GenSight BIOLOGICS

# Corporate Presentation

January 2022

A LEADING Gene Therapy BIOTECHNOLOGY COMPANY

GENSIGHT-BIOLOGICS.COM

# Disclaimer

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# Investment Case – Transitioning from R&D to Commercial Organization

| | | |
|---|---|---|
| 1 | **Late-stage Biotech company** | Public company founded in 2012 dedicated to developing and commercializing gene therapies for neurodegenerative retinal diseases and diseases of the central nervous system.<br>Euronext Listed SIGHT / €265m Market Cap / Avg. 30-day Daily volume: 0.5% of O/S |
| 2 | **Seasoned management team / Potential NASDAQ Listing** | Management team with strong and highly relevant Biotech experience in R&D and commercialization<br><br>Solid investor base of Healthcare specialist investors, including US based investors. Contemplating potential secondary NASDAQ listing |
| 3 | **LUMEVOQ® Strong clinical data in LHON** | LUMEVOQ® completed 3 Phase III studies in Leber Hereditary Optic Neuropathy (ND4 LHON), a rare and highly debilitating genetic ophthalmic disease leading to sudden loss of central vision and affecting c. 1,200 – 1,500 new patients / year in Europe and the US |
| 4 | **H1 2023 LUMEVOQ® European launch** | Dedicated team in place to accelerate/optimize LUMEVOQ® access in key European territories<br>Available in France through ATU at €700,000 for a bilateral injection<br>EU regulatory review ongoing - on track for potential approval in Q4 2022 and launch in Q1 2023<br>Ongoing discussion with US FDA to confirm regulatory timeline |
| 5 | **Cutting hedge optogenetics in Retinitis Pigmentosa** | GS030 outstanding early findings reporting blind patients to precisely identify objects (published in Nature Medicine in May 21)<br>Extension cohort currently being recruited |



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# 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)



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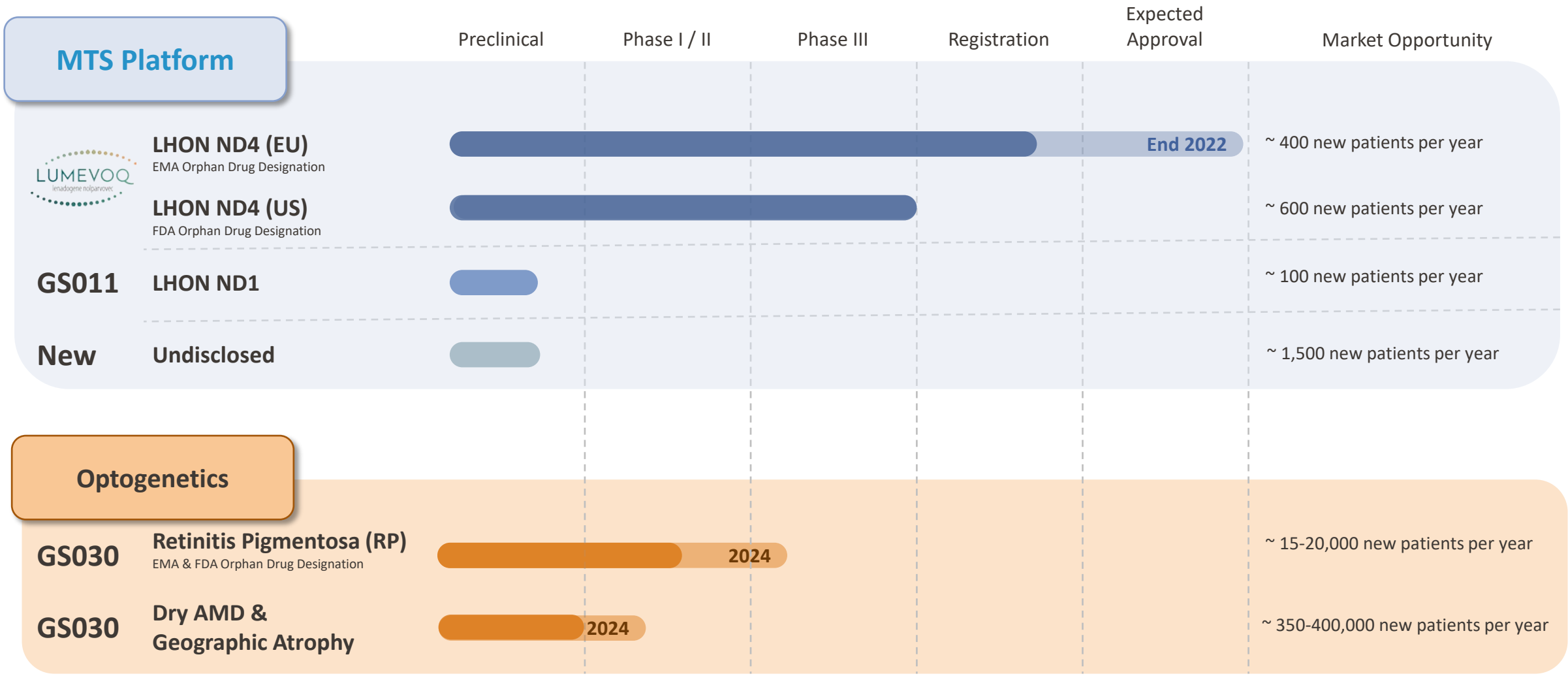
# Pipeline: solid and advanced product portfolio in ophthalmic Gene Therapy



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# LUMEVOQ® in LHON-*ND4*

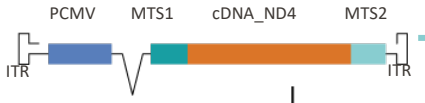
- 3 Phase III completed
- European regulatory submission ongoing in Leber Hereditary Optic Neuropathy
- Commercial preparation ongoing for early 2023 European launch

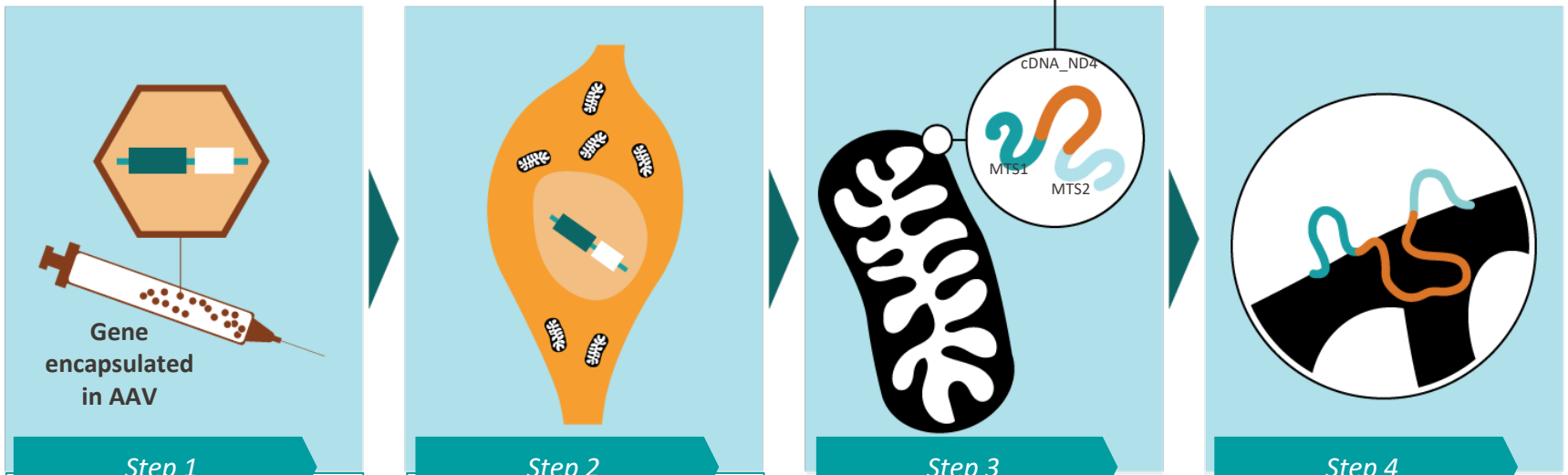
# LUMEVOQ® introduces Gene Therapy solution

