GenSight BIOLOGICS

Corporate Presentation

May 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. Euronext Listed SIGHT / €95m Market Cap / Avg. 30-day Daily volume: 0.5% of O/S
2	**Seasoned management team / Solid investor base**	Management team with strong and highly relevant Biotech experience in R&D and commercialization Solid investor base of Healthcare specialist investors, including US based investors.
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	**H2 2023 LUMEVOQ® European launch**	Dedicated team in place to accelerate/optimize LUMEVOQ® access in key European territories Available in France through ATU at €700,000 for a bilateral injection EU regulatory review ongoing - on track for potential approval in Q3 2023 and subsequent launch 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) 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

Sissel Rodahl
SVP Commercial Head

NOVARTIS (AVEXIS) (2018-2021)
RAPTOR PHARMA (2014-2017)
SHIRE (2009-2014)
MERCK SERONO (1994-2009)

Scott Jeffers
Chief Technical Officer

REDPIN THERAPEUTICS (2021-2022)
UNIQURE (2019-2021)
SELECTA BIOSCIENCES (2018-2019)
BRAMMER BIO (2015-2018)

Ph.D. in virology

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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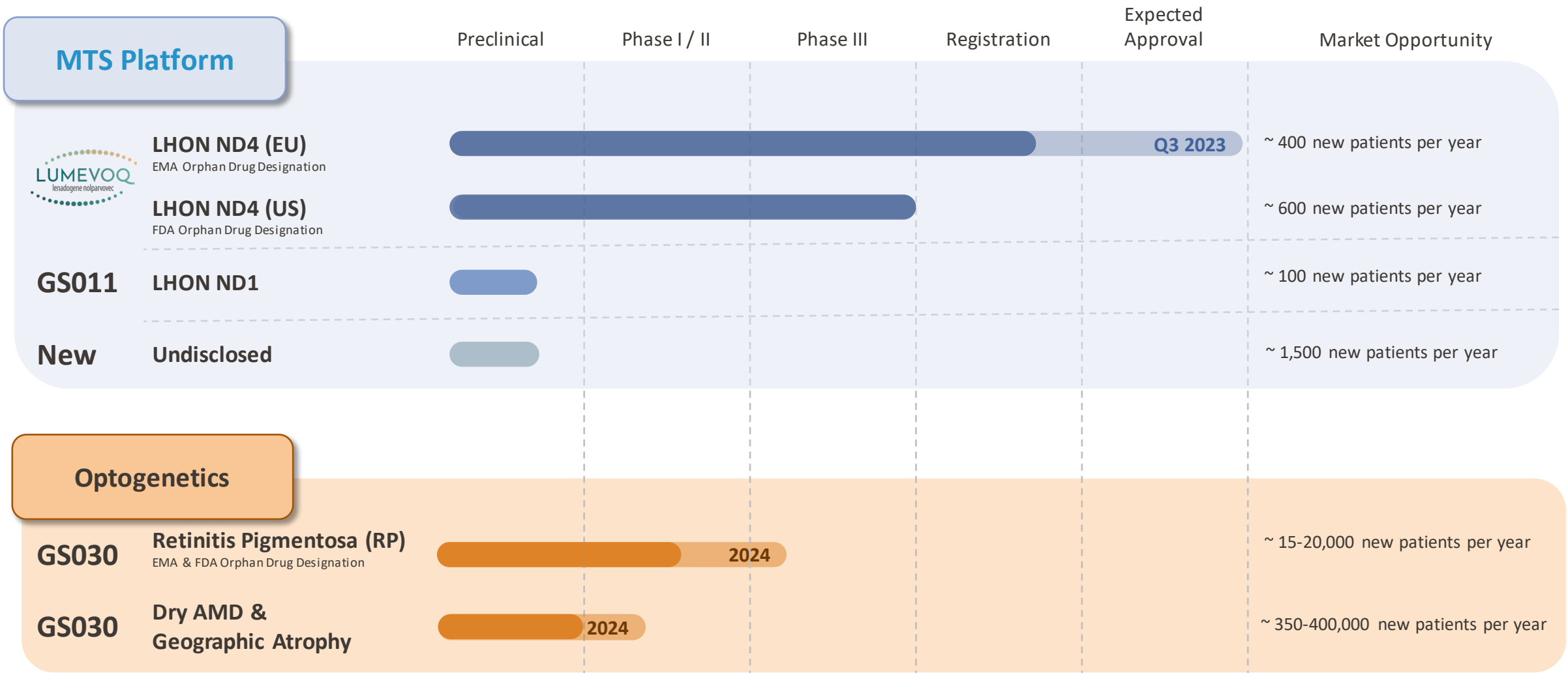
Pipeline: solid and advanced product portfolio in ophthalmic Gene Therapy



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LUMEVOQ® in LHON-*ND4*

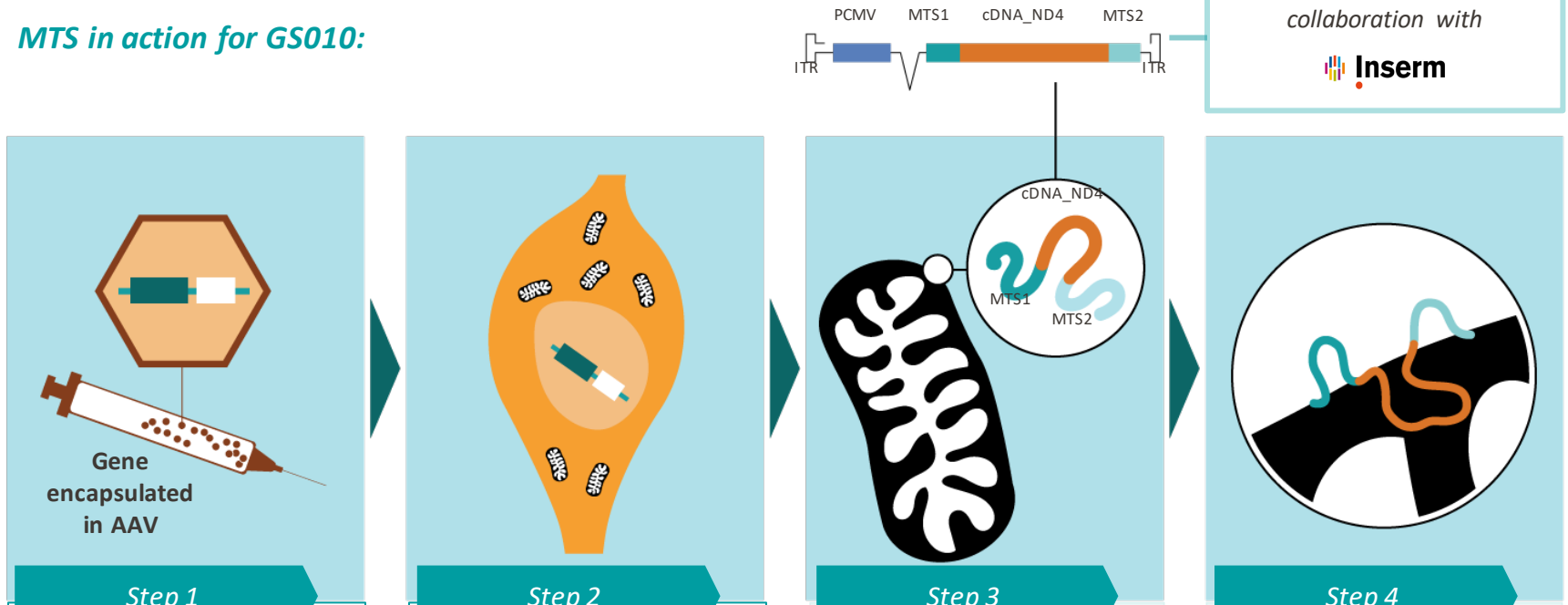
- 3 Phase III completed
- European regulatory submission ongoing in Leber Hereditary Optic Neuropathy
- Commercial preparation ongoing for H2 2023 European launch

