



Corporate Presentation

September 2023

A LEADING Gene Therapy BIOTECHNOLOGY COMPANY

[GENSIGHT-BIOLOGICS.COM](https://www.gensight-biologics.com)

Disclaimer

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Investment Case – Transitioning from R&D to Commercial Organization



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 Gidoïn
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



Scott Jeffers
Chief Technical Officer

REDPIN THERAPEUTICS (2021-2022)
UNIQUIRE (2019-2021)
SELECTA BIOSCIENCES (2018-2019)
BRAMMER BIO (2015-2018)
Ph.D. in virology

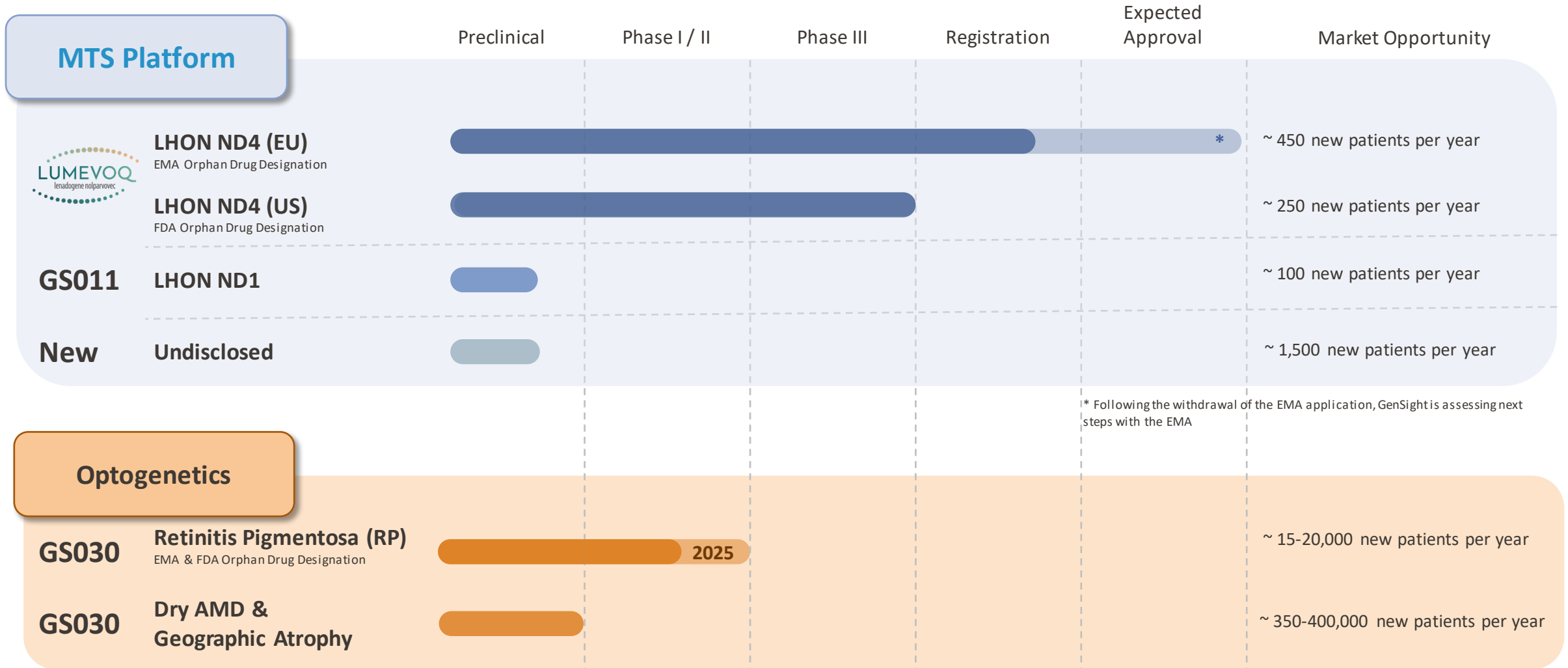


Philippe Motté
SVP, Regulatory & Quality

GENFIT (2020-2022)
MEDDAY (2019-2020)
ABBVIE (2013-2018)
IPSEN (2004-2013)
ROCHE (1998-2004)
GSK (1991-1998)
SANOFI (1989-1991)

Pharm.D. & Ph.D. in human biology

Pipeline: solid and advanced product portfolio in ophthalmic Gene Therapy



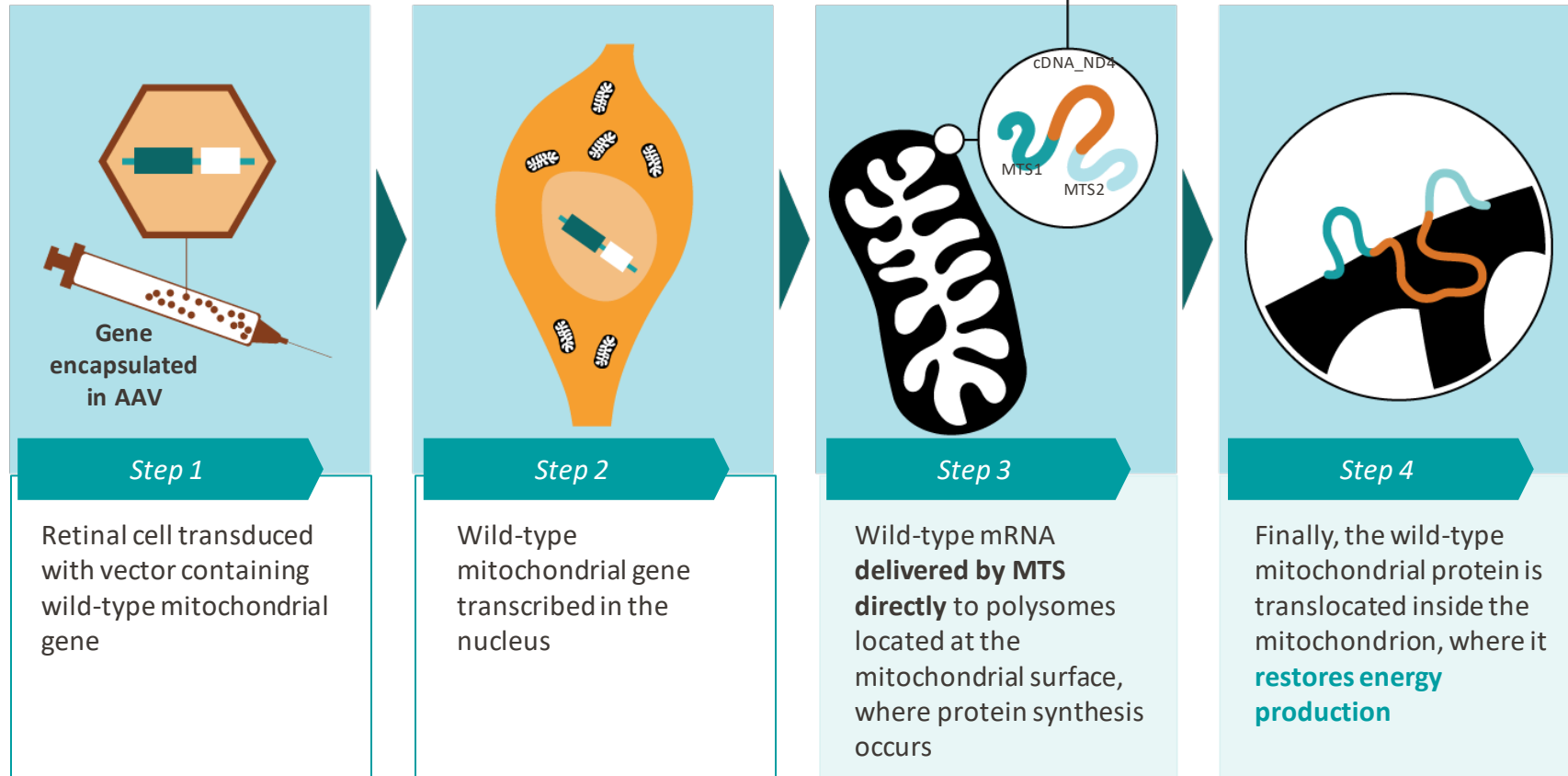
LUMEVOQ® in LHON-ND4

- 3 Phase III completed
 - Pending European regulatory new submission in Leber Hereditary Optic Neuropathy
- 

