



# Corporate Presentation

January 2022

A LEADING Gene Therapy BIOTECHNOLOGY COMPANY

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

# Disclaimer

This document contains forward-looking statements and estimates made by the GenSight Biologics S.A. (the “Company”), including with respect to the anticipated future performance of the Company, its subsidiaries and affiliates, and the market in which they operate. They include all matters that are not historical facts. These forward-looking statements can be identified by the use of forward-looking terminology including the terms “developments,” “estimates,” “expects,” “intends,” “may,” “milestones,” “potential,” “value,” “time to market,” “targeting,” “on track,” “planned,” “will,” “move to,” or other variations or comparable terminology, or by discussions of strategy and funding, as well as the Company’s, its subsidiaries’ and affiliates’ technology, and are based on financial and non-financial information, including projections as to the future regulatory situation and other information and assumptions. Such statements, forecasts and estimates are based on various assumptions and assessments of known and unknown risks, uncertainties and other factors, which were deemed reasonable when made but may or may not prove to be correct. Actual events are difficult to predict and may

depend upon factors that are beyond the Company’s control. Therefore, actual results, the financial condition, performance or achievements of the Company, its subsidiaries and affiliates or industry results, may turn out to be materially different from any future results, performance or achievements expressed or implied by such statements, forecasts and estimates. Forward-looking statements, forecasts and estimates only speak as of the date of this forward-looking statement, and no representations are made as to the accuracy or fairness of such forward-looking statements, forecasts and estimates. The Company, its subsidiaries and affiliates disclaim any obligation to update any such forward-looking statement, forecast or estimates to reflect any change in the Company’s expectations with regard thereto, or any events, or changes in conditions or circumstances on which any such statement, forecast or estimate is based.

# 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 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



**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*

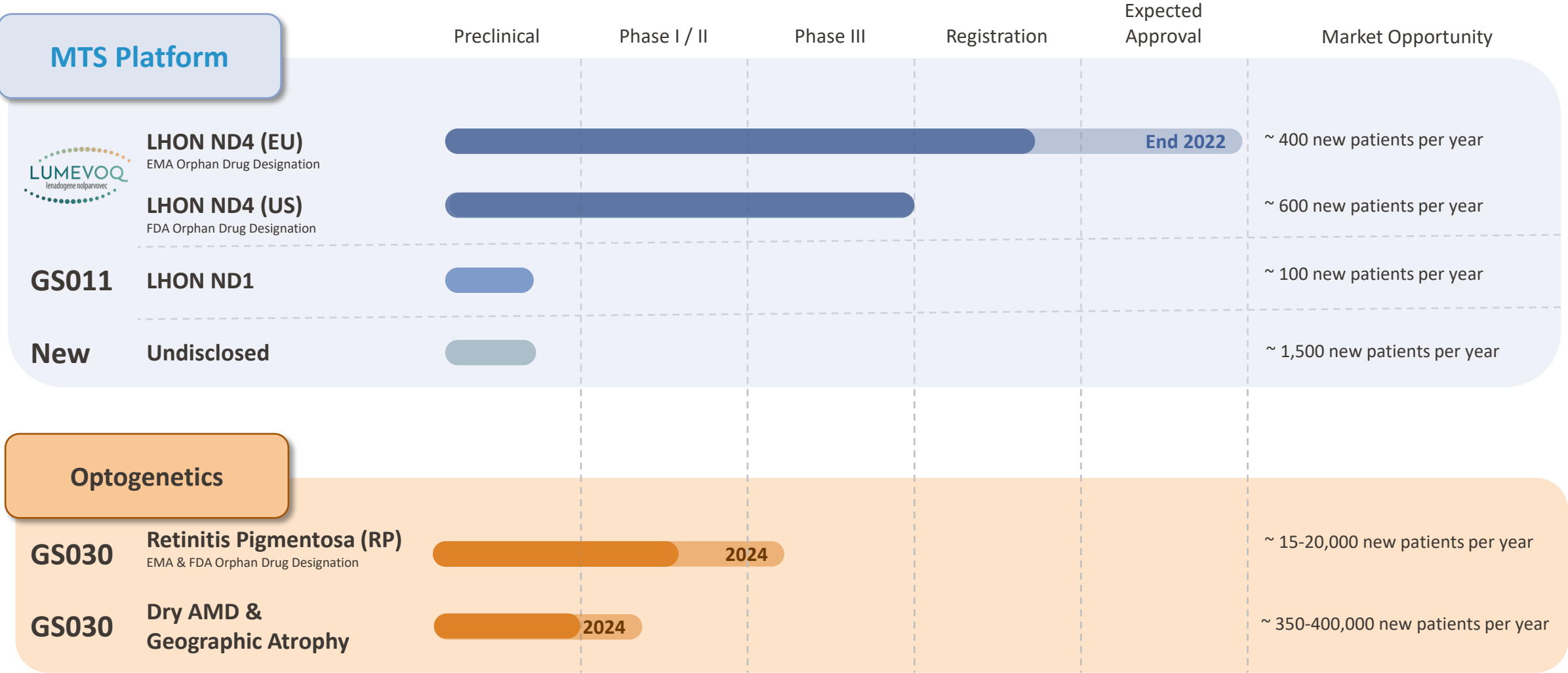
**EXELTIS SANTE** (2016-2019)  
**PFIZER** (2015-2016)  
**ABBVIE** (2014-2015)  
**GALDERMA** (2012-2013)  
**LABORATOIRE LAFON (TEVA)** (1993-2012)  
Pharm.D.



**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)

# Pipeline: solid and advanced product portfolio in ophthalmic Gene Therapy



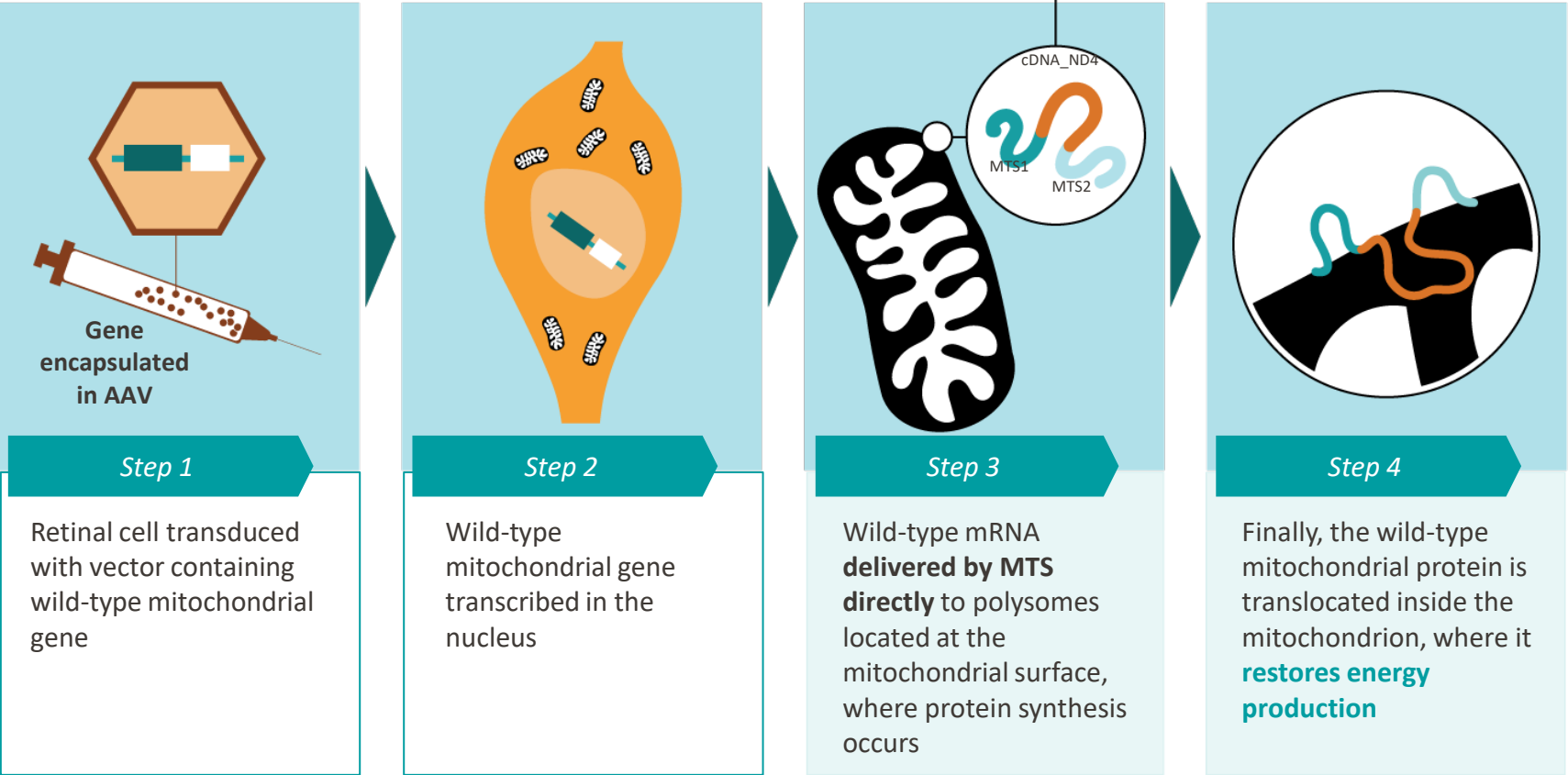
# LUMEVOQ® in LHON-ND4

- 3 Phase III completed
- European regulatory submission ongoing in Leber Hereditary Optic Neuropathy
- Commercial preparation ongoing for early 2023 European launch

