

GenSight Biologics announces publication of positive safety data from Phase I/II trial of GS010 in the *JAMA Ophthalmology*

Intravitreal administration of GS010 in patients with LHON was safe and well tolerated

Paris, France, February 12, 2019, 7:30 a.m. CET – GenSight Biologics (Euronext: SIGHT, ISIN: FR0013183985, PEA-PME eligible), a biopharma company focused on discovering and developing innovative gene therapies for retinal neurodegenerative diseases and central nervous system disorders, today announced publication of detailed safety data from the Phase I/II clinical trial of GS010 in Leber Hereditary Optic Neuropathy (LHON) patients in the *Journal of the American Medical Association (JAMA) Ophthalmology*. This study demonstrates that GS010 (rAAV2/2-ND4) is both safe and well tolerated 2 years after a single unilateral intravitreal administration.

The study was an open-label single-center Phase I/II clinical trial that included 4 dose-escalation cohorts and an extension cohort. Fifteen subjects with LHON carrying the ND4-G11778A mutation were prospectively enrolled. Each subject received a single intravitreal injection of rAAV2/2-ND4 in the worse-seeing eye. The study design included an initial follow-up period of 48 weeks, followed by longer-term follow-up for an additional 4 years. The primary objective was to ascertain the safety and tolerability of escalating doses of rAAV2/2-ND4. Secondary objectives included bio-dissemination and immunogenicity of rAAV2/2-ND4 and evaluation of visual functions.

The analysis included 15 patients (mean [SD] age, 47.9 [17.2] years; 13 men and 2 women) enrolled in the 5 cohorts of the clinical trial. Thirteen patients experienced intraocular inflammation after rAAV2/2-ND4 administration. Mild anterior chamber inflammation and vitritis were reported at all doses, and all cases were responsive to treatment. A maximum ocular inflammation score (OIS) of 9.5 was observed in a patient with history of idiopathic uveitis. Overall, OIS was not associated with the viral dose administered. No neutralizing antibodies (NAbs) against AAV2 were detected in aqueous humor before treatment. Two patients tested positive for cellular immune response against AAV2 at baseline and after treatment. Humoral immune response was not associated with either the dose administered or with the immune status of patients at baseline. No association was found between OISs and serum NAbs titers.

Dr. Barrett Katz, Chief Medical Officer of GenSight, commented “*Our findings have implications for all gene therapies employing viral vectors that are administered intravitreally. The tolerability of our vector and safety of our drug offer further support for the application of this technology to future trials. This confirms our confidence in continuing this journey searching for answers in blinding diseases for which adequate treatment is wanting.*”

The publication entitled “*Immune Response and Intraocular Inflammation in Patients With Leber Hereditary Optic Neuropathy Treated With Intravitreal Injection of Recombinant Adeno-Associated Virus 2 Carrying the ND4 Gene: A Secondary Analysis of a Phase 1/2 Clinical Trial*” is available online at <https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2723597>.

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About GenSight Biologics

GenSight Biologics S.A. is a clinical-stage biopharma company focused on discovering and developing 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, GS010, is in Phase III trials in Leber Hereditary Optic Neuropathy (LHON), a rare mitochondrial disease that leads to irreversible blindness in teens and young adults. Using its gene therapy-based approach, GenSight Biologics' product candidates are designed to be administered in a single treatment to affected eyes by intravitreal injection to offer patients a sustainable functional visual recovery.

About GS010

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.

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 1,400 to 1,500 new patients who lose their sight every year in the United States and Europe.