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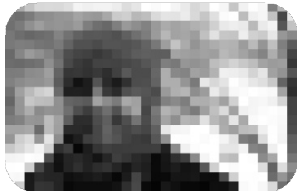
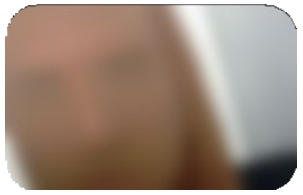
Leber Hereditary Optic Neuropathy (LHON-ND4) high unmet medical need

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

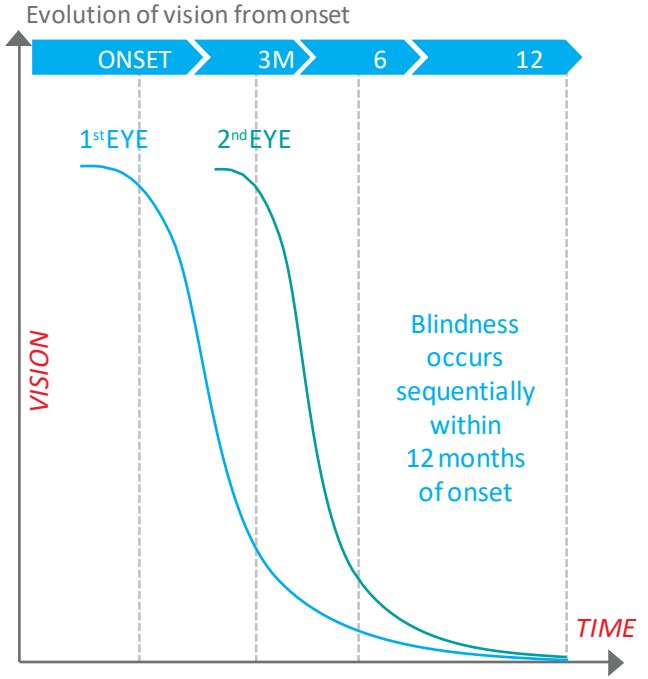


Image source: illustrated from Newman NJ et al., Am J Ophthalmo. 141(6), 1061-1067,2006

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

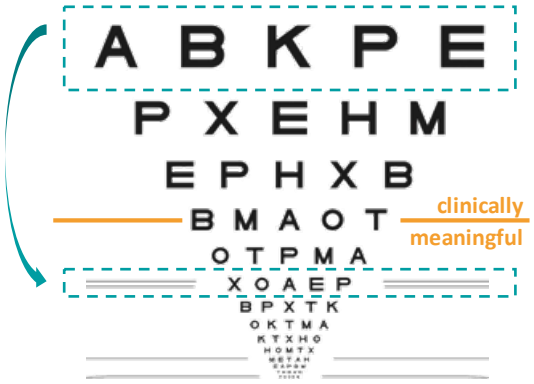
98 patients
with vision loss ≤ 1 year

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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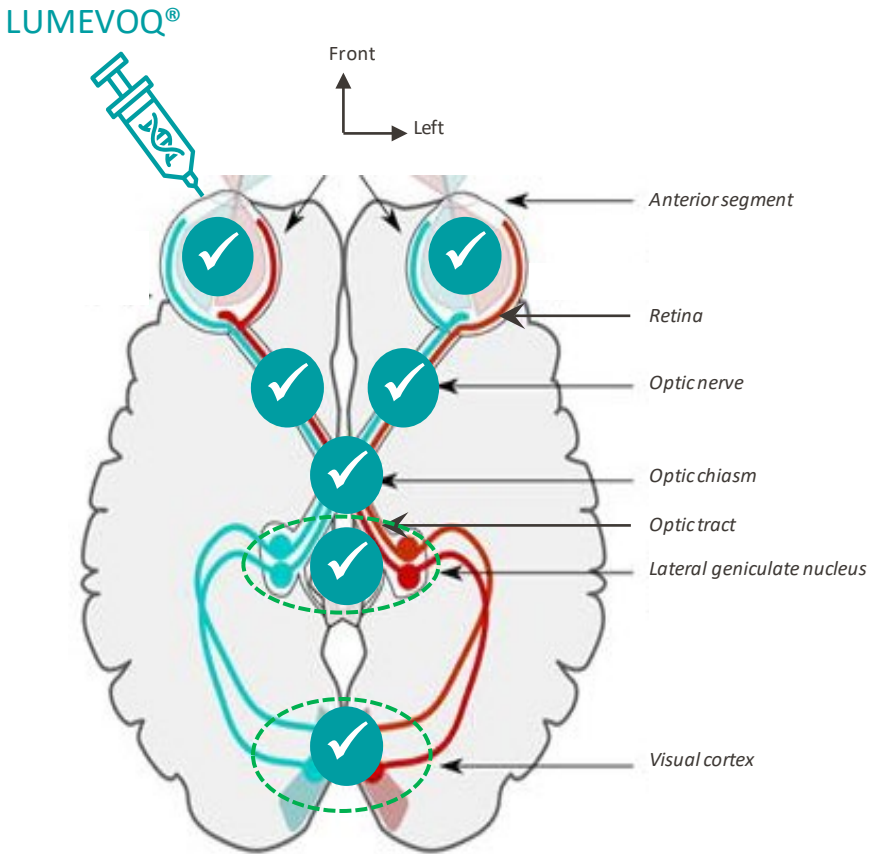
The Bilateral Effect Demonstrated – LUMEVOQ also detected in contralateral eyes



