



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



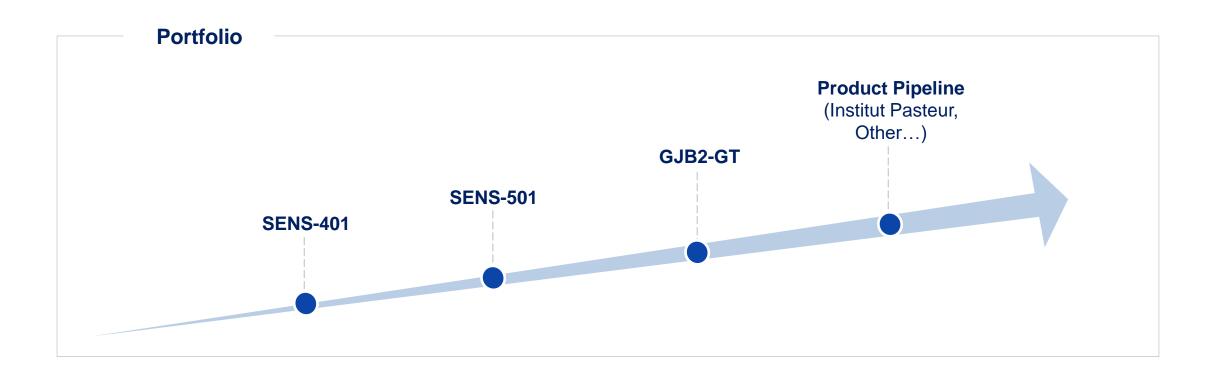
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Sensorion: Overview

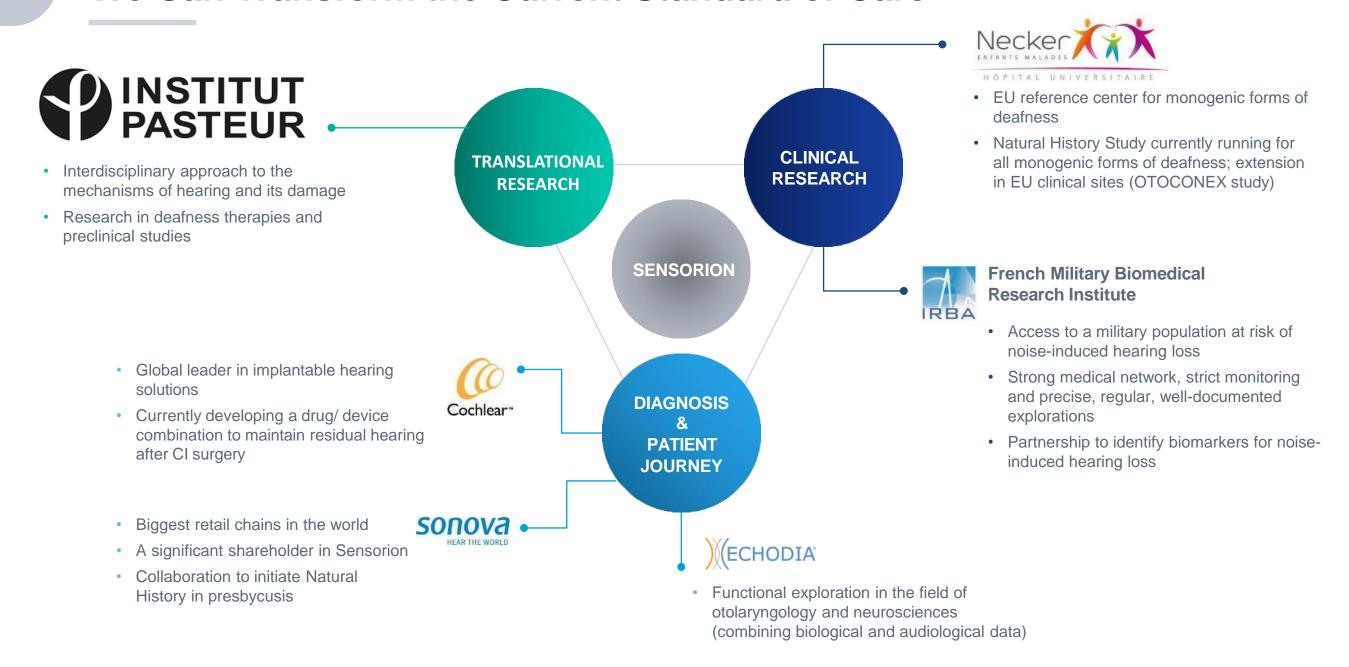
- Sensorion currently develops two **Gene Therapy** (GT) programs in the ear, targeting monogenic forms of deafness with **pediatric** and **adult** onset:
 - SENS-501 (OTOF-GT) caused by mutations of the gene encoding for otoferlin, EU & US ODD, US RPDD, CTA filed in the UK and in Europe
 - GJB2-GT related to mutations in GJB2 gene (candidate selected)
 - Prospective natural history studies ongoing, strong European eco-system in place
- Oral small molecule asset SENS-401, for the prevention and treatment of hearing loss:
 - Sensorion and Cochlear Ltd collaboration (ongoing clinical Proof-of-Concept study Positive preliminary results)
 - Cisplatin-Induced Ototoxicity (ongoing clinical Proof-of-Concept study)
 - Sudden Sensorineural Hearing Loss (completed Phase 2 study)
- Exclusive relationship with the Institut Pasteur in the field of hearing genetics, several GT programs initiated under strategic collaboration
- Strong partnerships with key players in hearing care and devices, including Necker Hospital (Paris, FR), Cochlear Ltd. (ASX listed) and Sonova (global hearing aid market leader)
- Strong shareholder base including leading blue-chip investors; listed on Euronext Growth.
 - Successful €35m capital raise in August 2023 led by Redmile Group alongside existing investors Invus and Sofinnova Partners

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 Provides GT Pipeline

GENE THERAPY

Otoferlin deficiency (OTOF-GT) – SENS-501 CTA filed (UK MHRA & Europe)

