

SENSORION



Copyright by Sensorion - 2022 - All Rights Reserved

DISCLAIMER

- This document has been prepared by Sensorion (the "Company") and is provided for information purposes only. This document does not purport to contain comprehensive or complete information about the Company and is qualified in its entirety by the business, financial and other information that the Company is required to publish in accordance with the rules, regulations and practices applicable to companies listed on Euronext Paris. No reliance may be placed for any purposes whatsoever on the information or opinions contained in this document or on its accuracy or completeness.
- This presentation does not constitute an offer to sell, a solicitation of, or an invitation to subscribe for or to buy, securities of Sensorion in any jurisdiction.
- The information and opinions contained in this document are provided as of the date of this document only and may be updated, supplemented, revised, verified or amended, and thus such information may be subject to significant changes. The Company is not under any obligation to update the information or opinions contained herein which are subject to change without prior notice.
- The information contained in this document has not been subject to independent verification. No representation, warranty or undertaking, express or implied, is made as to the accuracy, completeness or appropriateness of the information and opinions contained in this document. The Company, its subsidiaries, its advisors and representatives accept no responsibility for and shall not, under any circumstance, be held liable for any loss or damage that may arise from the use of this document or the information or opinions contained herein.
- This document contains information on the Company's markets and competitive position, and more specifically, on the size of its markets. This information has been drawn from various sources or from the Company's own estimates which may not be accurate and thus no reliance should be placed on such information.
- This document contains certain forward-looking statements. These statements are not guarantees of the Company's future performance. These forward-looking statements relate to the Company's future prospects, developments and marketing strategy and are based on analyses of earnings forecasts and estimates of amounts not yet determinable. Forward-looking statements are subject to a variety of risks and uncertainties as they relate to future events and are dependent on circumstances that may or may not materialize in the future. Forward-looking statements cannot, under any circumstance, be construed as a guarantee of the Company's future performance and the Company's actual financial position, results and cash flow, as well as the trends in the sector in which the Company operates, may differ materially from those proposed or reflected in the forward-looking statements contained in this document. Important factors that could cause actual results to differ materially from the results anticipated in the forward-looking statements include those discussed or identified in the "Risk Factors" section of our 2021 Annual Financial Report published on April 28, 2022, and available on our website (www.sensorion.com). Even if the Company's financial position, results, cash-flows and developments in the sector in which the Company operates were to conform to the forward-looking statements contained in this document, such results or developments cannot be construed as a reliable indication of the Company's future results or developments. The Company does not undertake any obligation to update or to confirm projections or estimates made by analysts or to make public any correction to any prospective information in order to reflect an event or circumstance that may occur after the date of this document.
- Certain figures and numbers appearing in this document have been rounded. Consequently, the total amounts and percentages appearing in the tables may not necessarily equal the sum of the individually rounded figures, amounts or percentages.
- All persons accessing this document must agree to the restrictions and limitations set out above.

Investments Highlights

- Sensorion is focused on innovative treatments that can restore, treat and prevent hearing loss
 - Its oral small molecule asset SENS-401 currently in clinical development in the following indications:
 - Sensorion and Cochlear Ltd. CTA approved for SENS-401 in patients scheduled for cochlear implantation in H1 2022 in France and Australia. First patient enrolled in Sept 2022
 - Cisplatin-Induced Ototoxicity clinical POC study continued with CTA amendment approval in H2 2022
 - Sudden Sensorineural Hearing Loss indication looking for potential partner
 - Two gene therapy programs, OTOF-GT and GJB2-GT, targeting monogenic forms of deafness:
 - caused by a mutation of the gene encoding for otoferlin
 - related to mutation in GJB2 gene
- **Exclusive relationship with Institut Pasteur** providing exclusive rights of first negotiation for all patents in the field of the genetics of hearing during the timeframe of the agreement
- Strong partnerships with Necker Hospital, Cochlear Ltd. and Sonova
- Strong shareholders support from **leading blue-chip investors**

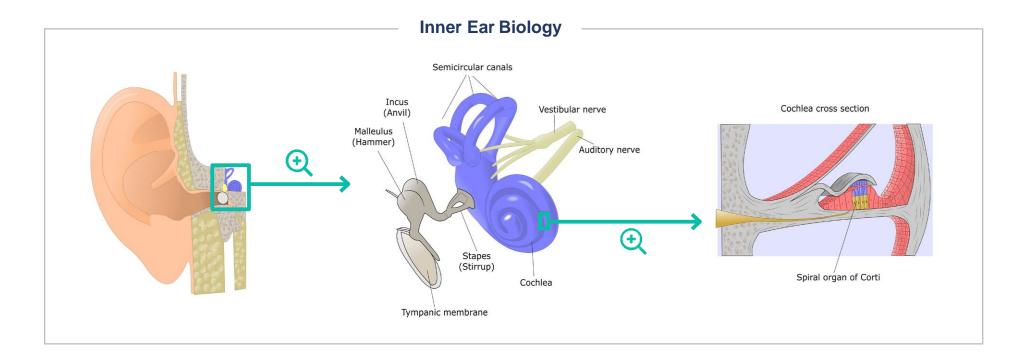




FINANCIALOVERVIEW

Date Established	
IPO	
Euronext Paris	ALSEN.PA
Cash (June 30, 2022)	≈€39m
Cash runway until end of Q3 2023	

