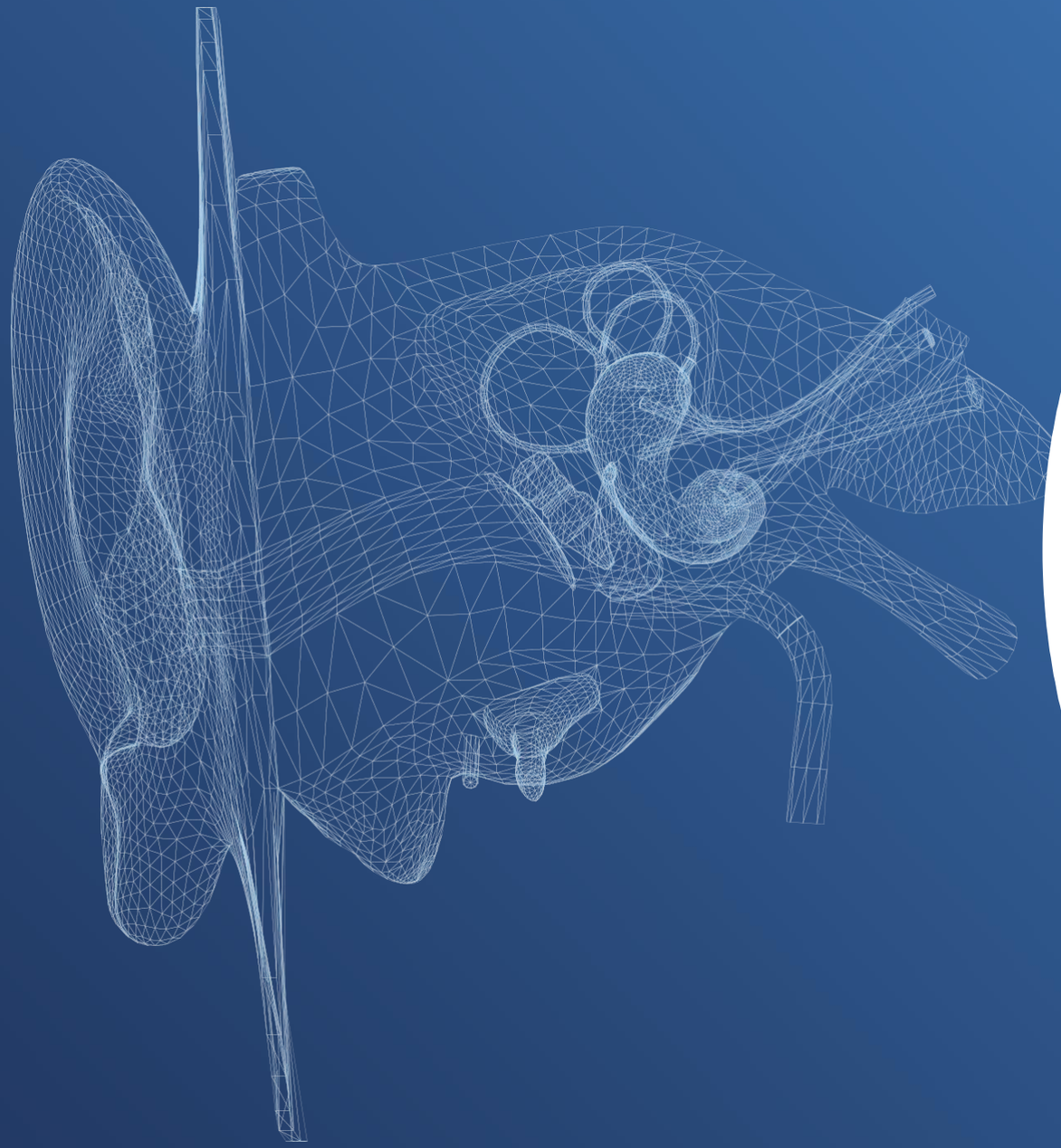

Sensorion

June 2022

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SENSORION

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Investments Highlights

- Sensorion is focused on **innovative treatments** that can **restore**, **treat** **and** **prevent** **hearing loss**
  - **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**
  - **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. First patient enrolled by mid-2022
    - **Cisplatin-Induced Ototoxicity** clinical PoC study continued with CTA amendment in H2 2022
    - **Sudden Sensorineural Hearing Loss** indication looking for potential partner
- **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**