Hearing restoration in DFNB9 pediatric patients

Connexin 26 deficiency (GJB2-GT)

Candidate selected

- 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 study completed

- Meaningful and statistically significant effect on PTA change over time in a large idiopathic population
- Complete PTA recovery in 50% of treated patients

Cochlear Implantation (CI)

Ph2 study ongoing – Positive Preliminary Results

- Assess preservation of the residual hearing after cochlear implantation
- Evaluate the presence of SENS-401 in the perilymph

Cisplatin-Induced Ototoxicity (CIO)

NOTOXIS Ph2 study ongoing

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

Sensorion's Portfolio Of Advanced Hearing Loss Therapies



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

We Have Established Internal Capabilities to Ensure Successful Execution



PRECLINICAL -SMALL MOLECULES & GT PROGRAMS

- Cell Model Platform: assays development, target & drug discovery, biomarkers
- Animal Pharmacology platform: from the POC to the dose-finding studies in disease-relevant rodent models, surgery
- Technology & Innovation platform: design and select the best drug candidate (capsid & promoter selection)



CLINICAL EXPERIENCE

- 400 people enrolled in Sensorion led clinical trials
- Set-up audio tests in different countries, languages
- Central reading of audiometry testing
- In-house audiology expertise of more than 20 years for the pediatric and adult populations and cochlear implants



CMC GENE THERAPY FACILITIES

- Process development: non-GMP manufacturing from small scale up to 50L in bioreactor
- Analytical development: development of productspecific analytical methods, in-house generic assays to support process development and AAV manufacturing



REGULATORY EXPERTISE

- Develop regulatory strategies to ensure expedited product development including gene therapy
- Regulatory Agency interaction (EU/US)
- Shape the treatment guidelines and standardize clinical endpoints



PATIENT ACCESS

- Working with prominent payers from the EU5
- Obtaining consultation about our early Clinical Development Program within EU and US
- Building capabilities cross-functionally

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Our Team has Significant Experience in Gene Therapy Clinical Development

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

10

Preclinical

4

Clinical

1

BLA filing

... using different technologies...

15

Gene therapy (AAVs / LVs)

1

Cell therapy 1

Gene editing

... across different organs and indications...









... with multiple organizations



























Sensorion's Gene Therapy Programs Target Rare Auditory Diseases

FIRST PROGRAMS RESULTING FROM THE INSTITUT PASTEUR COLLABORATION

OTOFERLIN DEFICIENCY

- 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
- Clinical Trial Application Filed (UK MHRA & Europe)

GJB2-RELATED HEARING LOSS

We have identified three forms of hearing loss associated with *GJB2* gene mutations:

- Early onset of severe presbycusis
- Childhood onset
- Congenital onset
- ~100,000 patients between 30 and 69 years old thought to be affected by a monogenic form of presbycusis due to GJB2 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 GJB2 mutations

Sources: Akil et al. 2019 (<u>link</u>), Orphanet (<u>link</u>), NIH (<u>link</u>), company estimates based on publicly available population data, Chardan 2020 report, Bryan, Garnier & Co 2019 report, Institut Pasteur, Boucher et al. 2020 (link)

DELAYED DIAGNOSIS – NOT SUSPECTED AT FIRST SIGHT

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

Aiming To Develop Best-in Class And First-in Class Gene Therapy

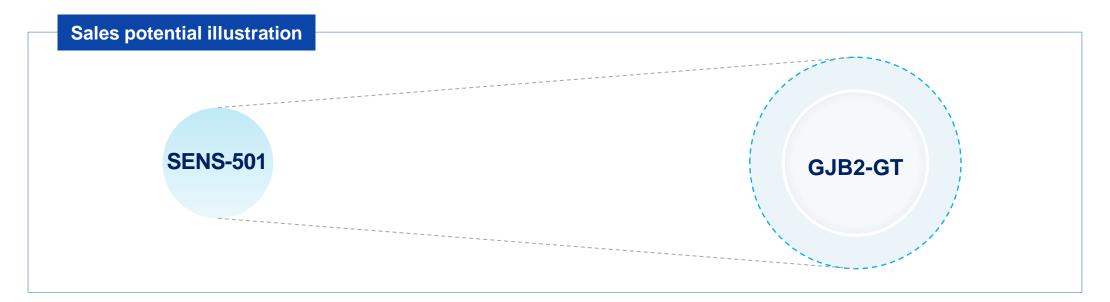
CRITERIA	SENSORION
AAV capsid selected for high-level of target cells specificity	
GT product showing high level of target cells transduction	
Limited off-target tissue biodistribution	
Surgical approach developed and mastered by ENTs surgeons	
Natural History Study preparing execution of the clinical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

Gene Therapy Pediatric Indications Have Blockbuster Sales Potential CTA Submitted in UK (MHRA) and Europe

SENS-501 (OTOF-GT) is the perfect pilot program

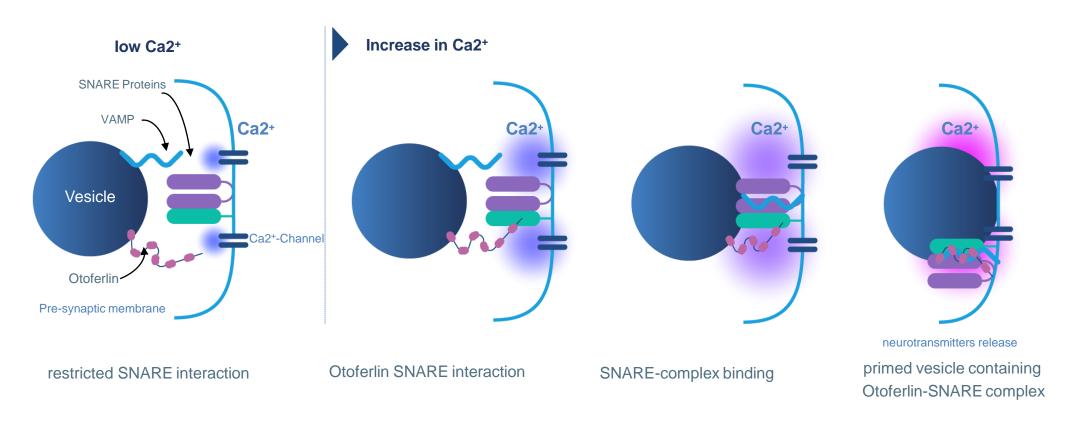
- Well understood biology and pathology of the otoferlin deficiency
- Full functionality of the remaining chain
- High specificity for the inner hair cells (IHCs), no off-target effect expected