The inner ear: one of the most delicate organs in the human body



KEY FACTS

Limited number of hair cells:

• 3,500 Inner Hair Cells

• 12,000 Outer Hair Cells

Hair cells do not naturally regenerate

According to the WHO*:

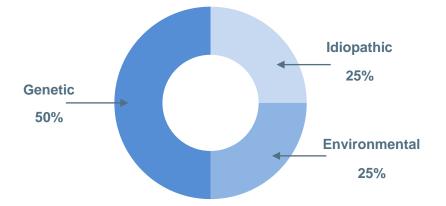
~ 400m people affected by disabling hearing loss worldwide including 34m children

~ **700m people projected** to be affected by 2050

*World Health Organization, 2021 World report on Hearing

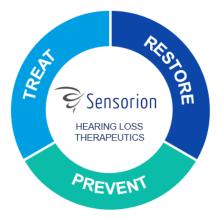
Our strategy: **RESTORE**, **TREAT & PREVENT** hearing loss

Causes of hearing loss



SMALL MOLECULE APPROACH

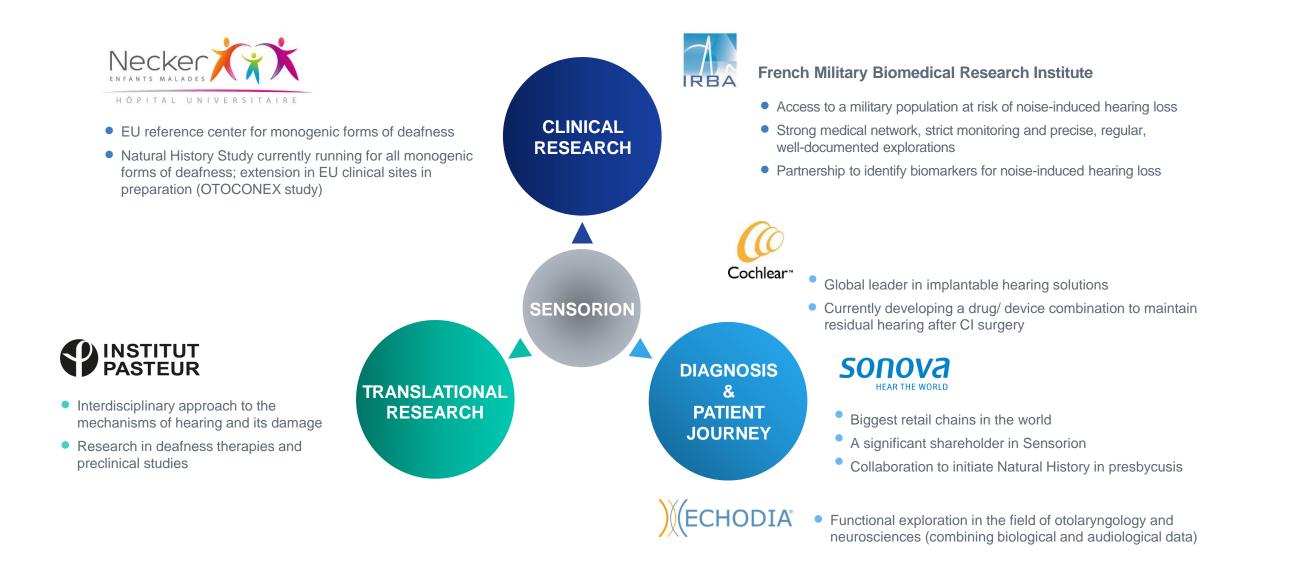
- Phase 2 study completed with SENS-401 to **TREAT** Sudden Sensorineural Hearing Loss Exploring partnering opportunities
- Phase 2a study with SENS-401 to **PREVENT** residual hearing loss after cochlear implantation
- Phase 2a study with SENS-401 to **PREVENT** hearing loss caused by Cisplatin-Induced Ototoxicity



GENE THERAPY APPROACH

- Exclusive collaboration signed with Institut Pasteur in Gene Therapy to **RESTORE** auditory functions
- Program to RESTORE hearing in otoferlin deficiency (DFNB9 deafness), one of the most common forms of congenital deafness
- Program to **RESTORE** hearing in *GJB2*-related hearing loss, the most common form of congenital deafness, also involved in adult early onset forms of severe presbycusis and in childhood onset forms of hearing loss

Our critical strategic alliances from bench to bedside



Our pipeline: a comprehensive portfolio to **RESTORE**, **TREAT & PREVENT** hearing loss



*Option to obtain a licence from Institut Pasteur (pre-defined financial terms and other terms to be negotiated)

An experienced team, Board of Directors and SAB



NAWAL OUZREN Chief Executive Officer

SENSORION (Since 2017)

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



GÉRALDINE HONNET Chief Medical Officer

> SENSORION (Since 2020)

GENETHON (2011-2020) Director of Development



OTMANE BOUSSIF Chief Technical Officer & CSO ad interim

> SENSORION (Since 2021)

NOVARTIS (2015-2021) Head Cell & Gene Therapy T. Dev.