# LUMEVOQ® introduces Gene Therapy solution

Replacing affected mitochondrial mRNA via proprietary *MTS\** technology

*MTS in action for GS010:*

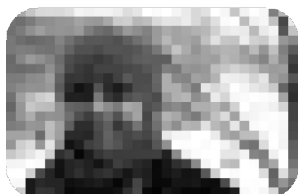


\*MTS = mitochondrial targeting sequence

# 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**<sup>(1)</sup> reached during acute phase

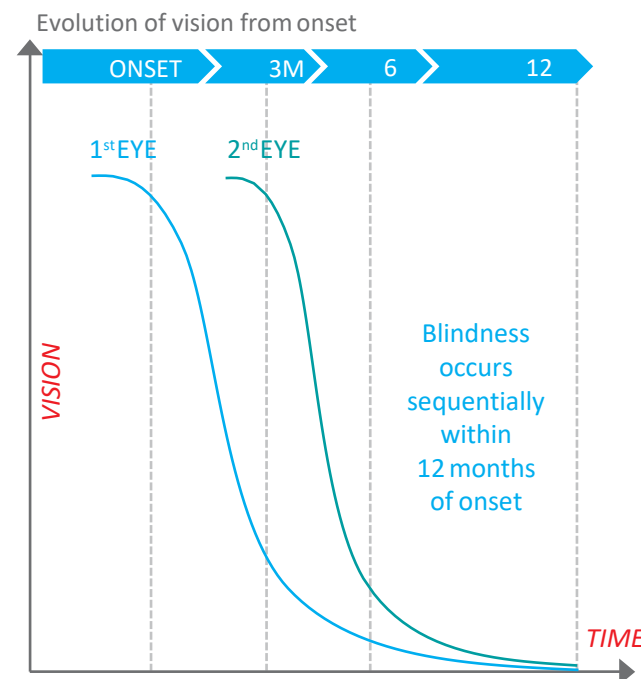


Image source: illustrated from Newman NJ et al., Am J Ophthalmol. 141(6), 1061-1067, 2006

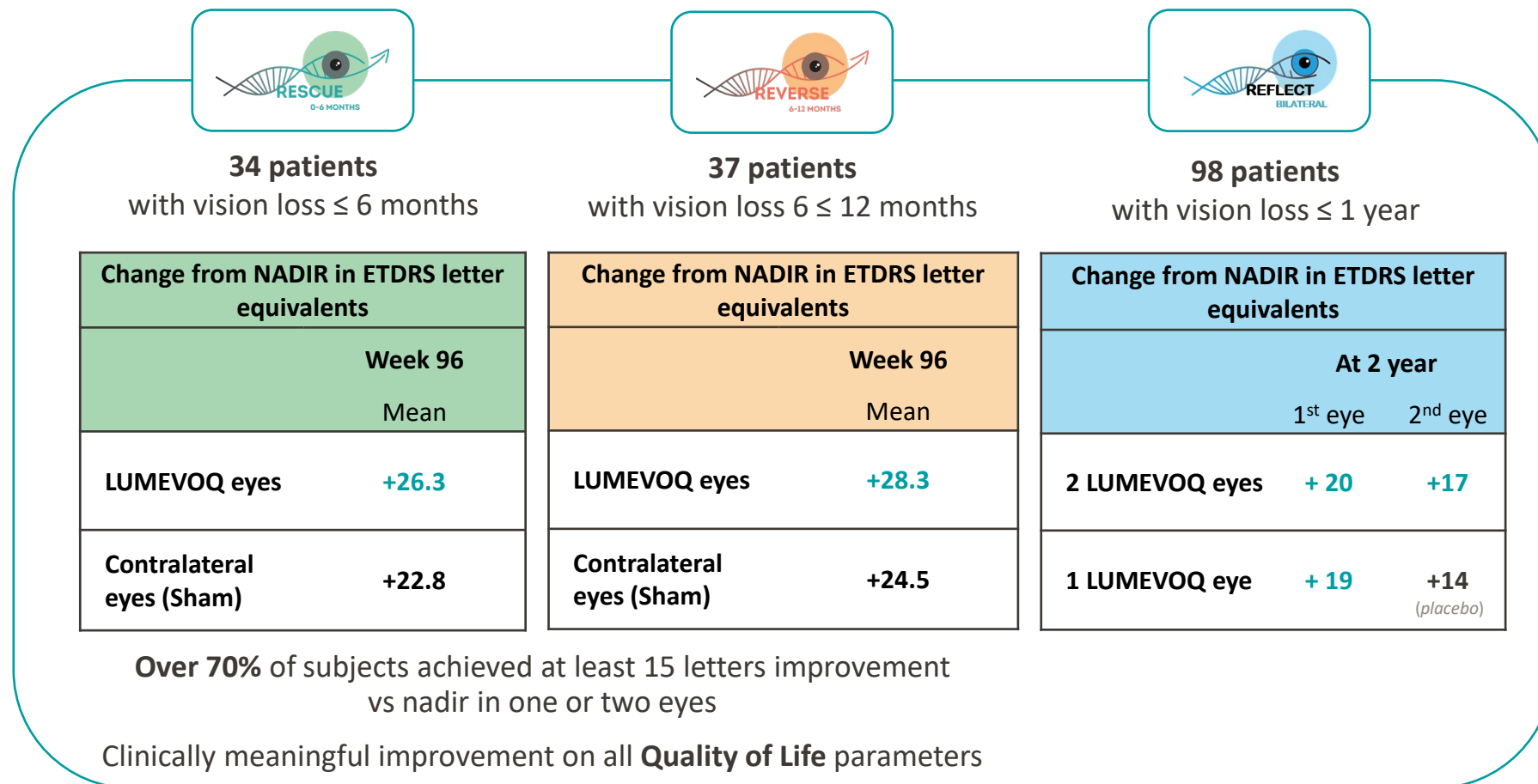
## Current treatment paradigm

- 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)<sup>(2)</sup>
- Demonstrated **6 letters improvement** vs placebo ( $p=0.078$  / NS) at week 24 in Change in best Visual Acuity<sup>(2)</sup>

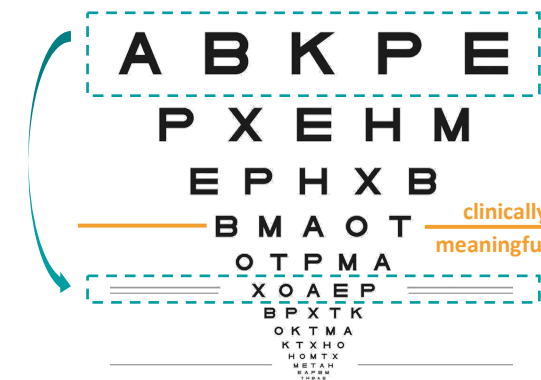
(1) Nadir: worst visual acuity from baseline

