GenSight BIOLOGICS

# Corporate Presentation

June 2020

A LEADING Gene Therapy BIOTECHNOLOGY COMPANY

GENSIGHT-BIOLOGICS.COM

# Disclaimer

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# Corporate Overview – Transitioning from R&D to Commercial organization

**GenSight at the forefront of Gene Therapy in ophthalmology**

- Publicly traded Biotech company
- Seasoned management team with strong BioPharma and Financial markets experience
- Technology platform leveraging disruptive gene therapies in ophthalmology
- Lead product targets mitochondrial diseases, applicable to broad number of diseases
- Second compound targets large indications such as Dry Age-related Macular Degeneration
- ATU granted in France in December 2019

**Differentiated Gene Therapy approach**

- Focus on ophthalmological diseases:
  - Through mitochondrial DNA correction (LUMEVOQ®)
  - By shaping retinal ganglion cells into photoreceptors (GS030)
- Using AAV2 as vector with proven safety and efficiency in human as well as well established manufacturing process

**LUMEVOQ® (GS010) - Preparing for regulatory submission in 2020 and commercial launch in 2021**

- Strong clinical benefit vs Natural History and/or nadir in 2 completed Phase III studies in rare ophthalmic disease with no/limited competition
- Commercial strategy and contract manufacturing capabilities close to completion

| | |
|---|---|
| Established in 2012 / IPO in 2016 | |
| EuroNext Paris: | SIGHT |
| Market Cap (June 11, 2020): | € 104m |
| Avg 30-day Daily volume: | 1.8% of O/S |
| Cash (Mar. 31, 2020): | € 12.8m |



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# Investment Case

**Targeting the LHON ND4 market with high unmet medical need and no widely approved treatment**

- Disease affects ~15,000/22,000 patients in the US/EU with 800/1,200 new cases each year
- Commercial strategy and manufacturing capabilities close to completion
- Bilateral injection priced at €700,000 / patient in French named patient Temporary Authorization for Use

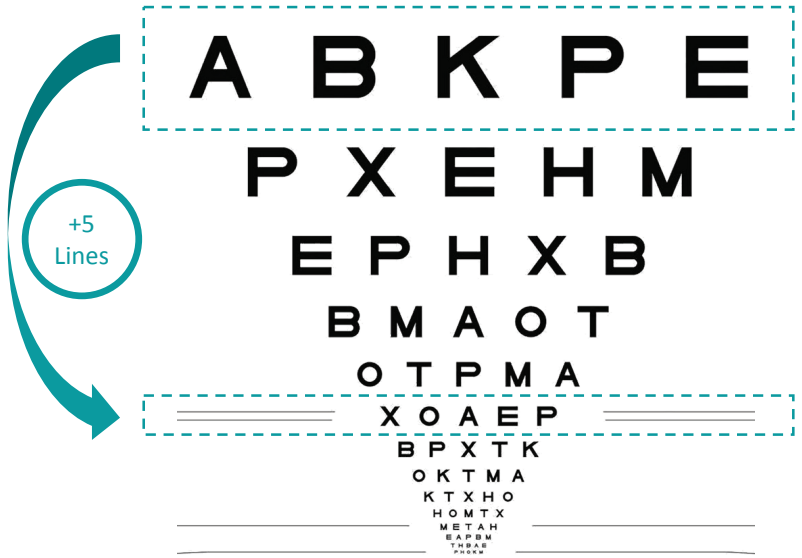
**Unparalleled clinical benefit demonstrated with LUVEMOQ™ in Leber Hereditary Optic Neuropathy (LHON) in two Phase III studies**

- +28/+26 ETDRS letters (i.e. over **5 lines** on visual scale) improvement vs nadir(1) in the two-Phase III studies
- Clinically meaningful improvement on all Quality of Life parameters at week 96

**Additional opportunities through technology platform**

- Large number of mitochondrial diseases making Mitochondrial Targeting Sequence (MTS used in GS010) a pipeline in itself
- GS030 in Retinitis pigmentosa and dry-AMD (Phase I/II)

Improvement vs nadir in REVERSE and RESCUE




(1) Nadir: worst visual acuity from baseline



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# Seasoned Executive Team

**Bernard Gilly**
*Chief Executive Officer*

**PIXIUM VISION** (Since 2011)
Chairman of the Board, Founder

**FOVEA PHARMA** (2005-2009)
Chairman & CEO – sold to Sanofi

**SOFINNOVA PARTNERS** (2000-2005)
Managing Partner

**TRANSGENE** (1992-2000)
Chairman & CEO

Ph.D. in biology and bio-economics

**Thomas Gidoin**
*Chief Financial Officer*

**DBV TECHNOLOGIES** (2012-2015)
VP of Finance

**IPSEN** (2008-2011)
UK Operations Controller (London)
Senior Financial Analyst (Paris)

**ERNST & YOUNG** (2007-2008)
Auditor

**Magali Taiel**
*Chief Medical Officer*

**ProQR THERAPEUTICS** (2016-2018)
VP of Clinical Development

**ELI LILLY** (2004-2016)
Medical Department Lead

**PFIZER** (2001-2004)
Medical Advisor

**SERVIER** (1999-2001)
R&D International Project Manager

MD, Board-certified ophthalmologist

**Catherine Cancian**
*Vice President Pharmaceutical Operations*

**GENETHON** (2015-2017)
Project Leader

**SANOFI PASTEUR** (1998-2014)
Industrial Operations and Regulatory Affairs

**Julio Benedicto**
*Vice President Marketing*

**IMS CONSULTING** (2011-2017)
Principal

**BOOZ & COMPANY** (2010-2011)
Principal

**MONITOR GROUP** (1994-2009)
Global Account Manager



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

| Technology | Product Candidate | Indication | Research | Preclinical | Phase I/II | Phase III | Registration | |
|---|---|---|---|---|---|---|---|---|
| MTS platform | LUMEVOQ® (FDA & EMA Orphan Drug Designation) | LHON ND4 (EU) | → | → | → | → | → | REVERSE: Phase III top-line data reported in Apr (48w) & Oct (72w) 2018 and in May 2019 (96w) |
| | | LHON ND4 (US) | → | → | → | → | | RESCUE: Phase III top-line data reported in Feb (48w), Apr (72w) and Sep (96w) 2019<br>REFLECT*: Phase III recruitment completed in July 2019, top-line data expected in Q1 2021 |
| | GS011 | LHON ND1 | → | | | | | Initiate preclinical studies following GS010 Phase III clinical data |
| | Undisclosed Mitochondrial Target | Undisclosed | → | | | | | |
| Optogenetics | GS030 (FDA & EMA Orphan Drug Designation) | RP | → | → | → | | | PIONEER: Start of 3rd cohort after DSMB#2 approval in PIONEER Phase I/II clinical trial.<br>Report interim data one year after last subject treated |
| | GS030 | Dry AMD & Geographic Atrophy | → | | | | | |