STEPHANIE FILIPE Head of PMO

> SENSORION (Since 2020)

CELLECTIS (2016-2020) Program Leader & Preclinical Manager

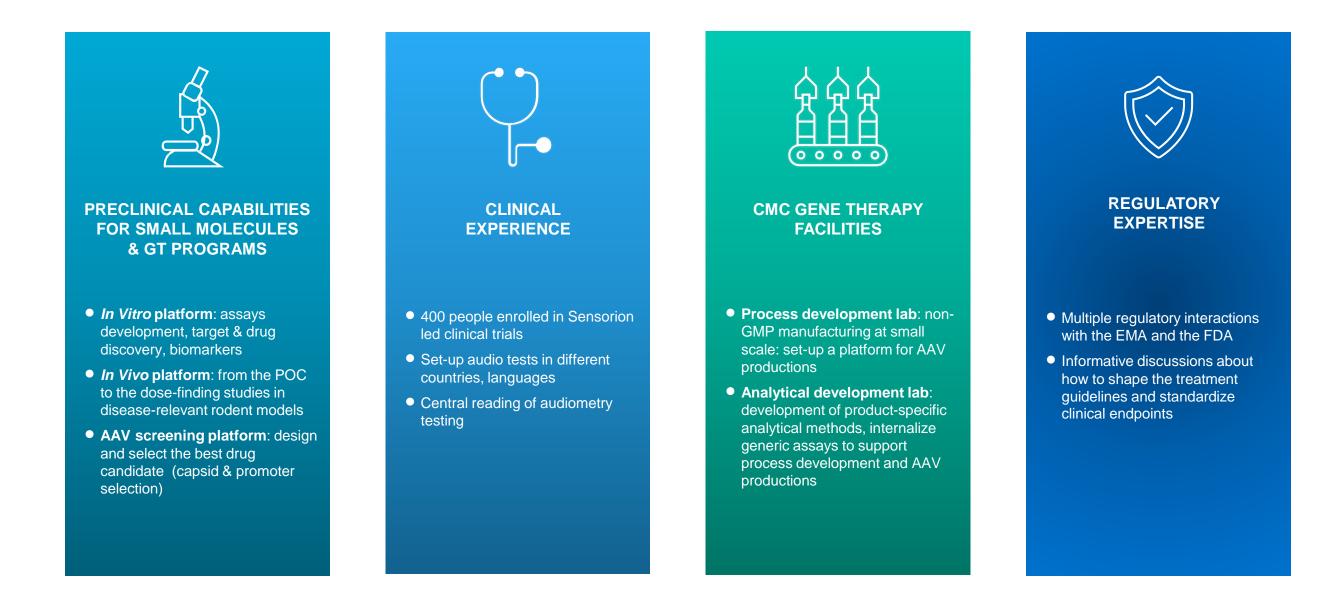
Board of Directors

- Scott D. Myers, USA, Chairman, Independent Director
- Khalil Barrage, USA, Director representing Invus
- Julien Miara, France, Director representing Invus
- Cédric Moreau, France, Director representing Sofinnova Partners
- John Furey, USA, Independent Director
- Eric de la Fortelle, France, Independent Director
- Aniz Girach, UK, Independent Director
- Jean-François Morin, France, Director representing BPI Investment

Scientific Advisory Board

- Pr Christine Petit, France, Chair, 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



SENS-401 TREAT AND PREVENT



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

Sudden Sensorineural Hearing Loss SSNHL

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

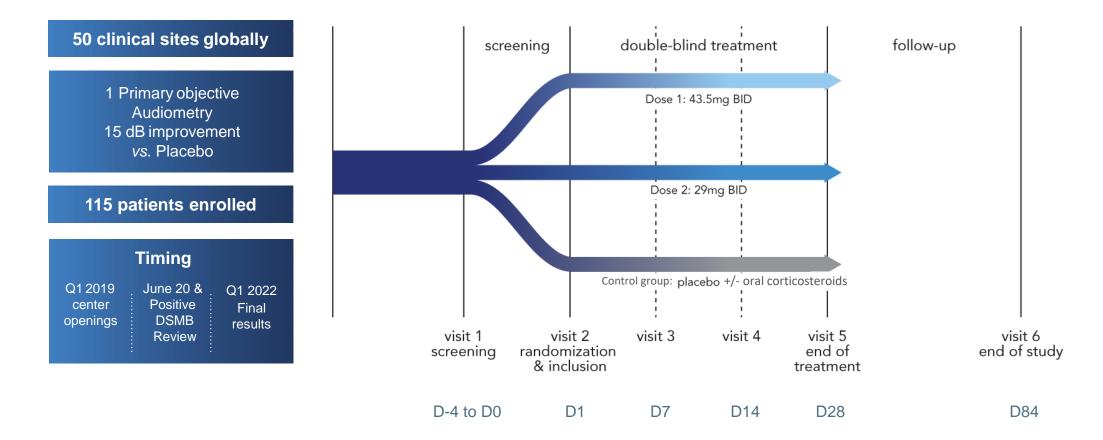
Incidence: 27-35 per 100,000 (218,000 patients in 2017 in G7 countries)¹

