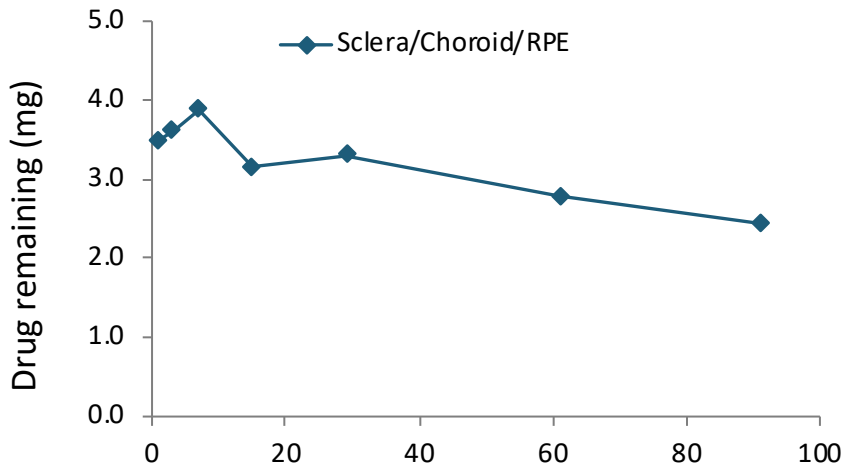




Concentration presented as mean ± SEM

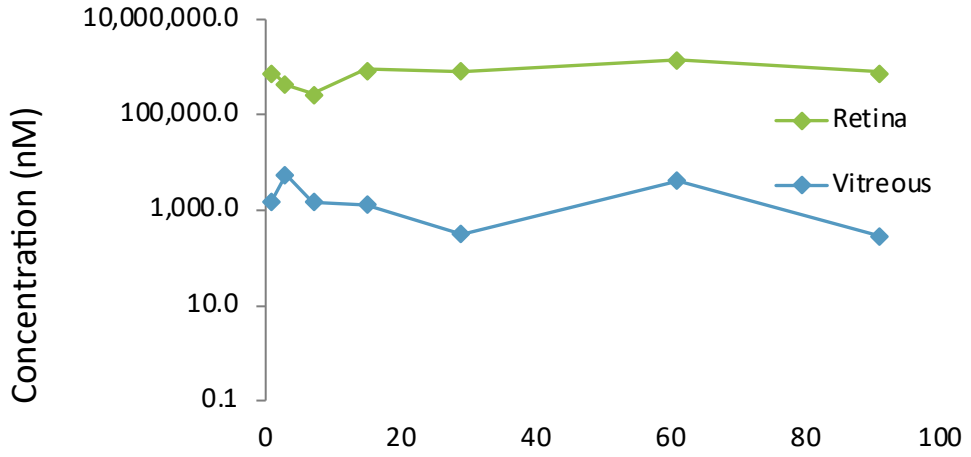


Based on non-clinical data

# High Drug Levels Maintained in RPE-Choroid-Sclera Tyrosine Kinase Inhibitor




- At 3 months > 60 % of TKI remaining
- Half-life > 3 months




- Retina levels of TKI are far greater than what is required to block the VEGF pathway
- Plasma levels below quantification limit: <1 ng/mL



Based on non-clinical data

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# Platform Expansion via Partnership: Ocular Oncology


## The Opportunity: Aura Biosciences

1. Non-surgical alternative to intravitreal delivery of Aura's oncology drug candidates
2. Choroidal melanoma is the most common, primary intraocular tumor in adults
3. Potential future financial upside for Clearside from pre-specified milestone payments and sales royalties

# Financial Summary

| (in millions) | June 30, 2019 |
|---|---|
| Cash and cash equivalents | $26.2 |
| Total assets | $29.9 |
| Long-term debt (including current portion) | $10.1 |
| Total liabilities | $17.0 |
| Total stockholders' equity | $12.9 |
| Common shares outstanding (as of August 7, 2019) | 37.8 |

# Experienced Leadership Team

## George Lasezkay

Pharm.D., J.D. | Interim CEO and Director

30 years experience
Allergan, Acucela, Novagali, Amakem, RetroSense

## Thomas Ciulla

M.D., MBA | Chief Medical Officer

27 years experience
Spark Therapeutics, Ophthotech, Indiana University School of Medicine

