GenSight BIOLOGICS

Corporate Presentation

June 2021

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

LUMEVOQ® – Filed for Approval in Europe in September 2020 and preparing for commercial launch in H1 2022

- **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

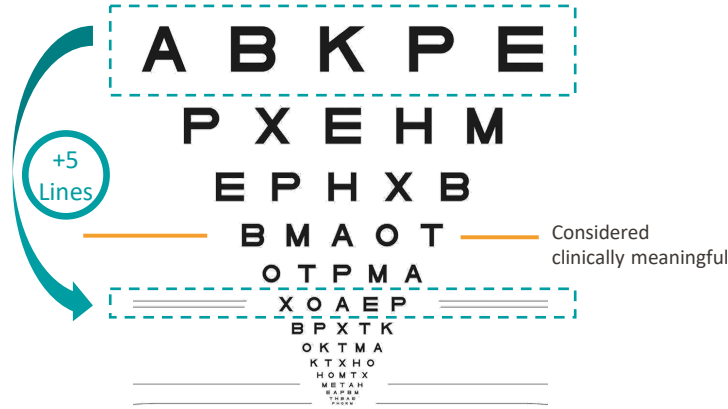
Commercial strategy and manufacturing capabilities close to completion

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

(1) Nadir: worst visual acuity from baseline

Established in 2012 / IPO in 2016	
EuroNext Paris:	SIGHT
Market Cap (May 3, 2021):	€ 423m
Avg 30-day Daily volume:	1.0% of O/S
Cash (March 31, 2021):	€ 61.1m

Improvement vs nadir in REVERSE and RESCUE



Seasoned Executive Team

Bernard Gilly
Chief Executive Officer

PIXIUM VISION (Since 2011)
FOVEA PHARMA (2005-2009)
SOFINNOVA PARTNERS (2000-2005)
TRANSGENE (1992-2000)

Ph.D. in biology and bio-economics

Thomas Gidoin
Chief Financial Officer

DBV TECHNOLOGIES (2012-2015)
IPSEN (2008-2011)
ERNST & YOUNG (2007-2008)

Magali Taiel
Chief Medical Officer

ProQR THERAPEUTICS (2016-2018)
ELI LILLY (2004-2016)
PFIZER (2001-2004)
SERVIER (1999-2001)

M.D., Board-certified ophthalmologist

Leigh Shaw
VP of Regulatory Affairs

UNITED NEUROSCIENCE (2017-2020)
NIGHTSTARX (2015-2017)
GREGORY FRYER ASSOCIATES (2005-2015)
HUNTINGDON LIFE SCIENCES (2002-2005)
CANTAB PHARMACEUTICALS (1995-2001)

Catherine Cancian
VP of Pharmaceutical Operations

GENETHON (2015-2017)
SANOFI PASTEUR (1998-2014)

Julio Benedicto
VP of Marketing

IMS CONSULTING (2011-2017)
BOOZ & COMPANY (2010-2011)
MONITOR GROUP (1994-2009)

Marie-Claude Holtz
VP of Quality

EXELTIS SANTE (2016-2019)
PFIZER (2015-2016)
ABBVIE (2014-2015)
GALDERMA (2012-2013)
LABORATOIRE LAFON (TEVA) (1993-2012)

Pharm.D.

Marion Ghibaudo
Chief Technical Officer

MAUNA KEA TECHNOLOGIES (2018-2021)
L'OREAL (2009-2018)

PhD in biophysics

Isabelle Scarabin
Director, Business Development

LYONBIOPOLE (2006-2013)
GREATER LYON (2002-2006)
RESSOURCES EN INNOVATION (1999-2002)
SANOFI PASTEUR MSD (1998-1999)

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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	Expected Approval	
MTS platform	LUMEVOQ® (FDA & EMA Orphan Drug Designation)	LHON ND4 (EU)						H1 2022	REVERSE: Phase III top-line data reported in Apr (48w) & Oct (72w) 2018 and in May 2019 (96w)
		LHON ND4 (US)					Q2 2022		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 June 2021
	GS011	LHON ND1							Initiate preclinical studies following GS010 Phase III clinical data
	Undisclosed Mitochondrial Target	Undisclosed							
Optogenetics	GS030 (FDA & EMA Orphan Drug Designation)	Retinitis Pigmentosa (RP)							PIONEER: Extension cohort in PIONEER Phase I/II clinical trial to be completed by end 2021. Early findings in Q2 2021
	GS030	Dry AMD & Geographic Atrophy							

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

LUMEVOQ® commercial launch in Europe expected in H1 2022

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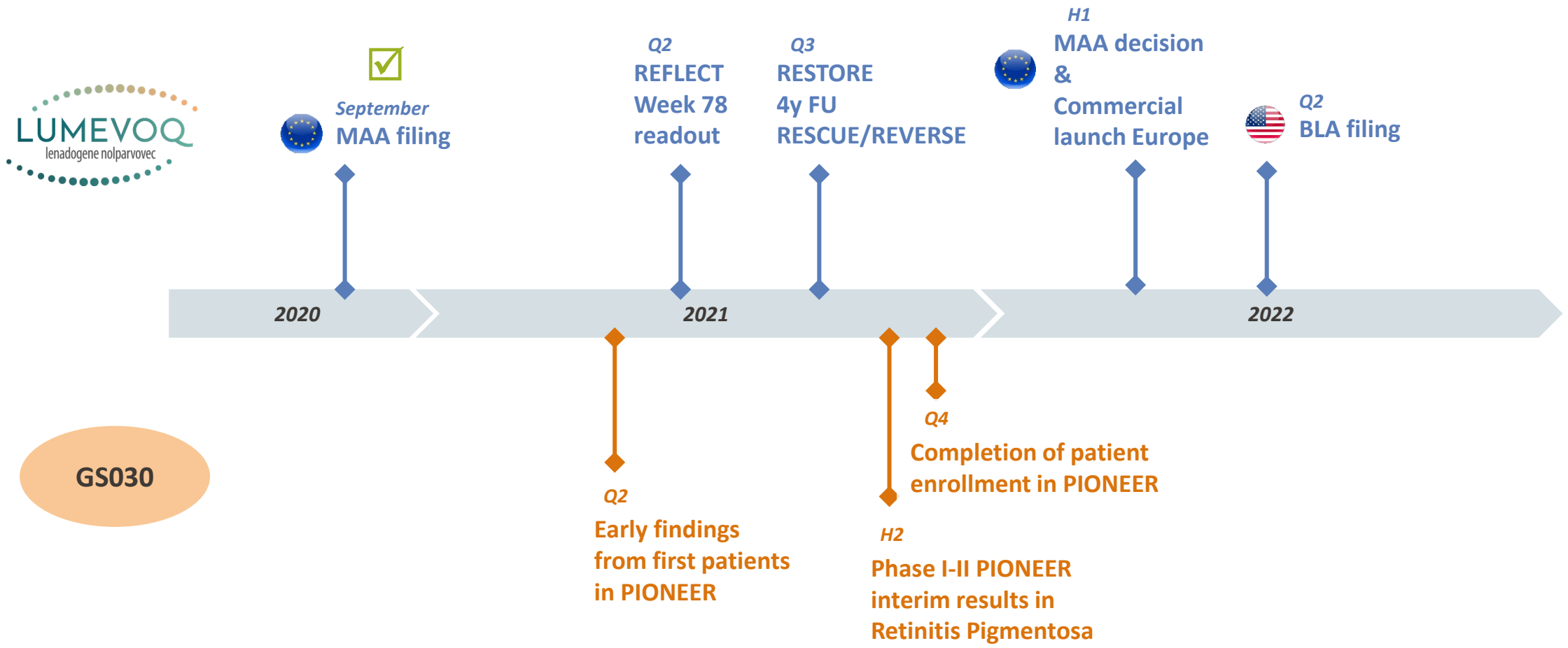
Rich upcoming news flow with numerous inflexion points



