Press Release

GenSight Biologics announces publication of positive data from Phase I/II trial and long-term follow-up of GS010 in *Ophthalmology*, the journal of the *American Academy of Ophthalmology*

- GS010 confirmed as safe and well tolerated 2 years after a single unilateral intravitreal injection
- Sustained improvement of visual acuity at 2 years of follow-up in LHON subjects with less than 2 years of visual loss prior to treatment

Paris, France, February 20, 2018, 7.30 am 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 results from the Phase I/II clinical trial and long-term follow-up of GS010 in Leber Hereditary Optic Neuropathy (LHON) patients in *Ophthalmology*, the journal of the *American Academy of Ophthalmology*. The study demonstrated that GS010 (rAAV2/2-ND4) is safe and well tolerated 2 years after a single unilateral intravitreal administration.

"This first-ever scientific publication of clinical data with GS010 is a major step forward for patients afflicted with LHON – a blinding disease affecting those in the prime of their life," commented **Dr. Catherine Vignal**, investigator of the study and Chief of the Department of Ophthalmology at the *Rothschild Foundation Hospital* in Paris. "*If these promising results are confirmed in the ongoing Phase III studies, GS010 would offer a meaningful and life changing therapy for those so afflicted and become the standard of care for LHON."*

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 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.

At week 96, there were no unexpected TEAEs, no serious adverse events related to the treatment or procedure, and no suspected unexpected serious adverse reactions. No deaths and no TEAEs leading to study discontinuation were reported. 94% of TEAEs were mild in intensity. The most frequent ocular TEAEs were intraocular inflammation and intraocular pressure (IOP) elevation. All ocular events resolved spontaneously or after appropriate therapy with IOP-lowering or anti-inflammatory therapy, except for 1 subject with ongoing mild vitritis (0.5+ vitreous cell, no vitreous haze, no treatment required at last visit), subsequently lost to follow-up but without documented worsening of vision. At week 96, no related TEAEs required ongoing treatment.

GenSight Biologics is currently conducting two Phase III clinical studies (RESCUE and REVERSE) in Europe and the United States to assess the efficacy of GS010 in subjects affected with LHON due to the *ND4* mutation, with vision loss up to one year at the time of treatment. Topline results at 48 weeks for REVERSE and RESCUE are expected in April 2018 and the third quarter of 2018, respectively.

The publication entitled "*Safety of rAAV2/2-ND4 Gene Therapy for Leber Hereditary Optic Neuropathy*" is available online (www.aaojournal.org/article/S0161-6420(17)33673-4/fulltext) and is *in press* for *Ophthalmology,* the journal of the *American Academy of Ophthalmology.*

Part of this data will also be presented at the *North American Neuro-Ophthalmology Society* (NANOS) conference in Big Island, Hawaii, March 3–8, 2018 and the *Association for Research in Vision and Ophthalmology* (ARVO) conference to be held in Honolulu, Hawaii, April 29 to May 3, 2018.

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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 each eye 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 works 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.

About RESCUE and REVERSE

RESCUE and REVERSE are two separate randomized, double-masked, sham-controlled pivotal Phase III trials designed to evaluate the efficacy of a single intravitreal injection of GS010 (rAAV2/2-ND4) in subjects affected by LHON due to the G11778A mutation in the mitochondrial *ND4* gene.

The primary endpoint will measure the difference in efficacy of GS010 in treated eyes compared to sham-treated eyes based on Best Corrected Visual Acuity (BCVA), as measured with the ETDRS at 48 weeks post-injection. The patients' LogMAR (Logarithm of the Minimal Angle of Resolution) scores, which are derived from the number of letters

patients read on the ETDRS chart, will be used for statistical purposes. Both trials have been adequately powered to evaluate a clinically relevant difference of at least 15 ETDRS letters between treated and untreated eyes adjusted to baseline.

The secondary endpoints will involve the application of the primary analysis to best seeing eyes that received GS010 compared to those receiving sham, and to worse seeing eyes that received GS010 compared to those that received sham. Additionally, a categorical evaluation with a responder analysis will be evaluated, including the proportion of patients who maintain vision (< ETDRS 15L loss), the proportion of patients who gain 15 ETDRS letters from baseline and the proportion of patients with Snellen acuity of >20/200. Complementary vision metrics will include automated visual fields, optical coherence tomography, and color and contrast sensitivity, in addition to quality of life scales, bio-dissemination and the time course of immune response.

The trials are conducted in parallel, in 37 subjects for REVERSE and 39 subjects for RESCUE, in 7 centers across the United States, the UK, France, Germany and Italy. Topline results of REVERSE at 48 weeks are expected in April 2018, while RESCUE is expected to read out in Q3 2018.

ClinicalTrials.gov Identifiers:
REVERSE: NCT02652780
RESCUE: NCT02652767