LUMEVOQ® introduces Gene Therapy solution

Replacing affected mitochondrial mRNA via proprietary *MTS* technology*

MTS in action for GS010:

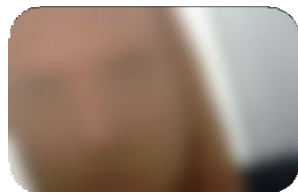
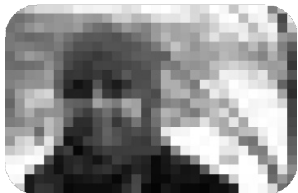


*MTS = mitochondrial targeting sequence

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

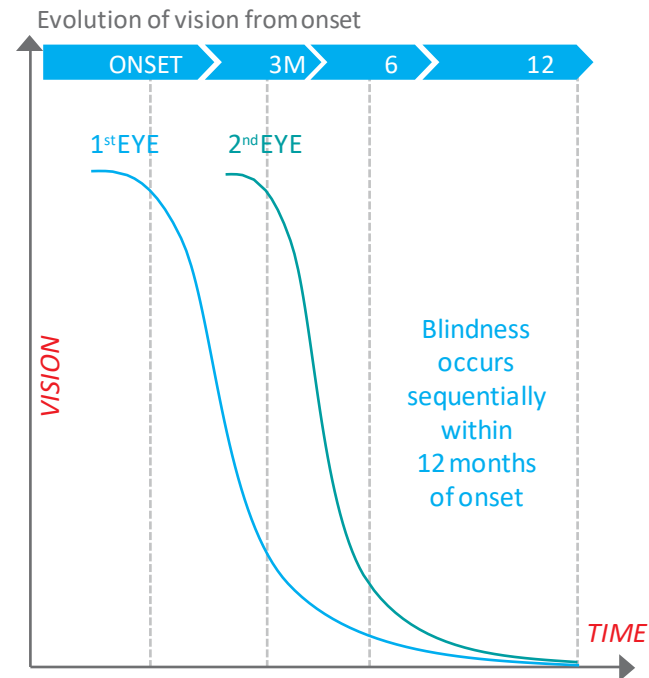


Image source: illustrated from Newman NJ et al., Am J Ophthalmol. 141(6), 1061-1067, 2006

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® in LHON in 3 Phase III studies



34 patients
with vision loss \leq 6 months

Change from NADIR in ETDRS letter equivalents	
Week 96	
Mean	
LUMEVOQ eyes	+26.3
Contralateral eyes (Sham)	+22.8



37 patients
with vision loss $6 \leq$ 12 months

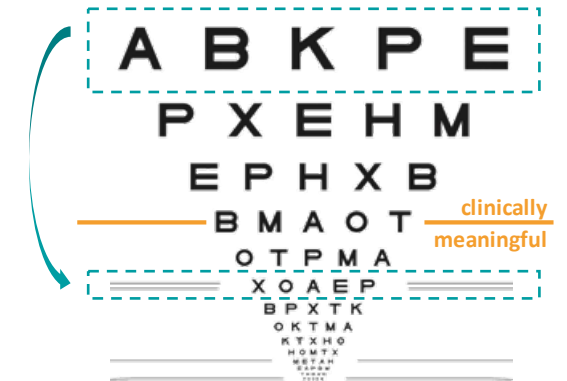
Change from NADIR in ETDRS letter equivalents	
Week 96	
Mean	
LUMEVOQ eyes	+28.3
Contralateral eyes (Sham)	+24.5



98 patients
with vision loss \leq 1 year

Change from NADIR in ETDRS letter equivalents		
At 2 year		
	1 st eye	2 nd eye
2 LUMEVOQ eyes	+ 20	+17
1 LUMEVOQ eye	+ 19	+14 <i>(placebo)</i>

3+ lines of visual acuity improvement vs Nadir is highly clinically relevant

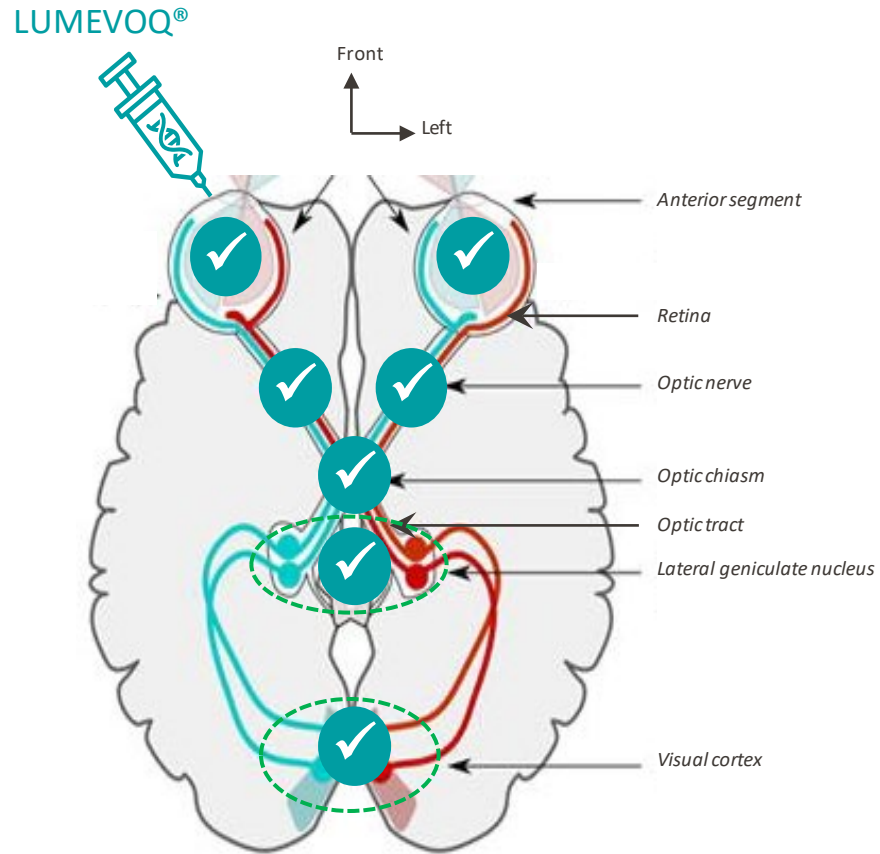


Over 70% of subjects achieved at least 15 letters improvement vs nadir in one or two eyes

Clinically meaningful improvement on all **Quality of Life** parameters

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

The Bilateral Effect Demonstrated – LUMEVOQ® also detected in contralateral eyes



Study¹ conducted on 6 non-human primates :