LUMEVOQ® (GS010) in LHON-*ND4*

Last Phase III ongoing in Leber Hereditary Optic Neuropathy

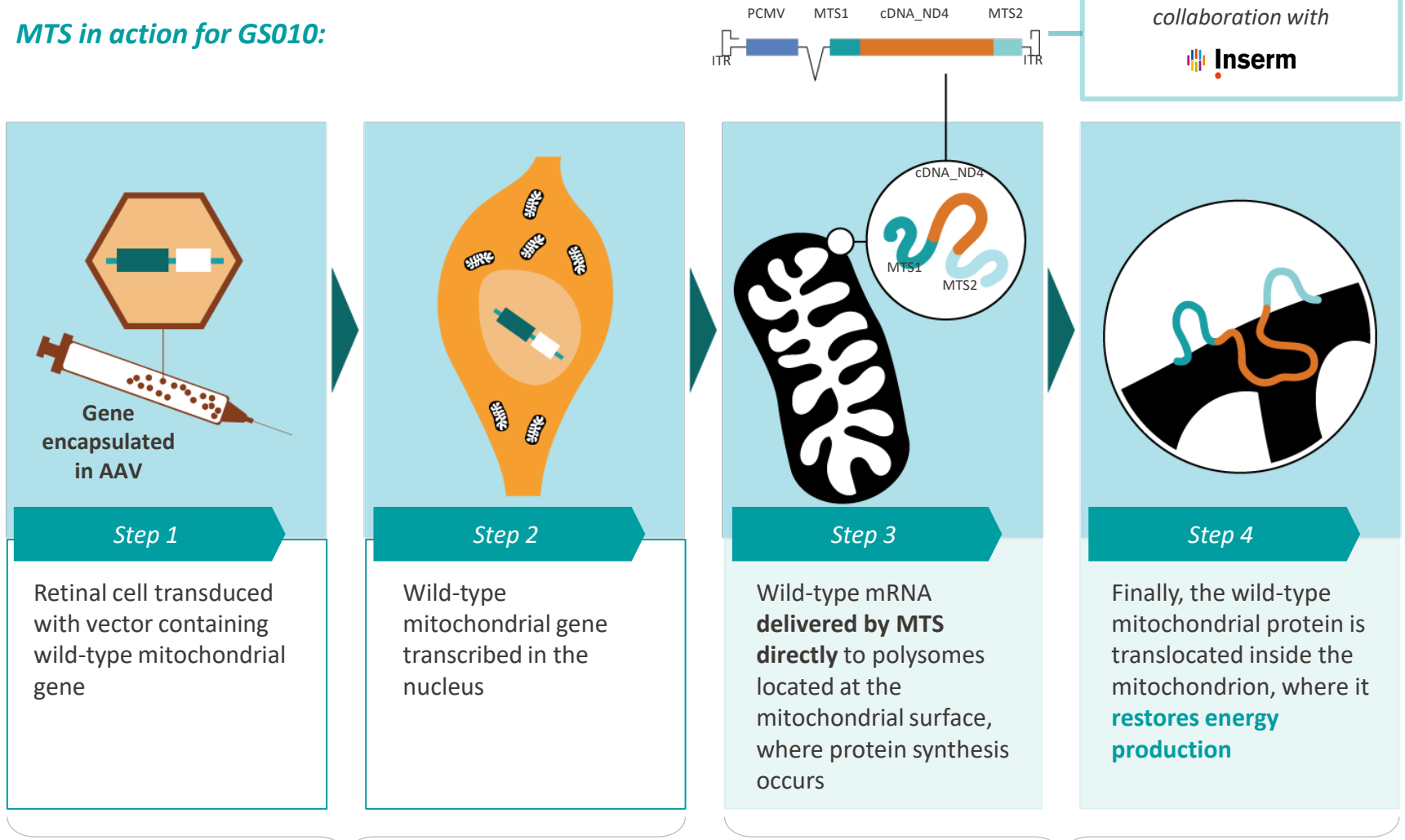
Commercial preparation ongoing for 2022 European launch

LUMEVOQ® introduces Gene Therapy solution

Replacing affected mitochondrial mRNA via proprietary *MTS* technology*

The product of research collaboration with Inserm

MTS in action for GS010:



*MTS = mitochondrial targeting sequence

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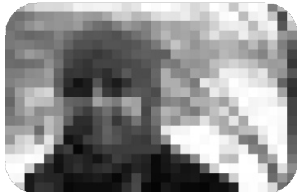
Leber Hereditary Optic Neuropathy (LHON-ND4) high unmet medical need

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

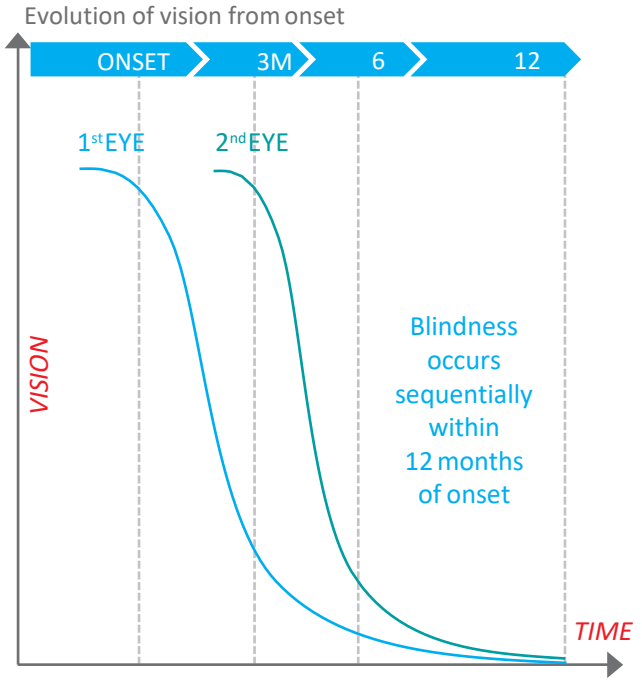


Image source: illustrated from Newman NJ et al., Am J Ophthalmo. 141(6), 1061-1067,2006

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

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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

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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

[1]The 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.