- 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



Sources: Sensorion, AT Kearney market research

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 Leads to Long-term Hearing Recovery in a Translational Model of Otoferlin Deficiency

120

100

80

60

40

20

15

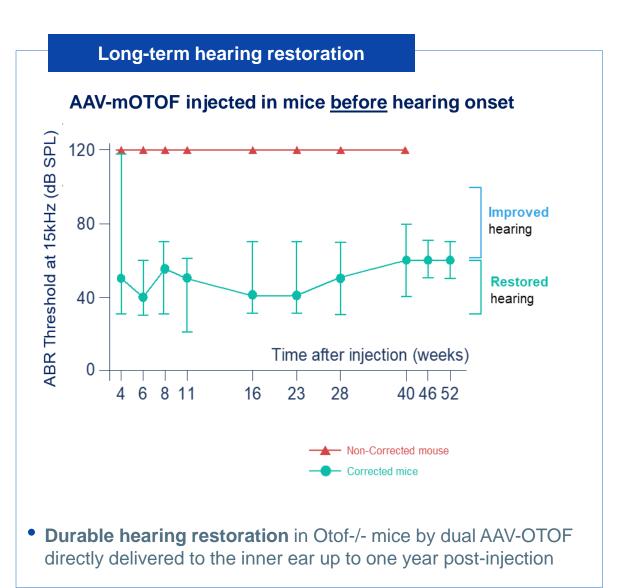
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SPL)

(dB

Threshold

ABR





Hearing restoration corrlates with de novo OTOF expression

OHC

Untreated - no hearing

Improved hearing

Restored hearing

Normal hearing

SENS-501 injected in mice after hearing onset

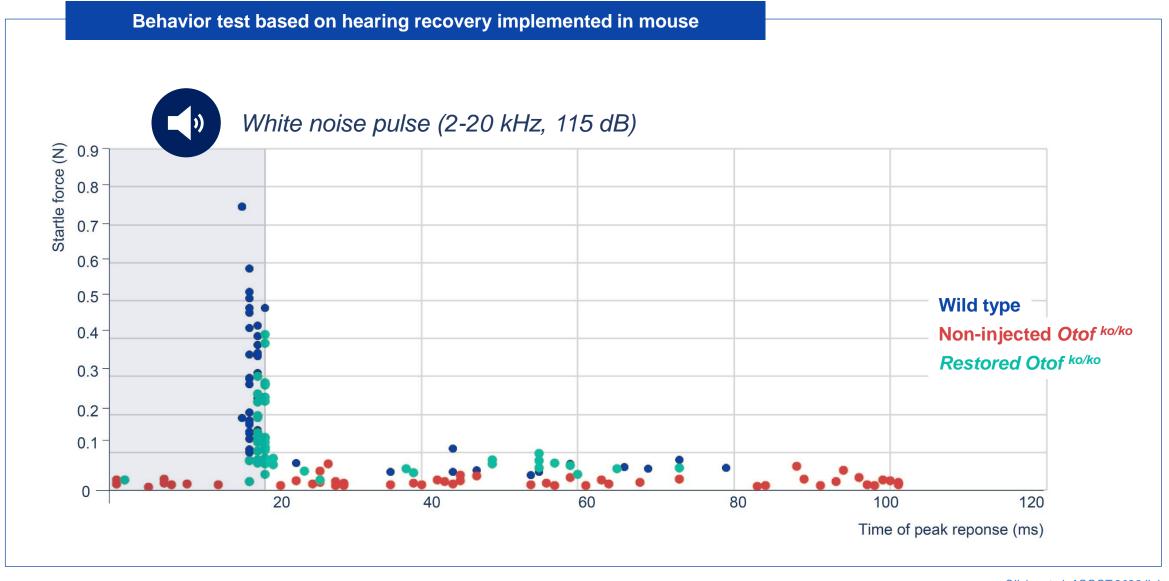
- Both doses of SENS-501 demonstrated efficacy in improving hearing in KO mice
- SENS-501 leads to Otoferlin expression in Inner Hair Cells

****: p<0.0001; ***: p<0.001; two-way ANOVA, Dunnett's Multiple comparison test with a single pooled variance

Olivier et al. ASGCT 2023 link

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SENS-501 Leads to Restoration of Efficient Sound Processing in Behavioural Test



Olivier et al. ASGCT 2023 link

Dedicated Surgical Approach for Gene Therapy

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

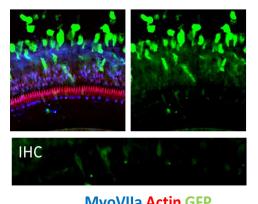
1 Fenestration

(Round window membrane)



Used for cochlear implant

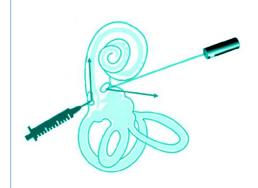
- Overpressure
- Limited volume
- Backflow
- Irregular transduction rate



MyoVIIa Actin GFP

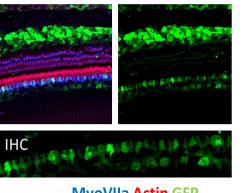
2 FENESTRATIONS

(Round window membrane + oval window)