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

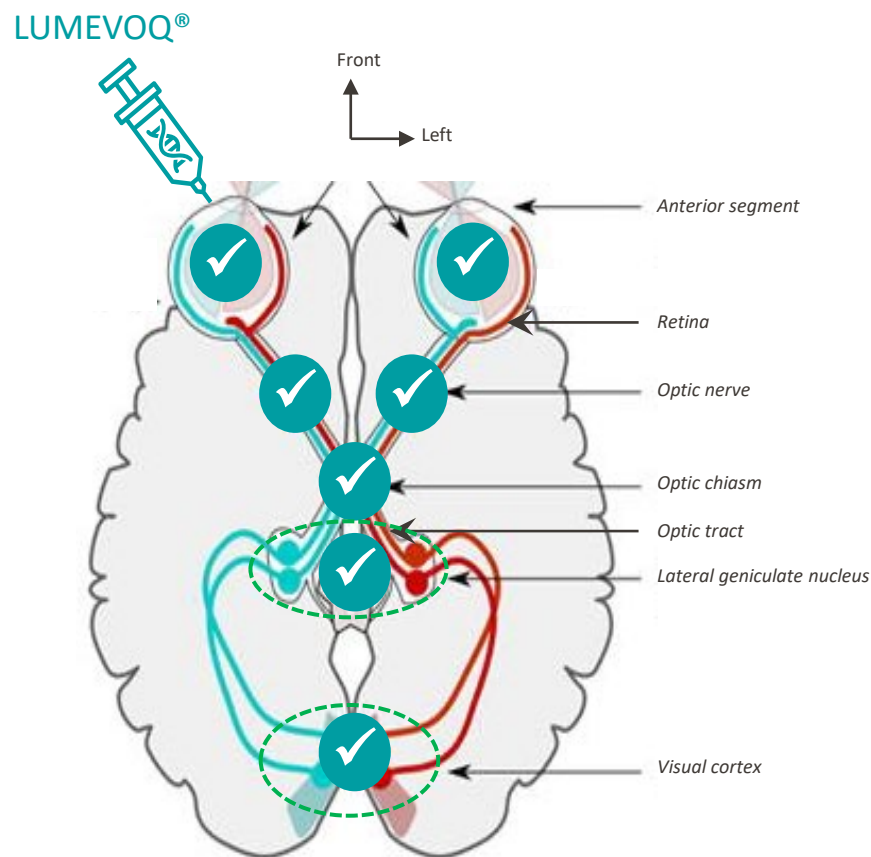


**3+ lines** of visual acuity improvement vs Nadir is highly clinically relevant



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



Study<sup>1</sup> 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 previously<sup>2</sup>
- Provides mechanistical explanation of contralateral effect observed in LUMEVOQ clinical trials

LUMEVOQ injection in one eye

Transfer of LUMEVOQ to  
uninjected eye

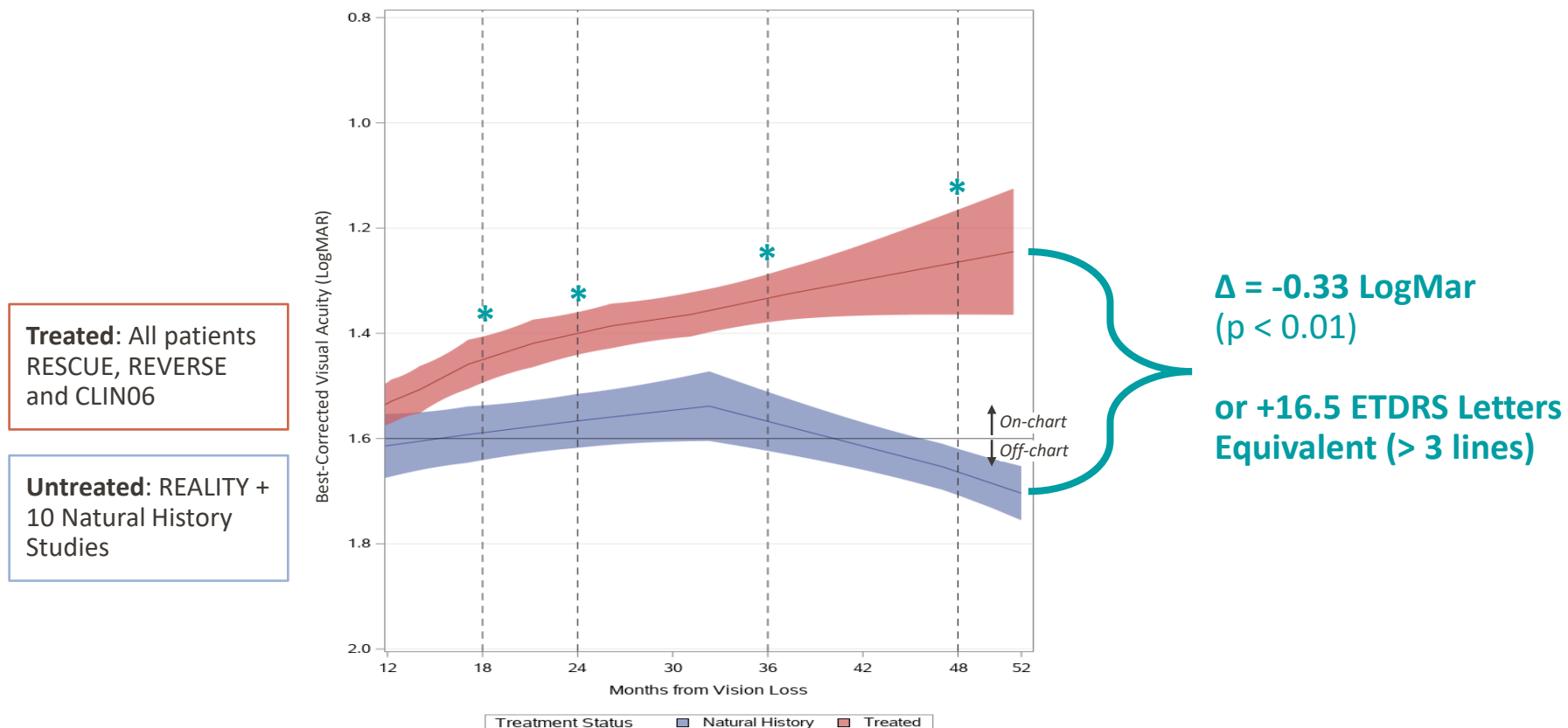
LUMEVOQ present in both eyes

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

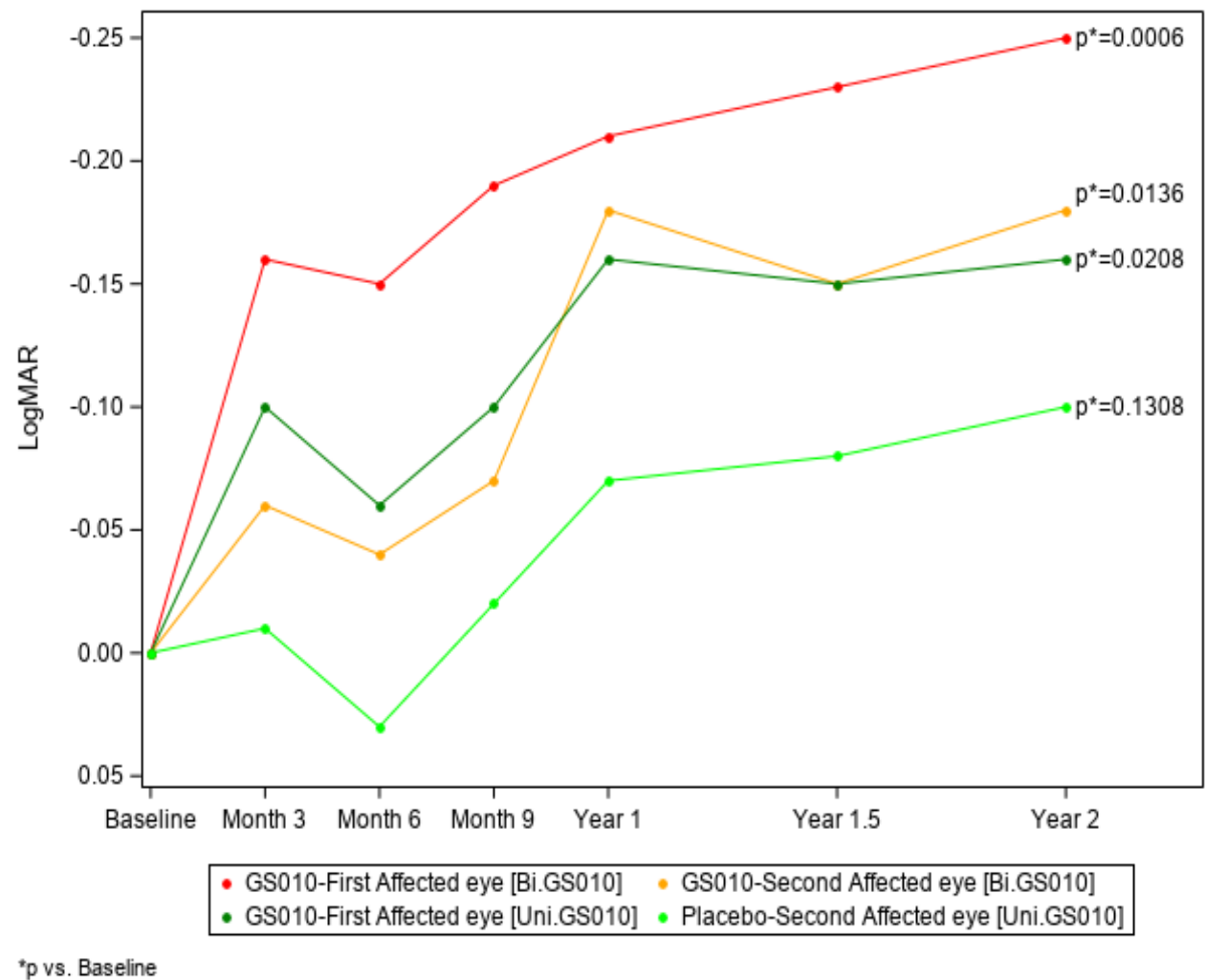
Figure 1. Evolution of Visual Acuity in LUMEVOQ®-treated Patients (N=76) versus Untreated Patients (N=208)