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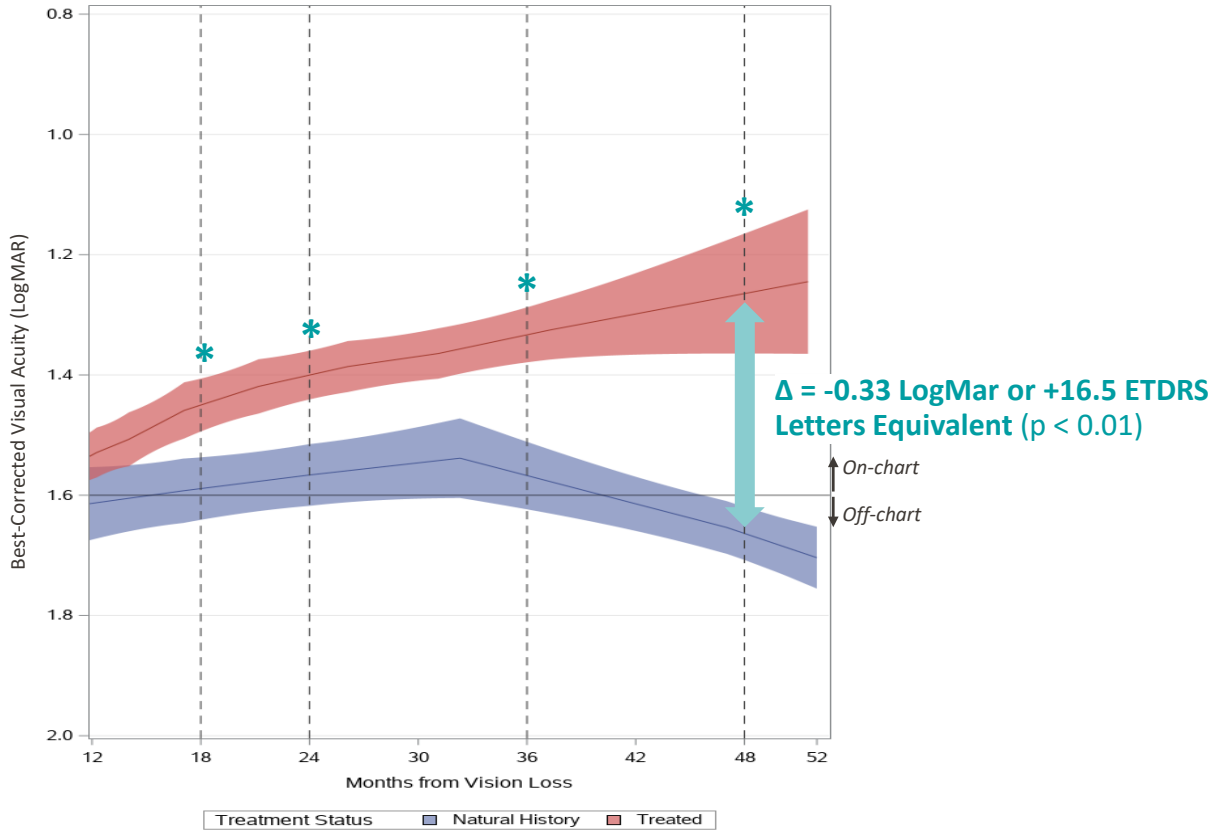
LUMEVOQ® modifies disease outcome

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)

Treated: All patients RESCUE, REVERSE and CLIN06

Untreated: REALITY + 10 Natural History Studies



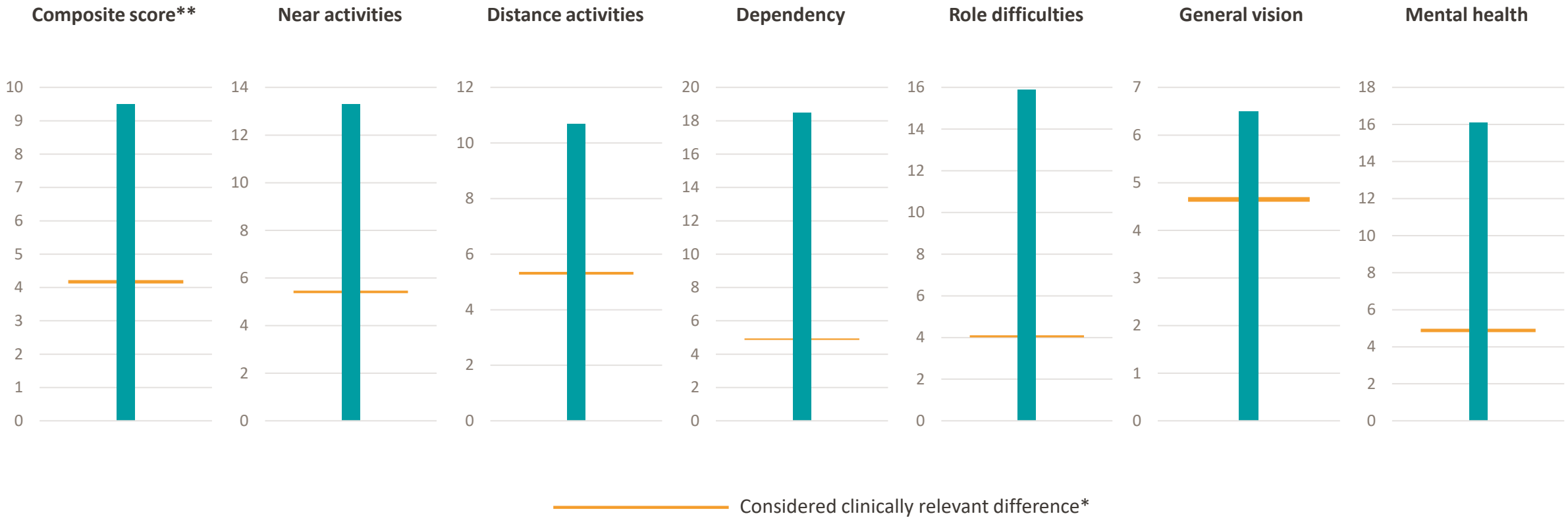
Note: All patients had a confirmed G11778A mutation in the *ND4* mitochondrial gene and were at least 15 years old. The diagram shows the Locally Estimated Scatterplot Smoothing (LOESS) curves for visual acuity in LUMEVOQ®-treated patients and untreated patients. The shaded areas represent the 95% confidence 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 studies[1] (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

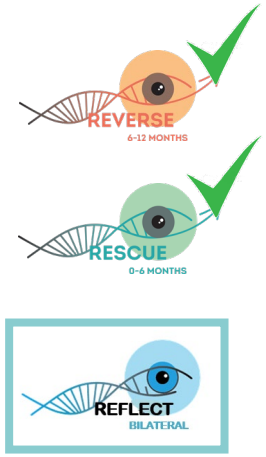


***** Suñer *et al.* (2009): clinically relevant score differences based on a clinically significant 15-letter BCVA improvement at 12 months.
** The composite score is an average of the vision-targeted sub-scale scores, excluding the general health rating question.