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

*The product of research collaboration with* Inserm

***MTS in action for GS010:***




**Step 1**

Retinal cell transduced with vector containing wild-type mitochondrial gene

**Step 2**

Wild-type mitochondrial gene transcribed in the nucleus

**Step 3**

Wild-type mRNA **delivered by MTS directly** to polysomes located at the mitochondrial surface, where protein synthesis occurs

**Step 4**

Finally, the wild-type mitochondrial protein is translocated inside the mitochondrion, where it **restores energy production**

*Gene Therapy*

*MTS**

*MTS = mitochondrial targeting sequence



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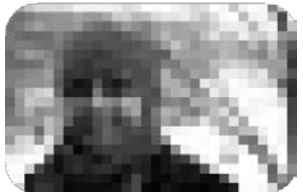
# Leber Hereditary Optic Neuropathy (LHON-ND4) high unmet medical need

## 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

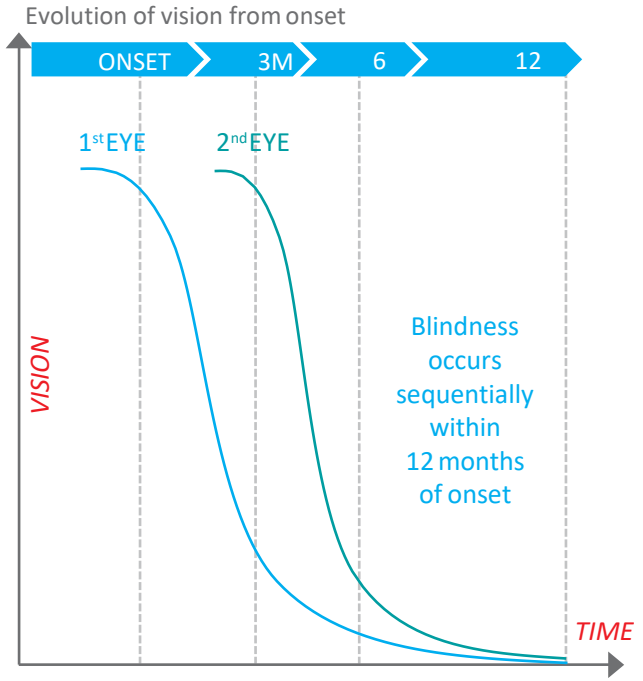



Image source: illustrated from Newman NJ et al., Am J Ophthalmo. 141(6), 1061-1067,2006

## 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® in LHON in 3 Phase III studies

RESCUE 0-6 MONTHS

**34 patients**
with vision loss ≤ 6 months

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

REVERSE 6-12 MONTHS

**37 patients**
with vision loss 6 ≤ 12 months

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

REFLECT BILATERAL

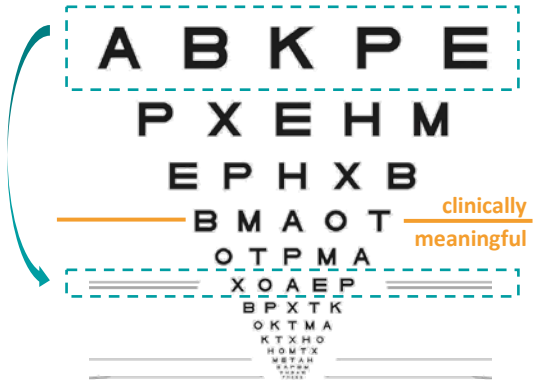
**98 patients**
with vision loss ≤ 1 year

| Change from NADIR in ETDRS letter equivalents | At 2 year 1st eye | At 2 year 2nd eye |
|---|---|---|
| **2 LUMEVOQ eyes** | **+ 20** | **+17** |
| **1 LUMEVOQ eye** | **+ 19** | **+14** (*placebo*) |

**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

**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)*



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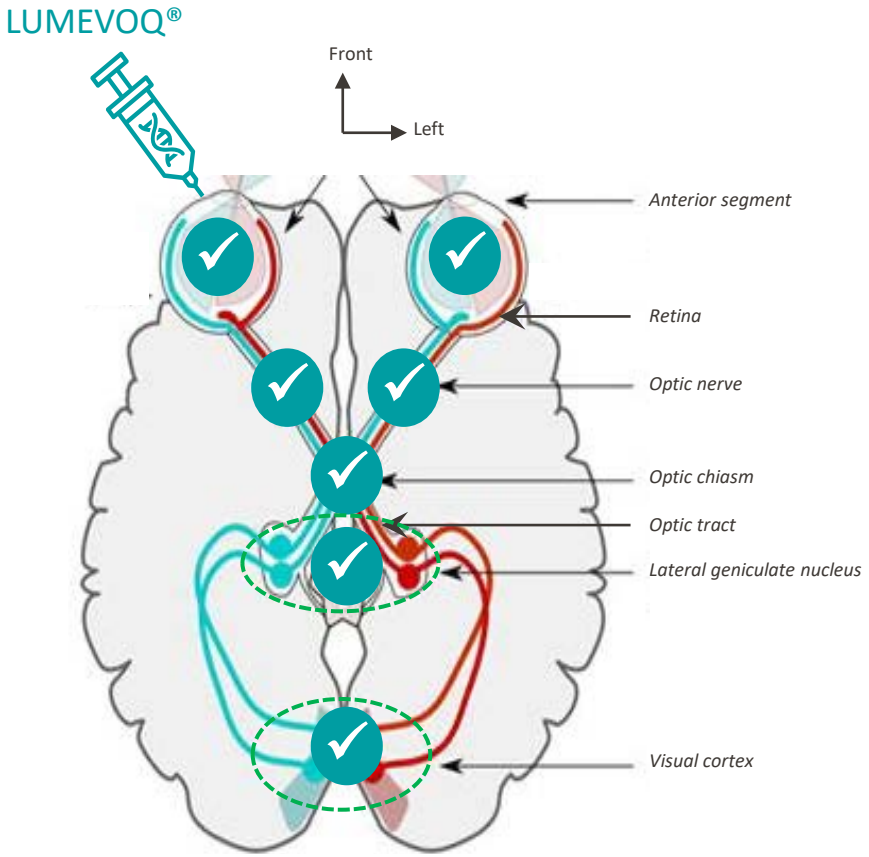
# The Bilateral Effect Demonstrated – LUMEVOQ also detected in contralateral eyes




Study[1] 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[2]
- 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.



