



Corporate Presentation

April 2019

A close-up photograph of a human eye, showing the iris and pupil. The eye has a light blue or green tint. The background of the slide is a soft, out-of-focus version of this image.

A LEADING GENE THERAPY BIOTECHNOLOGY COMPANY

GENSIGHT-BIOLICS.COM

Disclaimer

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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



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

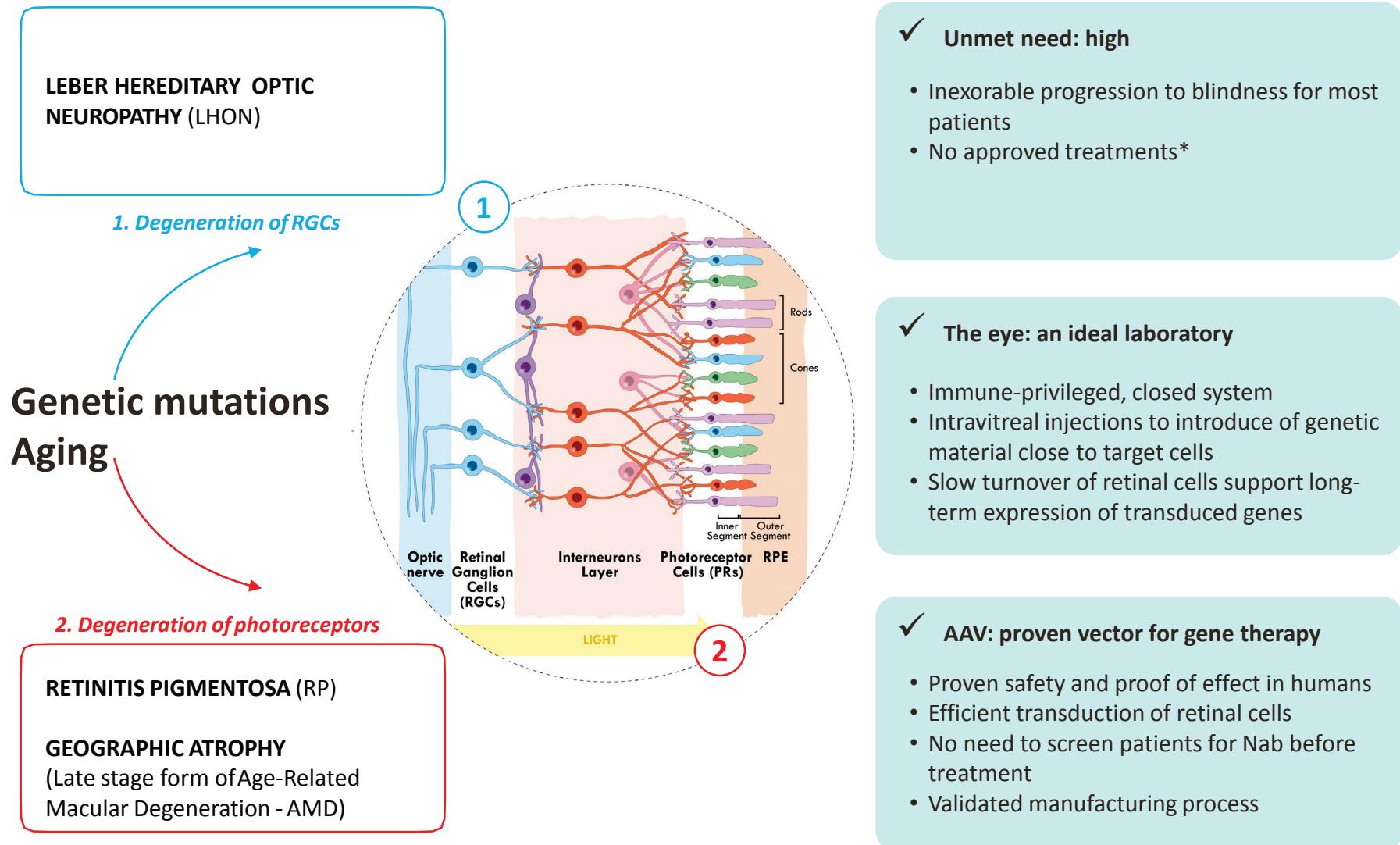
DBV TECHNOLOGIES (2012-2015)
VP of Finance
IPSEN (2008-2011)
UK Operations Controller (London)
Senior Financial Analyst (Paris)
ERNST & YOUNG (2007-2008)
Auditor



Barrett Katz
Chief Medical Officer

MONTEFIORE MED CENTER & A. EINSTEIN COLLEGE OF MEDICINE, NY, USA (2011-2017)
Prof. of Ophthalmology, Neurology and Neurosurgery
DANUBE PHARMA (2009-2011)
CEO
FOVEA PHARMA (2007-2009)
CMO
EYETECH (2005-2007)
VP of Medical Affairs and Strategy
MD, Board-certified ophthalmologist & neurologist

Our target: degenerative retinal diseases with underlying genetic causes



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) and Oct (72w) 2018. 96w expected in May 2019.
	GS011	LHON ND1		● →				RESCUE: Phase III top-line data reported in Feb (48w) and Apr (72w) 2019. 96w expected in Sep 2019.
	Undisclosed Mitochondrial Target	Undisclosed		● →				REFLECT* : Phase III recruitment ongoing, top-line data expected in Q2 2020
	GS030 (FDA & EMA Orphan Drug Designation)	RP		● →				PIONEER: First cohort enrolled in ongoing Phase I/II clinical trial. Report interim data one year after last subject treated
Optogenetics	GS030	Dry AMD & Geographic Atrophy		● →				

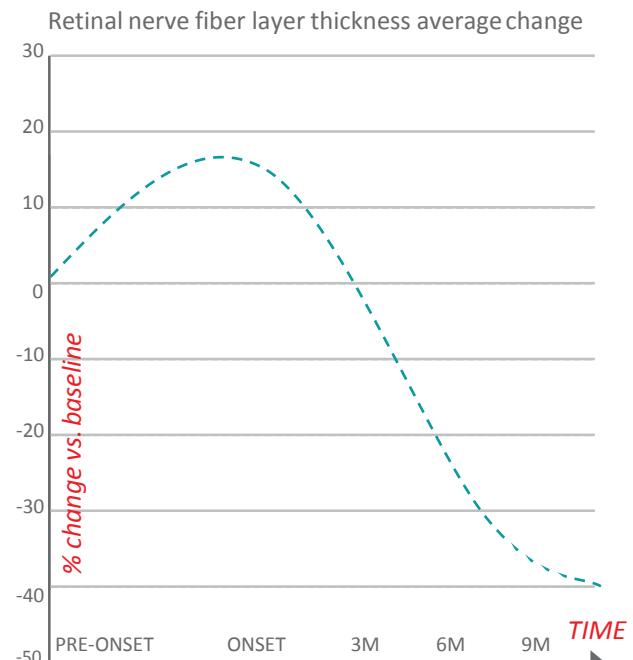
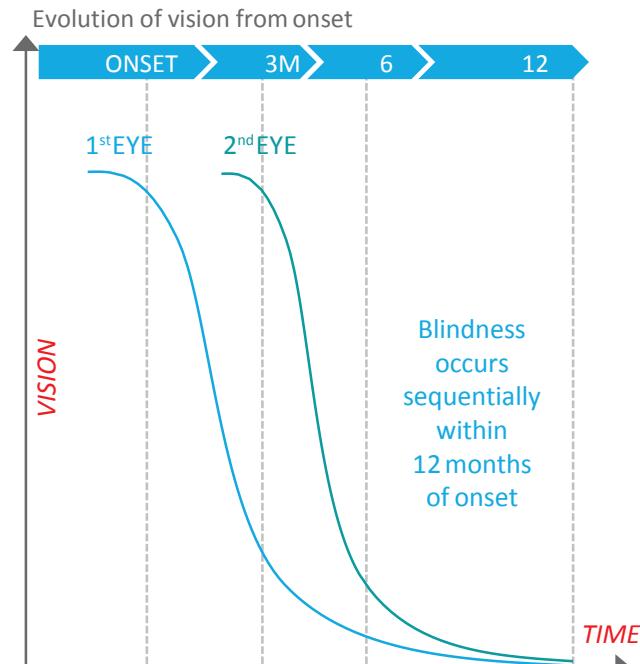
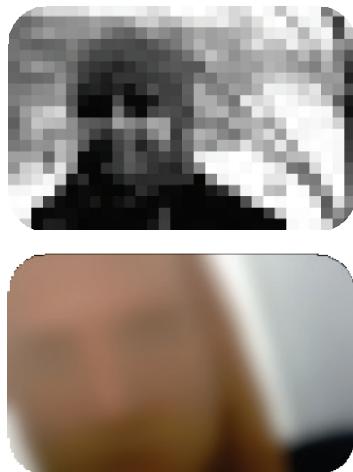
*Conducting this trial under a special protocol assessment with the FDA

