GenSight BIOLOGICS

Corporate Presentation

November 2019

A LEADING GENE THERAPY BIOTECHNOLOGY COMPANY

GENSIGHT-BIOLOGICS.COM

Disclaimer

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GenSight BIOLOGICS

Corporate Overview

Clinical-stage gene therapy company

- Focused on severe retinal degenerative pathologies leading to blindness as well as CNS diseases
- Well positioned to advance disruptive gene therapy technologies in ophthalmology to commercialization

Two disruptive technology platforms

- Mitochondrial targeting sequence (MTS)
- Optogenetics

Lead projects target:

- GS010 - Leber Hereditary Optic Neuropathy (Phase III)
- GS030 - Retinitis pigmentosa and dry-AMD (Phase I/II)

Listed on Euronext Paris (SIGHT)

- Established in 2012, IPO in July 2016 (EUR45m)
- GenSight Biologics Inc incorporated in the US in May 2017

GenSight BIOLOGICS

Executive Team

Bernard Gilly
Chief Executive Officer

PIXIUM VISION (Since 2011)
Chairman of the Board, Founder

FOVEA PHARMA (2005-2009)
Chairman & CEO – sold to Sanofi

SOFINNOVA PARTNERS (2000-2005)
Managing Partner

TRANSGENE (1992-2000)
Chairman & CEO

Ph.D. in biology and bio-economics

Thomas Gidoin
Chief Financial Officer

DBV TECHNOLOGIES (2012-2015)
VP of Finance

IPSEN (2008-2011)
UK Operations Controller (London)
Senior Financial Analyst (Paris)

ERNST & YOUNG (2007-2008)
Auditor

Magali Taiel
Chief Medical Officer

ProQR THERAPEUTICS (2016-2018)
VP of Clinical Development

ELI LILLY (2004-2016)
Medical Department Lead

PFIZER (2001-2004)
Medical Advisor

SERVIER (1999-2001)
R&D International Project Manager

MD, Board-certified ophthalmologist

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Our target: degenerative retinal diseases with underlying genetic causes

LEBER HEREDITARY OPTIC NEUROPATHY (LHON)

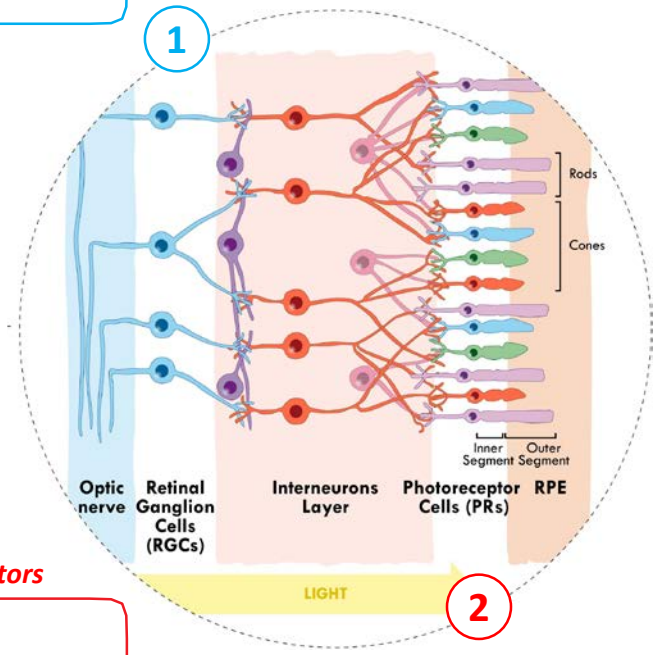
1. Degeneration of RGCs

Genetic mutations
Aging

2. Degeneration of photoreceptors

RETINITIS PIGMENTOSA (RP)

GEOGRAPHIC ATROPHY
(Late stage form of Age-Related Macular Degeneration - AMD)



✓ **Unmet need: high**

- Inexorable progression to blindness for most patients
- No approved treatments*

✓ **The eye: an ideal laboratory**

- Immune-privileged, closed system
- Intravitreal injections to introduce of genetic material close to target cells
- Slow turnover of retinal cells support long-term expression of transduced genes

✓ **AAV: proven vector for gene therapy**

- Proven safety and proof of effect in humans
- Efficient transduction of retinal cells
- No need to screen patients for Nab before treatment
- Validated manufacturing process

Source: Company
*Except for exceptional circumstances for idebenone in Europe

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Pipeline: solid and advanced product portfolio in ophthalmic gene therapy

Technology	Product Candidate	Indication	*Research*	*Preclinical*	*Phase I/II*	*Phase III*	*Registration*	Next Expected Events
MTS platform	**GS010** (FDA & EMA Orphan Drug Designation)	**LHON ND4**	→	→	→	→		**REVERSE**: Phase III top-line data reported in Apr (48w) & Oct (72w) 2018 and in May 2019 (96w) **RESCUE**: Phase III top-line data reported in Feb (48w), Apr (72w) and Sep (96w) 2019 **REFLECT***: Phase III recruitment completed in July 2019, top-line data expected in Q3 2020
	GS011	**LHON ND1**	→					Initiate preclinical studies following GS010 Phase III clinical data
	Undisclosed Mitochondrial Target	Undisclosed	→					
Optogenetics	**GS030** (FDA & EMA Orphan Drug Designation)	**RP**	→	→	→			**PIONEER**: Second cohort ongoing in PIONEER Phase I/II clinical trial. Report interim data one year after last subject treated
	GS030	**Dry AMD & Geographic Atrophy**	→					

*Conducting this trial under a special protocol assessment with the FDA

Lead candidate, GS010, is expected to file for MAA in Europe in the coming year

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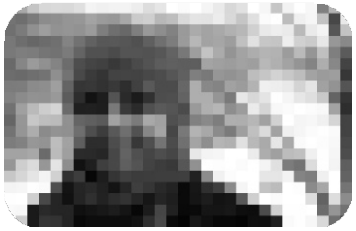
GS010

Fully enrolled Phase III trials for our lead product candidate dedicated to Leber Hereditary Optic Neuropathy (LHON)

GS010 aim: treat LHON, the most common mitochondrial disease causing bilateral blindness in the prime of life



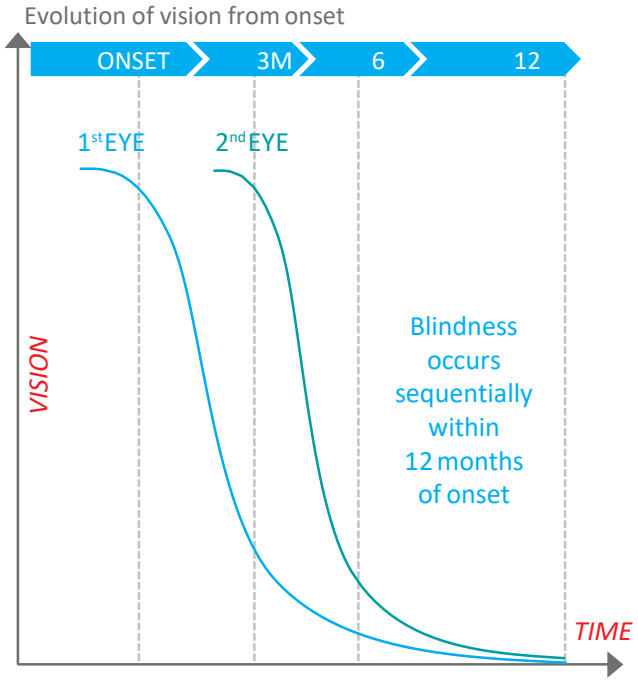


Image source: illustrated from Newamn NJ et al., Am J Ophthalmom. 141(6), 1061-1067,2006

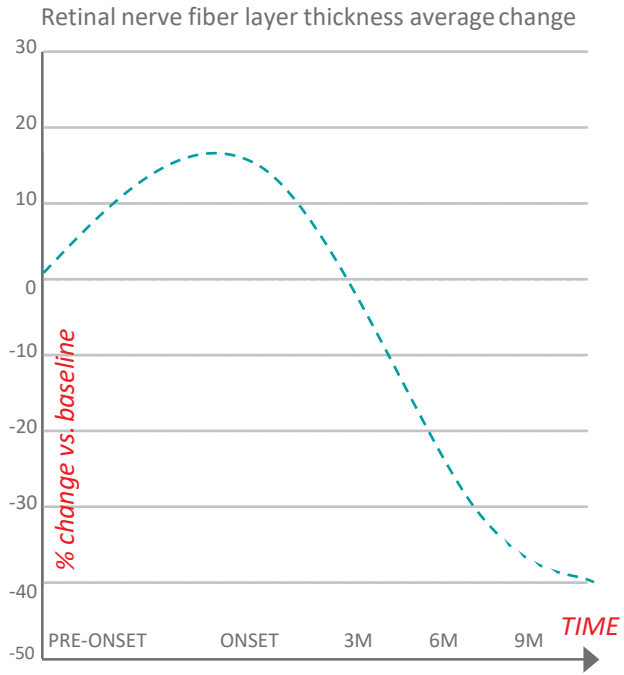


Image source: illustrated from Barboni et al Natural History of Leber's Hereditary Optic Neuropathy: An OCT Study

Incidence	0.15/100,000
Prevalence	1/31k-40k
Blindness	15-35y

- **Orphan maternally inherited mitochondrial disease**
- **Painless sudden loss of central vision** in the 1st eye with 2nd eye sequentially impaired: **symmetric disease with poor visual recovery**
- **Thinning of the Ganglion Cell Layer** occurs after the onset of vision loss and stabilizes at approximately 6 months
- **97%** of patients have bilateral involvement < 1 year / 25% of cases are simultaneous
- **Targets ND4** which accounts for ~75% of LHON in North America & Europe