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

Lead candidate, LUMEVOQ®, is expected to file for **MAA in Europe this year**



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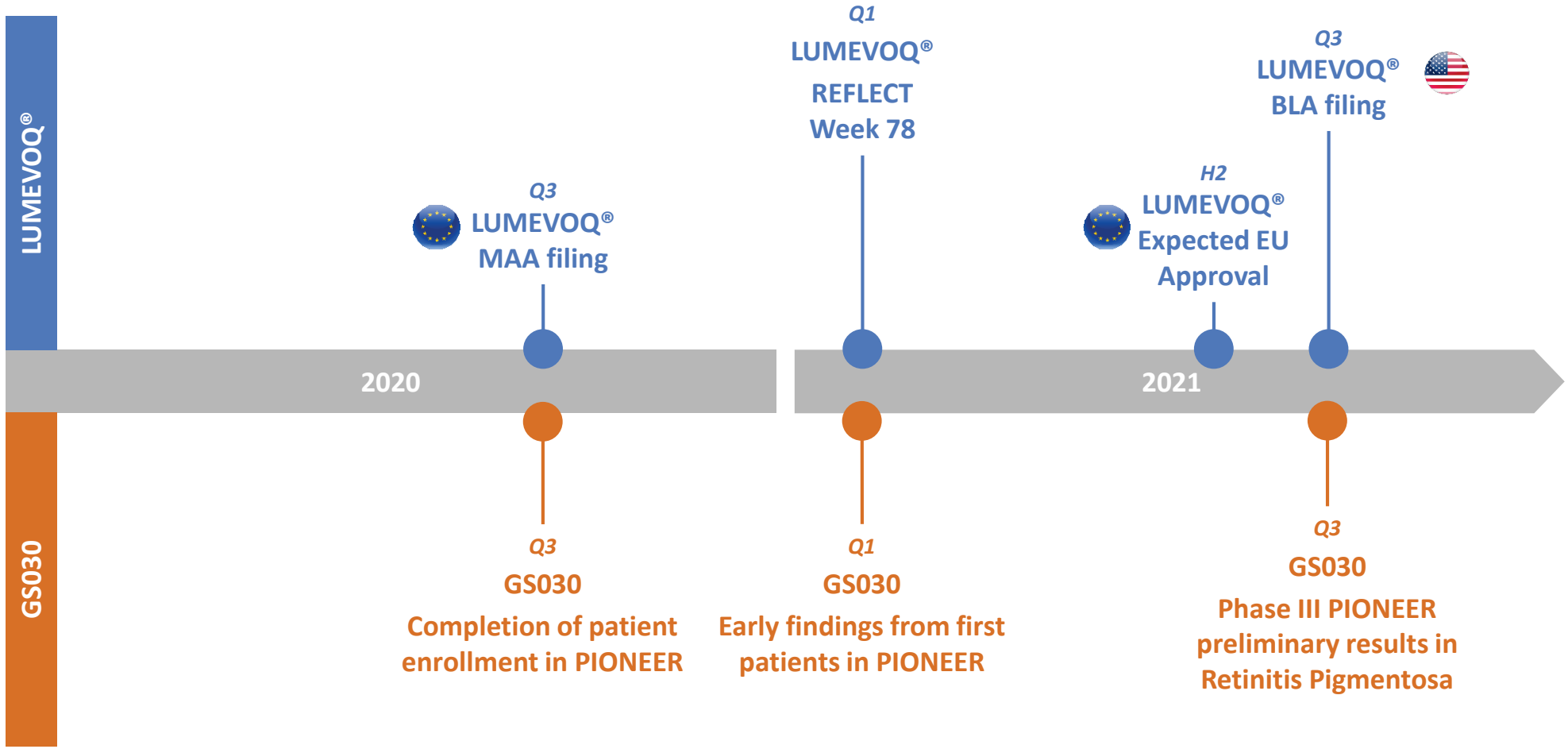
# Rich upcoming news flow with numerous inflexion points



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# LUMEVOQ® (GS010) in LHON-ND4

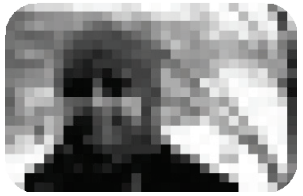
Last Phase III ongoing in Leber Hereditary Optic Neuropathy

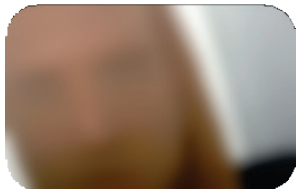
Commercial preparation ongoing for 2021 launch

# 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

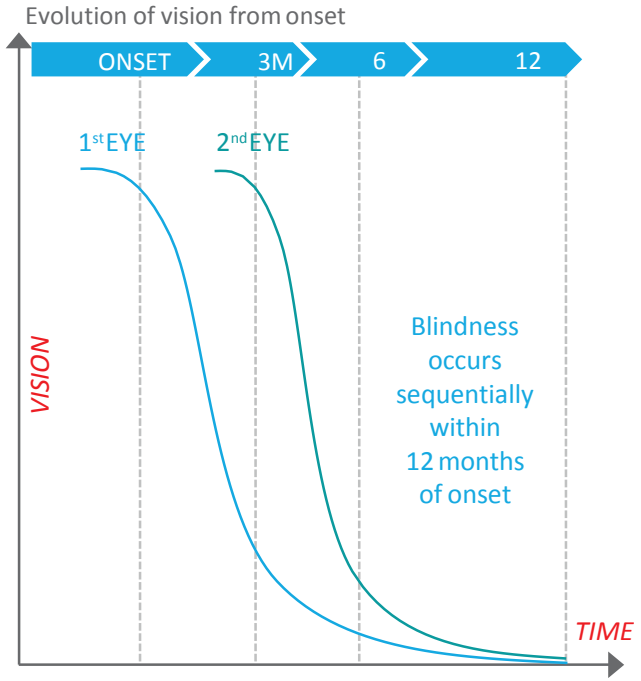



Image source: illustrated from Newamn NJ et al., Am J Ophthalmom. 141(6), 1061-1067,2006

## 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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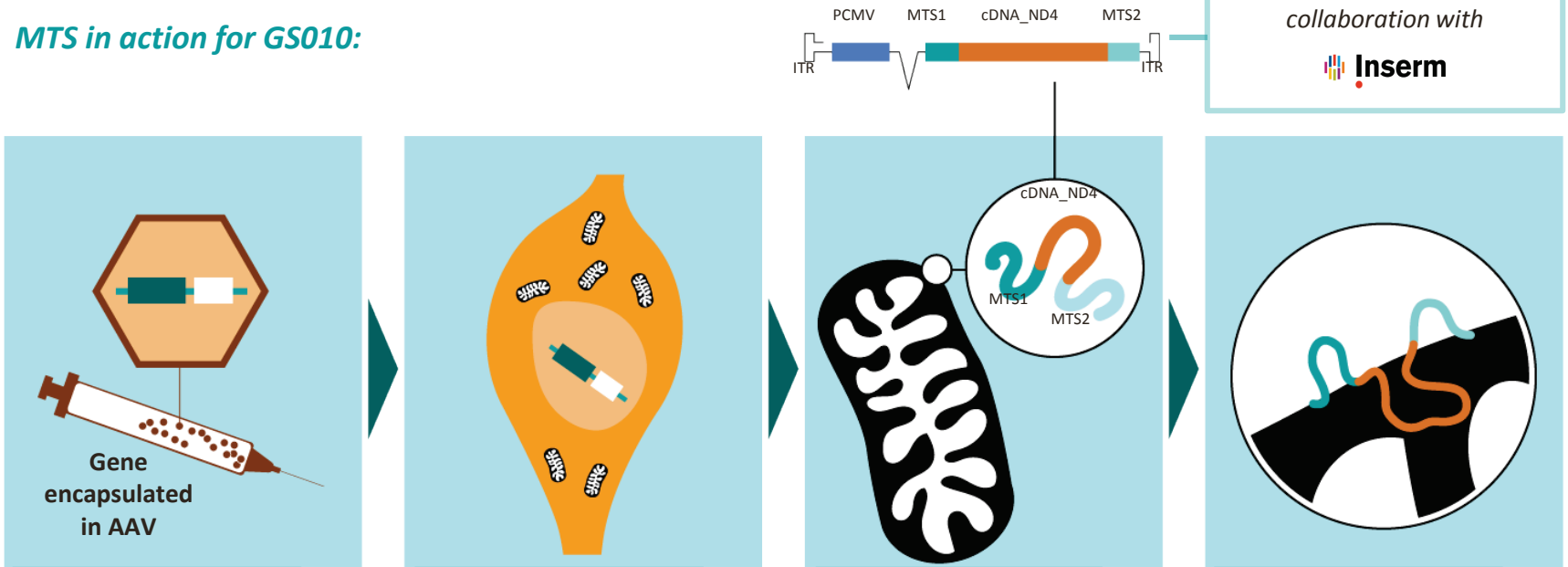
# LUMEVOQ® introduces Gene Therapy solution

