GenSight BIOLOGICS

CORPORATE PRESENTATION

A leading gene therapy biotechnology company

www.gensight-biologics.com

Disclaimer

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Corporate Overview

Clinical-stage gene therapy company

- Focused on severe retinal degenerative pathologies leading to blindness as well as CNS diseases
- Well positioned to advance disruptive gene therapy technologies in ophthalmology to commercialization

Two disruptive technology platforms

- Mitochondrial targeting sequence (MTS)
- Optogenetics

Lead projects target:

- GS010 - Leber Hereditary Optic Neuropathy (Phase III)
- GS030 - Retinitis pigmentosa and dry-AMD (Pre-clinical)

Listed on Euronext Paris (SIGHT)

- Established in 2012, IPO in July 2016 (EUR45m)
- GenSight Biologics Inc incorporated in the US in May 2017

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 Finance

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

ERNST & YOUNG (2007-2008)
Auditor

Barrett Katz
Chief Medical Officer

MONTEFIORE MED CENTER & A. EINSTEIN COLLEGE OF MEDICINE, NY, USA (2011-2017)
Prof. of Ophthalmology, Neurology and Neurosurgery

DANUBE PHARMA (2009-2011)
CEO

FOVEA PHARMA (2007-2009)
CMO

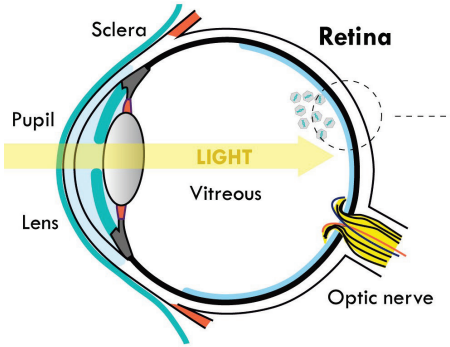
EYETECH (2005-2007)
VP of Medical Affairs and Strategy

MD, Board-certified ophthalmologist & neurologist

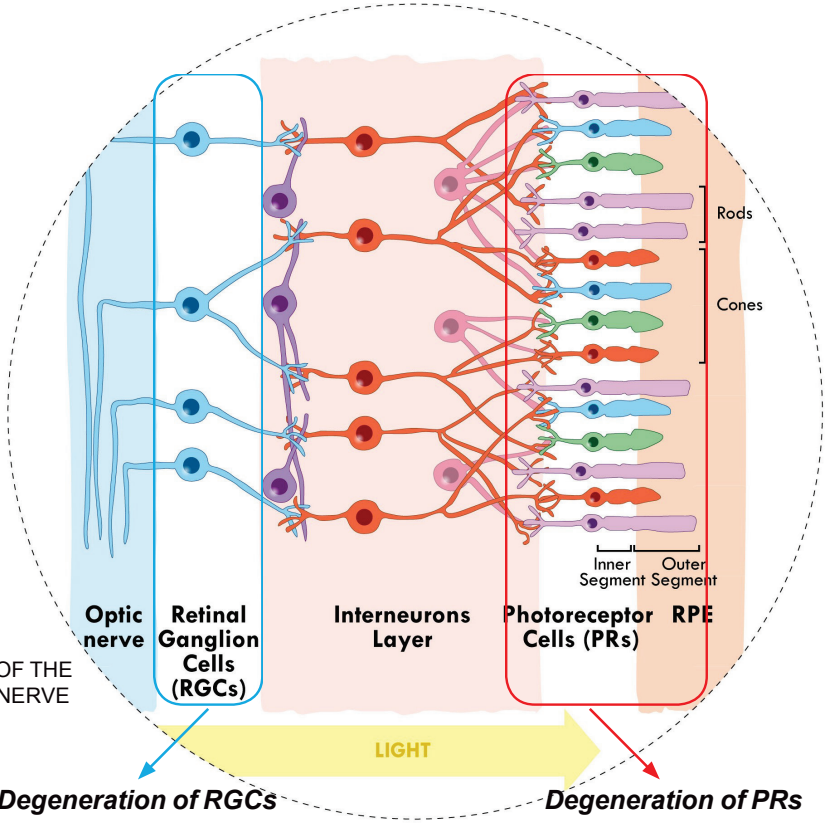
Degenerative retinal diseases

GenSight targets 3 areas of unmet needs: LHON, RP & DRY AMD

PHOTORECEPTOR CELLS TRANSFORM LIGHT INTO ELECTRIC SIGNALS IN THE EYE



ELECTRIC SIGNALS ARE SENT TO THE VISUAL CORTEX OF THE BRAIN VIA THE GANGLION CELLS FORMINGTHE OPTIC NERVE



LEBER HEREDITARY OPTIC NEUROPATHY (LHON)

RETINITIS PIGMENTOSA (RP)
GEOGRAPHIC ATROPHY
(Late stage form ofAge-Related Macular Degeneration - AMD)

Source: Company

Gene therapy in the eye - Methodology

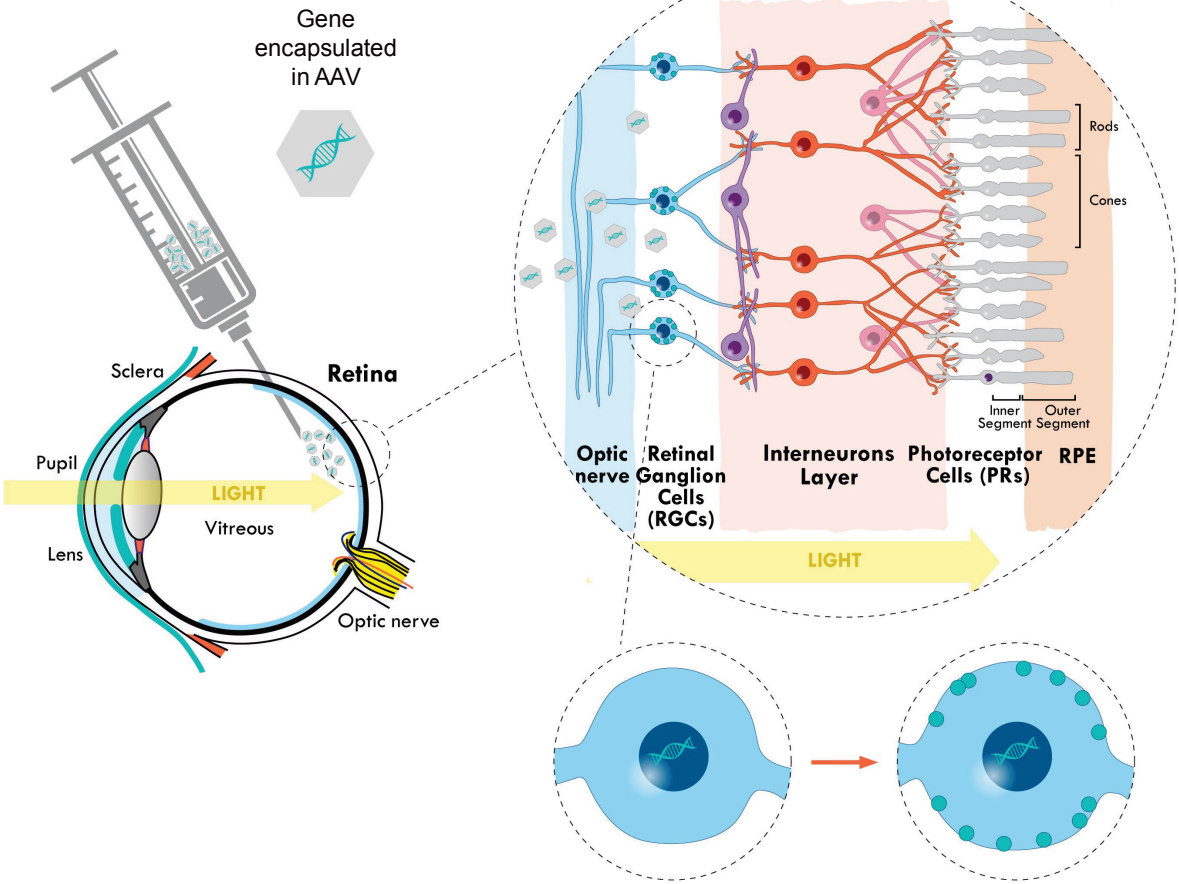
1. Genetic disorders and aging are responsible for retinal degenerative diseases that lead to blindness