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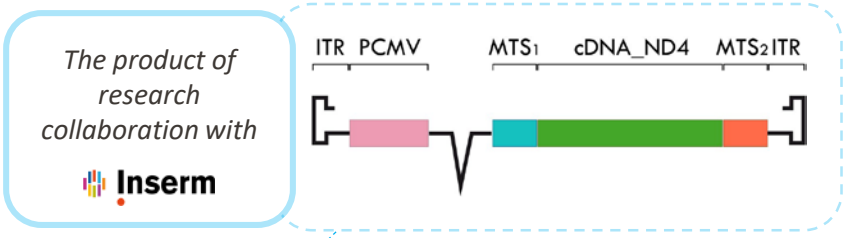
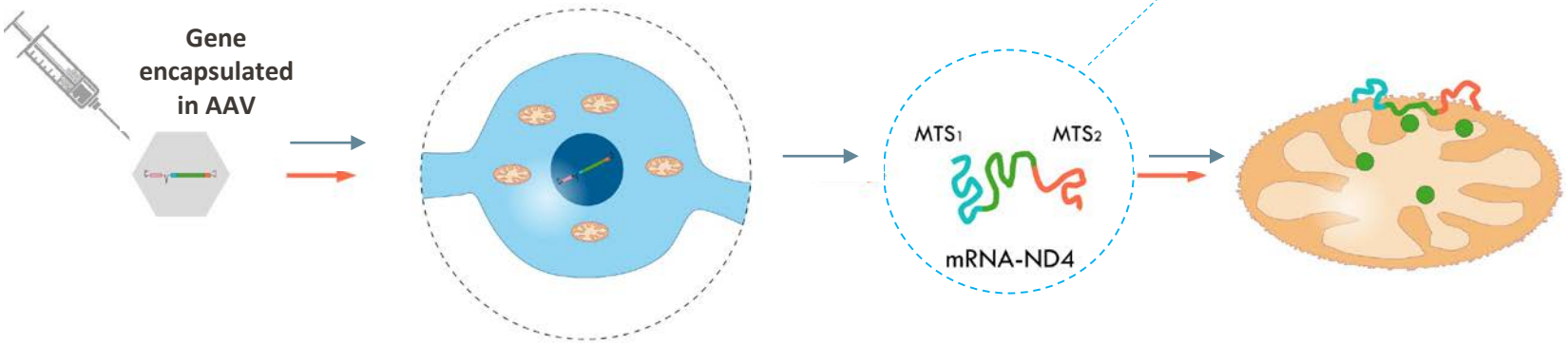
Solution: Gene therapy to produce working mRNA, with ***MTS* technology*** to shuttle mRNA directly to affected mitochondria

MTS in action for GS010:

The product of research collaboration with Inserm





Step 1

Retinal cell transduced with vector containing wild-type mitochondrial gene

Step 2

Wild-type mitochondrial gene transcribed in the nucleus

Step 3

Wild-type mRNA **delivered by MTS directly** to polysomes located at the mitochondrial surface, where protein synthesis occurs

Step 4

Finally, the wild-type mitochondrial protein is translocated inside the mitochondrion, where it **restores energy production**

Gene therapy

*MTS**

*MTS = mitochondrial targeting sequence

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RESCUE & REVERSE Phase III trials

Time-based strategy to assess GS010 efficacy

Different patient inclusion criteria → **Same design** → **Same endpoints at Week 48**

REVERSE

- Onset of disease
  6 months to ≤ 1 year
- 37 patients enrolled
- Fully enrolled Feb 2017

RESCUE

- Onset of disease
  ≤ 6 months
- 39 patients enrolled
- Fully enrolled July 2017

- Double-masked, multi-center
- One eye randomized to GS010; other eye received sham injection

Group 1

GS010 in right eye

SHAM in left eye

Group 2

SHAM in right eye

GS010 in left eye

Primary

- Mean difference change from baseline, ETDRS letters, drug treated eyes vs. sham treated eyes (LogMAR used for statistical analysis) at Week 48

Secondary

- SD-OCT, visual field, color and contrast vision
- Responders analysis:
  - Gain from baseline of 15 or more ETDRS letters
  - Snellen acuity > 20/200
- Treated vs. sham eyes' BCVA for best-seeing and worst-seeing eyes
- Quality of life assessments

Source: Company

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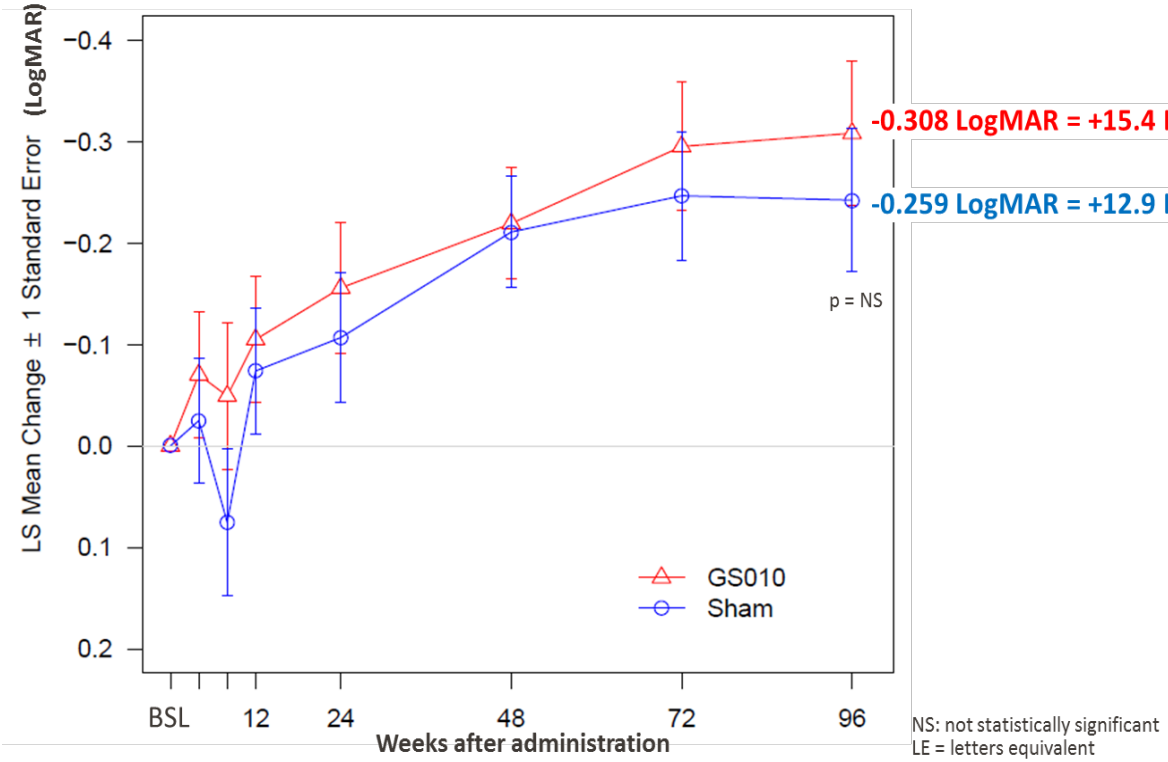
Visual Acuity: REVERSE 96-week

Visual Acuity bilaterally improved by +15 and +13 ETDRS letters equivalent from baseline to Week 96 in GS010- and sham-treated eyes, respectively, sustaining the gain at Week 72

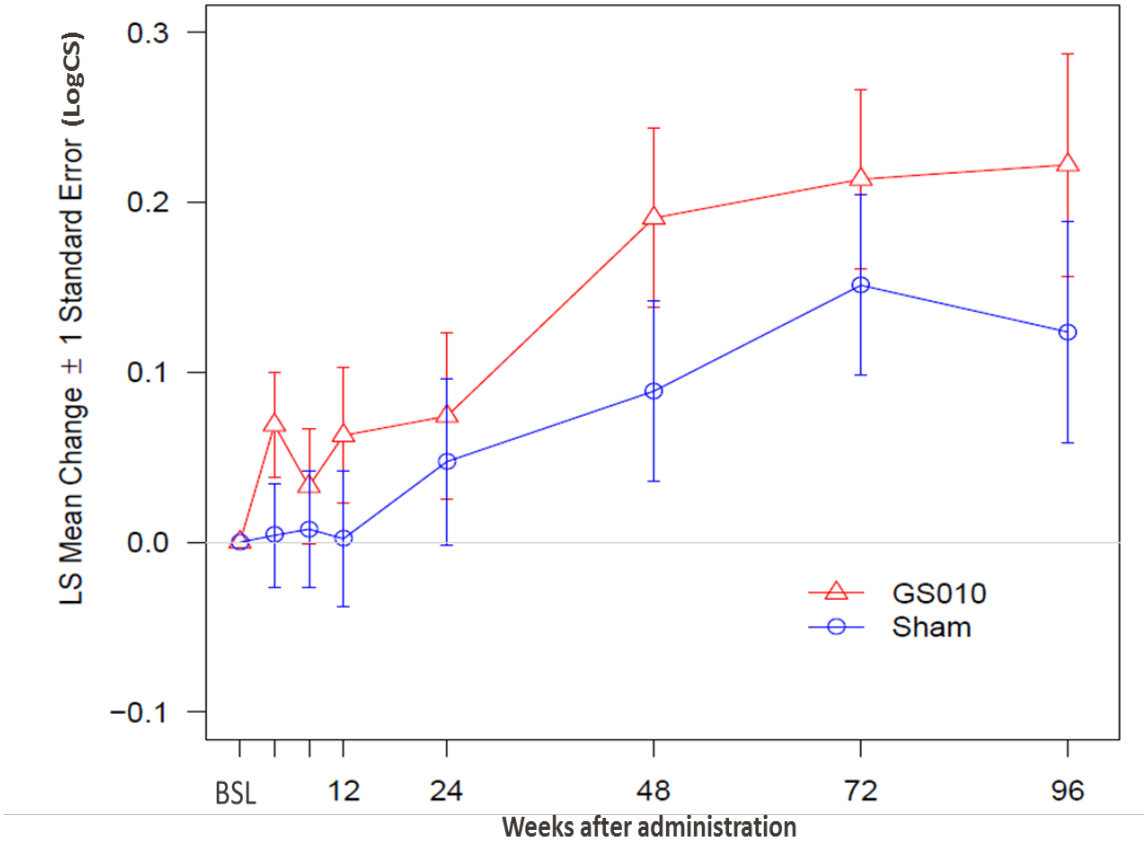


NS: not statistically significant
LE = letters equivalent

Mean visual acuity (BCVA) among GS010-treated eyes and sham-treated eyes evolved with similar trajectories, worsening to a post-treatment low point, or nadir, before recovering at Week 96 by +28 and +24 ETDRS letters equivalent, respectively

