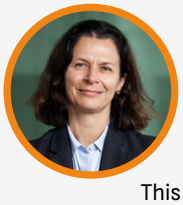
Shareholder Newsletter

October 2025

EDITORIAL



Dear Madam, Dear Sir,
Dear Shareholders,

We are delighted to reconnect with you this fall, which marks the beginning of ambitious projects that will be decisive for the future of our company.

This summer has been particularly productive for our team. In line with our commitments, we submitted, on August 11, 2025, the **dose-ranging study** requested by the ANSM. All documents required for validating this project are currently under review by the Agency and are progressing according to the regulatory timeline established under the European Clinical Trials Regulation. A regulatory decision regarding the clinical trial is expected before the end of 2025.

At the same time, we are successfully advancing the **technology transfer** with our new partner. The target timeline is being met, and the results obtained so far confirm this strategic choice. We are now approaching the final confirmation stage of the transfer. After this confirmation batch, we will move on to a GMP (Good Manufacturing Practice) production cycle. Ensuring a level of quality for our drug candidate GS010/Lumevoq® equivalent to that of the batches used in previous clinical trials is a key requirement for the submission and successful conduct of the RECOVER phase III trial.

In this issue, our Chief Medical Officer, Magali Taiel, presents the objectives and key milestones of the **RECOVER trial**, which has benefited, and will continue to benefit, from the feedback of both U.S. and European agencies. We remain fully committed to initiating RECOVER in the second half of 2026, subject to our obtaining the applicable regulatory approvals. We also wanted to share with you the regulatory steps required for securing approval for a **clinical trial** in France. Our Chief Regulatory & Quality Officer, Magali Gibou, will walk you through this demanding process.

We continue to execute our roadmap rigorously and remain focused on our primary goal: delivering innovative treatments to patients with unmet medical needs. We thank you for your continued trust and remain at your disposal to share operational information that matters the most to you.

Kind regards,

Laurence Rodriguez
CEO GenSight Biologics

NEWSFLOW

EVENTS AND PUBLICATIONS

Looking back

September 19-20, 2025

Congreso MitoSpain, Madrid, Spain

Dr. Magali Taiel, GenSight Biologics CMO

"Terapia Génica para LHON" (Gene therapy for LHON)

August 18-21, 2025

BioProcessing Summit: Filière Thérapie génique
17e Congrès Annuel
Scott Jeffers, GenSight Biologics CTO

Keynote Presentation: "Comparability Studies Following Process Change"

Looking forward

October 7-9, 2025

London, UK

October 9-11, 2025

Florence, Italy

October 17, 2025

Orlando, FL, USA

October 17-20, 2025

Ophthalmic Genetics Study Club 2025
Orlando, FL, USA

At the international congresses EVER and AAO, LHON experts Drs. Patrick Yu-Wai-Man, Valerio Carelli, Chiara La Morgia, Alfredo Sadun, Nancy Newman, Valérie Biousse, and Piero Barboni will present the latest data on the drug candidate GS010/Lumevoq®. In total, 6 presentations are scheduled at EVER and 3 presentations at AAO.

Financial Update

Strong Progress on Cost Management and Funding

We are pleased to announce the release of our half-year financial statements on September 29. The results demonstrate our continued success in reducing expenses to sustainable levels that support ongoing operations. Our Board approved these accounts on September 26, and our auditors have issued their reports.

We successfully raised €3.7 million on September 25 from three existing investors, including Heights and Invus. This funding round follows our €4.5 million private placement completed in early July, utilizing the same structure of shares and warrants, including pre-funded warrants.
These developments reinforce our commitment to financial discipline while securing the resources needed for continued growth.

Initial Public Offering	July 12, 2016	**Fiscal year-end date**	December 31
ISIN/Mnemonic code	FR0013183985/SIGHT	**Number of shares**	103.825.959 shares
Listing market	Euronext Paris – Compartiment C	**Liquidity agreement**	Oddo & Cie

The RECOVER Study

Magali Taiel
Chief Medical Officer

We are finalizing the protocol for the **RECOVER** phase III trial. Further interactions with European and U.S. regulatory agencies (EMA and FDA) will take place soon.

This pivotal study, designed with input from regulators, will, if successful, support global marketing authorization applications for our gene therapy, intended for patients with Leber Hereditary Optic Neuropathy (LHON) caused by the *ND4* mutation.

RECOVER

Study Objective

The RECOVER study evaluates the efficacy and safety of bilateral intravitreal injections of our drug candidate GS010 in patients with *ND4*-related LHON.

It is an international, multi-center, two-armed, double-blind, placebo-controlled Phase III trial.

Scientific Background

In all previous Phase III studies, bilateral improvement in visual acuity was observed in patients treated unilaterally. This prevented the achievement of the primary endpoint (a difference in the improvement of treated and untreated eyes) and suggested a contralateral therapeutic effect from the product.

