



Corporate Presentation | May 2020

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 forwardlooking 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, 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 & Delivering Treatments that Restore & 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



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



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





Core Advantages of Treating Via the Suprachoroidal Space





TARGETED

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

COMPARTMENTALIZED

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

BIOAVAILABLE PROLONGED PK

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

for durability



for efficacy

for safety

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.

Preclinical Data Leads to Clinical Results

TARGETED

for efficacy

20%

0%

7



n=45

CLS-TA

(N=96)

p<0.001

15.6%

n=10

Control

(N=64)

COMPARTMENTALIZED for safety

Values are area under the curve ratios (SCS / IVT) over 12x 91 days in rabbit eyes clera/Choroid Outer Retina Drug not detected in the aqueous from 1x Neural Retina SCS injection 0.002x Lens 0.03x Iris and Ciliary Body



BIOAVAILABLE PROLONGED PK for durability







Pipeline of SCS Treatments with Broad Applicability

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

PARTNER PROGRAMS using SCS Microinjector®

PARTNER	INDICATION	PRE- CLINICAL	IND- Enabling	PHASE 1	PHASE 2	PHASE 3	NDA
BAUSCH HEALTH	Macular edema associated with uveitis (XIPERE™)						
ARCTIC VISION	Macular edema associated with uveitis (XIPERE™)						
REGENXBIO	Wet AMD						
REGENXBIO	Diabetic Retinopathy						
AURA BIOSCIENCES	Ocular Oncology / Choroidal Melanoma						



Internal Pipeline Opportunities



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

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

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



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

TREATMENT BURDEN	At 1 year, "real-world" patients receive only 6-7 injections ^{4,5}	Under-treatment contributes to poor real-world outcomes
LIMITED OUTCOMES	At 1 year, with on-label anti-VEGF dosing ¹⁻³ : ~1/5 of patients lose BCVA	At 1 year, "real-world" patients improve by
	~1/2 do not achieve ≥ 20/40 ~2/3 do not gain ≥ 3 lines BCVA	only 1-3 letters ^{4,5}
CEILING OF EFFICACY	Increased anti-VEGF dosage or more intense regimens yield no additional BCVA benefit ^{1,6,7}	

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-C¹VEGF-D²
- 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

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Suprachoroidal Axitinib 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 models³⁻⁷
- More effective than other TKIs for experimental corneal neovascularization in animal models
- Better ocular cell biocompatibility than other TKIs⁸

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-vitro and in-vitro 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 Kinaes, on Laser-Induced Choroidal Neovascularization in Clore Surface. Surface Surface



CLS-AX:

High Drug Levels Maintained in the Retina after SCS administration







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.



Potential to Disrupt the AMD Treatment Landscape

Focused VEGF Blockade

Broad VEGF Blockade





Exploratory Preclinical PK Study Complement Inhibitor and the Suprachoroidal Space

Suprachoroidal delivery of complement inhibitor small molecule suspension resulted in targeted, compartmentalized, and sustained ocular levels in rabbits



- Targeted & Compartmentalized: High exposure for 90+ days in RPE-choroid-sclera (RCS
- Sustained: Estimated half-life (T_{1/2}) of 66, 66, and 76 days at 0.03, 0.1, and 0.3 mg/eye level, respectively
- Meaningful drug levels: 3-5 orders of magnitude higher than the in-vitro (AP hemolysis assay) IC90 value (10nM)



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

The Opportunity

- Avoid risks of vitrectomy (surgery)
- Avoid risks of retinotomy, subretinal injection, and macular detachment
- Deliver larger genes using non-viral vectors
- Convert gene therapy into an office-based procedure
- Potential for broader retinal coverage
- Enhance patient access



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

Int	ternational Journal of Nanomedicine	Dovepress	
8	Steen Access Full Text Article	ORIGINAL RESEARCH	
D	NA nanoparticles are safe an on-human primate eyes	nd nontoxic in	
N 8M	CCESS Freety available ordine	:¢	PLOS ••
ongcha	ao Han ¹ , Shannon M. Conley ¹ , Rasha Makkia ¹ , J t of Cel Biology, University of Okishoma Health Sciences Center, Olidhoma No, United States of America	u njing Guo¹, Mark J. Cooper², Mu Oly, Oklahuma, United States of America, 2Copernis	u na L Naash ¹ ca Therapeutics, Ir
Abst	ract		
Gene	Ten Jourses, or Bousence, Conserver © 2003 by The American Society for Bochemistry and Molecular Hology, Inc.	Vol. 276, No. 26, Iseue of August 2	9, pp. 22578-22584, 20 Printed in U.S.
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Gene curre as co CIG0	The bound of Bangway of Bangway Compared Bandwardy and Mahndar Hadags Int. Nanoparticles of Compacted DNA Published Ge Liutif, DeShan LiY, Murali K, Pasumarel Susaannah Li Hyatti, Jennifer M. Paynet, T Tamare L. Finky, Osman Muhammady, Rol and Mark J. Coopert ¹⁴ From the LDepartment of Biochemistry, Case Western and Weight Thermostic Inc. Circleadad, Ohto d	Vol. 278, No. 38, Jacob of August 2 Transfect Postmitotic Ce Received for public , JBC Papers in Pruss, June 14, 2003, DOI 10.10 ay 7, Tomasz H. Kowalczyk 7, Christophe mothy J. Miller 8, Peter Brunovskis 7, ert C. Moeny, Richard W. Hansont, Reserve University School of Medicine, Cleveland 4106-3062	8, pp. 10137 - 20146, 20 Preside in U.S. IIIS* ation, June 2, 200 74/jbc M30577622 cr R. Gedeon3, , Ohio 44106