**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**



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# RESCUE & REVERSE Phase III trials with unilateral injection demonstrated unprecedented improvement

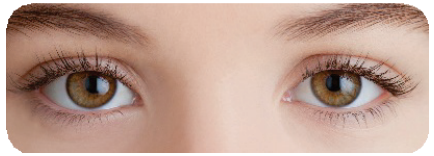
**Different patient inclusion criteria** | **Same design** | **Visual recovery at Week 96 and vs natural history**

## REVERSE

- Onset of disease
  **6 months to ≤ 1 year**
- 37 patients enrolled

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

***Group 1***

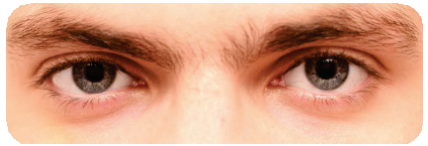


**GS010** in right eye | **SHAM** in left eye

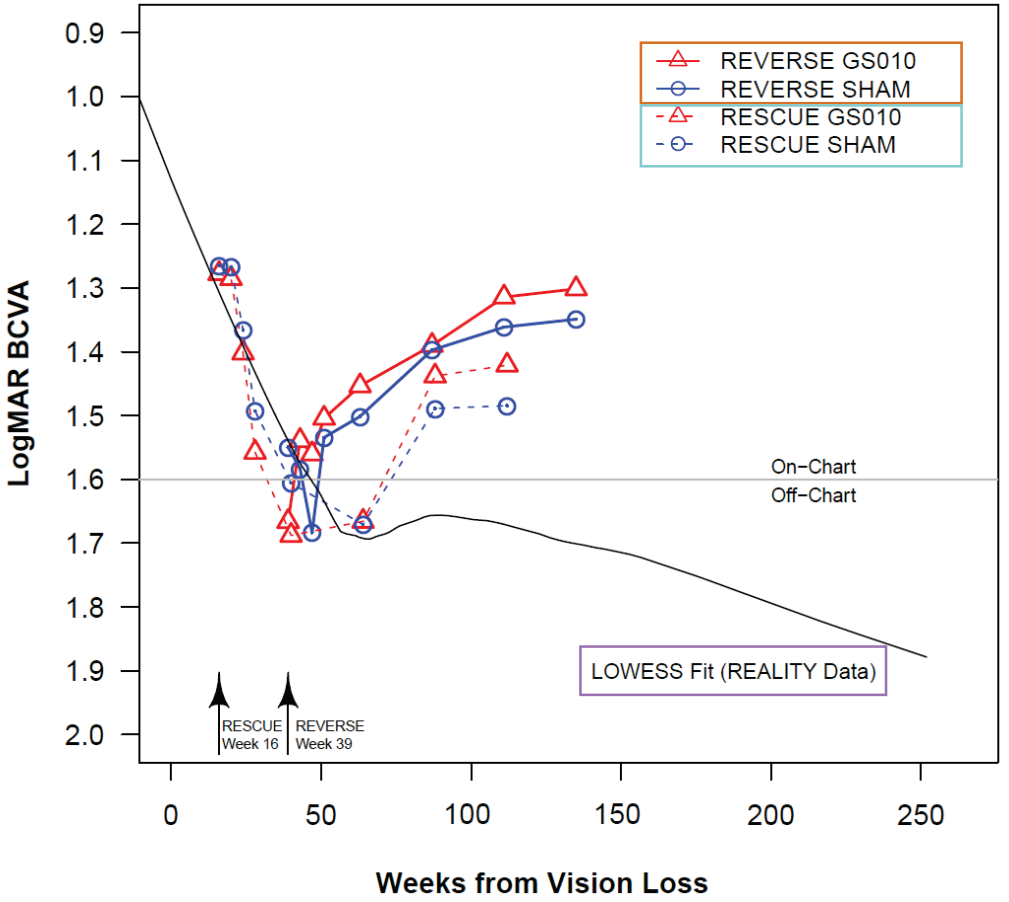
## RESCUE

- Onset of disease
  **≤ 6 months**
- 39 patients enrolled

***Group 2***



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




REVERSE 6-12 MONTHS
+28 ETDRS Letters vs nadir

RESCUE 0-6 MONTHS
+26 ETDRS Letters vs nadir

REALITY LHON REGISTRY
Retrospective Natural History



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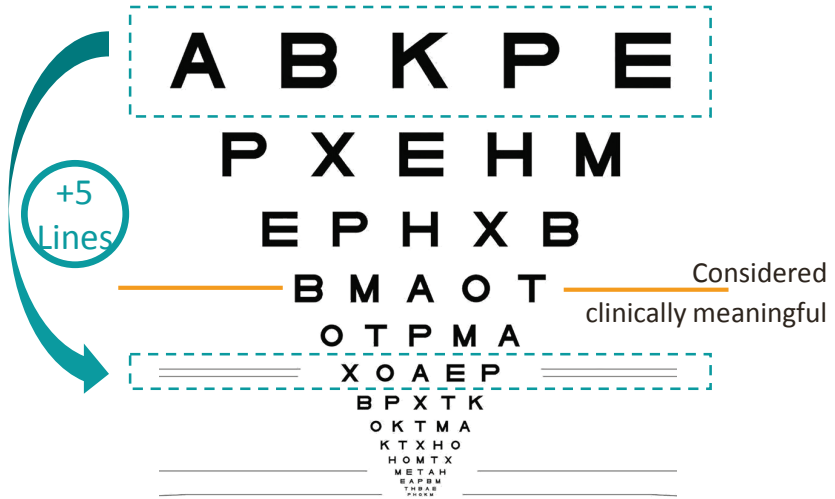
# Visual Acuity: Improvement of BCVA from NADIR

**Visual Acuity deteriorates to a low point before recovering significantly in both eyes**

| Change from NADIR in ETDRS letter equivalents | | |
|---|---|---|
| | Week 96 | |
| | n | Mean (SD) |
| **All-GS010 eyes** | 37 | +28.3 (22.5) |
| **All-sham eyes** | 37 | +24.5 (24.0) |

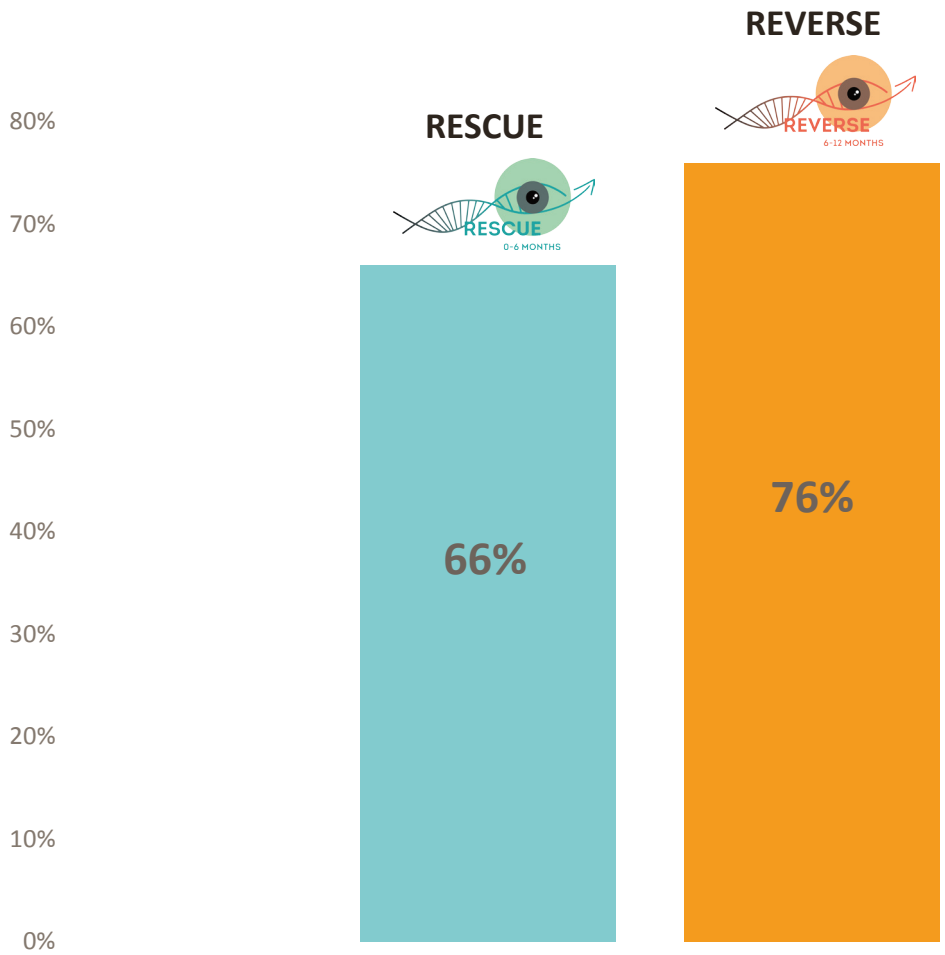
| Change from NADIR in ETDRS letter equivalents | | |
|---|---|---|
| | Week 96 | |
| | n | Mean (SD) |
| **All-GS010 eyes** | 34 | +26.3 (23.9) |
| **All-sham eyes** | 34 | +22.8 (24.2) |




