Press Release

GenSight Biologics Announces 1 Year Safety data and Efficacy signals from PIONEER Phase I/II Clinical Trial of GS030, an Optogenetic Treatment Candidate for Retinitis Pigmentosa

- GS030 is safe and well tolerated for at least 1 year after injection at all tested doses
- Encouraging efficacy signals observed in some patients
- Ongoing recruitment of GS030 extension cohort at the highest dose of 5e11 vg per eye

Paris, France, February 13, 2023, 7:30 am CET – GenSight Biologics (Euronext: SIGHT, ISIN: FR0013183985, PEA-PME eligible), a biopharma company focused on developing and commercializing innovative gene therapies for retinal neurodegenerative diseases and central nervous system disorders, today announced favorable safety data and encouraging efficacy signals at 1 year post-gene therapy administration for the PIONEER Phase I/II clinical trial evaluating GS030 for the treatment of retinitis pigmentosa (RP) in 9 patients, with a follow-up up to 4 years (n=1).

"While the primary endpoint of the study is safety and tolerability at 1 year after gene therapy administration, we have patients that are followed much longer and have already reached 3 and even 4 years post-injection, which continue to show good tolerability and safety," commented **Élise Boulanger-Scemama, MD**, Adolphe de Rothschild Foundation Hospital, Clinical Investigation Center CHNO des 15-20 and investigator of PIONEER. *"Those results for GS030 are particularly encouraging and could bring back hope for patients suffering from end-stage RP with currently no therapeutic solution."*

RP is a genetic blinding disease that affects between 15,000 and 20,000 new patients each year in the US and the EU for which there is currently no treatment. PIONEER is a first-in-human, multi-center, open-label dose escalation clinical trial evaluating the safety and tolerability of GS030, an optogenetic treatment candidate combining an AAV2-based gene therapy (GS030-DP) with the use of light-stimulating goggles (GS030-MD) in patients with end-stage RP. This therapeutic approach is independent of the causal mutation and therefore applicable to potentially all patients suffering from end-stage RP.

Three cohorts of three patients each were administered one of three doses of GS030-DP (5e10 vg; 1.5e11 vg; 5e11 vg) via a single intravitreal injection in their worst affected eye (i.e., the least-seeing eye). A Data Safety Monitoring Board (DSMB) reviewed the safety data of all treated subjects in each cohort and made recommendations before the extension cohort was enrolled. Based on the good safety profile of GS030, the DSMB recommended selecting the highest dose (5e11 vg) for the extension cohort where patients are currently being recruited.

The safety and tolerability results in the first three completed cohorts recorded only mild and moderate (grade 1 and 2) ocular adverse events (AEs) but no severe (grade 3) AEs, with a follow-up up to 4 years (n=1). The most common ocular AEs were mild intraocular inflammation responsive to corticosteroid treatment. Intraocular inflammation occurred in 70% of patients and resolved without sequalae in all patients.

The first use of GS030-MD was performed 8 weeks after injection under medical supervision and the light-stimulating goggles were well tolerated. Subjects performed multiple training sessions in parallel to scheduled study visits.

The patients from the highest dose cohort have reached 1-year post-gene therapy administration, enabling the assessment of efficacy signals at one year for the 3 cohorts. Encouraging signs of efficacy at 1 year were demonstrated in some patients after GS030 optogenetic treatment with a vision that improved from being barely able to perceive light before treatment to being able to locate and count objects, with the best results at the highest dose.

"Retinitis pigmentosa is the most frequent blinding genetic disorder for which there is currently no treatment. The safety data and early efficacy signals from our PIONEER trial are highly encouraging and suggest that our optogenetic treatment candidate could offer hope to the many patients affected," said **Bernard Gilly,** Co-Founder and Chief Executive Officer of GenSight Biologics. *" We are looking forward to further data from the extension cohort that is under recruitment and expect then to move GS030 to efficacy trials."*