Lead candidate, GS010, is expected to be less than 12 months away from MAA submission in Europe

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

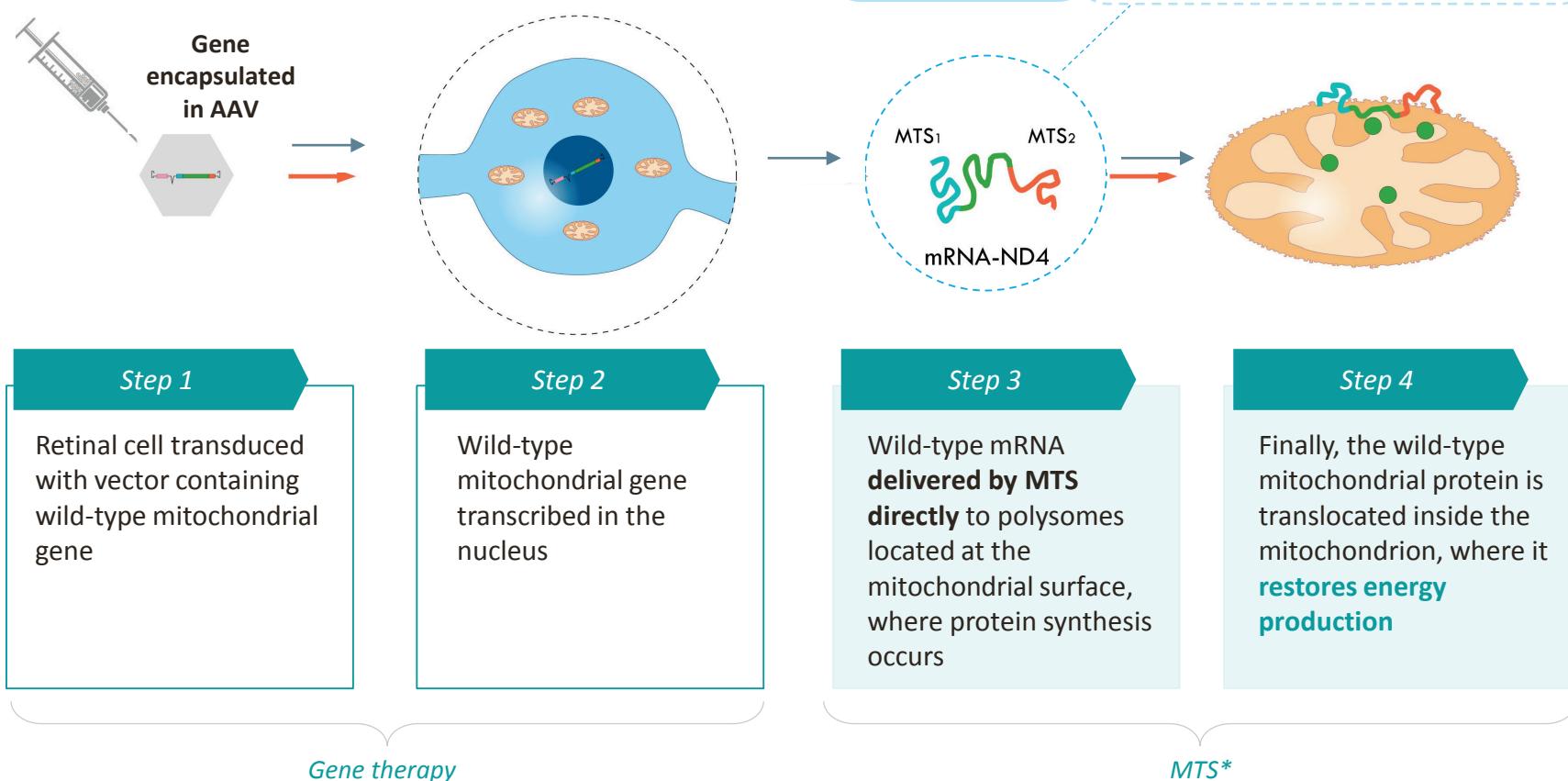


	Incidence	0.15/100,000
	Prevalence	1/31k-40k
	Blindness	15-35y

- 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

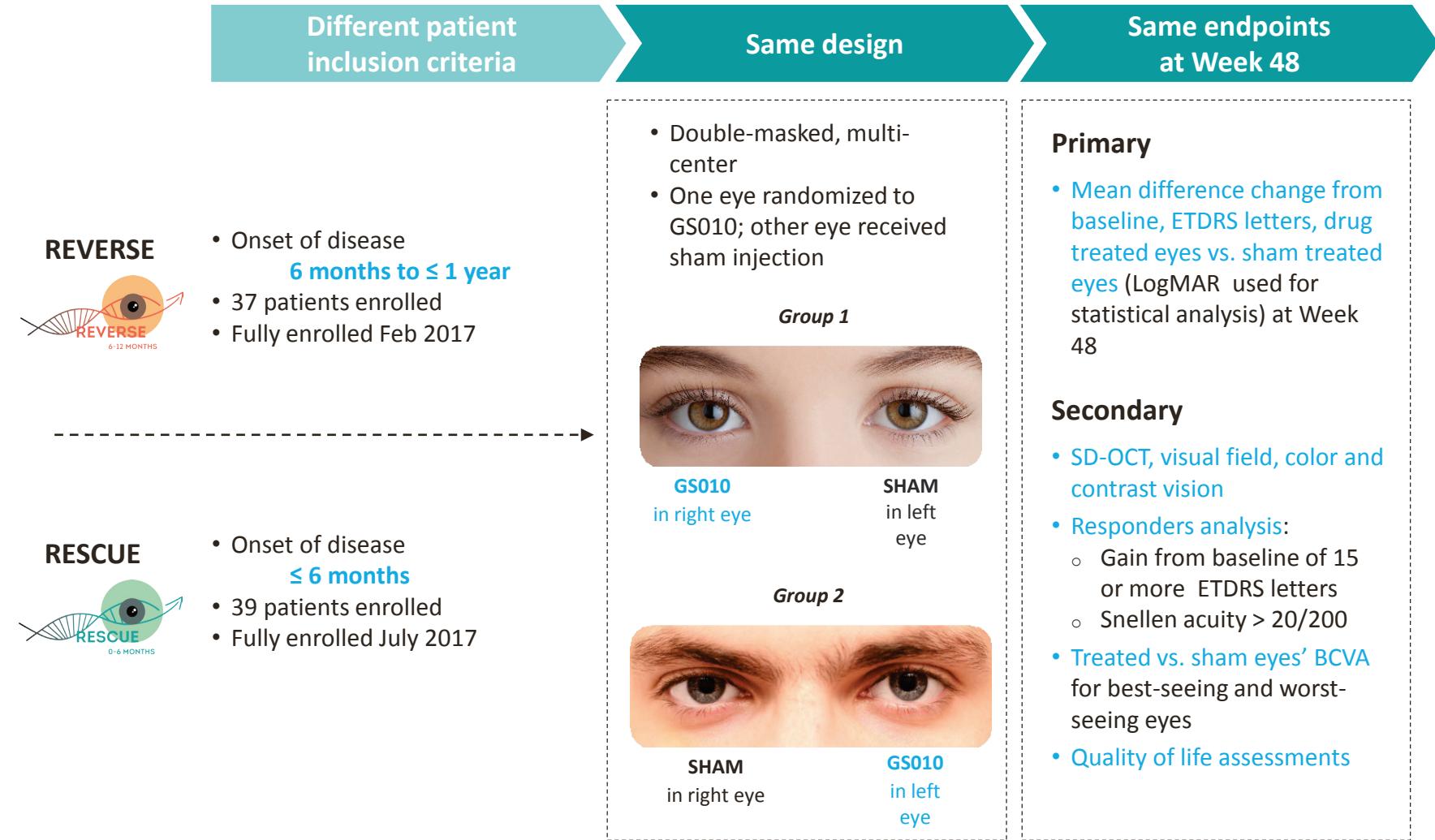
Solution: Gene therapy to produce working mRNA, with *MTS** technology to shuttle mRNA directly to affected mitochondria

MTS in action for GS010:



RESCUE & REVERSE Phase III trials

Time-based strategy to assess GS010 efficacy



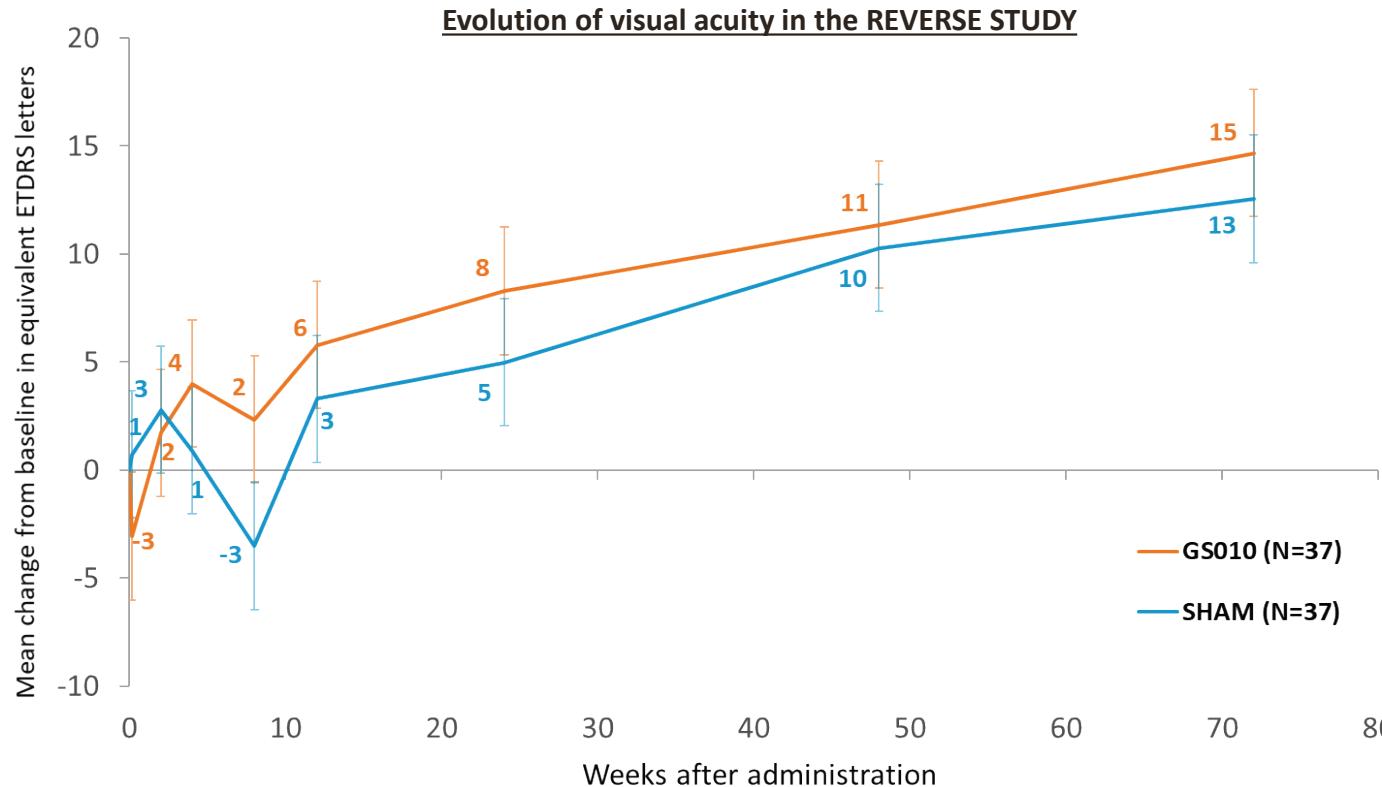
Source: Company



REVERSE 72-week Data: Improvement of central Visual Acuity

Sustained improvement of best-corrected visual acuity (BCVA), to clinically meaningful levels at Week 72

- A clinically meaningful improvement of +15 ETDRS letters reported in treated eyes
- A continuous bilateral improvement from Baseline to Week 72





REVERSE 72-week Data: Additional visual function outcomes

Improvement of Contrast Sensitivity

- **Contrast sensitivity** as determined by Pelli-Robson low contrast testing increased in both eyes from baseline to week 72:

Treated eyes: +0.21 LogCS

Untreated eyes: +0.15 LogCS

- Proportion of treated eyes that achieved a **clinically meaningful improvement of at least 0.3 LogCS** was statistically significantly higher than that of sham-treated eyes:

Treated eyes: 45.9%

Untreated eyes: 24.3%

$p = 0.0047$

GEE model predicting BCVA $\geq 20/200$

In a generalized estimating equation (GEE) model used to assess treatment effect on VA of $\geq 20/200$ acuity, GS010-treated eyes were significantly more likely to achieve 20/200 threshold than sham-treated eye.

$p = 0.0012$; odd ratio = 4.07



REVERSE 72-week Data: Anatomic targets successfully engaged

- SD-OCT demonstrated **statistically significant preservation** of retinal ganglion cells and **preservation** of retinal fiber layer in treated eyes vs. untreated eyes

- Change from baseline in retinal ganglion cell macular volume measured:

Treated Eyes	no loss
Untreated Eyes	-0.044 mm ³

p = 0.0060

- Change from baseline in thickness of the papillo-macular bundle:

Treated Eyes	+1.6 µm
Untreated Eyes	-1.4 µm

p = 0.0362

- Change from baseline in thickness of the temporal quadrant of the retinal nerve fiber layer:

Treated Eyes	-1.6 µm
Untreated Eyes	-3.6 µm

p = 0.0521

Sustained preservation of retinal anatomy in drug-treated eyes
demonstrates neuroprotective effect of GS010



REVERSE 72-week Data – NEI VFQ-25

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 at Week 48 and Week 72**
- Magnitudes of 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%
	+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%
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.

Improvement from baseline at Week 72 for other sub-scales: social functioning: +2.4 (23.3%); ocular pain: +1.4 (5.6%); color vision: +5.6 (20.8%); peripheral vision: +1.4 (15.5%). Missing values for general health subscale. Driving questions not pertinent to LHON patients.



RESCUE 72-week Data: Similar trajectories with nadir for visual acuity

Visual Acuity deteriorates to a low point before beginning to recover: **mean improvement from nadir to Week 72 of +21 and +22 ETDRS letter equivalent** in GS010- and sham-treated eyes, respectively

LS Mean (SE) ^a	Change from BASELINE			
	Week 48		Week 72	
	LogMAR	ETDRS Letter Equivalent	LogMAR	ETDRS Letter Equivalent
GS010 Eyes	+0.380 (0.129)	-19	+0.192 (0.104)	-10
Sham Eyes	+0.392 (0.129)	-20	+0.216 (0.104)	-11

^a Primary Endpoint was assessed using a mixed model of analysis of covariance (ANCOVA) was used with change from baseline at week 48 as the response, and subject, eyes of the subject as random factor, treatment and the baseline LogMAR value as covariates in the model.

Mean (SD) ^b	Change from NADIR ^a			
	Week 48		Week 72	
	LogMAR	ETDRS Letter Equivalent	LogMAR	ETDRS Letter Equivalent
GS010 Eyes	-0.257 (0.358)	+13	-0.413 (0.527)	+21
Sham Eyes	-0.236 (0.319)	+11	-0.435 (0.501)	+22