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

TREAT

SENS-401 SSNHL program: phase 2 design

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

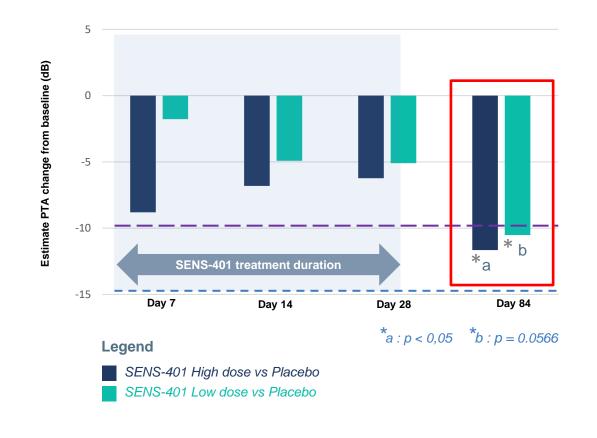


Primary endpoint definition:

"...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 shows a clinically meaningful effect at Day 84 in a large sub-population

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**.

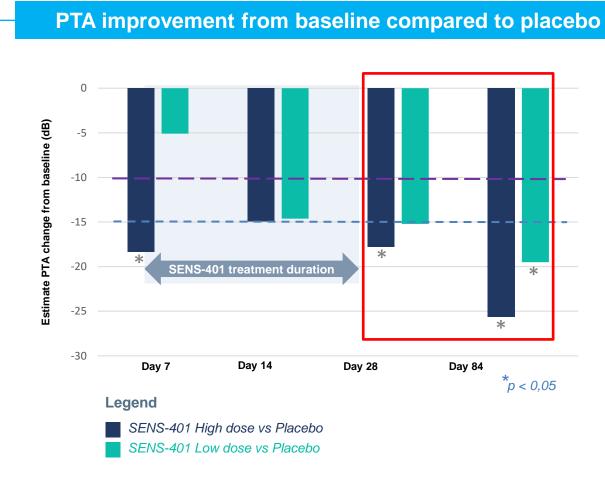
— — **10 dB change from baseline** considered as clinically meaningful.

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 sub-group (PTA \ge 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.

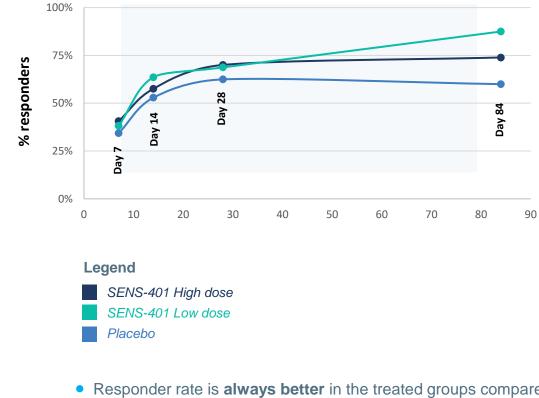
Sub-population

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.

Responder rate is always better in the treated groups compared to placebo

Responder analysis on ITT population



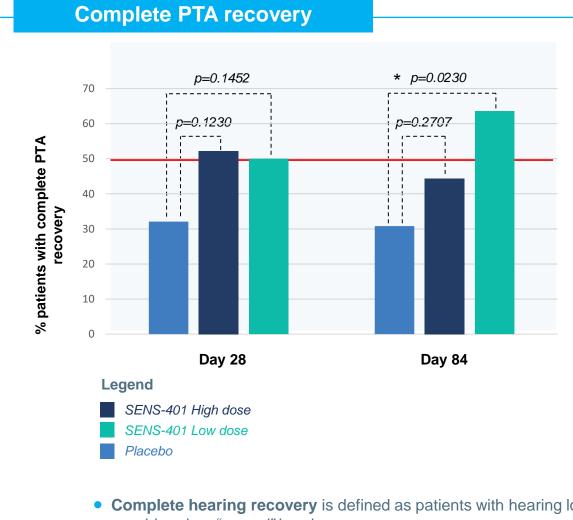
Population	showing an	improvement	greater than 30 dB
------------	------------	-------------	--------------------

n	Day 7	Day 14	Day 28	Day 84
High Dose	13	19	21	17
Low Dose	13	21	22	21
Placebo	11	18	20	18

Responder rate Calculated with the data available at each visit

- Responder rate is **always better** in the treated groups compared to placebo.
- Difference between treated groups and placebo increases over time.