Contrast Sensitivity: REVERSE 96-week

Like BCVA, contrast sensitivity (Pelli-Robson) showed a bilateral trend, improving from baseline to Week 96 in both GS010-treated and sham eyes



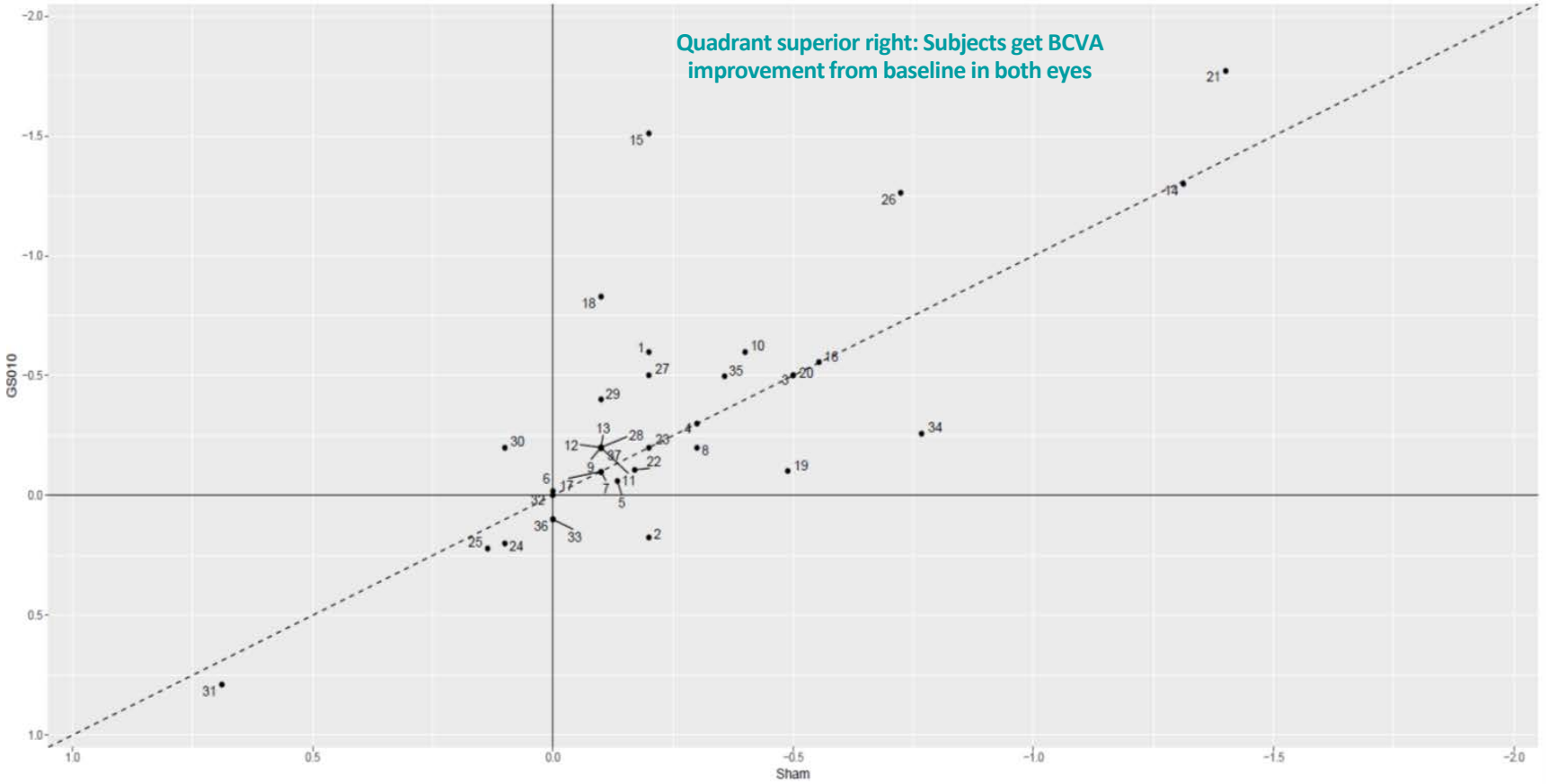
Mean contrast sensitivity for GS010-treated eyes showed a more robust improvement versus baseline over the course of the trial comparing to sham-treated eyes

Responder Analysis: Subjects Mapping in REVERSE at 96 weeks

Visual Acuity Change of Sham eyes was correlated with that of GS010 eyes in most REVERSE subjects
Subjects are well concentrated around the mean

REVERSE – Scatterplot of Change from Baseline at Week 96

Pearson Corr Coeff = 0.776; p – 1.677^{e}-08 / Spearman Corr Coeff = 0.727; p = 3.492^{e}-07



Natural History: REVERSE 96-week

Comparison to natural history based on a study by Santhera[1]

- In a **natural history study** conducted by Santhera[1], **15% of subjects** with the ND4 (*11778A*) mutation achieved the following definition of "clinically relevant recovery" (CRR) from baseline in at least one eye:
  - » Improved by at least 10 ETDRS letters from their on-chart visual acuity, or
  - » Improved from an off-chart level of visual acuity to being able to read at least 5 ETDRS letters (on-chart)

By comparison …

- **68% of REVERSE subjects** achieved this definition of CRR at Week 96, with GS010-treated eyes significantly more likely to achieve this than sham-treated eyes (62% vs. 43%, p = 0.0348, statistically significant difference).

"The data show that both the treated and the sham eye improved in both high and low contrast, defying the accepted natural history of this disease and improving upon it, based upon the clinical experiences of generations of neuro-ophthalmologists."

Dr. Robert C. Sergott

Director, Wills Eye Hospital, Neuro-Ophthalmology and Director, William H. Annesley, Jr, EyeBrain Center, Thomas Jefferson University, Philadelphia, PA

REVERSE subjects experienced a significantly higher rate of "clinically relevant recovery" than natural history

(1) Silva et al (2019), "Natural History of Leber's Hereditary Optic Neuropathy (LHON): Findings from a Large Patient Cohort", Poster presented at NANOS March 16-21, 2019; Poster Session II: Scientific Advancements; Poster: 163

Quality of Life: REVERSE 96-week

Sustained Quality of Life improvement

- Composite score and relevant sub-scores in the National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25) showed sustained improvements versus baseline at Week 48, Week 72 and Week 96
- Magnitudes of mean score improvement observed with GS010 correlate with clinically meaningful improvements in best-corrected visual acuity (BCVA)

NEI VFQ-25 Results from REVERSE

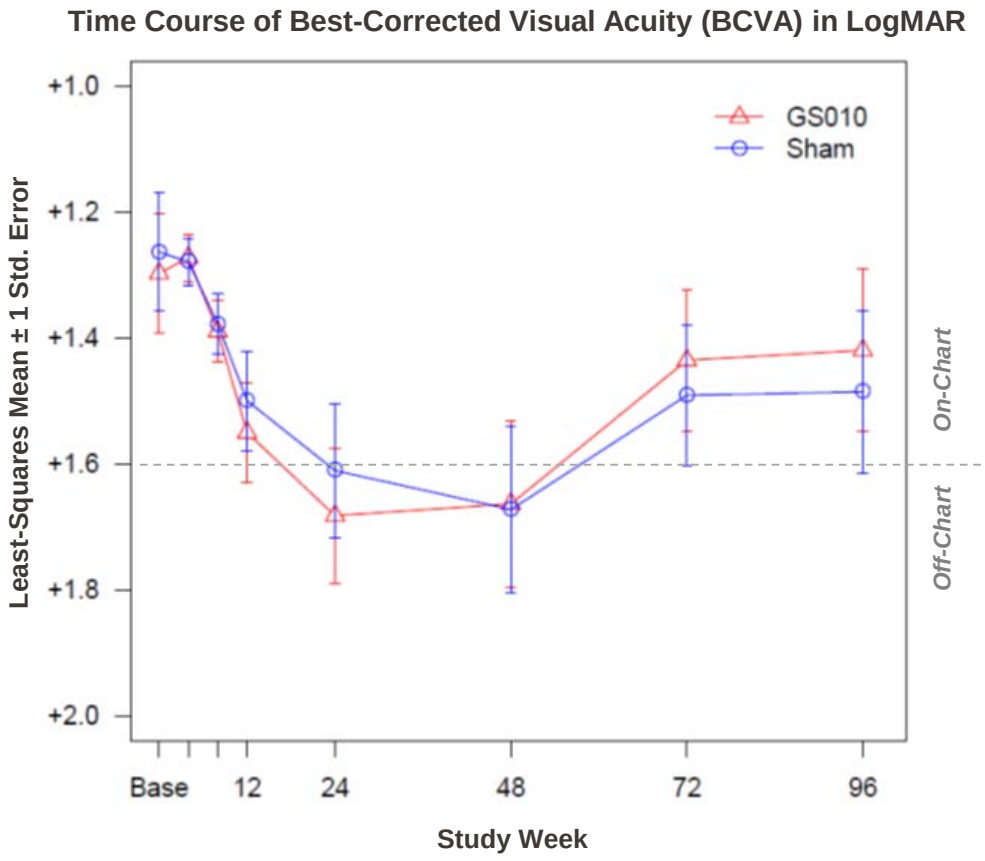
Mean change from baseline (absolute score and percent)

