

## GenSight Biologics Announces Publication of Meta-Analysis Confirming that Spontaneous Recovery in LHON is rare in the *Journal of Neuro-Ophthalmology*

**Paris, France, September 28, 2020, 7:30 am CEST** – GenSight Biologics (Euronext: SIGHT, ISIN: FR0013183985, PEA-PME eligible), a biopharma company focused on developing and commercializing innovative gene therapies for retinal neurodegenerative diseases and central nervous system disorders, today announced the recent publication of a new meta-analysis of the natural history of Leber Hereditary Optic Neuropathy (LHON) in the September 2020 issue of the *Journal of Neuro-Ophthalmology*, the official journal of the North American Neuro-Ophthalmology Society (NANOS).

The paper\*, written by leading global authorities on LHON, confirms the low rate of spontaneous visual recovery in patients with a mutated *ND4* gene, the most common cause of the disease. For those 15 years or older at onset of visual loss, only an estimated 11.3% experienced some degree of visual recovery.

LHON is a rare, inherited bilaterally blinding disease predominantly affecting otherwise healthy young individuals, mostly men. Some 800 to 1,200 new patients are affected each year in the US and in the EU. Clinicians who manage LHON patients have long agreed that patients only rarely recover their vision once disease onset begins, but they have found it challenging to estimate the rate of spontaneous recovery, given the small number of patients they personally encounter even after decades of clinical practice. The challenge was made more acute because different mutations had different prognoses. Those with the most common mutation, that in the *ND4* gene, were generally regarded as having the poorest prognosis.

The *Journal of Neuro-Ophthalmology* paper, entitled “*Visual Outcomes in Leber Hereditary Optic Neuropathy Patients with the m.11778G>A (MTND4) Mitochondrial DNA Mutation*”, overcame the challenge of small patient numbers by conducting a meta-analysis of 12 retrospective and 3 prospective studies, which were identified after an extensive review of the scientific and medical literature. Treatment with idebenone did not exclude patients from the sample. This approach enabled the authors to analyze the evolution of visual function in 695 patients with a mutated *ND4* gene.

“*Many papers have attempted to estimate the extent of spontaneous recovery in LHON, but it has been tricky to arrive at an aggregate rate for the most common underlying mutation, given the different approaches and samples used in the various studies,*” commented **Dr. Magali Taiel, MD**, Chief Medical Officer of GenSight Biologics and a co-author of the paper. “*The paper provides an extensive and exhaustive review of the literature and key insights in our knowledge of the disease.*”

The estimate of the rate of spontaneous recovery in the paper provides important context for the bilateral improvement observed in the pivotal trials RESCUE and REVERSE for GenSight Biologics’ lead product, LUMEVOQ®, a gene therapy for patients with LHON caused by a mutated *ND4* gene. In the trials, the rate of clinically meaningful improvement from nadir of at least 0.3LogMAR, or at least 3 lines on the Snellen chart, was 76% in REVERSE and 71% in RESCUE.

“*By reinforcing the insight that spontaneous recovery among LHON patients is rare, this new meta-analysis provides yet more support for bringing LUMEVOQ® to the market,*” said **Bernard Gilly**, Chief Executive

Officer of GenSight Biologics. *"We are eager to continue working with the authorities to provide a novel treatment to LHON patients."*

On the basis of the efficacy and safety demonstrated by its pivotal trials, other clinical and non-clinical data and an indirect comparison to natural history, LUMEVOQ®'s application for European marketing authorization was submitted in September 2020.

**\*About the article:**

**Visual Outcomes in Leber Hereditary Optic Neuropathy Patients with the m.11778G>A (MTND4) Mitochondrial DNA Mutation**

**Running Title:** Visual Function in m.11778G>A LHON Patients

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Dr. Newman, Dr. Carelli and Dr. Yu-Wai-Man are also primary investigators in RESCUE and REVERSE.

Abstract available online at:

[https://journals.lww.com/jneuro-ophthalmology/Abstract/9000/Visual\\_Outcomes\\_in\\_Leber\\_Hereditary\\_Optic.98886.aspx](https://journals.lww.com/jneuro-ophthalmology/Abstract/9000/Visual_Outcomes_in_Leber_Hereditary_Optic.98886.aspx)

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**About GenSight Biologics**

GenSight Biologics S.A. is a clinical-stage biopharma company focused on developing and commercializing innovative gene therapies for retinal neurodegenerative diseases and central nervous system disorders. GenSight Biologics' pipeline leverages two core technology platforms, the Mitochondrial Targeting Sequence (MTS) and optogenetics, to help preserve or restore vision in patients suffering from blinding retinal diseases. GenSight Biologics' lead product candidate, LUMEVOQ® (GS010; lenadogene nolparvovec), has been submitted for marketing approval in Europe for the treatment of Leber Hereditary Optic Neuropathy (LHON), a rare mitochondrial disease affecting primarily teens



and young adults that leads to irreversible blindness. Using its gene therapy-based approach, GenSight Biologics' product candidates are designed to be administered in a single treatment to each eye by intravitreal injection to offer patients a sustainable functional visual recovery.

#### **About Leber Hereditary Optic Neuropathy (LHON)**

Leber Hereditary Optic Neuropathy (LHON) is a rare maternally inherited mitochondrial genetic disease, characterized by the degeneration of retinal ganglion cells that results in brutal and irreversible vision loss that can lead to legal blindness, and mainly affects adolescents and young adults. LHON is associated with painless, sudden loss of central vision in the 1<sup>st</sup> eye, with the 2<sup>nd</sup> eye sequentially impaired. It is a symmetric disease with poor functional visual recovery. 97% of patients have bilateral involvement at less than one year of onset of vision loss, and in 25% of cases, vision loss occurs in both eyes simultaneously. The estimated incidence of LHON is approximately 800-1,200 new patients who lose their sight every year in the United States and the European Union.

#### **About LUMEVOQ® (GS010)**

LUMEVOQ® (GS010) targets Leber Hereditary Optic Neuropathy (LHON) by leveraging a mitochondrial targeting sequence (MTS) proprietary technology platform, arising from research conducted at the Institut de la Vision in Paris, which, when associated with the gene of interest, allows the platform to specifically address defects inside the mitochondria using an AAV vector (Adeno-Associated Virus). The gene of interest is transferred into the cell to be expressed and produces the functional protein, which will then be shuttled to the mitochondria through specific nucleotidic sequences in order to restore the missing or deficient mitochondrial function. "LUMEVOQ" was accepted as the invented name for GS010 (lenadogene nolparvovec) by the European Medicines Agency (EMA) in October 2018.