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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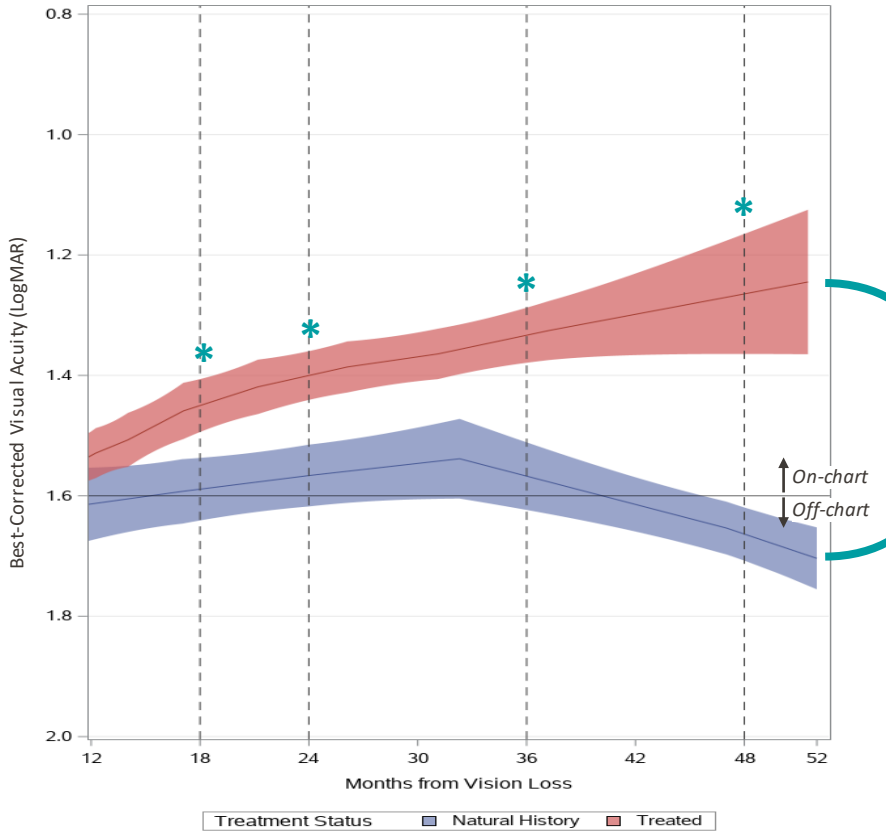
LUMEVOQ® modifies disease outcome compared to natural history

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.**

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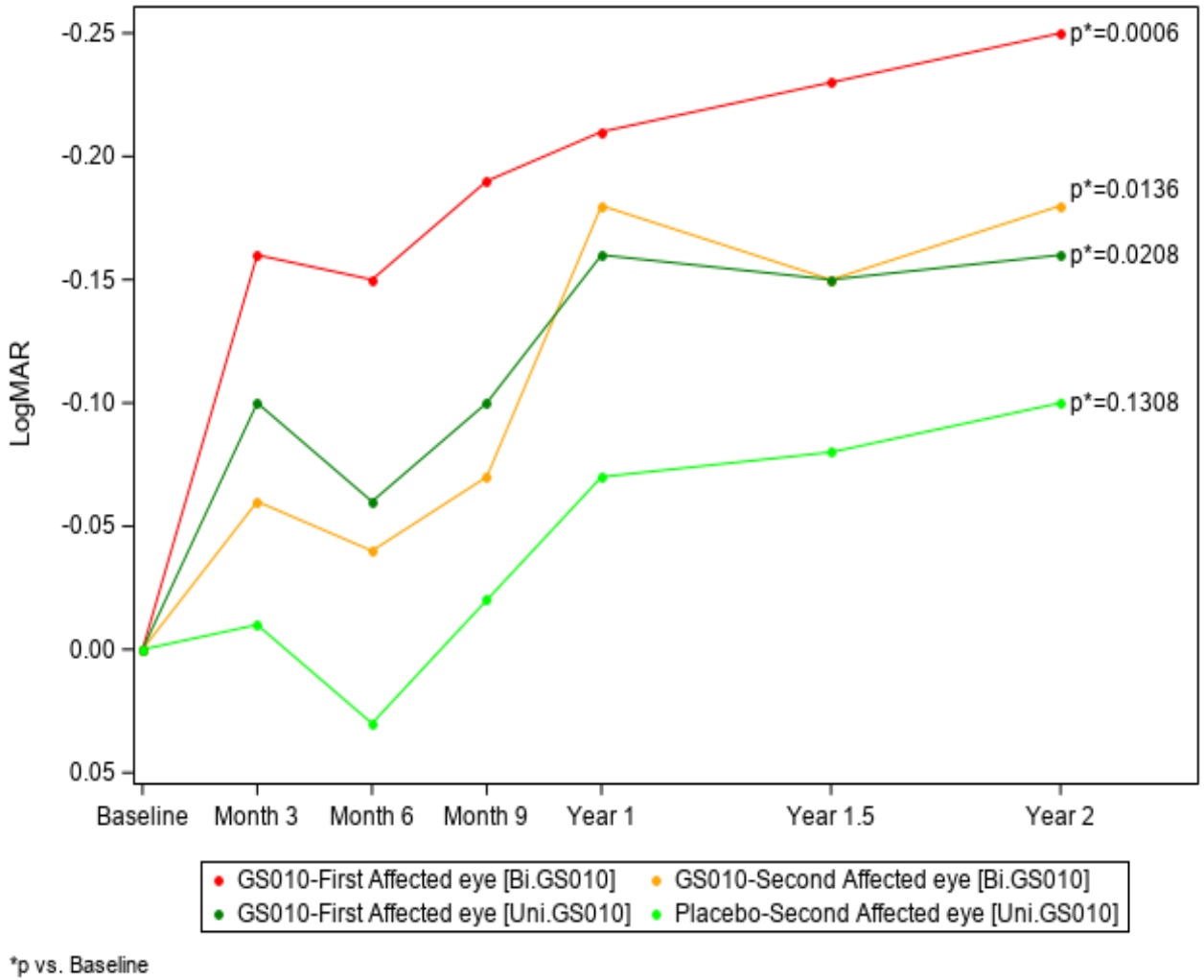
Better efficacy for bilaterally treated subjects demonstrated in REFLECT



