



Corporate Presentation

September 2020

A LEADING Gene Therapy BIOTECHNOLOGY COMPANY

GENSIGHT-BIOLOGICS.COM

Disclaimer

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Corporate Overview – Transitioning from R&D to Commercial organization

GenSight at the forefront of Gene Therapy in ophthalmology

- Publicly traded Biotech company
- Seasoned management team with strong BioPharma and Financial markets experience
- Differentiated gene therapy approach forming a technology platform leveraging disruptive gene therapies in ophthalmology and broader
 - Lead product (LUMEVOQ) targets mitochondrial disease
 - Second compound (GS030) uses optogenetic technology

Established in 2012 / IPO in 2016

EuroNext Paris:	SIGHT
Market Cap (July 3, 2020):	€ 101m
Avg 30-day Daily volume:	0.8% of O/S
Cash (June 30, 2020):	€ 16.8m

LUMEVOQ® – Filed for Approval in Europe in September 2020 and preparing for commercial launch in 2021

- **Market:** High unmet medical need; 1,200 – 1,500 new patients / yr EU + US
- **Efficacy:** Unparalleled clinical benefit demonstrated in two Phase III studies
 - +28/+26 ETDRS letters (i.e. over **5 lines** on visual scale) improvement vs nadir⁽¹⁾
- **Durability & Safety:** Excellent tolerability; Visual improvement maintained at least 3 years post-treatment
 - Clinically meaningful improvement on all Quality of Life parameters at week 96
- **Disease modifying:** Stark difference from Natural History

Commercial strategy and manufacturing capabilities close to completion

- Bilateral injection priced at €700,000 / patient in French named patient Temporary Authorization for Use

Improvement vs nadir in
REVERSE and RESCUE



Seasoned 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



Catherine Cancian

Vice President Pharmaceutical Operations

GENETHON (2015-2017)
Project Leader

SANOFI PASTEUR (1998-2014)
Industrial Operations and
Regulatory Affairs



Julio Benedicto

Vice President Marketing

IMS CONSULTING (2011-2017)
Principal

BOOZ & COMPANY (2010-2011)
Principal

MONITOR GROUP (1994-2009)
Global Account Manager

Pipeline: solid and advanced product portfolio in ophthalmic Gene Therapy

Technology	Product Candidate	Indication	Research	Preclinical	Phase I/II	Phase III	Registration	
MTS platform	LUMEVOQ® (FDA & EMA Orphan Drug Designation)	LHON ND4 (EU)	●—————→					REVERSE: Phase III top-line data reported in Apr (48w) & Oct (72w) 2018 and in May 2019 (96w)
		LHON ND4 (US)	●—————→					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 Q2 2021
	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: Start of 3 rd cohort after DSMB#2 approval in PIONEER Phase I/II clinical trial. Report interim data one year after last subject treated	
	GS030	Dry AMD & Geographic Atrophy	●————→					

MAA Filed in Europe

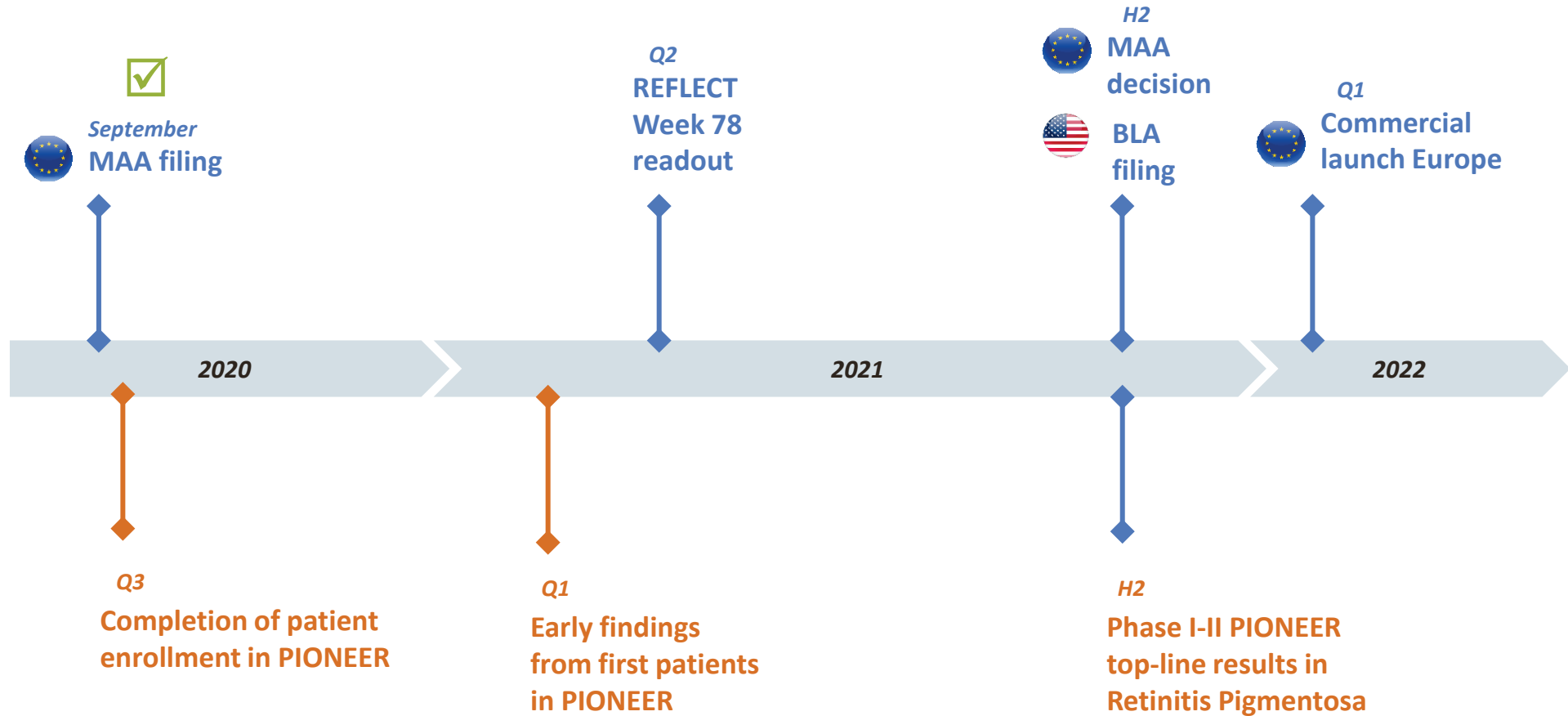
*Conducting this trial under a special protocol assessment with the FDA