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About GenSight Biologics

GenSight Biologics S.A. is a clinical-stage biopharma company focused on developing and commercializing 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, LUMEVOQ® (GS010; lenadogene nolparvovec), is an investigational compound and has not been registered in any country at this stage; a marketing authorization application is currently under review by the EMA for the treatment of Leber Hereditary Optic Neuropathy (LHON), a rare mitochondrial disease affecting primarily teens and young adults that leads to irreversible blindness. 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 GS030

GS030 leverages GenSight Biololgics' optogenetics technology platform, a novel approach to restore vision in blind patients using a combination of ocular gene therapy and tailored light-activation of treated retinal cells. The gene therapy, which is delivered via a single intravitreal injection, introduces a gene encoding for a light-sensitive protein (ChrimsonR-tdT) into retinal ganglion cells, making them responsive to light and bypassing photoreceptors killed off by diseases such as retinitis pigmentosa (RP). Because ChrimsonR-tdT is activated by high intensities of amber light, a wearable medical device is needed to stimulate the treated retina. The optronic light-stimulating goggles (GS030-MD) encode the visual scene in real-time and project a light beam with a specific wavelength and intensity onto the treated retina. Treatment with GS030 requires patients to wear the external wearable device in order to enable restoration of their visual function. With the support of the *Institut de la Vision* in Paris and the team of Dr. Botond Roska at the Friedrich Miescher Institute in Basel, GenSight is investigating GS030 as therapy to restore vision in patients suffering from late-stage RP. GenSight's optogenetics approach is independent of the specific genetic mutations causing blindness and has potential applications in other diseases of the retina in which photoreceptors degenerate, like dry age-related macular degeneration (dry-AMD). GS030 is an investigational compound and has been granted Orphan Drug Designation in the United States and Europe; GS030 is not approved by any regulatory authority in any country.

About Optogenetics

Optogenetics is a biological technique that involves the transfer of a gene encoding for a light sensitive protein to cause neuronal cells to respond to light stimulation. As a neuromodulation method, it can be used to modify or control the activities of individual neurons in living tissue and even in-vivo, with a very high spatial and temporal resolution. Optogenetics combines (1) the use of gene therapy methods to transfer a gene into target neurons with (2) the use of optics and electronics (optronics) to deliver the light to the transduced cells. Optogenetics holds clinical promise in the field of vision impairment or degenerative neurological disorders.

About Retinitis Pigmentosa

Retinitis pigmentosa (RP) is a family of orphan genetic diseases caused by multiple mutations in numerous genes involved in the visual cycle. Over 100 genetic defects have been implicated. RP patients generally begin experiencing vision loss in their young adult years, with progression to blindness by age 40. RP is the most widespread hereditary cause of blindness in developed nations, with a prevalence of about 1.5 million people throughout the world. In Europe and the United States, about 350,000 to 400,000 patients suffer from RP, and every year between 15,000 and 20,000 new patients with RP lose sight. There is currently no curative treatment for RP.

About the PIONEER Phase I/II trial

PIONEER (NCT03326336) is a first-in-man, multi-center, open label dose-escalation study to evaluate the safety and tolerability of GS030 in 12-18 subjects with late-stage retinitis pigmentosa. GS030 combines a gene therapy (GS030-DP) administered via a single intravitreal injection with a wearable optronic visual stimulation device (GS030-MD). Eligible patients in the first three cohorts are those affected by end-stage non-syndromic RP with no light perception (NLP) or light perception (LP) levels of visual acuity. The extension cohort will include patients with hand motion (HM) and counting fingers (CF) levels of visual acuity.

Three cohorts of three patients each were administered one of three doses of GS030-DP (5e10 vg; 1.5e11 vg; 5e11 vg) via a single intravitreal injection in their worst affected eye (i.e., the least-seeing eye). A Data Safety Monitoring Board (DSMB) reviewed the safety data of all treated subjects in each cohort and made recommendations before the extension cohort was enrolled. Based on the good safety profile of GS030, the DSMB recommended selecting the highest dose (5e11 vg) for the extension cohort, where patients are currently being recruited. The primary outcome analyses are on the safety and tolerability with a follow up to 5-year post-injection. PIONEER is being conducted in three centers in the United Kingdom, France and the United States.