*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
  - €5.3M revenues generated in 2021
  - 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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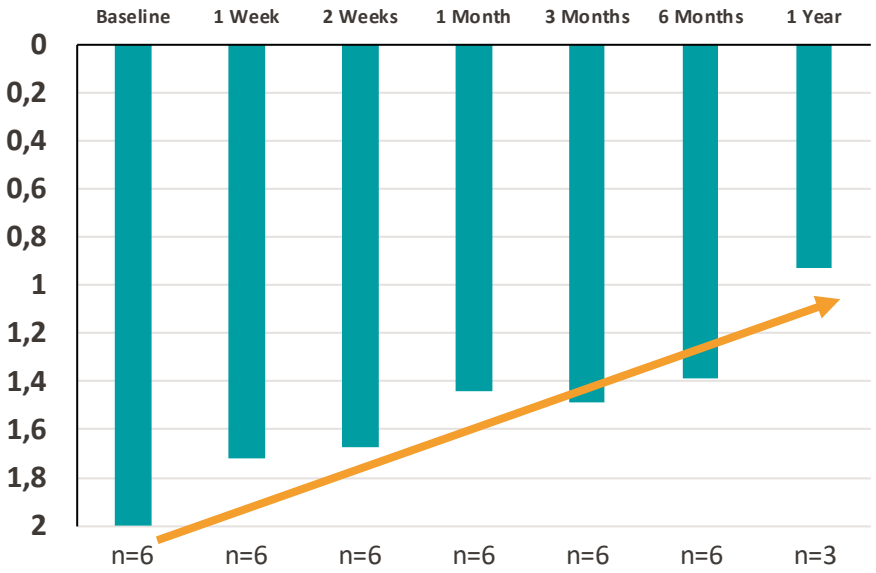
Real World Experience – US Compassionate Use Program

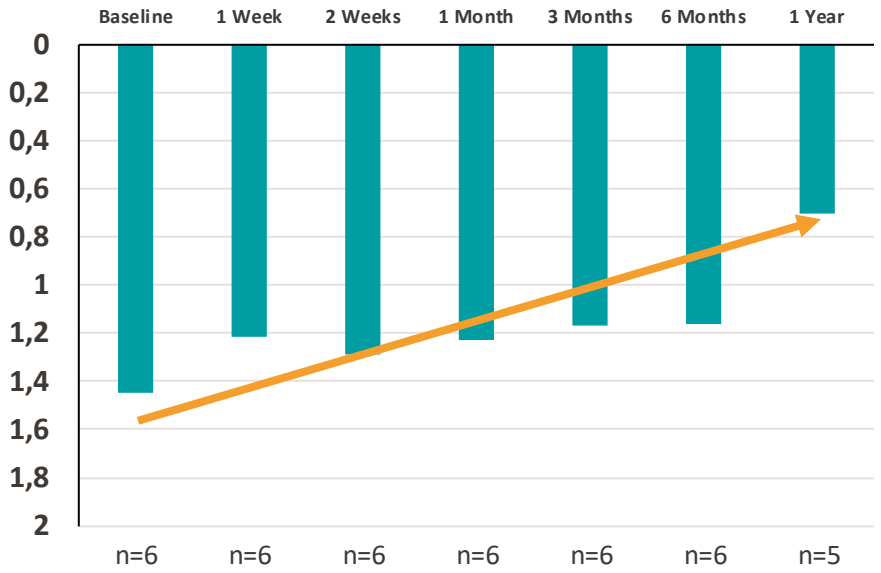
AVG **Worse** Eye BCVA Mean ETDRS Change (LogMAR)

11 lines of improvement



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

7.5 lines of improvement



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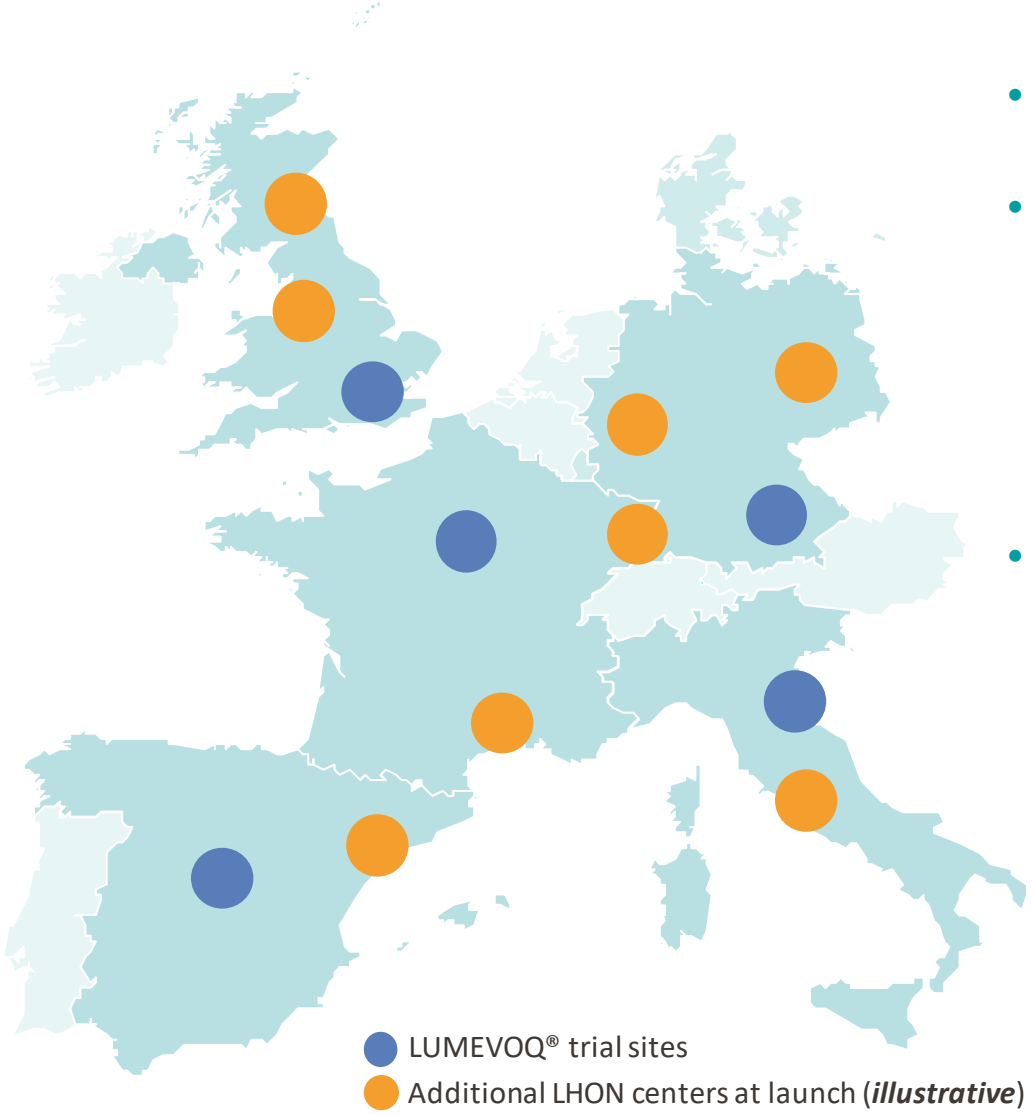
European Commercial Strategy – Leveraging LUMEVOQ® Clinical Centers to Build Network of LHON Centers of Excellence