## Charles Deignan

Chief Financial Officer

27 years experience
AtheroGenics, AAIPharma, Schering-Plough

## Brion Raymond

Chief Commercial Officer

17 years experience
Genentech, Carl Zeiss, Meditec, Xoma

## Leslie Zacks

General Counsel & Chief Compliance Officer

24 years experience
Arbor, Shionogi

## Rafael Andino

VP, Engineering & Manufacturing

26 years experience
CR Bard, CIBA Vision, Dupont, GE, IBM

## Rick McElheny

VP, Corporate Development

18 years experience
Sanofi, MEDA, Vidara

### Clearside Team Ophthalmic Experience

Alcon · Allergan · CIBA VISION · Genentech · MERCK · NOVARTIS · Spark THERAPEUTICS



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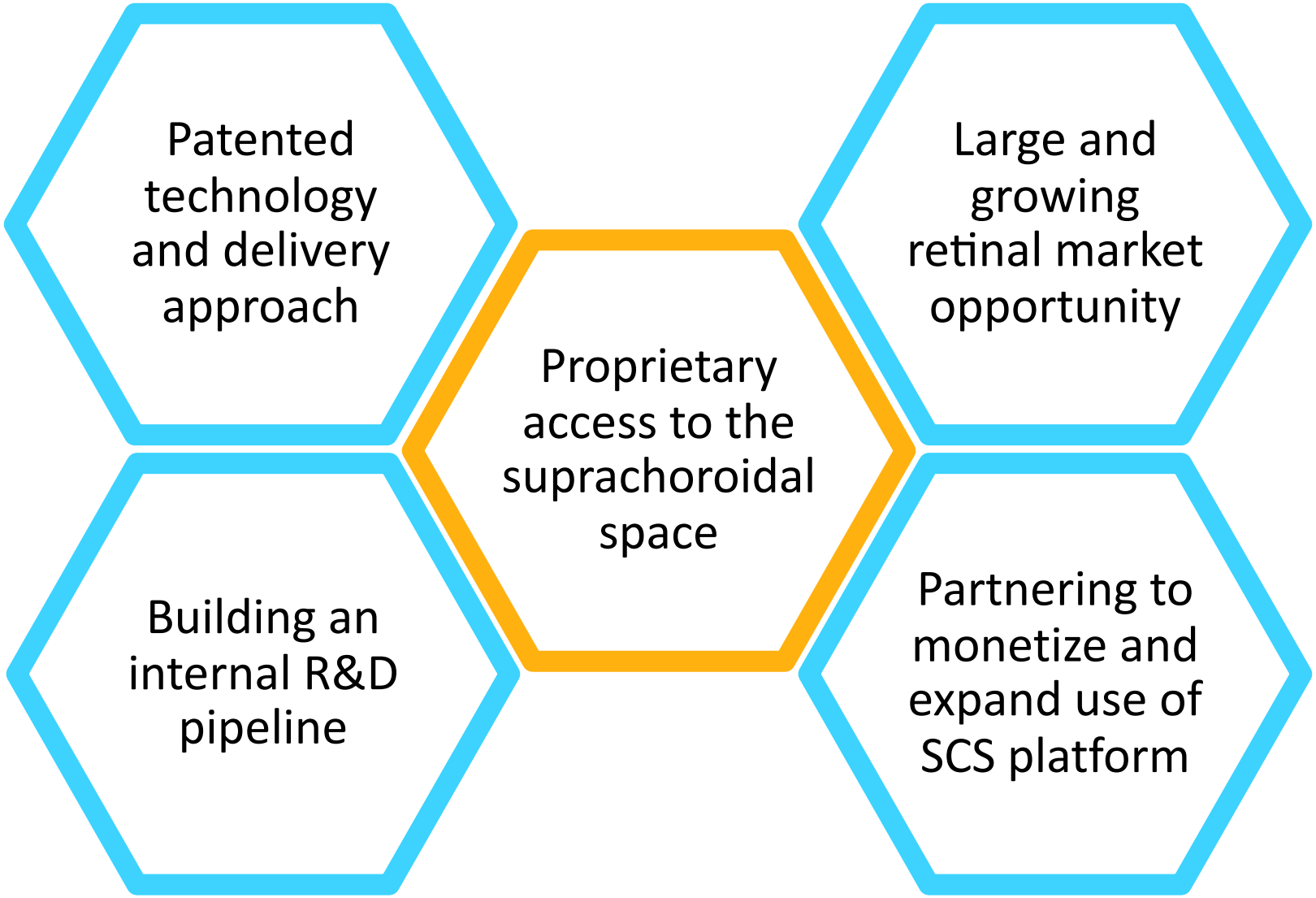
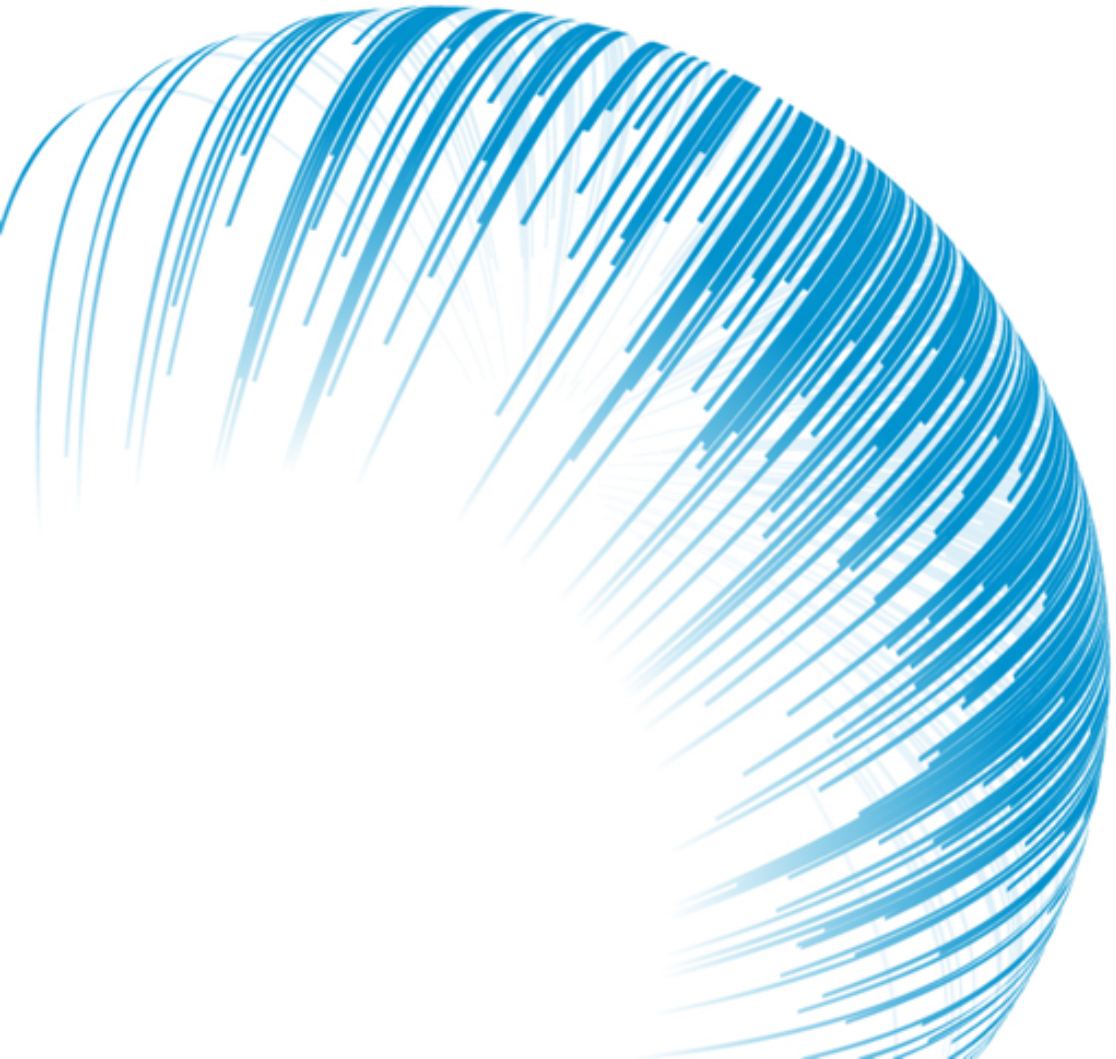
# Clearside Biomedical: Five Key Investment Themes





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