Combining 2 common surgical technics: cochlear implant and stapedotomy

- No overpressure
- No backflow
- Homogenous and efficient transduction rate



MyoVIIa Actin GFP

Surgical approach

- Surgical procedure is **similar to cochlear** implantation and well mastered by ENTs surgeons
- Optimized surgery uses stapedotomy procedure to maximize target cells exposure along the full length of the tonotopic axis
- New injection system device under development

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: expanding the Natural History Study across Europe

AUDINNOVE CONSORTIUM MEMBERS

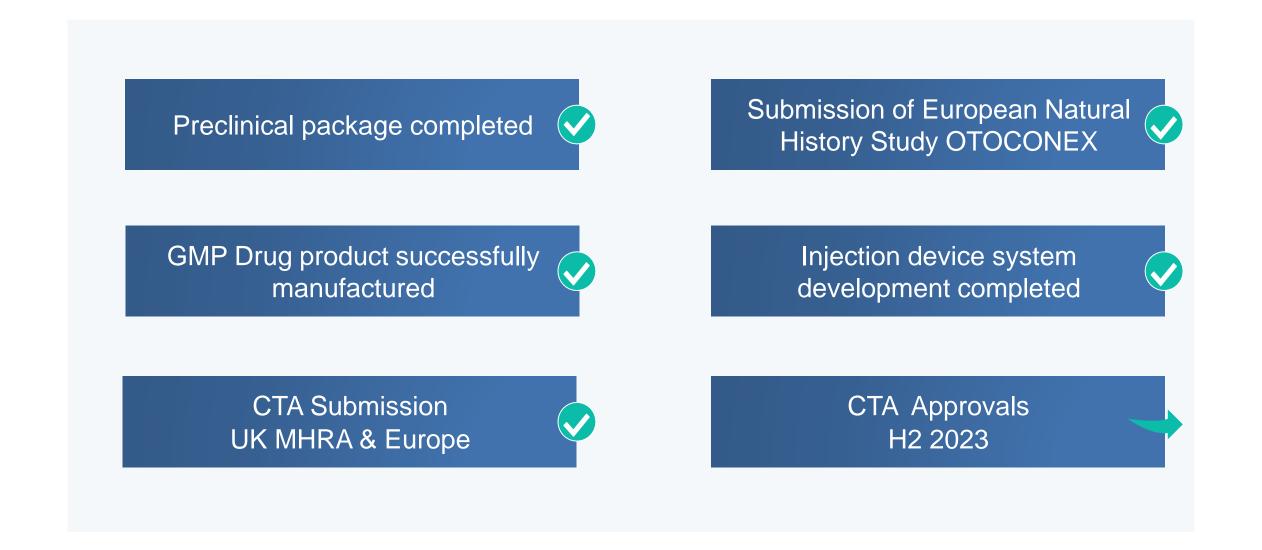






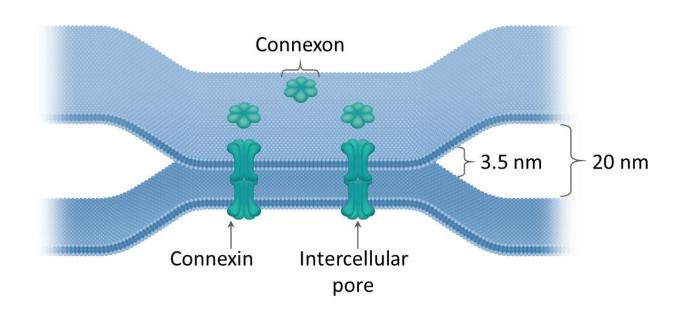


SENS-501 (OTOF) Gene Therapy Program Status – Progressing



Connexin 26: a Gap-junction Protein Encoded by *GJB2* Gene and Responsible for Tissue Homeostasis Mutations in the Gene Lead to Deafness

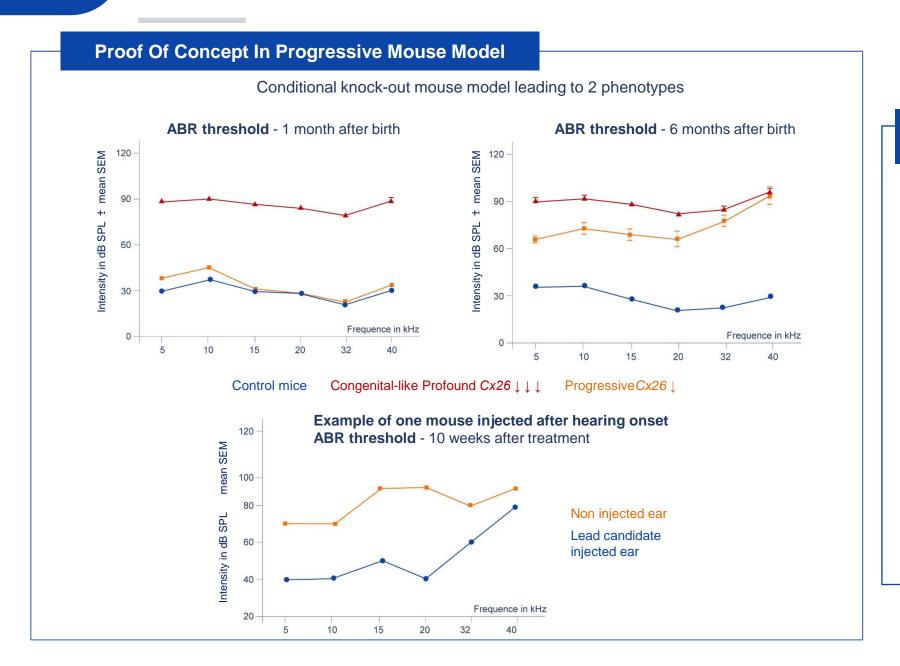
- GJB2 is the gene encoding for the Connexin 26 protein; one of 20 known connexins in humans and almost endemic to the cochlea (together with Cx30); a hexamer of 6 proteins forms Gap Junctions
- Gap Junctions are key for the intercellular exchange of molecules (miRNA, glucose, ions, etc.) hence responsible for tissue homeostasis
- *GJB*2 cDNA = 681 bp compatible with the use of a **single AAV**
- More than 100 recessive mutations origin Cx26 truncation / deletion leading to non-syndromic hearing loss and deafness
- GJB2 mutations are the most prevalent form of congenital deafness (DFNB1)
- Children are usually diagnosed during routine newborn screening and current SoC is cochlear implantation prior to language acquisition
- Prof. Christine Petit observed in an epidemiology study that some patients demonstrating early onset of severe presbycusis carried GJB2 mutations^[1]