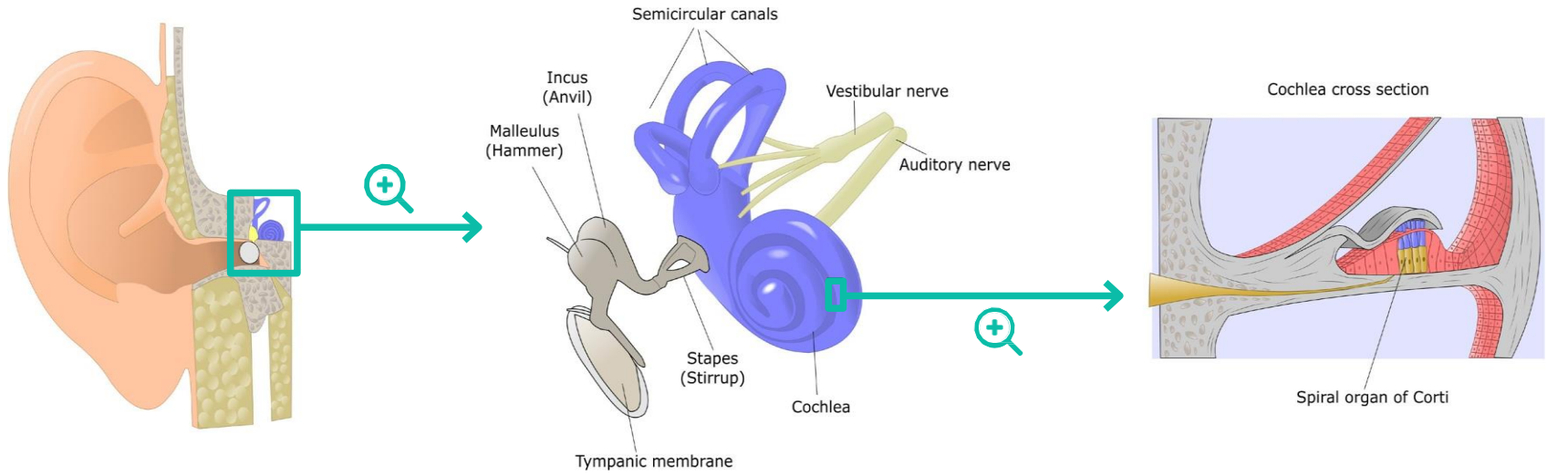
INVUS SOFINNOVA bpifrance

FINANCIAL OVERVIEW

Date Established..... 2009
IPO 2015
Euronext Paris ..... ALSEN.PA
Cash (Dec 31, 2021) ..... **≈€50m**
Cash runway until end of Q2 2023

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

Inner Ear Biology



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*:

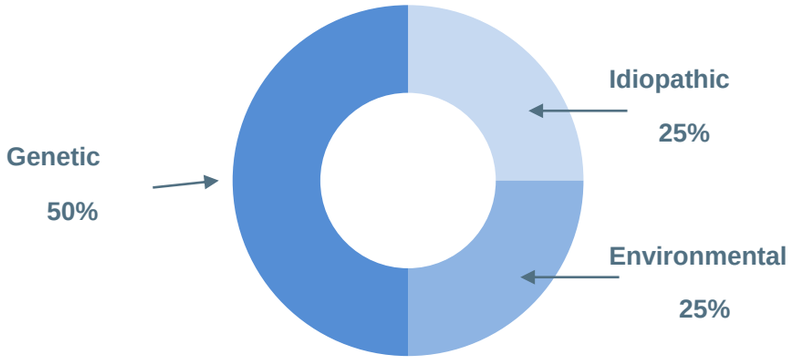
~ 400m people affected by disabling hearing loss worldwide including 34m children

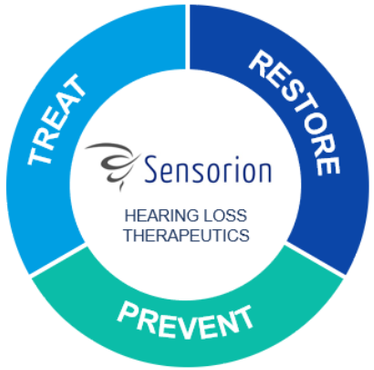
~ 700m people projected to be affected by 2050