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

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

Q2 2021
LUMEVOQ®
REFLECT
Week 78
Read-out



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 78

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

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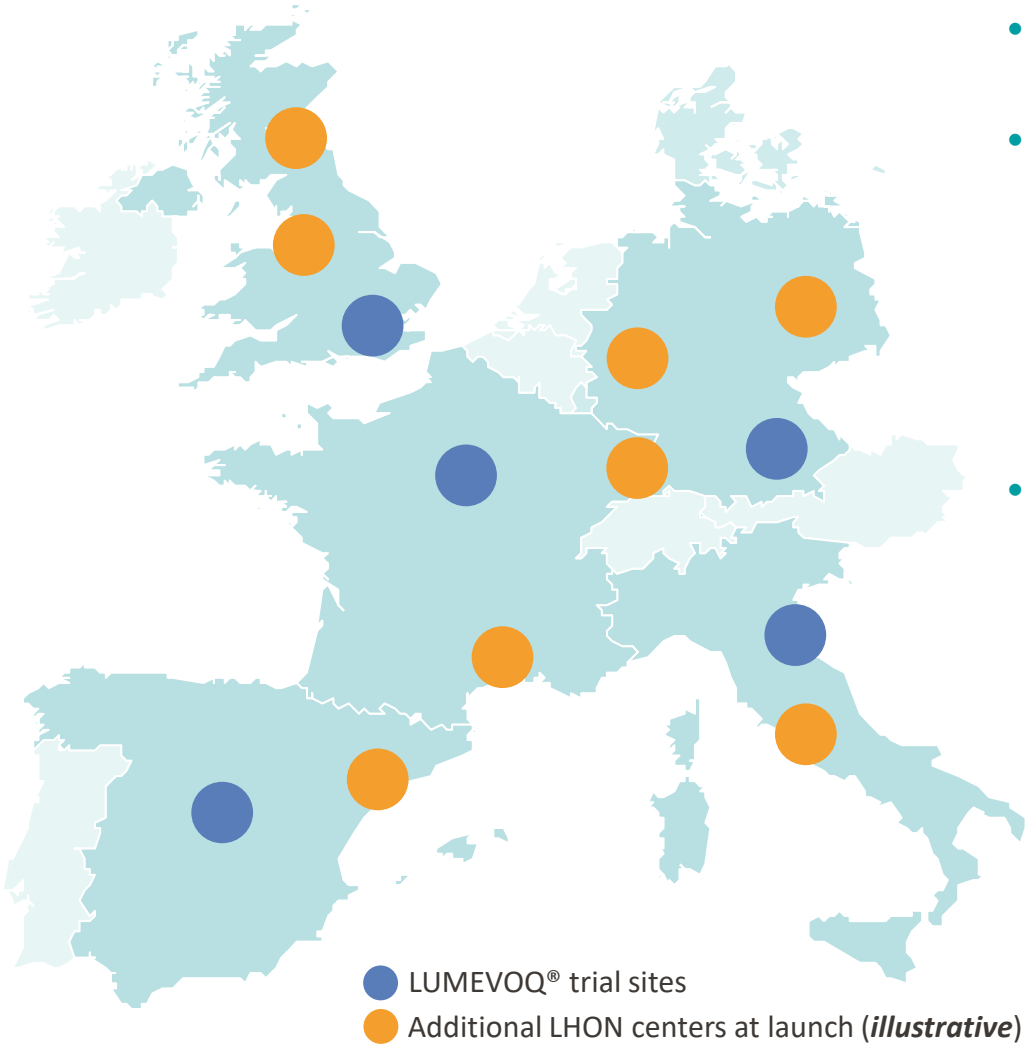
European Commercial Strategy – Leveraging LUMEVOQ® Trial Centers to Build Network of LHON Centers of Excellence



- 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

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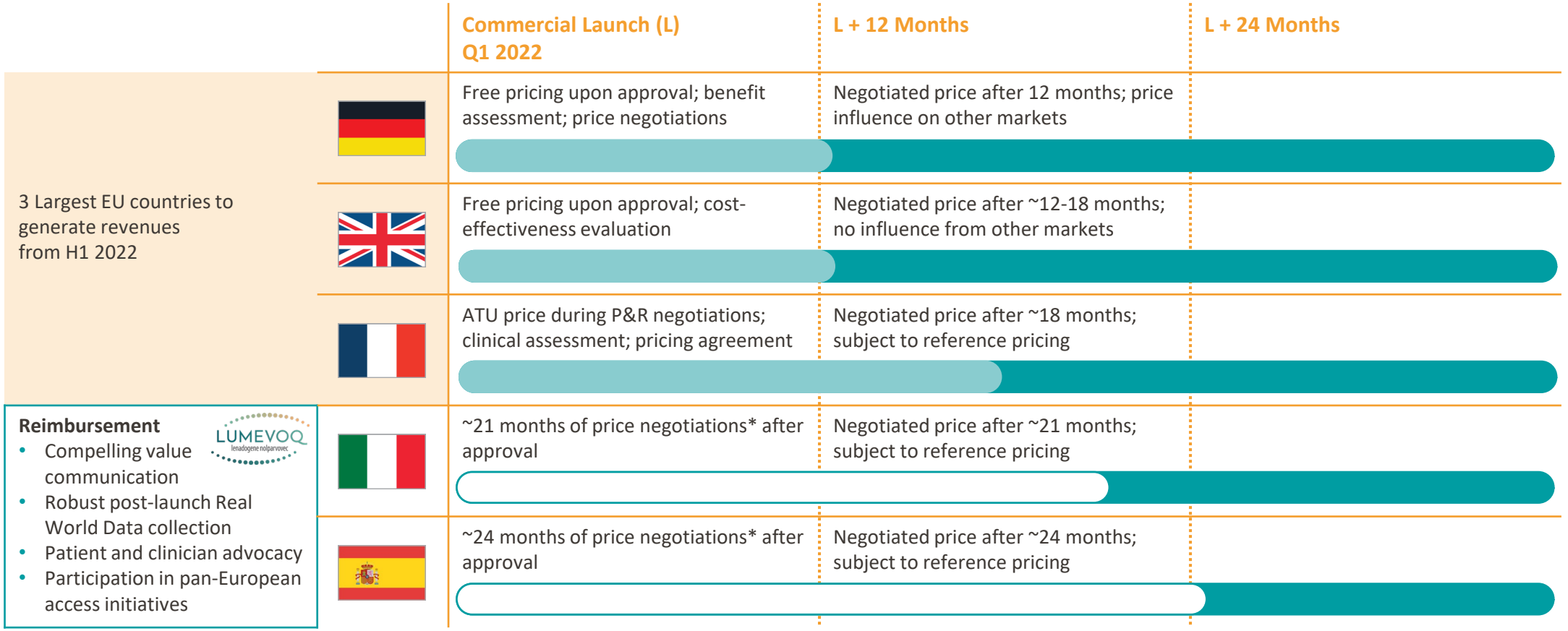
European Reimbursement Strategy – Short Term Revenues Generation Expected in H1 2022



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

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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

- 8 individual patients Expanded Access INDs so far approved by the FDA for LUMEVOQ® (lenadogene nolparvovec)
- These 8 subjects have been treated (bilateral GS010 IVT) under the investigator-sponsored programs since 2019
- Additional 10 individual patients Expanded Access INDs to be processed

- *"ATU Nominative"* - named patient Temporary Authorization for Use - for LUMEVOQ® granted by ANSM to CHNO of the *Quinze-Vingts* in Paris
- Bilateral injections priced at €700,000 per patient
  - €4.4M revenues generated in 2020
  - Increasing demand from physicians in 2021
  - Reimbursement warranted by the national Social Security up to €30M/year
- Named-Patient or Cohort Expanded Access Programs (EAP) in other European countries being set up to leverage LUMEVOQ® treatment for the benefit of patients accross Europe and beyond