	Composite Score**	Near Activities	Distance Activities	Dependency	Role Difficulties	General Vision	Mental Health
Week 48	+7.2 *+23.2%*	+10.4 *+65.1%*	+9.6 *+49.8%*	+12.4 *+100.6%*	+14.5 *+65.0%*	+10.3 *+50.9%*	+11.2 *+81.9%*
Week 72	+8.1 *+25.2%*	+9.5 *+58.1%*	+8.2 *+42.5%*	+18.9 *+130.2%*	+15.2 *+70.9%*	+11.9 *+54.1%*	+15.2 *+105.6%*
Week 96	+9.5 *+28.8%*	+13.3 *+78.1%*	+10.7 *+47.4%*	+18.5 *130.2%*	+15.9 *+78.9%*	+6.5 *+32.4%*	+16.1 *+108.2%*
Clinically relevant difference*	+3.90 to +4.34	+4.67 to +6.06	+5.15 to +5.38	+4.72 to +4.98	+3.31 to +4.70	+4.38 to +4.82	+4.70 to +4.88

*Suñer *et al.* (2009): clinically relevant score differences based on a clinically significant 15-letter BCVA improvement at 12 months.
**The composite score is an average of the vision-targeted sub-scale scores, excluding the general health rating question.

Visual Acuity: RESCUE 96-week

Visual Acuity bilaterally improved by +26 and +23 ETDRS letters from nadir to week 96 in GS010- and sham-treated eyes, respectively. Mean visual acuity has transitioned **from off-chart to on-chart.**



Mean visual acuity (BCVA) among GS010-treated eyes and sham-treated eyes evolved with similar trajectories, worsening to a lowest point, or nadir, before significantly improving to week 96 – coherent with REVERSE

Natural History: RESCUE 96-week

Comparison to LHON Natural History

- In a natural history study conducted by Santhera[(1)], **28% of subjects** with the ND4 (*11778A*) mutation achieved the following definition of "clinically relevant recovery" (CRR) from nadir in at least one eye:
  - »Improved by at least 10 ETDRS letters from their visual acuity, or
  - »Improved from an off-chart level of visual acuity to being able to read at least 5 ETDRS letters

- **63% of RESCUE subjects** achieved this definition of CRR at Week 96, with GS010-treated eyes as likely to achieve this as sham-treated eyes (58% vs. 45%, p = 0.0956).

"Patients in RESCUE were treated before the nadir so, as expected, they continued to worsen early on. But then from week 48 until week 96 they experienced a recovery from the nadir. That is much better than the natural history in any prior studies."

Dr. Mark L. Moster

Neuro-Ophthalmology, Wills Eye Hospital, Professor of Neurology and Ophthalmology at Thomas Jefferson University, Philadelphia, PA, and Principal Investigator in the REVERSE and RESCUE trials

RESCUE subjects experienced a significantly higher rate of "clinically relevant recovery" than natural history

(1) Silva et al (2019), "Natural History of Leber's Hereditary Optic Neuropathy (LHON): Findings from a Large Patient Cohort", Poster presented at NANOS March 16-21, 2019; Poster Session II: Scientific Advancements; Poster: 163

Visual Acuity: Improvement from Baseline

REVERSE: Continuous bilateral improvement of Visual Acuity up to Week 96
RESCUE: Worsening VA compared to baseline reflects brutal progression of LHON

LS Mean (SE) [a]	Change from BASELINE					
	Week 72			Week 96		
	n	LogMAR	ETDRS Letters Equivalent	n	LogMAR	ETDRS Letters Equivalent
GS010 Eyes	37	-0.294 (0.063)	**+15**	37	-0.308 (0.068)	**+15**
Sham Eyes	37	-0.246 (0.063)	**+12**	37	-0.259 (0.068)	**+13**

LS Mean (SE) [a]	Week 72			Week 96		
	n	LogMAR	ETDRS Letters Equivalent	n	LogMAR	ETDRS Letters Equivalent
GS010 Eyes	34	+0.192 (0.104)	**-10**	34	+0.168 (0.132)	**-8**
Sham Eyes	33	+0.216 (0.104)	**-11**	34	+0.238 (0.132)	**-12**

[a] Efficacy Endpoint was assessed using a mixed model of analysis of covariance (ANCOVA), with change from baseline at week of interest as the response, and subject, eyes of the subject as random factor, treatment and the baseline LogMAR value as covariates.
Missing data were not imputed.

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Visual Acuity: Recovery from Nadir

Visual Acuity deteriorates to a low point before recovering significantly in both eyes

REVERSE 6-12 MONTHS	Change from NADIR [a]					
	Week 72			Week 96		
Mean (SD) [b]	**n**	**LogMAR**	**ETDRS Letters Equivalent**	**n**	**LogMAR**	**ETDRS Letters Equivalent**
GS010 Eyes	37	-0.553 (0.444)	**+27.6**	37	-0.566 (0.450)	**+28.3**
Sham Eyes	37	-0.478 (0.498)	**+23.9**	37	-0.490 (0.480)	**+24.5**

RESCUE 0-6 MONTHS	Week 72			Week 96		
Mean (SD) [b]	**n**	**LogMAR**	**ETDRS Letters Equivalent**	**n**	**LogMAR**	**ETDRS Letters Equivalent**
GS010 Eyes	34	-0.509 (0.496)	**+25.4**	34	-0.526 (0.479)	**+26.3**
Sham Eyes	33	-0.452 (0.495)	**+22.6**	34	-0.457 (0.485)	**+22.8**

[a] NADIR: Nadir was defined as the **lowest Visual Acuity** value **from baseline** up to Week of interest. LP/NLP vision was assigned a LogMAR value of 4.0 and 4.5 respectively.
[b] Mean change from nadir was calculated using observed values (no data were imputed).

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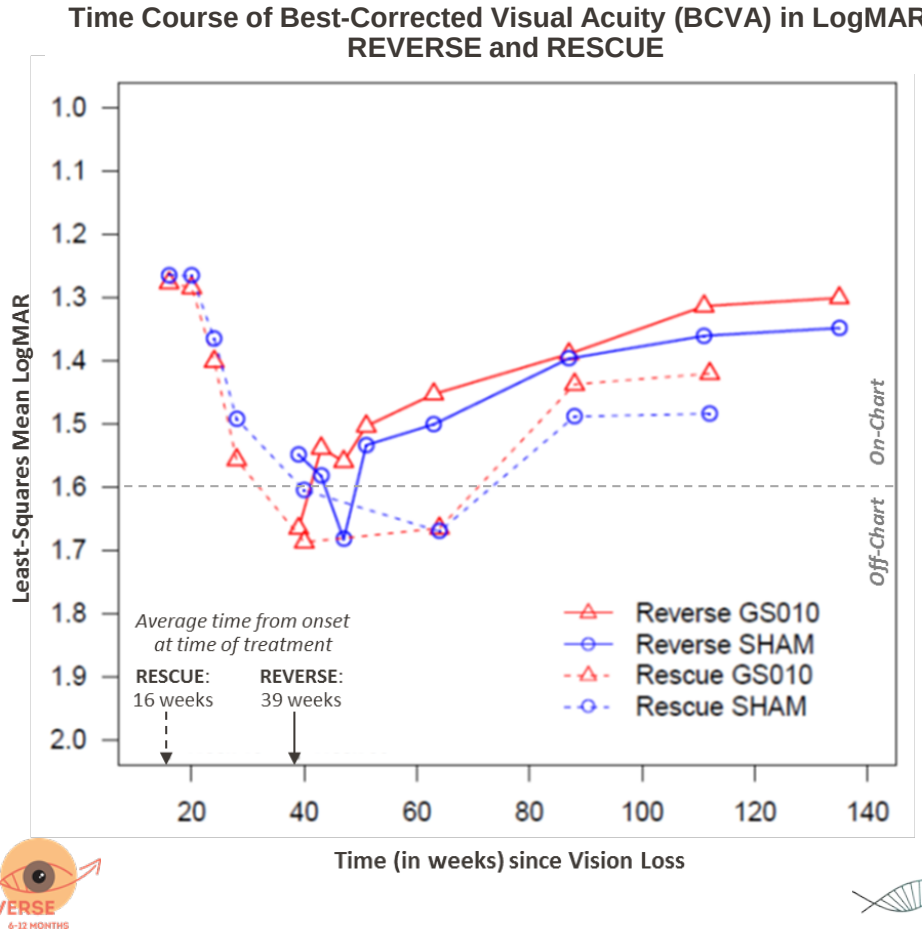
Visual Acuity: Time Course in LogMAR values in REVERSE and RESCUE

REVERSE and RESCUE show coherent pattern of meaningful and durable bilateral visual recovery from nadir



LogMAR All eyes Baseline	GS010 1.67 (0.50)	Sham 1.55 (0.42)	All 1.61 (0.46)

LogMAR All eyes Baseline	GS010 1.31 (0.52)	Sham 1.27 (0.62)	All 1.29 (0.57)

Safety: REVERSE & RESCUE

Favorable safety and tolerability profile

- GS010 was well tolerated throughout both studies
- No serious adverse events in GS010-treated eyes, and no discontinuation due to ocular events
- Most frequently seen ocular adverse events in the therapy group were mainly related to the injection procedure
- Except for the occurrence of intraocular inflammation:
  - likely related to GS010
  - accompanied by elevation of intraocular pressure in some patients
  - responsive to conventional treatment and without sequelae
- No systemic serious adverse events or discontinuations that were related to study treatment or study procedure.