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

**Unparalleled clinical benefit demonstrated with LUVEMOQ® (GS010) in LHON in two Phase III studies: +28/+26 ETDRS letters (i.e. over 5 lines on visual scale) improvement vs nadir**

# REVERSE and RESCUE  demonstrate that over 2/3 of patients benefit from treatment



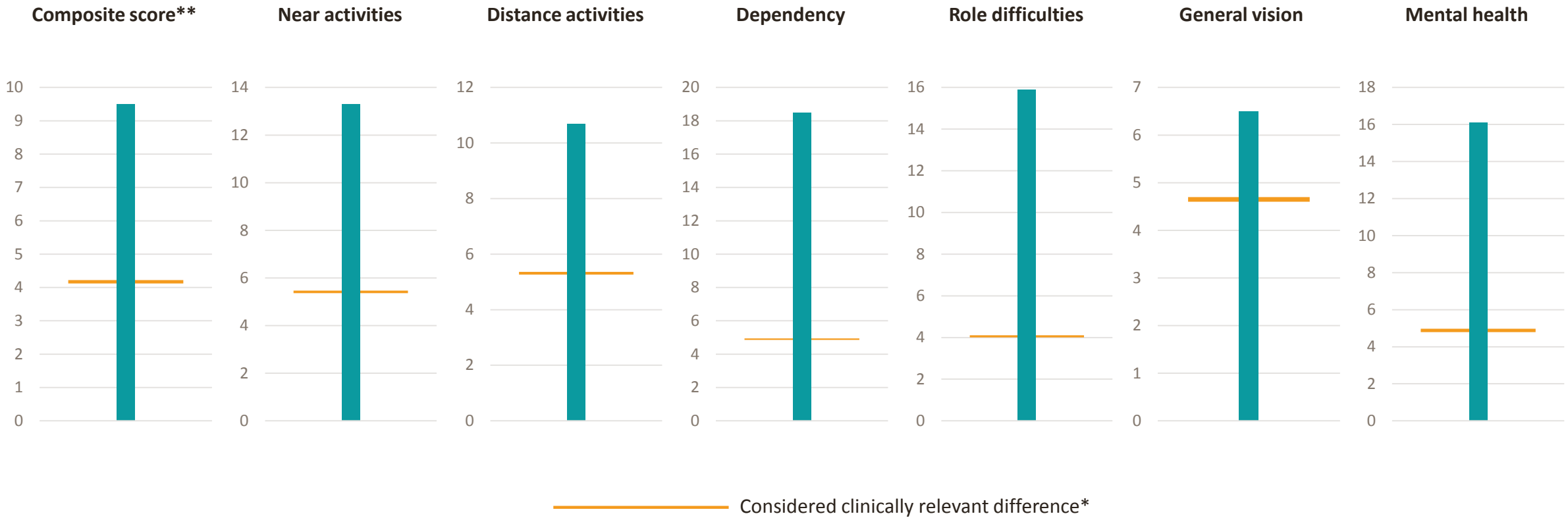

**76% of REVERSE subjects** achieved at least 15 letters improvement vs nadir in one or two eyes

**66% of RESCUE subjects** achieved at least 15 letters improvement vs nadir in one or two eyes

# LUMEVOQ® shows meaningful improvement on Quality of Life metrics

**NEI VFQ-25 Results from REVERSE study**

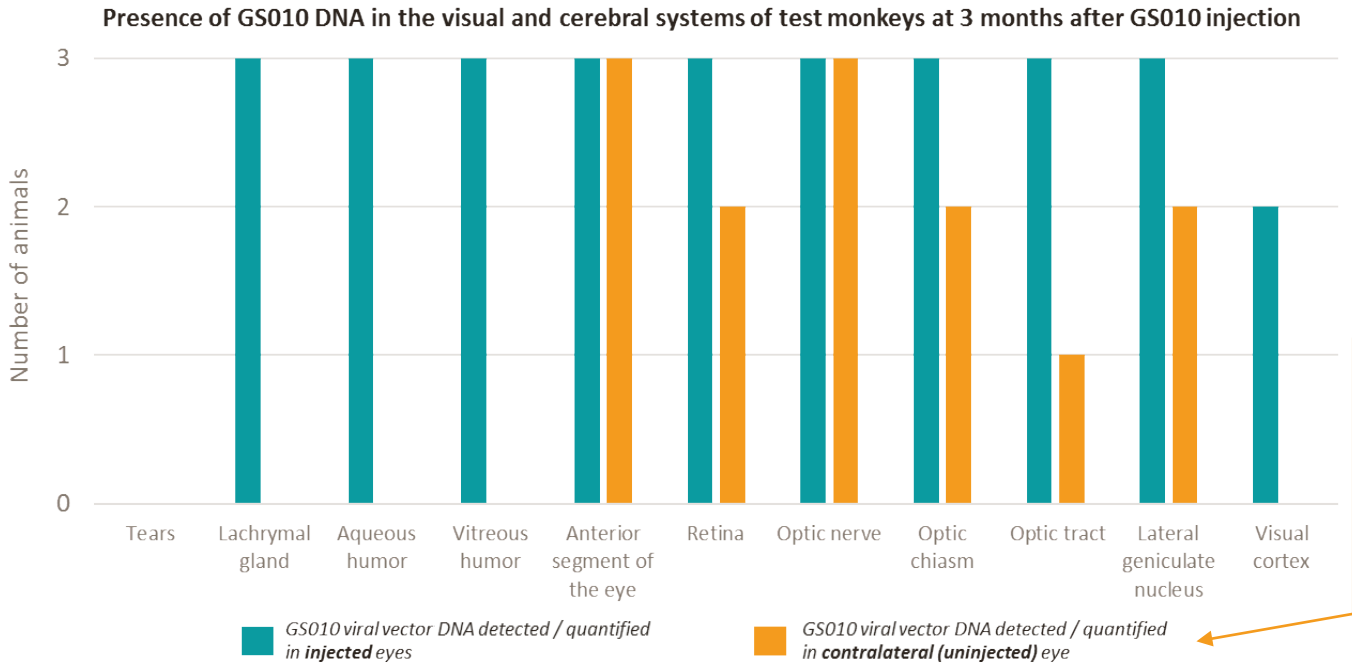
Mean change from baseline (absolute score) at week 96




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

# GS010 (LUMEVOQ®) viral vector DNA detection in uninjected eye of monkeys supports bilateral effect in REVERSE and RESCUE Phase III trials

## Viral vector DNA detected in uninjected eye → potential mechanism for bilateral effect in REVERSE and RESCUE




- Three test monkeys injected in one eye using dose equivalent of treatment in REVERSE and RESCUE trials
- Highly sensitive validated test for presence of GS010 DNA used on tissue samples from primates in study
- **Key finding:**
  - **GS010 viral vector DNA was detected/quantified in many tissue samples from contralateral (uninjected) eye**

*"The presence of viral vector DNA in the optic chiasm and optic nerve of the contralateral uninjected eye points towards a possible diffusion pathway."*

**Dr. Patrick Yu-Wai-Man**, Senior Lecturer & Honorary Consultant Ophthalmologist at the University of Cambridge, Moorfields Eye Hospital, and the UCL Institute of Ophthalmology, London, UK

*Notes*: One control monkey was injected in one eye with saline solution. Three test monkeys were injected with GS010 in one eye using dose allometrically equivalent to that used in REVERSE and RESCUE. Tissue samples were taken at 3 months after injection and tested using a protocol that specifically targeted the CMV promoter of the GS010 DNA. The sensitivity, specificity and accuracy of the test were validated in a dedicated study.

