

Unlocking the potential of advanced therapies for hearing loss



March 2023

SENSORION



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Sensorion: overview

- Sensorion specializes in GeneTherapies in the ear and currently develops two programs targeting monogenic forms of deafness in pediatrics and adult onset:
 - OTOF-GT caused by a mutation of the gene encoding for otoferlin
 - GJB2-GT related to mutation in GJB2 gene
 - Prospective natural histories ongoing, strong European eco-system in place
- Sensorion also has an **oral small molecule asset SENS-401** currently in clinical development in several indications:
 - Sensorion and Cochlear Ltd. CTA approved for combo with cochlear implantation
 - Cisplatin-Induced Ototoxicity clinical POC study ongoing
 - Sudden Sensorineural Hearing Loss positive Phase 2 secondary endpoints
- Exclusive relationship with Institut Pasteur in the field of hearing genetics providing product pipeline
- Strong partnerships with several key players in the space including Necker Hospital (Paris), Cochlear Ltd. (ASX listed) and Sonova (global hearing aid market leader)
- Strong shareholder base including leading blue-chip investors; listed on Euronext Growth





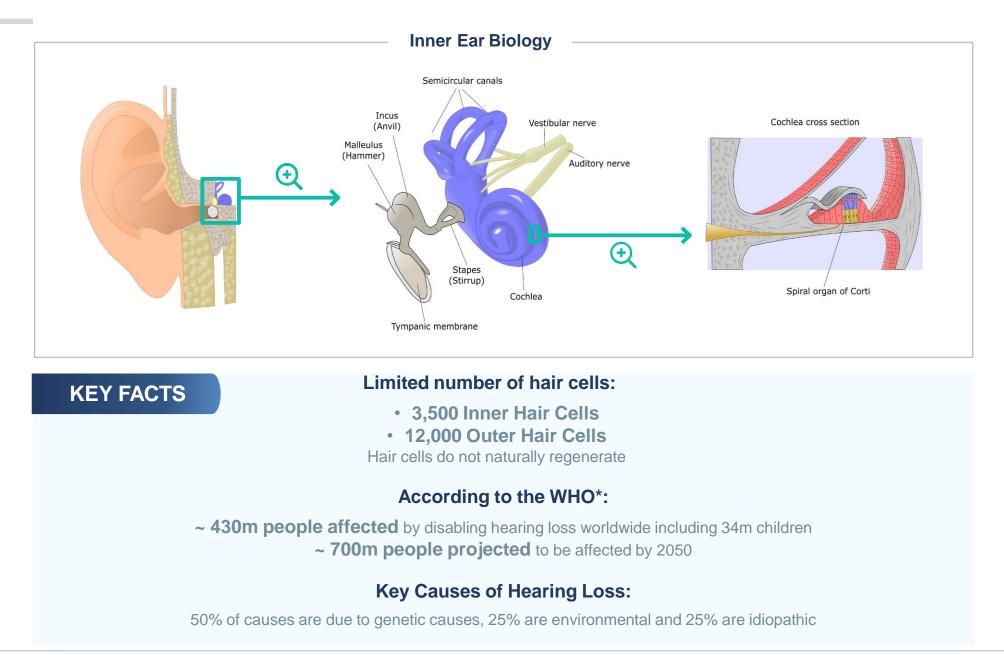




FINANCIALOVERVIEW

Date Established	2009
IPO	
Euronext Paris	ALSEN.PA
Cash (Dec 31, 2022)	≈€26.2m
Cash runway until end of 2023	

The Inner Ear: One Of The Most Delicate Organs In The Human Body



Sensorion Is Well Positioned To Transform The Hearing Landscape

THE LEADING FRANCHISE OF PRODUCT ASSETS AND INFRASTRUCTURE

GENE THERAPY

Otoferlin deficiency (OTOF-GT)

CTA enabling studies

• Hearing restoration in DFNB9 pediatric patients

Connexin 26 deficiency (GJB2-GT)

Lead selection

- 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

Cisplatin-Induced Ototoxicity (CIO)