2. Therapeutic gene is packaged in a virus vector (AAV)

   AAV is injected into the eye (intravitreal or subretinal)

3. AAV vector expresses a therapeutic protein in retinal cells

   It enables the retina to regain lost function



Source: Company

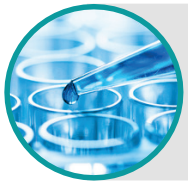
Advantages of gene therapy in ophthalmology

THE EYE: STRATEGIC TARGET

- No approved curative treatments for retinal degenerative diseases
- Immune privilege, closed system
- Easy access and ability to get gene to target cells
- Limited number of retinal cells
- Long-term expression of transduced gene due to low turnover rate of retinal cells

AAV: SUCCESSFUL IN RETINA

- Proven safety and proof of effect in humans
- Efficient transduction of retinal cells
- No need to screen patients for Nab before treatment
- Validated manufacturing process

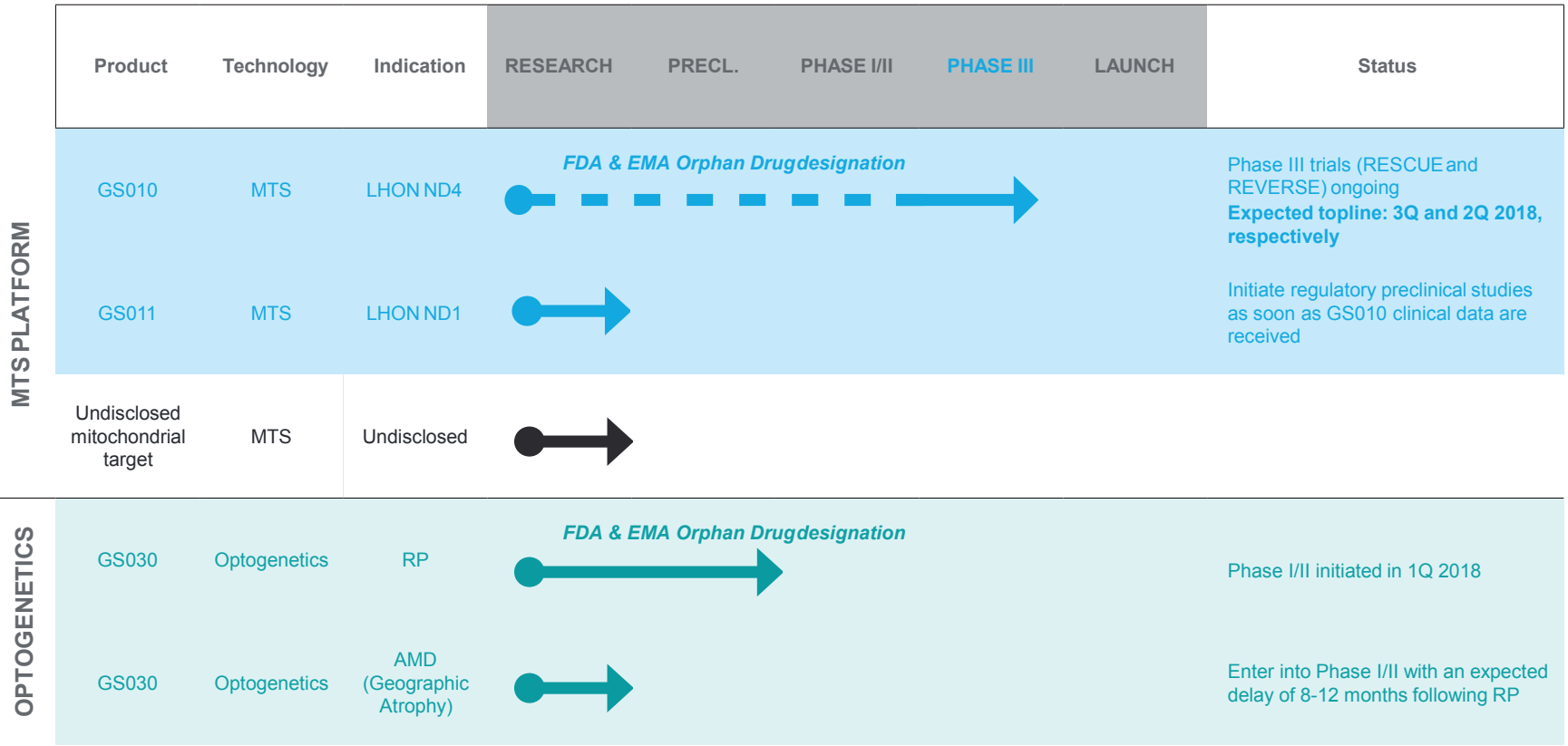


NO OTHER APPROVED THERAPEUTIC APPROACHES

- Genetic replacement therapy for diseases caused by single gene mutations (LHON)
- In-situ insertion of therapeutic gene to stimulate sight in patients with severe vision loss due to multiple causes, such as RP and AMD

Source: Company

Pipeline: solid and advanced product portfolio in ophthalmic gene therapy



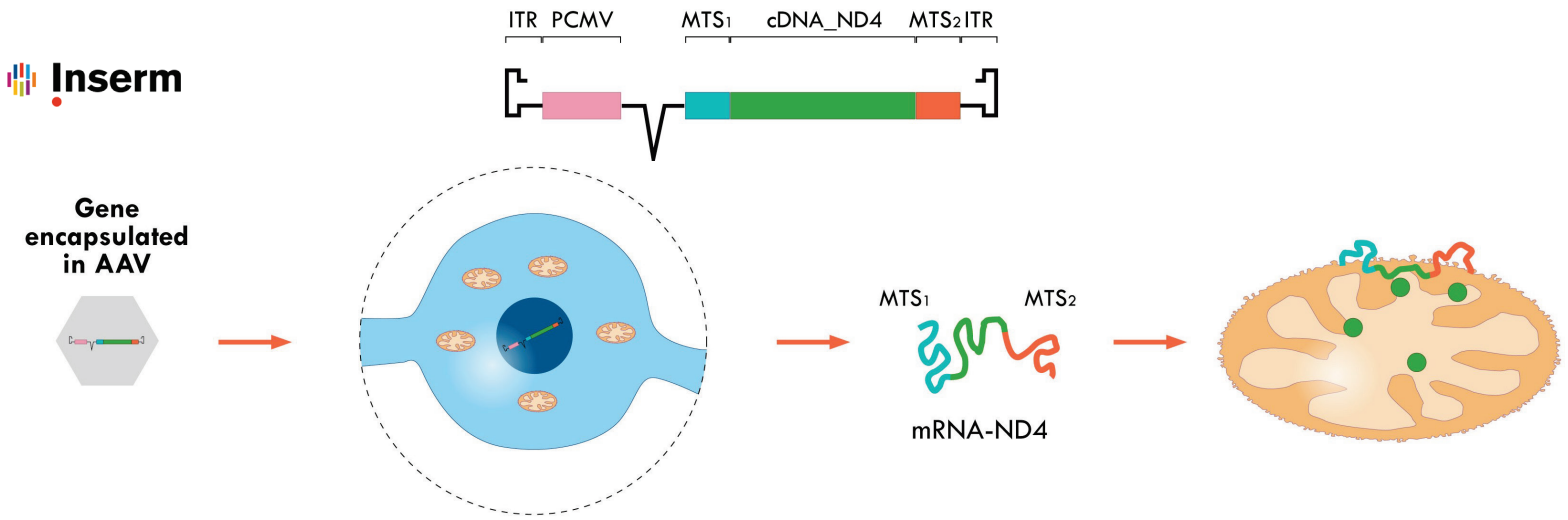
Lead candidate, GS010, is expected to be 18 months away from BLA and MAA submission

Note: Please refer to the 2016 Registration Document for a detailed description of regulatory strategy.