GS010 was well-tolerated through 96 weeks after injection

Efficacy key findings: REVERSE & RESCUE

REVERSE: 96-Week Follow-Up

- **Sustained bilateral improvement in visual acuity (BCVA) at Week 96**
  - **Versus baseline: +15 ETDRS letters equivalent** in GS010 eyes and **+13 ETDRS letters equivalent** in sham eyes
  - **Versus nadir: +28 ETDRS letters equivalent** in GS010 eyes and **+24 ETDRS letters equivalent** in sham eyes
- **68% of REVERSE subjects** attained **Clinically Relevant Recovery (CRR) from baseline** in at least one eye**, compared to 15%** in a **natural history** study
- **78% of REVERSE subjects** attained **Clinically Relevant Recovery (CRR) from nadir** in at least one eye**, compared to 28%** in a **natural history** study
- Patients' **quality of life** scores continue to increase, especially in **ability to carry out vision-related activities**
- **Preservation of anatomy for both eyes, as observed for retinal layers of interest: GCL, Temporal and PMB RNFL**

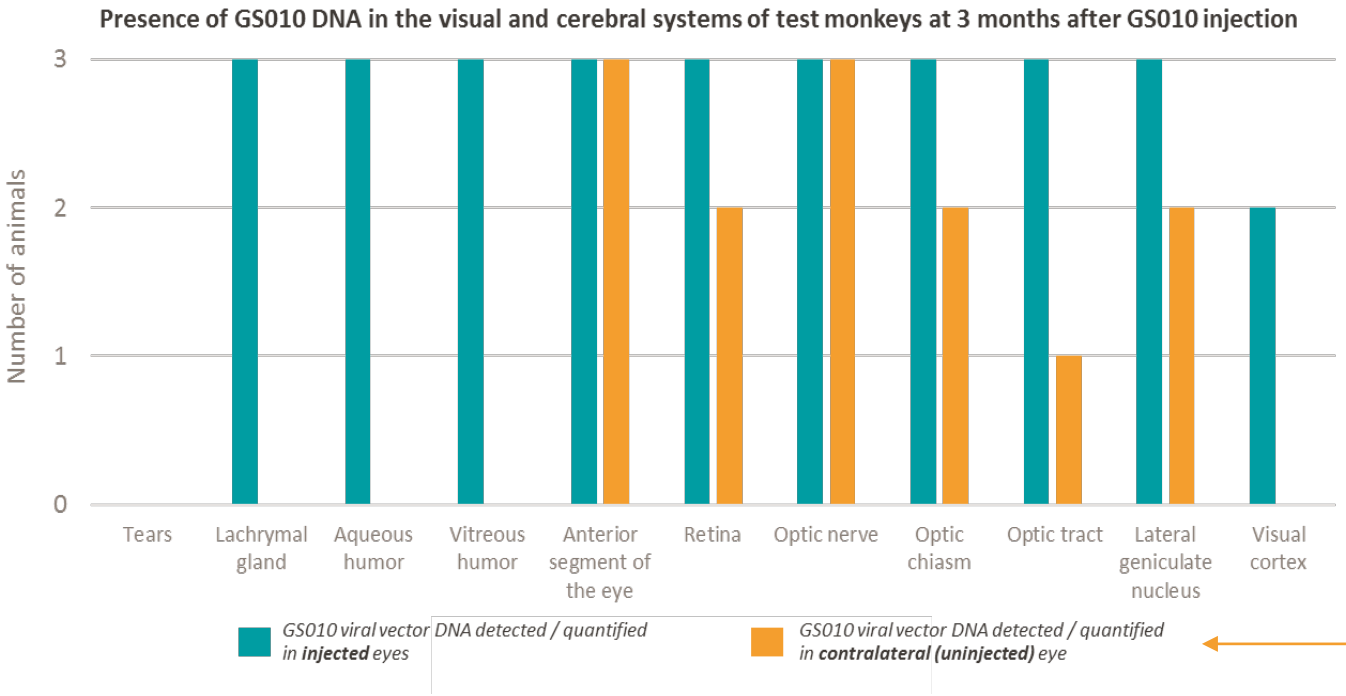
RESCUE: 96-Week Follow-Up

- **Sustained bilateral improvement** in **BCVA from Week 48 to Week 96**
  - **From Week 48 to Week 96: +10 ETDRS letters equivalent** in GS010 eyes and **+9 ETDRS letters** equivalent in sham eyes
- **Compelling bilateral improvement in BCVA** from **Nadir**
  - **Versus nadir: +26 ETDRS letters equivalent** in GS010 eyes and **+23 ETDRS letters equivalent** in sham eyes
- Clinically Relevant Recovery (CRR) from Nadir[1]
  - **63% RESCUE subjects attained CRR**
  - **compared to 28%** in a **natural history** study
- **Preservation of anatomy for both eyes, as observed for retinal layers of interest: GCL, Temporal and PMB RNFL**

[1] "Nadir" here is defined as the worst observed BCVA from baseline to the week of interest, including baseline. When the baseline is excluded from consideration, the proportion of RESCUE subjects achieving CRR is 58%.

GS010 Local Biodistribution: Evidence from Non-Clinical Primate Study

Viral vector DNA detected in uninjected eye → potential mechanism for bilateral effect in REVERSE and RESCUE



- Three test monkeys injected in <u>one</u> eye using dose equivalent of treatment in REVERSE and RESCUE trials
- Highly sensitive validated test for presence of GS010 DNA used on tissue samples from primates in study

- **Key finding:**
  - **GS010 viral vector DNA was detected/quantified in many tissue samples from contralateral (uninjected) eye**

"The presence of viral vector DNA in the optic chiasm and optic nerve of the contralateral uninjected eye points towards a possible diffusion pathway."

Dr. Patrick Yu-Wai-Man, Senior Lecturer & Honorary Consultant Ophthalmologist at the University of Cambridge, Moorfields Eye Hospital, and the UCL Institute of Ophthalmology, London, UK

Notes: One control monkey was injected in one eye with saline solution. Three test monkeys were injected with GS010 in one eye using dose allometrically equivalent to that used in REVERSE and RESCUE. Tissue samples were taken at 3 months after injection and tested using a protocol that specifically targeted the CMV promoter of the GS010 DNA. The sensitivity, specificity and accuracy of the test were validated in a dedicated study.

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REFLECT Phase III trial: assess efficacy and safety of bilateral injection

Double-masked, confirmatory study under Special Protocol Assessment from FDA

Patient inclusion criteria

- **98 patients** with vision loss ≤ 1 year
- **Initiation:** 4Q 2017 (1st patient treated in March 2018)
- Recruitment completed in July 2019

Design

Group 1

GS010 in first affected eye

GS010 in second affected eye

First affected eye always treated with GS010

Second affected eye randomized between GS010 and placebo

GS010 in first affected eye

Placebo in second affected eye

Group 2

Endpoints at Week 52

Primary

- Difference in change of vision compared to baseline between GS010 Treatment vs. Placebo in second affected/not yet affected eyes
  (LogMAR visual acuity used for statistical analysis)

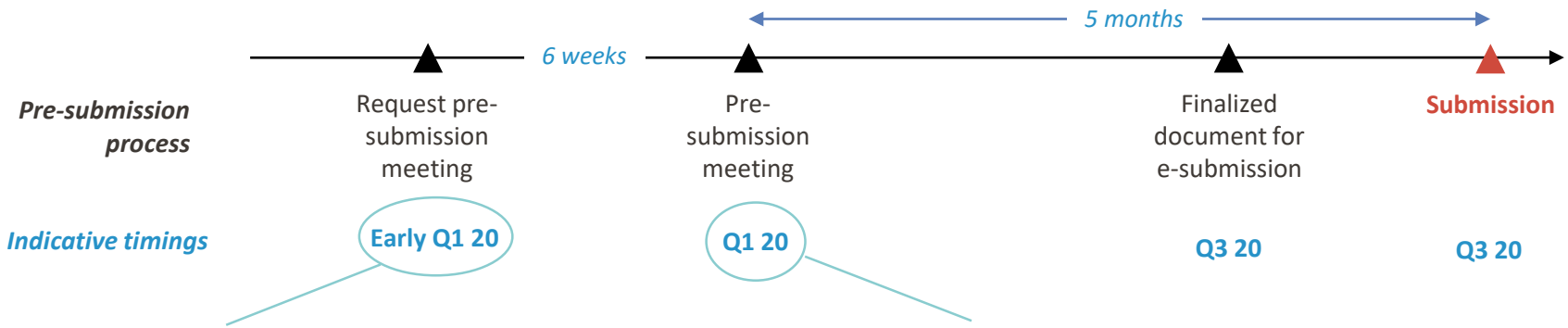
Secondary

- Best Corrected Visual Acuity at 2 years
- Spectral domain OCT biomarkers
- Humphrey visual field analysis
- Pelli Robson Low Vision Contrast Sensitivity
- Quality of life assessments

Source: Company

Engagement with EMA

Preparing for submission



Topics to be prepared

- Draft overviews for clinical, non-clinical and CMC data
- Draft SmPC, patient information leaflet, packaging
- Pediatric updates
- Information related to Conditional Marketing Authorisation and orphan market exclusivity
- Pharmacovigilance and other risk management aspects