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<sup>1</sup> (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



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

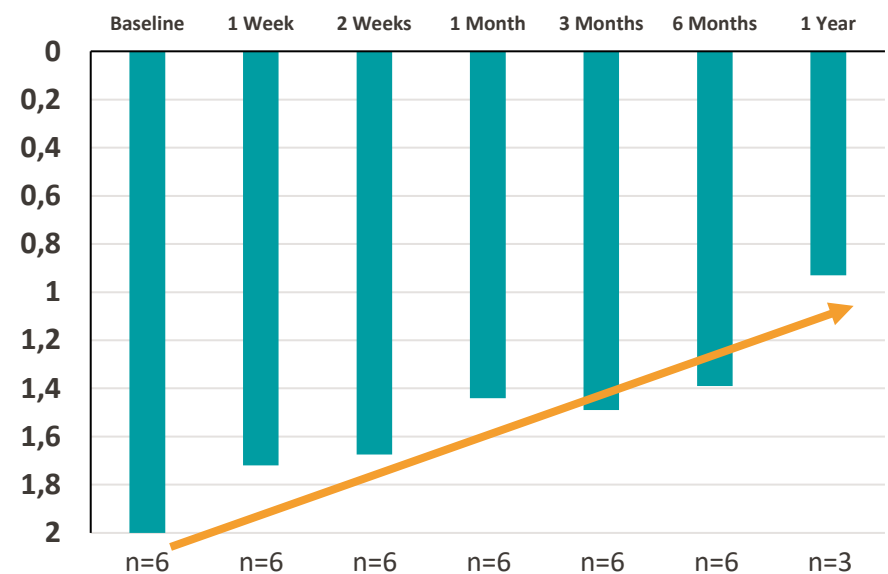


- “ATU de Cohorte” or ATUc - Cohort Temporary Authorization for Use - for LUMEVOQ® granted by ANSM to GenSight on July 5, 2021
  - “ATU Nominative or ATUn” - named patient Temporary Authorization for Use - for LUMEVOQ® first authorized by ANSM to CHNO of the *Quinze-Vingts* in Paris in December 2019
- Bilateral injections priced at €700,000 per patient
  - €4.4M revenues generated in 2020
  - Increasing demand from physicians in 2021 despite COVID restrictions
  - 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

# Real World Experience – US Compassionate Use Program

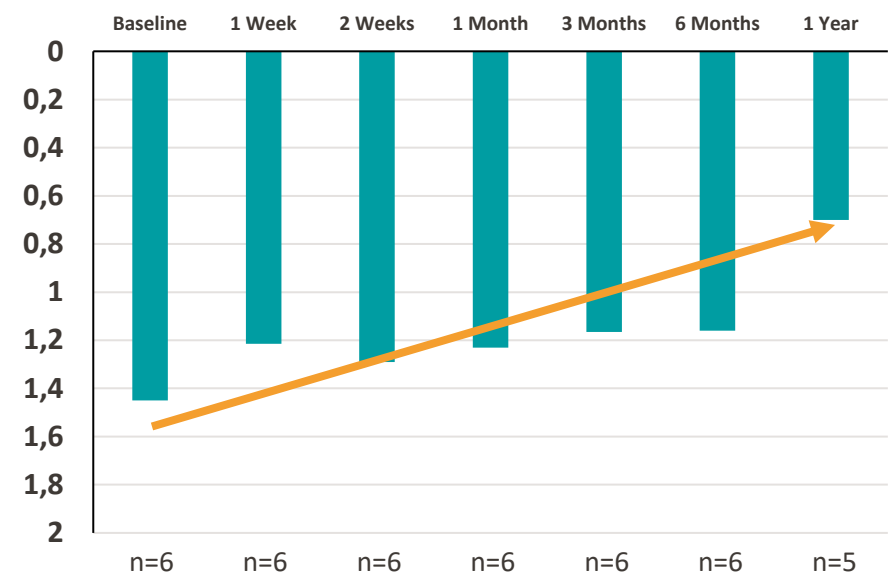
AVG **Worse** Eye BCVA Mean ETDRS  
Change (LogMAR)

11 lines of improvement

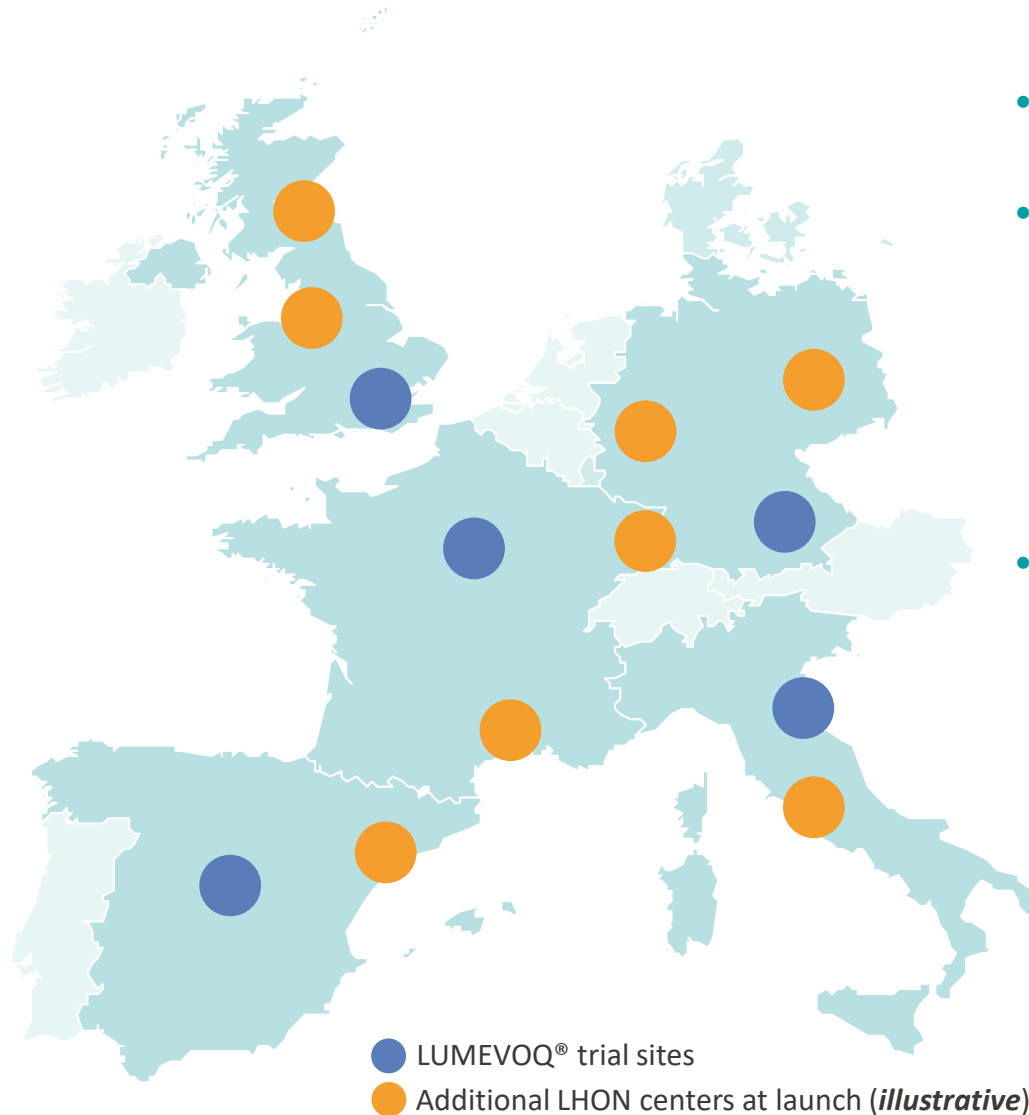


AVG **Better** Eye BCVA Mean ETDRS  
Change (LogMAR)