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

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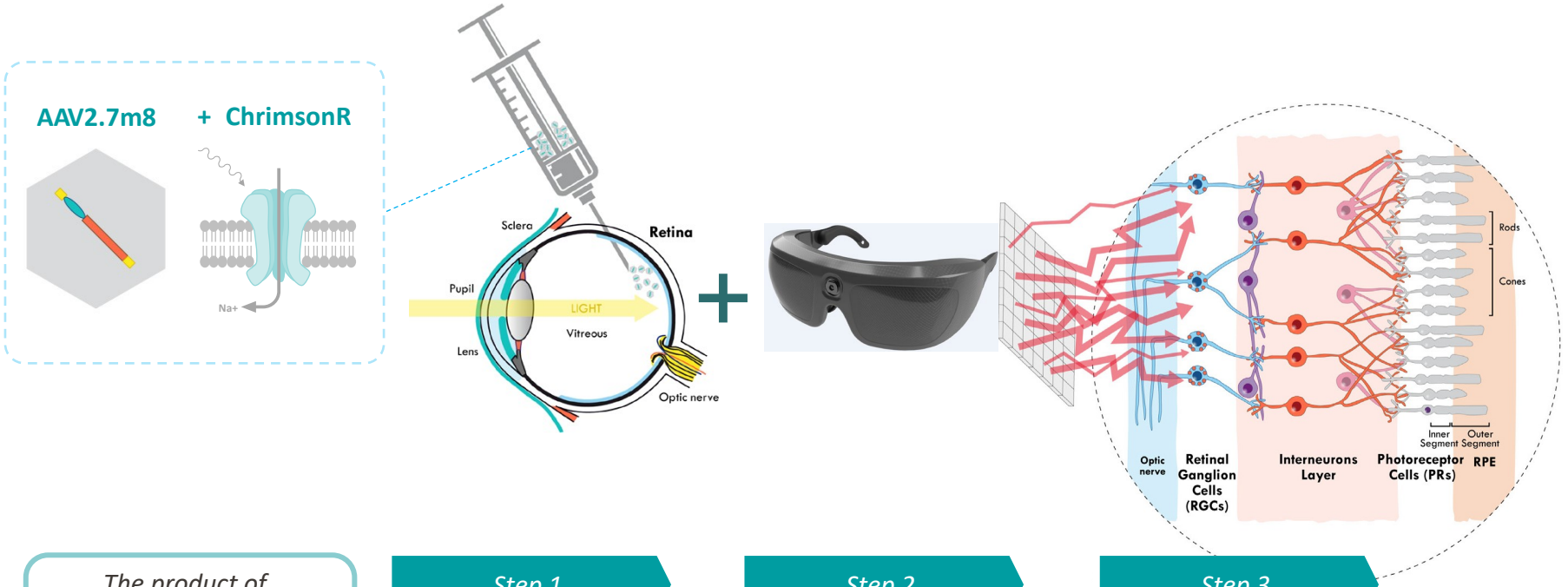
GS030: using Gene Therapy to rejuvenate production of light-sensitive protein and restore vision



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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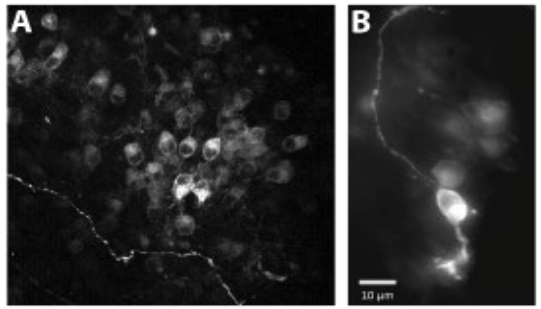
GS030 leads to functional vision restoration in monkey and rats

Localization of light-sensitive protein in NHP retina

Expression of ChrR-tdT in midget cells of monkey perifovea

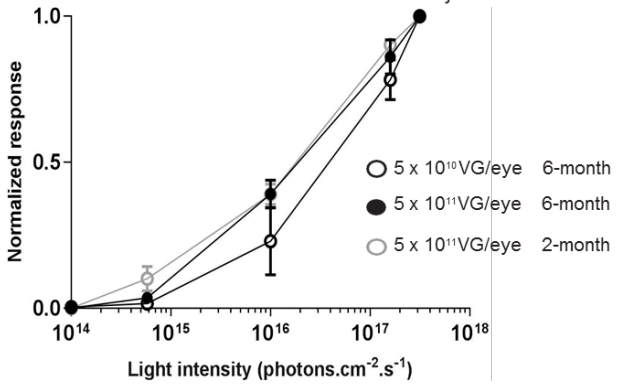
In vivo in NHP assessment 6 months after IVT injection



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



Recent publication

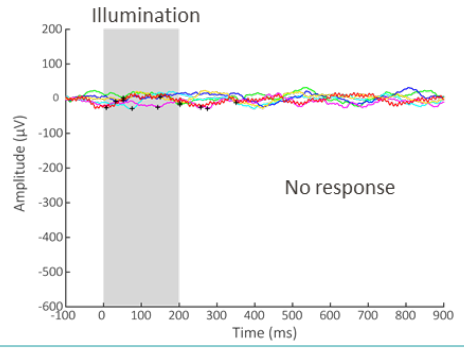
Optogenetic therapy: high spatiotemporal resolution and pattern discrimination compatible with vision restoration in non-human primates. Gauvain G. et al. **Communications Biology, Feb. 2021**
https://www.nature.com/articles/s42003-020-01594-w.

Restoration of a functional vision in P23H rats

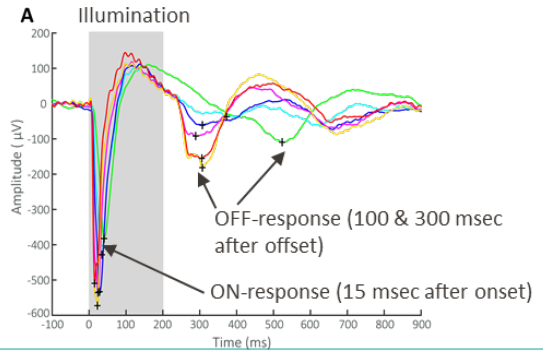
Light-induced visual evoked cortical responses

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

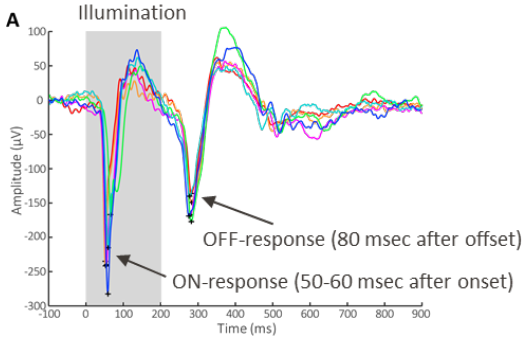
Untreated P23H rat



GS030-treated P23H rat



Normal Long-Evans rat



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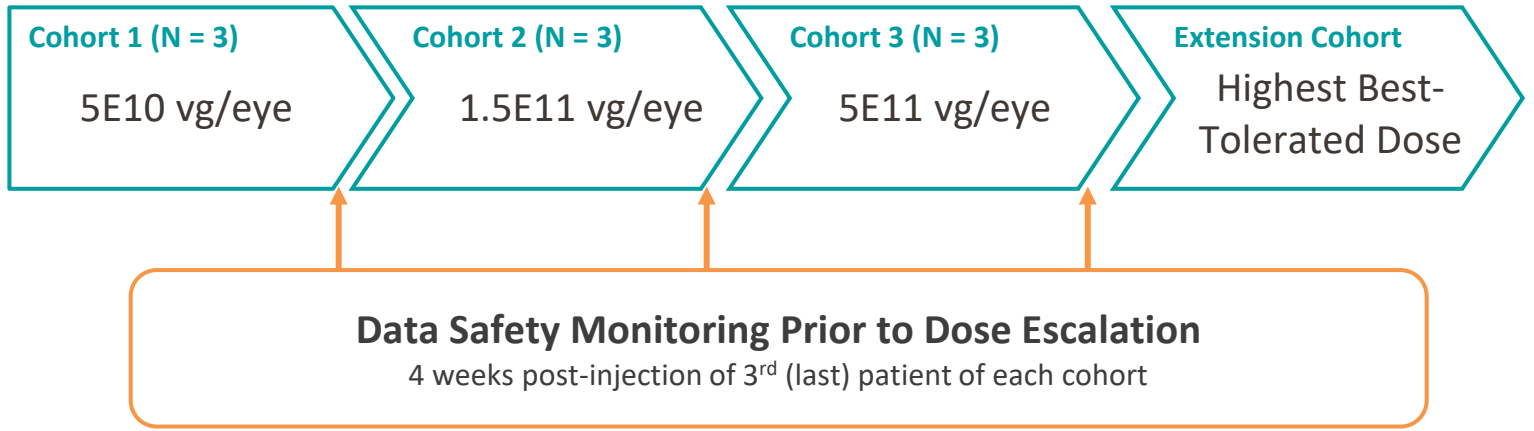
PIONEER Phase I/II clinical trial: A First-in-Man study

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

Recent publication

Partial recovery of visual function in a blind patient after optogenetic therapy.
Sahel J.A. et al., **Nature Medicine, May 2021**
https://www.nature.com/articles/s41591-021-01351-4

Video of the patient performing the tests available on www.gensight-biologics.com.

