Press Release

Sensorion Reports New Positive Clinical Results Presented at the World Congress of Audiology

- **Sensorion reported positive initial safety data on the First Patient Injected in Audiogene, its Phase 1/2 gene therapy clinical trial of SENS-501**
- **Sensorion announced positive final results of the Phase 2a clinical trial of SENS-401 after cochlear implantation**
- **Sensorion reported preliminary safety and efficacy data in the NOTOXIS trial, a Phase 2a clinical study of SENS-401 in the prevention of Cisplatin-Induced Ototoxicity**

Montpellier, September 23, 2024, 7.30 am CET – Sensorion (FR0012596468 – ALSEN) a pioneering clinical-stage biotechnology company which specializes in the development of novel therapies to restore, treat and prevent within the field of hearing loss disorders, today announces the detailed results of its clinical programs (SENS-501 and SENS-401), which were unveiled on September 20, 2024, during a symposium hosted by the Company and an oral presentation at the 36th World Congress of Audiology, held in Paris, France.

Nawal Ouzren, Chief Executive Officer of Sensorion, said: "*Sensorion is making tremendous progress across its hearing care franchise of innovative therapies for the restoration, prevention and treatment of hearing loss disorders. Notably, we have made significant advances in our gene therapy clinical trial, Audiogene, for the restoration of hearing in very young patients born with severe to profound hearing loss caused by mutations in the gene encoding for otoferlin. This program received regulatory approval in January 2024, and we are today confident that we will have treated the first cohort of patients by year end 2024, with one patient already injected and two additional patients already screened. I am very thankful to the parents of these patients for their trust and also to the study investigators participating in this study for their dedication.*
I am also very pleased with the progress made with SENS-401 portfolio. We have reported the final results, including the positive secondary efficacy endpoints, of our Phase 2a clinical trial for the preservation of residual hearing, developed in collaboration with Cochlear Limited. Our second Phase 2a clinical trial of SENS-401, in the prevention of Cisplatin-Induced Ototoxicity, is progressing as planned and I am looking forward to the completion of the recruitment in H1 2025.
Sensorion is more than ever striving to advance its innovative programs to potentially transform the quality of hearing of patients living with hearing disorders, a significant global unmet medical need."

- **SENS-501 (OTOF-GT) / Audiogene**

Sensorion announced that the first patient in the Audiogene trial has been injected in Q3 2024 in Australia by the team of Professor Catherine Birman, Otorhinolaryngologist, and Director of the Sydney Cochlear Implant Centre.

Audiogene aims to evaluate the safety, tolerability, and efficacy of intra-cochlear injection of SENS-501 for the treatment of OTOF gene-mediated hearing impairment in paediatric patients aged 6 to 31 months at the time of gene therapy treatment. Targeting the first years of life, the time period when the auditory system plasticity is optimal, will maximize the chances of these young children with pre-lingual hearing loss to acquire normal speech and language. The design of the study consists of two cohorts of two doses followed by an expansion cohort at the selected dose. While the safety will be the primary endpoint for the dose escalation cohort, the auditory brainstem response (ABR) will be the primary efficacy endpoint of the dose expansion cohort. Audiogene will also assess the clinical safety, performance, and usability of the administration device system developed by Sensorion.

According to the inclusion criteria, the first patient enrolled in Audiogene suffers from profound to severe hearing loss caused by mutations of the gene encoding for otoferlin. The administration of the gene therapy product was uneventful and well tolerated by the patient. Initial safety data indicate that no serious or adverse events were detected in the child following administration of SENS-501. The medical condition of the child (upper respiratory infection unrelated to SENS-501 injection) at the time of efficacy assessment (ABR Month 1) did not allow to get reliable hearing sensitivity. From early observations, changes in the child's behaviour and vocalisations were noted.

Sensorion continues the recruitment of patients in Audiogene Phase 1/2 study and announces that two additional patients have been screened. The Company anticipates the completion of the first cohort of patients (three patients) by the end of 2024 as well as the publication of initial efficacy data by year-end 2024. The recruitment completion of the second cohort (3 patients) is planned by the end of the first half of 2025.