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, considered as "normal" hearing.

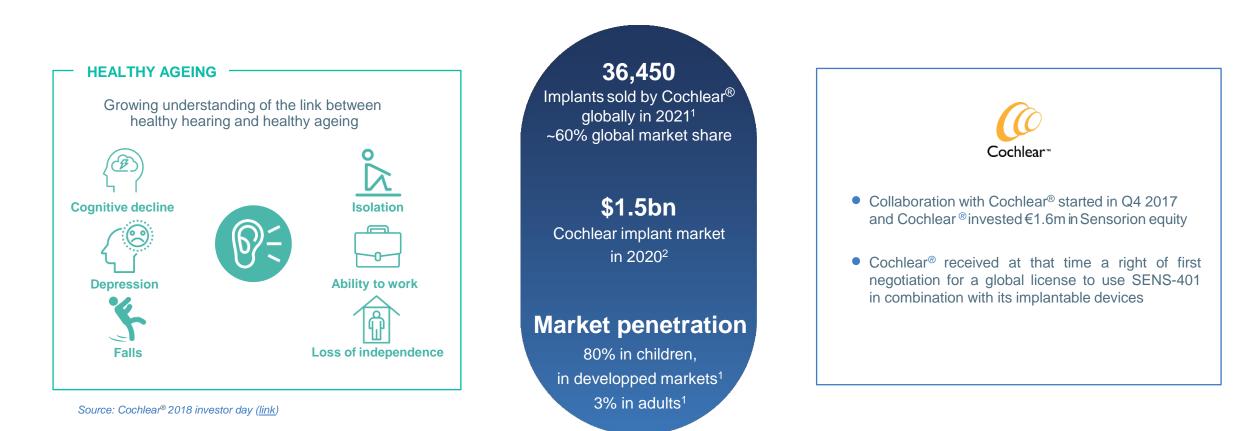
SENS-401 SSNHL phase 2 results summary Exploring partnering opportunities

AUDIBLE-S SECONDARY ENDPOINT RESULTS

- Safe and well tolerated in 115-patient SSNHL study; primary endpoint not met
- 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
- **Responder rate is always better in the treated group** compared to Placebo and difference with Placebo increases over time
- 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
- Complete PTA recovery is achieved in 50% of the SENS-401 treated patients

PREVENT SENS-401 to preserve residual hearing after cochlear implantation

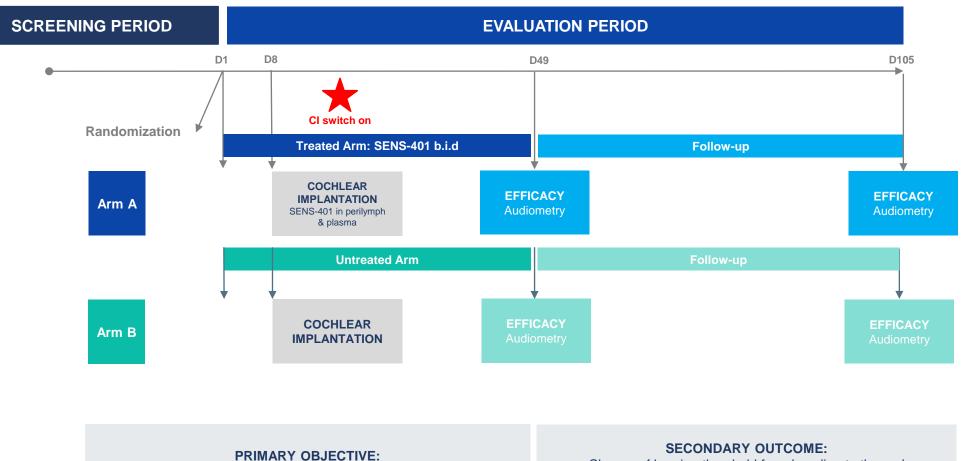
COMBINATION OF COCHLEAR IMPLANT WITH SENS-401 TO PREVENT CELL-DEATH POST COCHLEAR IMPLANT PROCEDURE



¹Cochlear[®] FY21 Result Presentation (<u>link</u>) ²Market estimates (<u>link</u>) SENS-401 proof-of-concept clinical study design approved in France and Australia with first patient enrolled in Sept. 2022

A PHASE IIA, MULTICENTER, RANDOMIZED, CONTROLLED, OPEN-LABEL STUDY





To evaluate the presence of SENS-401 in the perilymph

SECONDARY OUTCOME: Change of hearing threshold from baseline to the end of the study in the implanted ear at several frequencies

PREVENT

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)

