

Unlocking the potential of advanced therapies for hearing loss



SENSORION

Our vision is to help people with inner ear hearing disorders to live life with unlimited connections



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Sensorion: Establishing Global Leadership In Hearing Loss With Strong And Diversified Pipeline



Untapped opportunity with 1,5 bn people affected by hearing loss (HL); 0,5 bn suffer from disabling HL Multiple causes: genetic, environmental, idiopathic



Modality agnostic approach leveraging unparalleled understanding of the inner ear and world-leading, differentiated and exclusive partnerships (Institut Pasteur, Necker Hospital, Cochlear Ltd, Sonova)



Two gene therapies (GT): SENS-501 (for mutations in otoferlin encoding gene – Ph1/2 clinical study approved); **GJB2-GT** (for mutations in GJB2 gene – candidate selected – to enter the clinic in 2025) Prospective Natural History Studies ongoing



Small molecule, SENS-401, for the treatment, restoration and prevention of HL caused by Cochlear Implantation Cl (POC Ph2a ongoing), Cisplatin-Induced Ototoxicity ClO (POC Ph2a ongoing), and Sudden Sensorineural HL (Ph2b completed)



Multiple upcoming milestones across the GT and small molecule pipeline, including the full Ph 2a data readout for SENS-401 CI and first patient communication for the Ph 1/2 GT trial of SENS-501



Experienced and visionary management team Strong shareholder base backed by leading blue-chip life sciences investors; €100m raised since Aug 2023 giving cash runway until the end of 2025

Our Vision: A Global Franchise Establishing Leadership In The Hearing Space





Together With Best-In-Class Partners We Can Transform The Current Standard of Care



Sensorion Is Well Positioned To Transform the Hearing Landscape - Institut Pasteur Partnership Feeds GT Pipeline

GENE THERAPY

Otoferlin deficiency (SENS-501)

Audiogene Ph1/2 study approved in France; First Patient Communication in H2 2024

- Hearing restoration in DFNB9 pediatric patients aged 6 to 31 months
- Ph1/2 to evaluate safety, tolerability and efficacy of SENS-501

Connexin 26 deficiency (GJB2-GT)

Candidate selected

Considered Indications:

- Hearing restoration in DFNB1 pediatric patients
- Hearing restoration in **childhood onset** of hearing loss linked to *GJB2* mutations
- Hearing restoration in early onset severe **presbycusis** linked to *GJB2* mutations

SMALL MOLECULE: SENS-401

Sudden Sensorineural Hearing Loss (SSNHL)

AUDIBLE-S Ph2 Randomized and Controlled Study Completed

- Clinically and statistically significant effect on PTA (Pure Tone Audiometry) change over time in a large idiopathic population treated with oral corticosteroids
- Complete PTA recovery in 50% of treated patients

Cochlear Implantation (CI)

Ph2 Randomized and Controlled Study Ongoing Primary Endpoint Met

- Presence of SENS-401 detected in the perilymph of 100% of sampled patients
- Clinically significant difference at 6 and 14 weeks after CI in the residual hearing between SENS-401 and control groups at 500 Hz and in the average of 250-500-750 Hz

Cisplatin-Induced Ototoxicity (CIO)

NOTOXIS Ph2 Randomized and Controlled Study Ongoing Positive Preliminary Safety Results

 Assess prevention of the ototoxicity induced by Cisplatin in patients with neoplastic disease

Sensorion's Portfolio Of Advanced Hearing Loss Therapies

	Product	Indication	Discovery	In-vivo POC	Preclinical	Phase 1	Phase 2	Phase 3	Upcoming Milestones (estimated)
	SENS-501*	Otoferlin Deficiency		Communication on First Patient H2 2024					
RESTORE	GJB2-GT*	Adult Onset (presbycusis)					 		CTA/IND enabling preclinical activities
RESI	GJB2-GT*	Pediatric Progressive					 		CTA/IND enabling preclinical activities
	GJB2-GT*	Congenital Onset					1 1 1 1 1		CTA/IND enabling preclinical activities
PREVENT	SENS-401	Hearing Preservation after CI						Cochlear"	Final Data Readout Q3 2024
PREV	SENS-401	Cisplatin-Induced Ototoxicity							Preliminary Safety and Efficacy Data Sep 2024 during WCA
TREAT	SENS-401	SSNHL							Exploring Partnering Opportunities

3SBio has a right of first refusal with respect to licensing in Greater China of SENS-401 (except in combination with cochlear implants) and SENS-501 OTOF-GT *Option to obtain a licence from the Institut Pasteur (pre-defined financial terms and other terms to be negotiated)

We Have Established Internal Capabilities To Ensure Successful Execution



Our Team Has Significant Experience In Gene Therapy Clinical Development

The team has been involved in 15+ programs from preclinical to BLA filing...



