GenSight Biologics Enrolls First Patient in Pivotal Phase III Program of GS010 in Leber's Hereditary Optic Neuropathy

Paris, France, February 29, 2016 – GenSight Biologics S.A. (**GenSight**), a clinical-stage biotechnology company discovering and developing novel gene therapies for neurodegenerative retinal diseases, and in the future, of the central nervous system**,** today announced enrollment of the first patient in both RESCUE and REVERSE, two parallel pivotal Phase III trials with the Company's lead product candidate GS010 for the treatment of Leber's Hereditary Optic Neuropathy (LHON).

Bernard Gilly, PhD, Chairman & Chief Executive Officer of GenSight, commented: *"With the first patient recruited, we are now entering the last mile of GS010's development, which we hope will demonstrate GS010's ability to durably stop, if not restore, the brutal vision loss caused by LHON. GenSight continues to deliver on its strategy to develop novel approaches against blinding diseases."*

The pivotal trials are intended to determine whether GS010 can halt or reverse vision loss associated with LHON due to the NADH dehydrogenase 4 (ND4) mutation or be effective as prophylaxis for vision loss in an eye not yet affected. The trials will also seek to identify the therapeutic window of opportunity for treatment after onset of disease.

As early intervention is potentially a major factor in maximizing therapeutic success, the two clinical trials will focus on treating patients who have manifested visual decline for up to one year. RESCUE is expected to enroll 36 patients with an onset of vision loss up to 6 months in duration, while REVERSE is expected to enroll 36 patients with an onset of vision loss ranging from 7 to 12 months in duration.

GS010 will be administered as a single intravitreal injection to one eye of each subject, while the fellow eye will receive a sham procedure. At the end of the initial 48-week study period, a minimal three-year long term follow-up period will be initiated to determine the sustainability of efficacy outcomes and long-term safety of treatment.

Dr. Alfredo A. Sadun, MD, PhD, Doheny Eye Institute, UCLA Department of Ophthalmology, Pasadena, California (USA), commented: "*After three decades of study, I'm thrilled that we have reached this point where we may be able to offer effective treatment in LHON. We now have good reason to hope for a solution to this devastating bilateral cause of congenital blindness in young adults."*

Pr. José-Alain Sahel, MD, PhD, Director of the Institut de la Vision, Paris, Chairman of the Department of Ophthalmology at Centre Hospitalier National d'Ophtalmologie des XV-XX, Paris, and co-founder of GenSight added: "*We are eager to start enrolling European patients in the next few weeks in this first ever efficacy trial in LHON."*

The first patient in the entire program was injected at the Doheny Eye Institute, UCLA Department of Ophthalmology, Pasadena, California (USA) as part of the REVERSE trial, while the first RESCUE trial patient was injected at Wills Eye Hospital, Philadelphia, Pennsylvania (USA).

The trials will be conducted in parallel in 7 centers across the United States, the UK, France, Germany and Italy. European sites will open in the coming weeks upon final approval of regulatory agencies.

Topline results at 48 weeks are expected by the end of 2017.

More information

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' Log of the Minimal Angle of Resolution, or LogMAR, scores, which are derived from the number of letters they 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.

ClinicalTrials.gov Identifiers:
REVERSE: NCT02652780
RESCUE: NCT02652767

About Leber's Hereditary Optic Neuropathy (LHON)

LHON is a maternally-inherited genetic disease that causes the onset of irreversible and severe loss of sight leading to blindness and disability in teens and young adults. LHON greatly alters the patient's ability to perform daily life activities, reduces their autonomy and, in particular, affects their ability to read, drive and recognize facial features and expressions. The quality of life of patients with LHON is generally poor. LHON is estimated to affect approximately 1,400 to 1,500 new patients who lose their sight every year in the United States and Europe.

LHON is caused by defects in mitochondrial genes encoding for proteins called NADH dehydrogenase. These proteins are part of a large enzyme complex responsible for driving the production of adenosine triphosphate (ATP), which is the main source of energy within the cell. Three different genes encoding for four NADH dehydrogenases have been linked to LHON and are considered to be the primary mutations for the disease to manifest. The ND4 mutation accounts for over 75% of them.

About GenSight Biologics

GenSight Biologics S.A. (**GenSight**) is a clinical-stage biotechnology company discovering and developing novel therapies for neurodegenerative retinal diseases, and in the future, of the central nervous system. GenSight's pipeline leverages two core technology platforms, Mitochondrial Targeting Sequence (MTS) and optogenetics, to help preserve or restore vision in patients suffering from severe retinal diseases. GenSight's lead product, GS010, is in pivotal Phase III trials in Leber's Hereditary Optic Neuropathy (LHON), a rare mitochondrial disease that leads to irreversible sight loss in teens and young adults. Using its gene therapy-based approach, GenSight's product candidates are designed to be administered in a

single treatment to each eye by intravitreal injection in order to provide patients with a long-lasting functional cure, potentially for the rest of their lives.

For more information: www.gensight-biologics.com

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