**World Health Organization, 2021 World report on Hearing*

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

Causes of hearing loss





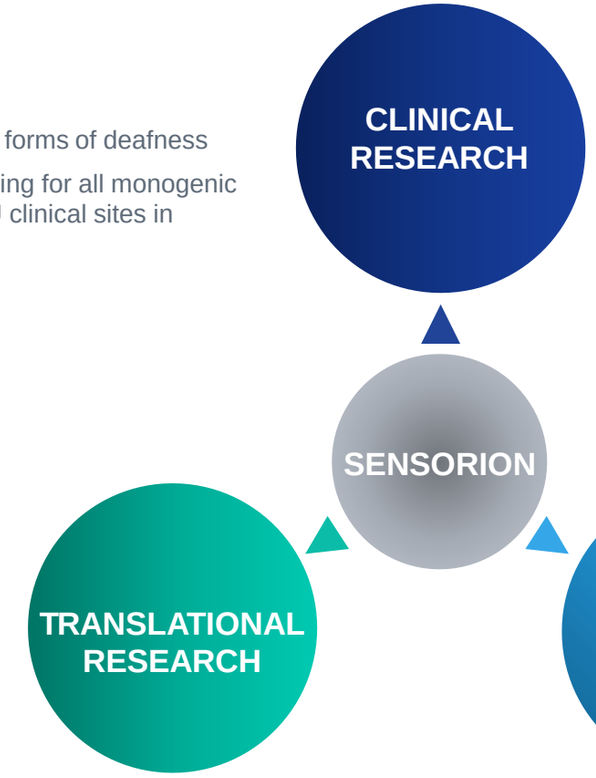
GENE THERAPY APPROACH

- 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

SMALL MOLECULE APPROACH

- Phase 2 study completed with SENS-401 to **TREAT** Sudden Sensorineural Hearing Loss – Looking for partnering
- Phase 2a to **PREVENT** residual hearing loss after cochlear implantation
- Phase 2a study with SENS-401 to **PREVENT** Cisplatin-Induced Ototoxicity

Our critical strategic alliances from bench to bedside



Necker Enfants Malades Hôpital Universitaire

- EU reference center for monogenic forms of deafness
- Natural History study currently running for all monogenic forms of deafness; extension in EU clinical sites in preparation (Otoconex study)

IRBA

French Military Biomedical Research Institute

- Access to a military population at risk of noise-induced hearing loss
- Strong medical network, strict monitoring and precise, regular, well-documented explorations
- Partnership to identify biomarkers for noise-induced hearing loss

Cochlear™

- Global leader in implantable hearing solutions
- Currently developing a drug/ device combination to maintain residual hearing after CI surgery

INSTITUT PASTEUR

- Interdisciplinary approach to the mechanisms of hearing and its damage
- Research in deafness therapies and preclinical studies

