Press Release

Key Opinion Leaders highlight GS010 efficacy and patient benefits in discussion of findings from REVERSE Phase III clinical trial

- Preservation of anatomic structures combined with visual function improvement (contrast sensitivity) demonstrate neuro-protection in human genetic disease
- Bilateral improvement deemed clinically relevant and not the result of placebo effect or natural history
- GenSight committed to push GS010 through regulatory approval in Europe and the United States as planned

Paris, France, June 20, 2018, 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, today reported key highlights from its recent Key Opinion Leader (KOL) Event hosted in New York City on June 12 and dedicated to GS010 and the REVERSE Phase III clinical trial in the treatment of Leber Hereditary Optic Neuropathy (LHON).

The panel of medical experts included **Nancy J. Newman, MD**[1], **Robert C. Sergott, MD**[2], **Mark Moster, MD**[3], and **José-Alain Sahel, MD**[4]. In addition, **Lissa Poincenot**, LHON patient advocate and mother of an LHON patient, presented the patient perspective on the results.

"This is revolutionary work that is being done," said Dr. Sergott, who presented the study's key findings. *"We are witnessing the best of translational, precision medicine."* The topline findings on Spectral-Domain Optical Coherence Tomography (SD-OCT) parameters are "***the first demonstrations of neuro-protection of neurons and of central nervous system axons in a human genetic disease,"*** according to Dr. Sergott.

Neuro-protection is an important outcome for LHON, a disease that in her disease overview, Dr. Newman had characterized as *"a disease in motion"* that inexorably resulted in bilateral vision loss in 97% of cases within a year of onset.

The evidence that GS010 engaged its biologic targets was coupled with a functional outcome. Low-contrast sensitivity, measured using the Pelli-Robson chart, almost doubled in the GS010-treated eyes compared to sham-treated eyes. Dr. Sergott noted that low-contrast sensitivity is a better indicator of real-life visual function than the more widely-used measure of visual acuity, which is based on the number of letters that can be read on a Snellen chart and which measures high-contrast sensitivity. He added: ***"LHON patients treated with GS010 have a statistically significant improvement in their ability to***

[1] Director, Neuro-Ophthalmology, and LeoDelle Jolley Professor of Ophthalmology, Emory University School of Medicine, Atlanta, GA
[2] Director, Neuro-Ophthalmology, Wills Eye Hospital; Director, William H. Annesley, Jr, EyeBrain Center, and Professor of Neurology and Ophthalmology at Thomas Jefferson University, Philadelphia, PA
[3] Neuro-Ophthalmology, Wills Eye Hospital and Professor of Neurology and Ophthalmology at Thomas Jefferson University, Philadelphia, PA
[4] Director of the Institut de la Vision (Sorbonne-Université/Inserm/CNRS), Paris; Chairman of the Department of Ophthalmology at Centre Hospitalier National d'Ophtalmologie des XV-XX, Paris; Professor and Chairman of the Department of Ophthalmology at University of Pittsburgh School of Medicine and UPMC (University of Pittsburgh Medical Center)

discern subtle shades of gray, a very precise measure of visual function, the ability to see better in low light environments that approximate real life conditions, both indoors and outdoors."

For Dr. Sergott, REVERSE results combined for the first time *"*evidence on *preserved retinal anatomy with evidence on improved visual function"*:

- At week 48, there was a statistically significant difference (p = 0.0189) between the change in retinal ganglion cell macular volume measured from baseline compared to all sham-treated eyes, with untreated eyes losing 0.038 cubic mm of macular ganglion cell volume while treated eyes preserved their ganglion cell volume (-0.003 cubic mm).
- In terms of the change in thickness of the temporal quadrant of the retinal nerve fiber layer from baseline to week 48, the trial demonstrated a large statistically significant difference (p = 0.0359) between all GS010-treated eyes and all sham-treated eyes, with untreated eyes showing a loss of 3.4 µm while treated eyes showed a limited loss of 0.6 µm.
- At week 48, GS010 treated eyes gained on average +0.20 LogCS, while the contrast sensitivity in sham-treated eyes remained stable (+0.08 LogCS on average). This difference was statistically significant, with a p-value of p = 0.0220.