7.5 lines of improvement

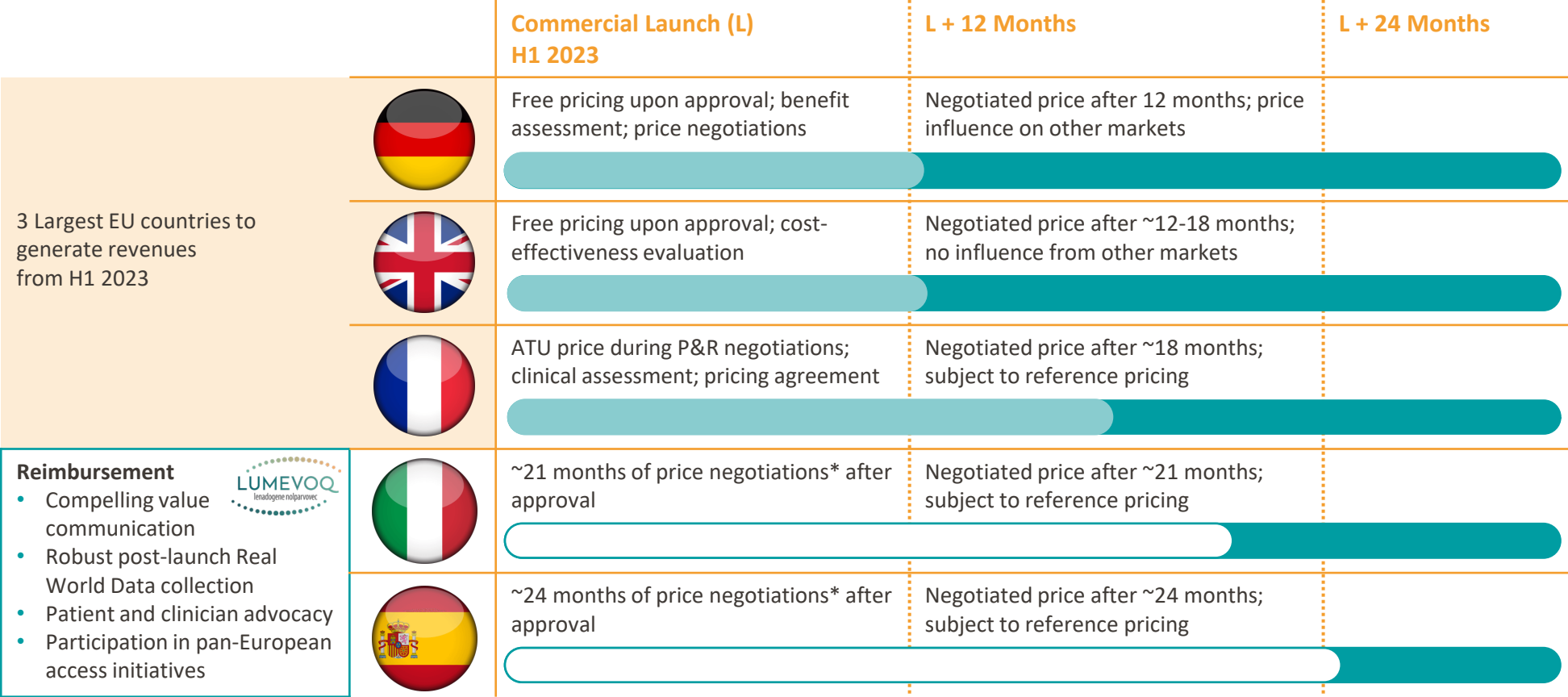


# European Commercial Strategy – Leveraging LUMEVOQ® Clinical Centers to Build Network of LHON Centers of Excellence

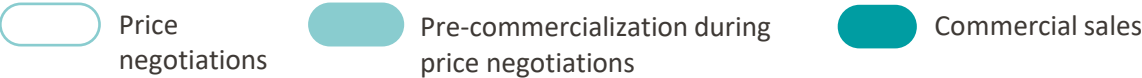


- LHON experts mapped in both major and smaller markets
- Progressively build the LHON clinical network working with LHON experts
  - Recognize varying levels of LHON expertise and patient mobilization across markets
  - Balance patient reach with logistical complexity
- LHON expert- and LHON patient-centric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

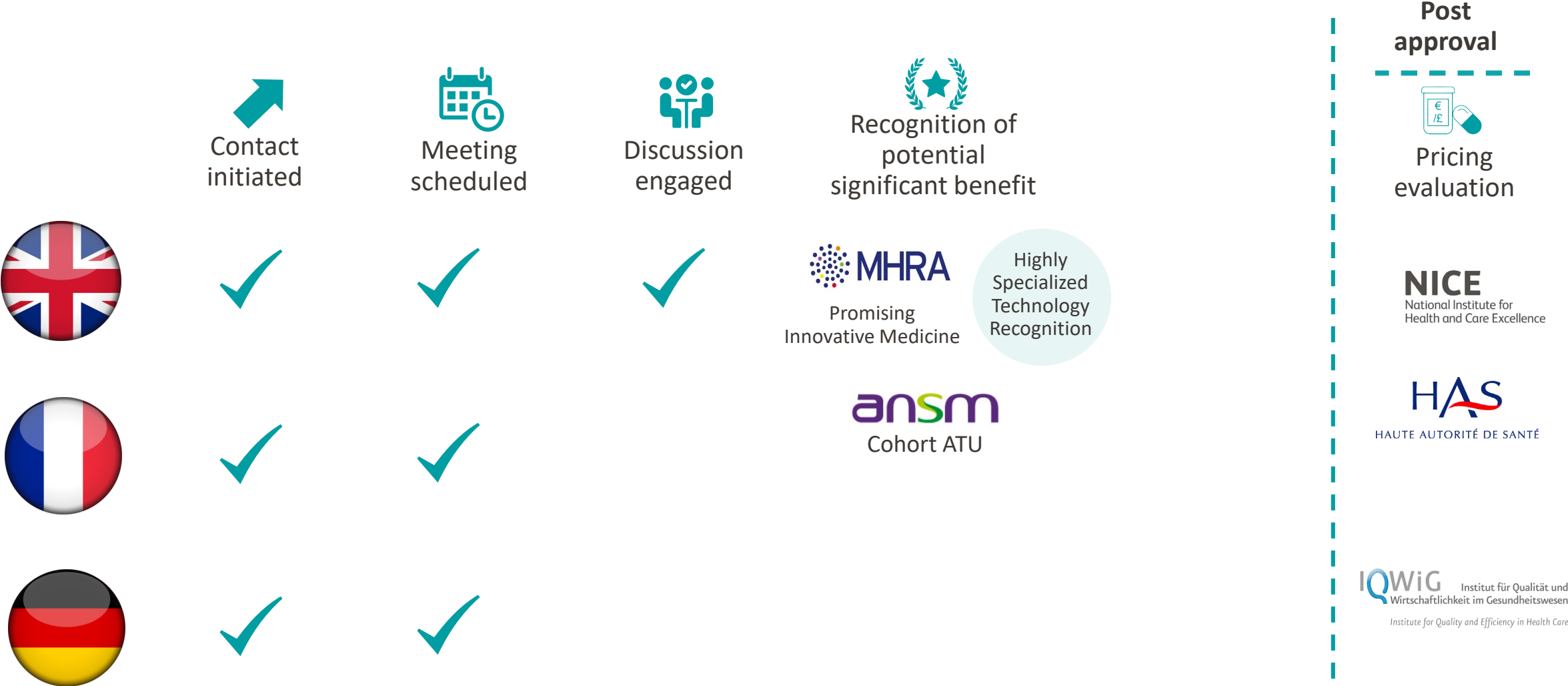
# European Reimbursement Strategy – Short Term Revenues Generation Expected in H1 2023