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



Published Preclinical Data on Viral Vectors in SCS

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







Corporate Collaborations



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



REGENXBIO Initiating Two Phase 2 Trials Using SCS Microinjector®

- RGX-314 for Treatment of Wet Age-Related Macular Degeneration (wet AMD)
 - REGENXBIO plans to initiate Phase 2 trial of suprachoroidal delivery of RGX-314 using SCS Microinjector[™] for treatment of wet AMD in <u>first half of 2020</u>.
 - Trial will build upon data from Phase 1/2a trial of RGX-314 and is expected to evaluate patients in two dose cohorts of RGX-314 versus a control arm. Interim data is expected from Cohort 1 by <u>end of 2020</u>.
- RGX-314 for Treatment of Diabetic Retinopathy (DR)
 - REGENXBIO expects to submit IND in <u>mid 2020</u> and plans to initiate Phase 2 trial of suprachoroidal delivery of RGX-314 using SCS Microinjector for treatment of DR in <u>second half of 2020</u> with interim data expected <u>in 2021</u>.





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
- Expect Aura to initiate clinical testing using our SCS Microinjector in the **second half of 2020**



The Terms:

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



Novel Approach to Targeting Uveitic Macular Edema Using SCS Microinjector[®]

(triamcinolone acetonide suprachoroidal injectable suspension) 40 mg/mL

- Macular edema is the leading cause of vision loss in patients with non-infectious uveitis
- 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 with three months additional stability data in Q4, 2020



Maximizing Commercial Potential of XIPERE™

The Opportunity: XIPERE Commercialization & Development

- Exclusive license for XIPERE commercialization and development in the U.S. and Canada
- Exclusive options for (i) Europe and the United Kingdom, (ii) Australia and New Zealand, (iii) South America & Mexico
- 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:

- Received \$5M upfront payment
- Up to \$15M in FDA approval and pre-launch milestones
- Up to \$57.3M in milestone payments
- Tiered royalties at increasing percentages from the high-teens to 20% on annual net sales





Maximizing Commercial Potential of XIPERE™

The Opportunity: XIPERE Commercialization & Development in Greater China and South Korea

- Exclusive license to develop and commercialize XIPERE for indications associated with uveitis in Greater China (mainland China, Hong Kong, Macau and Taiwan) and South Korea
- Right to develop and commercialize XIPERE for additional ophthalmic indications in Greater China and South Korea, with consent from Clearside

The Terms:

- Received \$4M upfront payment
- Up to \$31.5M in approval, development and sales milestones
- Tiered royalties of 10% to 12% based on annual net sales starting at product launch and going until the later of ten years after launch or loss of patent protection or marketing exclusivity in the territory





Four Partnering Deals to Drive Growth







Validates our investment in suprachoroidal delivery using our **SCS** Microinjector



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

Expands our overall internal and collaborative product development pipeline

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





Strong Intellectual Property Coverage of SCS Platform





Experienced Leadership Team



GEORGE LASEZKAY

Pharm.D., J.D. | CEO and Director 30 years experience Allergan, Acucela, Novagali, Amakem, RetroSense



THOMAS CIULLA

M.D., MBA | Chief Medical Officer 27 years experience

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



CHARLES DEIGNAN

Chief Financial Officer

27 years experience AtheroGenics, AAIPharma, Schering-Plough



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



LESLIE ZACKS General Counsel & Chief Compliance Officer

24 years experience Arbor, Shionogi

Clearside Team Ophthalmic Experience



🤹 Allergan

CIBA OVISION.









Research and Development Investment Highlights

Versatile therapeutic platform with proprietary access to the suprachoroidal space

Patented technology & delivery approach

Scientific presentations and publications

1Q 20

✓ Ophthalmology
✓ Angiogenesis
✓ Macula Society
2Q 20: ARVO
3Q 20: ASRS & Retina Society

4Q 20: AAO

Building an internal R&D pipeline

Mid 2020: IND submission for CLS-AX

2H 20: Initiation of Phase 1/2 trial for CLS-AX

Exploratory preclinical nonviral vector delivery studies ongoing Partnering to expand use of SCS platform

REGENXBIO: RGX-314* 1H 20: Initiate Phase 2 trial in wet AMD

Mid 20: Submit IND in DR

2H 20: Initiate P2 in DR

AURA: AU-011[^] 2H 20: Initiate clinical testing in choroidal melanoma