Schematic representation of a gap junction – adapted from Kemperman, Hoefsloot and Cremers J R Soc Med 2002:95: 171-177

[1]: Boucher et al. 2020

Selected Candidate Prevents Hearing Loss in Relevant Mouse Model



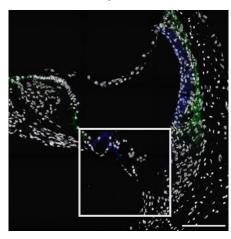
Hearing Loss Prevention Correlates With Connexin 26 Expression

Example of one mouse injected after hearing onset Connexin 26 expression in the cochlea

- 10 weeks after treatment

Lead candidate injected ear

Non injected ear



Left: Green staining demonstrates efficient Cx26 re-expression in target cells, which are otherwise depleted (right) in Cx26 in the GJB2 deficient model

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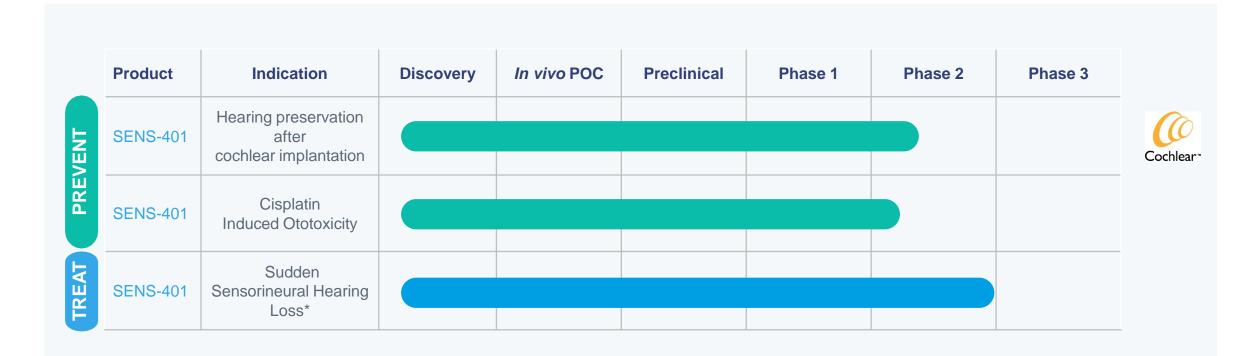
GJB2 Gene Therapy Program Next Steps







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

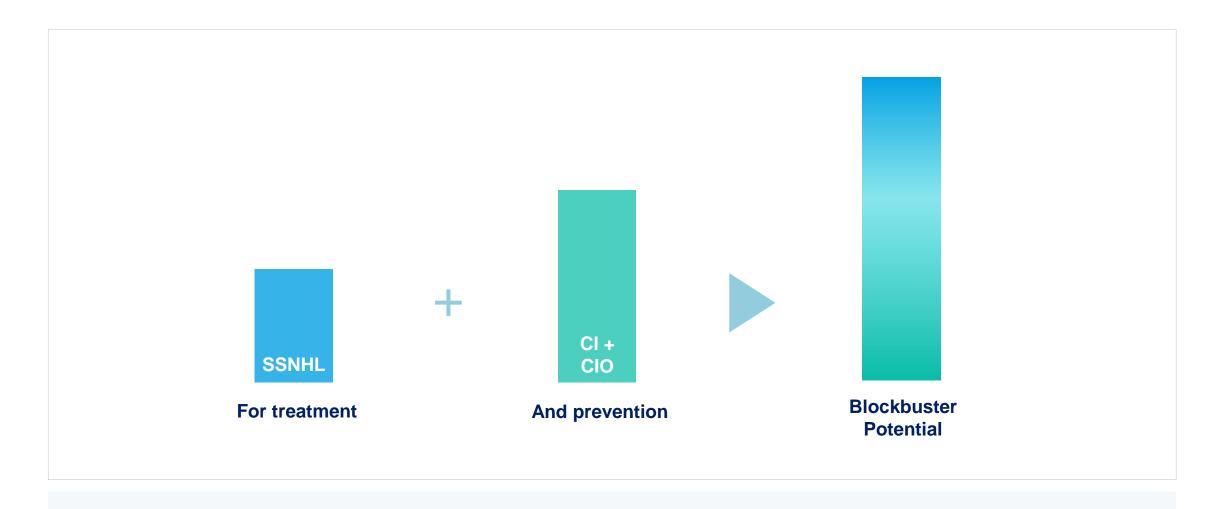


^{*&}quot;Patriot" Consortium (IRBA, Sensorion, Echodia, Institut Pasteur) awarded up to €10.8m non dilutive financing by French government, staged over the duration of the project. Sensorion will receive up to €5.6m to further develop SENS-401 in SSNHL French army

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SENS-401 - a Portfolio With Potential Blockbuster Value



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

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:

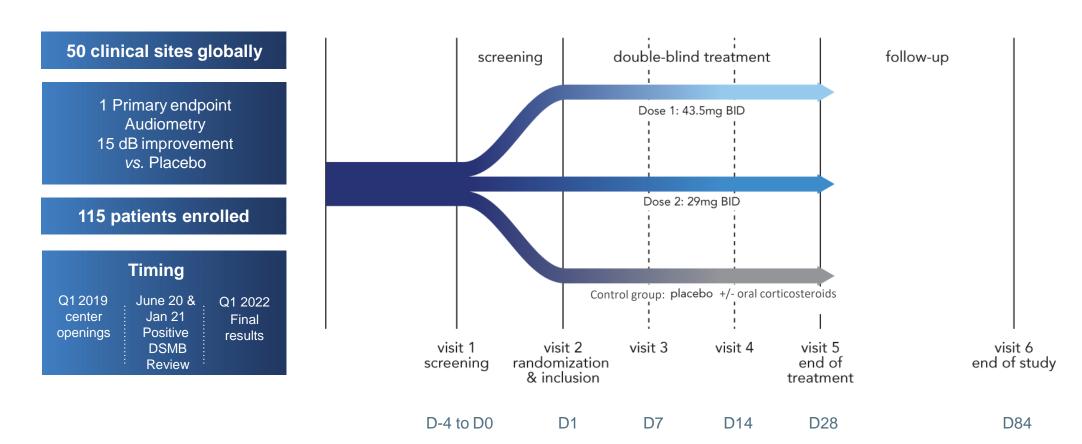
- Difficulties in communicating, social isolation, cognitive decline
- Accompanying tinnitus

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: Phase 2 Design

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

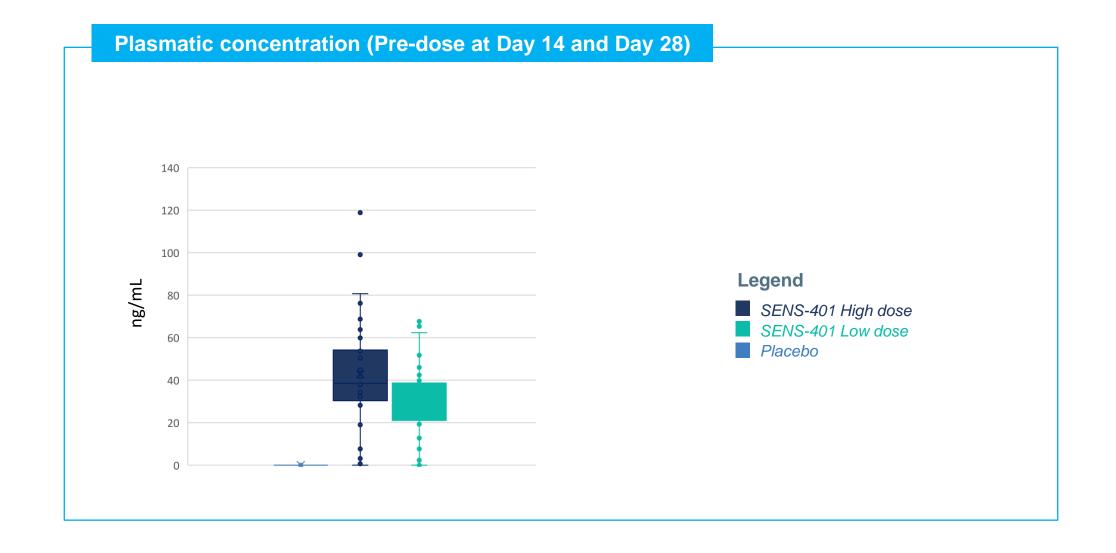


Primary endpoint definition:

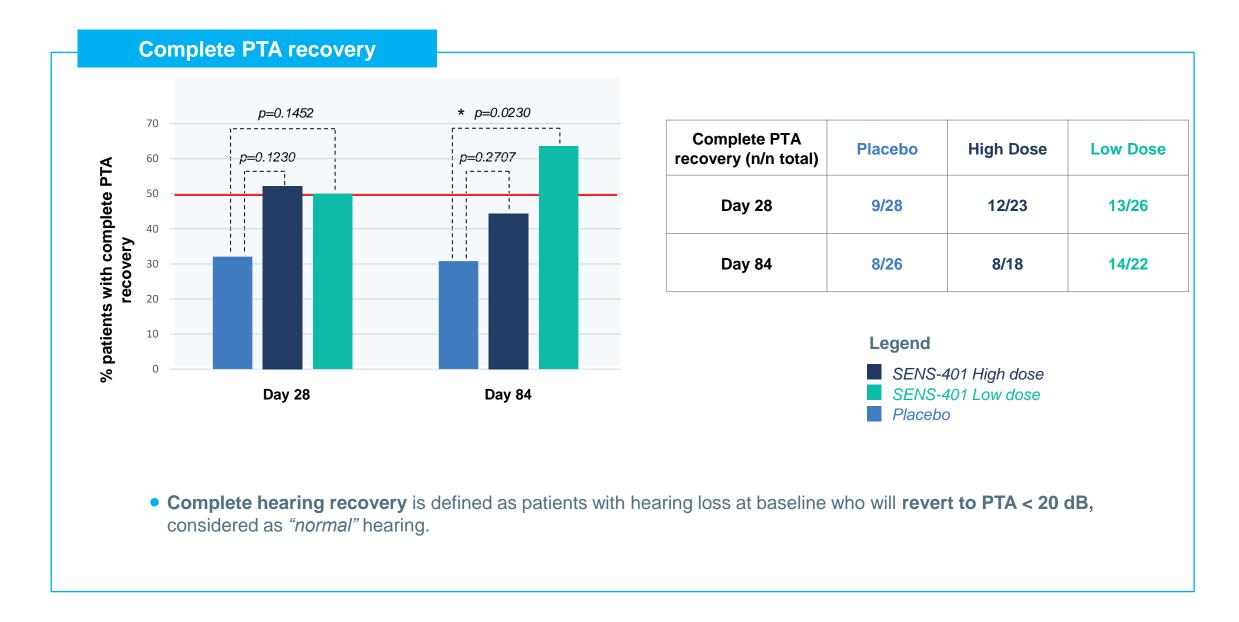
"...change in pure tone audiometry (PTA); average of the hearing threshold of 3 contiguous most affected hearing frequencies in decibels in the affected ear from baseline to the end of treatment visit (Visit 5/D28±3)"

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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

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)

KEY FIGURES

36,450

Implants sold by Cochlear[®] globally in 2021¹ (representing ~60% of global market share)