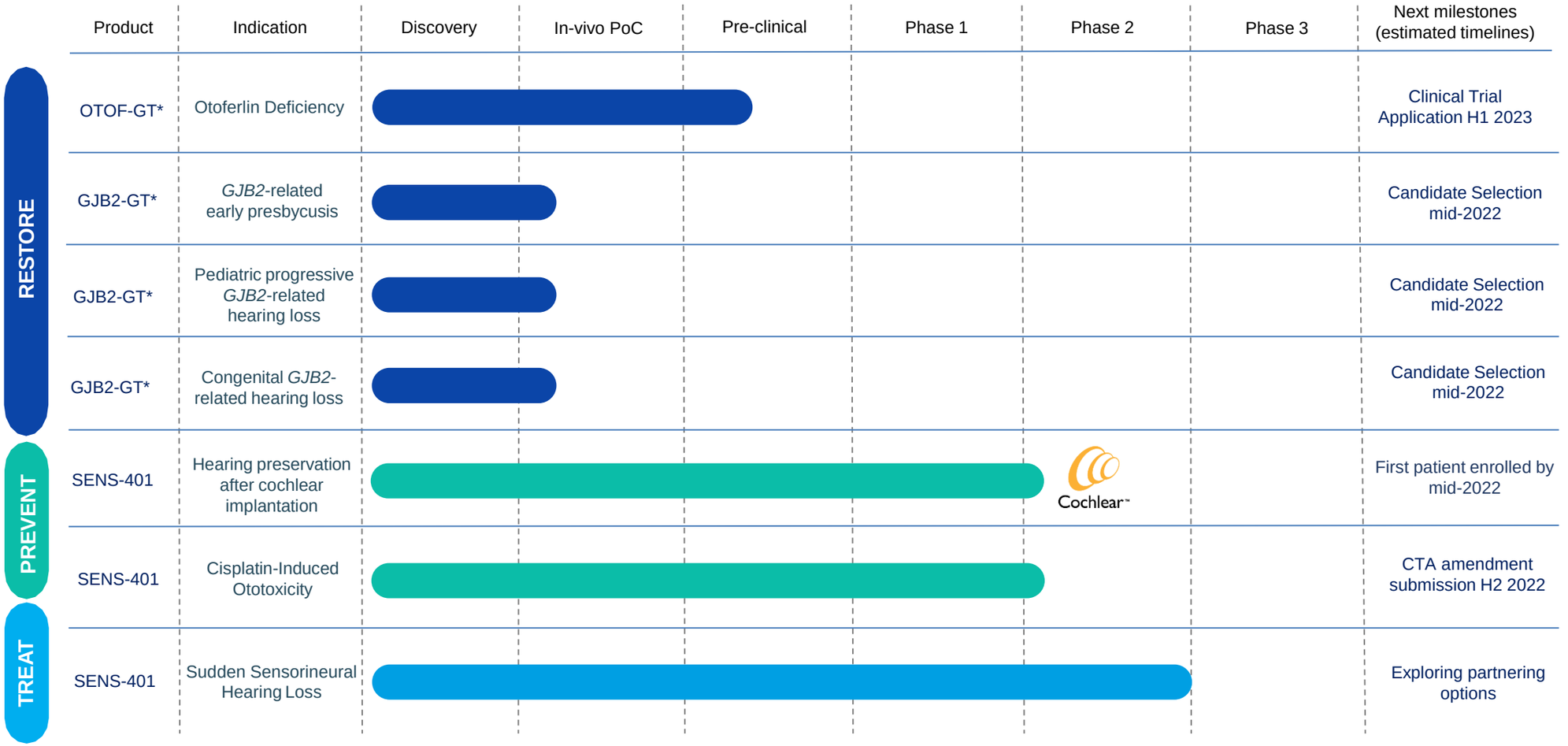
sonova HEAR THE WORLD

- Biggest retail chains in the world
- A significant shareholder in Sensorion
- Collaboration to initiate Natural History in presbycusis

ECHODIA

- Functional exploration in the field of otolaryngology and neurosciences (combining biological and audiological data)

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



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 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

NORA YANG
Chief Scientific Officer

SENSORION
(Since 2021)

STRATIFY
(2020-2021)
Cofounder and CSO

OTMANE BOUSSIF
Chief Technical Officer

SENSORION
(Since 2021)

NOVARTIS
(Since 2015)
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 ar the Helmholtz Center (Munich)*

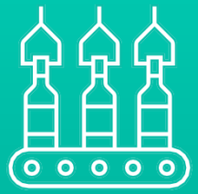
We have established internal capabilities to ensure successful execution

PRECLINICAL CAPABILITIES FOR SMALL MOLECULES & GT PROGRAMS

- ***In Vitro* platform**: assays development, target & drug discovery, biomarkers
- ***In Vivo* platform**: from the PoC to the dose-finding studies in disease-relevant rodent models
- **AAV screening 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



CMC GENE THERAPY FACILITIES

- **Process development lab**: non-GMP manufacturing at small scale: set-up a platform for AAV productions
- **Analytical development lab**: development of product-specific analytical methods, internalize generic assays to support process development and AAV productions

REGULATORY EXPERTISE

- Multiple regulatory interactions with the EMA and the FDA
- Informative discussions about how to shape the treatment guidelines and standardize clinical endpoints