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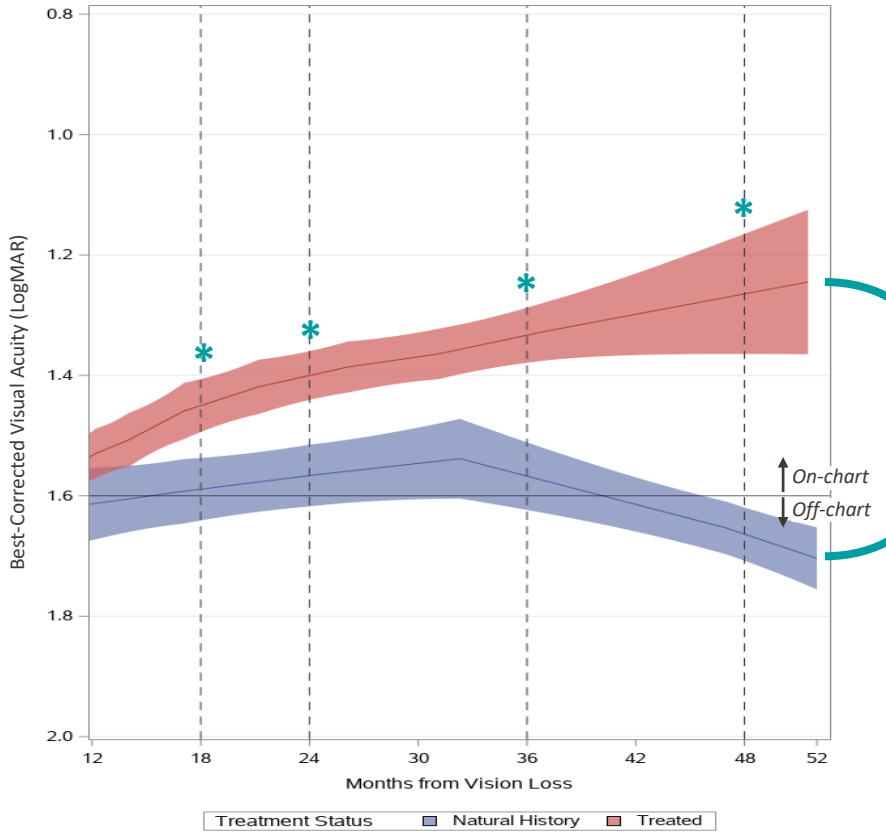
# LUMEVOQ® modifies disease outcome compared to natural history

## 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



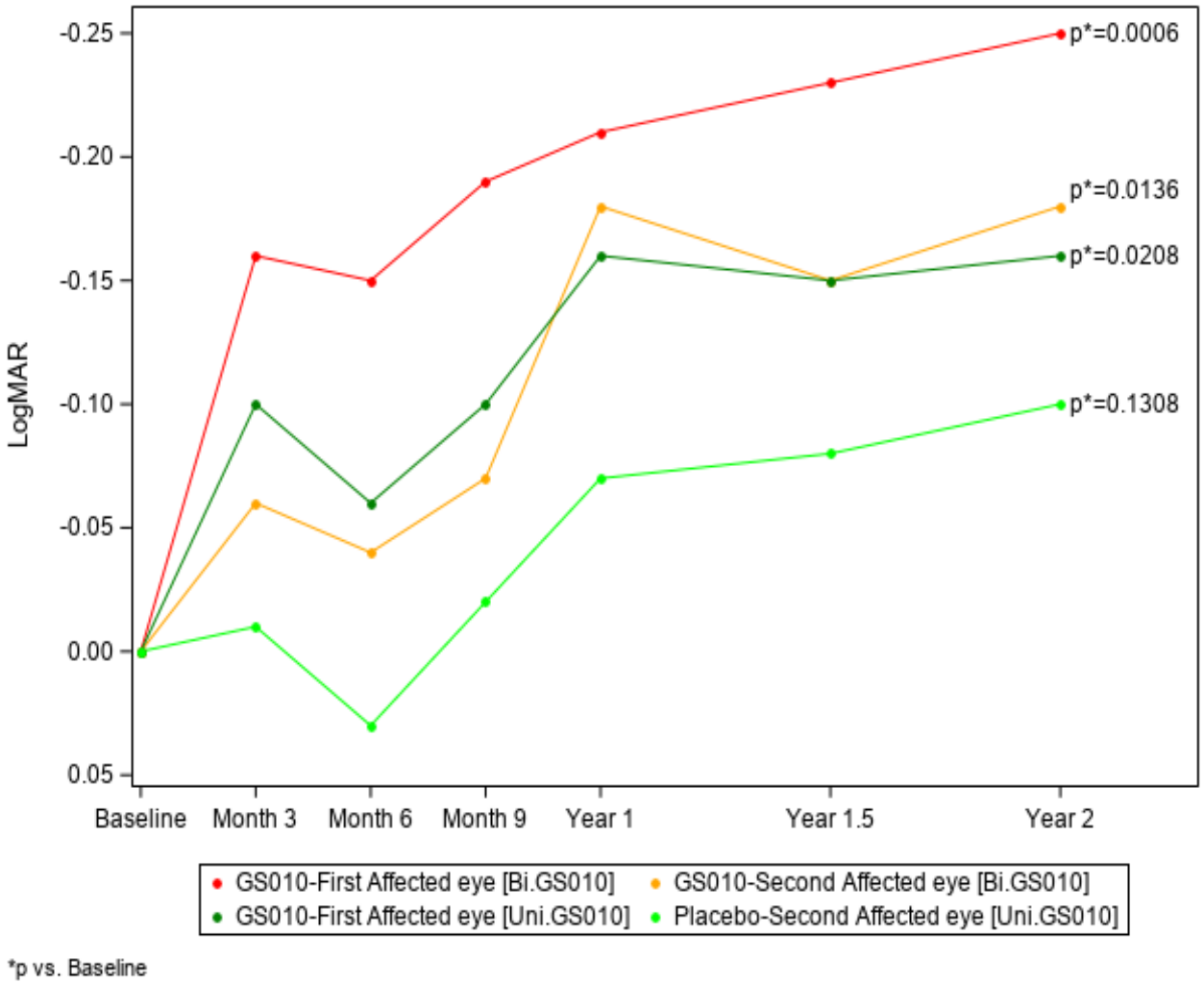

**Δ = -0.33 LogMar**
(p < 0.01)

**or +16.5 ETDRS Letters Equivalent (> 3 lines)**

*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.**

# 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


- "*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



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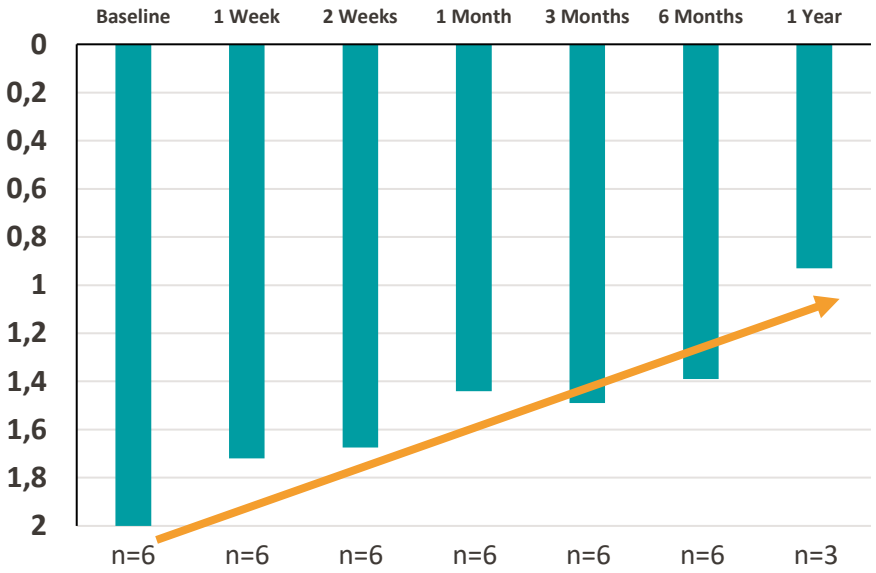
# Real World Experience – US Compassionate Use Program