\$1.5bn

Cochlear implant market in 2020²

80%

Market penetration in children in developed markets¹ and 3% in adults ¹

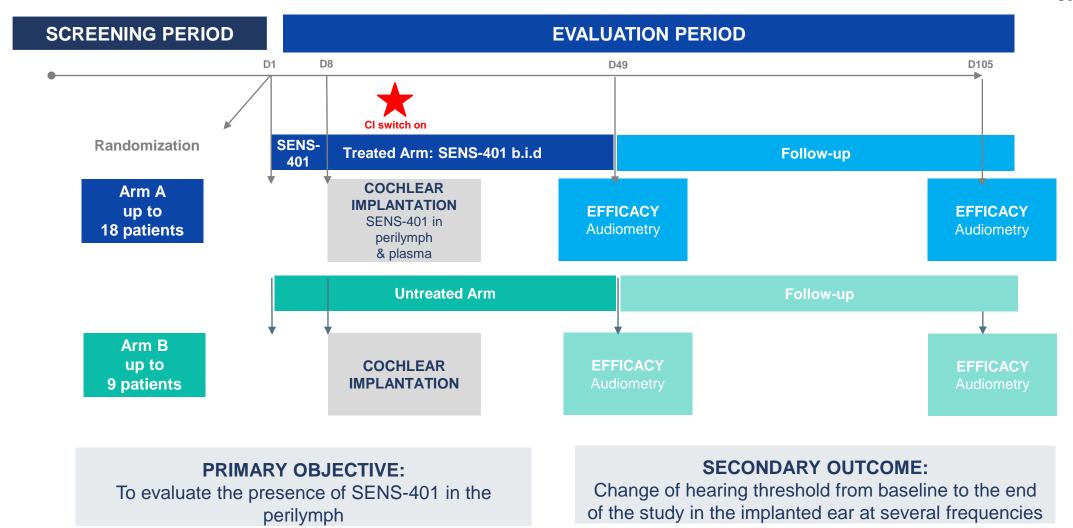
¹Cochlear® FY21 Result Presentation (<u>link</u>)

²Market estimates (link)

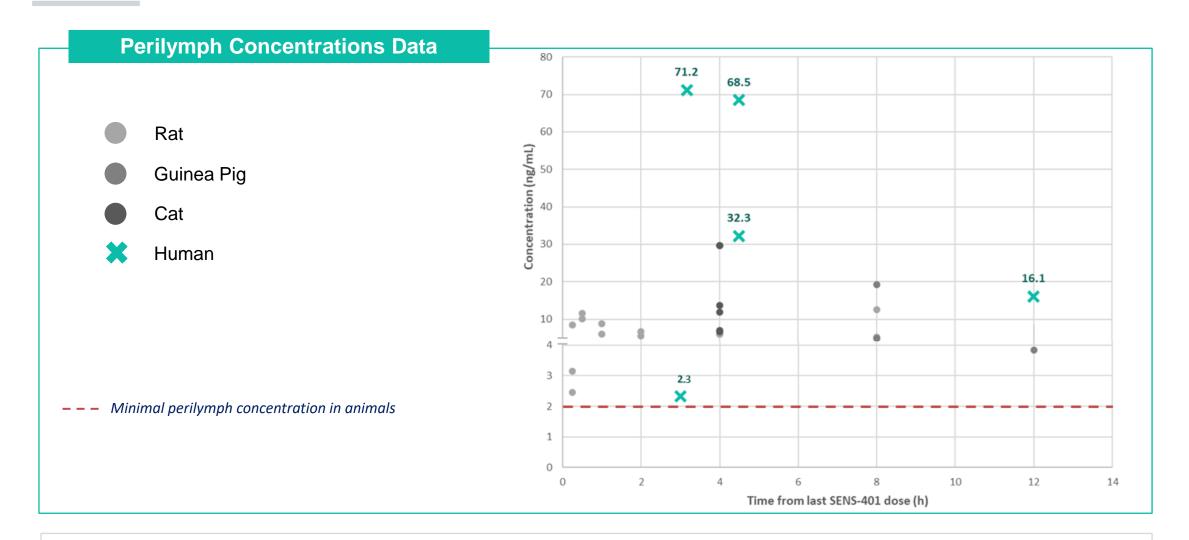
SENS-401 Study Commenced In Sept. 2022 Positive Preliminary Results Reported



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



SENS-401 is Detected in the Perilymph of the First 5 Treated Patients at Levels Consistent with Those Observed in Animals



- Plasma concentrations of SENS-401 in humans at steady state: dosing of 43.5 mg b.i.d range from 20-90 ng/mL
- Perilymph concentrations in animal models at equivalent plasma levels range from 2 to 30 ng/mL
- The observed values in the first 5 patients are in line with the predicted values, ranging from 2 to 70 ng/mL

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Residual Low Frequency Hearing Benefits for Cochlear Implant Users

Initial shift*

(2-4 weeks postoperative) between surgery and initial activation of the device

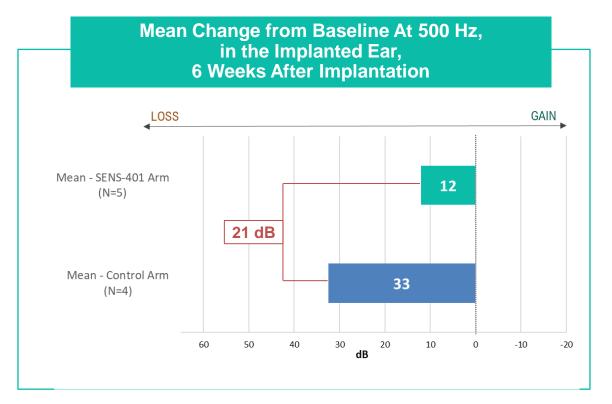
Attributed to perioperative factors

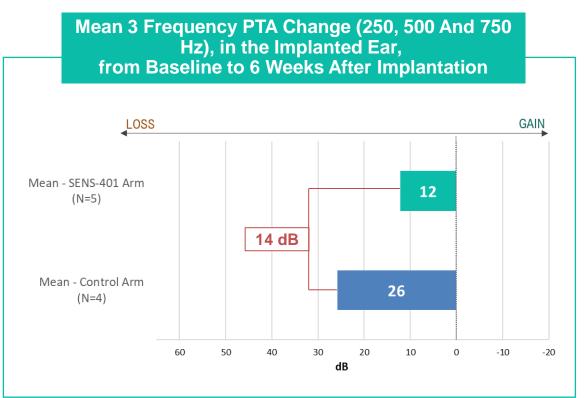
Second shift*
(3-6 months postoperative)