... across different organs and indications...



... using different technologies...



... with multiple organizations



GENE THERAPY PROGRAMS



Sensorion's Gene Therapy Programs Target Rare Auditory Diseases

FIRST PROGRAMS RESULTING FROM THE INSTITUT PASTEUR COLLABORATION

OTOFERLIN DEFICIENCY	GJB2-RELATED HEARING LOSS			
 Pediatric patients with mutations in OTOF suffer from severe to profound sensorineural prelingual non-syndromic hearing loss Otoferlin deficiency could be responsible for up to 8% of all cases of congenital hearing loss Prevalence ~20,000 in the USA + EU Incidence ~1,100 per year in USA + EU EU and US ODD, US RPDD 	 We have identified three forms of hearing loss associated with <i>GJB2</i> gene mutations: Early onset of severe presbycusis (adult population) Childhood onset (pediatric population) Congenital onset (pediatric population) ~100,000 patients between 30- and 69-years old thought to be affected by a monogenic form of presbycusis due to <i>GJB2</i> mutations Prevalence of congenital and childhood onset forms are estimated to be around 200,000 patients as around 50% of autosomal recessive non syndromic hearing loss cases are thought to be from <i>GJB2</i> mutations 			
Sources: Akil et al. 2019 (<u>link</u>), Orphanet (<u>link</u>), NIH (<u>link</u>), company estimates based & Co 2019 report, Institut Pasteur,				

DELAYED DIAGNOSIS – NOT SUSPECTED AT FIRST SIGHT

GENE THERAPY HAS A LIFE-CHANGING POTENTIAL FOR THESE AUDITORY DISEASES

SENS-501 Aiming To Develop Best-In Class And First-In Class Gene Therapy

CRITERIA	SENSORION
AAV capsid selected for high-level of target cells specificity	
GT product showing high level of target cells transduction	
Limited off-target tissue biodistribution	\checkmark
Surgical approach developed and mastered by ENTs surgeons	
Natural History Study preparing execution of the clinical trial	
Regular engagement with regulatory agencies	

SENS-501 Gene Therapy Pediatric Indications Have Blockbuster Sales Potential SENS-501 CTA Approved In France

SENS-501 (OTOF-GT) is the Perfect Pilot Program

- Well understood biology and pathology of the otoferlin deficiency
- Full functionality of the remaining chain
- High specificity for the inner hair cells (IHCs), no off-target effect expected

- SENS-501 will be the pilot program demonstrating that GT is a relevant medical approach for the inner ear
- SENS-501 will establish understanding of GT in the inner ear by the Regulators and the Payers for future GT programs
- Medical plausibility and target population have been confirmed through :
 - ✓ Orphan Drug Designation in the US and EU
 - ✓ Rare Pediatric Disease Designation with eligibility for voucher in the US
 - ✓ Clinical Trial Application approved in France, 1st patient communication H2 2024



Sources: Sensorion, AT Kearney market research

SENS-501 OTOF Gene Encodes Otoferlin, A Key Ca2⁺ Sensor Protein



Model illustrating calcium regulation of otoferlin/SNARE interaction in the hair cell – Adapted from Ramakrishnan et al. 2014

OTOF is the gene coding for the otoferlin protein, a Ca2⁺ sensor for vesicle fusion and vesicle pool replenishment at auditory hair cell ribbon synapses

SENS-501 SENS-501 Leads To Long-Term Hearing Recovery In A Translational Model Of Otoferlin Deficiency



• **Durable hearing restoration** in Otof-/- mice by dual AAV-OTOF directly delivered to the inner ear up to one year post-injection



- Both doses of SENS-501 demonstrated efficacy in improving hearing in KO mice
- SENS-501 leads to otoferlin expression in Inner Hair Cells

Olivier et al. ASGCT 2023 link

SENS-501 SENS-501 Leads To Restoration Of Efficient Sound Processing In Behavioural Test



Olivier et al. ASGCT 2023 link

SENS-501 Dedicated Surgical Approach For Gene Therapy

Non-Human Primates injected through the round window membrane (RWI) with or without stapedotomy (stap)



SENS-501 Phase 1/2 Audiogene Study (SENS-501) Approved In France First Patient Communication Anticipated In H2 2024