# LUMEVOQ® safe and well-tolerated through week 96 in REVERSE & RESCUE Phase III studies


- LUMEVOQ® was well-tolerated throughout both studies
- No serious adverse events in LUMEVOQ-treated eyes, and no discontinuation due to ocular events
- Most frequently seen ocular adverse events in the therapy group were mainly related to the injection procedure
- Occurrence of intraocular inflammation likely related to LUMEVOQ:
  - Accompanied by elevation of intraocular pressure in some patients “without any long-term sequelae”
  - Responsive to conventional treatment and without sequelae
- No systemic serious adverse events or discontinuations related to study treatment or study procedure

LUMEVOQ® was well-tolerated through **96 weeks** after injection



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

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

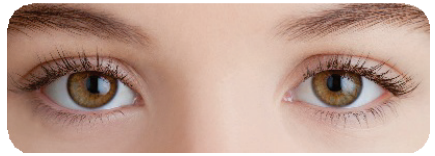
*Q1 2021*
LUMEVOQ®
REFLECT
Week 78
Read-out

## Patient inclusion criteria

- **98 patients**
  with vision loss ≤ 1 year
- **Initiation:** 4Q 2017
  (1st patient treated in March 2018)
- Recruitment completed in July 2019

## Design

***Group 1***



**GS010** in first affected eye

**GS010** in second affected eye

*First affected eye always treated with GS010*

*Second affected eye randomized between GS010 and placebo*

**GS010** in first affected eye

**Placebo** in second affected eye

***Group 2***

## Endpoints at Week 78

### Primary

- Difference in change of vision compared to baseline between GS010 Treatment vs. Placebo in second affected/not yet affected eyes
  (LogMAR visual acuity used for statistical analysis)

### Secondary

- Best-Corrected Visual Acuity at 2 years
- Spectral domain OCT biomarkers
- Humphrey visual field analysis
- Pelli-Robson Low Vision Contrast Sensitivity
- Quality of life assessments

*Source: Company*

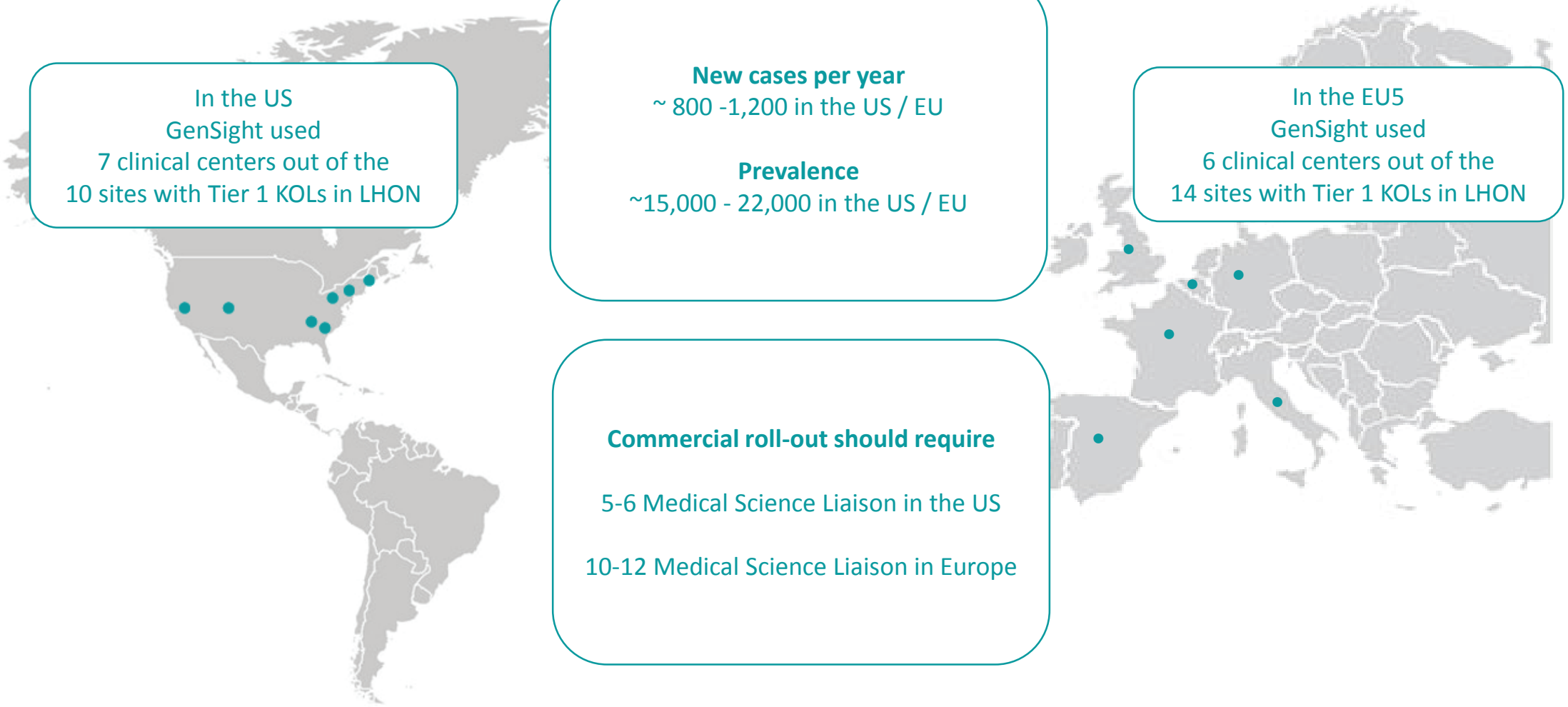
# LHON is treated in just a few hyper-specialized centers, requiring limited commercial infrastructure and allowing proximity to the patients

In the US
GenSight used
7 clinical centers out of the
10 sites with Tier 1 KOLs in LHON

**New cases per year**
~ 800 -1,200 in the US / EU

**Prevalence**
~15,000 - 22,000 in the US / EU

In the EU5
GenSight used
6 clinical centers out of the
14 sites with Tier 1 KOLs in LHON



**Commercial roll-out should require**

5-6 Medical Science Liaison in the US

10-12 Medical Science Liaison in Europe



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# Manufacturing strategy validated

Top quality toll manufacturer selected allowing:

- US based manufacturing
- Leverage manufacturing expertise and ability to scale up
- Lower production risk
- Reduce regulatory risk
- Increase flexibility
- No capex
- Optimize gross margin


Limited number of copies required per injection means:

- 5-6 manufacturing batches per year sufficient to treat EU/US expected demand
- 36-month shelf life provides flexibility to adjust to demand fluctuations