- All received a single injection of LUMEVOQ® in one eye at a dose equivalent to that used in humans, while 2 control animals received a placebo injection.
- Animals were monitored for 3 and 6 months following the injection. At 3 and 6 months, LUMEVOQ vector DNA was detected in the contralateral uninjected eye/visual tissue of 3 and 2 animals, respectively, and in the optic chiasm of all 6 animals.
- Demonstrates the transfer from the injected eye to the contralateral eye
- A similar mechanism of transfer was described previously²
- Provides mechanistical explanation of contralateral effect observed in LUMEVOQ clinical trials

LUMEVOQ injection in one eye

Transfer of LUMEVOQ to uninjected eye

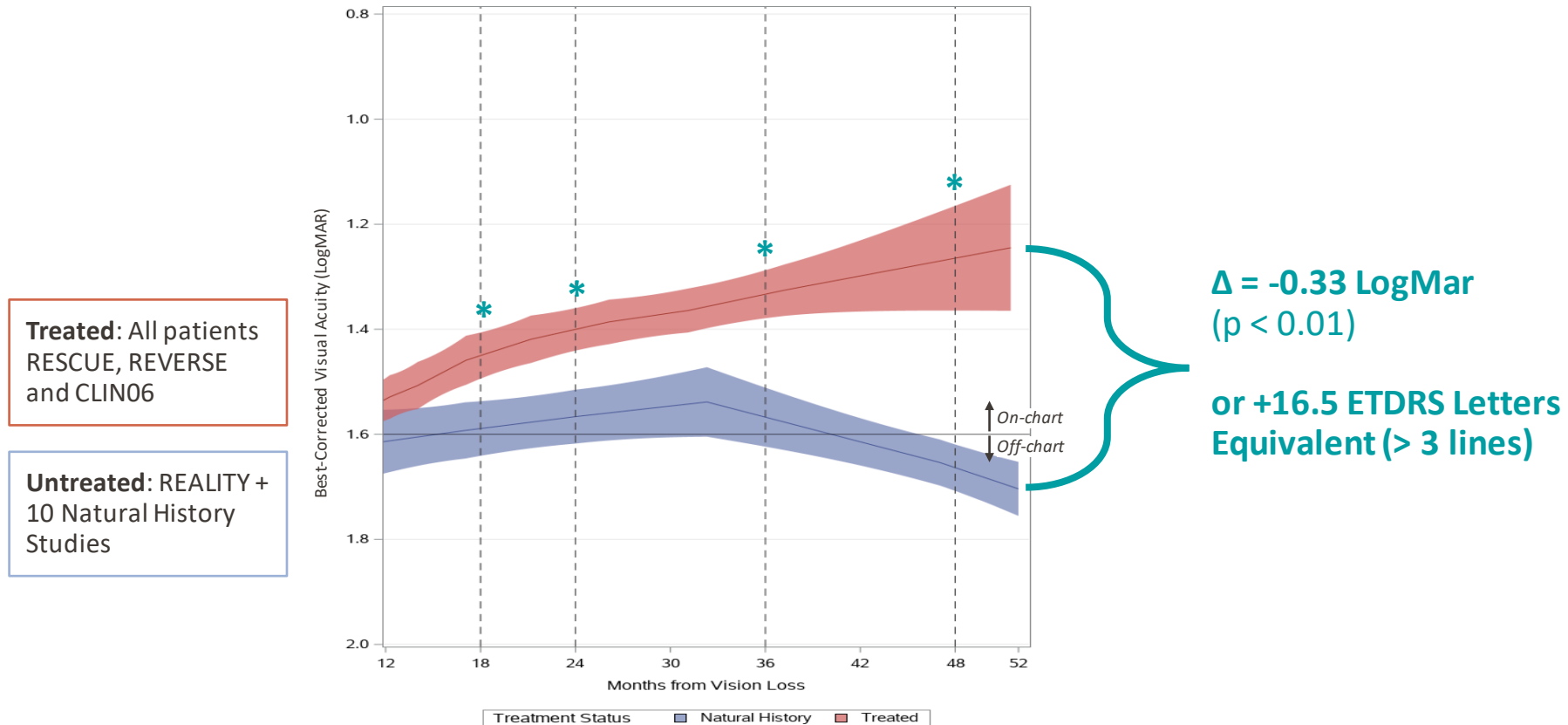
LUMEVOQ present in both eyes

1-Calkins *et al.* Biodistribution of intravitreal lenadogene nolparvovec gene therapy in nonhuman primates. *Mol Ther Methods clin Dev.* 2021 Oct 1;23:307-318. doi:10.1016/j.omtm.2021.09.013.
2-Lambert *et al.* Towards A Microbead Occlusion Model of Glaucoma for a Non-Human Primate. *Sci Rep.* 2019 Aug 9;9(1):11572. doi:10.1038/s41598-019-48054-y.

LUMEVOQ[®] modifies disease outcome compared to natural history

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)



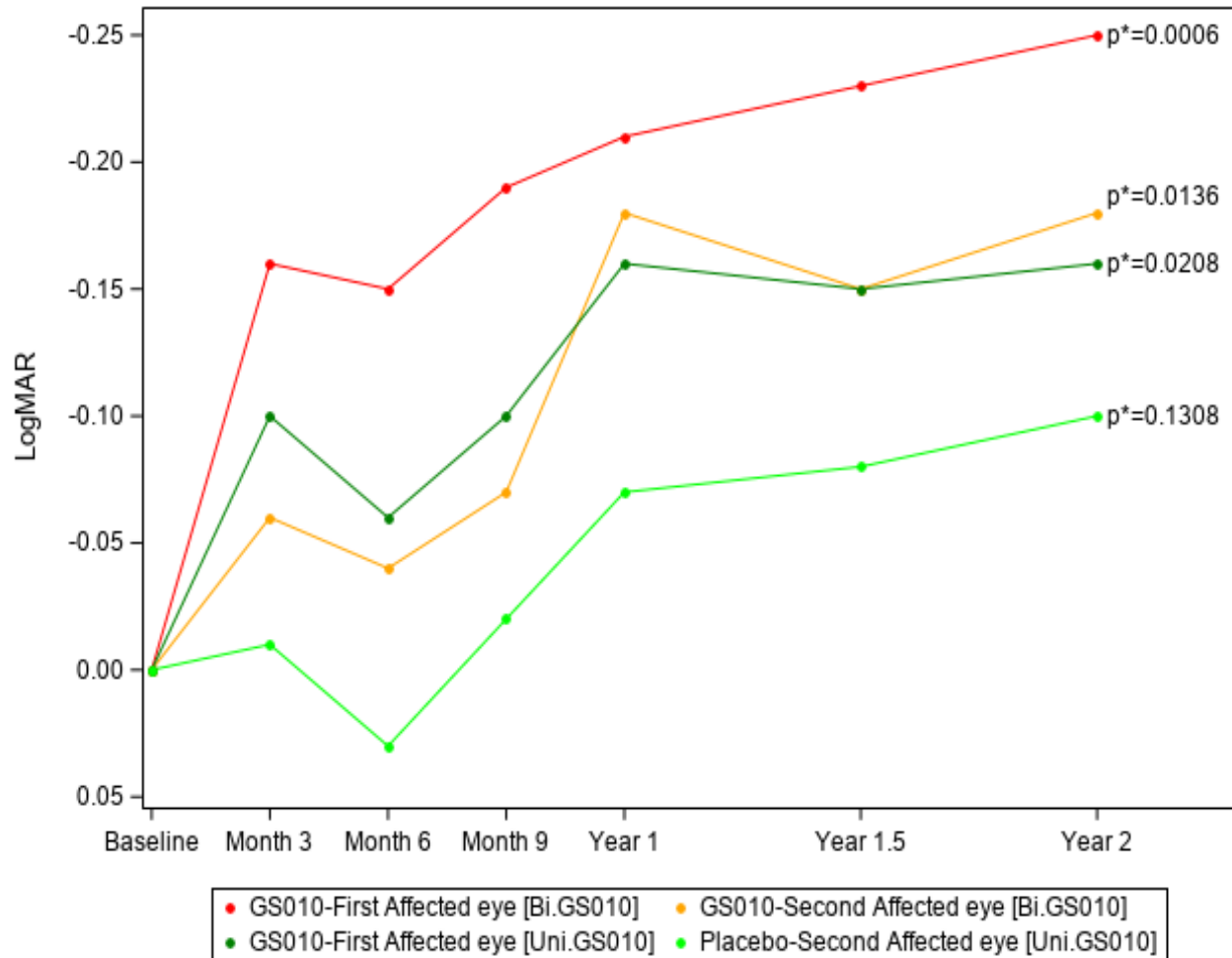
Treated: All patients RESCUE, REVERSE and CLIN06

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 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.