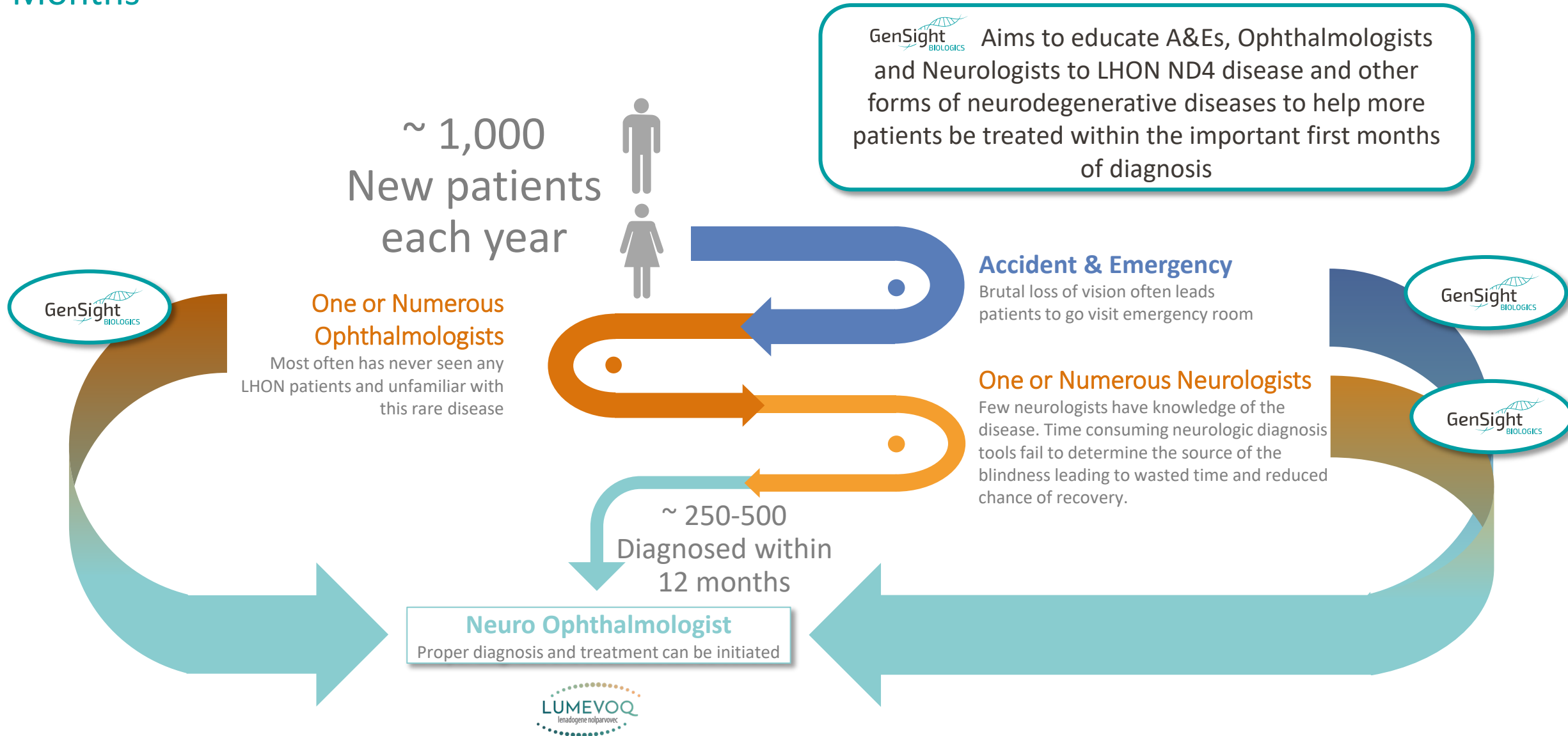
Note: Duration of negotiations depicted is based on industry benchmarks for recent rare disease launches; timings are illustrative



# Early Engagement Initiated with Key European payers



# 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)



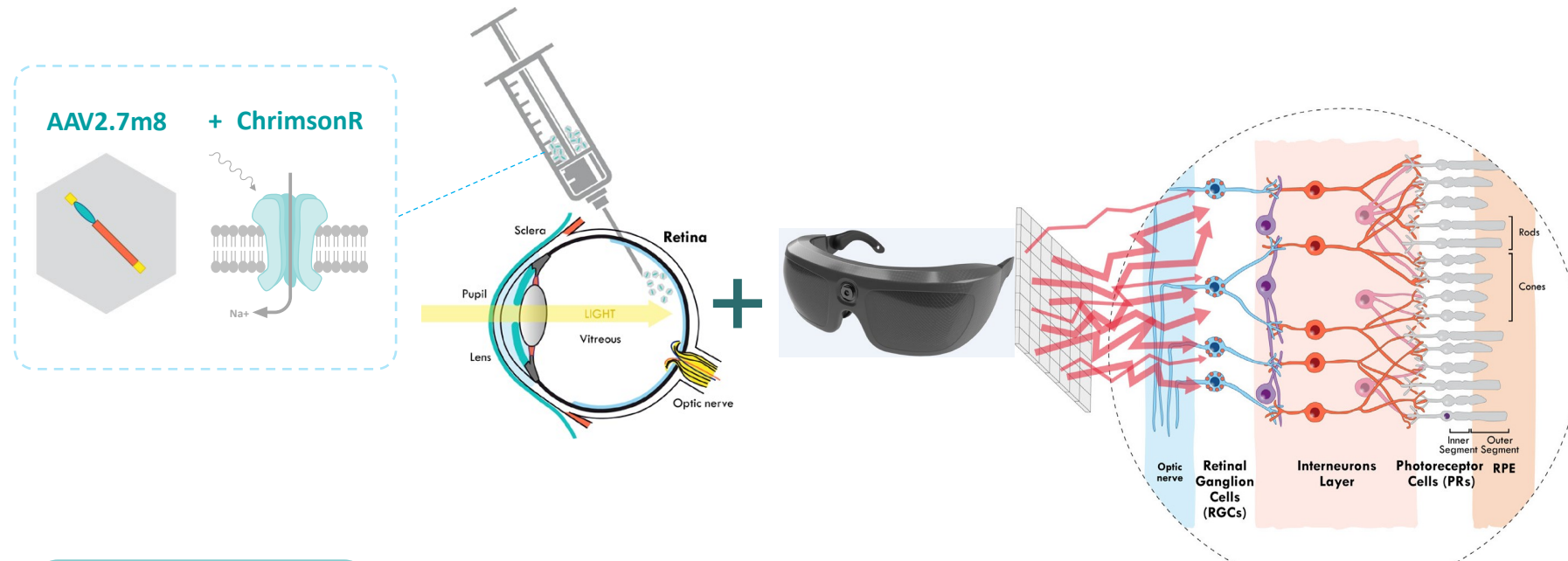
- Blinding genetic disease
- Mutations in over 100 different genes
- Photoreceptor degeneration leads to slow & irreversible progression to blindness, usually at age 40-45
- 15-20,000 new patients each year in the US and EU

## 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

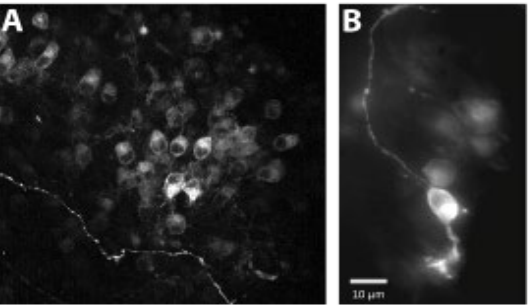
Retinal output sent  
to brain for image  
processing

# GS030 leads to functional vision restoration in monkey and rats

## Localization of light-sensitive protein in NHP retina

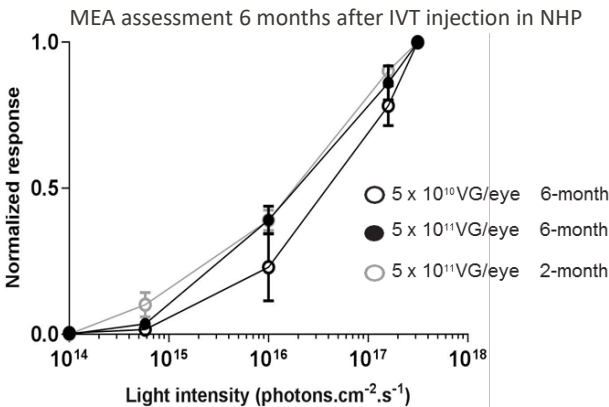
### Expression of ChrR-tdT in midget cells of monkey perifovea