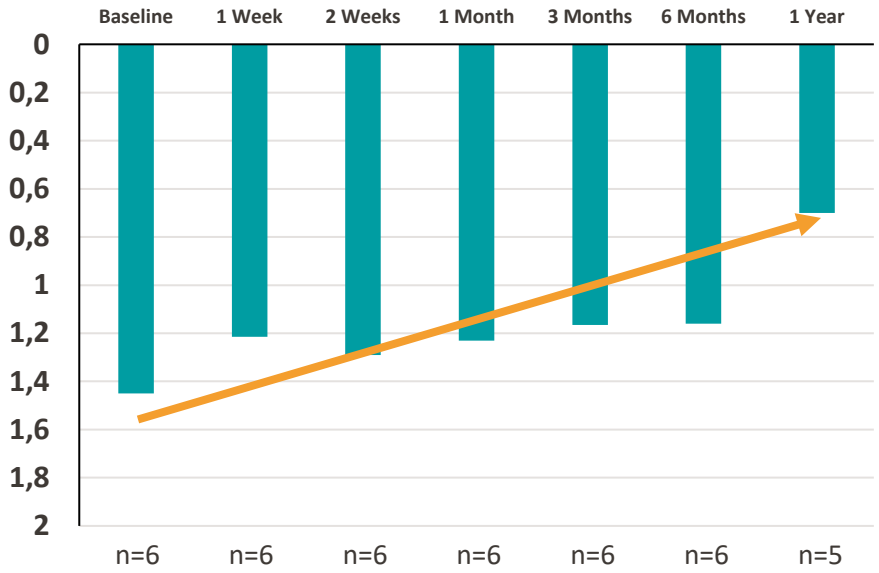
## AVG **Worse** Eye BCVA Mean ETDRS Change (LogMAR)

**11 lines of improvement**




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

**7.5 lines of improvement**



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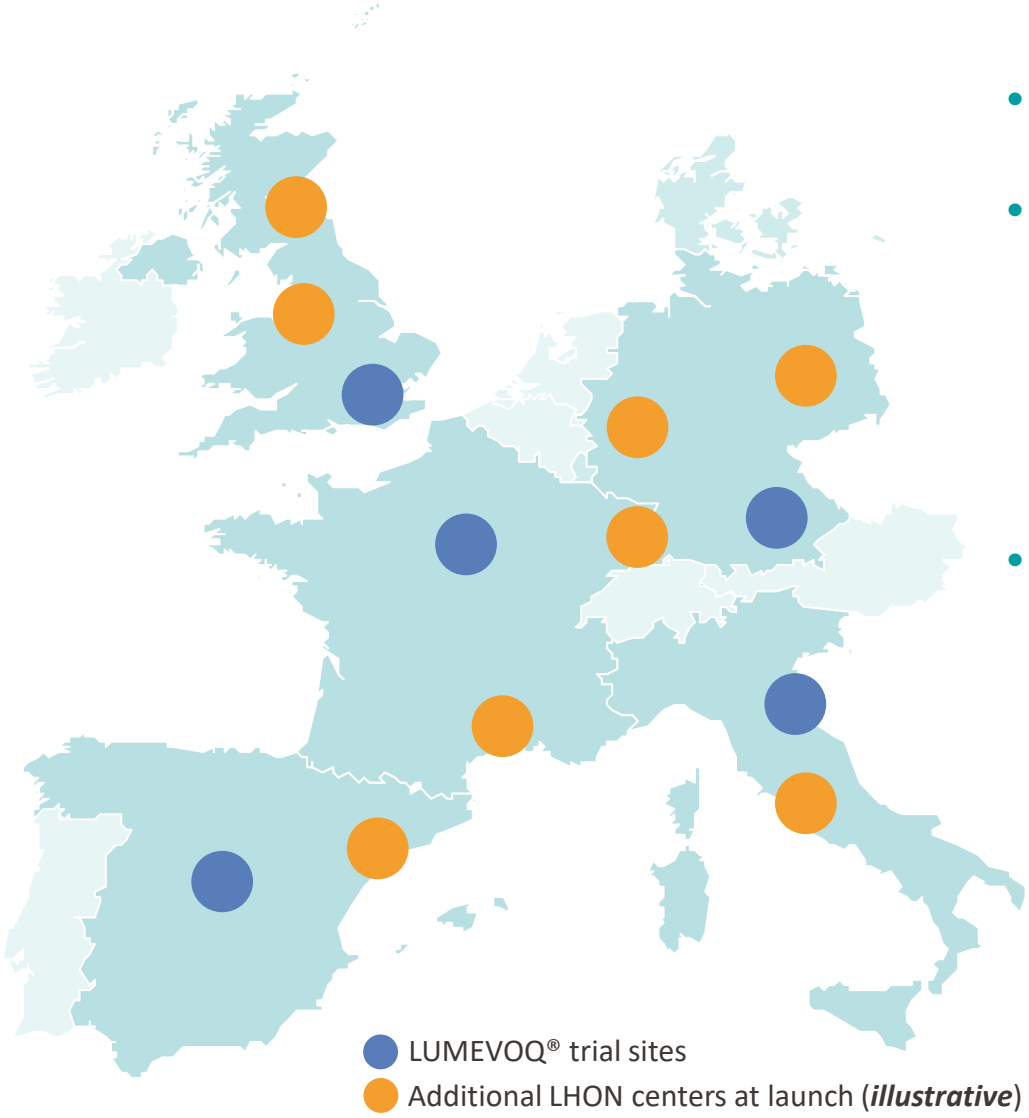
# European Commercial Strategy – Leveraging LUMEVOQ® Clinical Centers to Build Network of LHON Centers of Excellence




