Press Release

GenSight Biologics provides an update on the clinical and regulatory pathways for GS010

- Additional Week 72 (18-month) data point for REVERSE expected in early Q4 2018
- RESCUE topline results now expected in early Q1 2019 due to minor amendments in the Statistical Analysis Plan
- Filing for marketing authorization still expected in 2019 in Europe and 2020 in the US

Paris, France, September 13, 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 provided an update on the clinical and regulatory pathways for GS010, its gene therapy product currently in Phase III clinical development for the treatment of Leber Hereditary Optic Neuropathy (LHON). The revised regulatory pathway incorporates the findings of the REVERSE (CLIN03B) clinical trial, key results of which were announced in June this year.

The REVERSE trial is a randomized, double-masked, sham-controlled pivotal Phase III trial designed to evaluate the efficacy of a single intravitreal injection of GS010 (rAAV2/2-*ND4*) in subjects who were six to twelve months from initial onset of vision loss caused by LHON due to the G11778A mutation in the mitochondrial *ND4* gene. Subjects experienced an unexpected bilateral improvement – in both GS010-treated eyes as well as sham-treated eyes - in Best Corrected Visual Acuity (BCVA), as measured with the ETDRS chart at 48 weeks post-injection. Because of the unforeseen improvement seen in sham-treated eyes, the trial did not meet its primary efficacy endpoint. However, positive outcomes on secondary endpoints of both anatomic and visual functional measures demonstrated GS010's treatment effect.

- At Week 48, GS010-treated eyes demonstrated preserved ganglion cell volume whereas sham-treated eyes lost macular ganglion cell volume; the difference was statistically significant.
- Likewise, GS010-treated eyes demonstrated preserved retinal nerve fiber layer (NFL) while sham-treated eyes experienced a loss of NFL; the difference in the thickness of the temporal quadrant of the retinal nerve fiber layer at Week 48 was statistically significant.
- At Week 48, GS010-treated eyes showed improved visual function of contrast sensitivity (CS) as measured via Pelli-Robson testing. Sham-treated eyes showed no improvement of visual function, with their CS remaining stable; the difference was statistically significant.
- Post-hoc exploratory analyses also suggested subjects with less severe vision loss may benefit most from GS010.

The unexpected results on BCVA highlighted the importance of gaining more insights into the results observed at Week 48 by obtaining an earlier readout prior to the planned Week 96 analysis. GenSight has therefore added a Week 72 (18-month) readout to planned post-hoc analyses. This readout is expected in early Q4 of this year.

The REVERSE findings have been incorporated in ongoing discussions with regulatory authorities, particularly with the European Medicines Agency (EMA), for whom the REVERSE trial is one of two pivotal trials for GS010. The REVERSE Advisory Panel of Key Opinion Leaders has been discussing the findings ahead of a protocol assistance follow-up meeting with the EMA, which is scheduled in Q4 of this year. Protocol assistance is a special form of scientific advice provided by EMA to companies developing

designated orphan medicines for rare diseases. Final advice from EMA arising from the Q4 meeting is expected in early Q1 2019.

The REVERSE findings have also led GenSight to incorporate additional analyses into the statistical analysis plan (SAP) of RESCUE, the second Phase III trial considered pivotal by the EMA. RESCUE enrolled subjects up to six months from onset of visual loss, but otherwise identical disease and demographics enrollment criteria as those in REVERSE. The company conducted a thorough regulatory and clinical assessment of the option of amending the primary efficacy endpoint of RESCUE to CS but concluded that, based on consultations with the EMA and with experts, the expected benefit from such an amendment did not outweigh the risks associated with delaying GS010's application for marketing authorization. Topline RESCUE results are now expected in early Q1 2019, with full results in mid-Q1.

All findings will be included in discussions with both EMA and the US Food and Drug Administration (FDA) planned for Q1 next year. The FDA discussions will also feature updates on REFLECT, the third Phase III trial for GS010, which is covered by a Special Protocol Assessment (SPA) with the FDA. The company is currently evaluating options for investigating the bilateral improvement, observed in REVERSE, with an additional supportive ancillary study.

The topline and full results of REVERSE at Week 96 are expected in Q2 next year, providing a fuller picture of the benefits of GS010 for patients up to a year from initial visual loss. Based on ongoing discussions with the EMA, the company is targeting submission for European marketing authorization in Q4 2019. Based on the SPA and interim results of REFLECT, BLA submission in the US is targeted for H2 2020.

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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 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 early Q1 2019.

ClinicalTrials.gov Identifiers:
REVERSE: NCT02652780
RESCUE: NCT02652767