NOTOXIS Ph2 study ongoing

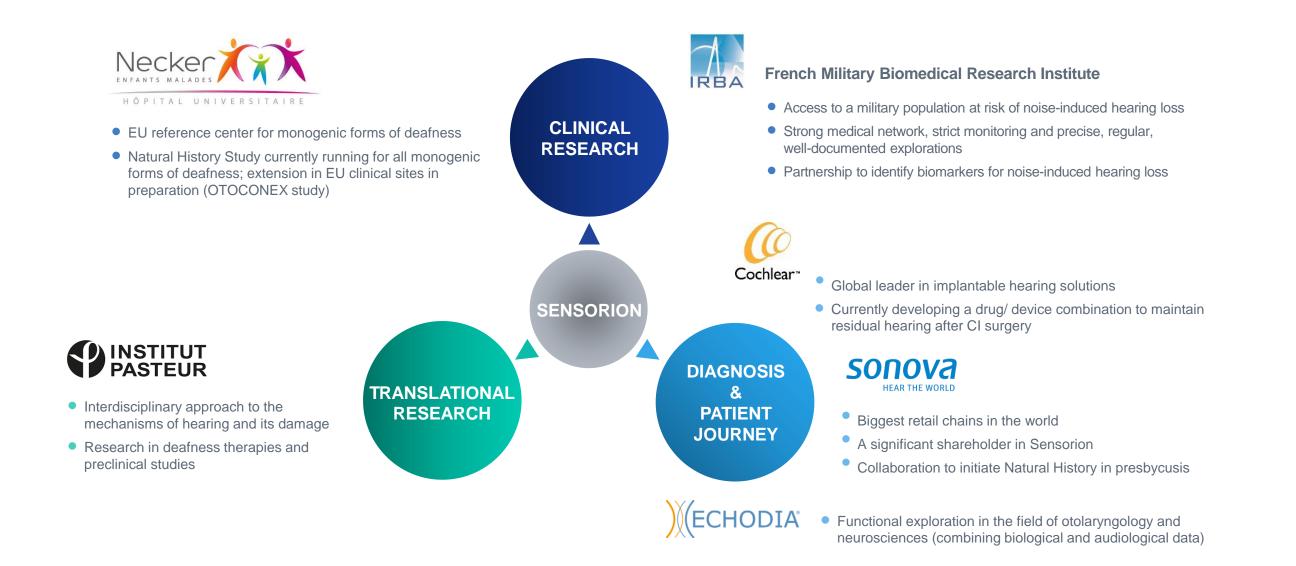
Assess prevention of the ototoxicity induced by Cisplatin in patients
 with neoplastic disease

Cochlear Implantation (CI)

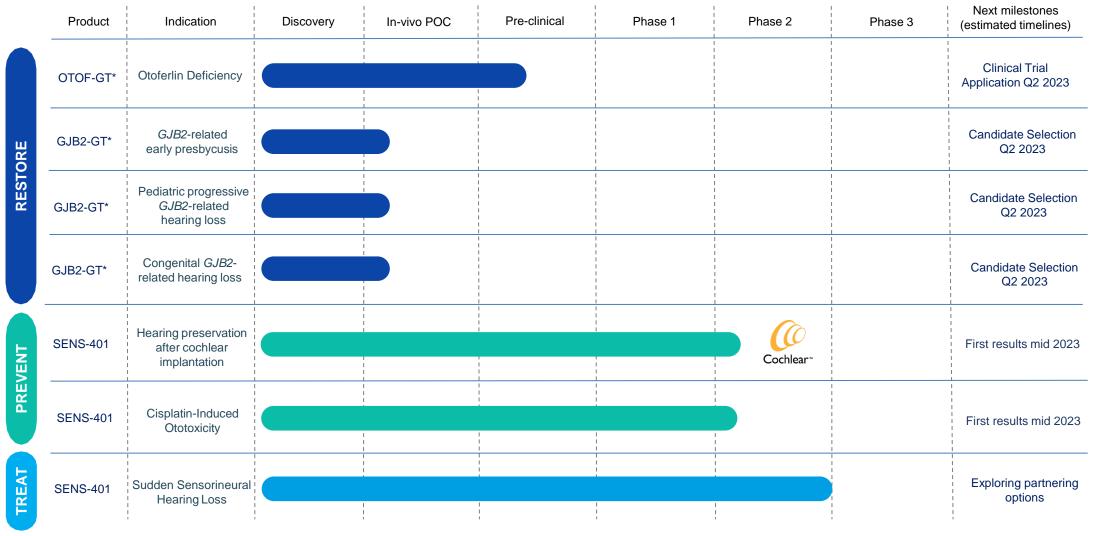
Ph2 study ongoing

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

Our Critical Strategic Alliances That Support The Franchise



Sensorion's Pipeline: A Comprehensive 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)

An Experienced Leadership Team and SAB



NAWAL OUZREN Chief Executive Officer

> SENSORION (Since 2017)

SHIRE (2016-2017) Head of the Global Genetic Diseases Franchise

BAXALTA (2014-2016) Vice President of the Global Hemophilia Franchise



GÉRALDINE HONNET Chief Medical Officer

SENSORION (Since 2020)

GENETHON (2011-2020) Director of Development

TRANSGENE (2007-2011) Responsible of development of infectious diseases programs



DAVID LAWRENCE Chief Financial Officer

> SENSORION (Since 2023)

