Press Release

GenSight Biologics Announces Positive Data Safety Monitoring Board Review of PIONEER Phase I/II Clinical Trial of GS030 as Optogenetic Treatment for Retinitis Pigmentosa

- DSMB finds no safety issue for highest dose of GS030
- DSMB recommends selecting the highest dose (5e11 vg/eye) for extension cohort
- Recruitment of the extension cohort has been initiated

Paris, France, September 15, 2021, 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 that the independent Data Safety Monitoring Board (DSMB) completed its third safety review of the ongoing PIONEER Phase I/II clinical trial of GS030 combining AAV2-based gene therapy with optogenetics for the treatment of Retinitis Pigmentosa (RP).

The DSMB found no safety issue in the third cohort of patients, who received an intravitreal injection with the highest dose (5e11 vg) among the three cohorts studied to date, followed by the use of a wearable optronic visual stimulation device. Based on GS030's safety profile, the DSMB recommended selecting this dose for the extension cohort and using the protocol without any modification. Recruitment of this cohort has begun.

"The DSMB's confirmation of GS030's safety and tolerability gives us added confidence to use the highest dose in our upcoming investigations of GS030's efficacy," commented **Bernard Gilly**, Co-Founder and Chief Executive Officer of GenSight. *"This adds momentum to our pursuit of a treatment for retinitis pigmentosa patients."*

PIONEER is the Phase I/II first-in-human, multi-center, open-label dose-escalation clinical trial to evaluate the safety and tolerability of GS030 in subjects with late-stage RP. A total of 12 to 18 subjects are planned to be enrolled. Three cohorts with three subjects each were administered an increasing dose of GS030-DP (5e10 vg; 1.5e11 vg; 5e11 vg) via a single intravitreal injection in their worse-seeing eye. An extension cohort would then receive the highest tolerated dose. A Data Safety Monitoring Board (DSMB) reviewed the safety data of all treated subjects in each cohort and made recommendations before the next cohort was enrolled. The primary outcome analysis will be the safety and tolerability at one year post-injection.

Eligible patients in the first three cohorts were those affected by end-stage non-syndromic Retinitis Pigmentosa with no light perception (NLP) or light perception (LP) levels of visual acuity. The extension cohort will expand the inclusion criteria by recruiting patients with hand motion (HM) and counting fingers (CF) levels of visual acuity.

GS030 was granted Orphan Drug Designation in the United States and Europe. PIONEER is being conducted in three centers across the United Kingdom, France, and the United States.

A case report of a patient, who was treated with a low dose (5e10 vg) of the gene therapy and subsequently experienced visual recovery, was published in *Nature Medicine* in June 2021. Additional interim results may be released in Q4 2021, and results of all treated patients with one year follow-up data are expected in 2023.

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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), has been submitted for marketing approval in Europe 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 has been granted Orphan Drug Designation in the United States and Europe.

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 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.

As per protocol, three cohorts with three subjects each will be administered an increasing dose of GS030-DP via a single intravitreal injection in their worse-seeing eye. An extension cohort will receive the highest tolerated dose. The DSMB will review the safety data of all treated subjects in each cohort and will make recommendations before a new cohort receives the next dose. The primary outcome analyses will be on the safety and tolerability at one year post-injection. PIONEER is being conducted in three centers in the United Kingdom, France and the United States.