- 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



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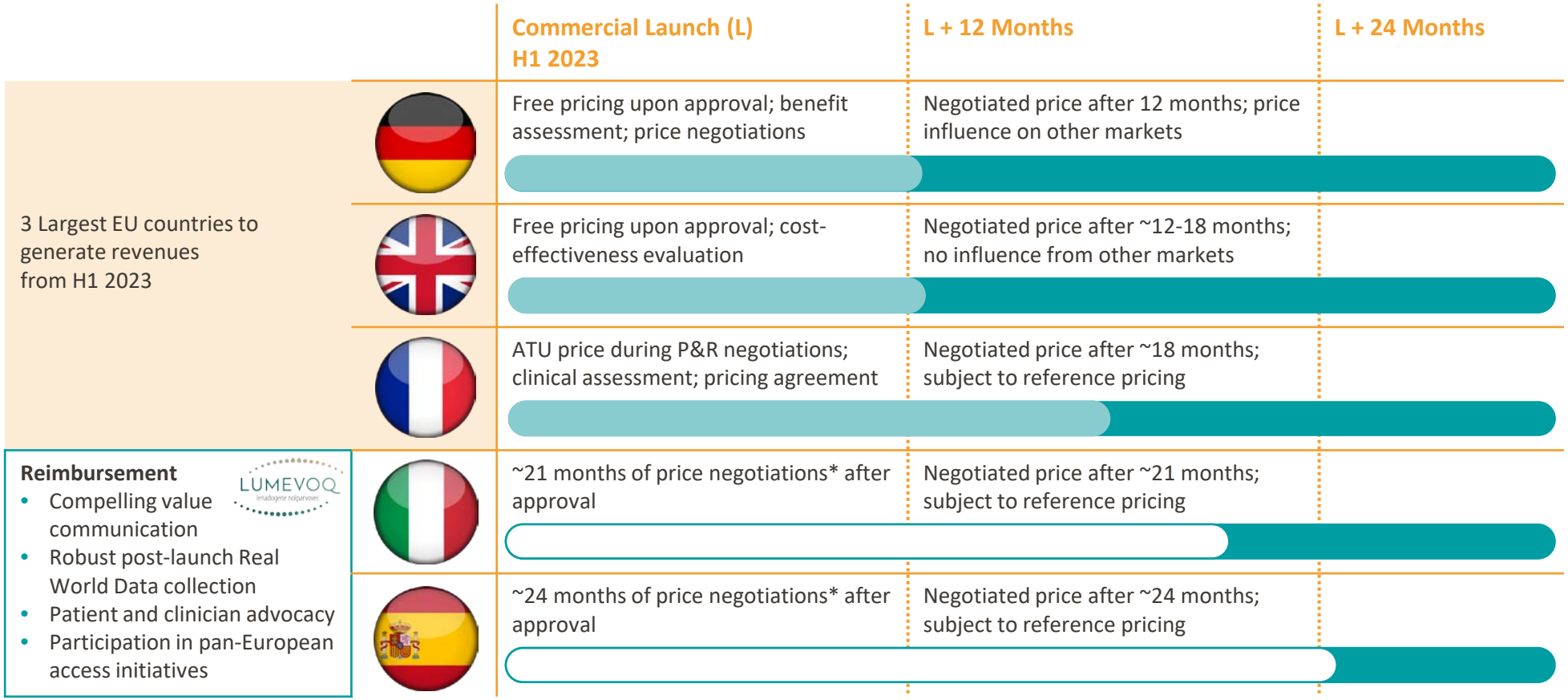
# European Reimbursement Strategy – Short Term Revenues Generation Expected in H1 2023




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



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# Early Engagement Initiated with Key European payers

| | Contact initiated | Meeting scheduled | Discussion engaged | Recognition of potential significant benefit |
|---|---|---|---|---|
|  | ✓ | ✓ | ✓ | MHRA Promising Innovative Medicine; Highly Specialized Technology Recognition |
|  | ✓ | ✓ | | ansm Cohort ATU |
|  | ✓ | ✓ | | |

**Post approval**

Pricing evaluation

NICE National Institute for Health and Care Excellence

HAS HAUTE AUTORITÉ DE SANTÉ

IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Institute for Quality and Efficiency in Health Care



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

GenSight BIOLOGICS Aims to educate A&Es, Ophthalmologists and Neurologists to LHON ND4 disease and other forms of neurodegenerative diseases to help more patients be treated within the important first months of diagnosis

~ 1,000
New patients
each year

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**One or Numerous Ophthalmologists**
Most often has never seen any LHON patients and unfamiliar with this rare disease

**Accident & Emergency**
Brutal loss of vision often leads patients to go visit emergency room

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**One or Numerous Neurologists**
Few neurologists have knowledge of the disease. Time consuming neurologic diagnosis tools fail to determine the source of the blindness leading to wasted time and reduced chance of recovery.

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~ 250-500
Diagnosed within
12 months

**Neuro Ophthalmologist**
Proper diagnosis and treatment can be initiated

LUMEVOQ
lenadogene nolparvovec



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# 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



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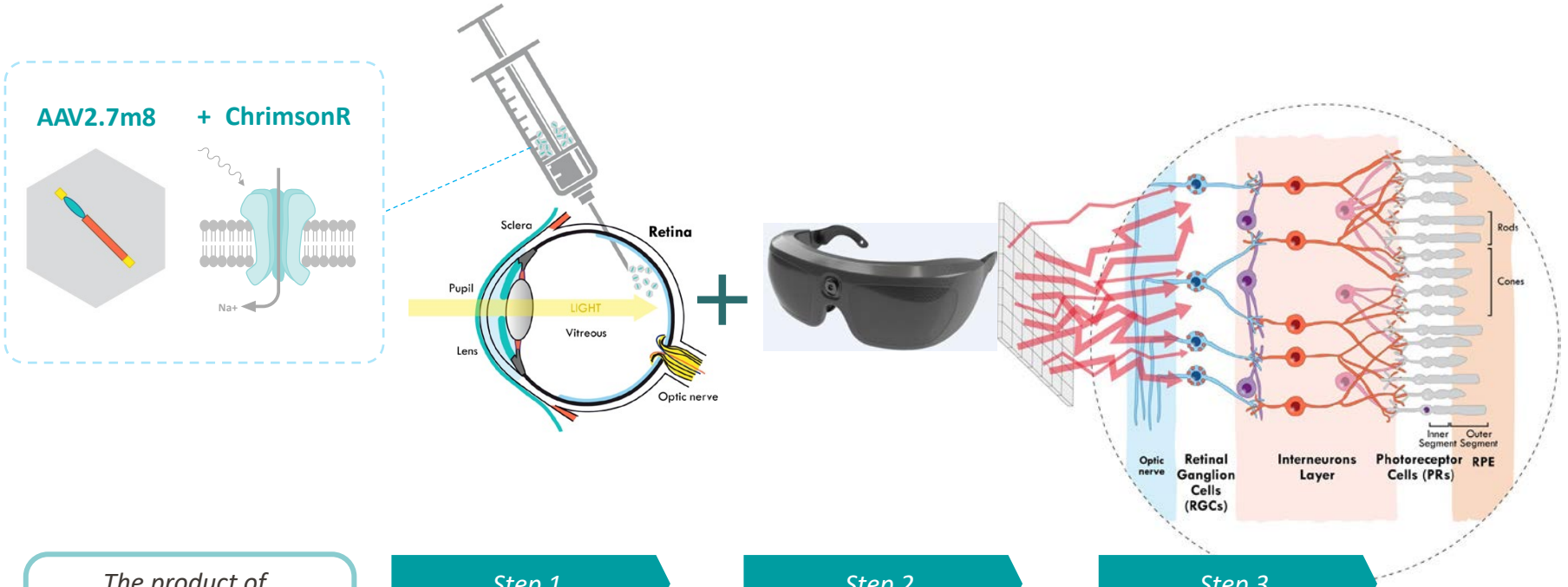
# GS030: using Gene Therapy to rejuvenate production of light-sensitive protein and restore vision