Cohort 3 ongoing without any modification after DSMB#2 approval

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

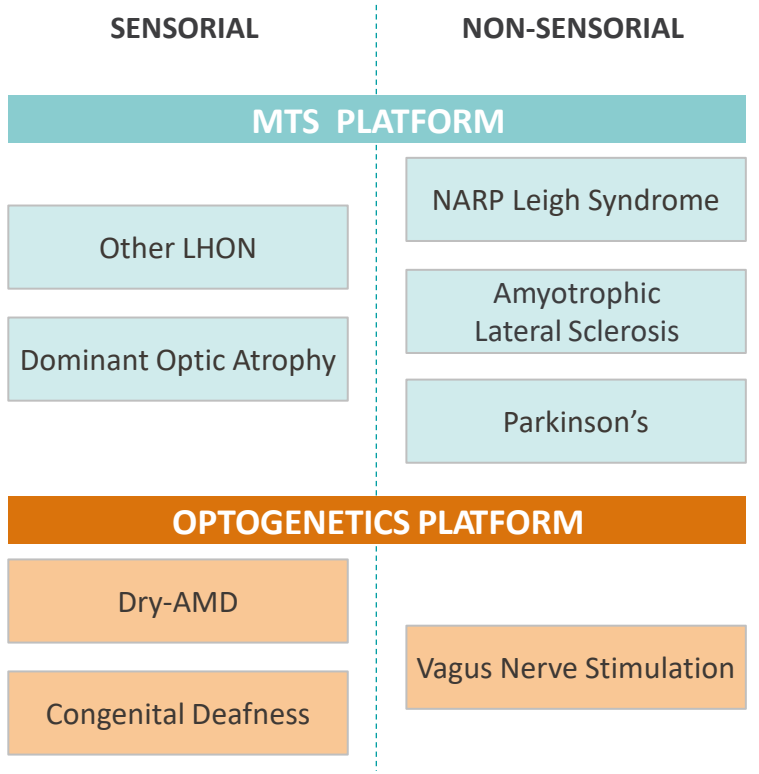
Gene Therapy increasingly attracts interest from investors and Large Pharma

» **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 pargeting large number of sensorial and non-sensorial diseases



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GenSight Biologics in numbers

Key financial information

Company Overview

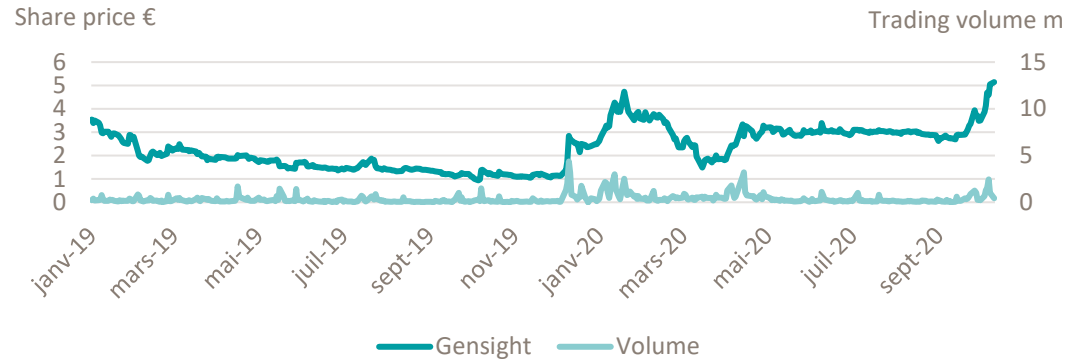
Market Cap*:	€ 423m
Cash Position (March 31, 2021):	€ 61.1m
Outstanding Shares:	46.0m
Latest Amount Raised (March 2021):	€ 30m
Raised to date	€ 197m
IPO Date	July 2016

Analyst Coverage

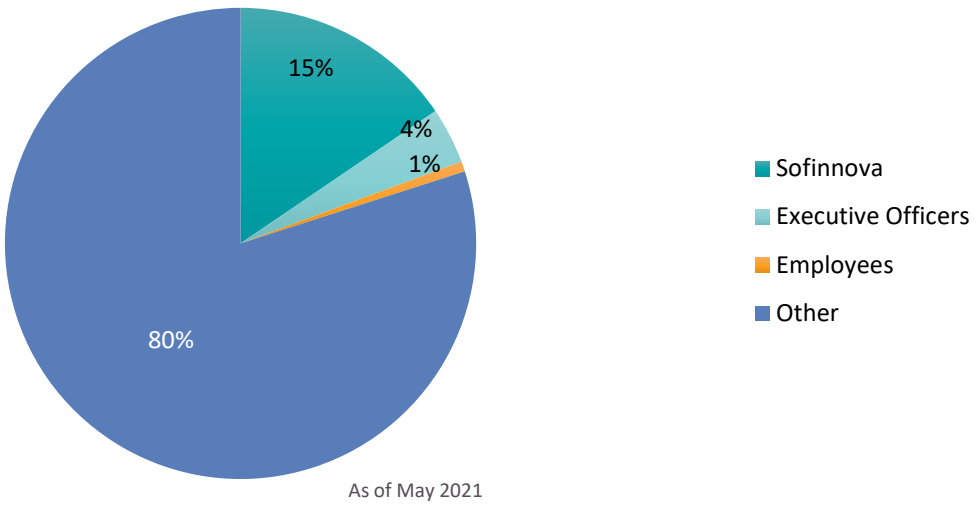
- Chardan: Gbola Amusa (US)
- Bryan Garnier: Dylan van Haaften (FR)
- Oddo BHF: Sébastien Malafosse (FR)

*As of May 3, 2021

Share price evolution and trading volume



Shareholder structure



As of May 2021

Corporate calendar

Corporate calendar	Date
2020 Full-Year Financial Update and Statements	March 10, 2021
2021 1Q Cash Position	April 20, 2021
Annual General Meeting	April 29, 2021
2021 First-Half Financial Update and Statements	July 29, 2021
2021 3Q Cash Position	October 19, 2021
2021 4Q Cash Position	January 18, 2022