PREVENT

SENS-401 CIO NOTOXIS Expecting CTA amendment approval in 2H 2022

SIGNIFICANTLY REDUCES CISPLATIN-INDUCED HEARING LOSS AND OUTER HAIR CELL DEATH IN PRE-CLINICAL MODELS

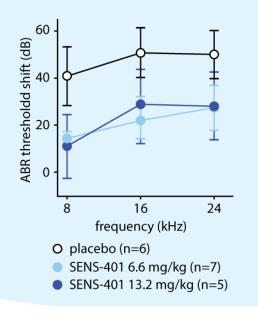
Significant improvement versus placebo 23-28 dB with 6.6 mg/kg (p<0.010) 22-30 dB with 13.2 mg/kg (p<0.013)

Significant enhancement of outer hair cells survival 22-264% for both doses

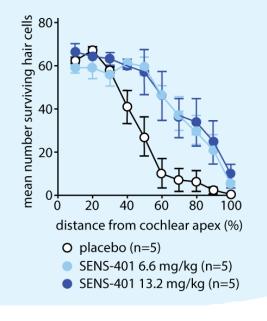
TREATMENT PROTOCOL

SENS-401 6.6 mg/kg, 13.2 mg/kg or placebo were administered to rats once-daily for 13 consecutive days after cisplatin infusion

Auditory brainstem response (ABR) threshold shift at day 14







Significantly more surviving outer hair cells were present after SENS-401 treatment compared with placebo (p<0.001), with up to 11-fold more in the basal turn of the cochlea

Source: Petremann et al. 2017, Otol Neurotol: Oral Administration of Clinical Stage Drug Candidate SENS-401 Effectively Reduces Cisplatin-induced Hearing Loss in Rats (link)

SENS-401 program next steps

CTA approval for SENS-401 study to preserve residual hearing post cochlear implementation in France and Australia 1H 2022

First patient enrolled in SENS-401 study to preserve residual hearing post cochlear implantation mid 2022