- 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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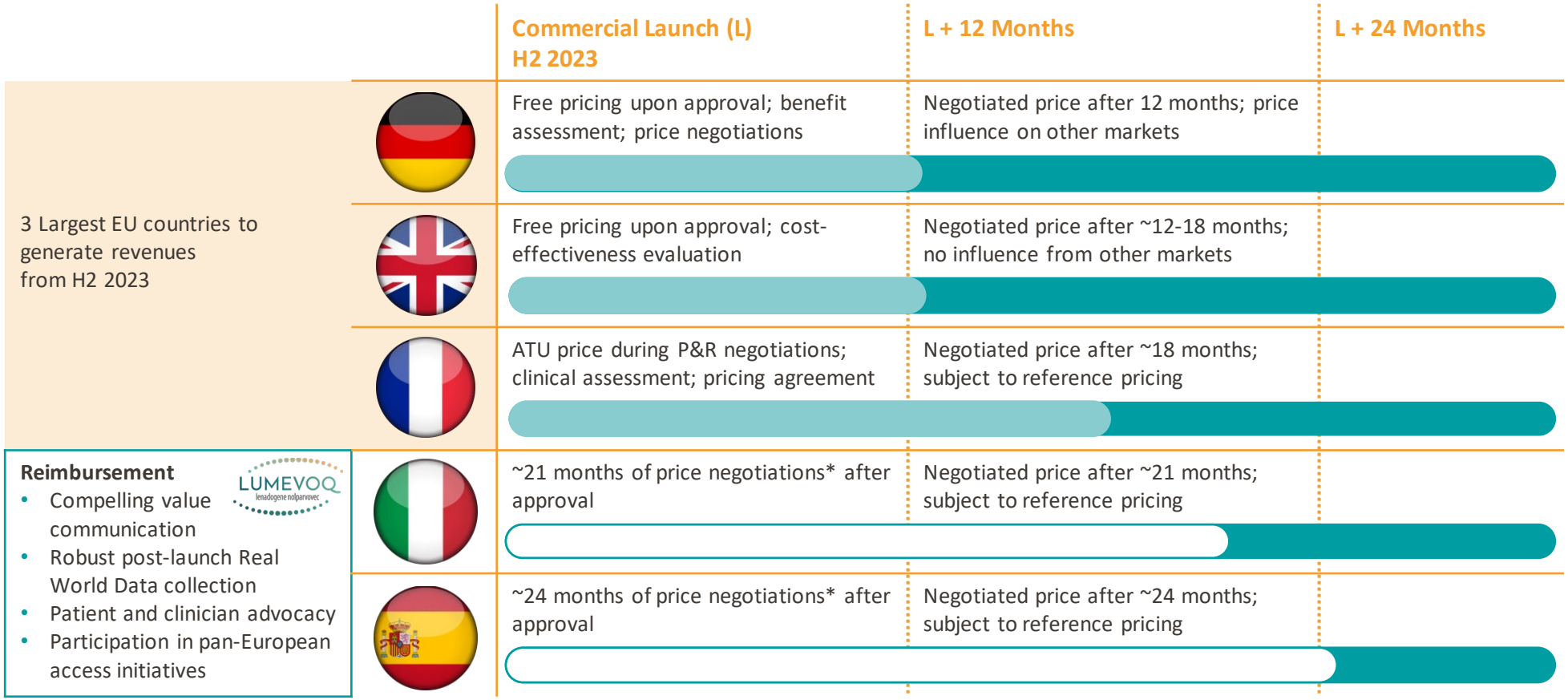
European Reimbursement Strategy – Short Term Revenues Generation Expected H2 2023