Lead candidate, LUMEVOQ® filed for MAA in Europe in September 2020

Rich upcoming news flow with numerous inflexion points



GS030



LUMEVOQ® (GS010) in LHON-ND4

Last Phase III ongoing in Leber Hereditary Optic Neuropathy

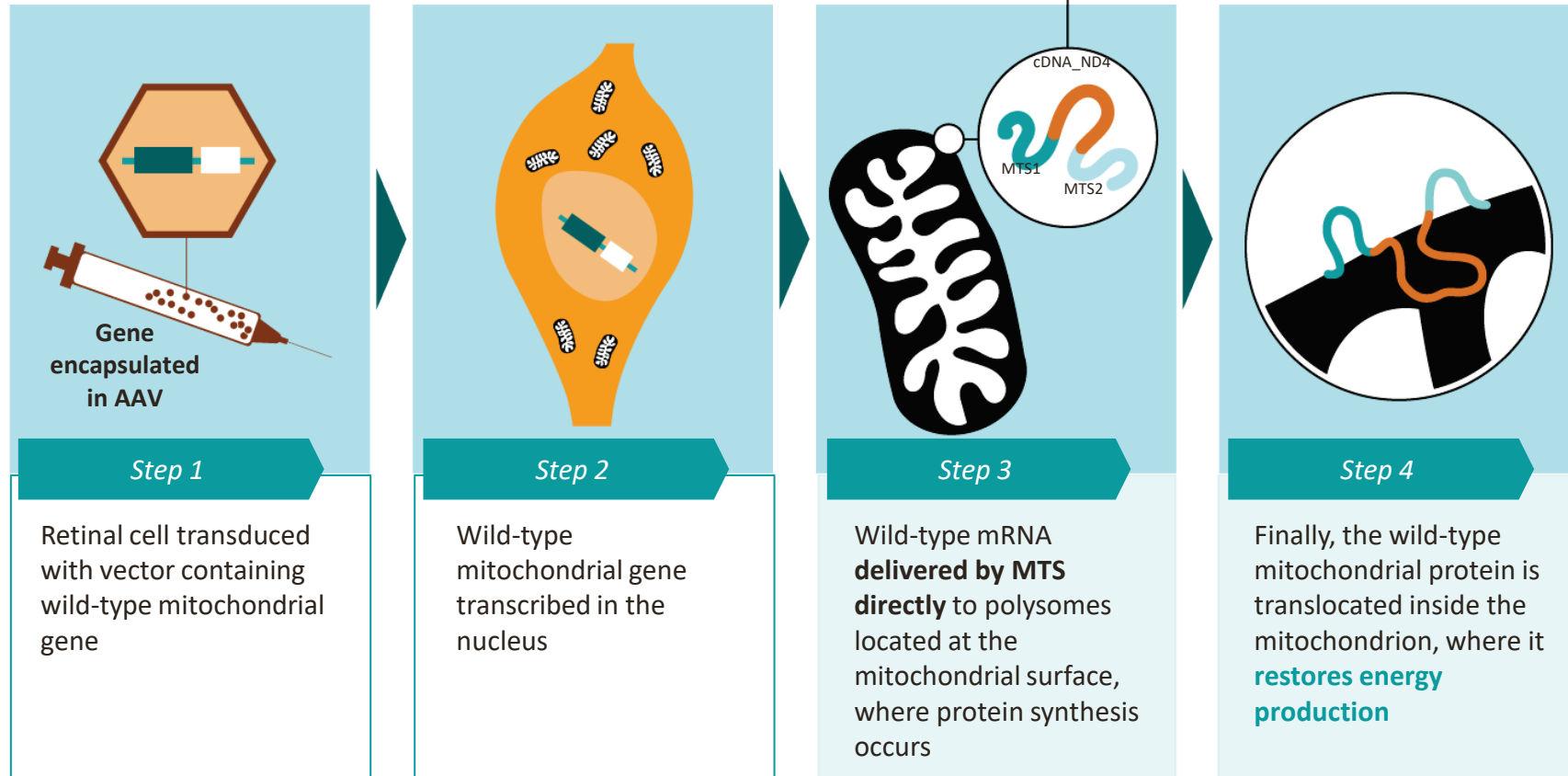
Commercial preparation ongoing for 2021 European launch



LUMEVOQ® introduces Gene Therapy solution

Replacing affected mitochondrial mRNA via proprietary *MTS** technology

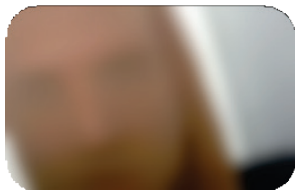
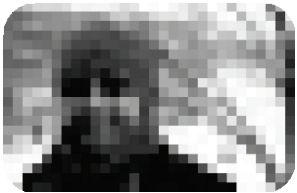
MTS in action for GS010:



Leber Hereditary Optic Neuropathy (LHON-ND4) high unmet medical need

What is LHON-ND4

- Rare inherited mitochondrial disease leading to degeneration of retinal ganglion cells (RGCs) and their axons, most often leading to **sudden loss of central vision**
- Sudden loss typically occurs at age 15-35, mostly in men
- **97%** of patients have bilateral involvement < 1 year / 25% of cases are simultaneous
- 90% of LHON patients have genes **MT-ND4** (~75% in **US/EU**), MT-ND1 and/or MT-ND6 affected



Incidence (new cases per year)

~800-1,200

Prevalence

~15,000-22,000

Progressive disease

- Rare recovery from vision **nadir**⁽¹⁾ reached during acute phase

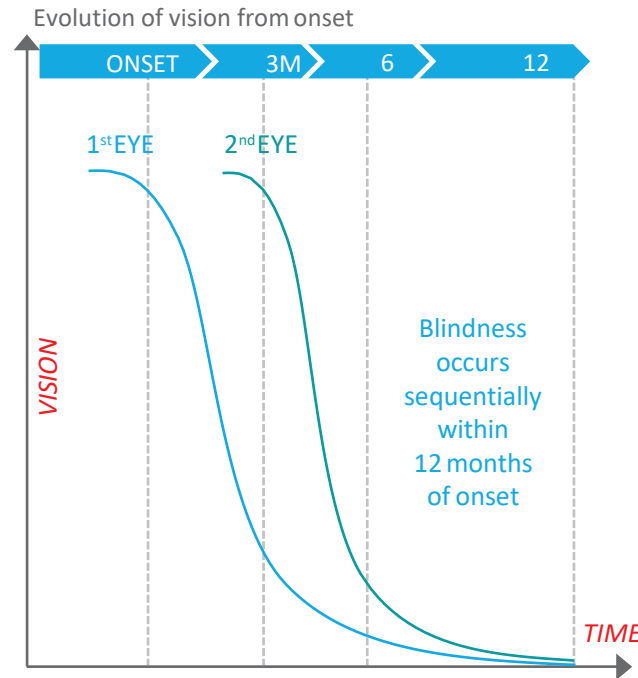


Image source: illustrated from Newman NJ et al., Am J Ophthalmol. 141(6), 1061-1067, 2006

Current treatment paradigm

- No cure for LHON-ND4
- Low-vision aids are primary supportive care
- Santhera's Raxone EU approved (under exceptional circumstances) in 2015 with mechanism of action partially relying on bypassing the dysfunctional complex I of the mitochondrial respiratory chain
 - Approved based on Phase 2 data, Phase 4 ongoing
 - Demonstrated **3 letters improvement** vs placebo ($p=0.291$ / NS) at week 24 in Best recovery of Visual Acuity (primary)⁽²⁾
 - Demonstrated **6 letters improvement** vs placebo ($p=0.078$ / NS) at week 24 in Change in best Visual Acuity⁽²⁾

(1) Nadir: worst visual acuity from baseline

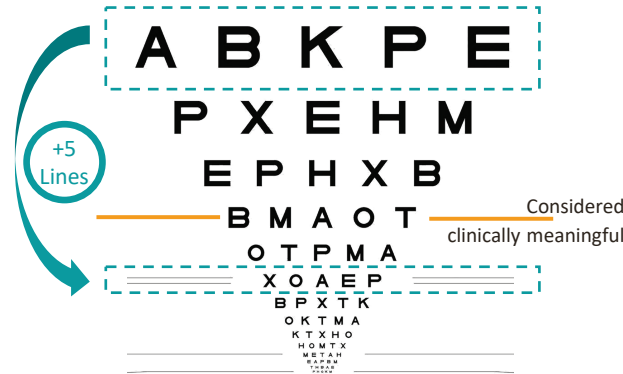
(2) Raxone European full prescribing information https://www.ema.europa.eu/en/documents/product-information/raxone-epar-product-information_en.pdf

Unparalleled clinical benefit demonstrated with LUMEVOQ® (GS010) in LHON in two Phase III studies

5 lines bilateral improvement of visual acuity



Change from NADIR in ETDRS letter equivalents		
	Week 96	
	n	Mean (SD)
All-GS010 eyes	37	+28.3 (22.5)
All-sham eyes	37	+24.5 (24.0)



Change from NADIR in ETDRS letter equivalents		
	Week 96	
	n	Mean (SD)
All-GS010 eyes	34	+26.3 (23.9)
All-sham eyes	34	+22.8 (24.2)

76% of REVERSE subjects achieved at least 15 letters improvement vs nadir in one or two eyes

71% of RESCUE subjects achieved at least 15 letters improvement vs nadir in one or two eyes

- **+28/+26 ETDRS letters (i.e. over 5 lines on visual scale) bilateral improvement vs nadir**
- **Stark difference from natural history outcome**
- **70+% of patients are gaining 15 letters or more**
- **Effect is maintained at least 3 years post administration**
- **Favorable safety profile**

*NADIR is defined as the **worst** BCVA from baseline to Week 96
Mean change from nadir was calculated using observed values (no data imputation)*

Other data complement the finding on sustained bilateral improvement



Insights on Mechanism of Bilateral Effect

- Non-human primate study detected/quantified GS010 viral vector DNA in many tissue samples from contralateral (uninjected) eye



Excellent Tolerability

- No serious adverse events in LUMEVOQ[®]-treated eyes, and no discontinuation due to ocular events
- Most frequently seen ocular adverse events in LUMEVOQ[®]-treated eyes were mainly related to the injection procedure
- Main ocular AE : mild intraocular inflammation – responsive to conventional treatment and without sequelae

Indirect comparison as a cornerstone for EMA Filing

External control group needed because of bilateral improvement in RESCUE and REVERSE trials