Audiogene, a Phase 1/2 clinical trial in children aged 6 to 31 months to assess safety, tolerability, and efficacy of SENS-501 following unilateral injection into the cochlea



Audiogene Study Design

Pediatric patients, aged 6 to 31 months at the time of the injection

Targeting the first years of life to maximize chances of acquiring speech and language



Dose escalation

• Primary endpoint: safety and tolerability

Dose expansion

• Primary endpoint: efficacy (ABR, Auditory Brainstem Response)



SENS-501 Otoferlin "Audinnove" Consortium Provides Privileged Access To Patients And Surgeons

Audinnove consortium received Hospital-University Research (RHU) prize:

- The consortium is eligible to receive up to €9.7m to develop a Gene Therapy program addressing otoferlin deficiency
- Audioferlin: Natural History Study: clinical evaluation and selection of patients
- Database compilation with genotypic and phenotypic characterization of children with congenital hearing loss
- Phase 1/2 Gene Therapy study (financing up to 1st patient in the clinical study)

Audinnove consortium is key to the understanding of the epidemiology and to build awareness of the emerging gene therapies

Necker-Enfants Malades Hospital

• The first dedicated pediatric hospital in the world

The Reference Center for Genetic Deafness at Necker coordinates the French and European genetic deafness networks



Audinnove is financed by the French State, via the National Research Agency through the "Investing for the future" program (ref: ANR-18-RHUS-0007)

OTOCONEX: Natural History Study running across Europe will support identification of DFNB9 patients for Audiogene.



SENS-501 SENS-501 (OTOF) Gene Therapy Program Status – Progressing



GJB2-GT

Connexin 26: A Gap-junction Protein Encoded By *GJB2* Gene and Responsible For Tissue Homeostasis

Mutations in the GJB2 Lead to Deafness

- *GJB2* is the gene encoding for the Connexin 26 protein; one of 20 known connexins
- Cx26 and Cx30 proteins are the dominating connexins in the cochlea; heteromeric or heterotypic hexamers forming Gap Junctions
- Gap Junctions are key for the intercellular exchange of molecules (miRNA, glucose, ions, etc.) hence responsible for tissue homeostasis
- More than 100 recessive mutations origin Cx26 truncation / deletion leading to non-syndromic hearing loss and deafness, most are addressable via gene replacement
- Severity of hearing loss correlates with degree of loss of GJB2 function



GJB2 Expression in the Cochlea Muse cochlea Organ of Corti top view Cochlea cross section Organ of Corti top view Image: Cochlea cross section Image: Cochlea cross section<

Phalloidin Cx26 DAPI

- Supporting cells of the organ of Corti
- Fibrocytes of the spiral limbus and the lateral wall
- Intermediate and basal cells of the stria vascularis
- Not expressed in hair cells

GJB2-GT Lead Candidate Was Selected To Answer Specific Development Criteria

CRITERIA	LEAD CANDIDATE
Natural and synthetic AAV capsid libraries screening for broad coverage of target cells	
Expression cassette design for high-level of target cells transduction, correct cellular localization, active gap-junctions	
Avoiding off-target expression (i.e. hair cells): promoter and regulatory sequences design	
Limited off-target tissue biodistribution	$\mathbf{\sim}$
Surgical approach developed and mastered by ENT surgeons	

Our Lead Candidate Was Designed to Ensure Broad Coverage of Relevant Cochlear Cells While Detargeting Hair Cells

GJB2-GT Lead Candidate Can Deliver Cx26 In The Appropriate Target Cells

Correct Delivery of Cx26 Using Lead Candidate Flag in Non-Human Primate Cochlea



GJB2-GT Lead Candidate Demonstrates Adequate Safety And Biodistribution Profile - Including Long-Term Local Tolerability In Mice And NHP



No impact on ABR up to 6 months following Lead Candidate injection

3-Month Exploratory Toxicity and Biodistribution in Non-Human Primate

- Lead Candidate is well tolerated and did not induce any macroscopic/organ weight changes or local/systemic microscopic findings
- Normal cochlear histology
- No lab and clinical findings
- Biodistribution: the vast majority of the vector remains in the injected ear, no dissemination observed in gonads, main organs, DRG

GJB2-GT Lead Candidate Prevents Hearing Loss In Relevant Mouse Model



Conditional knock-out mouse model leading to 2 phenotypes





GJB2-GT GJB2 Gene Therapy Program Next Steps

Submission of European Natural History Study OTOCONEX Submission of Natural History Study in collaboration with Sonova