Planning for manufacturing redundancy to further reduce manufacturing risk



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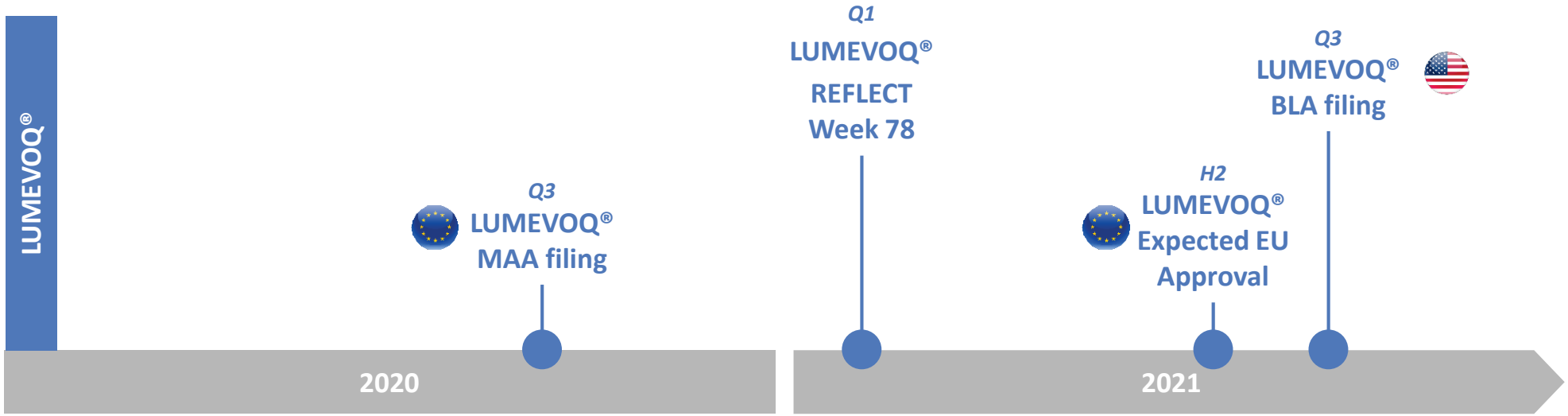
# LUMEVOQ® Key milestones



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# **Compassionate Use** for LUMEVOQ® (GS010)

**Seeking use of an investigational medication under circumstances a patient may not be able to participate in a clinical trial and before MA/BLA approval by regulatory authorities**

- 3 individual patients Expanded Access INDs have been approved by the FDA for GS010 (lenadogene nolparvovec)
- These 3 subjects have been treated (bilateral GS010 IVT) under the investigator-sponsored programs in 2019

- *"ATU Nominative"* - named patient Temporary Authorization for Use - for LUMEVOQ® granted by ANSM to CHNO of the *Quinze-Vingts* in Paris
  - 2 patients bilaterally treated in December 2019 and January 2020
- Bilateral injections priced at €700,000 per patient, expected to generate revenues in 2020
  - Reimbursement warranted by the national Social Security up to € 30M/year
- Next step : seeking for a Cohort ATU *"ATU de Cohorte"*

# GS030

Second product candidate targeting photoreceptor degenerative diseases:

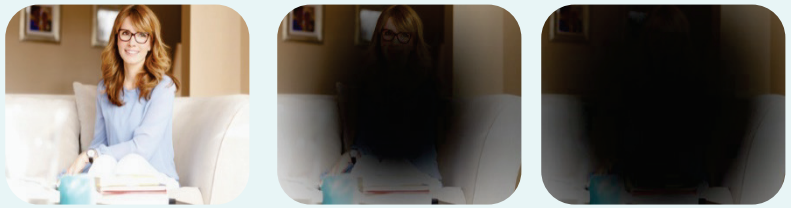
- Retinitis Pigmentosa (RP)
- Age-Related Macular Degeneration (AMD)

# Treating the 2 main degenerative diseases of photoreceptors that lead to blindness

## Retinitis Pigmentosa

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

## Geographic Atrophy (GA) in AMD (Age-Related Macular Degeneration)



- Early (dry-form) AMD evolves with age into late AMD, one of whose forms is GA
- Dry-AMD affects 350-400,000 new patients a year
- Prevalence of GA increases with age, from 3.5% among 75-year-olds to 22% among those over 90
- Late AMD patients with GA account for 10-20% of blind patients in their age group



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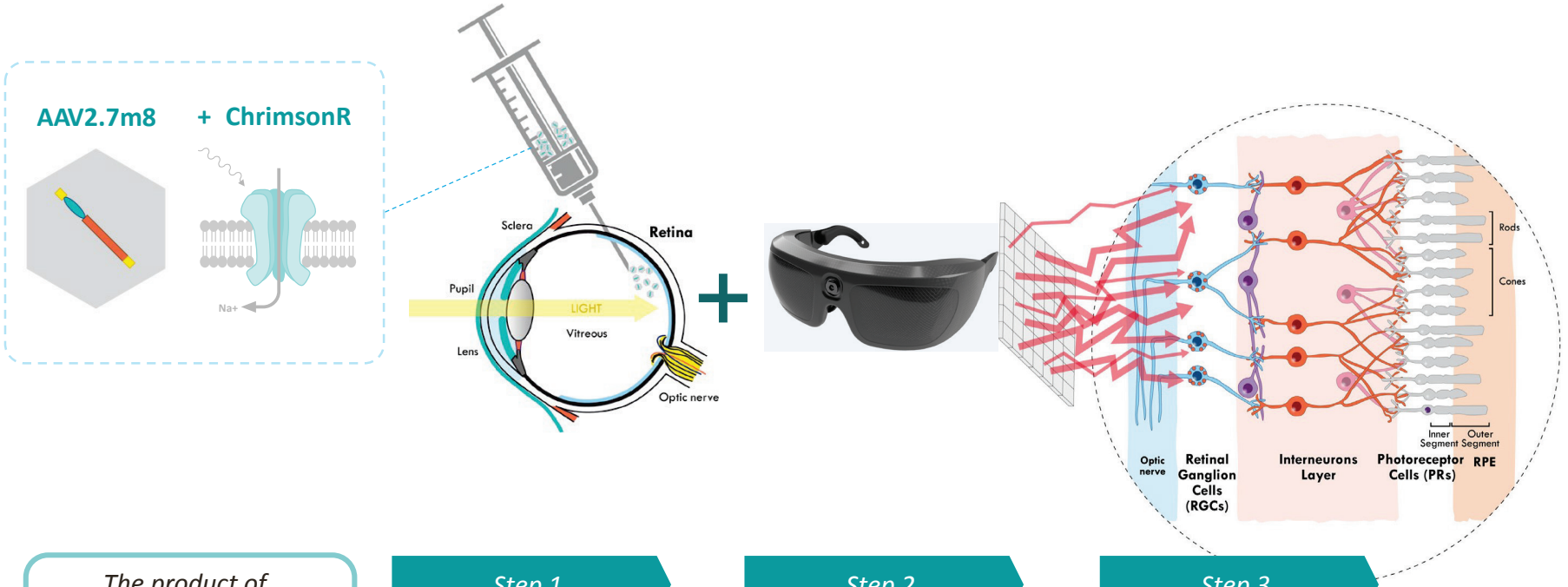
# GS030: using Gene Therapy to rejuvenate production of light-sensitive protein and restore vision




*The product of research collaboration with*

Massachusetts Institute of Technology

ADVERUM BIOTECHNOLOGIES

UPMC

**Step 1**

**Gene Therapy** transfer of the gene that encodes light-sensitive protein **Expression** in retinal ganglion cells (RGCs)

**Step 2**

Stimulation with **optoelectronic device** to transform external light stimuli into signal that can activate the RGCs

**Step 3**

Retinal output sent to brain for image processing



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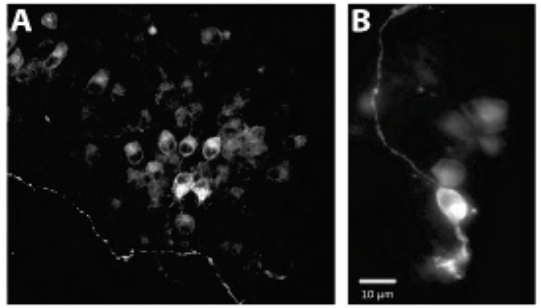
# GS030 leads to functional vision restoration in monkey and rats