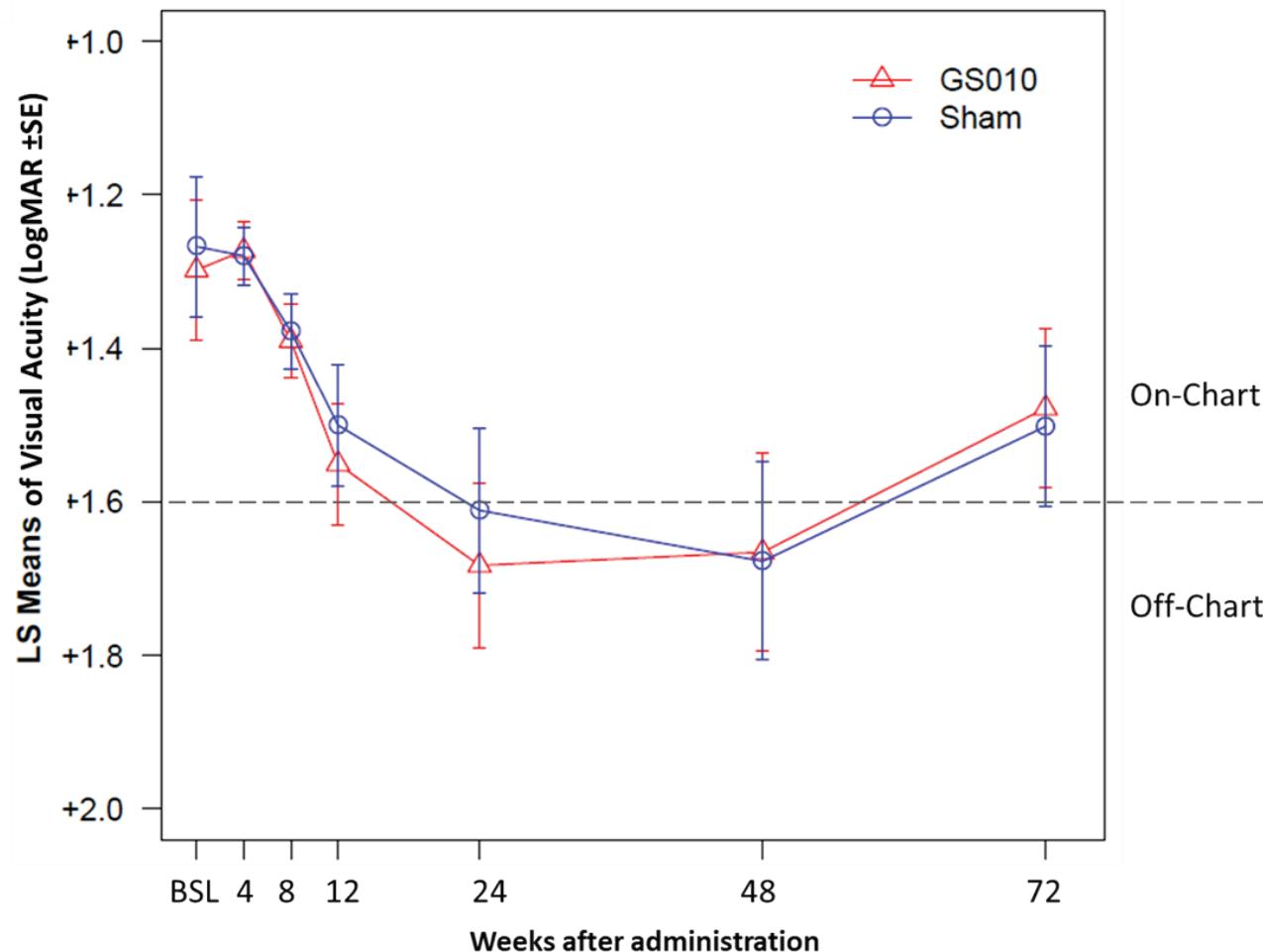
^a NADIR: lowest visual acuity measure post-treatment.

^b Mean change from nadir was calculated using observed values (no data were imputed).

- Worsening VA compared to baseline reflects brutal progression of LHON
- Worsening to nadir (lowest point of VA), then bilateral improvement
- As in REVERSE, visual acuity in GS010- and sham-treated eyes track together

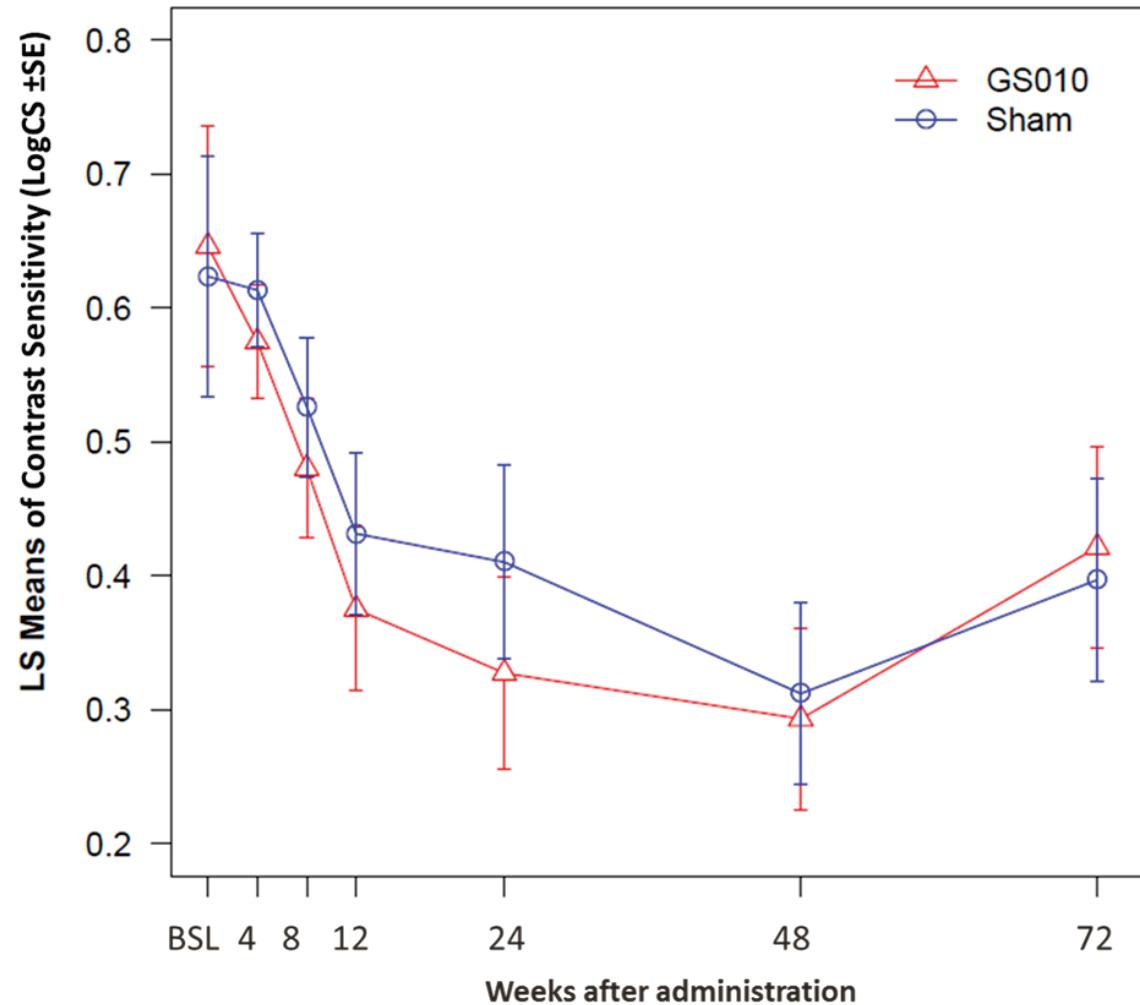
RESCUE 72-week Data: Visual acuity from off-chart to on-chart

Mean BCVA in both GS010- and sham-treated eyes improved from off-chart values at Week 48 to on-chart values at Week 72



RESCUE 72-week Data: Contrast sensitivity coherent with visual acuity

Contrast sensitivity bilaterally evolved similarly to BCVA: while values for GS010-treated eyes and sham-treated eyes remained below baseline, CS also recovered so that the gap to baseline diminished at Week 72 compared to Week 48.





RESCUE 72-week Data: Responder analysis in visual function

- **40% of eyes, both GS010-treated and sham-treated**, achieved a clinically meaningful BCVA improvement from nadir (0.3 LogMAR or 15 ETDRS letters) at Week 72.
- **58% of GS010-treated and 50% of sham-treated eyes** achieved a clinically meaningful BCVA improvement from nadir (0.2 LogMAR or 10 ETDRS letters) at Week 72.

“This improvement in visual function from Week 48 to Week 72, both in visual acuity and contrast sensitivity, strengthens our belief in the benefits of GS010, looking at the shift of the mean BCVA from off-chart to on-chart at Week 72. These results show a more favorable trend than the outcome we usually observe in clinical practice for LHON ND4 patients.”

Dr. Catherine Vignal

Head of the department of Neuro-Ophthalmology at the Rothschild Foundation,
Principal Investigator at the Department of Ophthalmology at Centre
Hospitalier National d’Ophthalmologie des XV-XX, Paris

Bilateral improvements in visual function corroborate previously observed parallel evolution of GS010- and sham-treated eyes in both RESCUE and REVERSE trials



RESCUE 72-week Data: Retinal anatomy

Anatomic outcomes so far do not indicate differential protection for the anatomy of GS010-treated eyes

In both drug-treated and sham-treated eyes, the relevant anatomy, as shown by various OCT measurements (tRNFL thickness, PMB thickness, GCL volume), continued to thin at Week 72, although the rate of thinning decreased between Week 48 and Week 72

“By design, the population in Rescue is very heterogeneous, and the structure of their retina is also highly variable, from marked atrophy of nerve fibers to edema. At unmasking, which happens after week 96, we will separate our subjects by their baseline OCT findings. In the subgroup with edema, thinning over time will be a good finding. In those with baseline atrophy of nerve fibers, increases in thickness will be a good sign. This mix of OCT findings at entry masks the true OCT findings at week 72 in Rescue.”

