Press Release

GenSight Biologics Announces the Publication of a Review of Gene Therapy Trials for LHON in *International Ophthalmology Clinics*

- Bilateral treatment effect following unilateral injection of gene therapy for *ND4*-LHON was independently reported by three research groups
- LUMEVOQ® is the first gene therapy treating a mitochondrial disease for which marketing approval has been requested from the European Medicines Agency

Paris, France, October 6, 2021, 7:30 am CET – 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 that the peer-reviewed journal *International Ophthalmology Clinics* has published a review of current and past gene therapy clinical trials for the treatment of Leber hereditary optic neuropathy (LHON).

The paper*, published in the October issue of the *International Ophthalmology Clinics* under the title "Gene Therapies for the Treatment of Leber Hereditary Optic Neuropathy", discusses the trials and the outcomes available to date.

Three research groups have developed gene therapies for *ND4*-LHON, the most prevalent and severe genotype of LHON[a,b]: GenSight Biologics (one Phase I/II trial and three Phase III trials)[c,d,e], the Huazhong University of Science and Technology (one Phase I and one open-label trial) and the Bascom Palmer Eye Institute of the University of Miami (one Phase I/II trial). Only GenSight's gene therapy, LUMEVOQ®, has completed Phase III trials and reached the registration phase.

"The active research on gene therapies to treat LHON answers the acute need for a safe and effective treatment for patients confronting this blinding disease," said **Magali Taiel, MD**, Chief Medical Officer of GenSight Biologics. *"We at GenSight Biologics are excited to be at the forefront of these efforts, particularly in Europe where we are already in the registration phase, aiming to bring a therapeutic solution to these patients in 2022."*

Across these clinical trials and different clinical development programs, a sustained and clinically meaningful bilateral benefit was reported in a substantial proportion of *ND4* patients who were unilaterally treated, at rates that surpass the expected natural history of the disease.

"This invited review provides a global perspective on the current gene-based approaches developed to tackle this devastating disease and discusses the positive outcomes observed with LUMEVOQ during the recent trials, bringing hope to our patients", commented lead author **José-Alain Sahel, MD,** Distinguished Professor and Chairman of the Department of Ophthalmology at the University of Pittsburgh School of Medicine and UPMC (University of Pittsburgh Medical Center), USA; Co-founder of GenSight Biologics; and Founder of the *Institut de la Vision* (Sorbonne-Université/Inserm/CNRS), Paris, France, which developed and patented the Mitochondrial Targeted Sequence (MTS) technology used in LUMEVOQ®.

Safety data from all the trials so far indicate that intravitreal injection constitutes a safe and easy route of administration, avoiding the complications of sub-retinal surgery. All gene therapies investigated provide excellent systemic tolerability and mostly mild ocular side effects, responsive to conventional ophthalmologic treatments.

LUMEVOQ® is the first gene therapy treating a mitochondrial disease for which marketing approval has been requested from the European Medicines Agency; the application was submitted in September 2020.

The paper is available at https://pubmed.ncbi.nlm.nih.gov/34584057/.

***About the paper:**

Gene Therapies for the Treatment of Leber Hereditary Optic Neuropathy

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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 1st eye, with the 2nd 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; lenadogene nolparvovec)

LUMEVOQ® (GS010; lenadogene nolparvovec) 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.