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

	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

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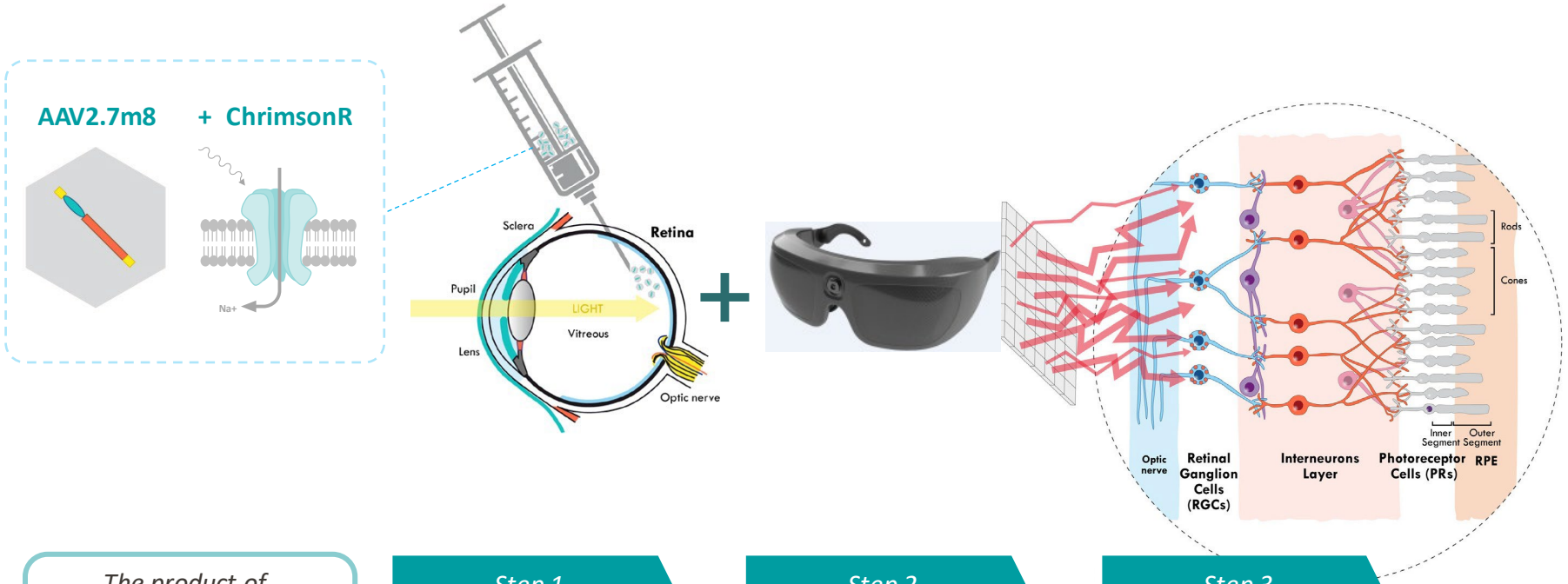
GS030: using Gene Therapy to rejuvenate production of light-sensitive protein and restore vision



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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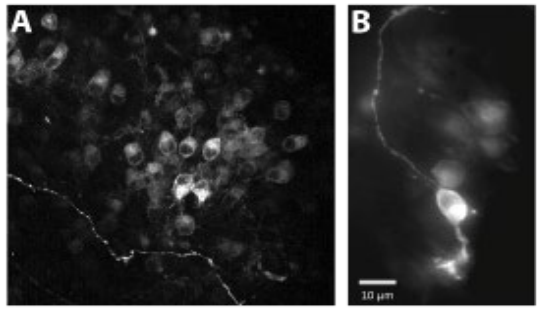
GS030 leads to functional vision restoration in monkey and rats

Localization of light-sensitive protein in NHP retina

Expression of ChrR-tdT in midget cells of monkey perifovea

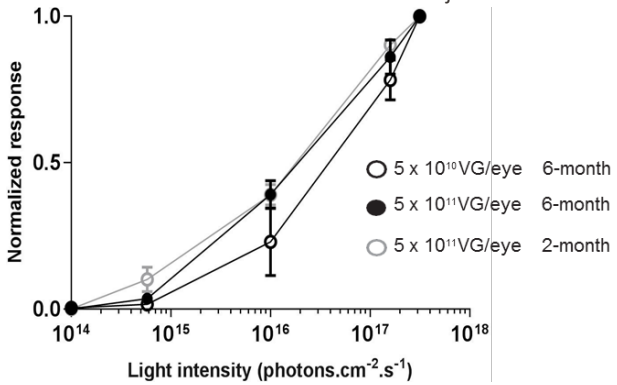
In vivo in NHP assessment 6 months after IVT injection



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

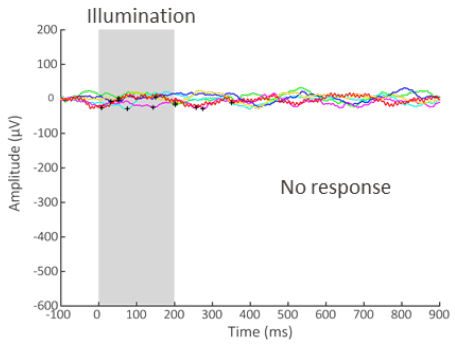
Optogenetic therapy: high spatiotemporal resolution and pattern discrimination compatible with vision restoration in non-human primates. Gauvain G. et al. **Communications Biology, Feb. 2021**
https://www.nature.com/articles/s42003-020-01594-w.

Restoration of a functional vision in P23H rats

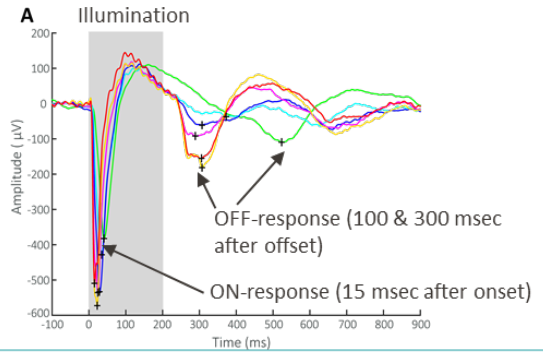
Light-induced visual evoked cortical responses