Dr. Robert C. Sergott

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

Anatomic measures showed similar trajectories for GS010-treated and sham-treated eyes – difference not statistically significant at Week 72



RESCUE 72-week Data: Safety and tolerability

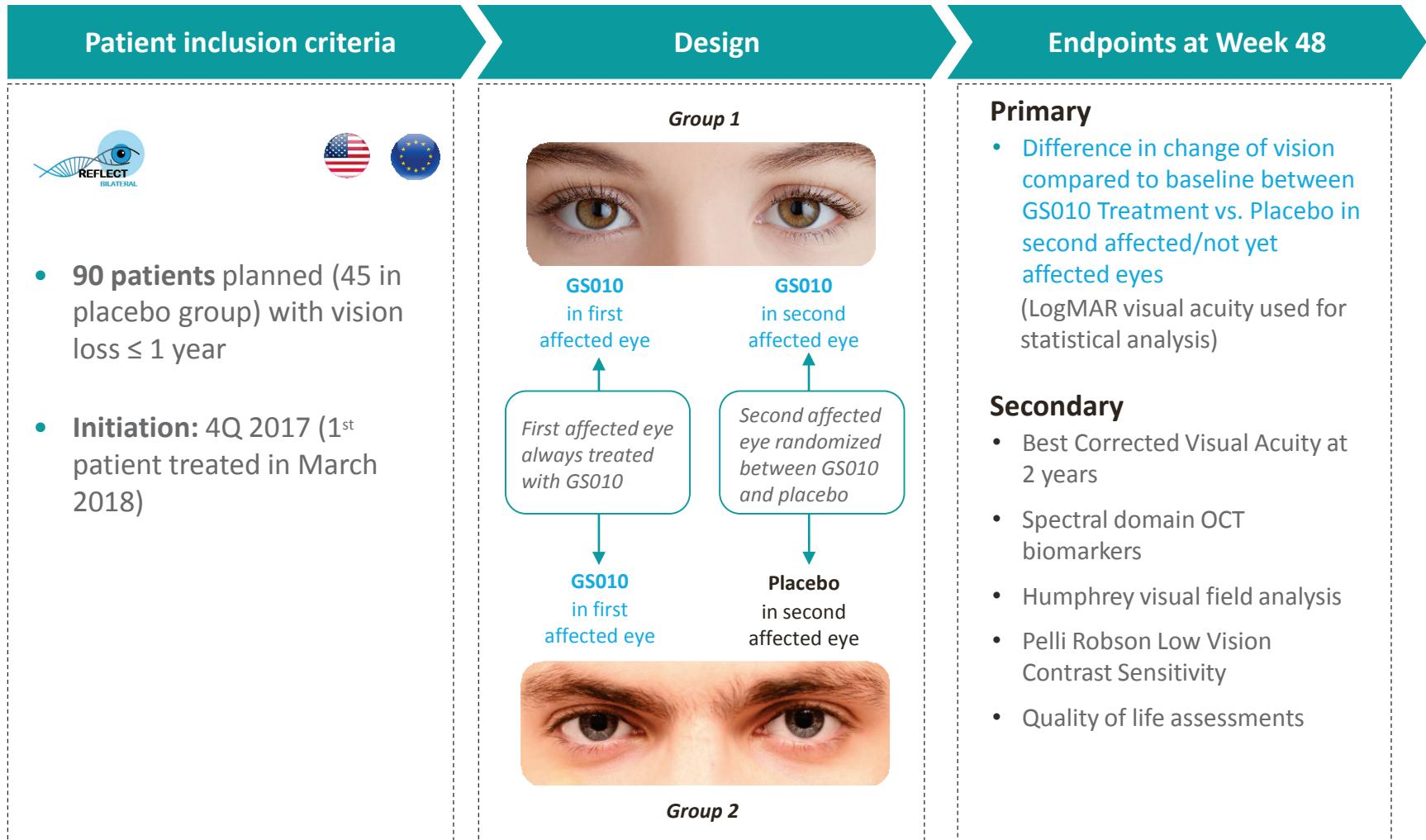
Favorable safety and tolerability profile

- No serious ocular adverse events or discontinuations due to ocular issues
- Most frequently seen ocular adverse events were related to injection procedure itself
- Transient elevations of intraocular pressure were occasionally seen but were secondary to intraocular inflammation, and likely due to administration of GS010
- Such episodes were without sequelae and responded to conventional treatment
- No systemic serious adverse events or discontinuations related to study treatment or study procedure

GS010 was well-tolerated through 72 weeks

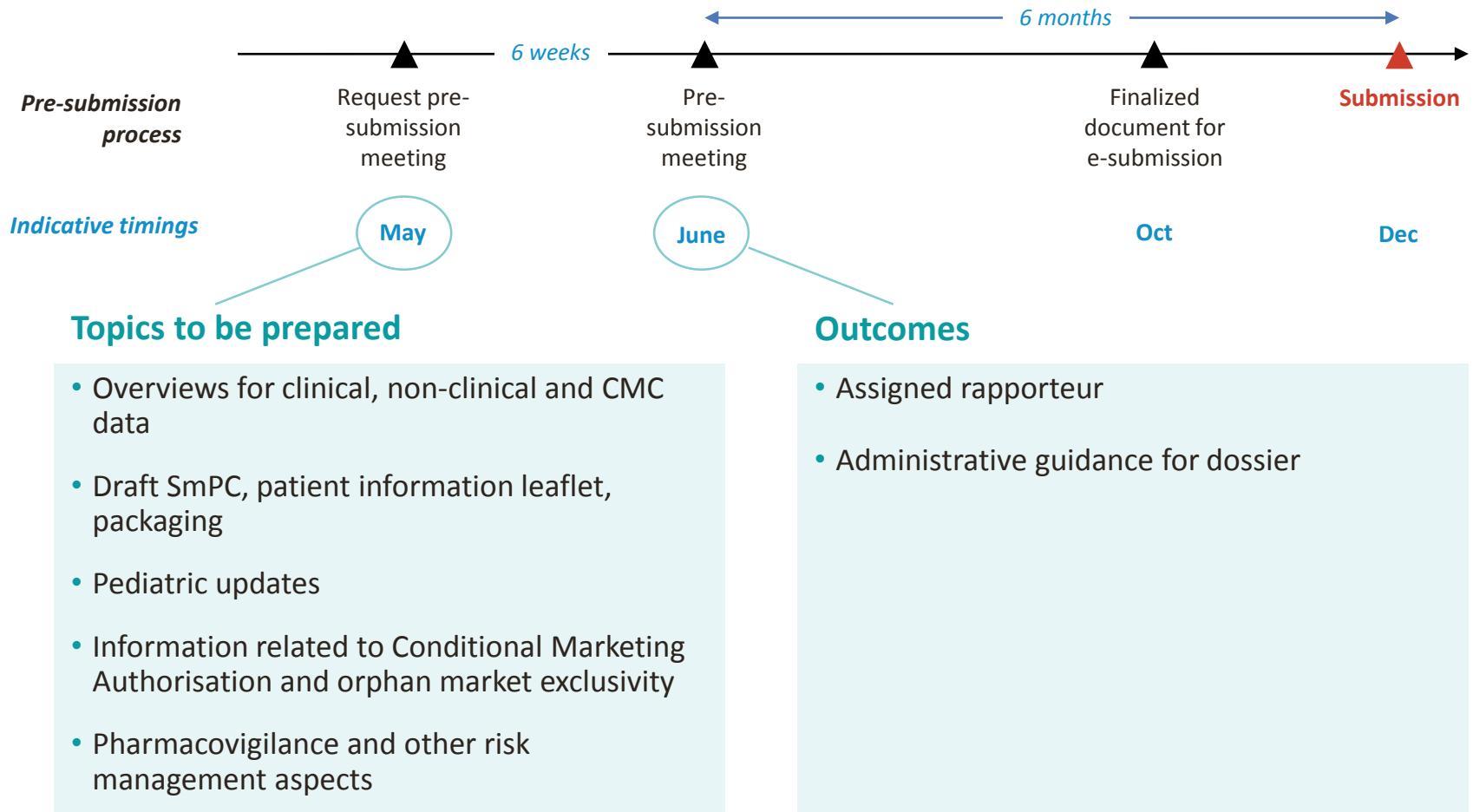
REFLECT Phase III trial: assess efficacy and safety of bilateral injection