- Contralateral effect eliminated the **control group** formed by the sham eyes, as defined in the studies' designs
- EMA scientific advice highlighted the importance of performing an indirect comparison of LUMEVOQ® data using an external control group

Treated Group 76 patients / 152 eyes

- All patients in RESCUE, REVERSE and long-term follow-up study CLIN06 (up to the last available observation)
- Sham eyes included in the treated group, in line with the contralateral effect
 - Treated as independent observations equivalent to injected eyes

Untreated Group (External Control) 208 patients / 408 eyes

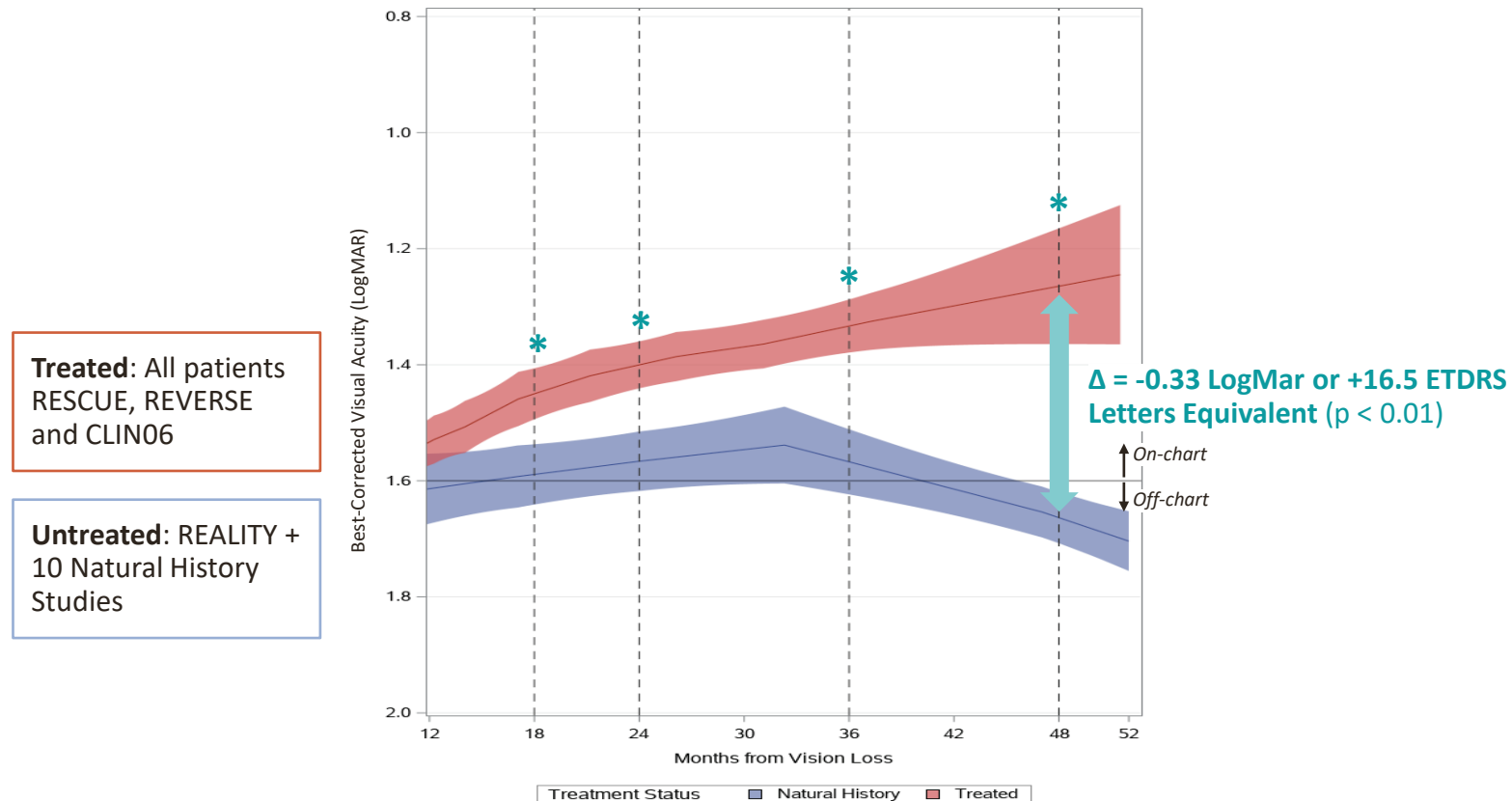
- All patients from REALITY registry study with *ND4* mutation and ≥ 15 years old, *and*
- Patients from 10 natural history studies (2 prospective, 8 retrospective)¹ identified after a systematic review of the LHON scientific literature
 - Must have individual patient data that included mutation type, age, BCVA associated with a time of onset for vision loss
 - Patients included only if they had confirmed *ND4* mutation and were ≥ 15 years old

¹The 10 studies that passed the inclusion criteria were: Hotta 1995, Lam 2014, Nakamura 1993, Newman 1991, Qu 2007, Qu 2009, Romero 2014, Sadun 2004, Yang 2016, and Zhou 2010.

LUMEVOQ[®] modifies disease outcome

Sustained improvement after LUMEVOQ[®] injection vs. absence of recovery among untreated patients

Figure 1. Evolution of Visual Acuity in LUMEVOQ[®]-treated Patients (N=76) versus Untreated Patients (N=208)



Note: All patients had a confirmed G11778A mutation in the *ND4* mitochondrial gene and were at least 15 years old. The diagram shows the Locally Estimated Scatterplot Smoothing (LOESS) curves for visual acuity in LUMEVOQ[®]-treated patients and untreated patients. The shaded areas represent the 95% confidence interval for the mean BCVA. "Treated" eyes refer to all eyes (LUMEVOQ[®] and sham) from the RESCUE, REVERSE and CLIN06 trials (N=76 patients / 152 eyes). Untreated eyes refer to patient-level data from the REALITY study and a matched data set from two prospective and eight retrospective natural history studies¹ (N=208 patients / 408 eyes).

*Statistically significant difference between mean visual acuity of treated and untreated eyes at M18, M24, M36 and M48, as illustrated by the non-overlapping confidence intervals.

LUMEVOQ® shows meaningful improvement on Quality of Life metrics



NEI VFQ-25 Results from REVERSE study

Mean change from baseline (absolute score) at week 96



— Considered clinically relevant difference*

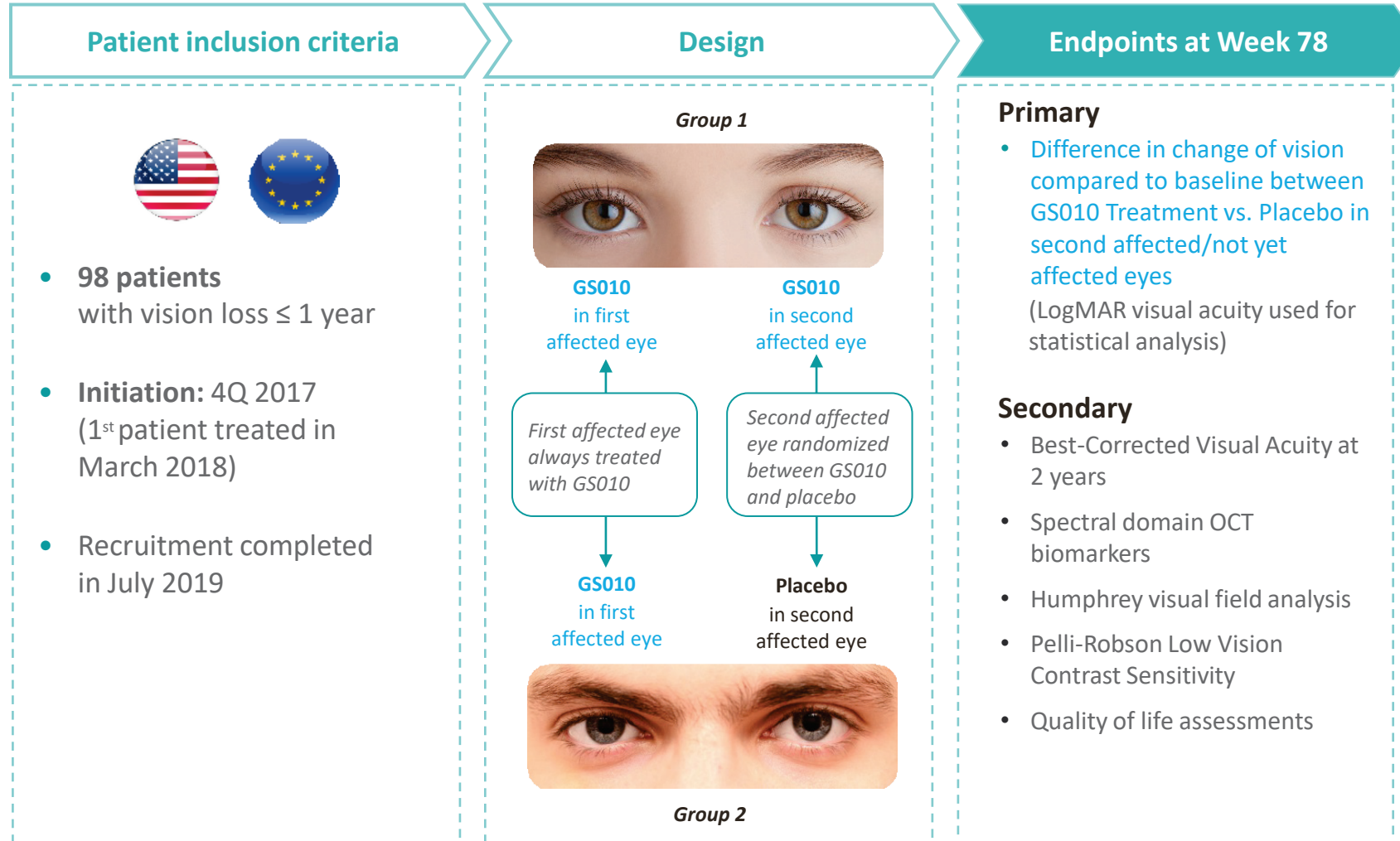
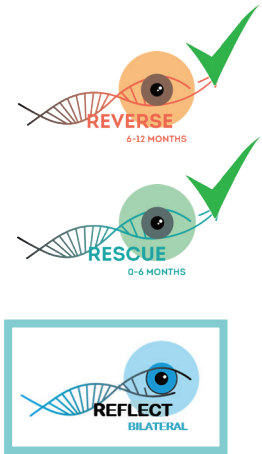
* Suñer *et al.* (2009): clinically relevant score differences based on a clinically significant 15-letter BCVA improvement at 12 months.