Since then, experimental evidence of contralateral transfer of the gene therapy has emerged from studies in mice and monkeys, as well as from clinical data in treated patients, explaining the contralateral effect. These findings led to the design of the RECOVER trial, which includes a control arm of untreated patients (bilateral placebo) until the primary efficacy analysis and eliminates bias from interocular transfer (i.e., the improvement of visual acuity in the untreated contralateral eye that had been intended as the comparator).

Regulatory Compliance

The RECOVER trial must comply with EMA and FDA requirements, which mandate a control arm without active treatment.

Regulatory authorization in each country hosting an investigational site will be required, as will approval from ethics committees. As GS010 contains genetically modified organisms (GMOs), RECOVER is also subject to "GMO authorization" by national competent authorities.

RECOVER Study Details

Clinical data from 252 patients treated with GS010 in earlier development stages enabled the optimal design of RECOVER.

- Total patients: > 100 randomized into 2 treatment arms
  - 1 arm receiving GS010 in both eyes
  - 1 arm receiving placebo in both eyes
- Population: Patients with ND4-related LHON, aged 15+
- Primary endpoint: Visual acuity 1.5 years post-treatment
- Follow-up: Long-term monitoring, as is standard for gene therapy studies
- Note: Patients in the placebo arm will be treated with GS010 when the primary efficacy endpoint outcome is achieved.
- The clinical trial is expected to start in the second half of 2026, subject to our obtaining the applicable regulatory approvals.

Regulatory Update

What are the regulatory steps for a clinical trial in France?

Magali Gibou
Chief Regulatory & Quality Officer

In France, clinical trials are governed by the **Public Health Code** and by **European Regulation (EU) No. 536/2014**, applicable in all EU member states and to all clinical trials as of January 31, 2025.

After **drafting the protocol** and all documents required to conduct the clinical trial, the sponsoring company must submit a single authorization application via the CTIS submission portal (the European platform that centralizes all clinical trial information), comprising a scientific section (Part I), assessed by the competent authority (ANSM), and a national Part II covering the ethical and data-protection aspects of the trial, in accordance with national requirements.

The Part I **assessment** consists of reviewing the general scientific documentation, notably the expected therapeutic benefits, the risks and inconveniences for participants, the requirements relating to manufacturing, importation and labeling, as well as the contents of the investigator's brochure.

The Part II assessment consists of reviewing the country-specific dossier, including the ethics committee. Reviewers from the ANSM and the ethics committee examine the procedures for recruiting participants and obtaining informed consent, the financial aspects of the study, the protection of personal data, the qualifications of the investigators (the physicians overseeing the conduct of the study), the suitability of the clinical sites to conduct the trial, compensation for harm (sponsor insurance), as well as the management and use of participants' biological samples.

During the assessment, the Agency and/or the ethics committee may request additional information from the sponsor, which must be provided within a predefined timeframe. At the end of the assessment, a single decision, taking into account the conclusions of the assessments of Parts I and II, is transmitted to the sponsor via CTIS. The decision may be an authorization, an authorization with conditions, or a refusal to allow conduct of the clinical trial.

The regulatory procedure governing the use of an investigational medicinal product containing GMOs, such as GS010/Lumevoq®, in a clinical trial is overseen by the ANSM and consists of a notification or an application for authorization for restricted use of the GMO, depending on the containment level required. The notification of restricted use of GS010 (containment class 1) for the "dose-ranging" study was submitted on August 12, 2025; the ANSM acknowledgment of receipt was received on August 19, 2025.

The **clinical trial** may begin once all these conditions are met: all regulatory authorizations have been granted; the product has obtained pharmaceutical release; an agreement has been signed between the sponsor and the clinical sites; full documentation and logistics have been put in place at the clinical sites; and all study personnel have been trained.

Enrollment of participants in the study is subject to the signing of informed consent and verification of their eligibility against the study's inclusion and exclusion criteria.

During the conduct of the clinical trial, the sponsor must fulfill certain regulatory obligations. In particular, the sponsor must ensure that the study is conducted in accordance with the approved protocol and the principles of Good Clinical Practice. The study data must be collected, processed and stored so that they can be accurately reported, interpreted and verified while maintaining the confidentiality of records and protecting personal data. Finally, the sponsor must monitor the safety of the investigational medicinal product in use—collect and analyze adverse events occurring during the study; and report serious and unexpected adverse reactions to the health authorities: this is pharmacovigilance.

After the last visit of the last patient included in the study, the **sponsor is required to declare the end of the study to the ANSM and to the ethics committee(s)**. A summary of the trial results needs to be submitted within one year from the end of the study via the CTIS portal.

The sponsor must archive and maintain the quality of all documents relating to the trial for **25 years**. Participants' medical records may be retained longer, in accordance with national requirements.

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