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



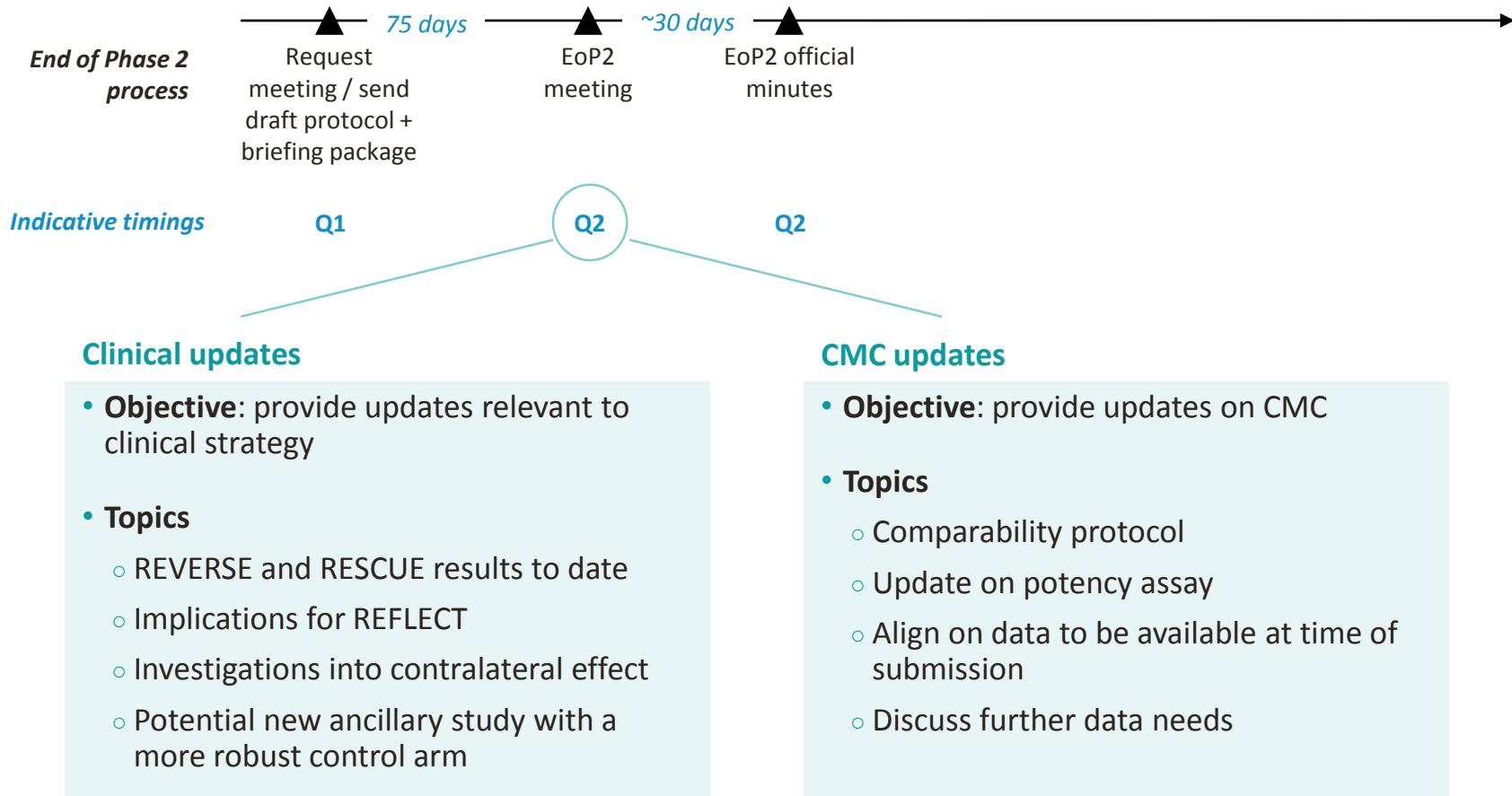
Engagement with EMA

Preparing for submission

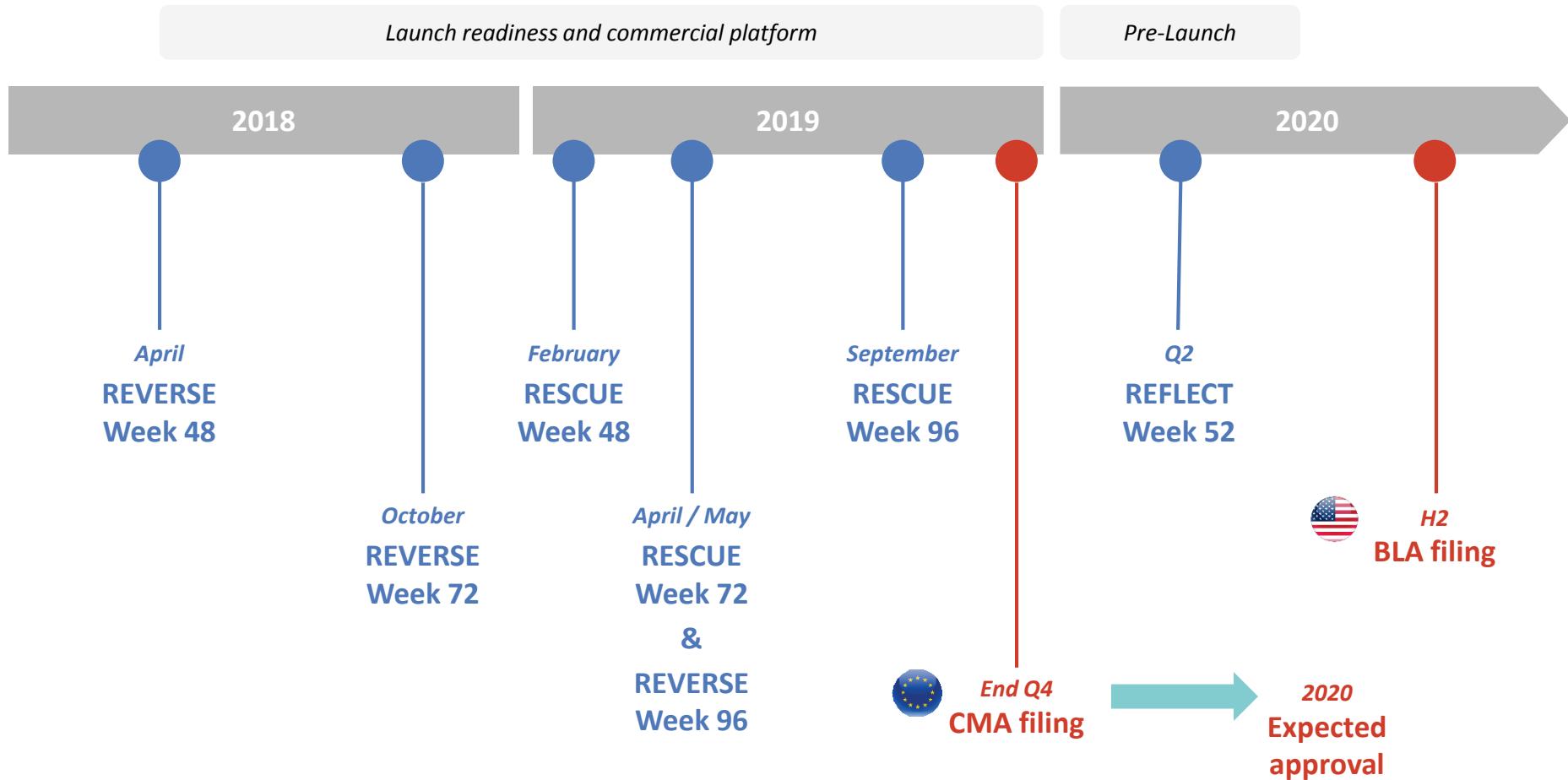


Engagement with FDA

End of Phase 2 (EOP2) meeting to provide updates



GS010 Path to Market



GS030

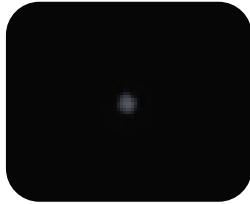
Second lead product
candidate targeting
photoreceptor degenerative
diseases (RP/AMD)