*In vivo* in NHP assessment 6 months after IVT injection



## Dose-ranging response to firing relationship in NHP

### Active dose range : $5 \times 10^{10}$ and $5 \times 10^{11}$ 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**

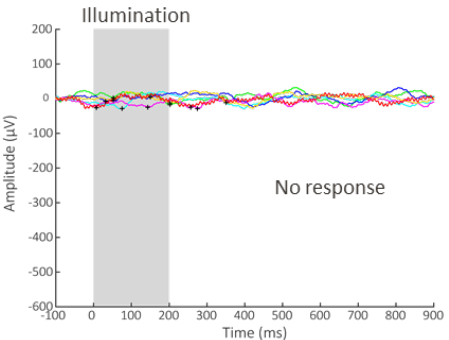
<https://www.nature.com/articles/s42003-020-01594-w>

## Restoration of a functional vision in P23H rats

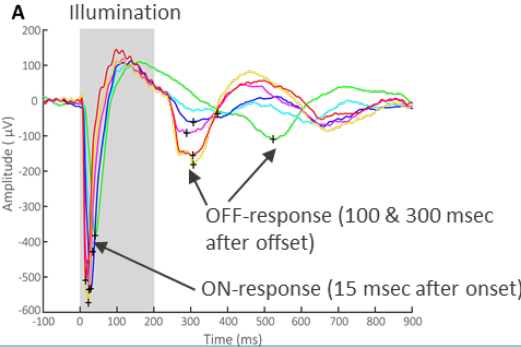
### Untreated P23H rat

### Light-induced visual evoked cortical responses

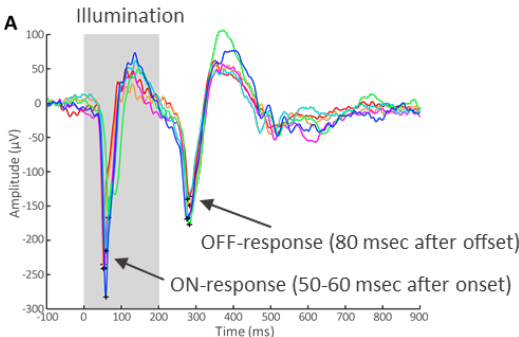
Full field 590 nm light from  $\sim 4.7 \times 10^{15}$  to  $1.1 \times 10^{17}$  photons/cm<sup>2</sup>/sec



### GS030-treated P23H rat



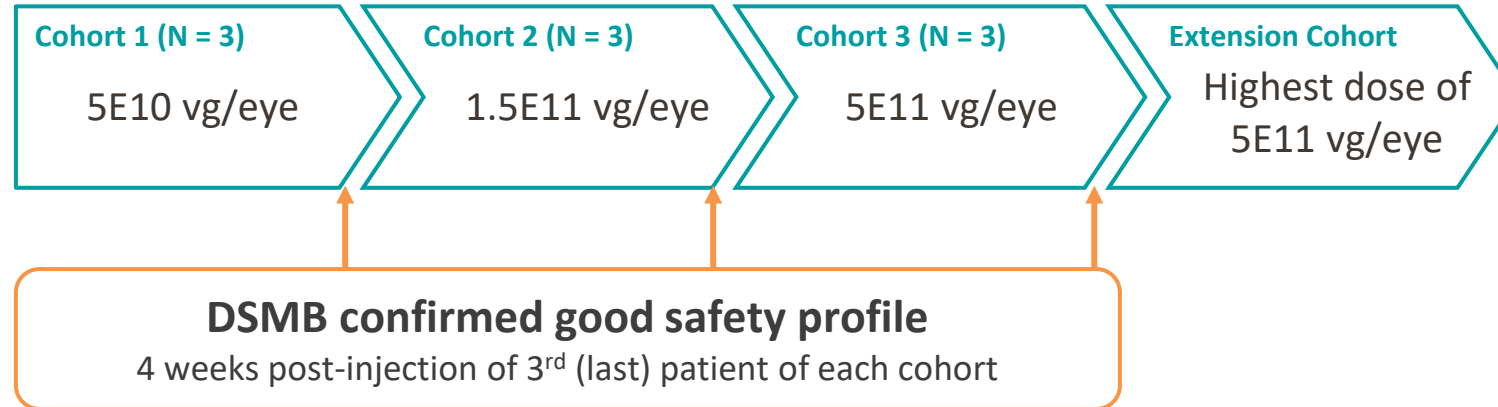
### Normal Long-Evans rat



# 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.

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

2<sup>nd</sup> 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

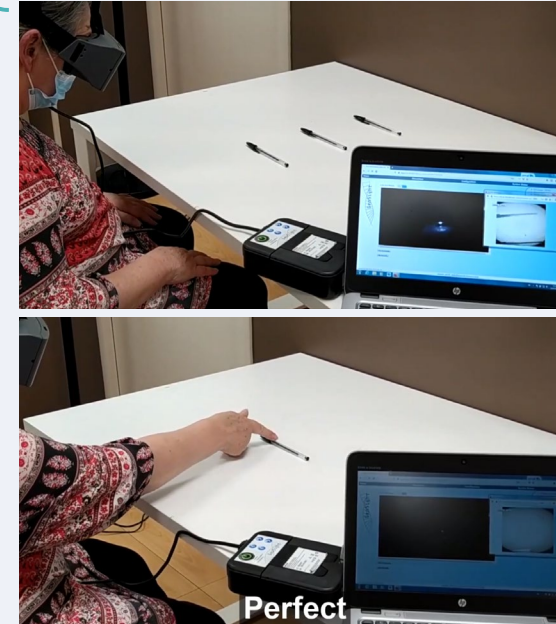
Partial recovery of visual function in a blind patient after optogenetic therapy.