VALNEVA (2017-2021) Chief Financial Officer

SYNPROMICS (2011-2019) Co-Founder & Board member

GSK/CHIRON/ACAMBIS (1988-2006)



STEPHANIE FILIPE Head of PMO

> SENSORION (Since 2020)

CELLECTIS (2016-2020) Program Leader & Preclinical Manager

OTR3 (2008-2015) R&D Director & Clinical Project Manager



LAURENT DESIRE Head of Preclinical Development

> SENSORION (Since 2020)

YPOSKESI (2017-2020) Head of Cellular & Molecular Biology Unit

DIAXONHIT (2012-2017) R&D Executive Director



CHRISTINE LE BEC Head of CMC Gene Therapy

> SENSORION (Since 2020)

GENETHON (1996-2020) Head of CMC Analytical Department

Scientific Advisory Board

- Pr Christine Petit, France, Chair SAB, Professor, Institut Pasteur
- Pr Alain Fischer, France, Professor, Collège de France
- Dr. Robert Dow, UK, Chief Medical Officer, Scendea
- **Dr. Paul Avan**, France, Head of the Center for Research, Hearing Institute (Paris)
- Dr. Diane Lazard, France, Principal Associate Investigator, Hearing Institute (Paris)
- Dr. Hernán López-Schier, Germany, Senior Group Leader & Research Unit Director at the Helmholtz Center (Munich)

We Have Established Internal Capabilities To Ensure Successful Execution



GENE THERAPY PROGRAMS



Sensorion's Gene Therapy Programs Aim To Treat Rare Auditory Diseases

FIRST TWO PROGRAMS RESULTING FROM THE INSTITUT PASTEUR COLLABORATION

OTOFERLIN DEFICIENCY	GJB2-RELATED HEARING LOSS
 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 FDA has granted RPDD 	 We have identified three forms of hearing loss associated with <i>GJB2</i> 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 <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
DELAYED DIAGNOSIS –	on publicly available population data, Chardan 2020 report, Bryan, Garnier & Co 2019 report, et al. 2020 (<u>link</u>) NOT SUSPECTED AT FIRST SIGHT IG 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	
CT product abouting high lovel of target calls transduction	
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	
Retard Theory Study proparing skeed of the similar that	
Regular engagement with regulatory agencies	

The GT Pediatric Indications Have Blockbuster Sales Potential

OTOF-GT is the perfect pilot program

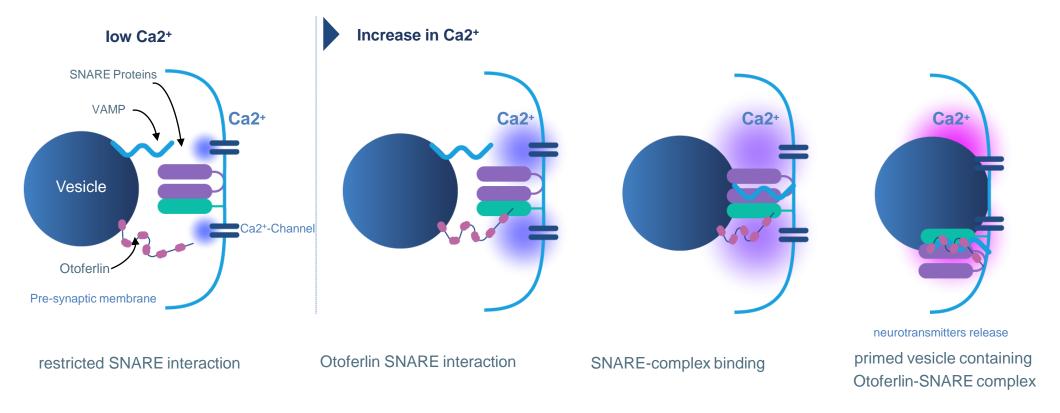
- Well understood biology and pathology of the otoferlin deficiency
- Full functionality of the remaining chain
- High specificity for the inner hair cells (IHCs), no off-target effect expected

- OTOF-GT will be the pilot program demonstrating that GT is a relevant medical approach for the inner ear
- OTOF-GT 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
 - \checkmark Rare Pediatric Disease Designation with eligibility for voucher in the US