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

Retinitis Pigmentosa



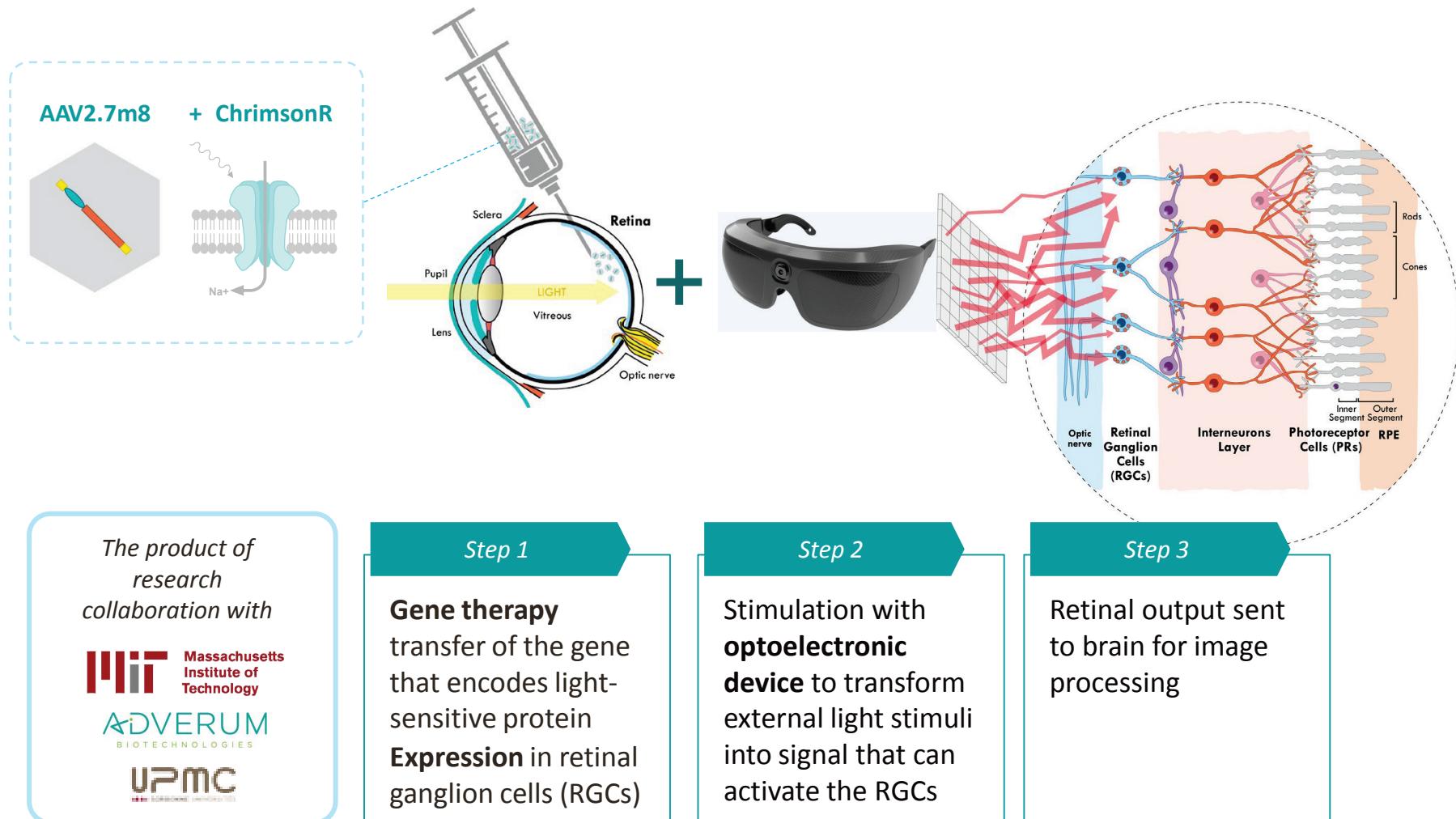
Geographic Atrophy (GA) in AMD (Age-Related Macular Degeneration)



- 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

- 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

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

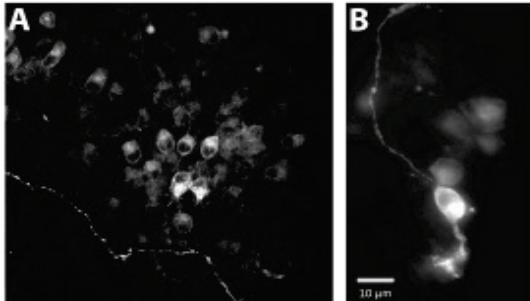


GS030: activated RGCs provide visual information to the higher visual centers

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

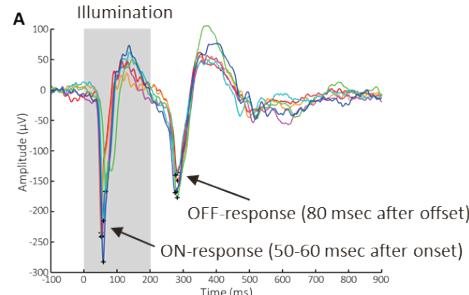


Restoration of a functional vision in P23H rats

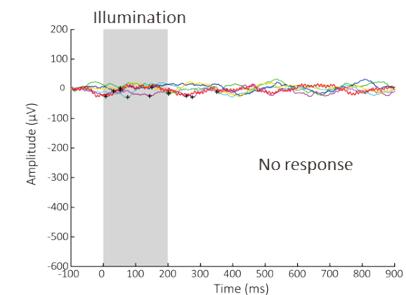
Light-induced visual evoked cortical responses

Full field 590 nm light from $\sim 4.7 \times 10^{15}$ to 1.1×10^{17} photons/cm²/sec

Normal Long-Evans rat



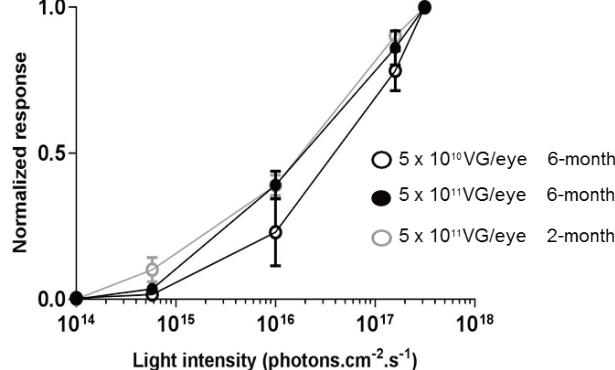
Untreated P23H rat



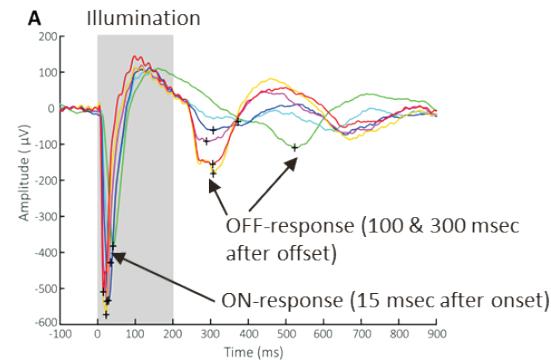
Dose-ranging response to firing relationship in NHP

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

MEA assessment 6 months after IVT injection in NHP



GS030-treated P23H rat



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 7.21×10^{10} VG/eye (low dose) vs 7.84×10^{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 7.84×10^9 VG/eye in 1 µL; 590 nm LED light at 1.4×10^{16} vs 1.7×10^{17} photons/cm²/s vs ambient room light

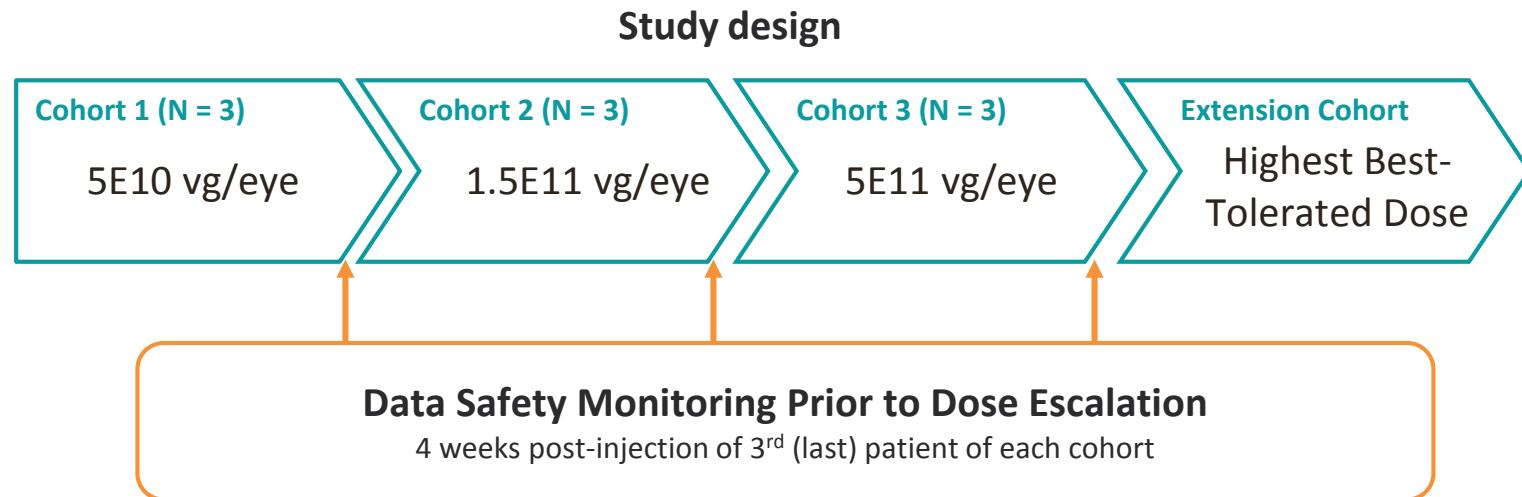
Local tolerance

- **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

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



- **First-in-man**, dose-escalation safety study, multi-center
- **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