** The composite score is an average of the vision-targeted sub-scale scores, excluding the general health rating question.

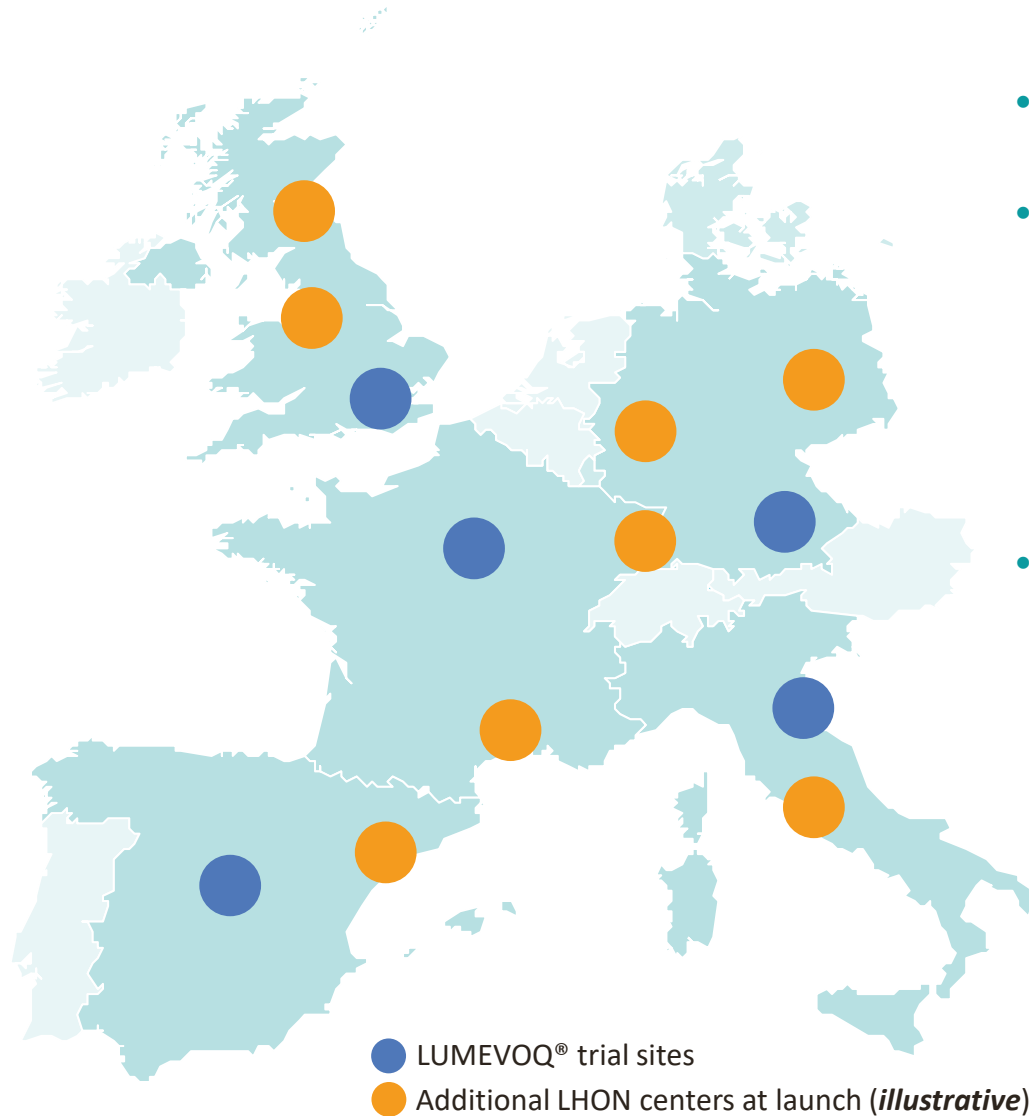
Last ongoing Phase III trial: REFLECT to assess efficacy and safety of bilateral injection

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

Q1 2021
LUMEVOQ®
REFLECT
Week 78
Read-out

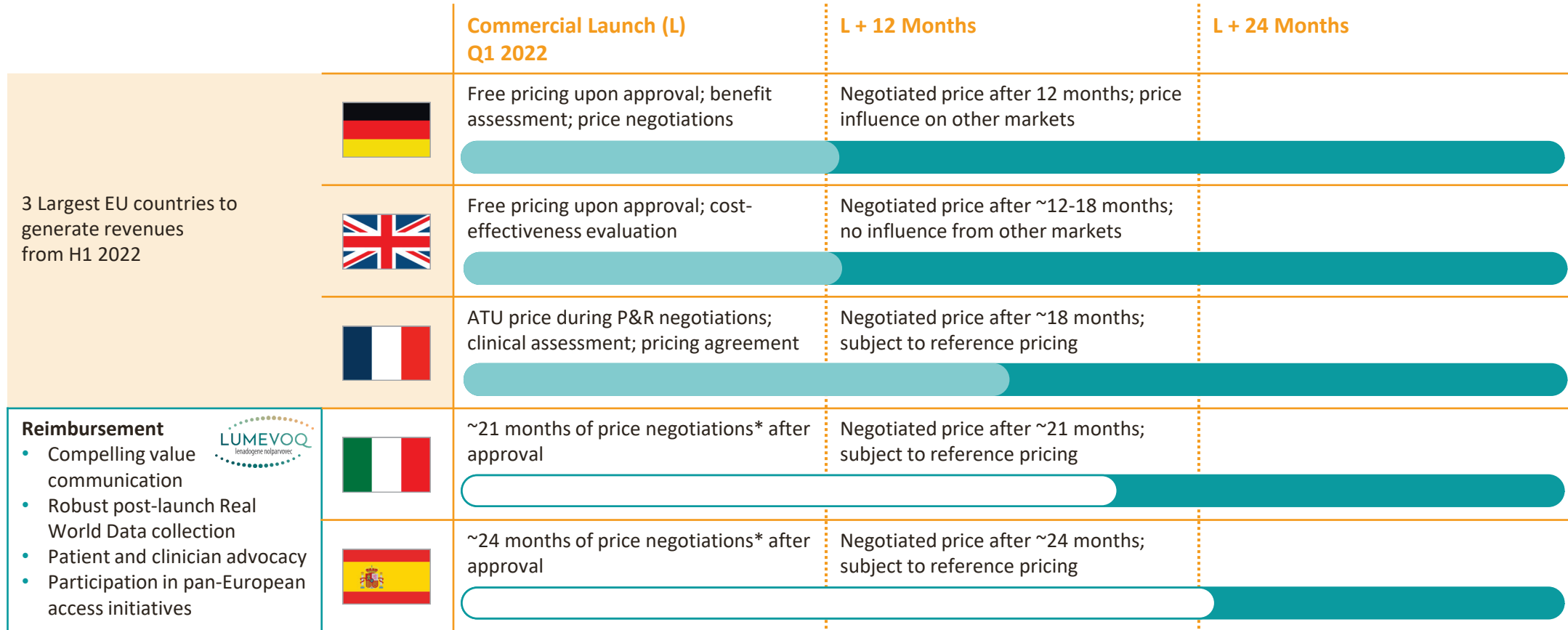


European Commercial Strategy – Leveraging LUMEVOQ® Trial Centers to Build Network of LHON Centers of Excellence