Professor Catherine Birman, ENT, Otorhinolaryngologist, and Director of the Sydney Cochlear Implant Centre, declared: "*I am very excited to participate in this groundbreaking gene therapy trial that may have the potential to transform the lives of the babies carrying the OTOF gene mutation. I am grateful to the family of the first patient to receive the gene therapy for placing their trust in this innovative approach and potentially paving the way for the use of gene therapies in the field of hearing loss. I am looking forward to following the progress of the first patient in the follow-up period and further recruitment of patients in Audiogene assessing SENS-501 efficacy*."

- **SENS-401 / Cochlear Implantation**

Sensorion's Phase 2a clinical study of SENS-401 for the preservation of residual hearing loss after cochlear implantation is now completed with the last patient having completed the follow-up period. Overall, 16 patients were treated with SENS-401 and 8 were in the control group. The Company reported the analysis of the final results during its symposium, held at the World Congress of Audiology, on September 20, 2024.

As a reminder, the study is a multicenter, randomized, controlled, open-label trial designed to assess the presence of SENS-401 in the perilymph after 7 days of repeated oral administration in adult participants over 18 years old undergoing cochlear implantation. On March 11, 2024, Sensorion confirmed the presence of SENS-401 in the perilymph at levels compatible with potential therapeutic efficacy in 100% of the patients sampled, 7 days after the start of the treatment. These results demonstrated that SENS-401 administered orally crossed the labyrinth barrier and confirmed that the primary endpoint was met.
The study design also included a number of secondary endpoints, notably the change of hearing threshold from baseline to the end of the treatment period in the implanted ear at several frequencies. Study entry criteria required patients to have a pure tone audiometry (PTA) threshold of 80 dB or better (i.e., ≤80 dB) at 500 Hz, defined as indicating a minimal level of residual hearing.

The final results show that after 7 weeks of treatment with SENS-401 (and 6 weeks after cochlear implantation), the reduction in residual hearing loss was systematically better at all frequencies in the treated group with SENS-401. This protective effect was also observed 8 weeks after cessation of treatment (14 weeks post-cochlear implantation). The results show that solely the SENS-401 treated patients showed a complete hearing preservation (40% of patients) compared to the control group (0% of patients).

Additionally, these data validate the favourable safety profile of SENS-401 in treated patients, in line with previous studies of 125 patients exposed to SENS-401.

These positive results strongly support the continuation of the clinical development of SENS-401 for hearing preservation in treated patients.

Stephen O'Leary, Head of otorhinolaryngology, University of Melbourne said: *"The final results of the SENS-401 Phase 2a study are very encouraging as they support the conclusion that the administration of SENS-401 preserves residual hearing in patients undergoing cochlear implantation. This represents a crucial step towards for cochlear implantation candidates as residual hearing is very important to maintain and improve the quality of hearing of such patients. Residual hearing loss usually occurs mainly in the first 6 months after surgery; thus, early action is crucial.*
These positive data encourage us to pursue the clinical development of SENS-401, in order to offer innovative therapeutic treatments to patients scheduled for cochlear implantation as the level of residual hearing preservation showed in the study means patients have a better chance of understanding speech against background noise and perceiving more natural sound quality with speech and sounds."

- **SENS-401 (Cisplatin-Induced Ototoxicity, CIO) / NOTOXIS**

Sensorion is conducting another clinical study of SENS-401 in the prevention of Cisplatin-Induced Ototoxicity (CIO). NOTOXIS is a Phase 2a, multi-center, randomized, controlled and open-label study designed to assess the efficacy of SENS-401 in the prevention of CIO in adult subjects with neoplastic disease. The preliminary analyses presented were conducted on 16 patients (7 in the treated with SENS-401 group, and 9 in the control group).

The preliminary results presented indicate that the incidence of ototoxicity in the control group is consistent with published data. Despite significant exposure to cisplatin in the treatment group, most participants showed only mild ototoxicity. The SENS-401 group received higher cumulative doses of cisplatin than the control group. The preliminary results suggest a potential trend toward an otoprotective effect of SENS-401 beyond a cisplatin dose of 300 mg/m2.

SENS-401 showed a favourable safety profile with no new or unexpected serious adverse events after 23 weeks of twice-daily oral exposure, a longer duration than previous studies. Safety results are consistent with previous studies involving a total of 125 patients exposed to SENS-401.
Adverse events reported included constipation and nausea, as expected.

These preliminary data suggest that the cumulative dose of cisplatin is a key factor in the severity of ototoxicity. So far, the data show no significant difference in ototoxicity between the 2 groups. Patients most exposed to cisplatin may benefit more from the otoprotective effect of SENS-401.