Better efficacy for bilaterally treated subjects demonstrated in REFLECT



*p vs. Baseline

Note: The LogMAR value of interest at 1.5 years was the first logMAR recorded after 518 days after IMP and for the 2 year analysis the LogMAR value of interest is the nearest LogMAR of 730 days recorded between 700 and 935 days post IMP. For 18 values, the logMAR taken into account for the analysis at 1.5 years is recorded after 700 days, these values are therefore taken into account in the two analyses- This is not a bias because the analyses at each moment of the graph are carried out independently

Driving patient and physicians' awareness through Compassionate Use for LUMEVOQ®



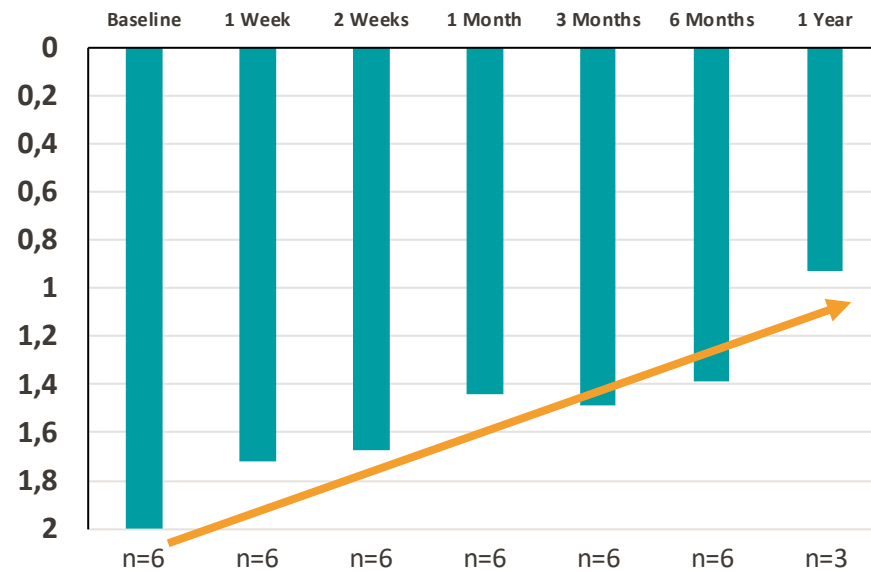
- 18 individual patients Expanded Access INDs so far approved by the FDA for LUMEVOQ®
- Additional individual patients Expanded Access INDs to be processed

- “*Autorisation d’Accès Compassionnel*” or AAP – Early Access program – for LUMEVOQ®, former ATU granted by ANSM
 - “*ATU Nominative* or ATUn” - named patient Temporary Authorization for Use - for LUMEVOQ® first authorized by ANSM to CHNO of the *Quinze-Vingts* in Paris in December 2019
- Bilateral injections priced at €700,000 per patient
 - €3.1M revenues generated in 2022 (one single quarter)
 - Currently paused pending product availability in Q1 2024
- 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

Real World Experience – US Compassionate Use Program

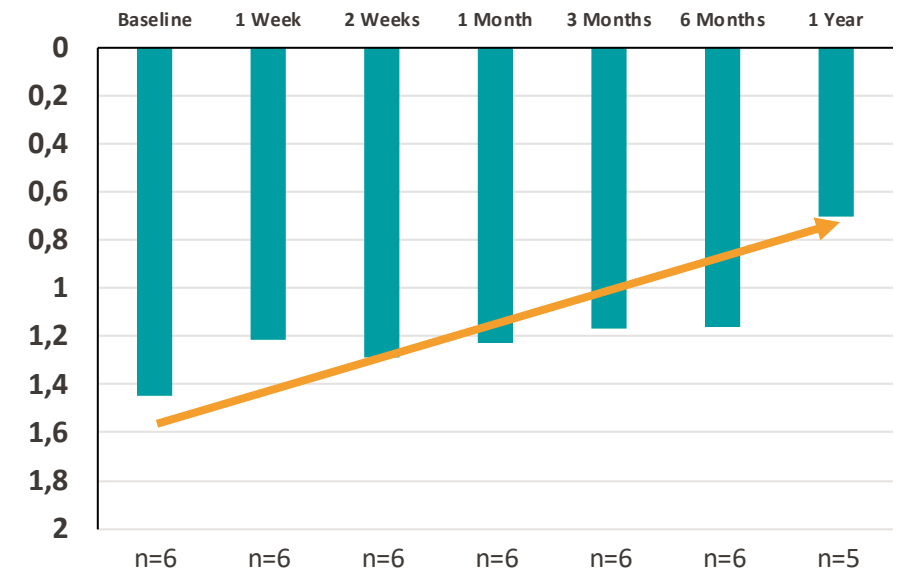
AVG **Worse** Eye BCVA Mean ETDRS Change (LogMAR)