*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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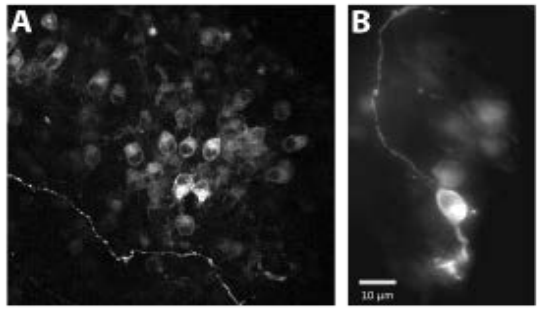
# GS030 leads to functional vision restoration in monkey and rats

*Localization of light-sensitive protein in NHP retina*

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

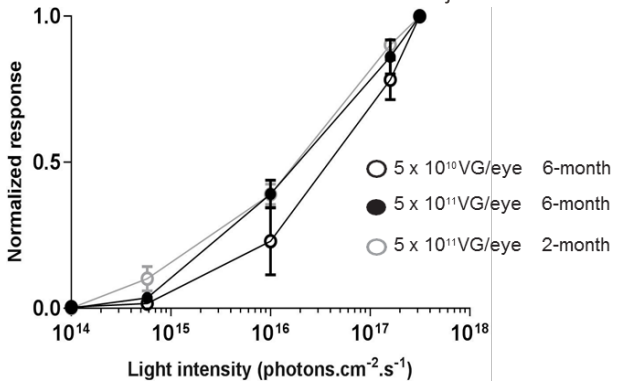
*In vivo* in NHP assessment 6 months after IVT injection




*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**

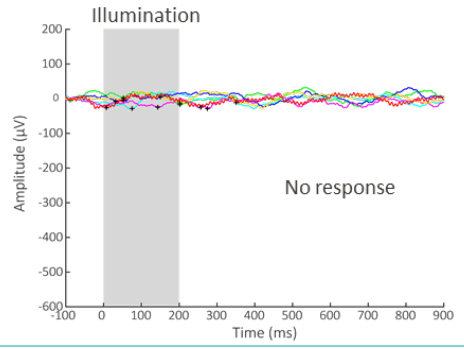
Optogenetic therapy: high spatiotemporal resolution and pattern discrimination compatible with vision restoration in non-human primates. Gauvain G. et al. **Communications Biology, Feb. 2021**
https://www.nature.com/articles/s42003-020-01594-w.

*Restoration of a functional vision in P23H rats*

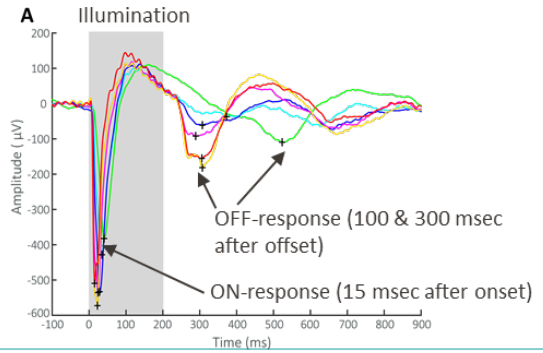
**Light-induced visual evoked cortical responses**

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

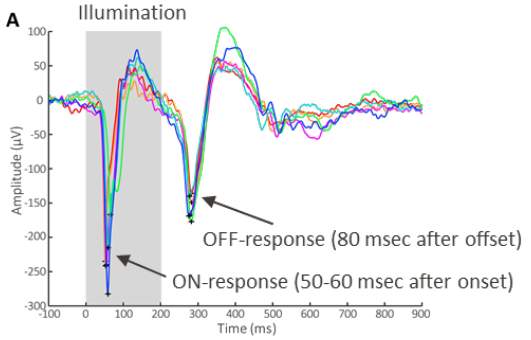
**Untreated P23H rat**




**GS030-treated P23H rat**




**Normal Long-Evans rat**



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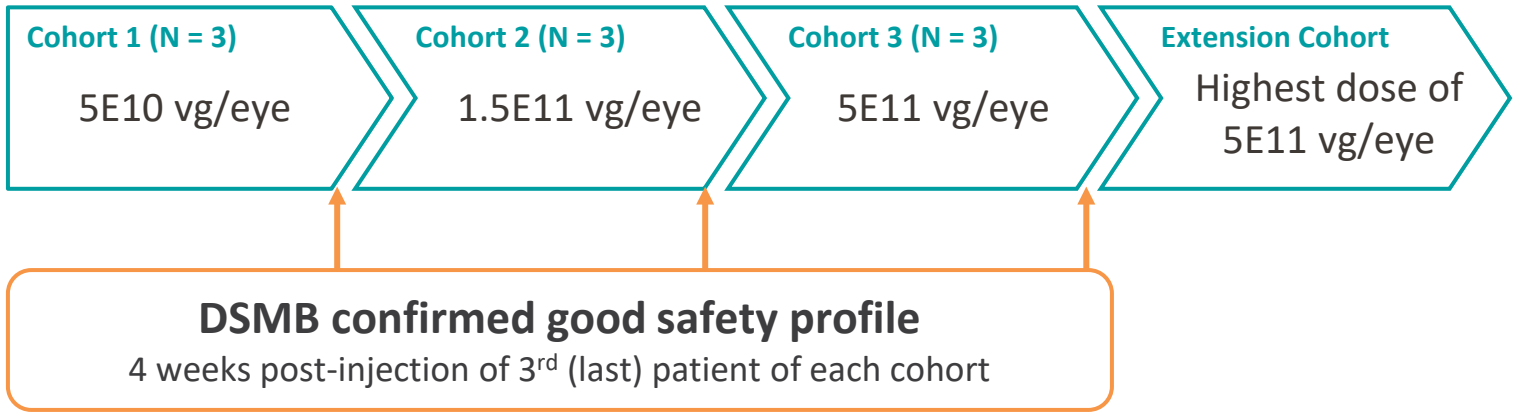
# **PIONEER** Phase I/II clinical trial: A First-in-Man study

**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

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.

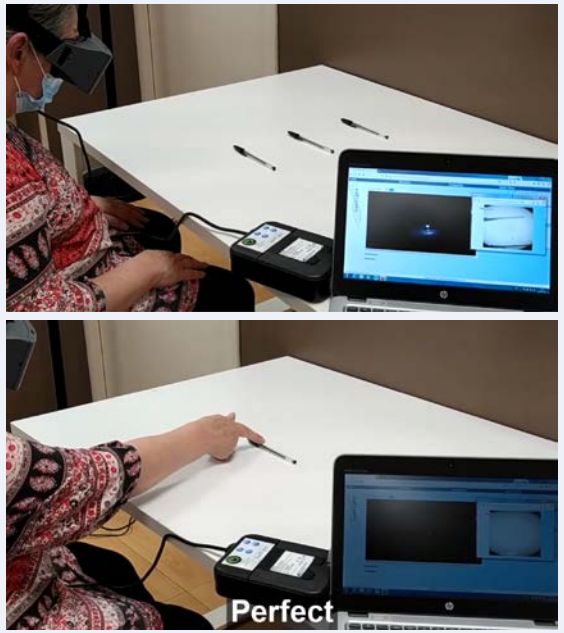
Training with the device started 4 months after injection.