Candidate selection Q2 2023



Preclinical IND enabling studies

Clinical Trial Applications Mid-Year 2025

SMALL MOLECULE PROGRAMS



SENS-401: Multiple Indications To Treat And Prevent Hearing Loss

Product	Indication	Discovery	In vivo POC	Preclinical	Phase 1	Phase 2	Phase 3	
SENS-401 aft	Hearing preservation							
	after cochlear implantation							
								C
SENS-401	Cisplatin Induced Ototoxicity							
SENS-401	Sudden Sensorineural Hearing							

*"Patriot" Consortium (IRBA, Sensorion, Echodia, Institut Pasteur) awarded up to €10.8m non dilutive financing by French government, staged over the duration of the project. Sensorion will receive up to €5.6m to further develop SENS-401 in SSNHL French army

SENS-401 - A Portfolio With Potential Blockbuster Value



SENS-401 SSNHL clinical data and insight **derisk** further development of SENS-401 in other indications

SENS-401 To Preserve Residual Hearing After Cochlear Implantation

COMBINATION OF COCHLEAR IMPLANT WITH SENS-401 TO PREVENT CELL-DEATH POST COCHLEAR IMPLANT PROCEDURE



Source: Cochlear® 2018 investor day (link)



¹Cochlear[®] FY21 Result Presentation (<u>link</u>) ²Market estimates (<u>link</u>)

CI

SENS-401 CI Study Design Primary Endpoint Met

A Phase 2a, Multicenter, Randomized, Controlled, Open-label Study





Primary Endpoint Of The Phase 2a Clinical Study For Residual Hearing Preservation Has Been Met



- Presence of SENS-401 in the perilymph is confirmed in 100% of the patients sampled following cochlear implantation.
- These results confirm that SENS-401 administered orally crosses the labyrinth barrier.

Residual Low Frequency Hearing Benefits For Cochlear Implant Users



Postoperative hearing preservation defined as: unaided air-conduction **thresholds < 85 dB HL** at 125, 250, and 500 Hz

*Jensen et al., Hearing Preservation After Cochlear Implantation, 2021

SENS-401 Provides Medically Significant Hearing Protection 6 Weeks Post-Cochlear Implantation



 SENS-401 administered one week before and six weeks after cochlear implantation leads to a lower loss of residual hearing (19 dB and 16 dB), as measured by hearing thresholds at the 500 Hz frequency and the average of three contiguous frequencies ranging from 250 to 750 Hz, compared to 32 dB in the control group.

* One participant in each group had a missing hearing threshold at the frequency 750 Hz at the baseline.

The Hearing Protection Provided By SENS-401 Post-Cochlear Implantation Continues For Up To 8 Weeks After End Of Treatment



Residual hearing loss is lower on average in patients treated with SENS-401 (25dB) compared to untreated patients with SENS-401 (36 dB) 8 weeks after the end of the treatment period.

* One participant in each group had a missing hearing threshold at the frequency 750 Hz at the baseline.
SENS-401 CI Conclusion Primary Enpoint Met



SENS-401 can cross the labyrinthine barrier to target cochlear hair cells in all patients sampled, confirming primary endpoint is met.



Six and Fourteen weeks post-cochlear implantation, the residual hearing loss whether assessed at 500 Hz or across an average of 3 consecutive frequencies exhibited a clinically significant difference for the treated group (19-dB), in comparison to the untreated group (32dB). This difference is maintained up to 14 weeks with 25 dB in the treated group vs 36 dB in the untreated group.



This supports the assumption that **SENS-401**, present in the perilymph fluid, reaches concentrations that are pharmacologically active.



SENS-401 taken for 6 weeks confirms it has a good safety profile.



These encouraging trends necessitate further validation across the full study participant group.



SENS- 401 has the potential to modify the outcome of CI while preserving residual hearing by improving speech perception in quiet and noise, music perception, spatial localization and maintaining more natural sound quality.



These results support the SSNHL phase 2 data and further development of SENS-401.

Cisplatin Administration For Chemotherapies Damages The Inner Ear And Leads To Hearing Loss, Tinnitus And Dizziness

WHAT IS CIO?

Hearing loss caused by cisplatin administration as chemotherapeutic treatment. Risk factors include young age as well as individual and cumulative cisplatin doses.

CIO leads to permanent inner ear problems in 50-60% of adult cases and in 90% of pediatric cases.

These complications significantly impact patients' quality of life due to:

- Hearing loss, tinnitus and dizziness impacting daily life activities
- Problems in language acquisition and learning for pediatric patients
- Difficulties in communicating, social isolation, cognitive decline

Potential treatments must not interfere with cisplatin efficacy.

