Press Release

GenSight Biologics enrolls first subject in first-in-man PIONEER Phase I/II clinical trial of GS030 combining gene therapy and Optogenetics for the treatment of Retinitis Pigmentosa

Paris, France, October 26, 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 announced that the first subject was treated in the first-in-man PIONEER Phase I/II clinical trial of GS030 at the Moorfields Eye Hospital in London, United Kingdom.

"We are thrilled to see our second lead program, GS030, now entering the Clinic. This is a fantastic achievement for the team, and a promising step forward for patients. Optogenetics has been studied for years in research laboratories, and it bears a great clinical promise in fighting vision impairment and other degenerative sensorial and neurological disorders," commented **Bernard Gilly**, Co-founder and Chief Executive Officer of GenSight. *"GenSight continues to deliver on its strategy to develop novel approaches for treating and curing blinding diseases."*

PIONEER is a first-in-man, multi-center, open label dose-escalation study to evaluate the safety and tolerability of GS030 in 18 subjects with Retinitis Pigmentosa. GS030 combines a gene therapy (GS030-DP) administered via a single intravitreal injection with a wearable optronic visual stimulation device (GS030-MD).

GS030 is based on the Optogenetics technology platform developed by GenSight, which uses gene therapy to introduce a gene encoding for a light-sensitive protein into retinal ganglion cells by a single intravitreal injection, thereby making them responsive to light and bypassing destroyed photoreceptors.

Eligible patients in the first three cohorts will be those affected by end-stage non-syndromic Retinitis Pigmentosa with no light perception (NLP) or light perception (LP) level of visual acuity. The extension cohort will also include less severe patients, with hand motion (HM) and counting fingers (CF) levels of visual acuity.

As per protocol, three cohorts of three subjects each will be administered an increasing dose of GS030-DP via a single intravitreal injection in their worse affected eye. A fourth extension cohort will receive the highest tolerated dose. An independent Data Safety Monitoring Board (DSMB) will review safety data of all treated subjects in each cohort and make recommendations before moving to the next dose.

The primary outcome analysis will be the safety and tolerability at one-year post-injection.

"I am particularly pleased with this milestone because it potentially paves the way for a substantial improvement in the quality of sight and life of patients with RP. It is also a recognition of the quality of the collaboration between the team at the Vision Institute and GenSight," commented **Dr. José-Alain Sahel**, Director of the *Institut de la Vision* (Sorbonne-Université/Inserm/CNRS), Paris; Chairman of the Department of Ophthalmology at *Centre Hospitalier National d'Ophtalmologie des XV-XX*, Paris; Professor and Chairman of the Department of Ophthalmology at University of Pittsburgh School of Medicine and UPMC (University of Pittsburgh Medical Center).

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

GenSight expects to complete enrollment by the fourth quarter of 2019. Early findings for the first cohort are expected in the first half of 2019, and topline results for all subjects are expected in the fourth quarter of 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 GS030

GS030 leverages GenSight's optogenetics technology platform, a novel approach to restore vision in patients by using gene therapy to introduce a gene encoding for a light-sensitive protein into specifically targeted cells of the retina by a single injection, thereby making them responsive to light. An external wearable medical device to specifically stimulate the transduced cells is developed to amplify the light signal and further enable vision. Patients will need to wear the external wearable device to enable optimal restoration of visual function. Using this optogenetics technology platform, and with the support of the Vision Institute in Paris and the team of Dr. Botond Roska at the Friedrich Miescher Institute in Basel, GenSight is developing its second product candidate, GS030, to restore vision in patients suffering from Retinitis Pigmentosa, or RP. GenSight's optogenetics technology platform is independent of the specific genetic mutations that lead to this family of disease. It is expected that GS030 would benefit patients from the early stages of RP. This technology offers the possibility of application to other diseases of the retina where photoreceptors have degenerated, and may be transferable to the dry form of Age Related Macular Degeneration (dry-AMD).

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 result, it is a neuromodulation method that 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 the use of gene therapy methods to transfer a gene into target neurons with the use of optics and electronics (optronics) to deliver the light to the transduced cells. Optogenetics is widely used by research laboratories throughout the world and holds clinical promise in the field of vision impairment or degenerative neurological disorders.

About Retinitis Pigmentosa (RP)

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 existing curative treatment for RP.