Outcomes

- Assigned rapporteur
- Administrative guidance for dossier

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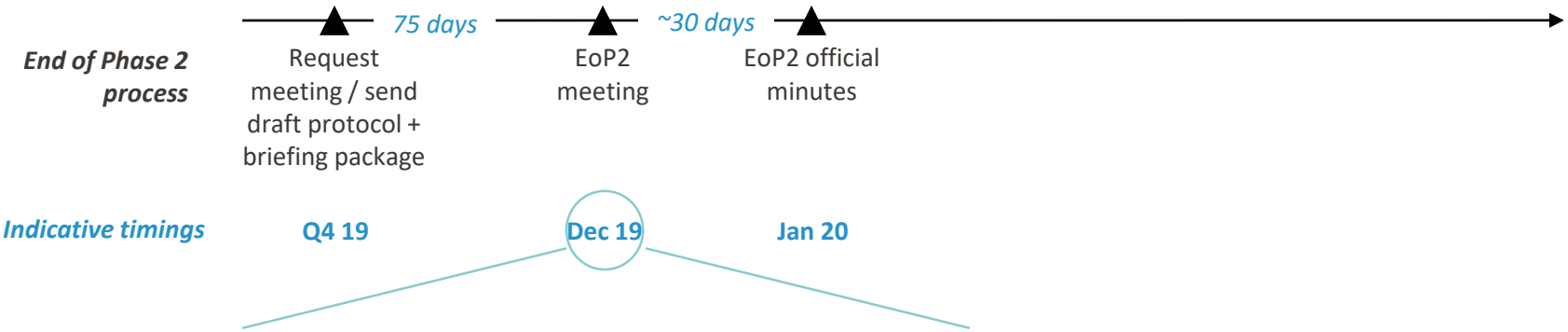
Engagement with FDA

Type B meeting to provide updates



Clinical updates

- **Objective**: provide updates relevant to clinical strategy
- **Topics**
  - REVERSE and RESCUE results to date
  - Implications for REFLECT
  - Investigations into contralateral effect
  - Potential new study with a more robust control arm

CMC updates

- **Objective**: provide updates on CMC
- **Topics**
  - Comparability protocol
  - Update on potency assay
  - Align on data to be available at time of submission
  - Discuss further data needs

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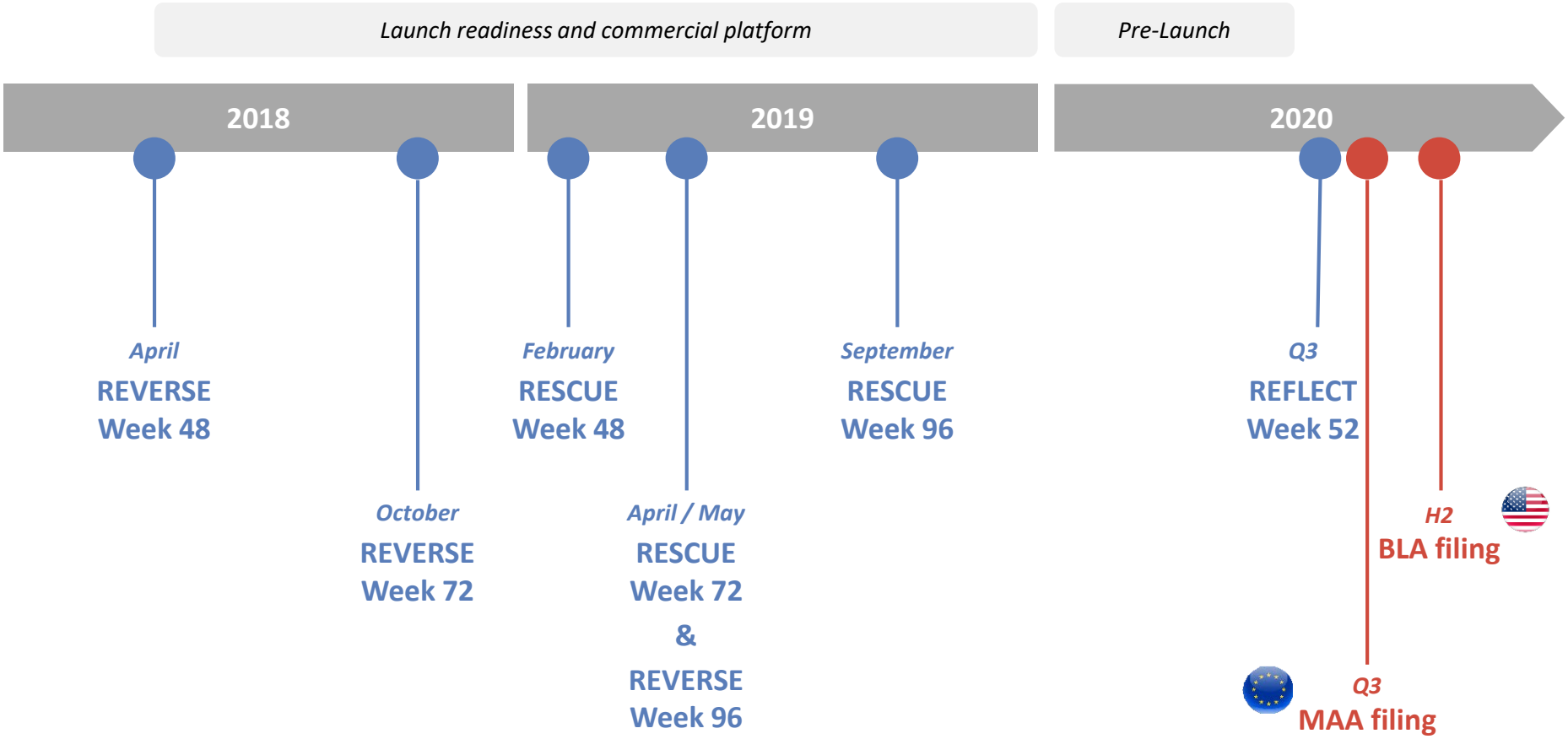
GS010 Path to Market

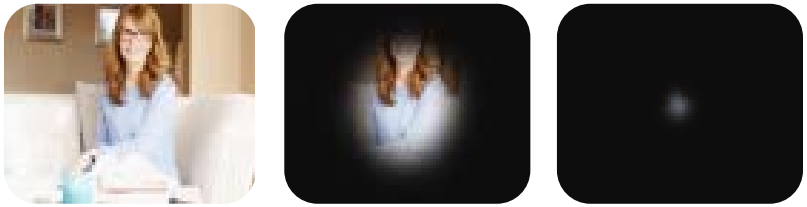


GS030

Second lead product candidate targeting photoreceptor degenerative diseases (RP/AMD)

GS030 aim: treat degenerative diseases of photoreceptors that lead to blindness

Retinitis Pigmentosa



- Blinding genetic disease caused by mutations in over 100 different genes
- Sequential photoreceptor degeneration leads to slow & irreversible progression to blindness, usually at age 40-45
- 15-20,000 new patients each year in the US and EU

Geographic Atrophy (GA) in AMD (Age-Related Macular Degeneration)

- Early (dry-form) AMD evolves with age into late AMD, one of whose forms is GA
- AMD strikes 350-400,000 new patients a year, most of them at 55-60 years of age
- Prevalence of GA increases with age, from 3.5% among 75-year-olds to 22% among those over 90
- Late AMD patients with GA account for 10-20% of blind patients in their age group

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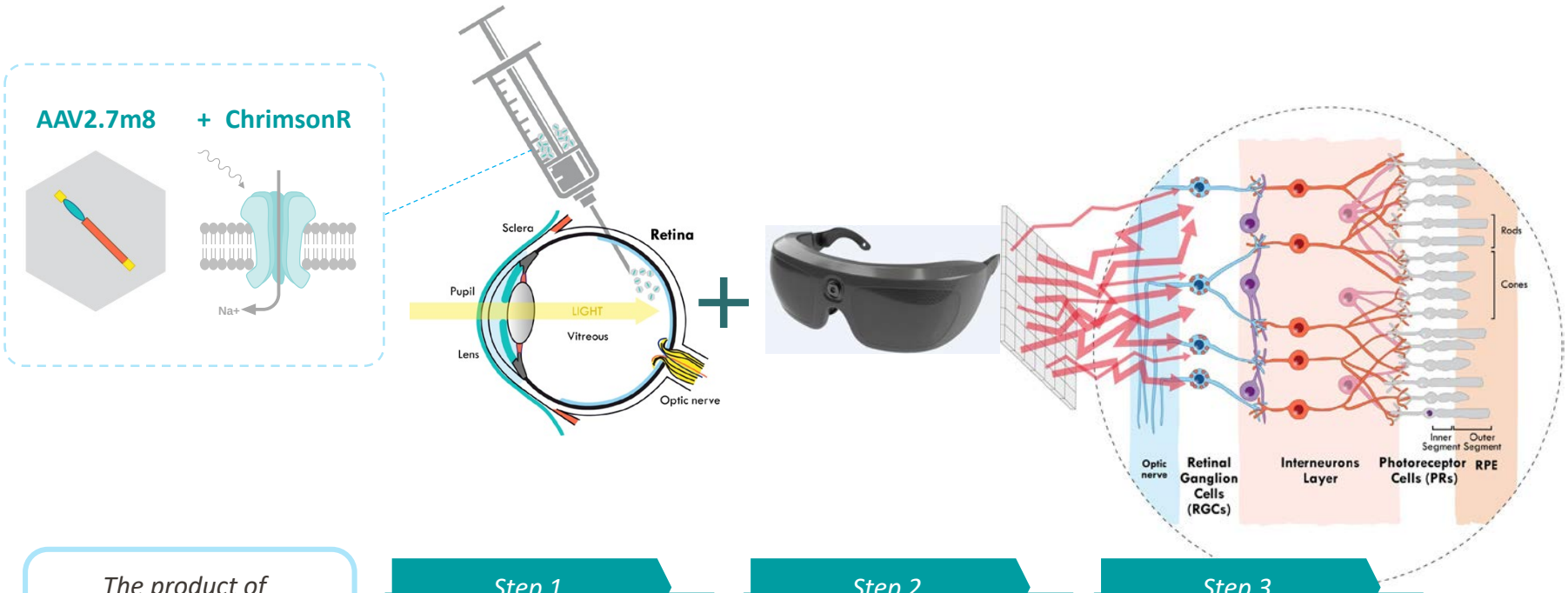
Optogenetics using GS030: gene therapy-based approach to restore light sensitivity