GS010

Fully enrolled ongoing Phase III for our lead product candidate dedicated to Leber Hereditary Optic Neuropathy (LHON)

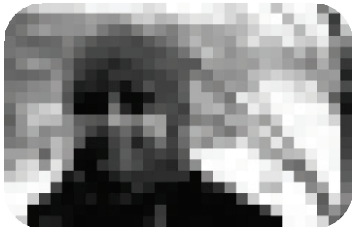
GenSight's proprietary gene sequencing encapsulated in AAV

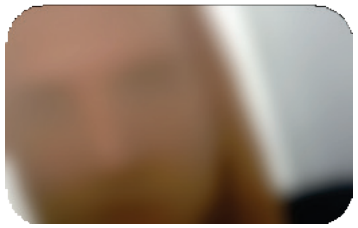


1. Transduction of retinal cell with replacement mitochondrial gene
2. Transcription of replacement mitochondrial gene in the nucleus
3. Delivery of replacement gene mRNA to polysomes located at the mitochondrial surface
4. Synthesis, translocation and proper localization of replacement mitochondrial protein

The only technology that permits missing mitochondrial proteins to be ***actively*** shuttled into the mitochondrion to restore energy production

LHON: the most common mitochondrial disease causing bilateral blindness at the prime of life





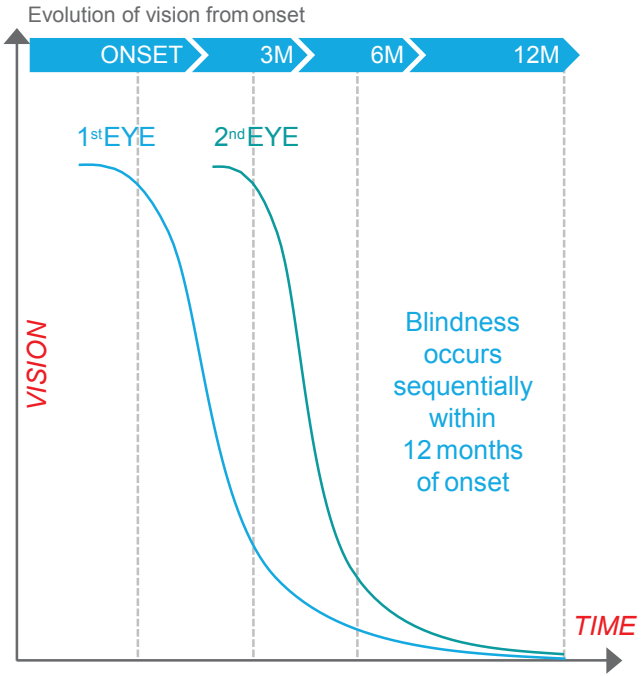


Image source: illustrated from Newamn NJ et al., Am J Ophthalmom. 141(6), 1061-1067,2006

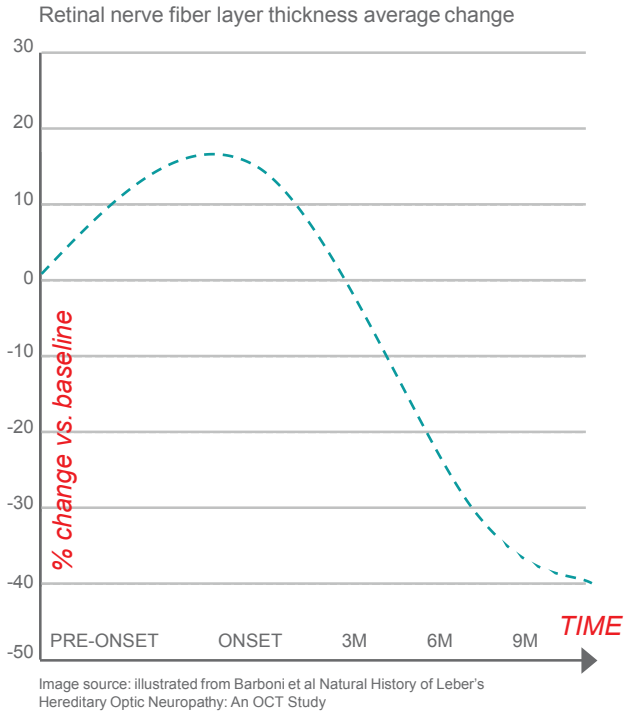


Image source: illustrated from Barboni et al Natural History of Leber's Hereditary Optic Neuropathy: An OCT Study

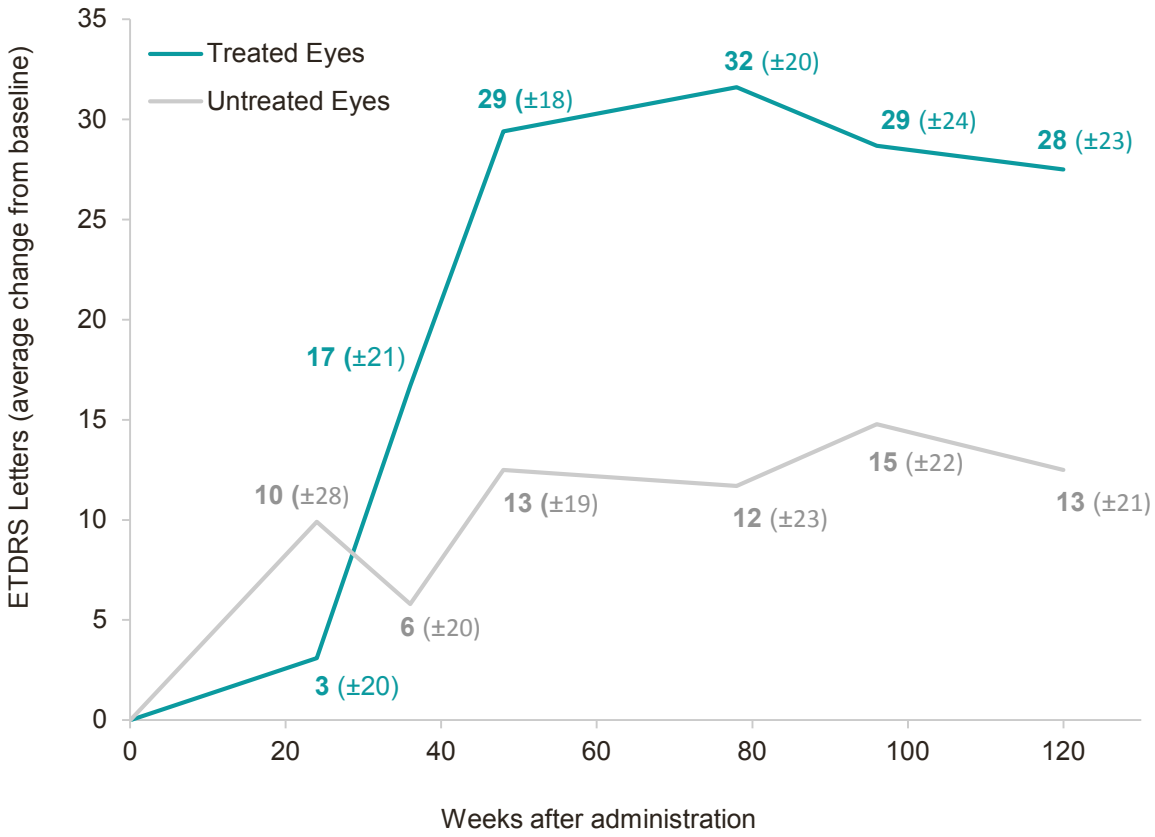
Incidence	0.15/100,000
Prevalence	1/31k-40k
Blindness	15-35y

- **Orphan maternally inherited mitochondrial disease**
- **Painless sudden loss of central vision** in the 1st eye with 2nd eye sequentially impaired: **symmetric disease with poor visual recovery**
- **Thinning of the Ganglion Cell Layer** occurs after the onset of vision loss and stabilizes at approximately 6 months
- **97%** of patients have bilateral involvement < 1 year / 25% of cases are simultaneous
- **Targets ND4** which accounts for ~75% of LHON in North America & Europe