2

GENE THERAPY

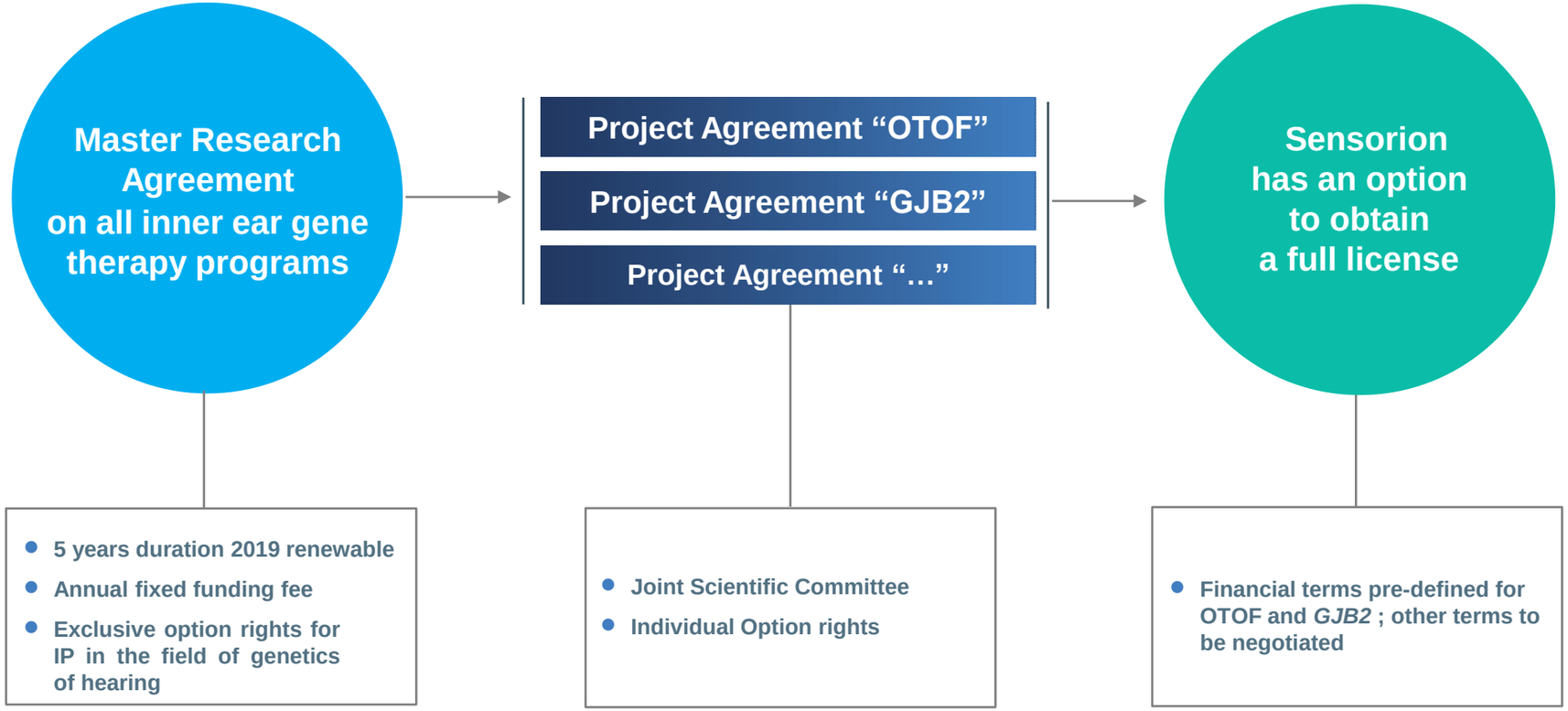
RESTORE

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

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 ~1100 per year in USA + EU

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

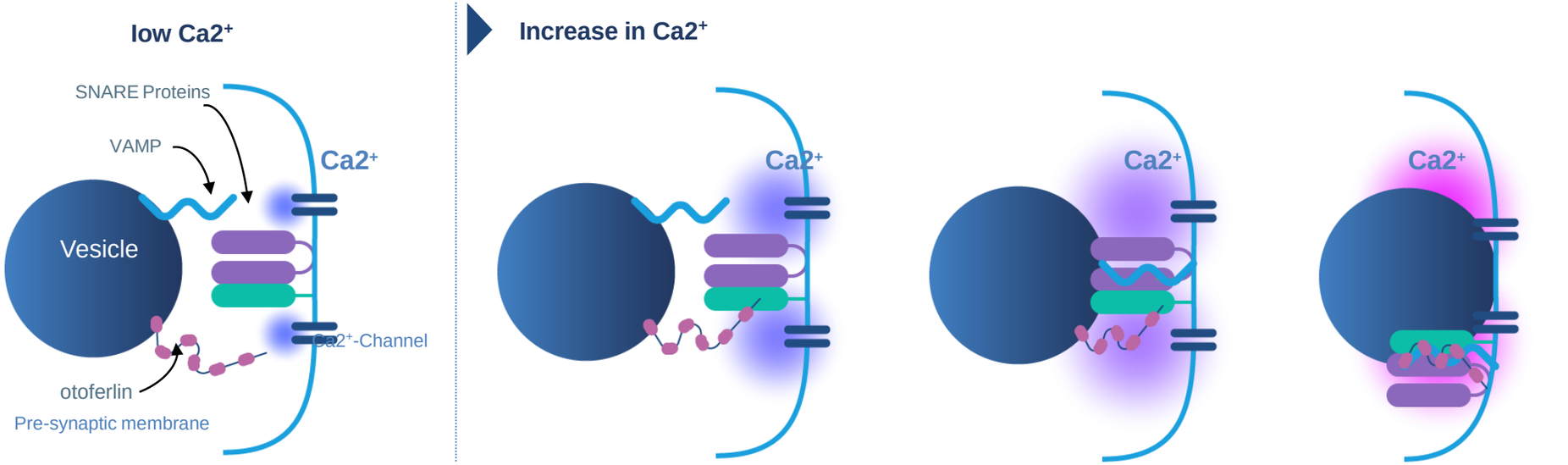
Sources: Akil et al. 2019 (link), Orphanet (link), NIH (link), company estimates based on publicly available population data, Chardan 2020 report, Bryan, Garnier & Co 2019 report, Institut Pasteur, Boucher et al. 2020 (link)