SENS-401 CIO NOTOXIS CTA amendment approval 2H 2022

SENS-401 SSNHL exploring potential partners for further developments

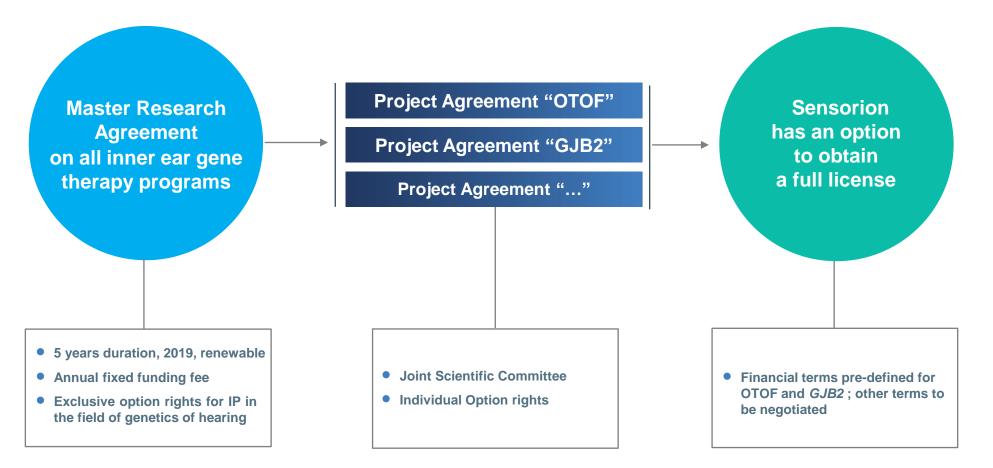
GENE THERAPY RESTORE



RESTORE Strategic R&D collaboration with Institut Pasteur on genetics of hearing

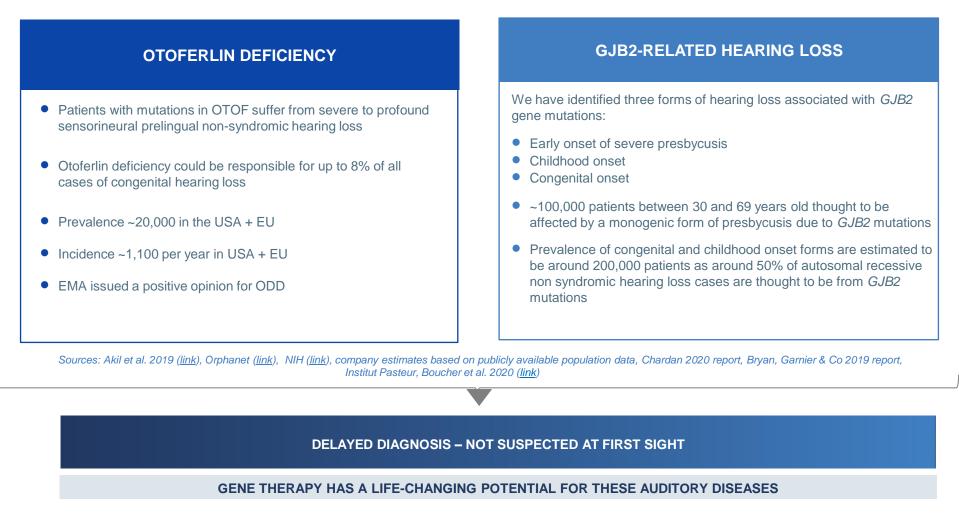
2 PROGRAMS INITIATED UNDER THE COLLABORATION AGREEMENT WITH INSTITUT PASTEUR

Rare disease, high unmet medical need

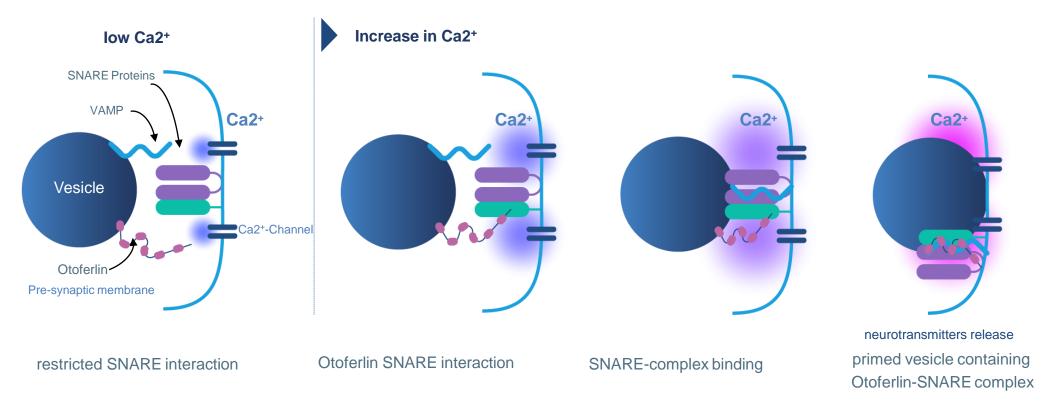


RESTORE Sensorion's gene therapy programs to treat rare auditory diseases

2 PROGRAMS INITIATED UNDER THE STRATEGIC COLLABORATION AGREEMENT WITH INSTITUT PASTEUR



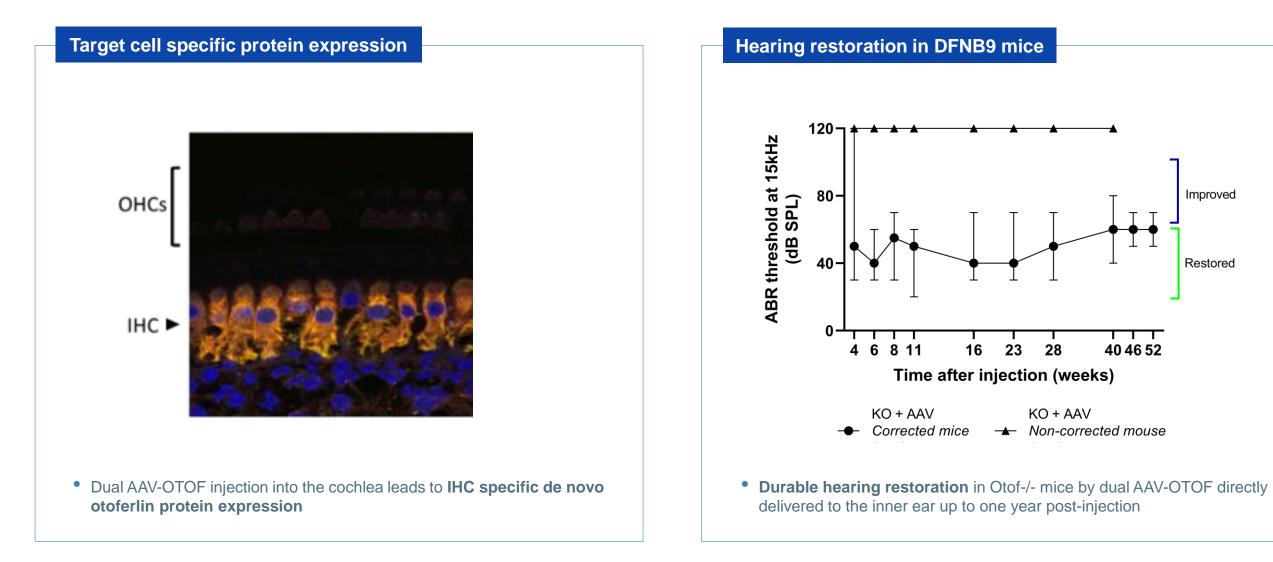
RESTORE OTOF Gene encodes otoferlin, a key Ca2+ sensor protein