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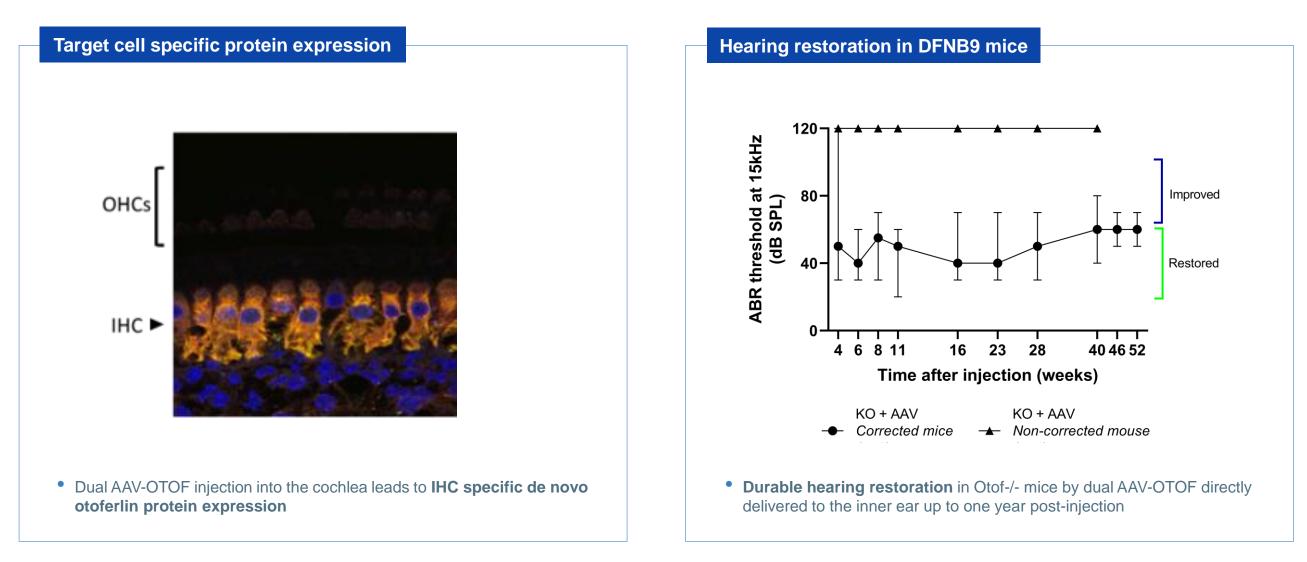
OTOF Gene Encodes Otoferlin, A Key Ca2+ Sensor Protein



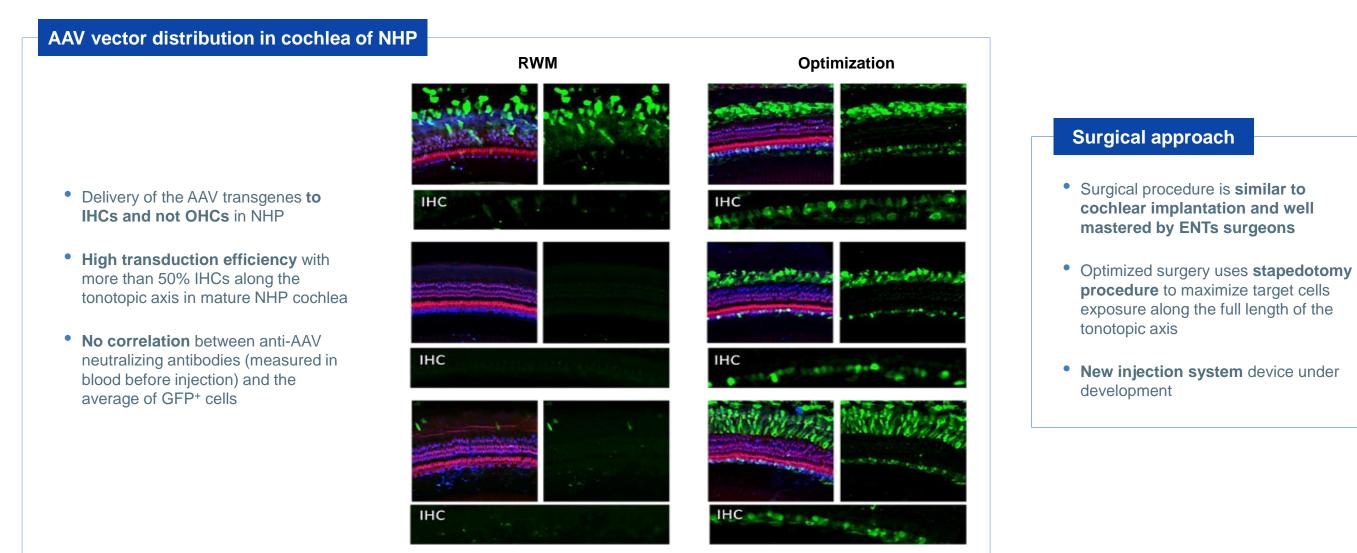
Model illustrating calcium regulation of otoferlin/SNARE interaction in the hair cell – Adapted from Ramakrishnan et al. 2014