11 lines of improvement

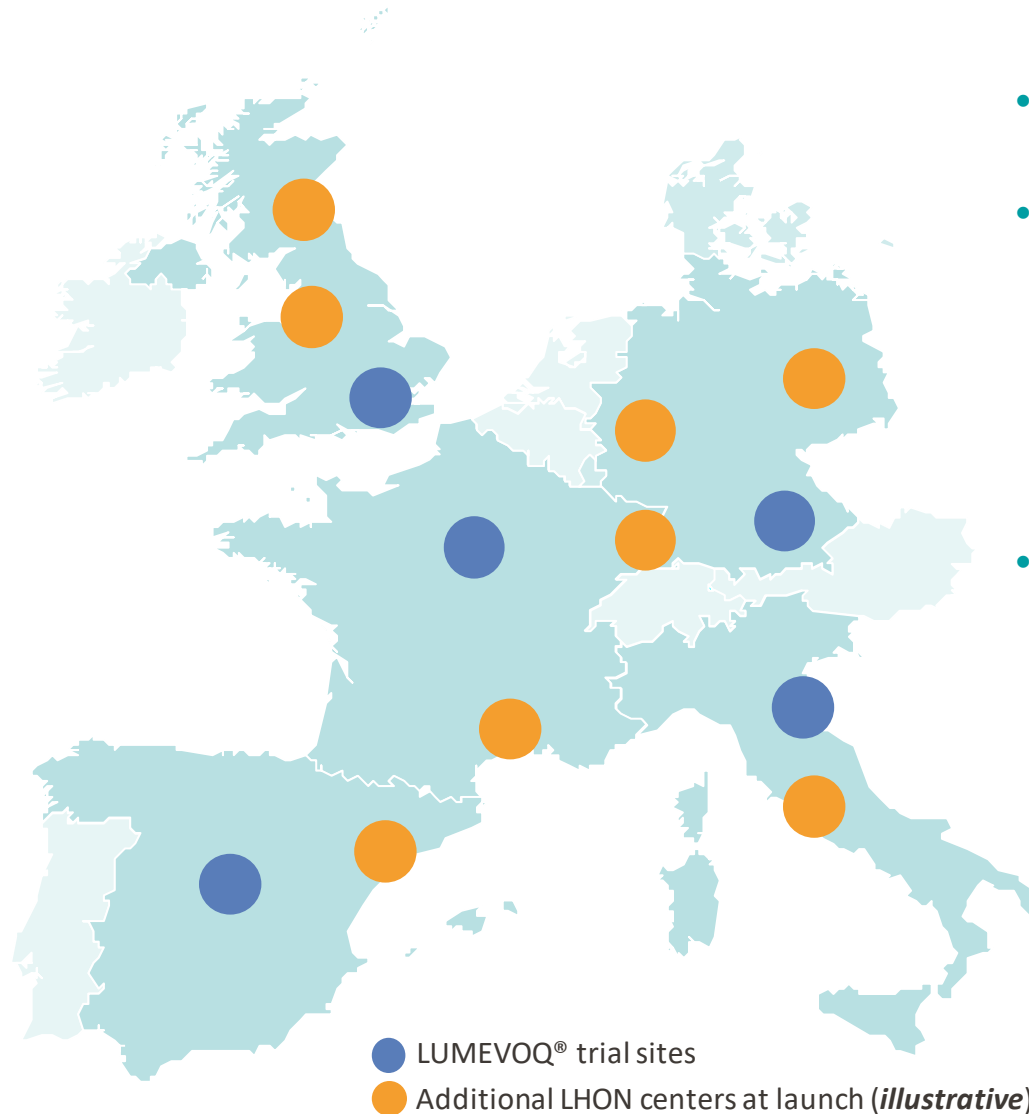


AVG **Better** Eye BCVA Mean ETDRS Change (LogMAR)

7.5 lines of improvement

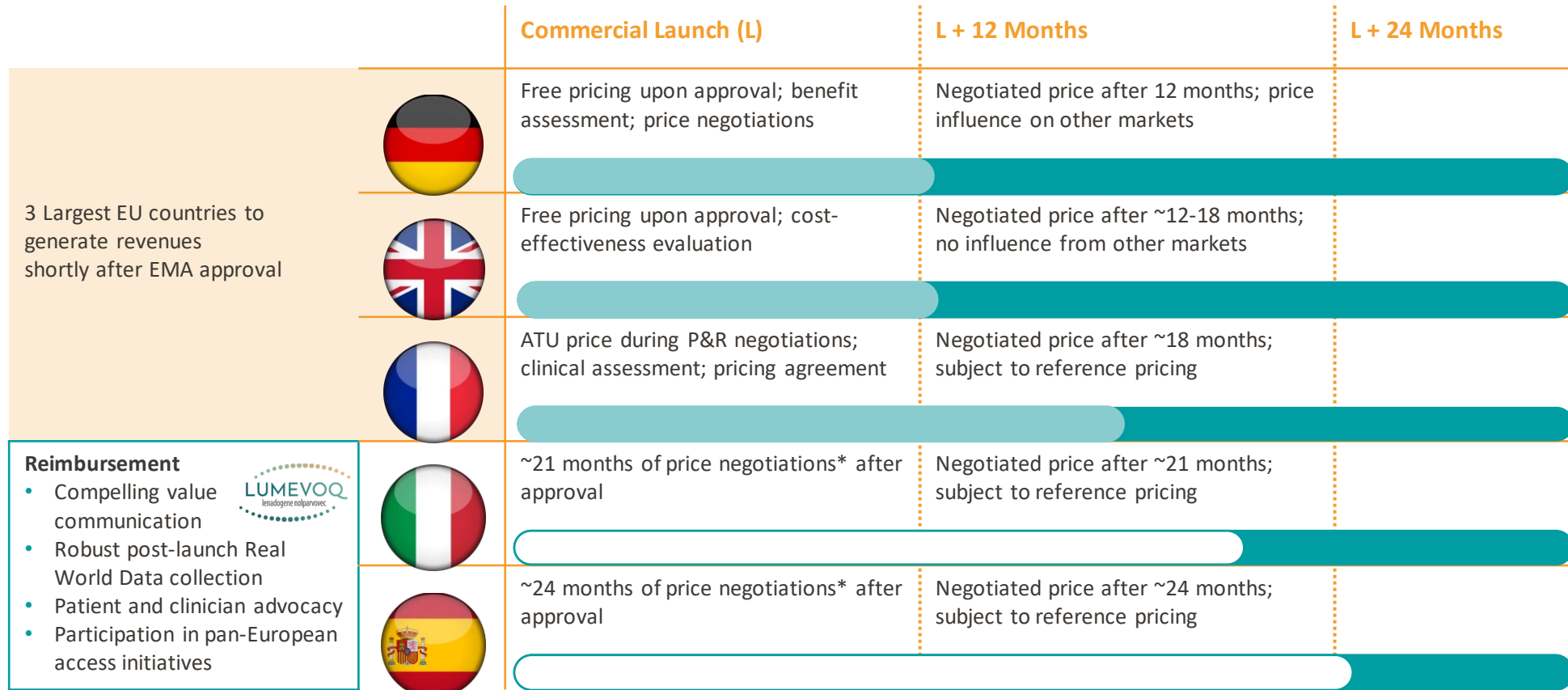


European Commercial Strategy – Leveraging LUMEVOQ® Clinical Centers to Build Network of LHON Centers of Excellence

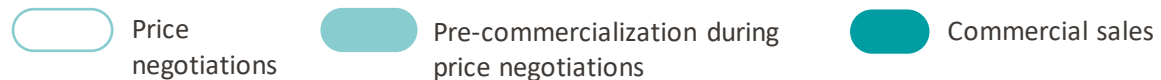


- LHON experts mapped in both major and smaller markets
- Progressively build the LHON clinical network working with LHON experts
 - Recognize varying levels of LHON expertise and patient mobilization across markets
 - Balance patient reach with logistical complexity
- LHON expert- and LHON patient-centric 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