Dr. Sergott acknowledged the topline finding that, at 48 weeks, there was no statistical difference between GS010-treated and sham-treated eyes in terms of improvement in high-contrast visual acuity, as measured by logMAR acuity. However, he pointed out that the timing and magnitude of the observed improvement in each eye were at odds with known facts of LHON natural history.

Dr. Moster, after reviewing published literature on the disease's natural history, had remarked, ***"Spontaneous recovery can occur, but only in a small subset of patients. And among the mutations that cause LHON, this phenomenon is rarest among patients with the 11778 mutation, which is the one targeted by GS010."*** He further highlighted that the instances of recovery tended to occur more than 20 months after vision is lost.

Dr. Sergott further asserted, *"It is a fallacy to consider the bilateral improvement a placebo effect."* In his discussion, Dr. Sahel explained that while a definitive explanation for the bilateral effect is still lacking, a number of hypotheses can be advanced based on observations in other disease areas and on animal models of ocular injury. Improvement in the contralateral eye is not without scientific precedent.

Dr. Sergott shared trends from *post hoc* analyses that, consistent with the progressive nature of LHON, support the notion that earlier intervention resulted in better clinical outcomes:

- Subjects who entered study with better vision (on-chart eyes) tended to have better clinical outcomes. At week 48, in on-chart best-seeing eyes, GS010-treated eyes gained on average +12 ETDRS letters (-0.236 LogMAR) compared to +4 ETDRS letters (-0.075 LogMAR) in sham-treated eyes.
- Subjects whose vision loss was less than 9 months tended to have better clinical outcomes. 75% of GS010-treated eyes that showed a trend in visual acuity improvement at week 48 had vision loss for less than 9 months at time of treatment administration.
- Subjects who were younger (< 21 years) at enrollment tended to have better clinical outcomes.
- The proportion of subjects who achieved a large improvement in visual acuity (0.5 logMar, 25 ETDRS letters) was higher than in sham-treated eyes.

"In my opinion, LHON is a genetic emergency," Dr. Sergott concluded.

In the panel discussion that followed, the medical experts were asked to interpret what the two-line visual acuity improvement observed in both eyes meant to patients. Dr. Newman cautioned against overemphasizing quantitative measures that may understate the actual improvement in patients' quality of life. *"There is good work being done on more meaningful measurement of the functional impact of improved central acuity for LHON patients, but these measures have yet to be discussed and agreed with authorities,"* said Dr. Newman. *"Ultimately, it's up to the patients to decide what a two-line improvement means; we should listen to them."* Ms. Poincenot echoed this assessment: ***"For patients, slight differences mean a lot in day-to-day life. A little improvement can translate into making life easier."***

Bernard Gilly, co-founder and CEO of GenSight, reaffirmed GenSight's push to bring GS010 to market. ***"We are committed to working with the relevant authorities to bring this product to the approval stage as soon as possible,"*** he said. Aiming to maintain its plan to submit dossiers to the FDA and EMA in Q2 2019, the company is scheduling consultations with those agencies to discuss REVERSE results and trends. These discussions will help frame the results from RESCUE, which will be available in October this year, and inform potential refinements to the design of REFLECT, which has begun patient recruitment.

The presentation is available in replay on the Company's website at https://www.gensight-biologics.com/2018/05/21/gensight-biologics-to-host-kol-event-on-june-12-2018/.

Contacts

GenSight Biologics
Thomas Gidoin
Chief Financial Officer
tgidoin@gensight-biologics.com
+33 (0)1 76 21 72 20

RooneyPartners
Media Relations
Marion Janic
mjanic@rooneyco.com
+1-212-223-4017

The Trout Group
US Investor Relations
Chad Rubin
crubin@troutgroup.com
+1-646-378-2947

James Palmer
Europe Investor Relations
j.palmer@orpheonfinance.com
+33 7 60 92 77 74

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 RESCUE at 48 weeks are expected in Q3 2018.

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 is 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, color and contrast sensitivity and quality of life scales. The first subject was treated in March 2018.

ClinicalTrials.gov Identifiers:
REFLECT: NCT03293524