DELAYED DIAGNOSIS – NOT SUSPECTED AT FIRST SIGHT

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

RESTORE

OTOF Gene encodes Otoferlin, a key $Ca2^+$ sensor protein



restricted SNARE interaction

Otoferlin SNARE interaction

SNARE-complex binding

primed vesicle containing Otoferlin-SNARE complex

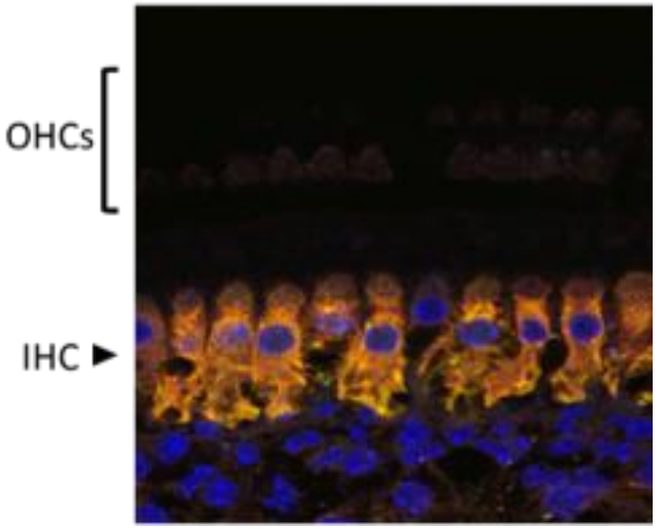
Model illustrating calcium regulation of Otoferlin/SNARE interaction in the hair cell – Adapted from Ramakrishnan *et al.* 2014

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

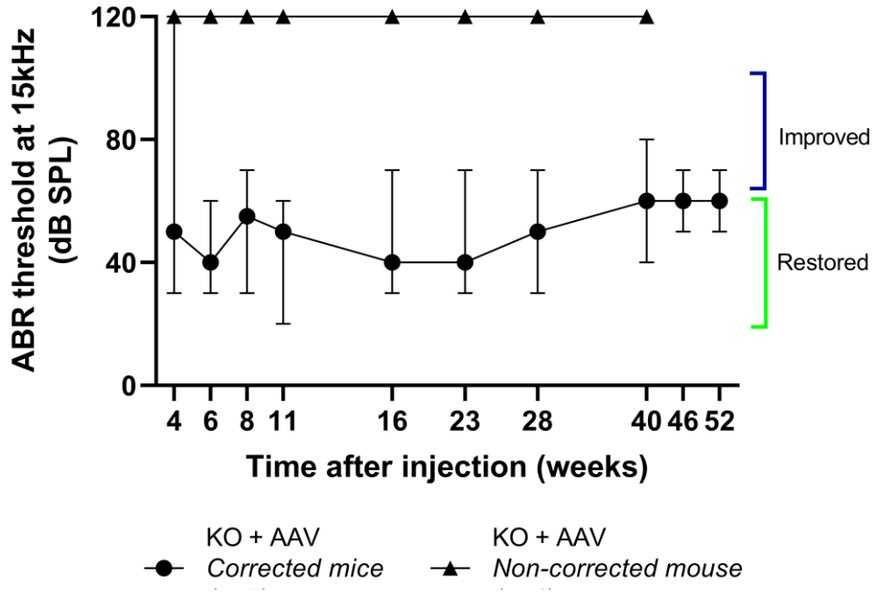
Dual AAV-OTOF resulted in IHCs specific expression and hearing restoration in DFNB9 mice

Target cell specific protein expression



- Dual AAV-OTOF injection into the cochlea leads to **IHC specific de novo Otoferlin protein expression**