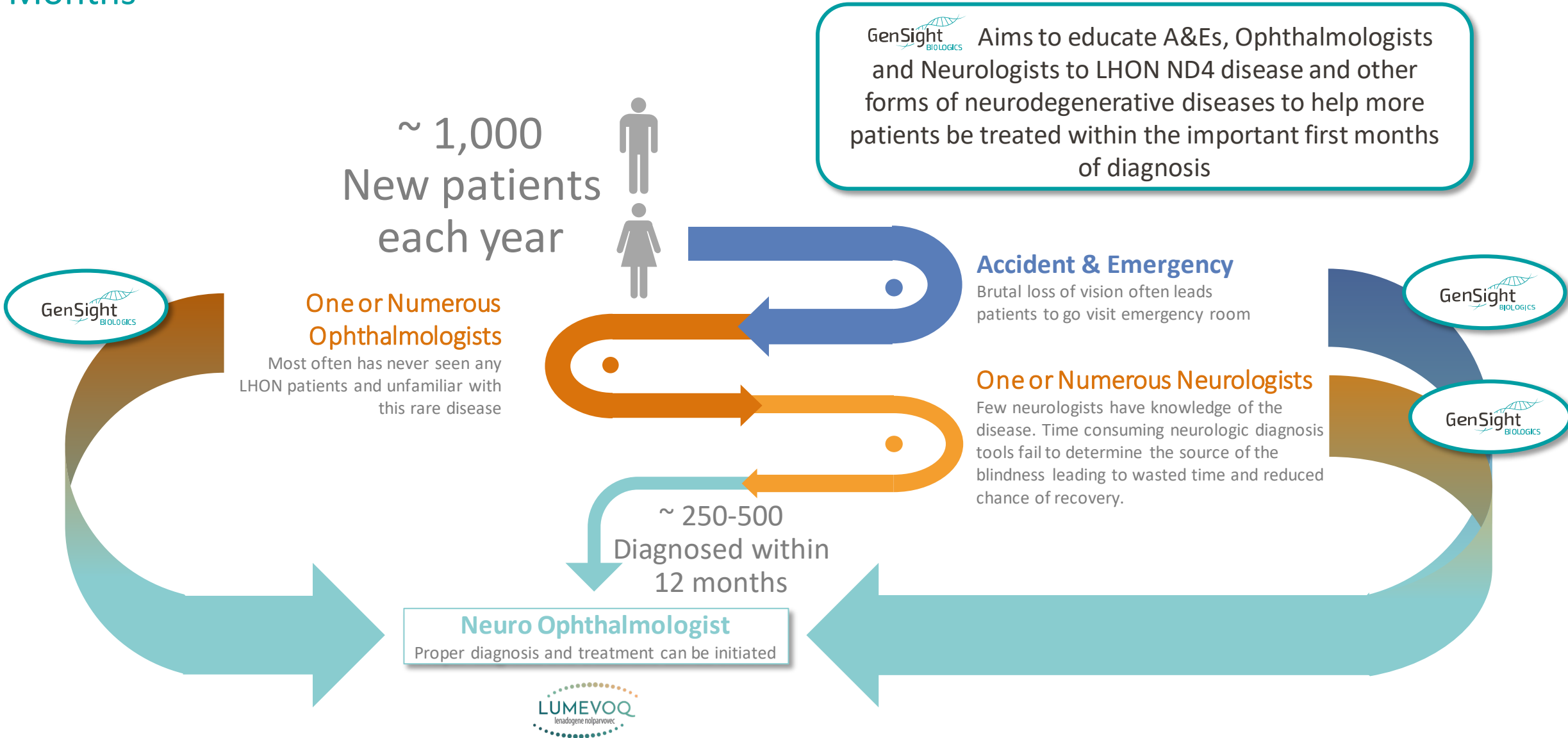
European Reimbursement Strategy – Short Term Revenues Generation After EMA Approval



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



A Targeted Approach to Accelerate Diagnosis and Get More Patients Treated Within 12 Months



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 (RP)



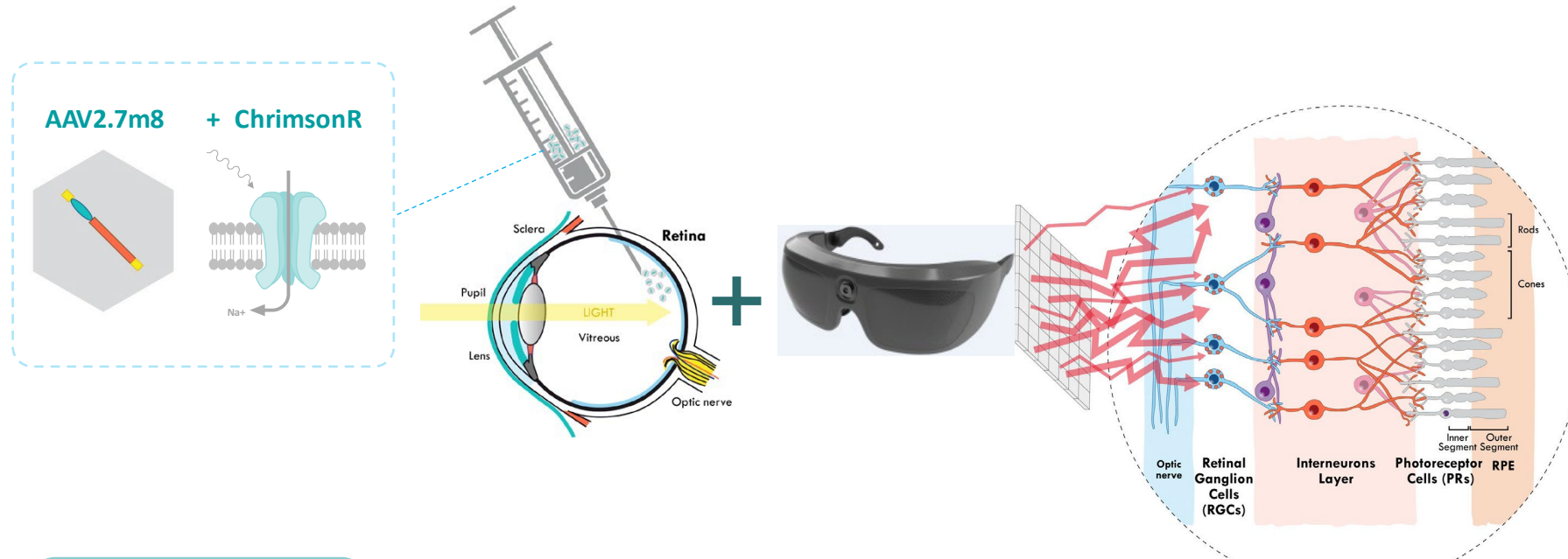
- Blinding genetic disease
- Mutations in over 100 different genes
- Photoreceptor degeneration leads to slow & irreversible progression to blindness, usually at age 40-45
- 15-20,000 new patients each year in the US and EU

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



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

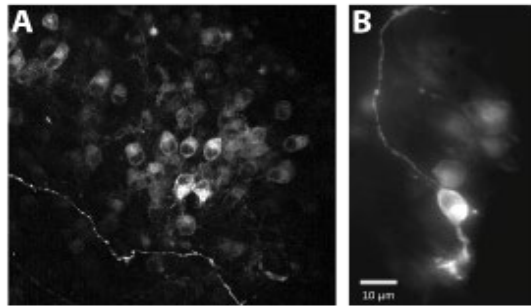
Retinal output sent to brain for image processing

GS030 leads to functional vision restoration in monkey and rats

Localization of light-sensitive protein in NHP retina

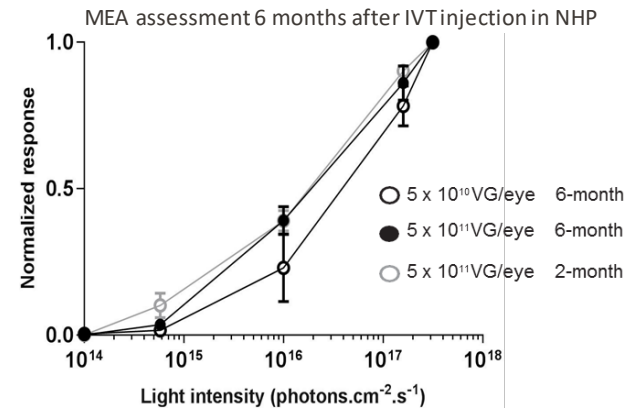
Expression of ChrR-tdT in midget cells of monkey perfovea

In vivo in NHP assessment 6 months after IVT injection



Dose-ranging response to firing relationship in NHP

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



Recent publication

Optogenetic therapy: high spatiotemporal resolution and pattern discrimination compatible with vision restoration in non-human primates. Gauvain G. et al.