Phase I/II follow-up

Sustained improvement after 2.5 years in patients with less than 2 years of vision loss

Mean change from Baseline

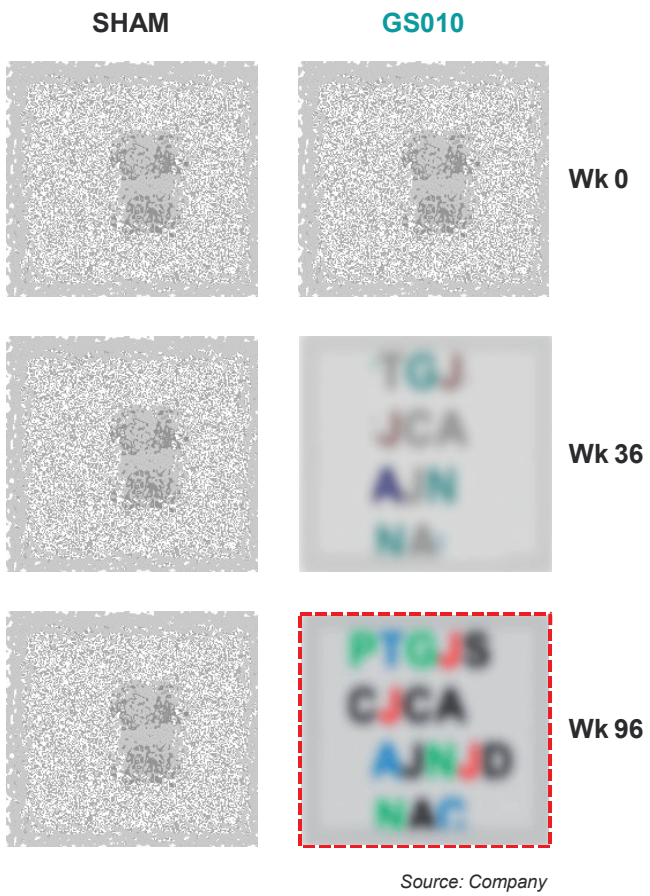


Subgroup 1 (n=5)

Vision loss duration ≤ 2 years and Baseline LogMAR ≤ 2.79

(ie excludes "hand motion" patients, in accordance with the Phase III protocol)

Illustration of visual benefit for patient



Source: Company

Phase I/II follow-up

Sustained improvement after 2.5 years in patients with less than 2 years of vision loss

ETDRS letters (LogMAR) Visual Acuity change from baseline **Δ TE vs UTE**	**1.0 year**	**1.5 year**	**2.0 years**	**2.5 years**
All patients (n = 14)	+3 letters (-0.06)	+8 letters (-0.16)	+0 letters (-0.00)	+7 letters (-0.14)
Patients with ≤ 2y disease duration (n = 5)*	+17 letters (-0.34)	+20 letters (-0.40)	+14 letters (-0.28)	+15 letters (-0.30)

Note (*): Excludes “hand motion” patients, in accordance with the Phase III protocol.

Trends of improved visual acuity
in patients with less than 2 years of vision loss

Phase I/II follow-up

Strong trends validate and inform our Phase III design

Symptom duration impacts magnitude of treatment effect

- VA beneficial positive trends after 2.5 years in patients ≤ 2y of vision loss with a clinically significant improvement (≥ 15 ETDRS letters)
- Color vision beneficial trends at week 48 in patients with ≤ 2y symptom duration, confirmed with subjective outcome from patients

Baseline vision status at treatment impacts magnitude of treatment effect

- Observed in visual field & color vision tests

Analysis supports protocol strategy for phase III

- Population divided by time from onset
- Effect analyzed on better seeing eye

> **Now I can see if a traffic light is red or green. In the subway, I can read the names of stations with large letters. I have better autonomy.**

"Phase 1 Patient"

RESCUE & REVERSE Phase III trials: time based strategy

Phase III Trials

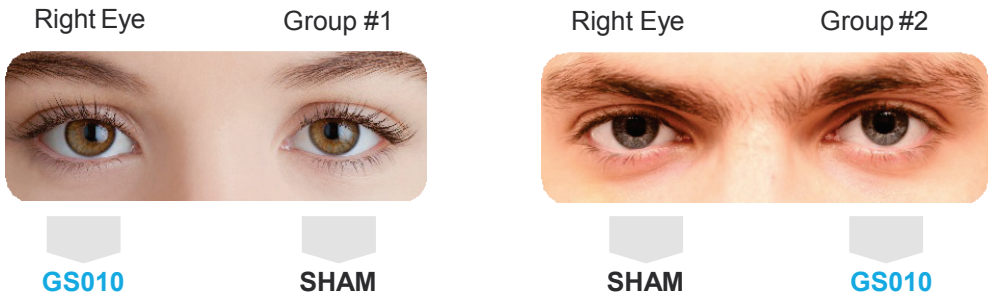
RESCUE
onset of disease
≤ 6 months

&

REVERSE
onset of disease
6 months to ≤ 1 year

- **Initiation:** 4Q 2015 (1st patient in February 2016)
- **39 patients in RESCUE** (recruitment completed in July 2017)
- **37 patients in REVERSE** (recruitment completed in February 2017)
- **Randomized (one eye treated vs. sham), double-masked, sham-controlled, multi-center**

One eye of each patient randomized to GS010 or sham



Endpoints at 48 weeks

Primary:

- Mean Difference in ETDRS of treated eyes compared to eyes receiving sham injection (LogMAR used for statistical analysis)

Secondary:

- Measure vision gain, vision stabilization, or reduction in vision decline
- Best or worst eyes vs. sham
- Responders analysis:
  - Gain from baseline of 15 or more ETDRS letters

    OR
  - Snellen acuity > 20/200
- SD-OCT, visual field, color and contrast vision

Source: Company

REFLECT Phase III trial: bilateral treatment

Phase III Trial

- **Initiation:** 4Q 2017 (1st patient expected 1Q 2018)
- **90 patients** planned (45 in each group) with vision loss ≤ 1 year
- **Randomized (two eyes treated vs. one eye treated + placebo in the other eye), double-masked, placebo-controlled, multi-center**
- **Conducted under a Special Protocol Assessment (SPA) from the FDA**

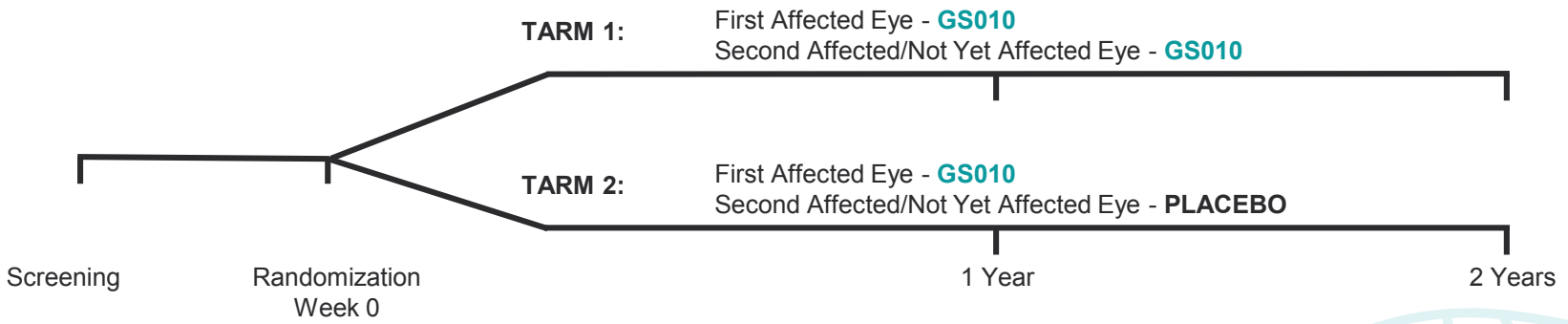
Endpoints at 48 weeks

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)