Hearing restoration in DFNB9 mice



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

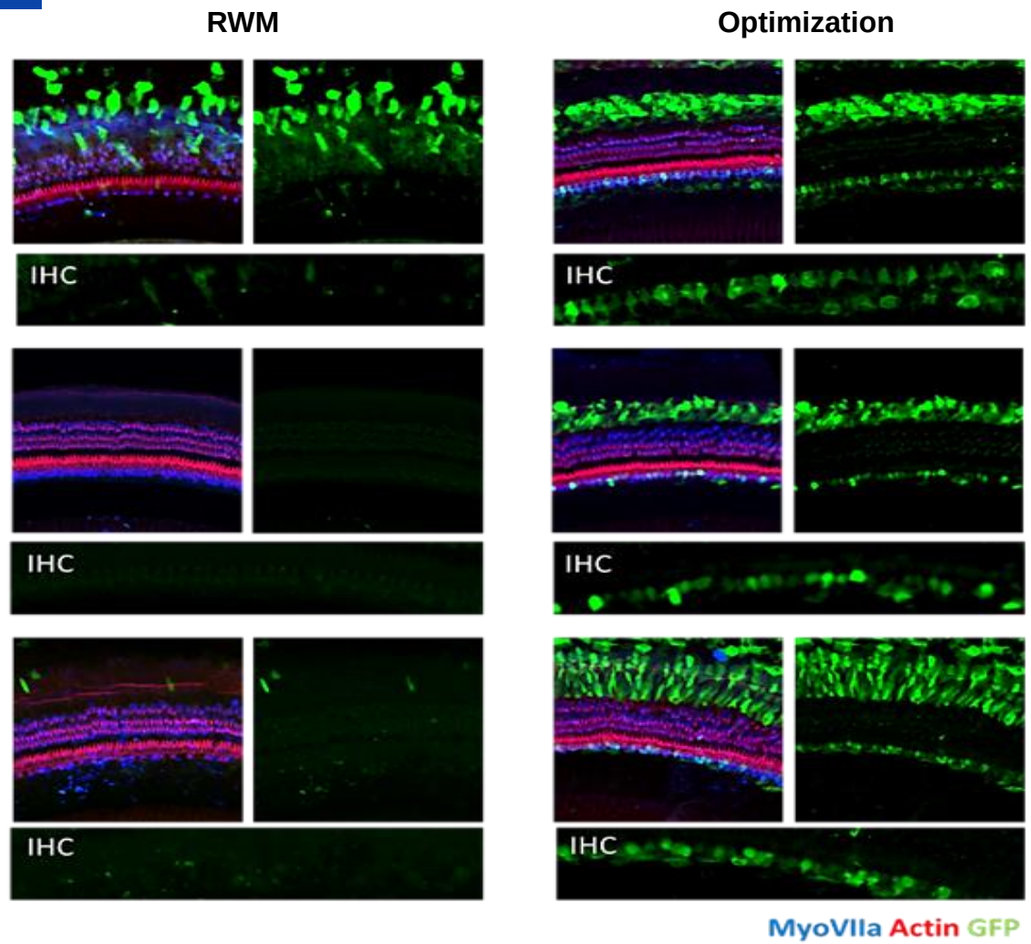
Lahlou et al. ARO 2022 link

RESTORE

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

AAV vector distribution in cochlea of NHP

- Delivery of the AAV transgenes **to IHCs and not OHCs** in NHP
- **High transduction efficiency** with more than 50% IHCs along the tonotopic axis in mature NHP cochlea
- **No correlation** between anti-AAV neutralizing antibodies (measured in blood before injection) and the average of GFP^+ cells



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

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

AUDINNOVE CONSORTIUM MEMBERS

Sensorion

INSTITUT PASTEUR

Necker ENFANTS MALADES HÔPITAL UNIVERSITAIRE

FONDATION POUR L'AUDITION À L'ÉCOUTE DE LA VIE

RESTORE

OTOF gene therapy program status

PoC data in mouse & PoC preliminary data in NHPs

Submission of European Natural History Study OTOCONEX

Product development and manufacturing agreement

Production of toxicological batches mid-2022

Advice from regulatory authorities

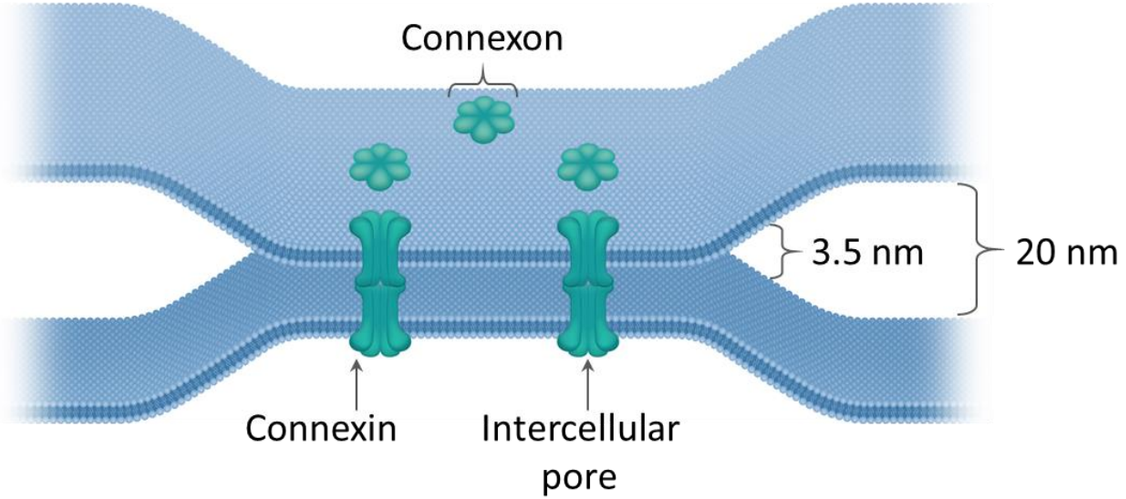
Clinical Trial Application H1 2023

RESTORE

CONNEXIN 26: a gap-junction protein encoded by *GJB2* gene and responsible for tissue homeostasis mutations in the gene leads 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]