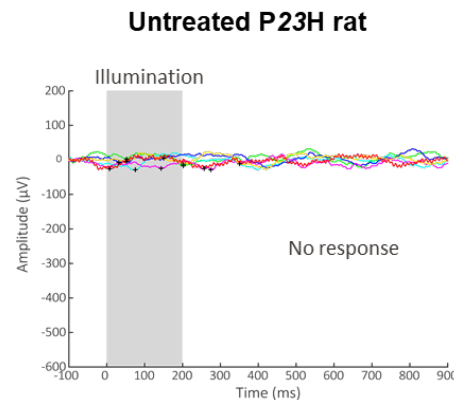
Communications Biology, Feb. 2021

<https://www.nature.com/articles/s42003-020-01594-w>

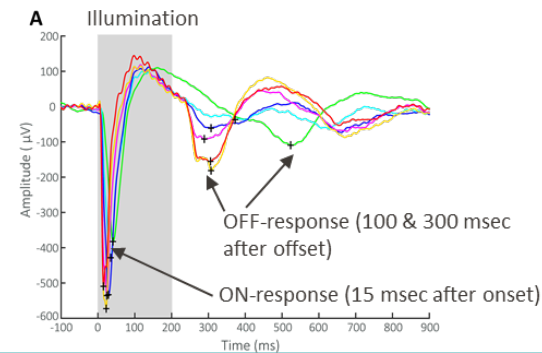
Restoration of a functional vision in P23H rats

Light-induced visual evoked cortical responses

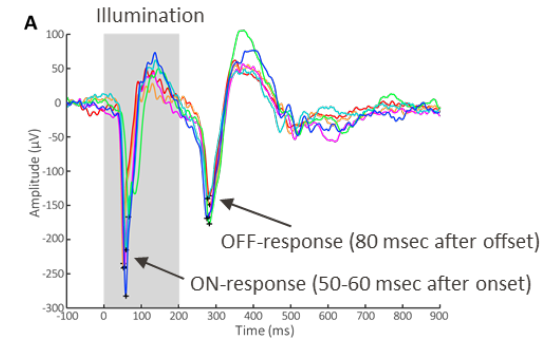
Full field 590 nm light from $\sim 4.7 \times 10^{15}$ to 1.1×10^{17} photons/cm²/sec



GS030-treated P23H rat



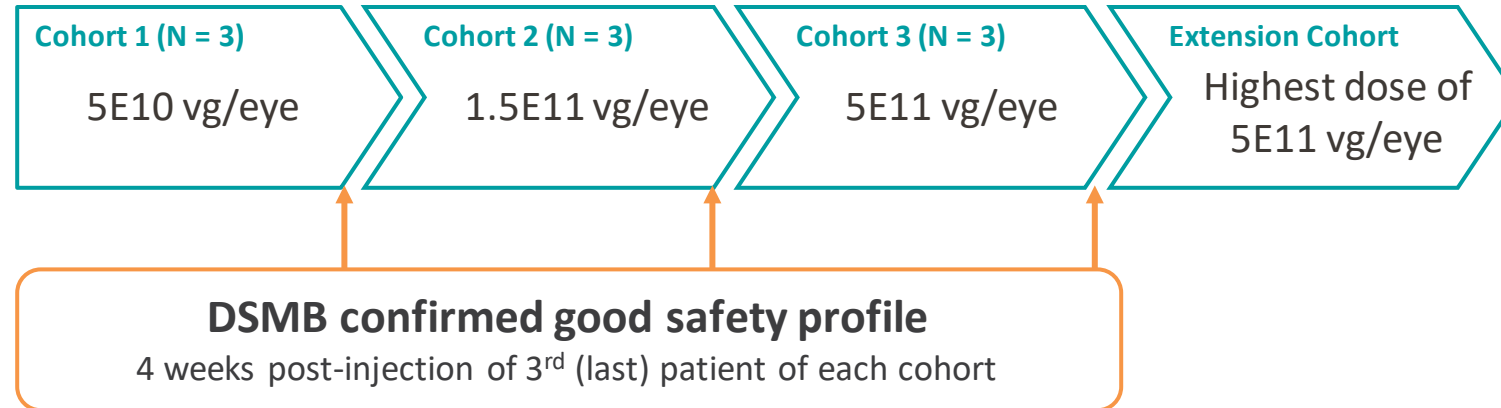
Normal Long-Evans rat



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

Extension Cohort recruiting with highest dose 5E11 vg/eye without any modification after DSMB#3 recommendation

PIONEER: encouraging preliminary findings from two patients



Outcome one year after gene therapy

Both treated patients experienced **significant vision improvement**, from being barely able to perceive light before treatment to being **able to locate and count objects**, one year after gene therapy.

1st patient: 40-year history of RP, received one intravitreal injection of 5E10 vg/eye of GS030 gene therapy in the worse-seeing eye.

2nd patient: 20 years after RP diagnosis, received one intravitreal injection of 1.5E11 vg/eye of GS030 gene therapy in the worse-seeing eye.

Training with the device started 4 months after injection.