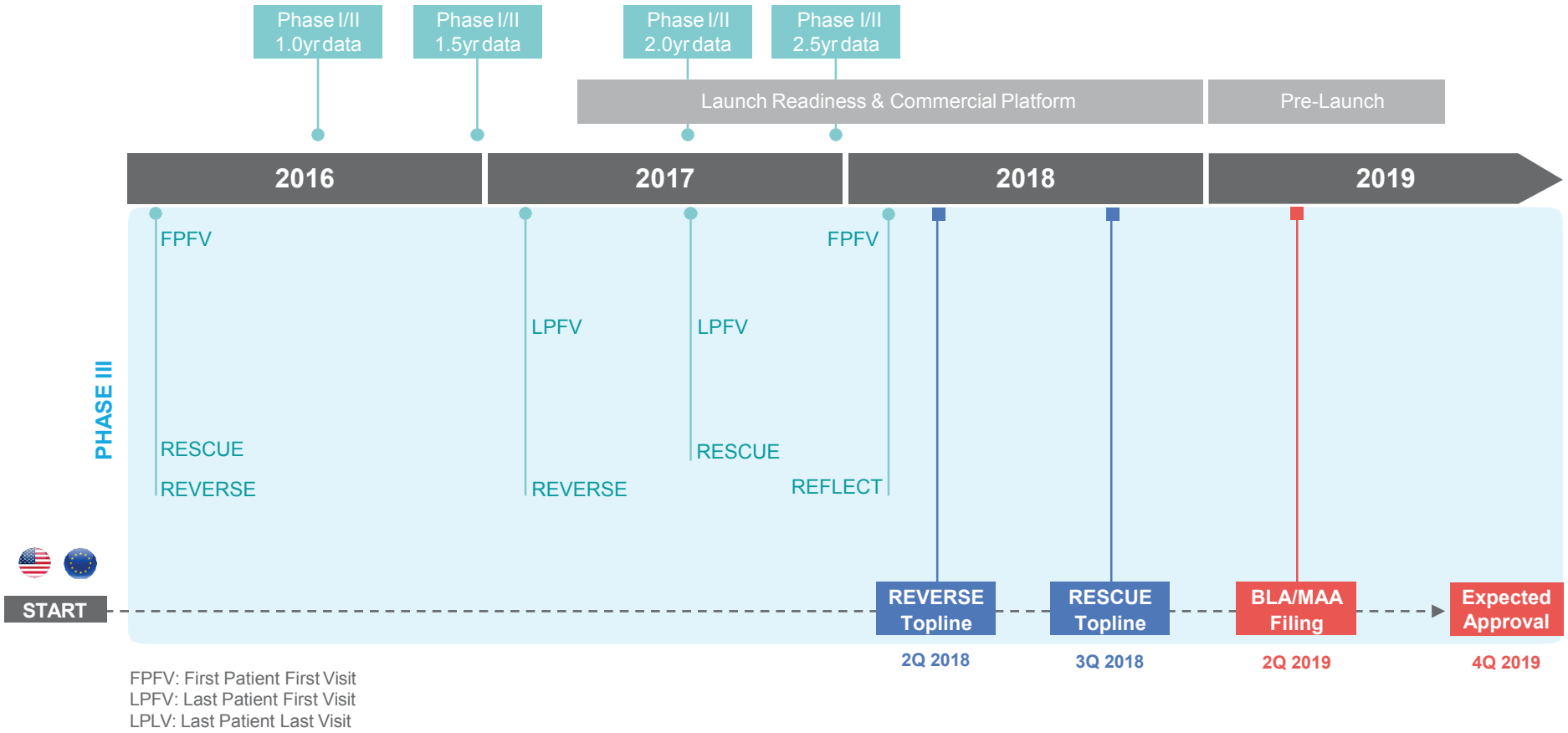
Secondary:

- 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



Confirmatory Phase III study to assess safety and efficacy of a bilateral injection of GS010

GS010: an accelerated path to market



FPFV: First Patient First Visit
LPFV: Last Patient First Visit
LPLV: Last Patient Last Visit

Objective: obtain marketing authorization for GS010 by the end of 2019

(1) FDA approval is expected to be conditional upon the initiation of a trial to evaluate bilateral dosing. Current discussions with the FDA remain ongoing. Please refer to the 2016 Registration Document for a detailed description of regulatory strategy.

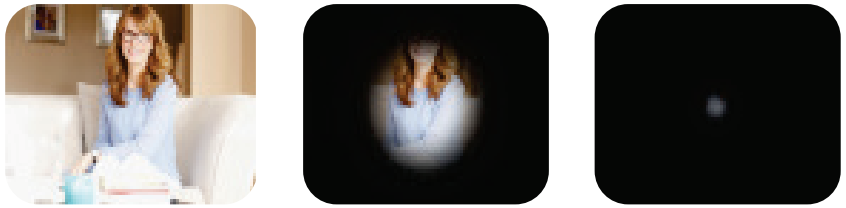
GS030

Second lead product candidate targeting photoreceptor degenerative diseases (RP/AMD)

RP / AMD: degenerative diseases of photoreceptors leading to blindness

Retinitis Pigmentosa (RP)

- Blinding genetic disease with multiple mutations (+100 genes)
- Sequential photoreceptor degeneration
- Slow & irreversible evolution leading to blindness



Incidence	15K-20K / year
Prevalence	350K-400K (1.5 M worldwide)
Blindness Occurence	40-45 years old

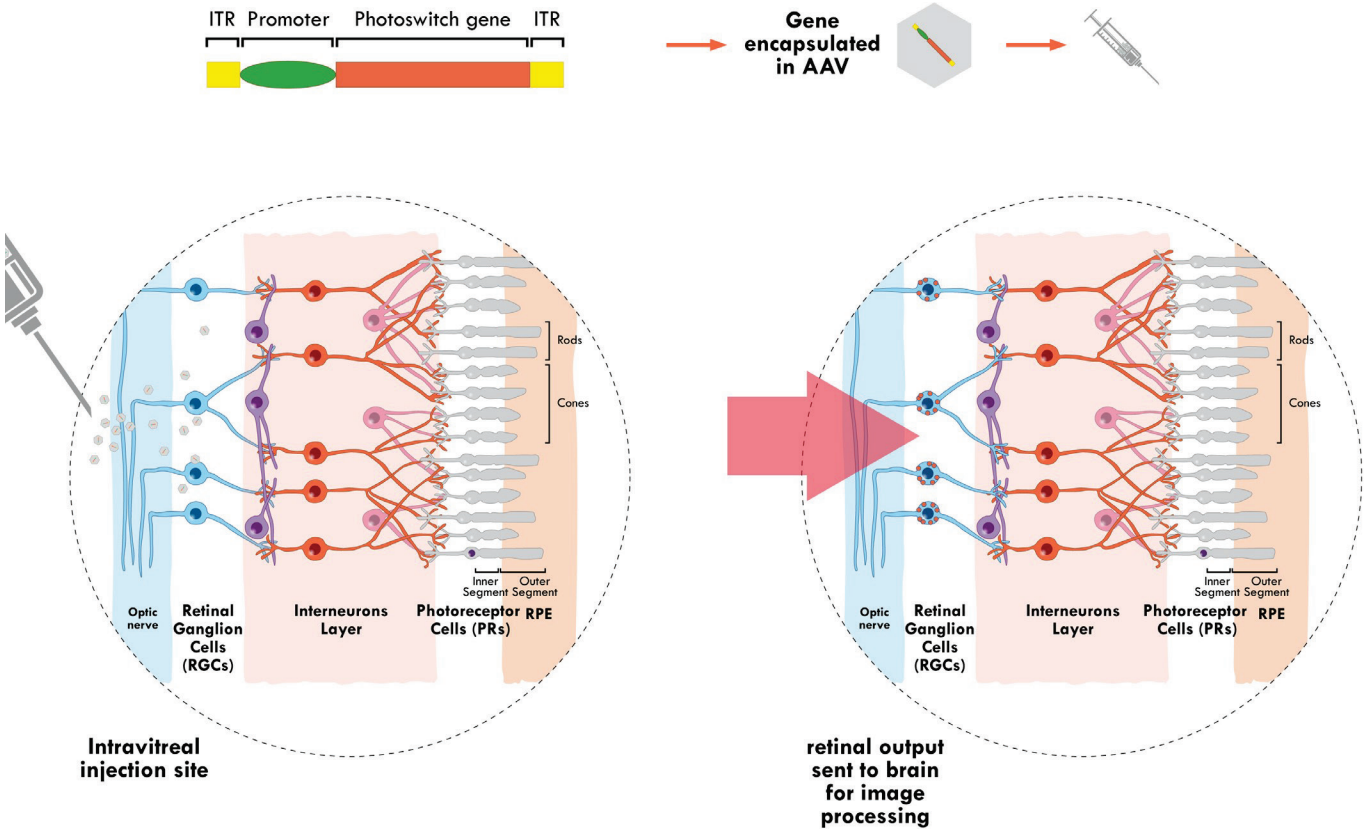
Age-Related Macular Degeneration (AMD)