- LHON experts mapped in both major and smaller markets
- Progressively build the LHON clinical network working with LHON experts
 - Recognize varying levels of LHON expertise and patient mobilization across markets
 - Balance patient reach with logistical complexity
- LHON expert- and LHON patient-centric commercial and medical teams executing focused local activities
 - Foster existing relationship with centers and LHON experts
 - Broaden LHON expert network locally and internationally
 - Manage patient and caregiver experience along the patient journey

European Reimbursement Strategy – Short Term Revenues Generation Expected in H1 2022



Note: Duration of negotiations depicted is based on industry benchmarks for recent rare disease launches; timings are illustrative

Compassionate Use for LUMEVOQ® (GS010)

Seeking use of an investigational medication under circumstances a patient may not be able to participate in a clinical trial and before MA/BLA approval by regulatory authorities



- 4 individual patients Expanded Access INDs have been approved by the FDA for GS010 (lenadogene nolparvovec)
- These 4 subjects have been treated (bilateral GS010 IVT) under the investigator-sponsored programs in 2019



ansm

- “ATU Nominative” - named patient Temporary Authorization for Use - for LUMEVOQ® granted by ANSM to CHNO of the *Quinze-Vingts* in Paris
 - 3 patients bilaterally treated
 - Additional requests approved
- Bilateral injections priced at €700,000 per patient, expected to generate revenues in 2020
 - Reimbursement warranted by the national Social Security up to € 30M/year
- Next step : seeking for a Cohort ATU “ATU de Cohorte”

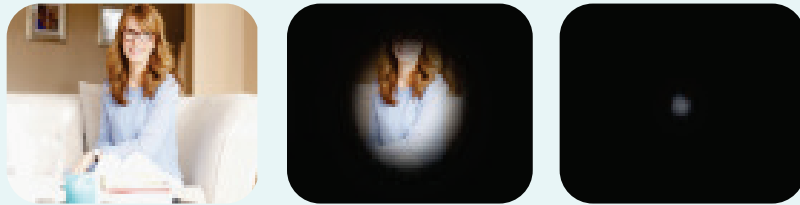
GS030

Second product candidate targeting photoreceptor degenerative diseases:

- Retinitis Pigmentosa (RP)
- Age-Related Macular Degeneration (AMD)

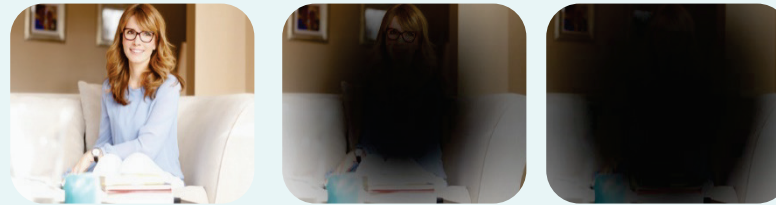
Treating the 2 main degenerative diseases of photoreceptors that lead to blindness

Retinitis Pigmentosa



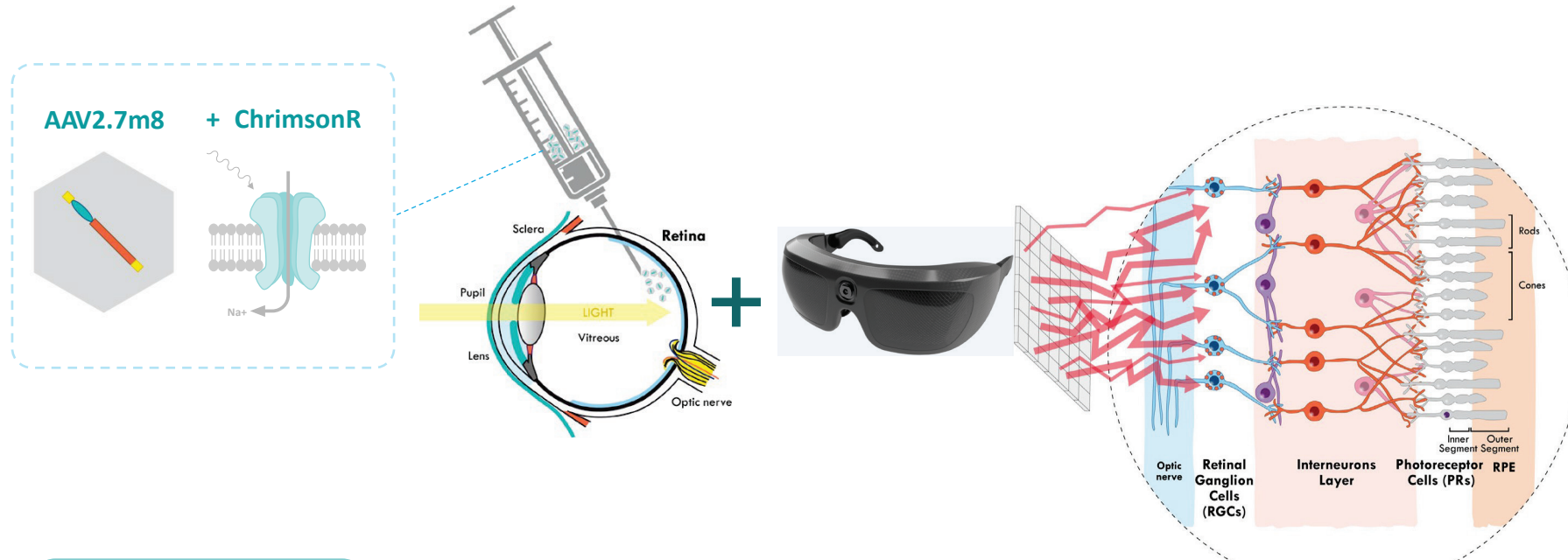
- Blinding genetic disease caused by mutations in over 100 different genes
- Sequential photoreceptor degeneration leads to slow & irreversible progression to blindness, usually at age 40-45
- 15-20,000 new patients each year in the US and EU

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
- Dry-AMD affects 350-400,000 new patients a year
- 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

GS030: using Gene Therapy to rejuvenate production of light-sensitive protein and restore vision



The product of research collaboration with

MIT Massachusetts Institute of Technology

ADVERUM BIOTECHNOLOGIES

UPMC UNIVERSITY PITTSBURGH MEDICAL CENTER

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

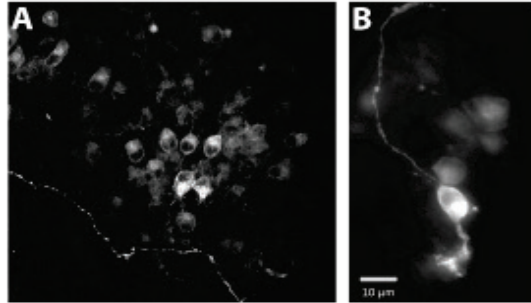
Retinal output sent to brain for image processing

GS030 leads to functional vision restoration in monkey and rats

Localization of light-sensitive protein in NHP retina

Expression of ChrR-tdT in midget cells of monkey perfovea

In vivo in NHP assessment 6 months after IVT injection

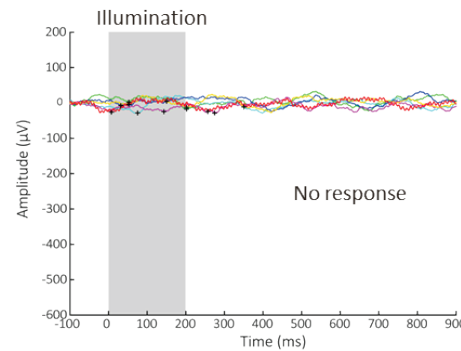


Restoration of a functional vision in P23H rats

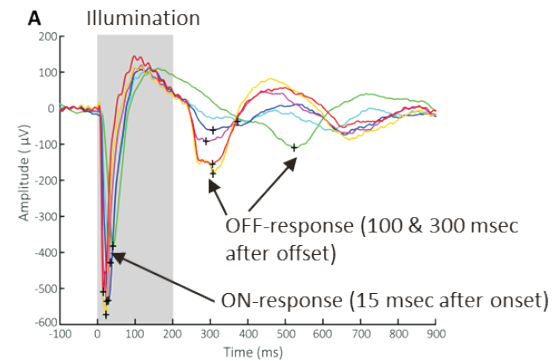
Light-induced visual evoked cortical responses