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

Dual AAV-OTOF Resulted In IHCs Specific Expression And Hearing Restoration In DFNB9 Mice



Optimized Surgical Procedure Leads To IHC Specific AAV-delivered Transgene Transduction In Mature NHP Cochlea



MyoVIIa Actin GFP

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Lahlou et al. ARO 2022 link

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

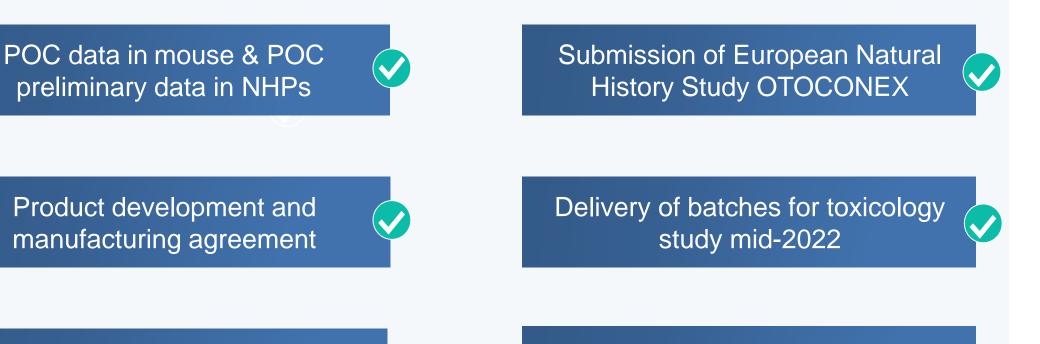


Audinnove is financed by the French State, via the National Research Agency through the "Investing for the future" program (ref: ANR-18-RHUS-0007)

OTOCONEX: expanding the Natural History Study across Europe



OTOF Gene Therapy Program Status – Progressing On Track

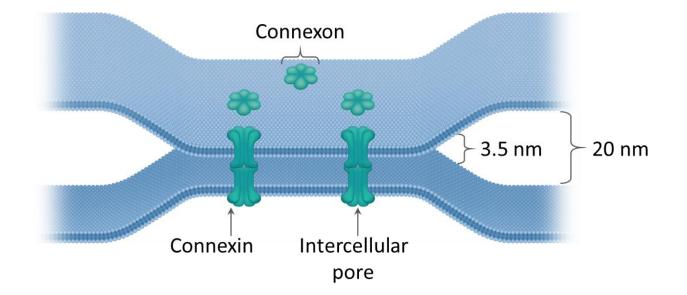


Clinical Trial Application Q2 2023



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
- *GJB2* 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

GJB2 Gene Therapy Program Next Steps



Submission of Natural History Study in collaboration with Sonova

Candidate selection H1 2023

Preclinical IND enabling studies

SMALL MOLECULE PROGRAMS

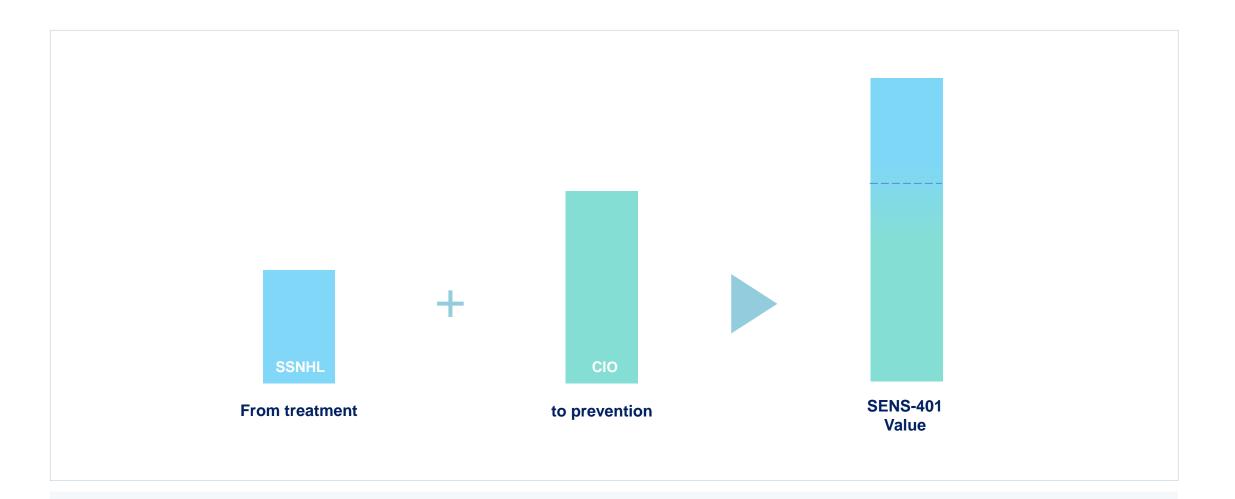


SENS-401: Multiple Indications To Treat And Prevent Hearing Loss

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

*"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 Is A Pipeline In Itself 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:

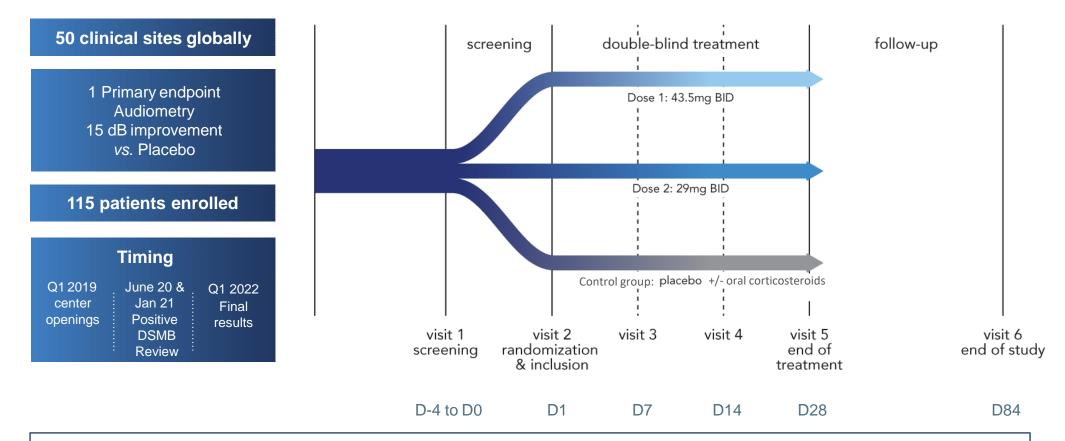
- Difficulties in communicating, social isolation, cognitive decline
- Accompanying tinnitus

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

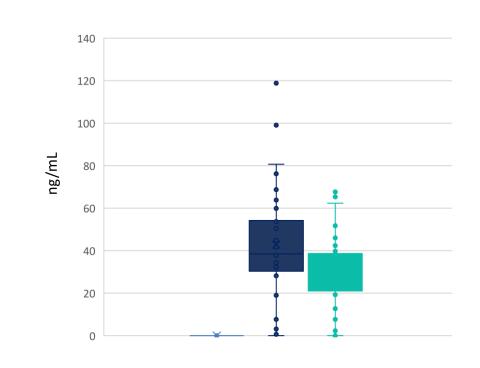


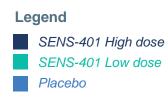
Primary endpoint definition:

"...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)"

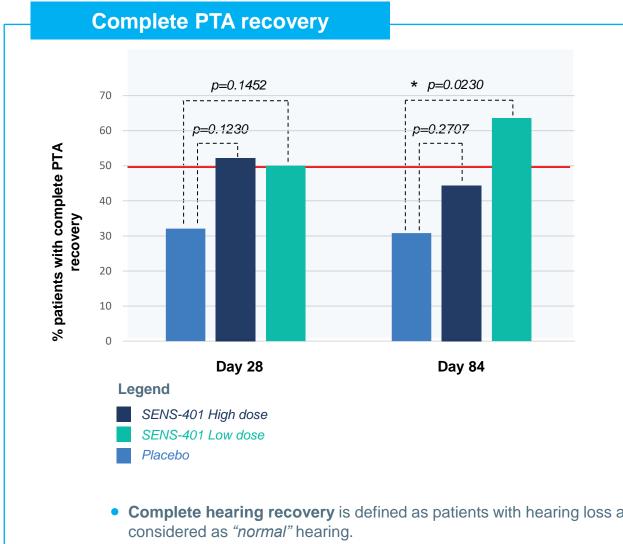
SENS-401 Plasmatic Exposure

Plasmatic concentration (Pre-dose at Day 14 and Day 28)





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

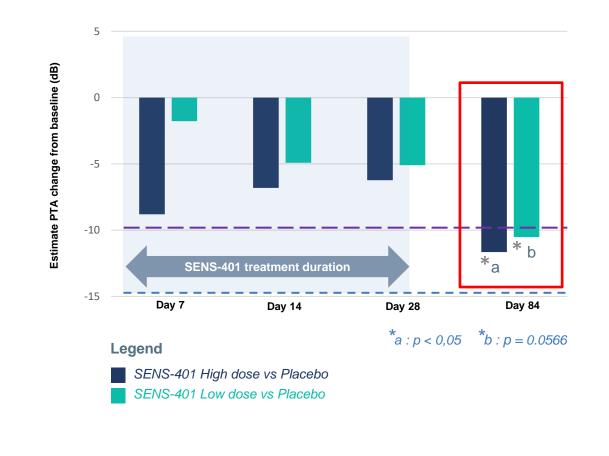


Complete PTA recovery (n/n total)	Placebo	High Dose	Low Dose	
Day 28	9/28	12/23	13/26	
Day 84	8/26	8/18	14/22	