## *Localization of light-sensitive protein in NHP retina*

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

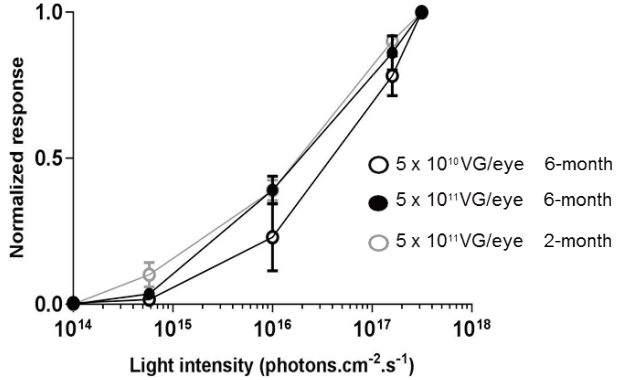
*In vivo* in NHP assessment 6 months after IVT injection




## *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

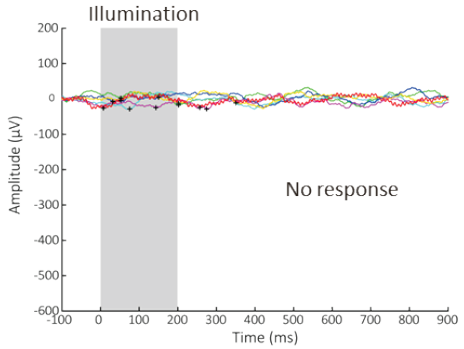



## *Restoration of a functional vision in P23H rats*

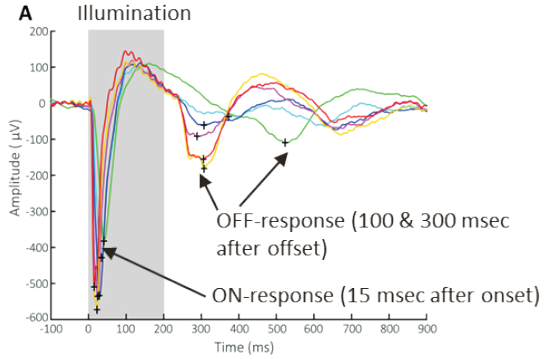
**Light-induced visual evoked cortical responses**

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

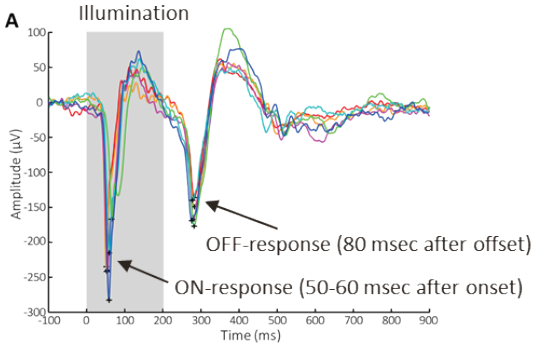
**Untreated P23H rat**




**GS030-treated P23H rat**




**Normal Long-Evans rat**

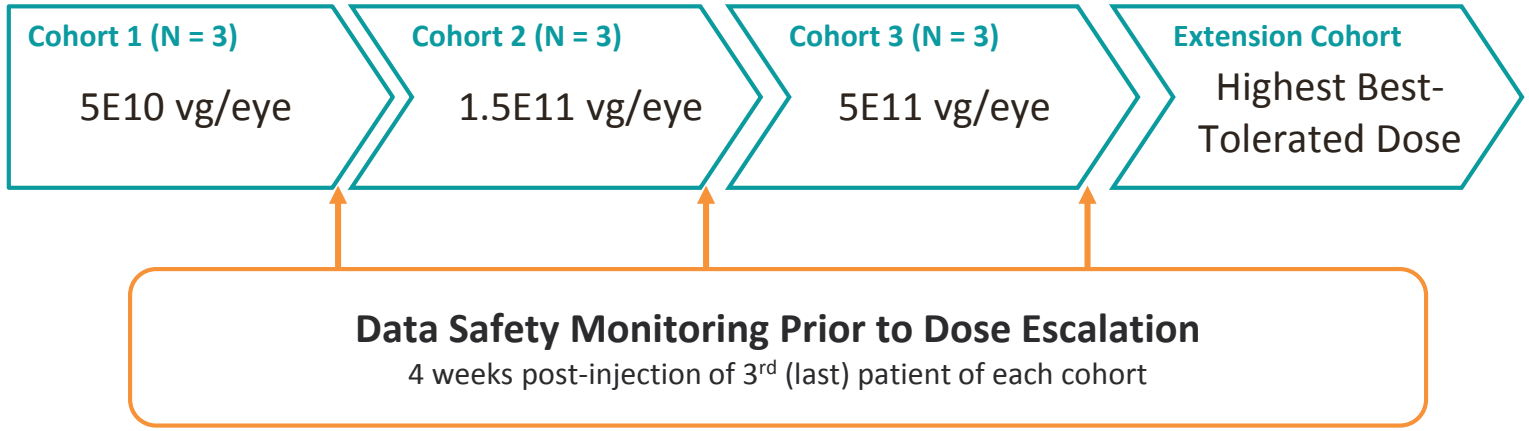





GenSight BIOLOGICS

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

**Study design**



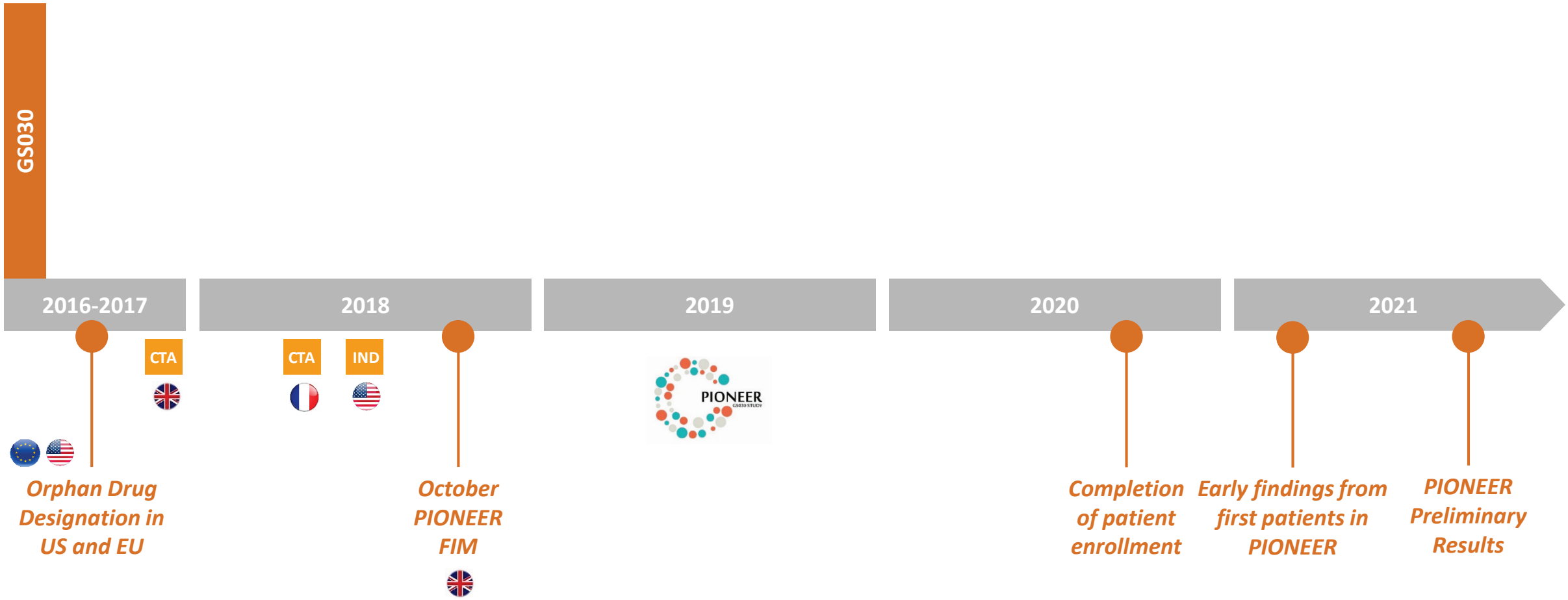

- **First-in-man**, dose-escalation safety study, multi-center (France, UK, US)
- **Study population:** end-stage non-syndromic RP (vision < Counting Fingers)
- **Primary analysis:** Safety at 1 year
- Single intra-vitreal injection in the **worst affected** eye
- Decision to increase the dose taken by a DSMB