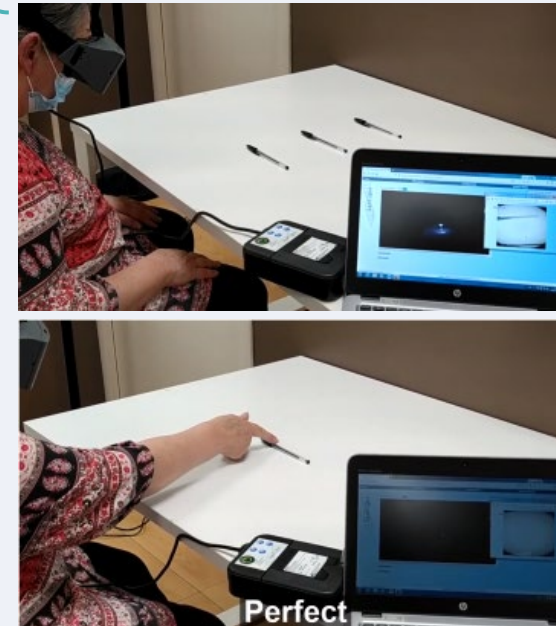
Recent publication

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>

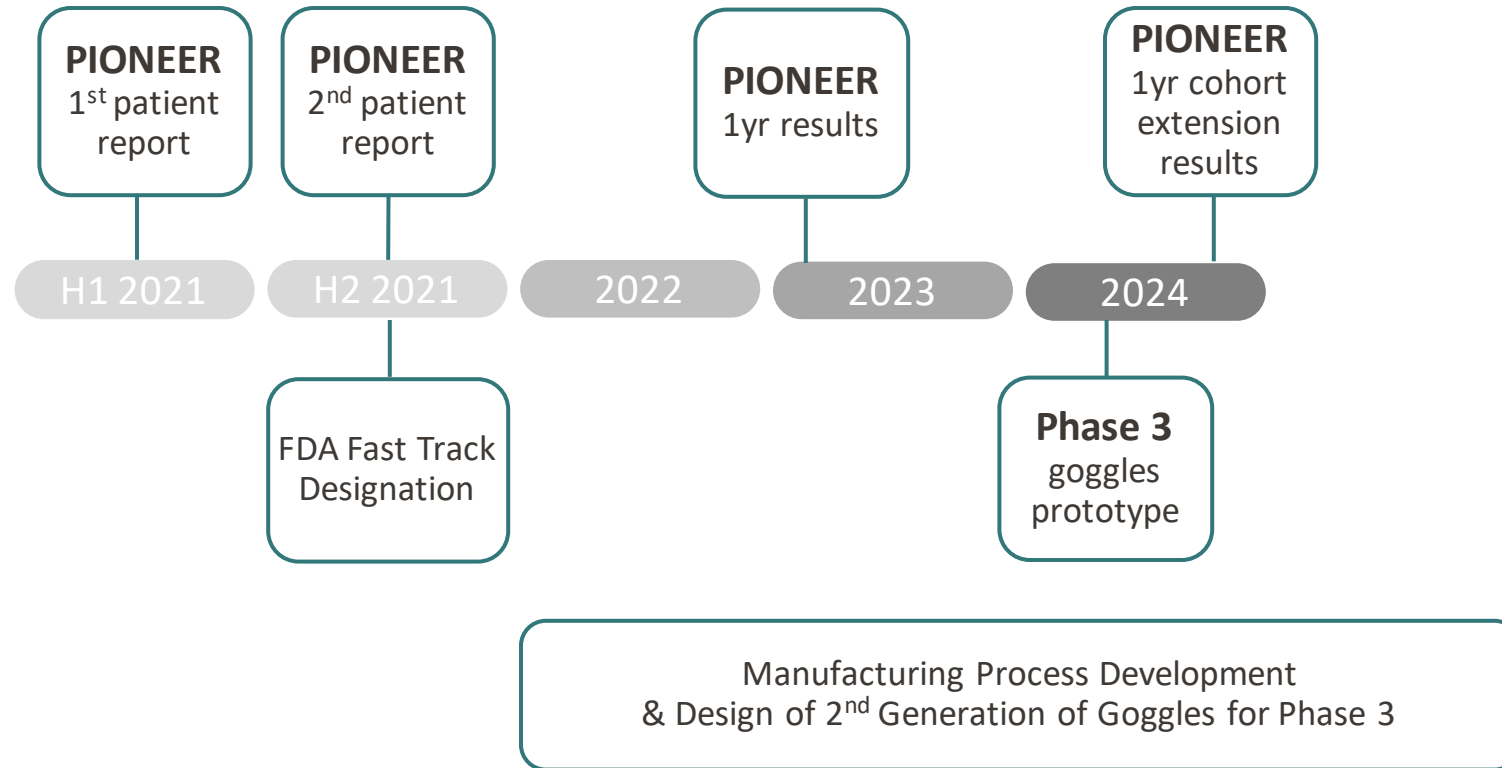


Video of treated patient



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

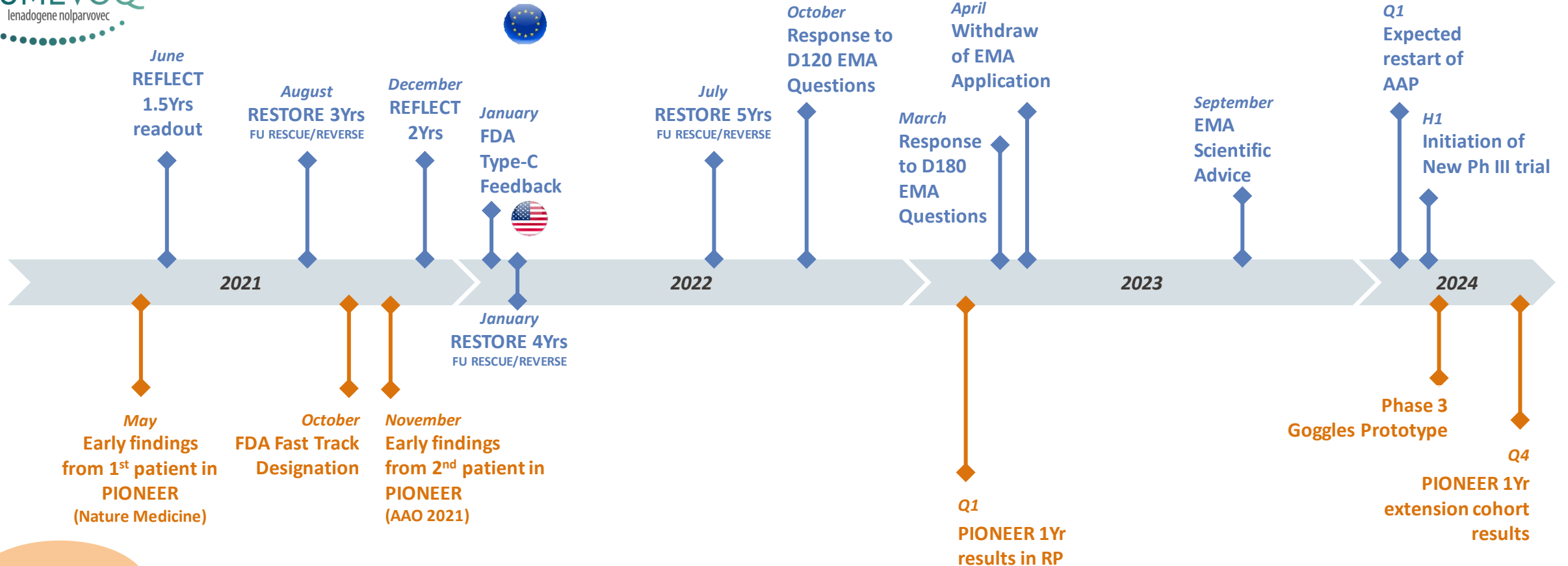
GS030 timeline



Building high strategic value



Rich upcoming news flow with numerous inflection points



GS030

GenSight Biologics in numbers

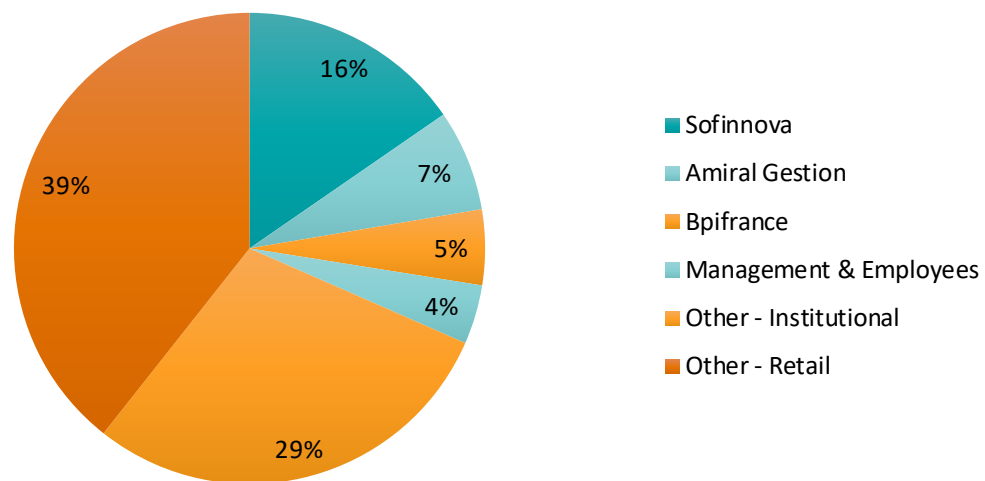
Key financial information

Company Overview

Market Cap* :	€ 20m
Cash Position : (Mar 31, 2023)	€ 0.9m + €10m <i>(financing announced on Aug 3)</i>
Outstanding Shares:	46.3m
Latest Amount Raised : (March 2021)	€ 30m
Raised to date	€ 197m
IPO Date	July 13, 2016

*As of September 6, 2023

Shareholder structure



As of June 2023

Analyst Coverage



Daniil Gataulin (US)



Ingrid Gafanhao (FR)



Damien Choplain (FR)



Sushila Hernandez (NL)



Justine Telliez (FR)

Corporate calendar

	Date
2023 First-Half Financial Update and Statements	September 15, 2023
2023 3Q Cash Position	October 26, 2023
2023 4Q Cash Position	January 25, 2024