- Onset of AMD: 55 to 60 years of age
- Early form: dry-AMD that evolves with aging to late AMD
- Late AMD can either be:
  - Neovascular form (wet-AMD)
  - Geographic atrophy
- Prevalence of geographic atrophy increases with age from 3.5% over 75 years to 22% over 90 years

Incidence of AMD	350k – 400k / year
Prevalence of Late AMD	1.47% with 0.81% geographic atrophy in at least one eye
Blindness Occurrence from Late AMD	250 000 with geographic atrophy accounting from 10 to 20% of blind patients

Optogenetics: gene therapy with photosensitive protein

Transferring a gene encoding light-sensitive protein to retinal ganglion cells to restore photoreceptor function in cells that are still wired to the visual cortex

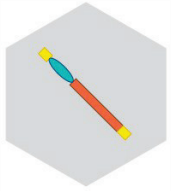


Restore photoreceptor function in cells by training RGCs to act as photoreceptors

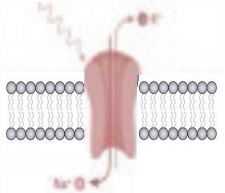
GS030: stimulating the eye with light through gene therapy

1

AAV2.7m8



+ ChrimsonR



Massachusetts Institute of Technology

ADVERUM BIOTECHNOLOGIES

GenSight BIOLOGICS

UPMC

Gene therapy transfer of light sensitive protein

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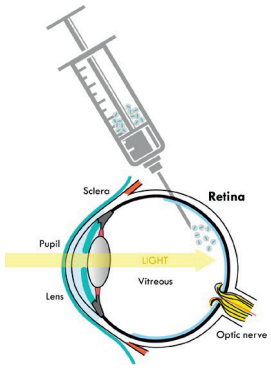
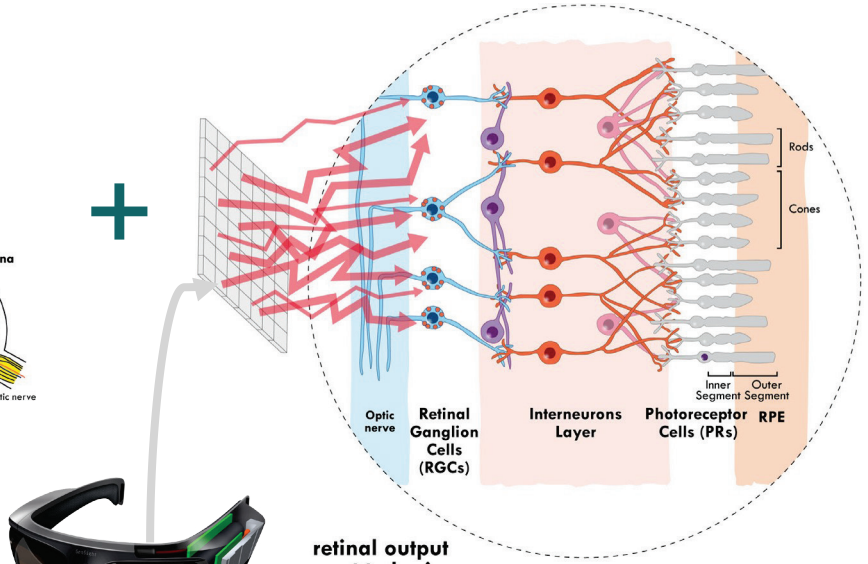


Expression in retinal ganglion cells

3



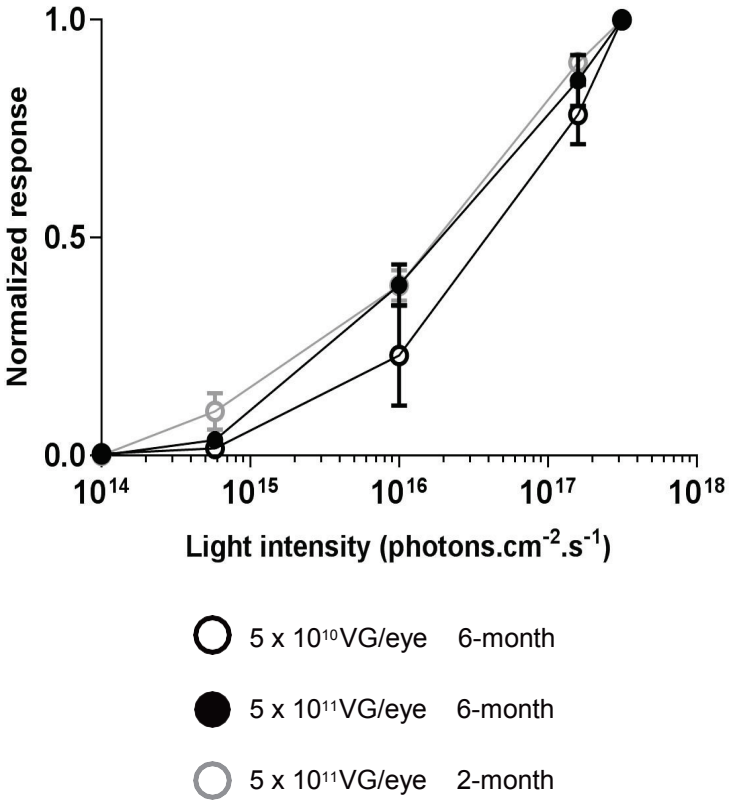
retinal output sent to brain for image processing

Stimulation with optoelectronic device
External visual interface transforms external light stimuli into signal that activates the transduced retinal ganglion cells