The product of research collaboration with

Massachusetts Institute of Technology

ADVERUM BIOTECHNOLOGIES

UPMC

Step 1

Gene therapy transfer of the gene that encodes light-sensitive protein **Expression** in retinal ganglion cells (RGCs)

Step 2

Stimulation with **optoelectronic device** to transform external light stimuli into signal that can activate the RGCs

Step 3

Retinal output sent to brain for image processing

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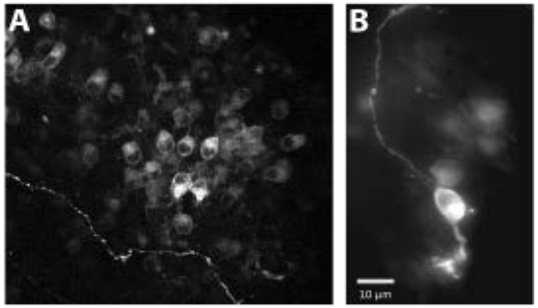
GS030: activated RGCs provide visual information to the higher visual centers

Localization of light-sensitive protein in NHP retina

Expression of ChrR-tdT in midget cells of monkey perifovea

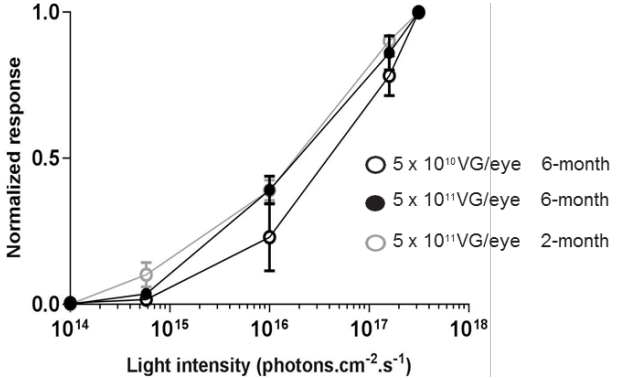
In vivo in NHP assessment 6 months after IVT injection



Dose-ranging response to firing relationship in NHP

Active dose range : $5x10^{10}$ and $5x10^{11}$ VG/eye

MEA assessment 6 months after IVT injection in NHP

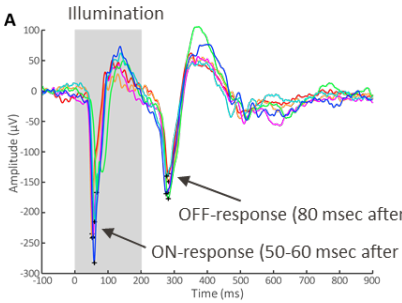


Restoration of a functional vision in P23H rats

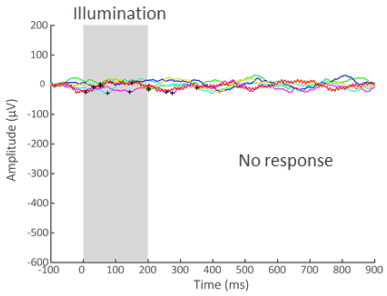
Light-induced visual evoked cortical responses

Full field 590 nm light from ~ $4.7x10^{15}$ to $1.1x10^{17}$ photons/cm^2/sec

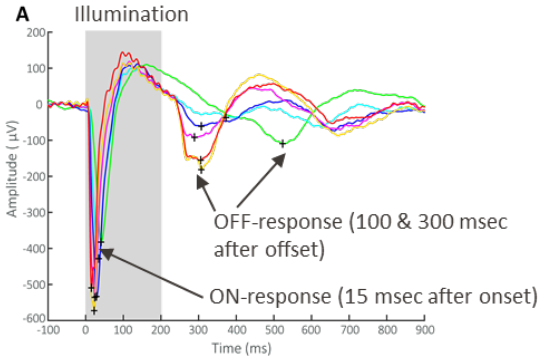
Normal Long-Evans rat



Untreated P23H rat



GS030-treated P23H rat



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GS030: well-tolerated and safe in pre-clinical studies

Toxicity study of GS030 product in non-human primates *(n=32)*

Bilateral IVT administration with vehicle vs $7.21x10^{10}$ VG/eye (low dose) vs $7.84x10^{11}$ VG/eye (high dose) in 100 µL

Ophthalmology

- **Dose-dependent ocular inflammation** in the anterior segment and vitreous, improving/resolving from Month 2 up to Month 6
- **Not associated with any retinal tissue destruction** or functional changes
- **No or very slight residual inflammation** in all animals at 6 months (**self-resolution**, no treatment before or after injection)

Histology

- **Dose-dependent minimal mononuclear cell infiltration** in eye tissues
- **No histological findings in other tissues**

Immunogenicity (anti-AAV2 NAb)

- **Expected humoral immune response** in serum starting at Day 15; tended to decrease at Week 13 then sustained up to Month 6
- **Dose-dependent local immune response** in aqueous humor and vitreous

Local tolerance of GS030 product with light exposure in rd1 blind mice *(n=36)*

Bilateral IVT administration with vehicle vs $7.84x10^{9}$ VG/eye in 1 µL; 590 nm LED light at $1.4×10^{16}$ vs $1.7×10^{17}$ photons/cm^2/s vs ambient room light

Local tolerance

- **No ophthalmic findings** related to gene therapy (GS030-DP) or to LED light
- **No microscopic findings** in the retina related to GS030-DP or to LED light
- **Transient corneal edema & lens opacity** linked to anesthesia procedure

ChrimsonR-tdTomato expression

- **Good expression** of ChrimsonR-tdTomato in retinas and optic nerves

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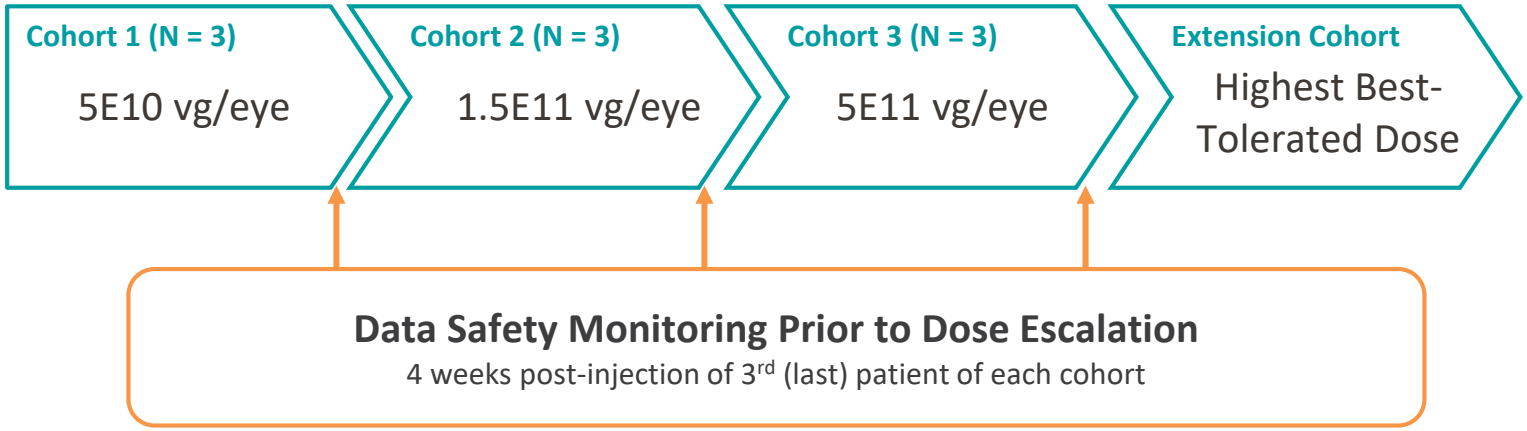
PIONEER Phase I/II clinical trial: A First-in-Man study

Study design



- **First-in-man**, dose-escalation safety study, multi-center (France, UK, US)
- **Study population:** end-stage non-syndromic RP (vision < Counting Fingers)
- **Primary analysis:** Safety at 1 year
- Single intra-vitreal injection in the **worst affected** eye
- Decision to increase the dose taken by a DSMB

1st DSMB recommended to continue with cohort 2 without modification on April 30, 2019

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GS030: CMC progress & Regulatory interactions

CMC

- **Manufacturing process developed up to 25L**
  - Toxicology batch produced at 25L scale
  - Drug Substance titers (> 2E13 vg/ml) and characteristics in line with expectations
  - Scale up to 100L batch successful
- **Manufacturing process successfully transferred to GMP**
  - GMP clinical supply ready
  - 100L GMP batches manufactured
- **Potency assay**
  - Development completed
  - Transfer in progress