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

RESCUE

- Onset of disease
  ≤ 6 months
- 39 patients enrolled

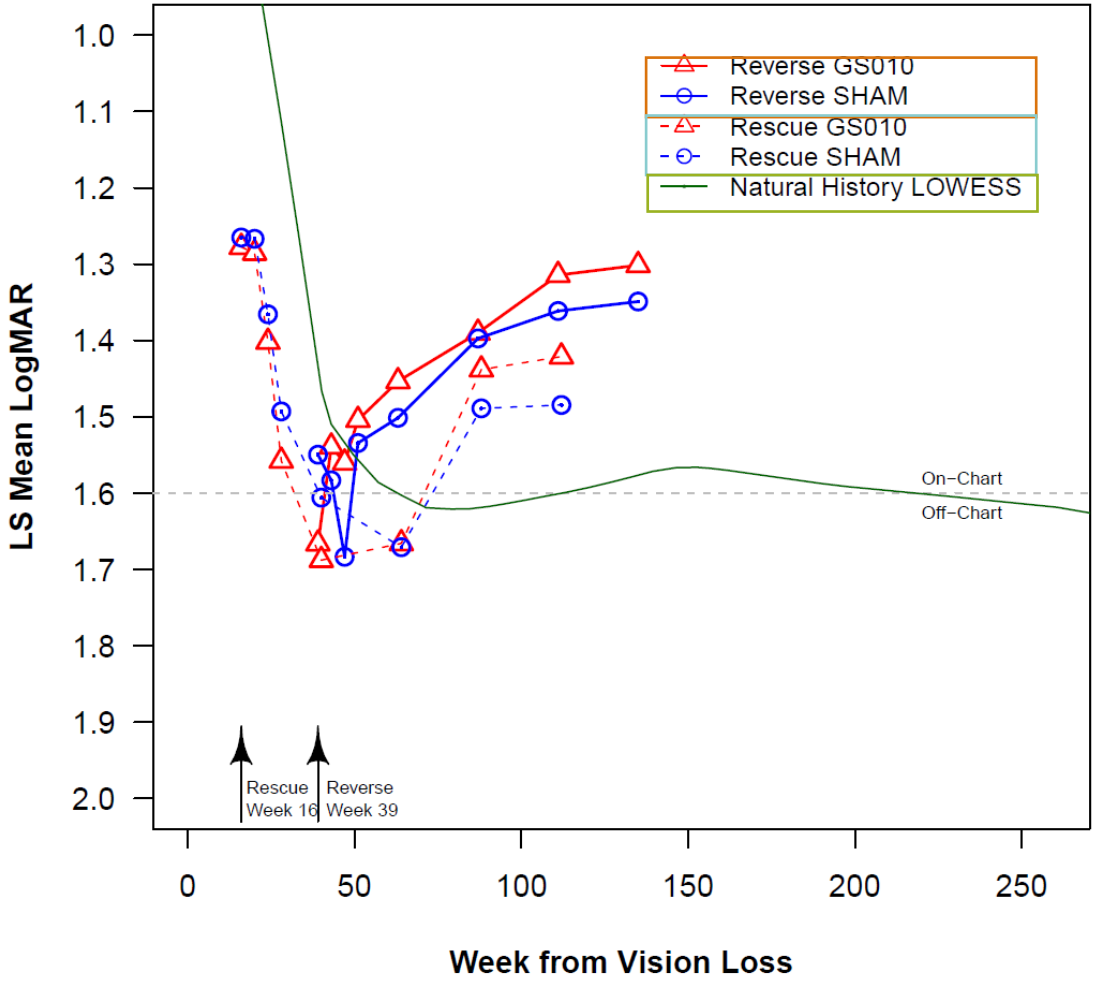
- Double-masked, multi-center
- One eye randomized to GS010; other eye received sham injection

Group 1

GS010 in right eye | **SHAM** in left eye

Group 2

SHAM in right eye | **GS010** in left eye



REVERSE 6-12 MONTHS

+28 ETDRS Letters vs nadir

RESCUE 0-6 MONTHS

+26 ETDRS Letters vs nadir

REVERSE and RESCUE: Final Results
75 *ND4* Subjects ≥ 15 years old – Over 2 year-follow-up

REALITY LHON REGISTRY

Retrospective Natural History

REALITY: Final Results
23* *ND4* Subjects ≥ 15 years old – Over 5 year-follow-up

**: Out of which, 15 had been treated with idebenone, the majority within 12 months of their vision loss*

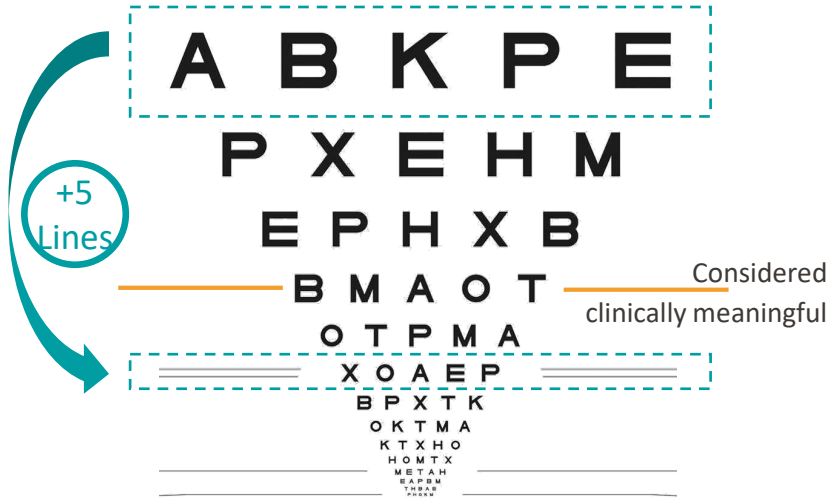
GenSight BIOLOGICS

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		
	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)



*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			
	n	Year 2 post-injection Mean (SD)	Year 3 post-injection 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)