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

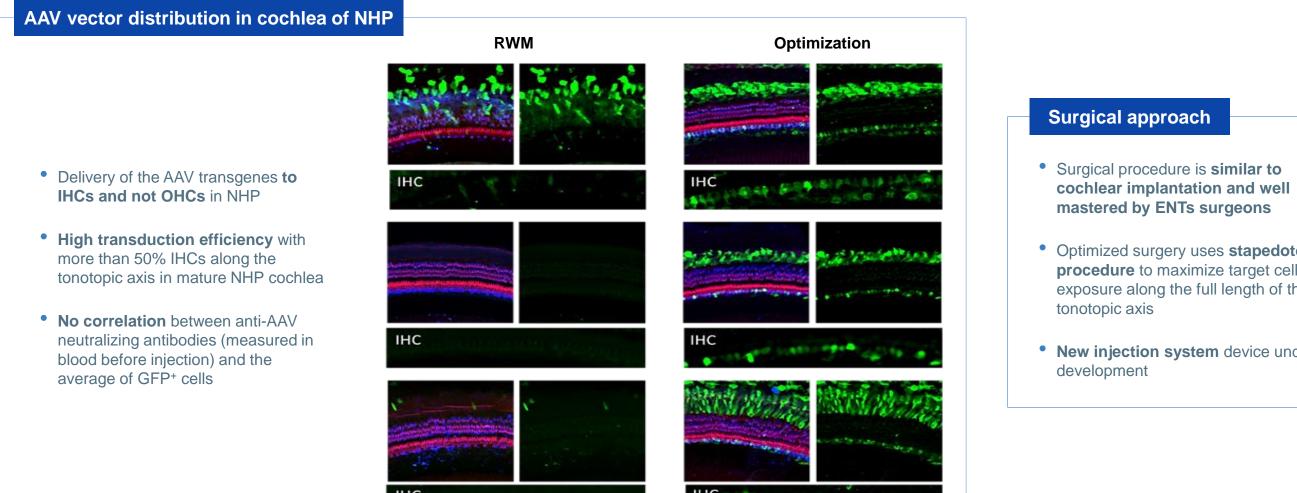
OTOF is the gene coding for the otoferlin protein, a Ca2⁺ sensor for vesicle fusion and vesicle pool replenishment at auditory hair cell ribbon synapses RESTORE

Dual AAV-OTOF resulted in IHCs specific expression and hearing restoration in DFNB9 mice



RESTORE

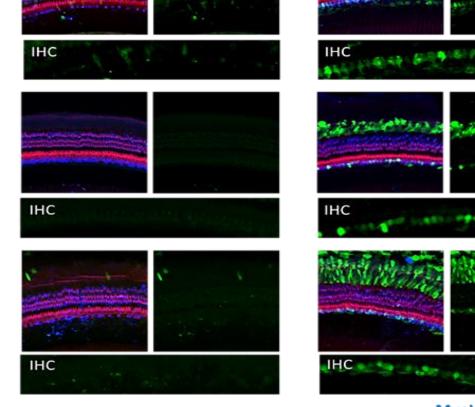
Optimized surgical procedure leads to IHC specific AAV-delivered transgene transduction in mature NHP cochlea



MyoVIIa Actin GFP

- Optimized surgery uses **stapedotomy** procedure to maximize target cells exposure along the full length of the
- New injection system device under

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



RESTORE OTOF gene therapy program status

POC data in mouse & POC preliminary data in NHPs

Submission of European Natural History Study OTOCONEX

Delivery of batches for toxicology study mid-2022

Clinical Trial Application 1H 2023

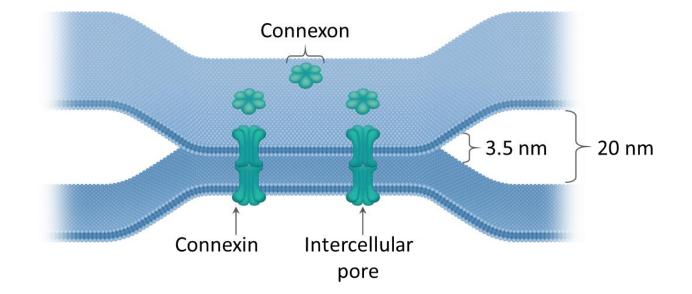
Advice from regulatory authorities

Product development and

manufacturing agreement

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 2H 2022

Preclinical IND enabling studies

Sensorion potential newsflow [estimated timelines]

- 1H 2022 SENS-401 in combination with cochlear implantation: CTA in France and in Australia
- Mid 2022 SENS-401 in combination with cochlear implantation: first patient enrolled
- Mid-2022 OTOF-GT: delivery of batches for toxicology study
- 2H 2022 GJB2-GT candidate selection
- 2H 2022 SENS-401 CIO: NOTOXIS CTA study amendment approval
- 1H 2023 SENS-401 in combination with cochlear implantation: first results
- 1H 2023 OTOF-GT: approval for U.S. ODD and RPDD
- 1H 2023 OTOF-GT: Submission of the Clinical Trial Application (CTA)

THANK YOU

Nawal Ouzren Chief Executive Officer <u>E: contact@sensorion-pharma.com</u>