• Complete hearing recovery is defined as patients with hearing loss at baseline who will revert to PTA < 20 dB,

Although Primary Endpoint Not Met, Data Supports Further Clinical Development

PTA improvement from baseline compared to placebo on per protocol idiopathic SSNHL



	Day 7	Day 14	Day 28	Day 84
High dose	N= 21	N= 23	N= 22	N= 17
Low dose	N= 26	N= 26	N= 26	N= 21
Placebo	N= 25	N= 28	N= 27	N= 25

- - - Primary analysis

Comparing SENS-401 treatment groups to Placebo at **Day 28** with a **target of an improvement of 15 dB**.

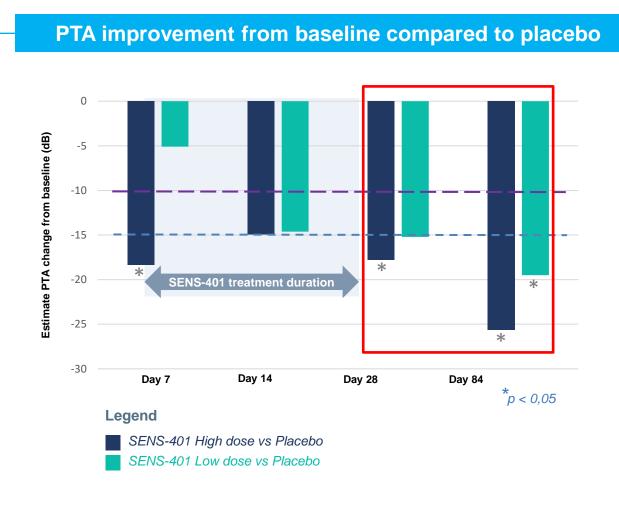
— — **10 dB change from baseline** considered as clinically meaningful.

Sub-population

Homogeneous idiopathic population of patients treated with corticosteroids.

• Statistically significant effect on PTA change with more than 10 dB change from baseline vs placebo observed over time in homogeneous idiopathic population of patients treated with corticosteroids.

SENS-401 Effect Is More Pronounced In A Profound Hearing Loss Subgroup (PTA ≥ 80 Db)



	Day 7	Day 14	Day 28	Day 84
High dose	N= 11	N= 11	N= 9	N= 9
Low dose	N= 11	N= 11	N= 9	N= 9
Placebo	N= 14	N= 15	N= 15	N= 13

– – – Primary analysis

Comparing SENS-401 treatment groups to Placebo at Day 28 with a **target of an improvement of 15 dB**.

— 10 dB change from baseline considered as clinically meaningful.

Sub-population

Homogeneous idiopathic population of patients with profound hearing loss (PTA \ge 80 dB) 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 hearing loss.
- A better response was observed in both treatment groups with a continuous improvement between Day 28 and Day 84.

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 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
- The change in PTA translates into functional improvement evidenced with speech audiometry tests
- Safe and well tolerated in 115-patient SSNHL study; primary endpoint not met
- **Responder rate is always better in the treated group** compared to Placebo and difference with Placebo increases over time

Cisplatin Administration For Chemotherapeutic Treatment Of Cancer 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

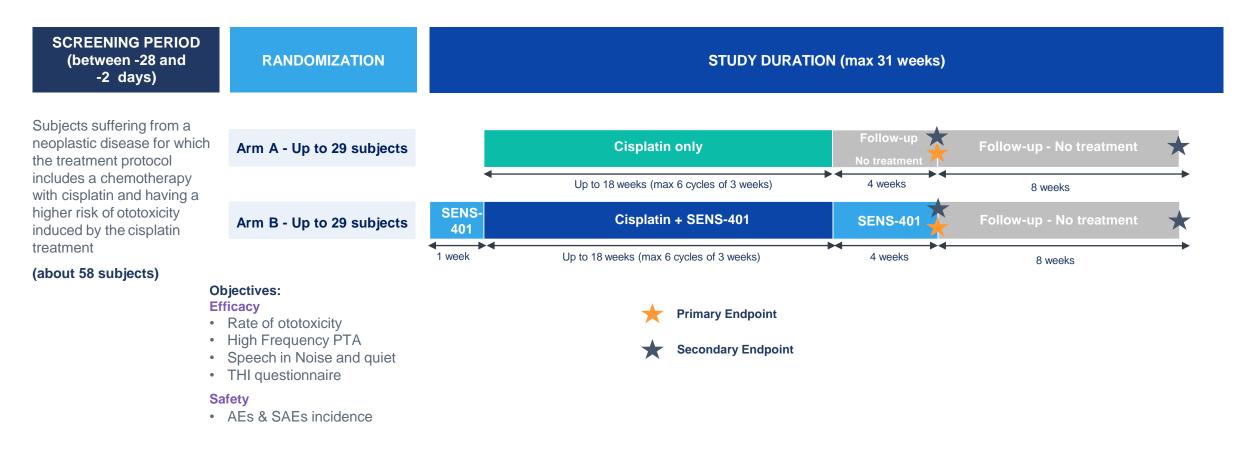
Potential treatments must not interfere with cisplatin efficacy.