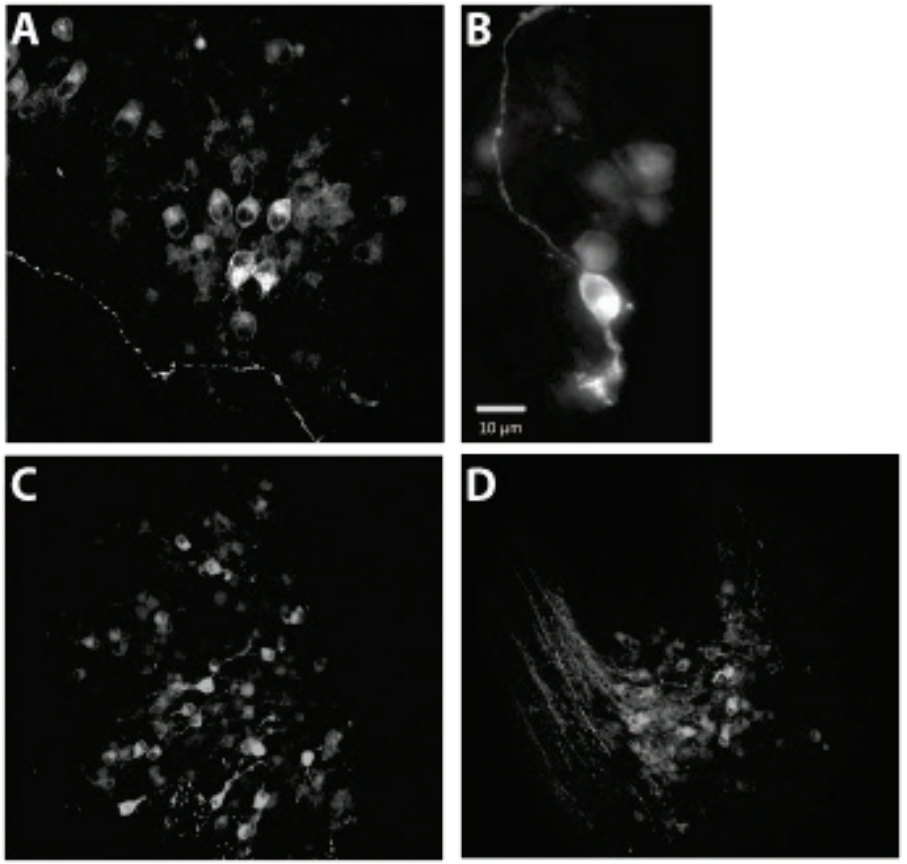
Source: Company

GS030: activation and stimulation of photoreceptors in monkeys

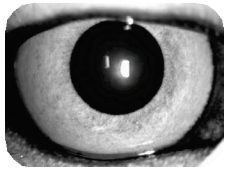
Irradiance-firing relationship

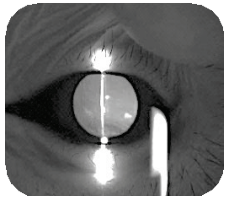


Expression of ChrR-tdT in midget cells of the perifovea



No adverse effect associated with GS030 in non-human primates





Bilateral IVT administration with 5x1011 VG/eye (in 100 µL)

Ophthalmology examinations	• **Normal in all animals at 2 months (n = 8 eyes)** • **Normal in all animals at 3 & 6 months (n = 4 eyes)**
Histopathology (n = 2 eyes/ timepoint)	• **Eye tissues: no ocular inflammation** • **Other tissues: no histological findings**
Retina structural modifications (n = 2 eyes/ timepoint)	• **No apparent structural modifications of the retina (layer thickness and structures)** • **No retinal cell degeneration or necrosis**

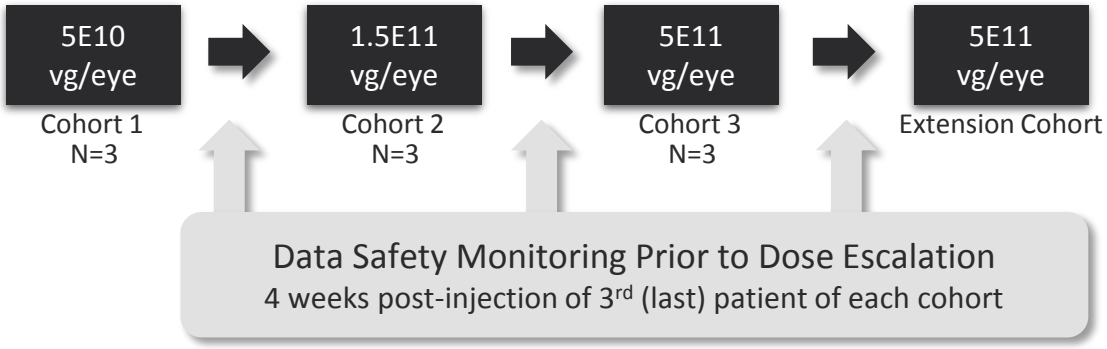
- Very mild increase in humoral immune response (NAb) in serum at 2 months, none at 6 months
- No NAb in aqueous humor from both eyes at 2 & 6 months

GS030 expression does not lead to retinal inflammation nor pathological modifications of the retina

Source: Company

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

Study design



- **First-in-man**, dose-escalation safety study, multi-center
- **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

First patient expected to be enrolled in 1Q 2018 in the UK

Source: Company

GS030: CMC progress & Regulatory interactions

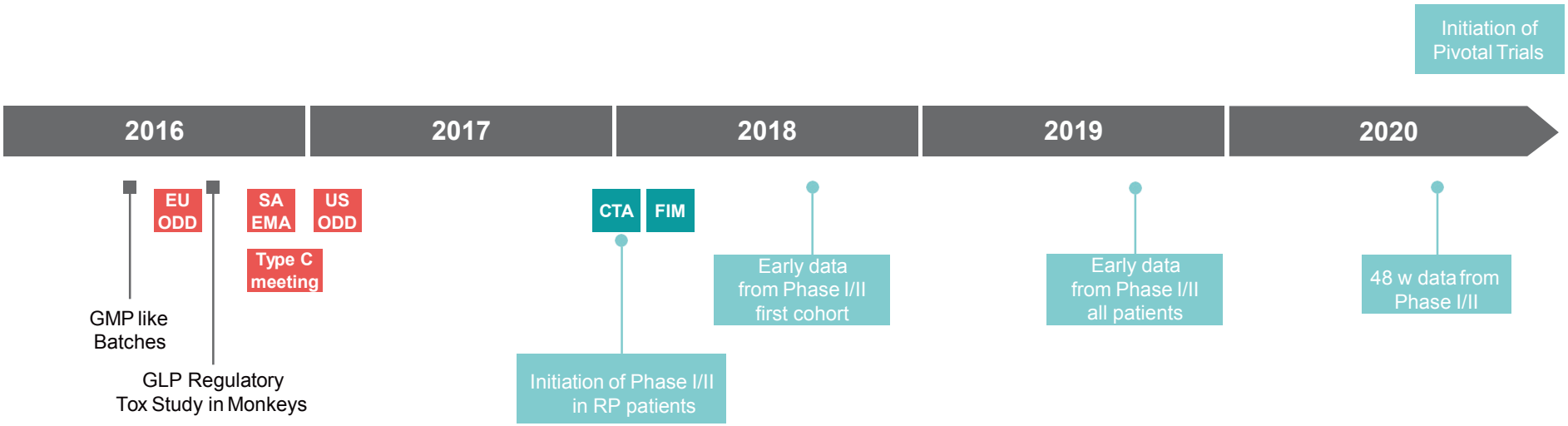
CMC

- **Manufacturing process developed up to 25L**
  - Toxicology batch produced at 25L scale
  - Drug Substance titers (> 2E13 vg/ml) and characteristics in line with expectations
  - Scale up to 100L batch successful
- **Manufacturing process transfer to GMP ongoing**
  - GMP clinical supply ready
- **Potency assay under development**

Regulatory

- **Orphan Drug Designation granted in the US and in Europe**
- **EMA Scientific advice & FDA type-C meeting**
  - Non clinical approach globally well received and endorsed in principle by agencies
  - Our future IND/CTA submissions will therefore include FDA & EMA recommendations to ensure optimal review process
- **Active strategy & interactions with US and EU Agencies to obtain advice on preclinical package to support FIM and exploit the existing process of expedited programs**

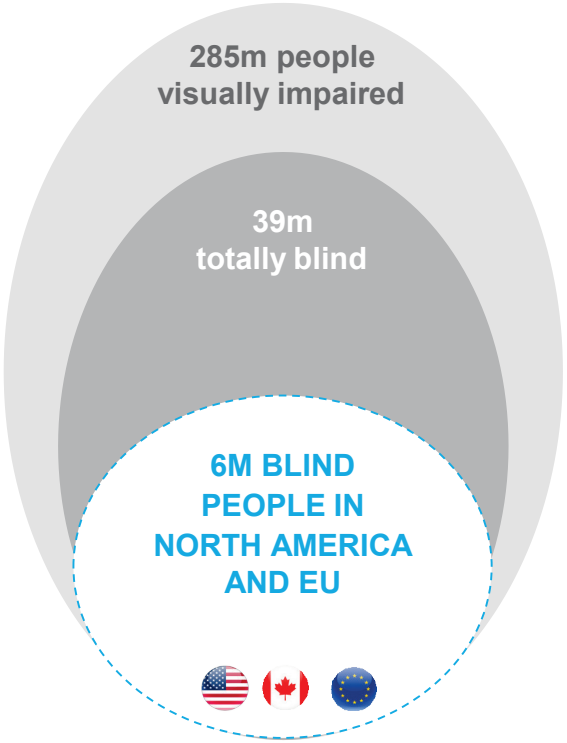
Key expected development milestones for GS030