Regulatory

- **Orphan Drug Designation** granted in the US and in Europe
- **Active strategy & interactions with US and EU Agencies** to obtain advice on preclinical package to support FIM and exploit the existing process of expedited programs
- **CTA approved in the UK and in France**
- **IND released by FDA in the US**

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GS030 Key Milestones

2016-2017

CTA

Orphan Drug Designation in US and EU

2018

CTA IND

October

PIONEER FIM

2019

PIONEER GS030 STUDY

2020

Completion of patient enrollment

Early findings from first patients in PIONEER

PIONEER Preliminary Results

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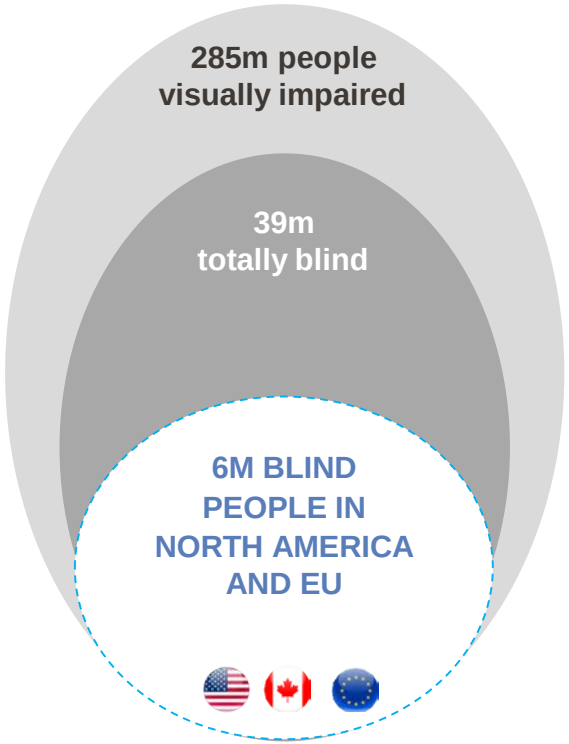
Building high strategic value

Curing blindness represents major market opportunity

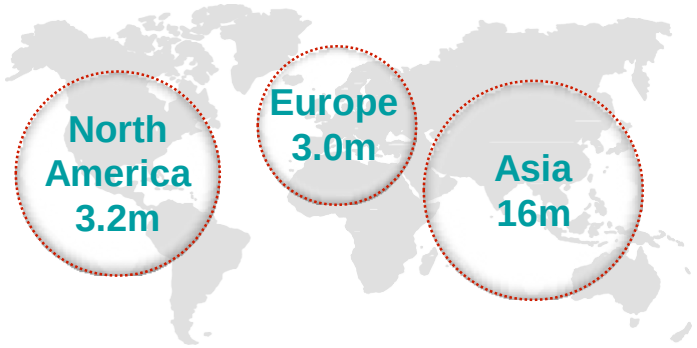


Source: WHO, IAPB-VISION2020, NORC-Univ. of Chicago / The Economic Burden of Vision Loss and Eye Disorders in the United States, 2014.

Favorable reimbursement conditions:

- Gene therapy in ophthalmology for rare diseases could be considered **similar to organ transplants for payers**
- Blindness imposes a **high burden** on health systems
  - Total blindness costs exceed tens of billions USD per annum
- **Absence of curative treatments**
  - Increasing pressure from patients and patients associations

Geographical Split – Blind people in major markets



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Pricing and reimbursement environments are evolving to accommodate curative potential of innovative cell and gene therapies

Early entrants are setting pricing and contracting benchmarks, and authorities signal flexibility to new thinking

LUXTURNA™ voretigene neparvovec-rzyl for subretinal injection

- Approved December 2017 for treatment of biallelic RPE65 mutation-associated retinal dystrophy
- List price: $425,000 *per eye*
- Early commercial agreements with select health plans
  - Pay-for-performance
  - Staggered payments
  - Special procurement process using specialty pharmacies
  - CMS policy (Medicare coverage) to be published in 2019

Strimvelis

- Approved May 2016 for treatment of ADA-SCID
- List price: 594,000€ *per patient*
- Positive HTA assessments in UK and IT; covered by ***EU Directive 2011/24****
  - Treatment administered only at the designated treatment center in Milan

Note: **Luxturna** received Marketing Authorization for Europe in November 2018.
So far, NHS England reached £613,410 per patient at full price ($744,000, -12% of US price).
A full list price has not yet been published.

+ Openness to alternative pay-for-performance / risk-sharing options among individual plans
+ Industry consultation into legislative initiatives covering new payment models for regenerative therapies
+ Ongoing cross-border initiatives in the EU, e.g., European reference networks (ERN EYE for ophthalmology)
+ HTA-industry consultations on refining cost effectiveness models for curative treatments

*The directive sets out the conditions under which a patient may travel to another EU country to receive medical care and reimbursement. It covers healthcare costs, as well as the prescription and delivery of medications and medical devices.

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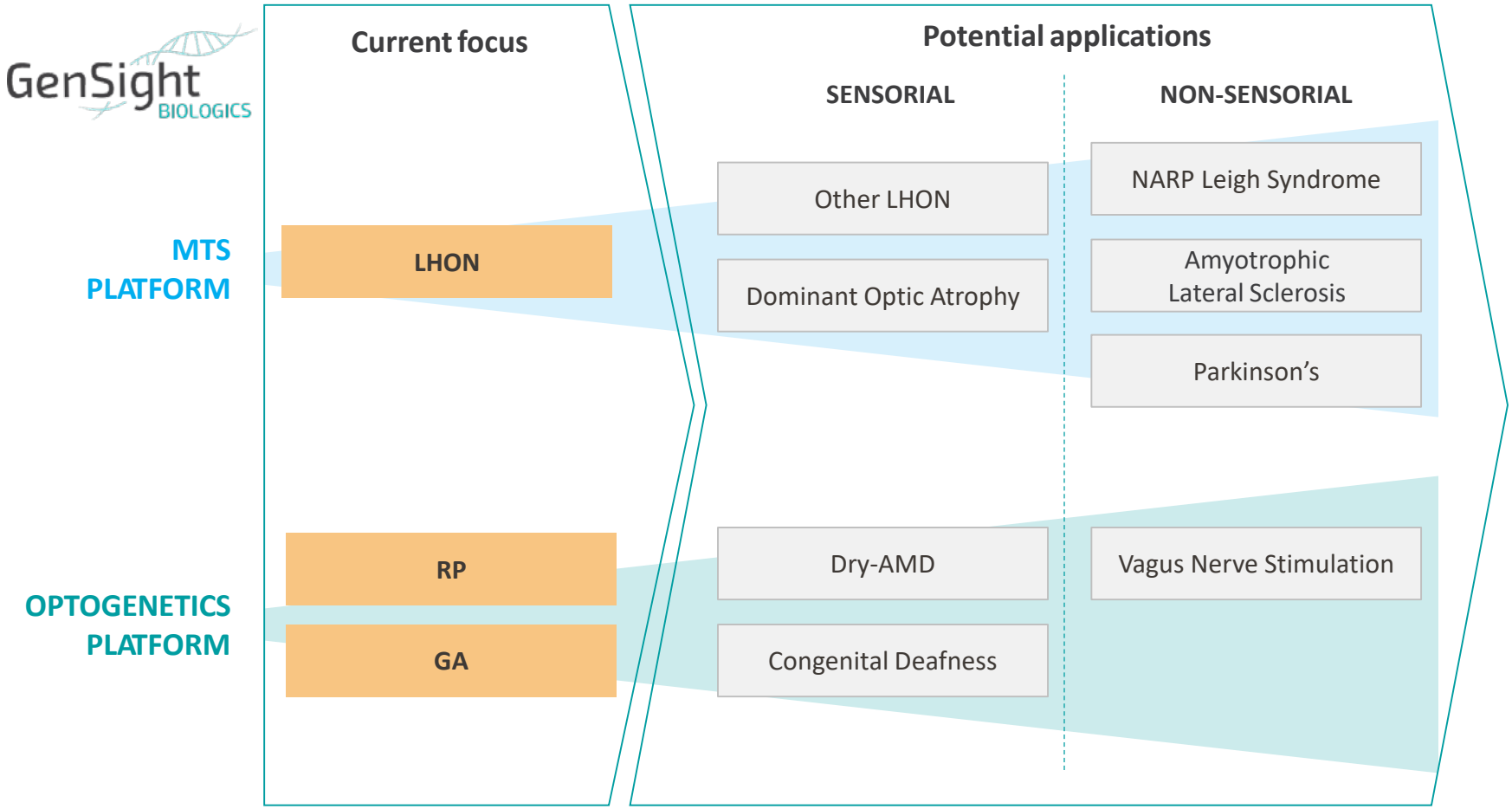
Potential applications of GenSight technology platforms



Ability to leverage technology platforms and significant expertise to expand the pipeline in ophthalmology and other neurodegenerative disorders

GenSight Biologics

Key financial information

Financing history

- March 2013 – Series A round – €20m
- June 2015 – Series B round – €32m
- July 2016 – Euronext IPO – €45m
- June 2017 – PIPE – €22m
- February 2019 – PIPE – €8m

Listed on Euronext Paris (SIGHT)

- Established in 2012, IPO in July 2016

Recognition from Blue-Chip specialist investors

- Perceptive, Fidelity, Abingworth, Versant, Sofinnova, JP Morgan AM and others

Analyst coverage

- Oddo & Cie – Martial Descoutures (FR)
- Gilbert Dupont – Jamila El Bougrini (FR)
- Chardan – Gbola Amusa (US)
- NIBC – Dylan van Haaften (NL)

Cash position
(as of Jun 30, 2019)

€14.3m

Number of outstanding shares

29.0m

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