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)

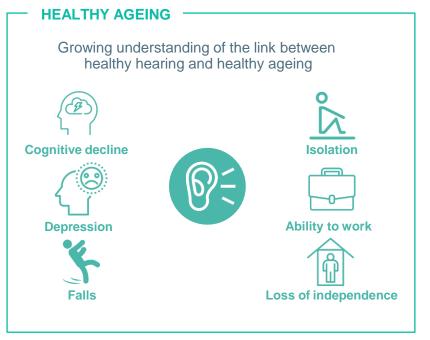
SENS-401 Phase 2a Proof-of-concept Study; First Data Expected Mid-2023

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



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)

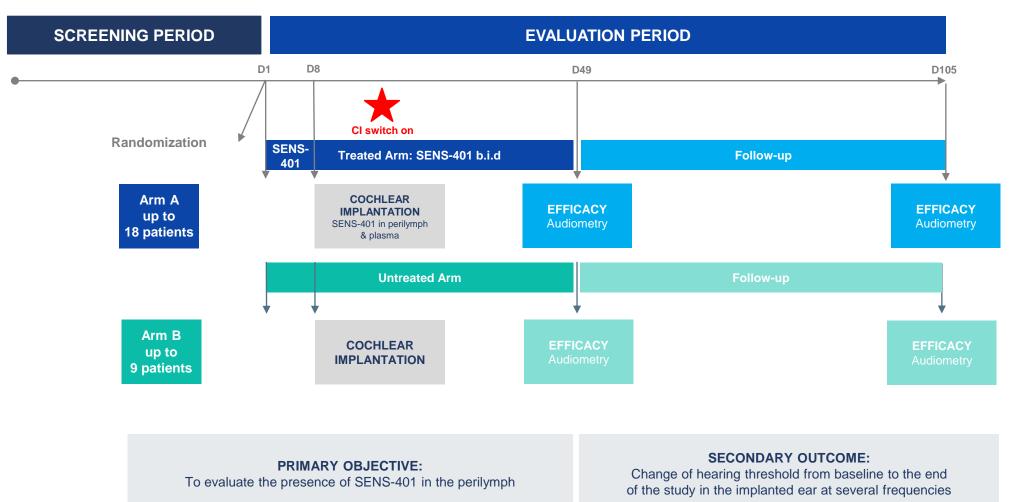


¹Cochlear[®] FY21 Result Presentation (<u>link</u>) ²Market estimates (<u>link</u>)

SENS-401 Study Commenced In Sept. 2022; First Data Expected Mid-2023

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





SENS-401 Program Key Milestones, Data Readouts In Q2 2023

First patient enrolled in SENS-401 CIO NOTOXIS Dec 2022



SENS-401 CIO NOTOXIS CTA amendment approved Oct 2022

SENS-401 CIO NOTOXIS - first results mid 2023

SENS-401 combo with cochlear implants - first results mid 2023

Sensorion potential newsflow [estimated timelines]

- Mid-2022 OTOF-GT: delivery of batches for toxicology study
 H2 2022 OTOF-GT: EMA's positive opinion for ODD
 H2 2022 SENS-401 CIO: NOTOXIS CTA study amendment approval
 H2 2022 OTOF-GT: FDA approval for RPDD
 H2 2022 OTOF-GT: FDA approval for US ODD
 April 6, 2023 Sensorion to host a Gene Therapy R&D day
 Mid-2023 SENS-401 in combination with cochlear implantation: first results
- Q2 2023 SENS-401 CIO: NOTOXIS first results
- Q2 2023 OTOF-GT: submission of the Clinical Trial Application (CTA)
- Q2 2023 GJB2-GT: candidate selection

THANK YOU

E: contact@sensorion-pharma.com