Incidence of cisplatin treated patients: 500,000 patients in 2025 in G7 countries¹



¹ Company/ estimates based on publicly available data (in the US, Japan, Germany, France, the UK, Italy and Spain)

CIO

SENS-401 Phase 2a Proof-Of-Concept Study NOTOXIS Positive Preliminary Safety Data

A Phase 2a, Multicenter, Randomized, Controlled, Open-label Study to Evaluate the Efficacy of SENS-401 to Prevent the Ototoxicity Induced by Cisplatin in Adult Subjects with a Neoplastic Disease



;y

- Rate of ototoxicity
- High Frequency PTA
- Speech in Noise and quiet
- THI questionnaire

Safety

AEs & SAEs incidence

Key Takeaways from Preliminary Study Data

- SENS-401 has a **favorable safety profile** when administered continuously for up to **11 weeks** in adult patients undergoing cisplatin-based chemotherapy
- Recruitment is progressing well, with over a third of the required study population enrolled (and eleven clinical centers open to date)
- Sensorion will provide preliminary safety and efficacy data of its POC Phase 2a clinical trial of SENS-401 CIO during the World Congress of Audiology, being held on September 19-22, 2024

CIO

SENS-401 Program Key Milestones, Data Readouts in 2024

SENS-401 with cochlear implants (CI) - Positive Preliminary Results Reported SENS-401 with cochlear implants (CI) - Primary Endpoint Readout H1 2024

SENS-401 CIO NOTOXIS - Preliminary Results S2 2023



SENS-401 CIO NOTOXIS
- Preliminary Safety and Efficacy Data
Sep. 2024 during WCA

SENS-401 with cochlear implants (CI) – Full Data Readout Q3 2024

Sensorion Newsflow [Estimated Timelines]



THANK YOU

E: contact@sensorion-pharma.com



Hearing Loss



Access And Clarity Are Mandatory For Optimal Outcomes



*Guideline criteria may vary slightly by manufacturer, device, and/or country

SENS-401



SENS-401 Mechanism Of Action



SSNHL



SSNHL

Sudden Sensorineural Hearing Loss (SSNHL) is a Severe Disease Affecting more than 200,000 Patients Per Year

WHAT IS SSNHL?

The sudden onset of a significant hearing loss due to dysfunction of the cells of the cochlea and central auditory structures.

Hearing loss develops over less than 72 hrs, hearing sensitivity is reduced by at least 30 dB (1,000 fold) in the affected ear(s).

>70% of cases are idiopathic, known causes include noise/head trauma, ischemia, infection.

>50% of patients suffer from permanent disabling hearing loss, mostly those with initial severe/profound hearing loss.

Complications significantly impact quality of life due to:

- Difficulties in communicating, social isolation, cognitive decline
- Accompanying tinnitus

Incidence: 27-35 per 100,000 (218,000 patients in 2017 in G7 countries)¹

¹ Company/ estimates based on publicly available data (in the US, Japan, Germany, France, the UK, Italy and Spain)

SENS-401 SSNHL Program: AUDIBLE-S Phase 2 Design

A RANDOMIZED, MULTICENTER, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL



Primary endpoint definition:

"...change in pure tone audiometry (PTA); average of the hearing threshold of 3 contiguous most affected hearing frequencies in decibels in the affected ear from baseline to the end of treatment visit (Visit 5/D28±3)"

SENS-401 Plasmatic Exposure



SENS-401 Induces Complete PTA Recovery In 50% Of Patients



SENS-401 SSNHL Phase 2 Results Summary

Seeking Partners For Late-Stage Development And Commercialization

AUDIBLE-S SECONDARY ENDPOINT RESULTS

- Complete PTA recovery is achieved in 50% of the SENS-401 treated patients
- SENS-401 shows a clinically meaningful and statistically significant effect on PTA change (at least 10 dB) over time in a large homogeneous idiopathic population of patients treated with corticosteroids
- SENS-401 induces a significative PTA change of at least 19 dB at day 28 and up to 25 dB at Day 84 allowing a reduction of the hearing loss degree from profound to mild, in large profound hearing loss sub-group
- A better response was observed in both treatment groups with a **continuous improvement between Day 28 and Day 84**
- The change in PTA translates into functional improvement evidenced with speech audiometry tests
- Safe and well tolerated in 115-patient SSNHL study; although primary endpoint not met data supports and informs further clinical development
- Responder rate is always better in the treated group compared to Placebo and difference with Placebo increases over time