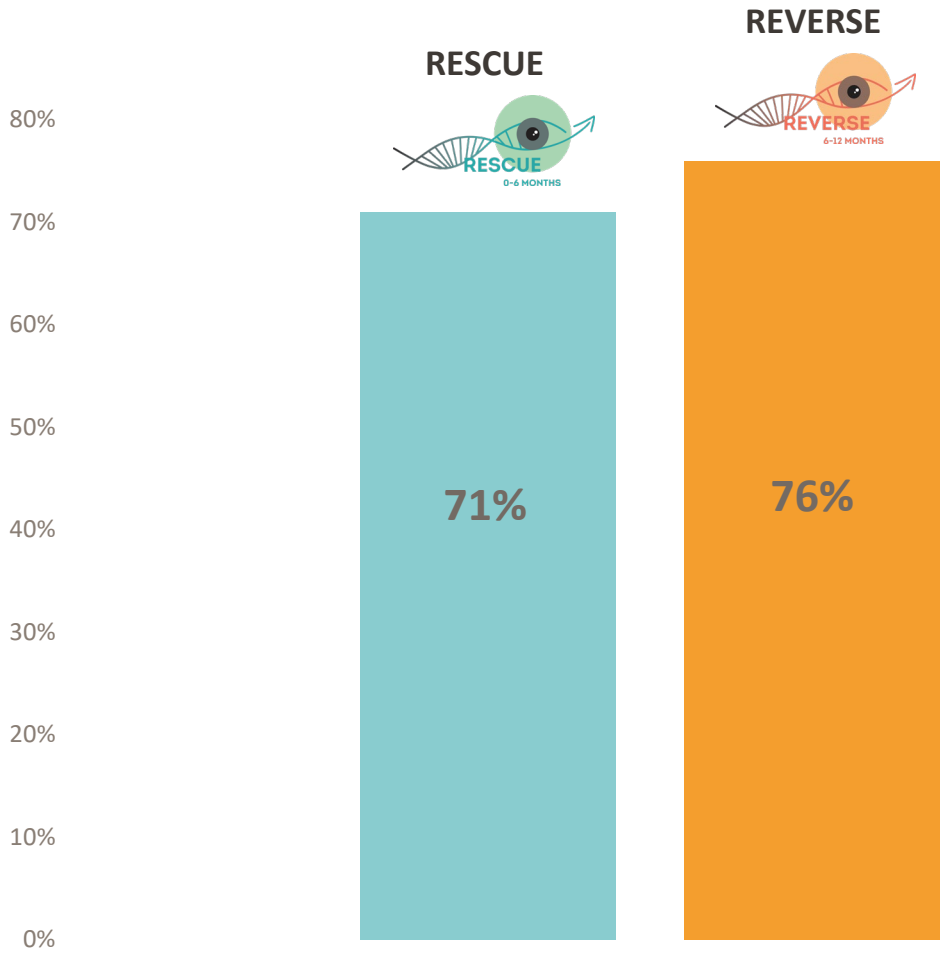
n=37 n=34

CLIN06 – long-term follow-up study

n=31 n=30

GenSight BIOLOGICS

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



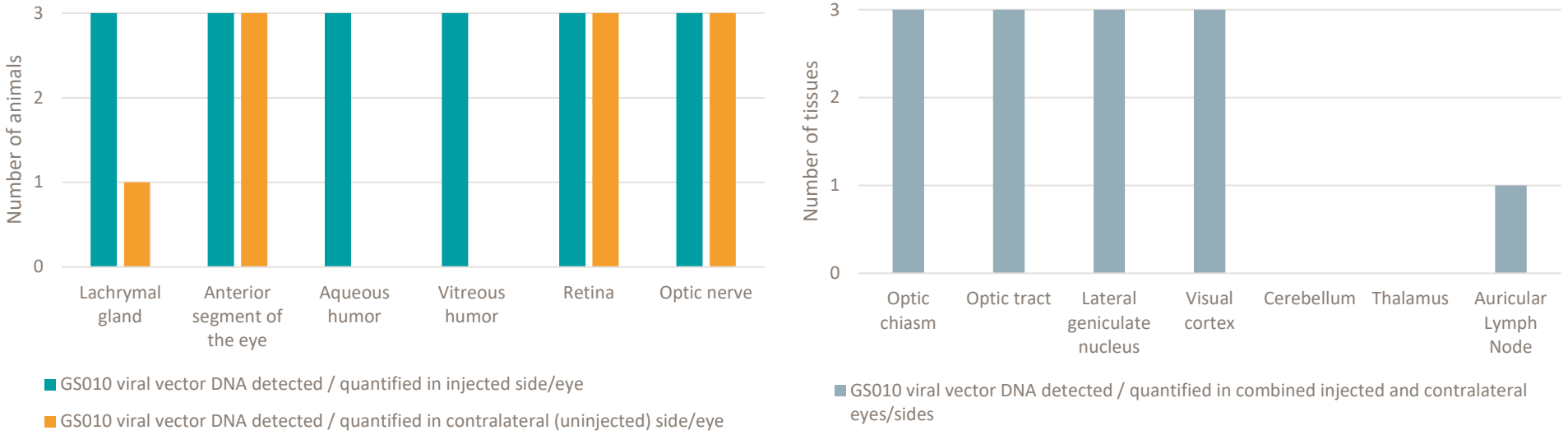
76% of REVERSE subjects achieved at least 15 letters improvement vs nadir in one or two eyes

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

Presence of GS010 DNA in the visual and cerebral systems of test monkey at 3 months after GS010 injection



- 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 bar graph indicates the number of animals (of three) in which rAAV2/2-*ND4* (GS010) DNA was present above the limit of detection (15.6 copies/µg of DNA).

Source: Yu-Wai-Man P. et al., Sci Transl Med. Dec. 2020

"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.

GenSight BIOLOGICS

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

Onset

- ✗ *Delay in recognizing onset of visual loss*

GenSight BIOLOGICS

- ✓ Disease awareness campaign and engagement with patient advocates educate potential LHON patients on sudden vision loss and hereditary factors
- ✓ Help potential patients find neuro-ophthalmologist to confirm diagnosis

Initial consultations and misdiagnoses

- ✗ *Lack of expertise in recognizing LHON*
- ✗ *Referral to wrong specialist*
- ✗ *Barriers to traveling to LHON centers of excellence*

GenSight BIOLOGICS

- ✓ Increase ophthalmologist and neurologist expertise in diagnosing LHON
- ✓ Create a network of experts (LHON Centers of Excellence) in main markets
- ✓ Work collaboratively with LHON patient associations

Confirmed diagnosis and treatment

GenSight BIOLOGICS

- ✓ Patient and center of excellence services to
  - Speed access to genetic testing and counselling
  - Minimize administrative burden of reimbursement

Follow-up care

GenSight BIOLOGICS

- ✓ Patient services to facilitate monitoring of LUMEVOQ® benefit and safety
- ✓ Feedback to and engagement with LHON patient community

GenSight BIOLOGICS

LUMEVOQ®: From lab to hospital (1/2)

The optimized allotopic expression of ND1 or ND4 genes restores respiratory chain complex I activity in fibroblasts harboring mutations in these genes	Bonnet C. et al., Biochim Biophys Acta., May 2008
Optimized allotopic expression of the human mitochondrial ND4 prevents blindness in a rat model of mitochondrial dysfunction	Ellouze S. et al., Am J Hum Genet., Sep. 2008
Nuclear expression of mitochondrial ND4 leads to the protein assembling in complex I and prevents optic atrophy and visual loss	Cwerman-Thibault H. et al., Mol Ther Methods Clin Dev., Feb. 2015
Safety of rAAV2/2-ND4 Gene Therapy for Leber Hereditary Optic Neuropathy	Vignal C. et al., Ophthalmology, Feb. 2018
Immune Response and Intraocular Inflammation in Patients With Leber Hereditary Optic Neuropathy Treated With Intravitreal Injection of Recombinant Adeno-Associated Virus 2 Carrying the ND4 Gene: A Secondary Analysis of a Phase 1/2 Clinical Trial	Bouquet C. et al., JAMA Ophthalmol., April 2019
Bilateral visual improvement with unilateral gene therapy injection for Leber hereditary optic neuropathy	Yu-Wai-Man P. et al., Sci Transl Med. Dec. 2020

GenSight BIOLOGICS

LUMEVOQ®: From lab to hospital (2/2)

Efficacy and safety of intravitreal gene therapy for Leber hereditary optic neuropathy treated within 6 months of disease onset	Newman N.J. et al., Ophthalmology, Jan. 2021
Safety of intravitreal gene therapy for treatment of subjects with Leber Hereditary Optic Neuropathy due to mutations in the mitochondrial ND4 gene – The REVEAL study	Vignal-Clermont C. et al. BioDrugs, Feb. 2021
Natural History of Patients with Leber Hereditary Optic Neuropathy – Results from the REALITY Study	Yu-Wai-Man P. et al., Eye, April 2021
Intravitreal Gene Therapy vs. Natural History in Patients with Leber Hereditary Optic Neuropathy Carrying the m.11778G>A ND4 Mutation: Systematic Review and Indirect Comparison	Newman N.J., et al., Front. Neurol., May 2021

Recent scientific publications related to LHON

Visual Outcomes in Leber Hereditary Optic Neuropathy Patients With the m.11778G.A (MTND4) Mitochondrial DNA Mutation	Newman N.J., et al., J. Neuro-Ophthalmol Dec. 2020 - Volume 40 - Issue 4 - p 547-557