Sahel J.A. et al., **Nature Medicine**, May 2021

<https://www.nature.com/articles/s41591-021-01351-4>

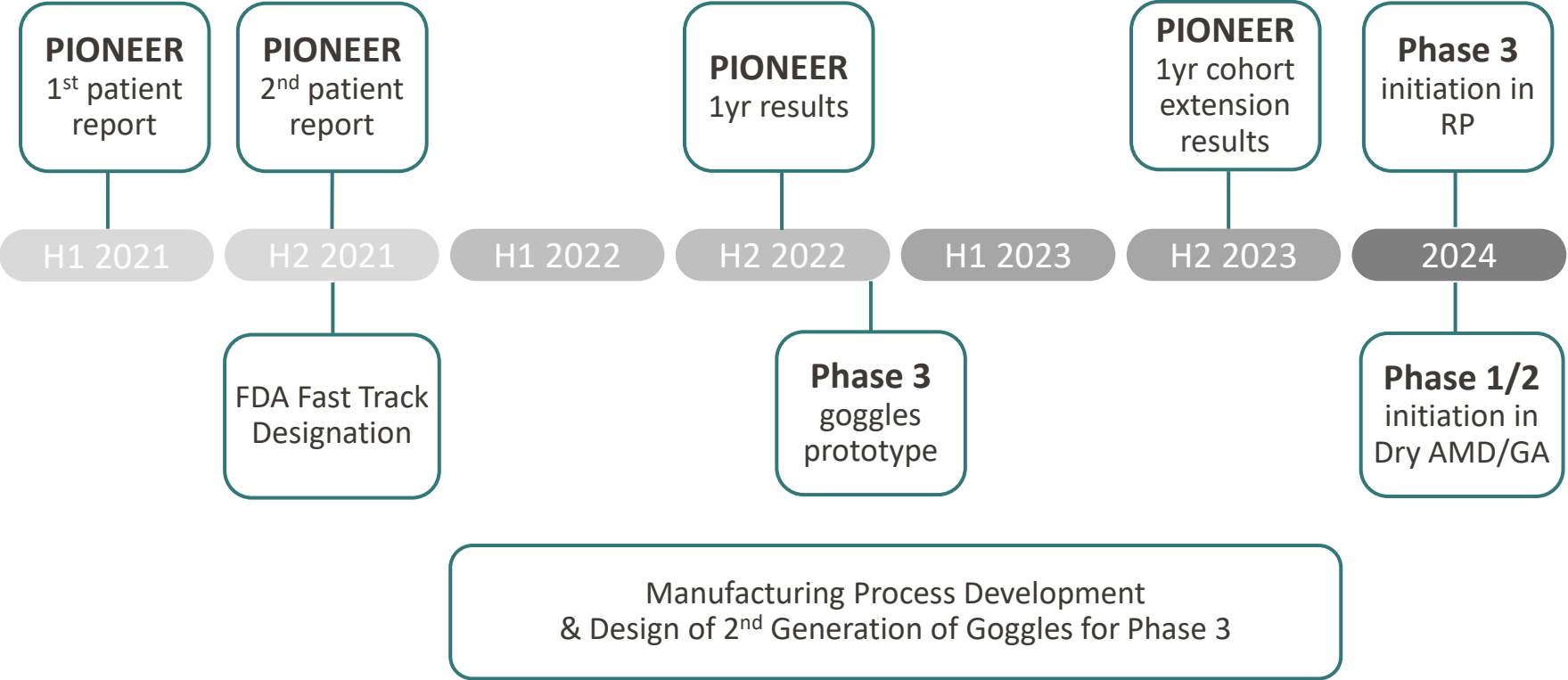


## Video of treated patient



Video of the patient performing the tests available on [www.gensight-biologics.com](http://www.gensight-biologics.com).

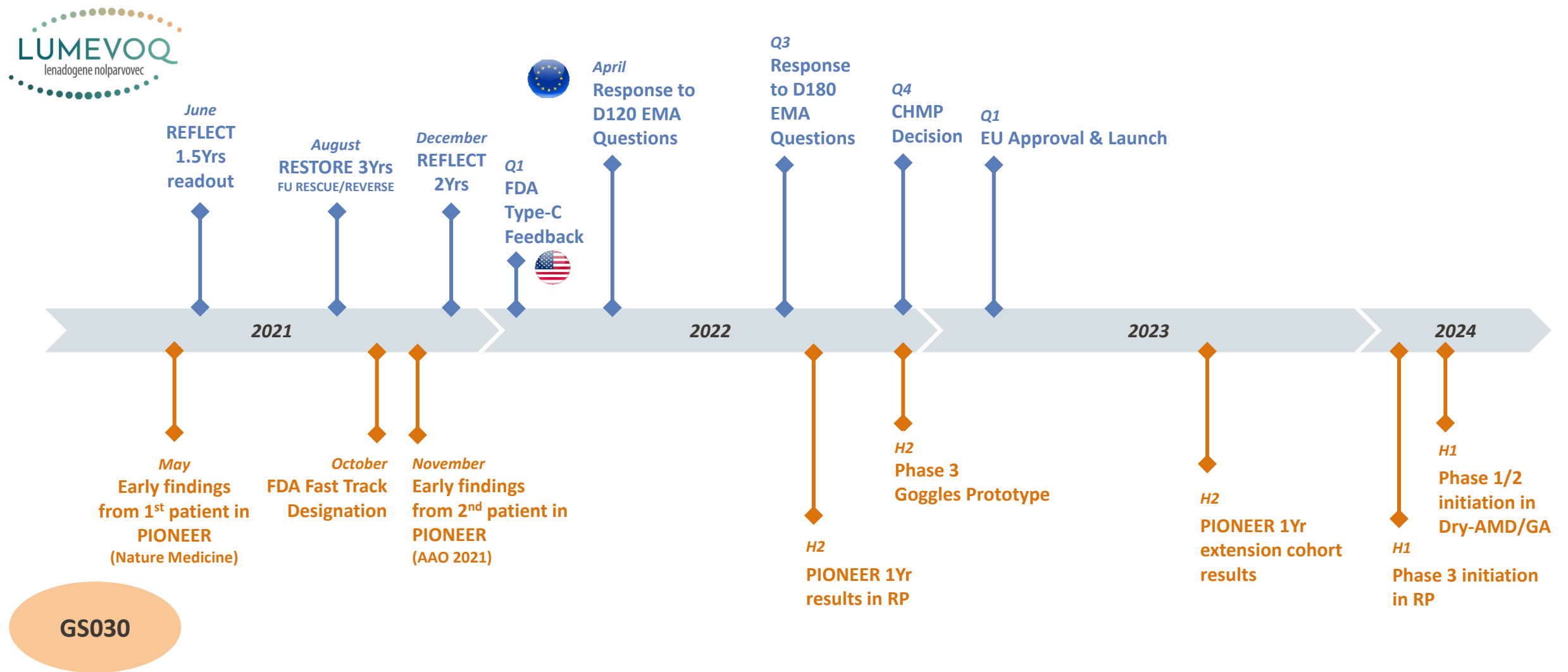
# GS030 timeline



Building high strategic value



# Rich upcoming news flow with numerous inflection points



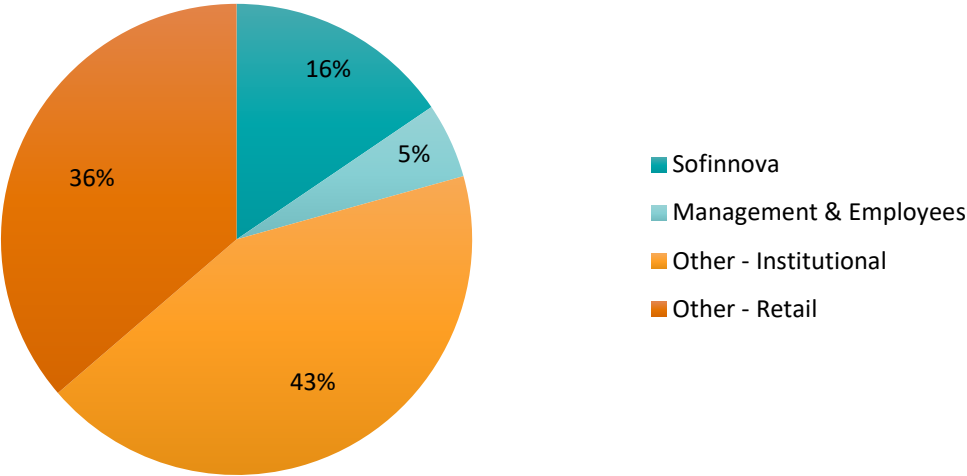
# GenSight Biologics in numbers

## Key financial information

Company Overview		
Market Cap* :	€ 265m	<b>Analyst Coverage</b> <ul style="list-style-type: none"><li>• Chardan: Geulah Livshits (US)</li><li>• Bryan Garnier: Dylan van Haaften (FR)</li><li>• ODDO BHF: Martial Descoutures (FR)</li><li>• Kempen : René Wouters (NL)</li></ul>
Cash Position : (September 30, 2021)	€ 49.1m	
Outstanding Shares:	46.0m	
Latest Amount Raised : (March 2021)	€ 30m	
Raised to date	€ 197m	
IPO Date	July 13, 2016	

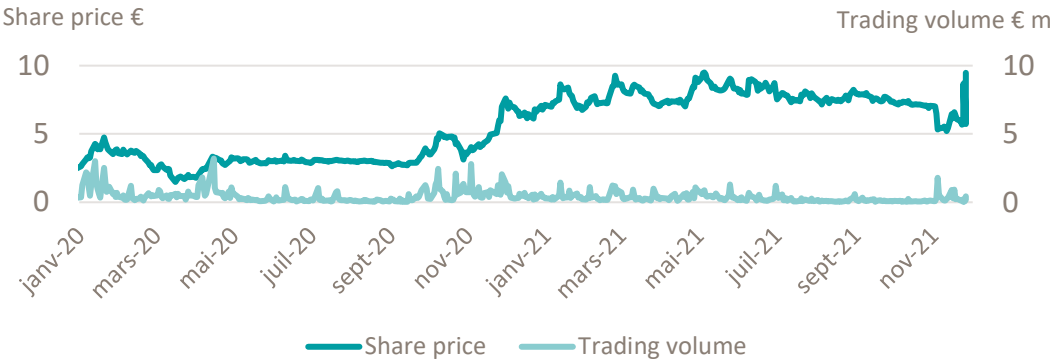
\*As of January 3, 2021

## Shareholder structure



As of July 2021

## Share price evolution and trading volume



## Corporate calendar

2021 4Q Cash Position

January 18, 2022

# Impressive Development Track Record from Concept to Clinic