**First patient treated in October 2018 at the Moorfields
Eye Hospital in the UK**

GS030: CMC progress & Regulatory interactions

CMC

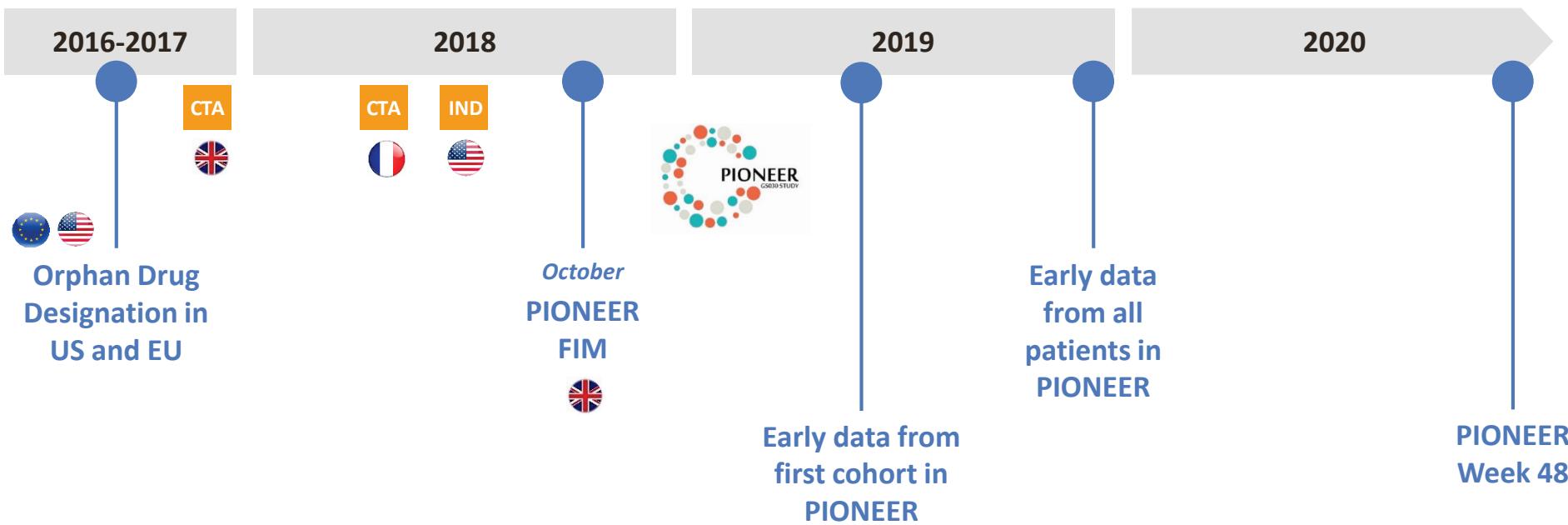
- **Manufacturing process developed up to 25L**
 - Toxicology batch produced at 25L scale
 - Drug Substance titers (> 2E13 vg/ml) and characteristics in line with expectations
 - Scale up to 100L batch successful
- **Manufacturing process successfully transferred to GMP**
 - GMP clinical supply ready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

GS030 Key Milestones

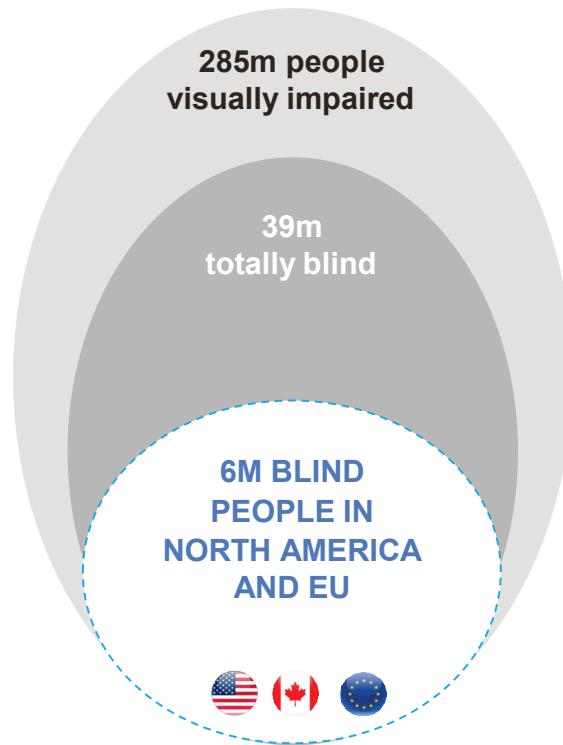
Pivotal trial expected to
be initiated in 2020



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



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



- 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



Stimvelis

- 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 but a 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

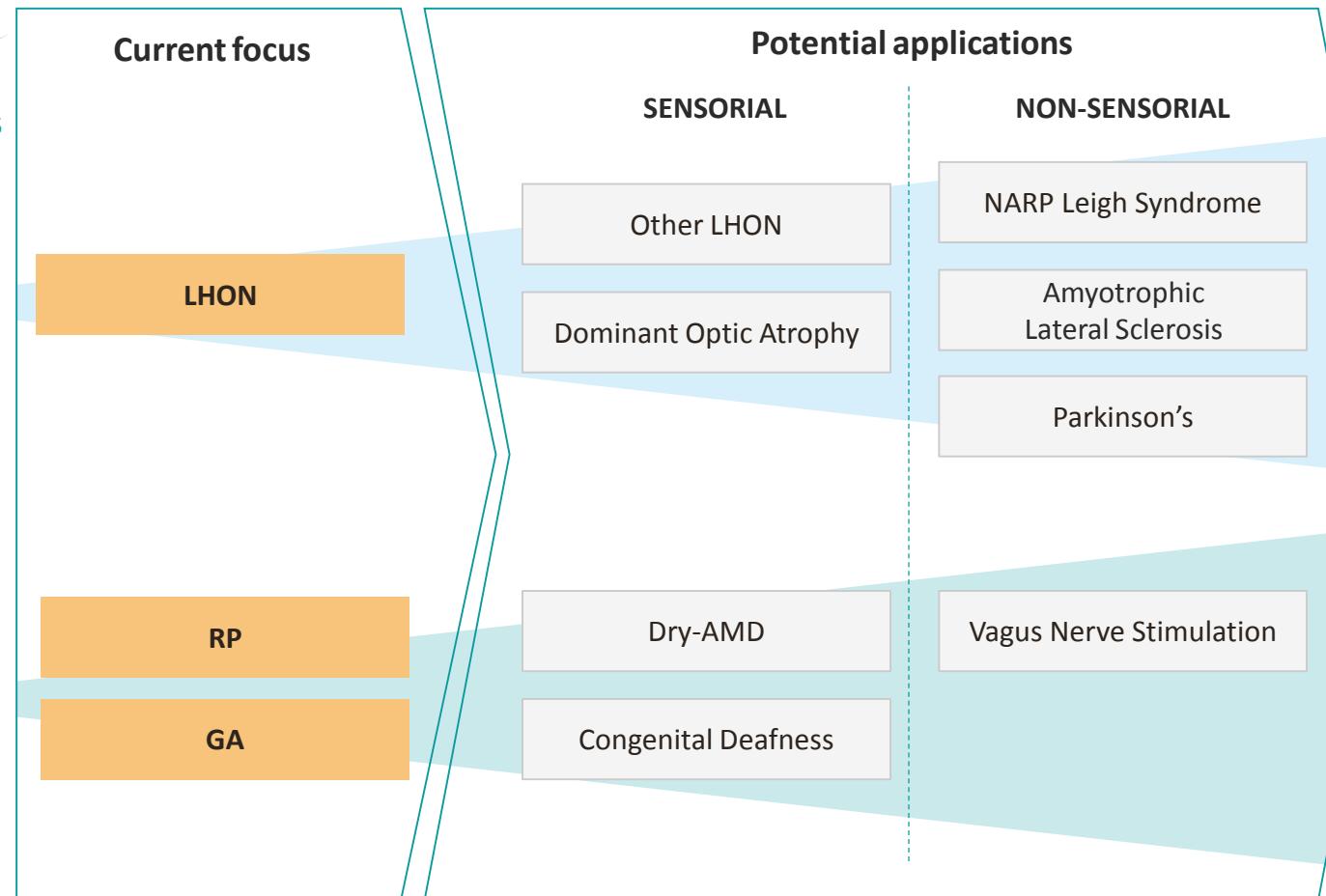
*The directive sets out the conditions under which a patient may travel to another EU country to receive medical care and reimbursement. It covers healthcare costs, as well as the prescription and delivery of medications and medical devices.

Potential applications of GenSight technology platforms



**MTS
PLATFORM**

**OPTOGENETICS
PLATFORM**



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 Mar 31, 2019)

€24.0m

Number of outstanding shares

28.7m