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

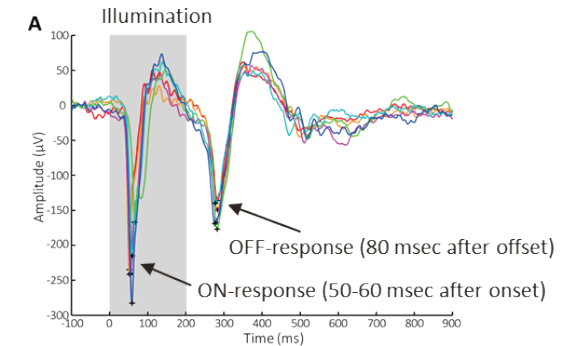
Untreated P23H rat



GS030-treated P23H rat



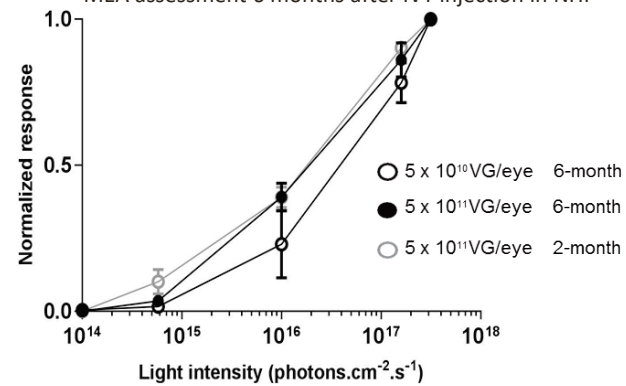
Normal Long-Evans rat



Dose-ranging response to firing relationship in NHP

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

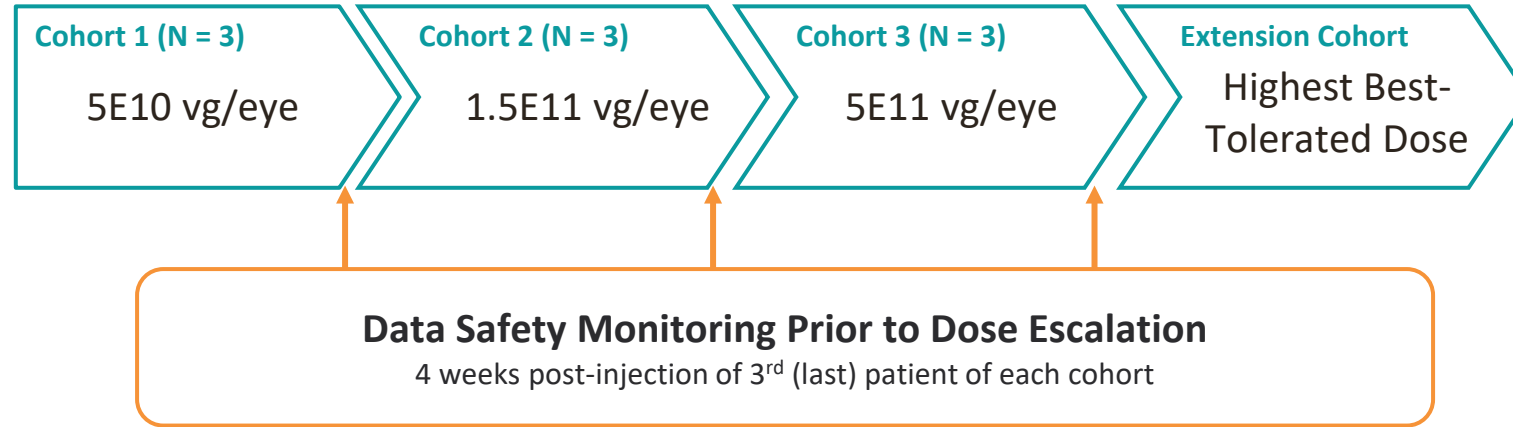
MEA assessment 6 months after IVT injection in NHP



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

2nd cohort fully enrolled and treated
DSMB#2 approved to move to cohort 3 without any modification

Building high strategic value



A company developing innovative and versatile technology platforms nearing commercialization and evolving in an area where value is increasingly being recognized by the market

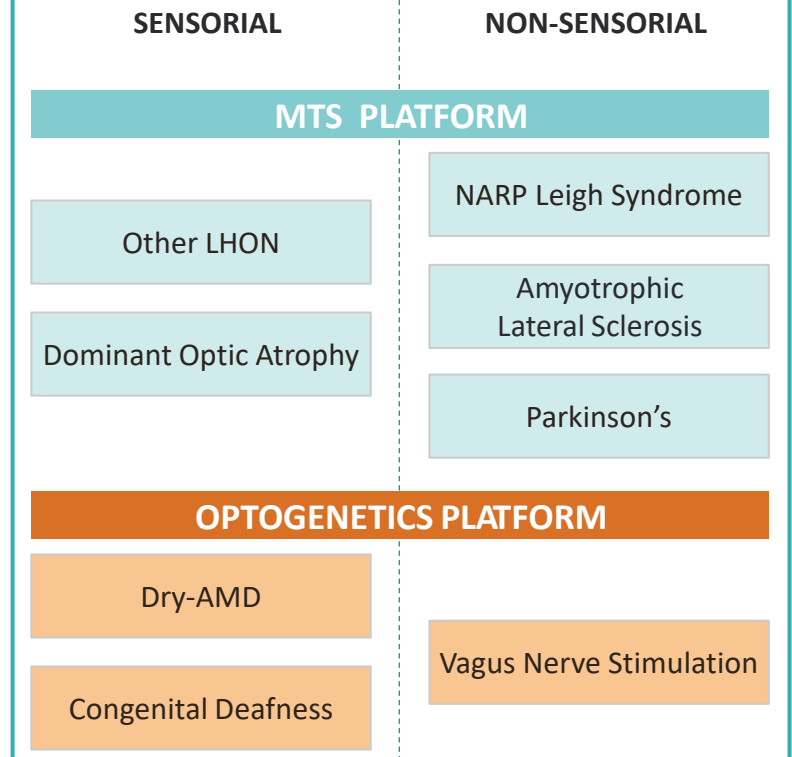
GenSight at the forefront of Gene Therapy with potential product launch in 2021

- » **LUMEVOQ® in LHON-ND4**
 - Strong clinical data
 - Upcoming confirmatory Phase III trial
- » **Targets attractive market**
 - High unmet medical need
 - Virtually no competition
 - Well defined path to commercial success
- » **Proprietary MTS technology**
 - Broad range of mitochondrial diseases
- » **Rich news flow** in 2020 and 2021

Gene Therapy increasingly attracts interest from investors and Large Pharma

- » **Viable therapeutic option** (already 3 approved therapies)
- » **Pricing reflective of significant therapeutic benefit**
- » **Large Pharma increasingly involved in the field**

LUMEVOQ® and Beyond: Two platforms targeting large number of sensorial and non-sensorial diseases