ODD: Orphan Drug Designation
CTA: Clinical Trial Application
EMA: European Medicines Agency
IDE: Investigational Device Exemption

Building a high strategic value

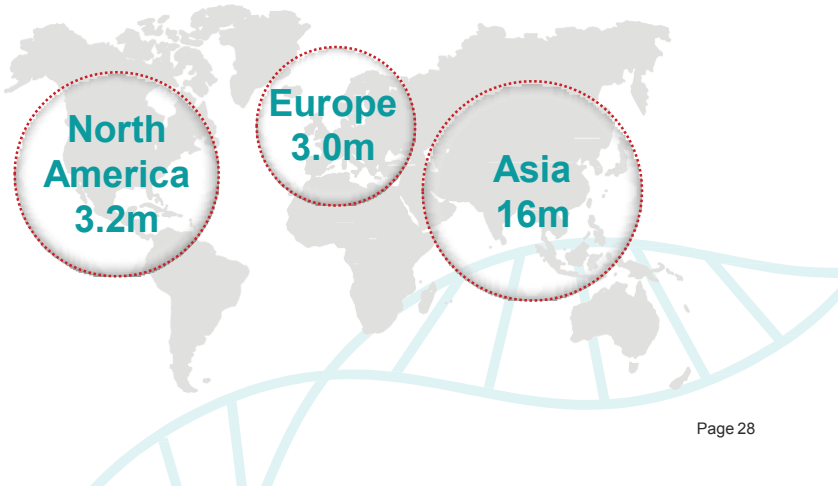
Curing blindness represents major market opportunity



Favorable reimbursement conditions:

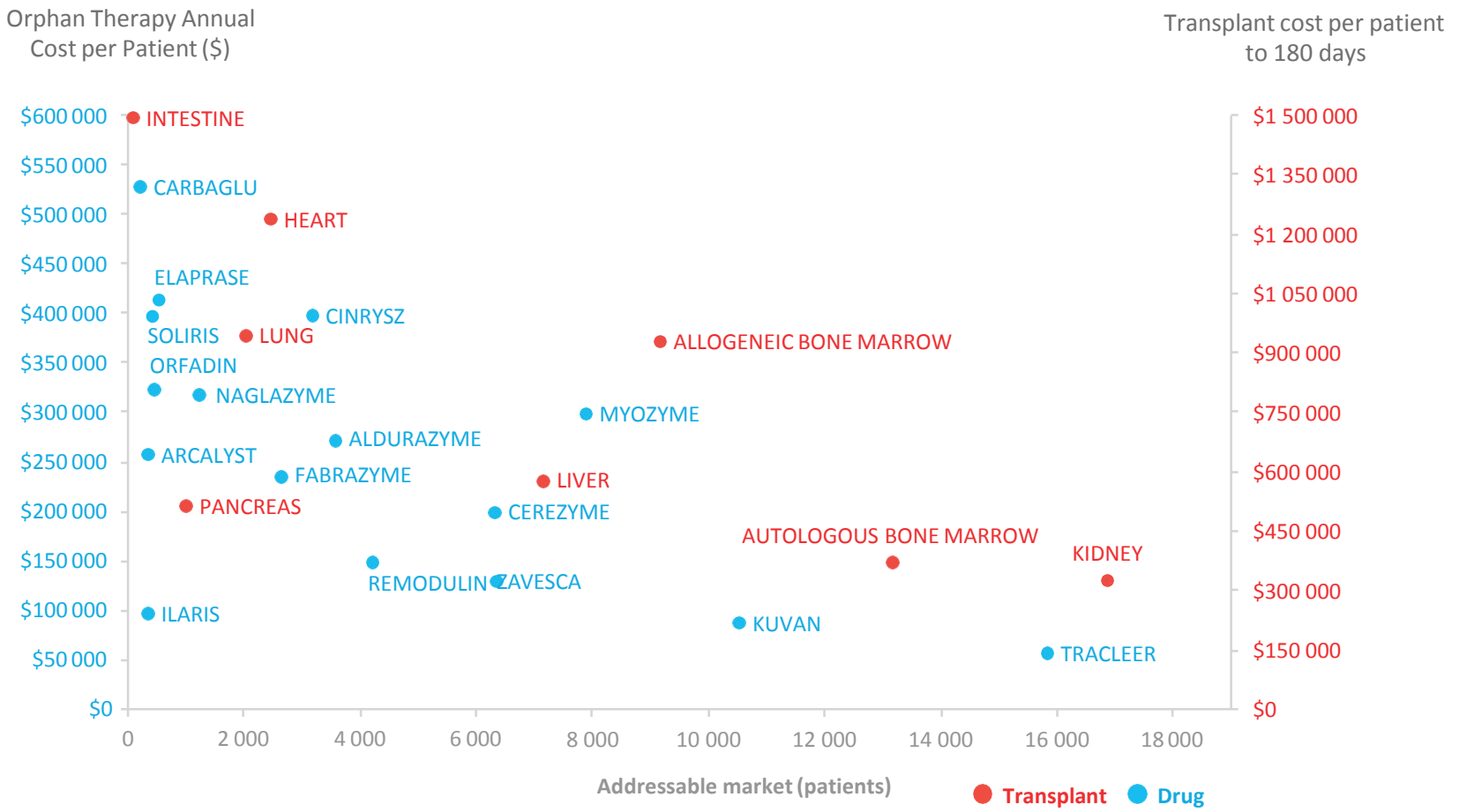
- Gene therapy in ophthalmology for rare diseases could be considered **similar to organ transplants for payers**
- Blindness imposes a **high burden** to health systems
  - Total blindness costs exceed tens of billions USD per annum
- **Absence of curative treatments**
  - Increasing pressure from patients and patients associations

Geographical Split – Blind people in major markets



Source: WHO, IAPB-VISION2020, NORC-Univ. of Chicago / The Economic Burden of Vision Loss and Eye Disorders in the United States, 2014.

Pricing and prevalence: organ transplant / gene therapy



Orphan therapies and transplants: a relevant pricing benchmark

Source: Nature Biotechnology, Volume 33, Number 9, September 2015: The payers' perspective on gene therapy.

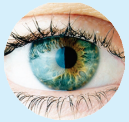
Potential applications of GenSight technology platforms

Current focus

- LHON
- RP
- AMD

GenSight BIOLOGICS

Potential applications



MTS PLATFORM

- Other LHON
- Dominant Optic Atrophy
- NARP Leigh Syndrome
- Amyotrophic Lateral Sclerosis
- Parkinson's

OPTOGENETICS PLATFORM

SENSORIAL

- Dry-AMD
- Congenital Deafness

NON-SENSORIAL

- Vagus Nerve Stimulation

Ability to leverage technology platforms and significant expertise to expand the pipeline in ophthalmology and other neurodegenerative disorders

GenSight Biologics
Key financial information

Financing history
- March 2013 – Series A round – €20m
- June 2015 – Series B round – €32m
- July 2016 – Euronext IPO – €45m
- June 2017 – PIPE – €22m

Listed on Euronext Paris (SIGHT)
- Established in 2012, IPO in July 2016

Recognition from Blue-Chip specialist investors
- Perceptive, Fidelity, Abingworth, Versant, JP MorganAM and others

Analyst coverage
- Oddo & Cie – *Sébastien Malafosse* (FR)
- Gilbert Dupont – *Damien Choplain* (FR)
- Chardan – *Gbola Amusa* (US)

Cash position
(as of September 30, 2017)

€59.5m

Number of outstanding shares
(as of December 31, 2017)

24.2m
Fully diluted: 27.2m