 Attributed to intracochlear fibrosis, excitotoxic changes from electrical and acoustic stimulation

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

SENS-401 Preserves Early Loss of Residual Hearing - As Shown in all Five Patients Treated so far

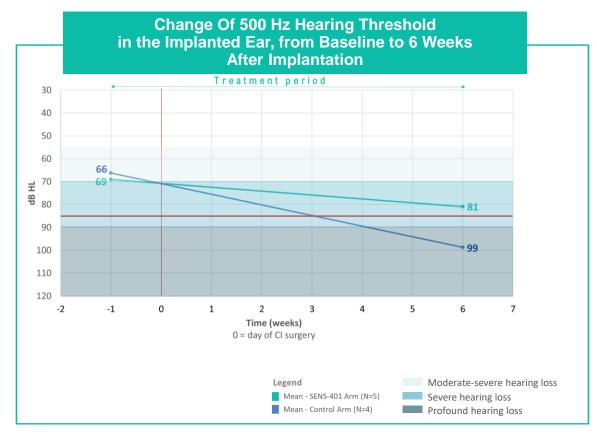


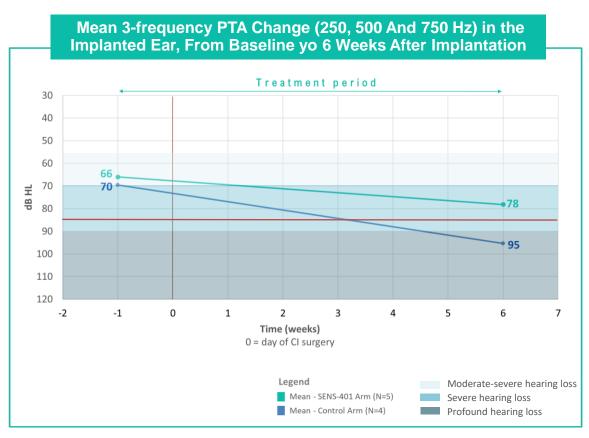


PTA = Pure Tone Average

A clinically significant difference of 21 dB and 14 dB in the early loss of residual hearing between SENS-401 and control
groups is observed at 500 Hz and in the average of 3 frequencies respectively, 6 weeks after cochlear implantation

SENS-401 Also Preserves Post-Operative Hearing - As Measured at the End of the Treatment Period





Postoperative hearing preservation defined as unaided air-conduction thresholds <85 dB HL (adaptation of Jensen et al., 2021)

- The SENS- 401 treated group remains above the defined threshold of postoperative hearing preservation
- Shift in hearing loss degree: patients not treated with SENS-401 are progressing from moderate-severe hearing loss to profound hearing loss

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SENS-401 CI Preliminary Results Conclusion



Preliminary key results are promising and suggest that SENS-401 can cross the labyrinthine barrier to target cochlear hair cells.



Six 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, favorable trend for the treated group (12 dB), in comparison to the untreated group. (33 dB), resulting in a difference of clinical significance of 21 dB



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



SENS-401 taken for 7 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.

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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



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



SENS-401 Phase 2a Proof-of-Concept Study First Data Expected H2 2023

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

SCREENING PERIOD (between -28 and -2 days)

Subjects suffering from a neoplastic disease for which the treatment protocol includes a chemotherapy with cisplatin and having a higher risk of ototoxicity induced by the cisplatin treatment

(about 58 subjects)

RANDOMIZATION STUDY DURATION (max 31 weeks) Follow-up Follow-up - No treatment **Cisplatin only** Arm A - Up to 29 subjects Up to 18 weeks (max 6 cycles of 3 weeks) 4 weeks 8 weeks **SENS-**Cisplatin + SENS-401 Follow-up - No treatment **SENS-401** Arm B - Up to 29 subjects 401 Up to 18 weeks (max 6 cycles of 3 8 weeks week weeks) weeks **Objectives: Primary Endpoint Efficacy Secondary Endpoint** Rate of ototoxicity High Frequency PTA · Speech in Noise and quiet

Safety

AEs & SAEs incidence

THI questionnaire

SENS-401 Program Key Milestones, Data Readouts in 2023



First patient enrolled in SENS-401 CIO NOTOXIS Dec 2022



SENS-401 with cochlear implants
- Final data readout H1 2024

SENS-401 CIO NOTOXIS
- preliminary results H2 2023

Sensorion Newsflow [estimated timelines]

H1 2024 – SENS-501: First Patient Inclusion

 H2 2022 – SENS-501: EMA & FDA ODD, FDA RPDD 	
TIZ ZUZZ OLINO UUT. LIVIT OTT ODD, I DITTIT DD	
 Q2 2023 – GJB2-GT: Candidate selection 	
 Mid-2023 – SENS-401 in combination with cochlear implantation: preliminary results 	
 Q2 2023 – SENS-501: Clinical Trial Application (CTA) first submission (MHRA) 	
 July 2023 – SENS-501: CTA submission in Europe 	Ø
 August 2023 – Successful €35m capital raise 	
 H2 2023 – SENS-401 CIO: NOTOXIS preliminary results 	
 H2 2023 – SENS-501: CTA Approvals 	
 H1 2024 – SENS-401 in combination with cochlear implantation: full data readout 	

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THANK YOU

E: contact@sensorion-pharma.com