2nd cohort fully enrolled and treated
DSMB#2 approved to move to cohort 3 without any modification



GenSight BIOLOGICS

# GS030 Key Milestones






GenSight BIOLOGICS

# Building high strategic value

# A company developing innovative and versatile technology platforms nearing commercialization and evolving in an area where value is increasingly being recognized by the market

## GenSight at the forefront of Gene Therapy with potential product launch in 2021

» **LUMEVOQ® in LHON-ND4**
- Strong clinical data
- Upcoming confirmatory Phase III trial

» **Targets attractive market**
- High unmet medical need
- Virtually no competition
- Well defined path to commercial success

» **Proprietary MTS technology**
- Broad range of mitochondrial diseases

» **Rich news flow** in 2020 and 2021

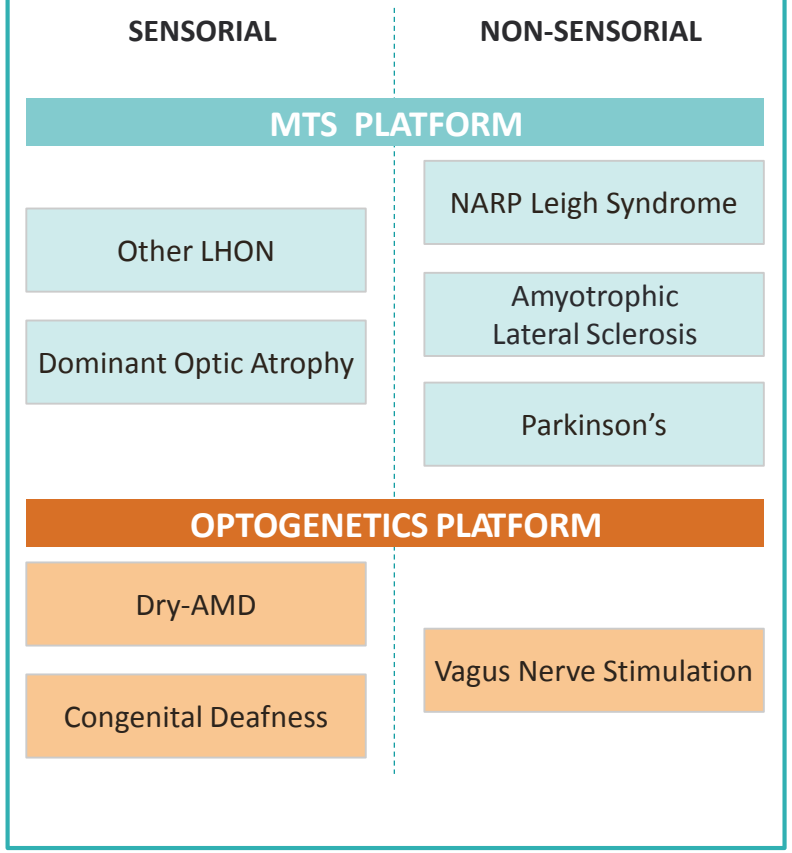
## Gene Therapy increasingly attracts interest from investors and Large Pharma

» **Viable therapeutic option** (already 3 approved therapies)

» **Pricing reflective of significant therapeutic benefit**

» **Large Pharma increasingly involved in the field**

## LUMEVOQ® and Beyond: Two platforms pargeting large number of sensorial and non-sensorial diseases






GenSight BIOLOGICS

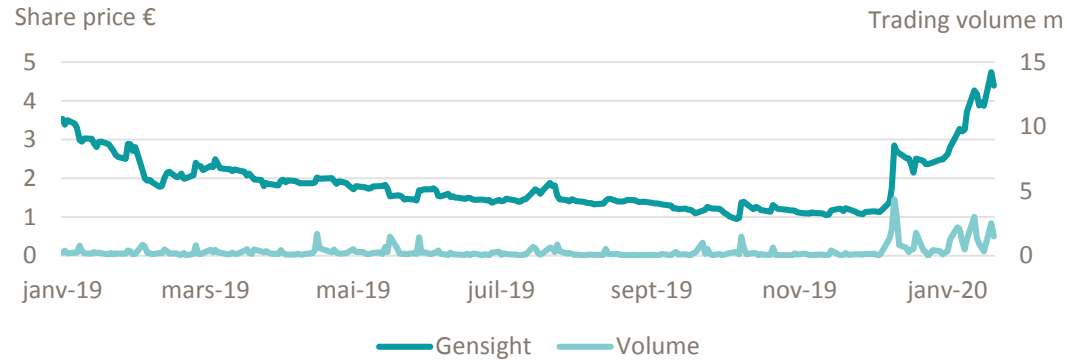
# GenSight Biologics in numbers

## Key financial information

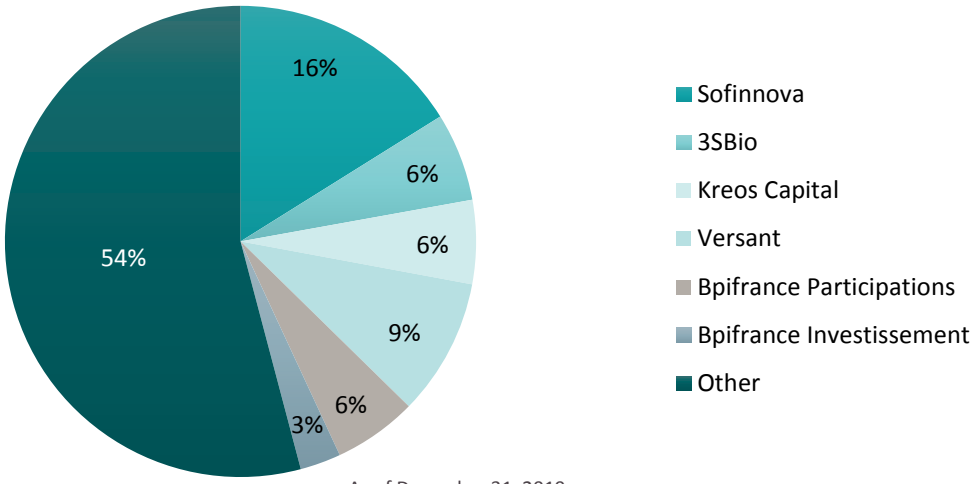
| Company Overview | | |
|---|---|---|
| Market Cap*: | € 104m | **Analyst Coverage** |
| Cash Position (Mar. 31, 2020): | € 12.8m | • Oddo & Cie: Martial Descoutures (FR) |
| Outstanding Shares: | 32.8m | • Gilbert Dupont: Jamila El Bougrini (FR) |
| Latest Amount Raised (Dec 20, 2019): | € 15m | • Chardan: Gbola Amusa (US) |
| Raised to date | € 142m | |
| IPO Date | July 2016 | |

*As of June 11, 2020

### Share price evolution and trading volume




### Shareholder structure




As of December 31, 2019

| Corporate calendar | Date |
|---|---|
| 2019 Full-Year Financial Update and Statements | March 12, 2020 |
| 2020 1Q Cash Position | April 21, 2020 |
| Annual General Meeting | April 29, 2020 |
| 2020 First-Half Financial Update and Statements | July 30, 2020 |
| 2020 3Q Cash Position | October 20, 2020 |
| 2020 4Q Cash Position | January 19, 2021 |