## 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

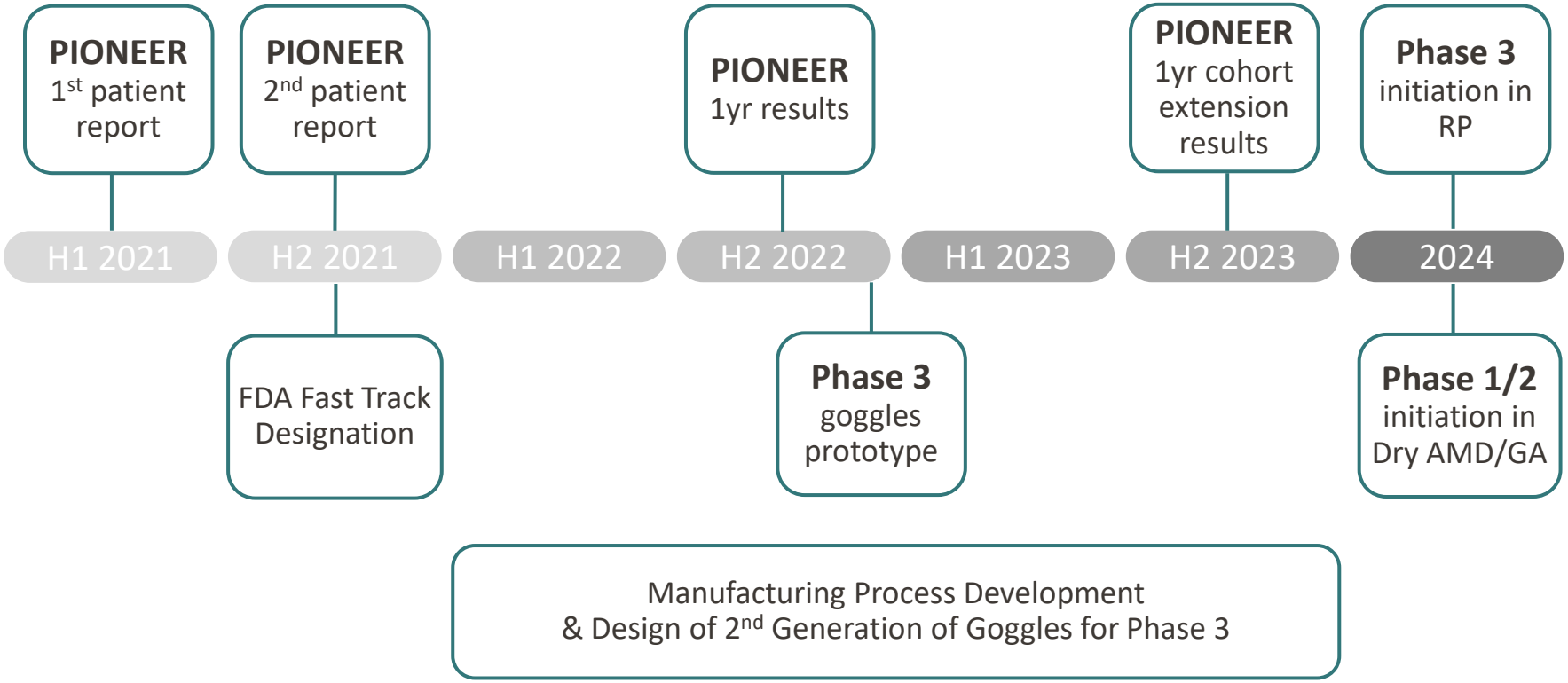



Video of the patient performing the tests available on www.gensight-biologics.com.



GenSight BIOLOGICS

# GS030 timeline



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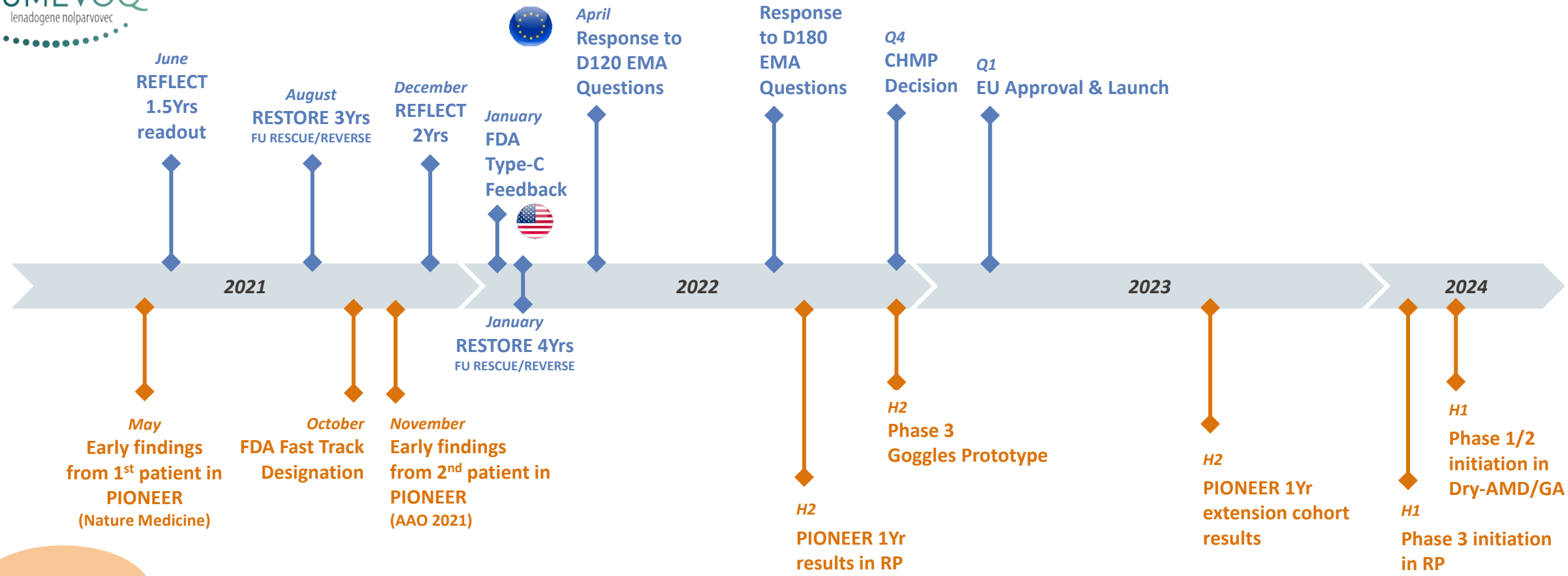
# Building high strategic value

# Rich upcoming news flow with numerous inflection points

LUMEVOQ
lenadogene nolparvovec




GS030



GenSight BIOLOGICS

# GenSight Biologics in numbers

## Key financial information

### Company Overview

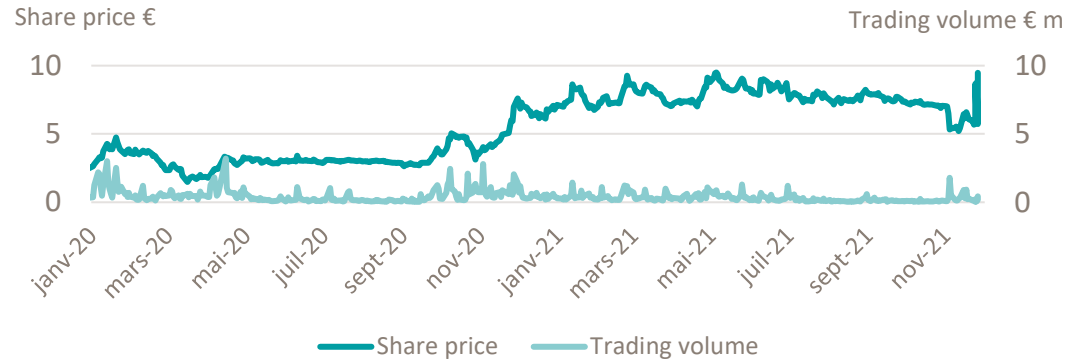
| | |
|---|---|
| Market Cap* : | € 208m |
| Cash Position : (December 31, 2021) | € 44.3m |
| Outstanding Shares: | 46.3m |
| Latest Amount Raised : (March 2021) | € 30m |
| Raised to date | € 197m |
| IPO Date | July 13, 2016 |