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

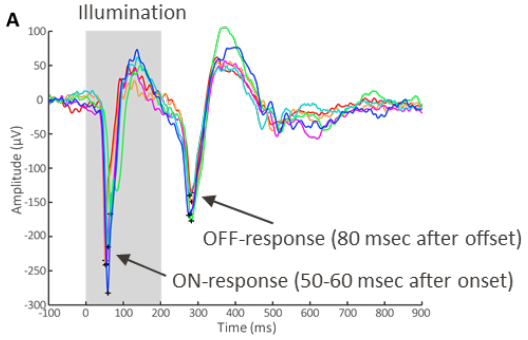
Untreated P23H rat



GS030-treated P23H rat

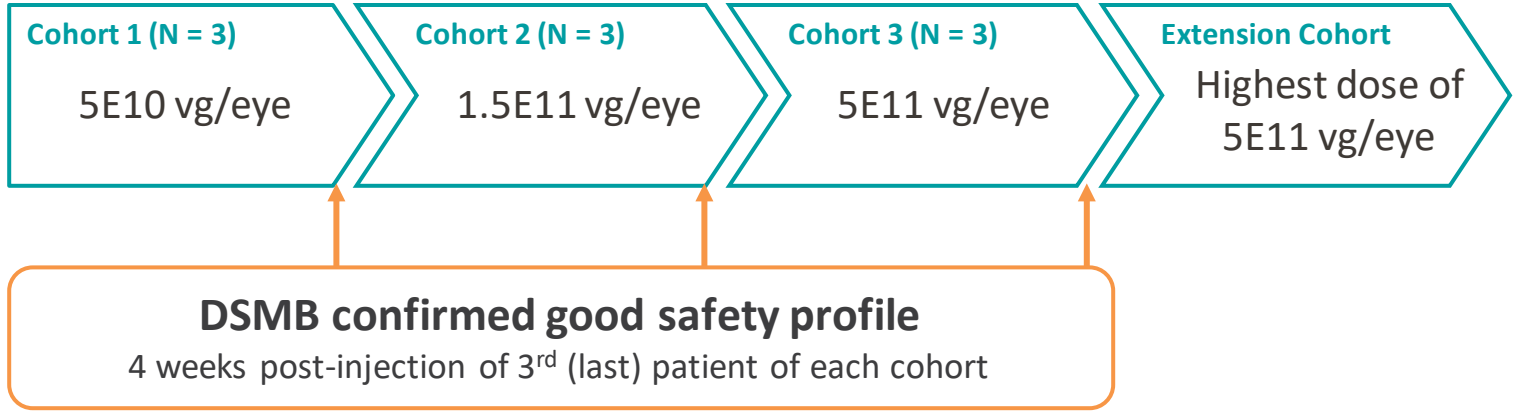


Normal Long-Evans rat



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.

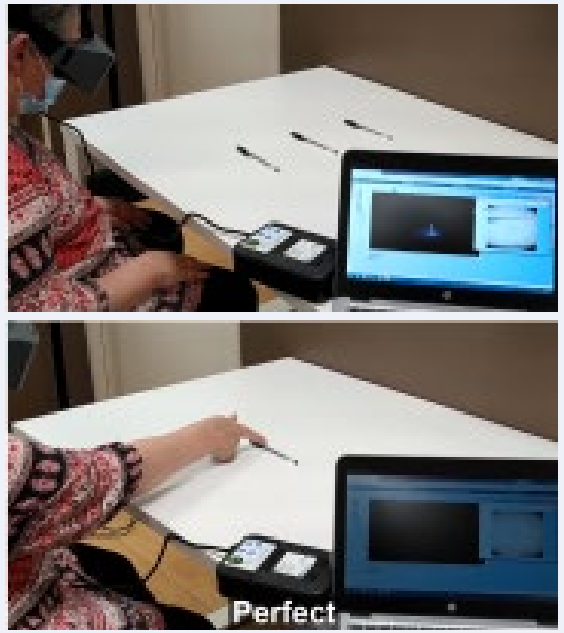
Training with the device started 4 months after injection.

Recent publication

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

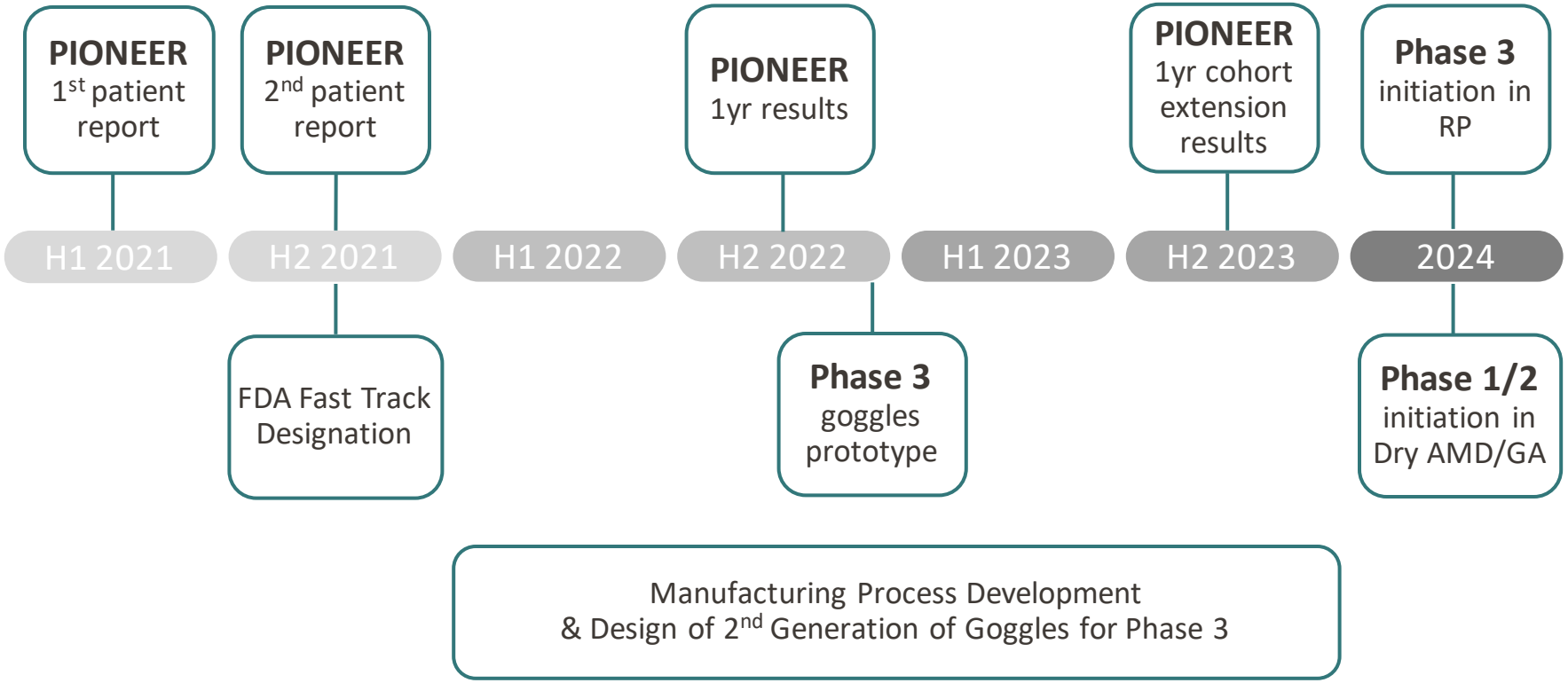
Sahel J.A. et al., **Nature Medicine, May 2021**
https://www.nature.com/articles/s41591-021-01351-4