Sensorion anticipates the patient recruitment completion in H1 2025. A more detailed analysis will be carried out on all patients at the end of the study.

Professor Yann Nguyen, ENT Surgeon, Pitié Salpétrière Hospital, Paris, France, declared: *"The results of the Phase 2a study of SENS-401 in the NOTOXIS program are encouraging. Ototoxicity is a debilitating condition in patients following cisplatin-based chemotherapy. Hearing loss caused by cisplatin is often diagnosed when it's too late, and it is permanent and irreversible. Therefore, it is paramount to pursue the development of a therapeutic solution, that has the potential to prevent cisplatin-induced ototoxicity without interfering with cisplatin efficacy. I am very satisfied with the drug safety profile and the otoprotective trend suggested by the preliminary data, and I am impatient to advance Sensorion's small molecule further in this study."*

A recording of the symposium held on September 20, 2024, at the World Congress of Audiology will be available on the Company's website in the coming days.

About SENS-501

SENS-501 (OTOF-GT) is an innovative gene therapy program developed to treat a specific form of congenital deafness linked to mutations in the OTOF (otoferlin) gene. This gene plays a key role in the transmission of auditory signals between the hair cells of the inner ear and the auditory nerve. When this gene is defective, affected individuals are born with severe to profound hearing loss.
The aim of SENS-501 (OTOF-GT) is to restore hearing by introducing a functional copy of the OTOF gene directly into hair cells via viral vector technology (AAV). By replacing the defective gene, this therapy aims to restore the normal process of converting sound into electrical signals, enabling patients

to regain their hearing ability.
Currently in the pre-clinical research phase, this gene therapy program represents significant hope for families affected by this rare form of genetic deafness. SENS-501 (OTOF-GT) embodies a commitment to scientific innovation in the field of hearing, with the potential to dramatically improve the quality of life of patients suffering from genetic deafness.
This gene therapy for patients suffering from otoferlin deficiency has been developed in the framework of RHU AUDINNOVE, a consortium composed of Sensorion with the Necker Enfants Malades Hospital, the Institut Pasteur, and the Fondation pour l'Audition. The project is partially financed by the French National Research Agency, through the "investing for the future" program (ref: ANR-18-RHUS-0007).

About SENS-401

SENS-401 (Arazasetron), Sensorion's clinical stage lead drug candidate, is an orally available small molecule that aims to protect and preserve inner ear tissue from damage responsible of progressive or sequelae hearing impairment. Sensorion currently develops SENS-401 in a Phase 2 clinical trial for the prevention of Cisplatin-Induced Ototoxicity and has completed a Phase 2a study to prevent residual hearing loss in patients scheduled for cochlear implantation. SENS-401 has been granted Orphan Drug Designation by the EMA in Europe for the treatment of sudden sensorineural hearing loss, and by the FDA in the U.S. for the prevention of platinum-induced ototoxicity in pediatric population.

About Sensorion

Sensorion is a pioneering clinical-stage biotech company, which specializes in the development of novel therapies to restore, treat, and prevent hearing loss disorders, a significant global unmet medical need. Sensorion has built a unique R&D technology platform to expand its understanding of the pathophysiology and etiology of inner ear related diseases, enabling it to select the best targets and mechanisms of action for drug candidates.
It has two gene therapy programs aimed at correcting hereditary monogenic forms of deafness, developed in the framework of its broad strategic collaboration focused on the genetics of hearing with the Institut Pasteur. SENS-501 (OTOF-GT) currently being developed in a Phase 1/2 clinical trial, targets deafness caused by mutations of the gene encoding for otoferlin and GJB2-GT targets hearing loss related to mutations in GJB2 gene to potentially address important hearing loss segments in adults and children. The Company is also working on the identification of biomarkers to improve diagnosis of these underserved illnesses.
Sensorion's portfolio also comprises clinical-stage small molecule programs for the treatment and prevention of hearing loss disorders. Sensorion's clinical-stage portfolio includes one Phase 2 product: SENS-401 (Arazasetron) progressing in a planned Phase 2 proof of concept clinical study of SENS-401 in Cisplatin-Induced Ototoxicity (CIO) and, with partner Cochlear Limited, has completed in a study of SENS-401 in patients scheduled for cochlear implantation. A Phase 2 study of SENS-401 was also completed in Sudden Sensorineural Hearing Loss (SSNHL) in January 2022.
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