Press Release

GenSight Biologics to present new GS010 data at the 2019 Annual Meeting of the American Academy of Ophthalmology

Paris, France, October 8, 2019, 7.30 am CEST – 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, announced that the full top-line results from its REVERSE and RESCUE Phase III clinical trials of GS010, as well as new mechanistic data, were accepted for an oral presentation at the 2019 Annual Meeting of the American Academy of Ophthalmology in San Francisco, CA, October 12-15, 2019. Members of the management team will also present at several meetings prior to the conference.

The Future is Now: Leaders in Ocular Gene Therapy
October 9, 2019 – San Francisco (CA, USA)
Magali Taiel, MD, Chief Medical Officer, will present on October 9, 2019 at Hotel Nikko in San Francisco.

11th Annual Ophthalmology Innovation Summit (OIS) @AAO
October 9, 2019 – San Francisco (CA, USA)
Thomas Gidoin, Chief Financial Officer, will present on October 10, 2019 at Hilton San Francisco Union Square in San Francisco.

American Academy of Ophthalmology (AAO)
October 12-15, 2019 – San Francisco (CA, USA)
"Efficacy of rAAV2/2-ND4, an Investigational Gene Therapy for ND4 LHON: Top-line Results of Phase 3 Clinical Trial REVERSE" will be presented by **Patrick Yu-Wai Man, MD**, Senior Lecturer and Honorary Consultant Ophthalmologist at the University of Cambridge, Moorfields Eye Hospital, and the UCL Institute of Ophthalmology, London, United Kingdom (Investigator in REVERSE and RESCUE trials).

- *Oral Presentation*
- *Session: Neuro-Ophthalmology Original Papers*
- *Abstract Number: PA021*
- *Sunday, October 13, 2019, 3:00 - 3:07 pm PDT*

"The PIONEER Study: A Phase 1/2 Optogenetic Retinal Gene Therapy Clinical Trial for Non-syndromic RP" will be presented by **Simona Degli Esposti, MD**, Locum Research Consultant, NIHR Clinical Research Facility, Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom (Investigator in PIONEER trial).

- *ePoster Theater Presentation*
- *Session: Retina, Vitreous*
- *Abstract Number: PO396*
- *Sunday, October 13, 2019, 5:10 pm PDT*

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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 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 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. Readouts for these endpoints are at 48, 72 and 96 weeks after injection.

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. Week 96 results were reported in 2019 for both trials, after which patients were transferred to a long-term follow-up study that will last for three years.

ClinicalTrials.gov Identifiers:
REVERSE: NCT02652780
RESCUE: NCT02652767

About REFLECT

REFLECT is a multi-center, randomized, double-masked, placebo-controlled study to evaluate the safety and efficacy of bilateral injections of GS010 in subjects with LHON due to the NADH dehydrogenase 4 (*ND4*) mutation.

The trial planned to enroll 90 patients with vision loss up to 1 year in duration and will be conducted in multiple centers in Europe and in the US.

In the active arm, GS010 will be administered as a single intravitreal injection to both eyes of each subject. In the placebo arm, GS010 will be administered as a single intravitreal injection to the first affected eye, while the fellow eye will receive a placebo injection.

The primary endpoint for the REFLECT trial is the BCVA reported in LogMAR at 1-Year post-treatment in the second-affected/not-yet-affected eye. The change from baseline in second-affected/not-yet-affected eyes receiving GS010 and placebo will be the primary response of interest. The secondary efficacy endpoints include: BCVA reported in LogMAR at 2-Years post-treatment in the second-affected/not-yet-affected eye compared to both placebo and the first-affected eye receiving GS010, OCT and contrast sensitivity and quality of life scales. The first subject was treated in March 2018, and enrolment was completed in July 2019, ahead of schedule.

ClinicalTrials.gov Identifiers:
REFLECT: NCT03293524

About GS030

GS030 leverages GenSight's optogenetics technology platform, a novel approach to restore vision in patients by using gene therapy to introduce a gene encoding for a light-sensitive protein into specifically targeted cells of the retina by a single injection, thereby making them responsive to light. An external wearable medical device to specifically stimulate the transduced cells is developed to amplify the light signal and further enable vision. Patients will need to wear the external wearable device to enable optimal restoration of visual function. Using this optogenetics technology platform, and with the support of the Vision Institute in Paris and the team of Dr. Botond Roska at the Friedrich Miescher Institute in Basel, GenSight is developing its second product candidate, GS030, to restore vision in patients suffering from Retinitis Pigmentosa, or RP. GenSight's optogenetics technology platform is independent of the specific genetic mutations that lead to this family of disease. It is expected that GS030 would benefit patients from the early stages of RP. This technology offers the possibility of application to other diseases of the retina where photoreceptors have degenerated, and may be transferable to the dry form of Age Related Macular Degeneration (dry-AMD).