Video of treated patient



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

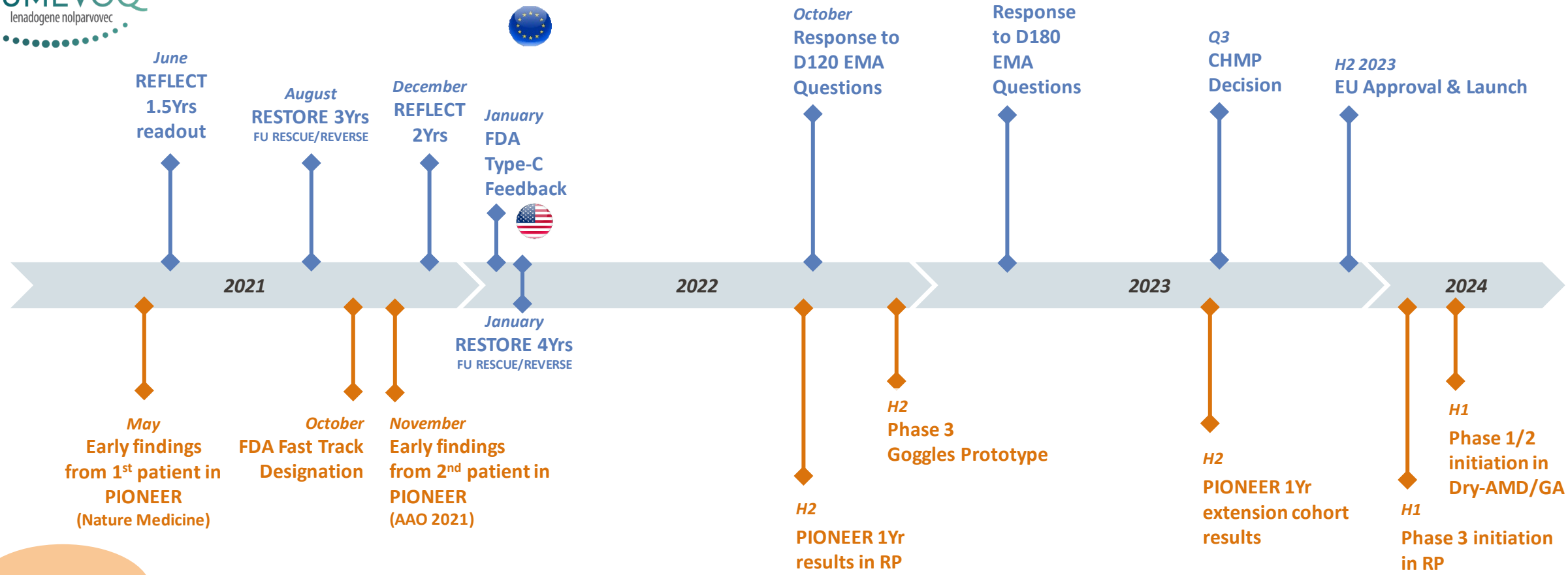
GS030 timeline



Building high strategic value

Rich upcoming news flow with numerous inflection points

LUMEVOQ
lenadogene nolparvovec



GS030

GenSight BIOLOGICS

GenSight Biologics in numbers

Key financial information

Company Overview

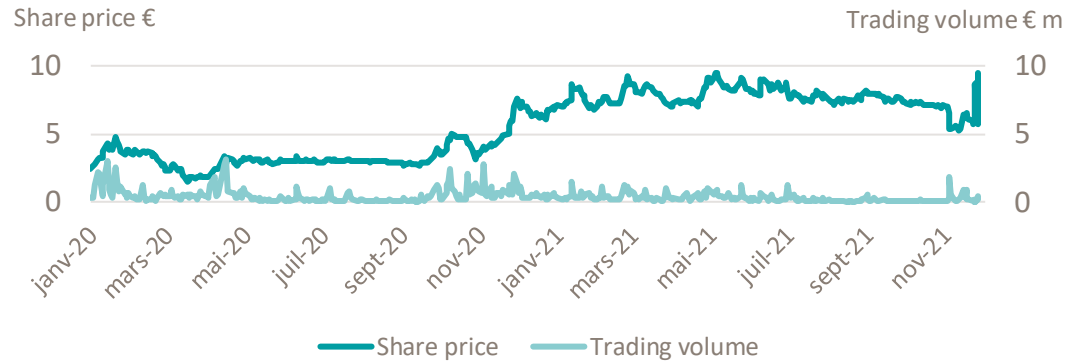
Market Cap* :	€ 95m
Cash Position : (March 31, 2022)	€ 36.0m
Outstanding Shares:	46.3m
Latest Amount Raised : (March 2021)	€ 30m
Raised to date	€ 197m
IPO Date	July 13, 2016

Analyst Coverage

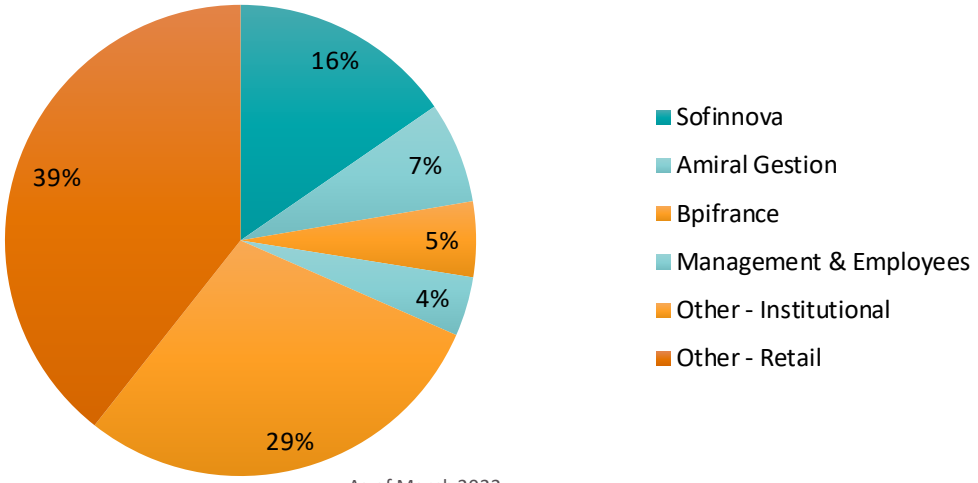
- Chardan: Geulah Livshits (US)
- Bryan Garnier: Dylan van Haaften (FR)
- ODDO BHF: Martial Descoutures (FR)
- Kempen : René Wouters (NL)

*As of April 25, 2022

Share price evolution and trading volume



Shareholder structure



As of March 2022

Corporate calendar

Corporate calendar	Date
Annual General Meeting	**May 25, 2022**
2022 First-Half Financial Update and Statements	July 28, 2022
2022 3Q Cash Position	October 27, 2022
2022 4Q Cash Position	January 26, 2023