**Analyst Coverage**

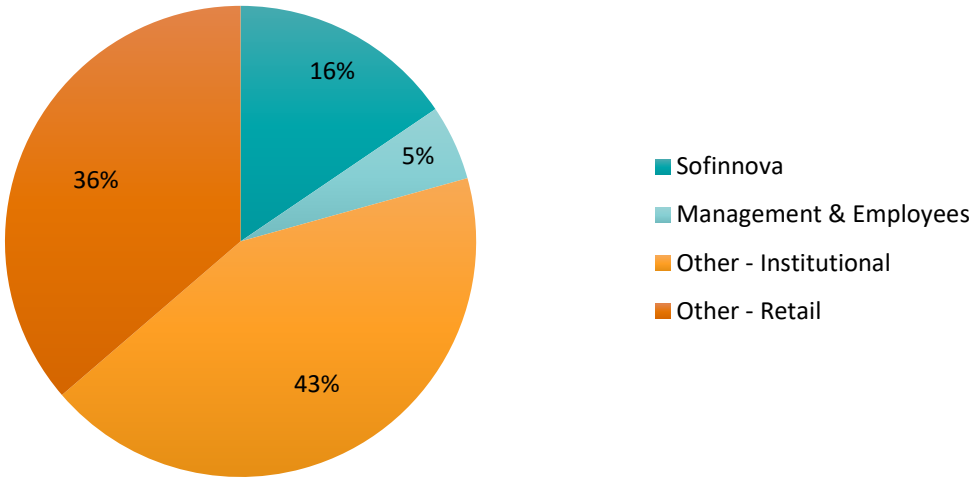
- Chardan: Geulah Livshits (US)
- Bryan Garnier: Dylan van Haaften (FR)
- ODDO BHF: Martial Descoutures (FR)
- Kempen : René Wouters (NL)

*As of January 18, 2022

### Share price evolution and trading volume



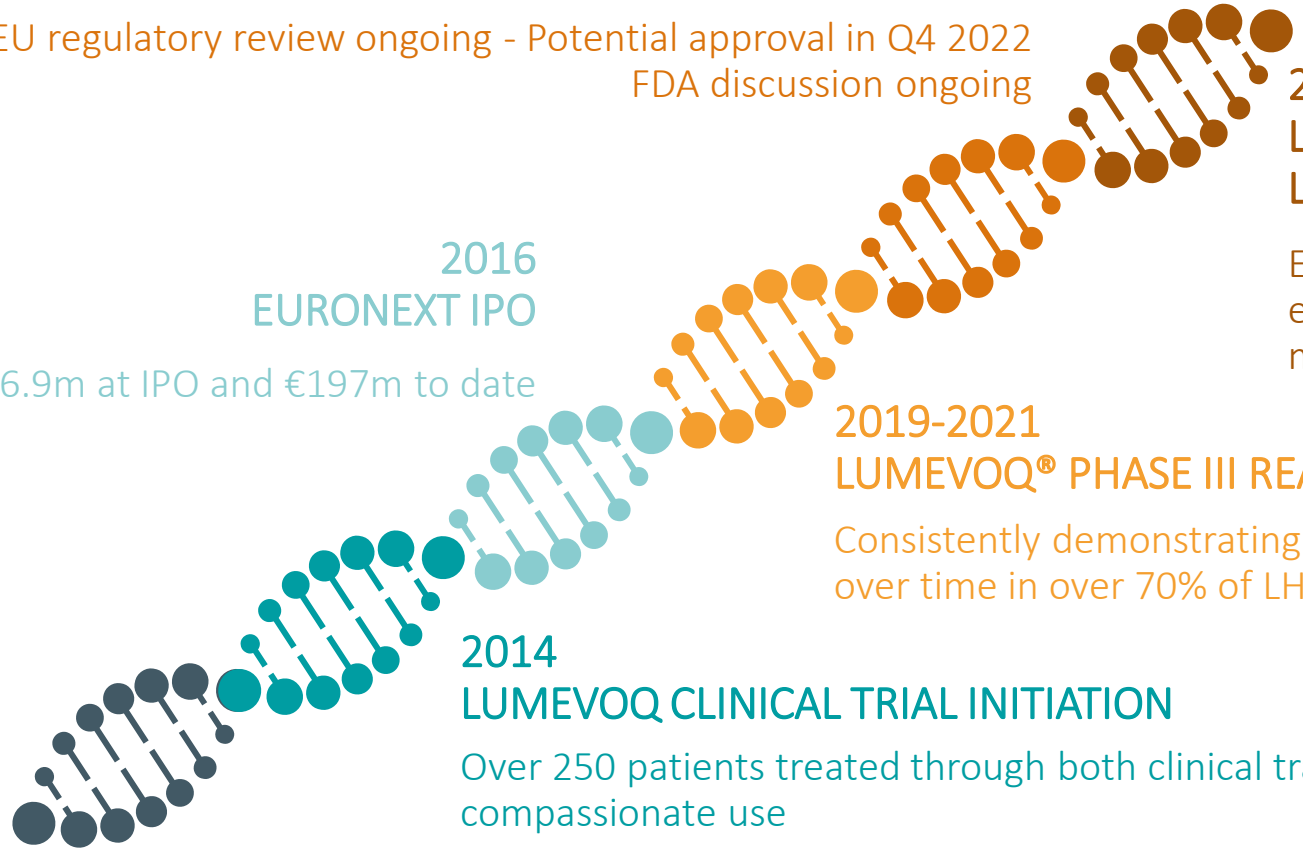

### Shareholder structure




As of July 2021

| Corporate calendar | Date |
|---|---|
| **2021 Financial Results** | **March 10, 2022** |

# Impressive Development Track Record from Concept to Clinic



**2012**
**CREATION**

Discovery and development of gene therapies for neurodegenerative retinal diseases and diseases of the central nervous system

**2014**
**LUMEVOQ CLINICAL TRIAL INITIATION**

Over 250 patients treated through both clinical trails and compassionate use

**2016**
**EURONEXT IPO**

Raised €46.9m at IPO and €197m to date

**2019-2021**
**LUMEVOQ® PHASE III READ-OUTS IN EUROPE AND THE US**

Consistently demonstrating good safety and visual improvement over time in over 70% of LHON ND4 patients

**2021-2022**
**REGULATORY REVIEW IN EU AND IN THE US**

EU regulatory review ongoing - Potential approval in Q4 2022
FDA discussion ongoing

**2023**
**LUMEVOQ® EXPECTED EUROPEAN LAUNCH**

European commercial team started executing on fast launch potential and market access strategy

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