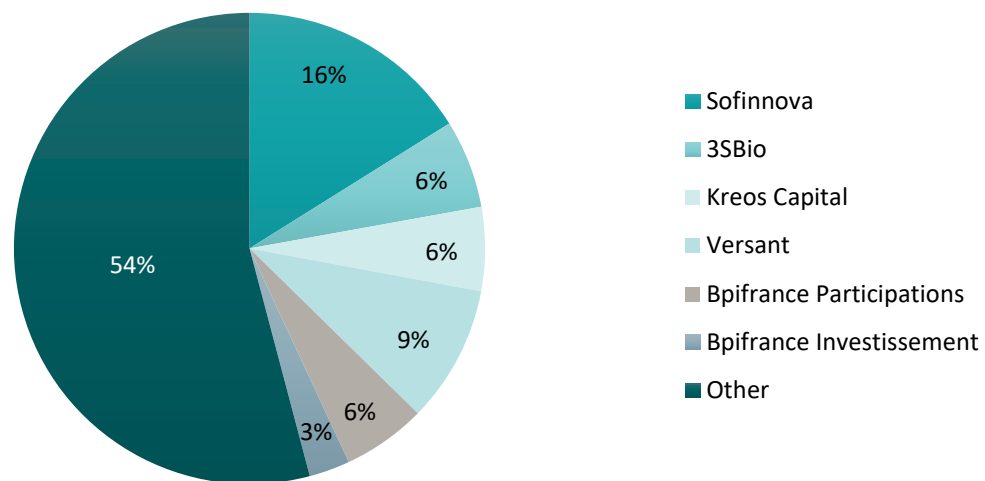
GenSight Biologics in numbers

Key financial information

Company Overview		
Market Cap*:	€ 101m	Analyst Coverage
Cash Position (June 30, 2020):	€ 16.8m	
Outstanding Shares:	32.8m	
Latest Amount Raised (Dec. 20, 2019):	€ 15m	• Oddo & Cie: Martial Descoutures (FR)
Raised to date	€ 142m	• Gilbert Dupont: Jamila El Bougrini (FR)
IPO Date	July 2016	• Chardan: Gbola Amusa (US)

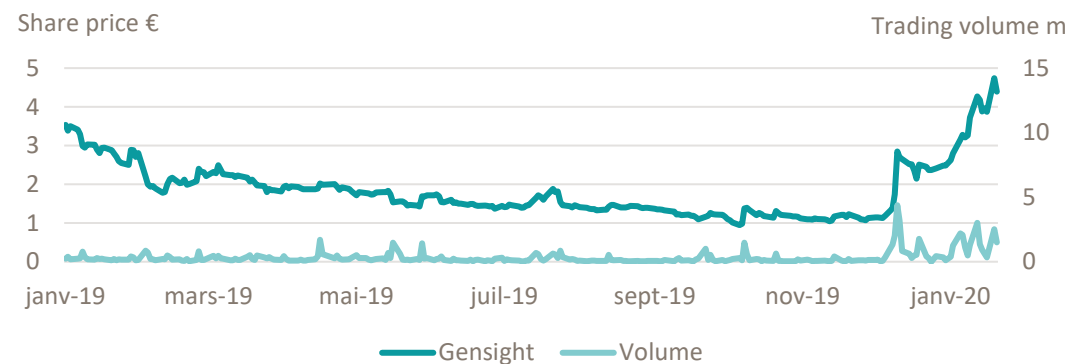
*As of July 3, 2020

Shareholder structure



As of December 31, 2019

Share price evolution and trading volume



Corporate calendar

Corporate calendar	Date
2019 Full-Year Financial Update and Statements	March 12, 2020
2020 1Q Cash Position	April 21, 2020
Annual General Meeting	April 29, 2020
2020 First-Half Financial Update and Statements	July 30, 2020
2020 3Q Cash Position	October 20, 2020
2020 4Q Cash Position	January 19, 2021

Appendix



RESCUE & REVERSE Phase III trials with unilateral injection demonstrated unprecedented improvement

Different patient inclusion criteria

Same design

Visual recovery at Week 96 and vs natural history

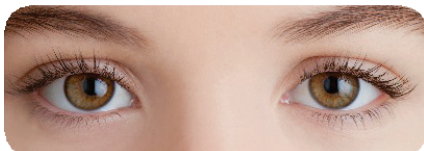
REVERSE



- Onset of disease **6 months to ≤ 1 year**
- 37 patients enrolled

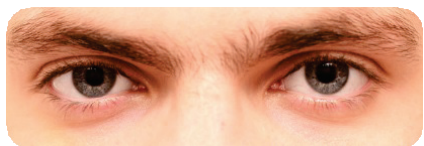
- Double-masked, multi-center
- One eye randomized to GS010; other eye received sham injection

Group 1



GS010 in right eye SHAM in left eye

Group 2

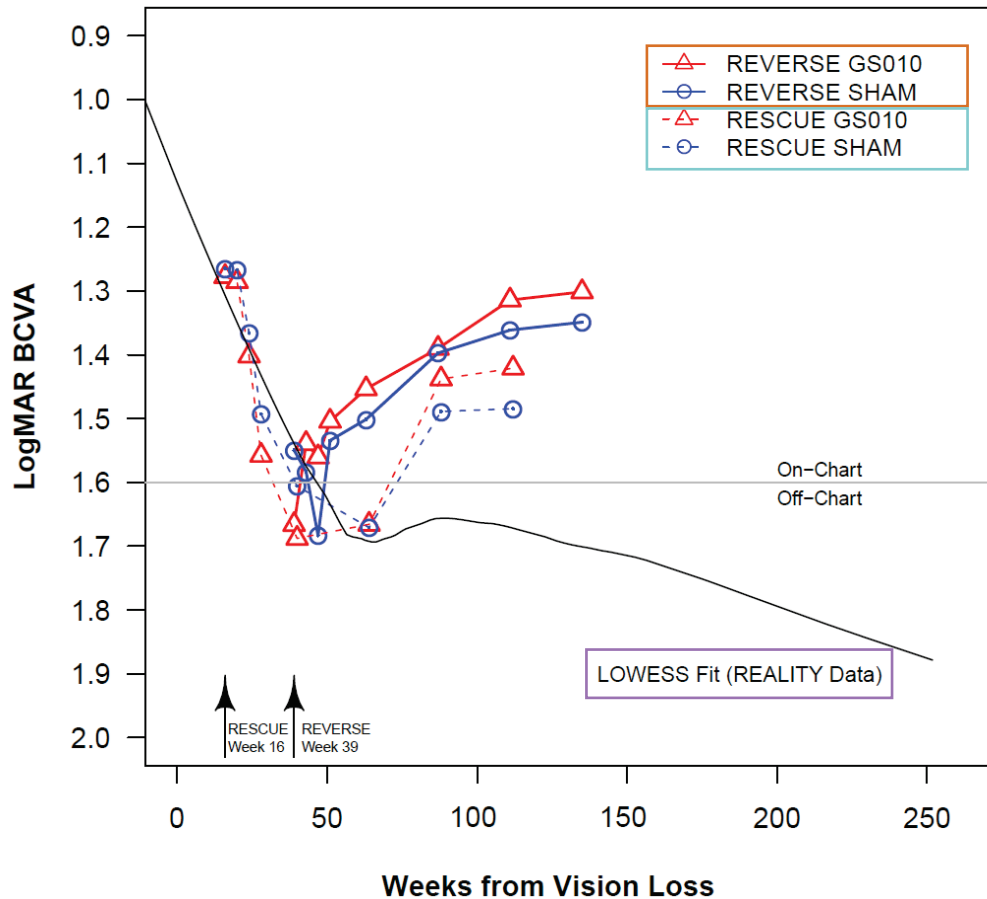


SHAM in right eye GS010 in left eye

RESCUE



- Onset of disease **≤ 6 months**
- 39 patients enrolled



+28 ETDRS Letters vs nadir



+26 ETDRS Letters vs nadir



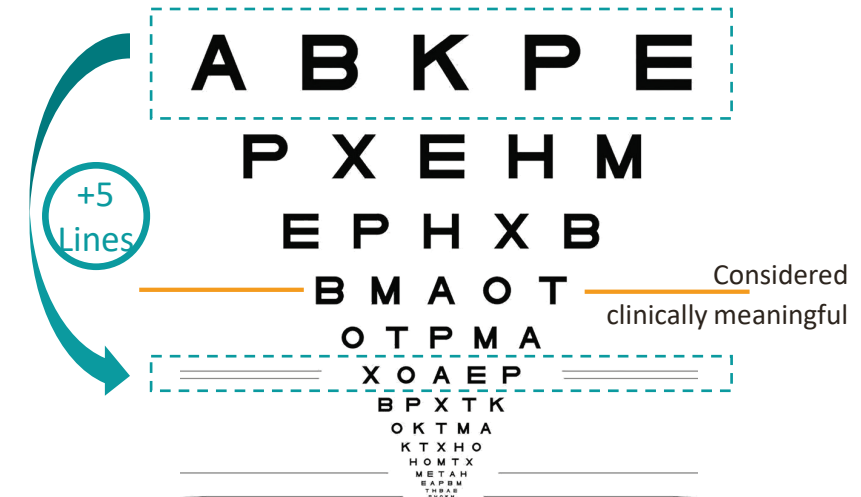
Retrospective Natural History

Visual Acuity: Improvement of BCVA from NADIR

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



Change from NADIR in ETDRS letter equivalents			Change from NADIR in ETDRS letter equivalents		
Week 96			Week 96		
	n	Mean (SD)		n	Mean (SD)
All-GS010 eyes	37	+28.3 (22.5)	All-GS010 eyes	34	+26.3 (23.9)
All-sham eyes	37	+24.5 (24.0)	All-sham eyes	34	+22.8 (24.2)



