Press Release

GenSight Biologics Announces FDA Grant of Fast Track Designation for Optogenetic Therapy GS030 as Treatment for Retinitis Pigmentosa

Paris, France, October 12, 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 U.S. Food & Drug Administration (FDA) has granted Fast Track Designation to GS030, which combines AAV2-based gene therapy with optogenetics to treat Retinitis Pigmentosa (RP).

"The Fast Track designation granted by the FDA to GS030 highlights the significant unmet need for a safe and effective treatment of all forms of retinitis pigmentosa," commented **Bernard Gilly**, Co-Founder and Chief Executive Officer of GenSight. *"Following the publication of a promising first case report in Nature Medicine in June, and with more data from the PIONEER trial expected later this year, we are in a great position in our quest to provide a cutting-edge treatment for retinitis pigmentosa patients."*

Fast Track is a process intended to facilitate the development and expedite the review of drugs for the treatment of serious conditions where there is an unmet medical need. The purpose is to get important new drugs to the patient earlier. Drugs that receive Fast Track designation may be eligible for more frequent communications and meetings with FDA to discuss the drug's development plan, including the design of the proposed clinical trials, and ensure collection of appropriate data needed to support drug approval. Drugs with Fast Track designation may also qualify for Accelerated Approval, Priority Review or Rolling Review of New Drug Applications (NDA) or Biologic License Applications (BLA) if relevant criteria are met.

Optogenetic therapies combine cellular expression of light-sensitive opsins with light stimulation using a medical device. GS030 uses an optimized viral vector (GS030-DP) to express the light-sensitive opsin ChrimsonR in retinal ganglion cells and proprietary light-stimulating goggles (GS030-MD) to project the right wavelength and intensity of light onto the treated retina. Granted Orphan Drug Designation in the United States and Europe, GS030-DP is administered via an intravitreal injection.

PIONEER, a 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, 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. The Data Safety Monitoring Board recently recommended that the highest dose of the gene therapy (5e11 vg) be used for the extension cohort in the PIONEER trial. 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, and Fast Track designation by the U.S. Food & Drug Administration (FDA).

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 were administered an increasing dose of GS030-DP via a single intravitreal injection in their worse-seeing eye. The DSMB reviewed the safety data of all treated subjects in each cohort and made recommendations before a new cohort receives the next dose. The DSMB recommended selecting the highest dose (5e 11 vg/eye) for the extension cohort currently recruiting. 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.