NADIR was defined as the **worst BCVA** from baseline to Week 96
 Mean change from nadir was calculated using observed values (no data imputation)

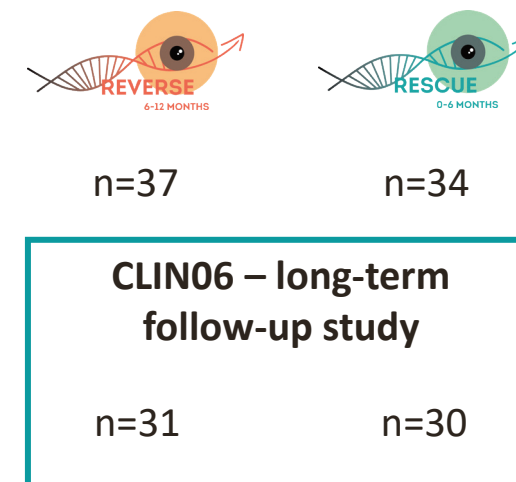
**Unparalleled clinical benefit demonstrated with LUMEVOQ® (GS010) in LHON in two Phase III studies:
 +28/+26 ETDRS letters (i.e. over 5 lines on visual scale) improvement vs nadir**

3-year long-term follow-up: sustained efficacy and safety

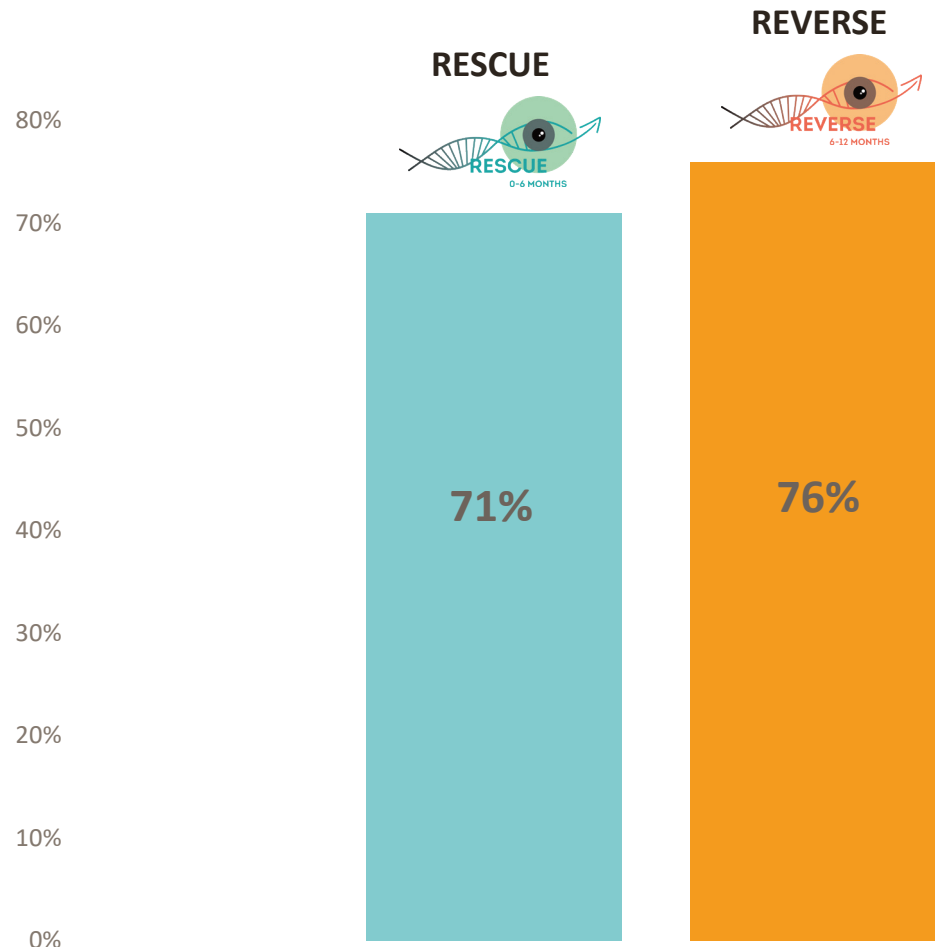
Change from NADIR in ETDRS letter equivalents			
		Year 2 post-injection	Year 3 post-injection
	n	Mean (SD)	Mean (SD)
All-GS010 eyes	61	+18.8 (15.3)	+20.5 (18.3)
All-sham eyes	61	+17.3 (14.6)	+19.4 (18.5)

The CLIN06 sample consists of the RESCUE and REVERSE participants who accepted to be followed in the CLIN06 study

NADIR was defined as the **worst BCVA** from baseline to Week 96 and 144
Mean change from nadir was calculated using observed values (no data imputation)



REVERSE and RESCUE demonstrate that over 70% of patients benefit from treatment

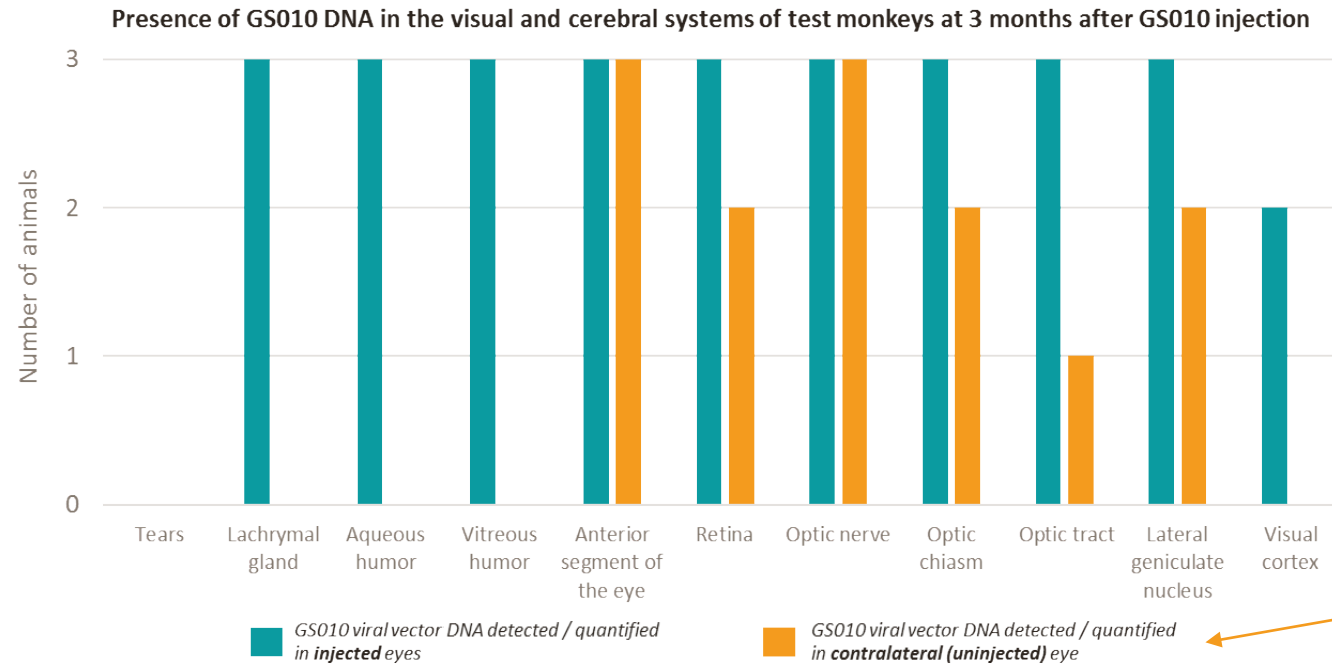


76% of REVERSE subjects achieved at least 15 letters improvement vs nadir in one or two eyes

71% of RESCUE subjects achieved at least 15 letters improvement vs nadir in one or two eyes

GS010 (LUMEVOQ®) viral vector DNA detection in uninjected eye of monkeys supports bilateral effect in REVERSE and RESCUE Phase III trials

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



- Three test monkeys injected in one 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.

European Commercial Strategy - Facilitate and Speed Up Patient Access to LUMEVOQ®