[1]: Boucher et al. 2020



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

RESTORE

GJB2 gene therapy program next steps

Submission of European Natural History Study OTOCONEX

Submission of Natural History Study in collaboration with Sonova

Candidate selection mid-2022

Preclinical IND enabling studies

3

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
PREVENT	SENS-401	Hearing preservation after cochlear implantation					Cochlear™	
TREAT	SENS-401	Cisplatin Induced Ototoxicity						
TREAT	SENS-401	Sudden Sensorineural Hearing Loss*						

**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*

TREAT

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)

SENS-401 SSNHL program: phase 2 design

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

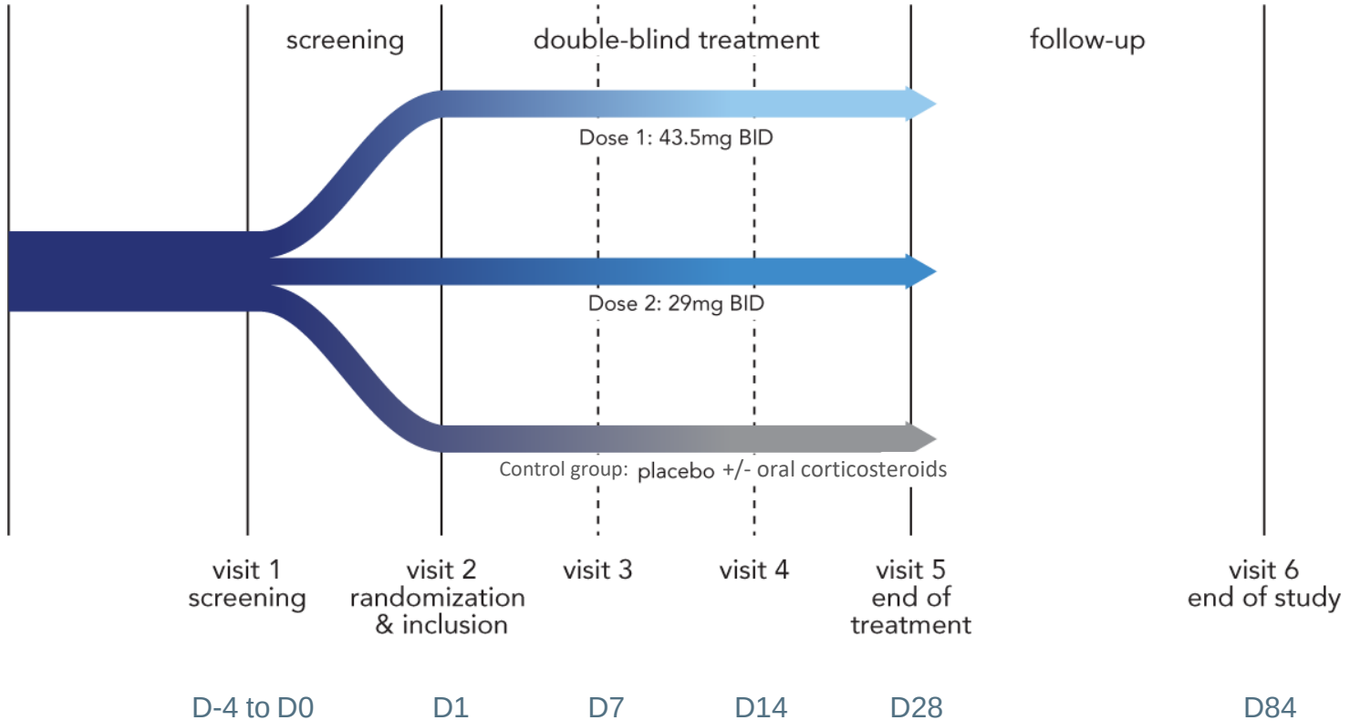
50 clinical sites globally

1 Primary objective
Audiometry
15 dB improvement
vs. Placebo

115 patients enrolled

Timing

Q1 2019 center openings	June 20 & Positive DSMB Review	Q1 2022 Final results

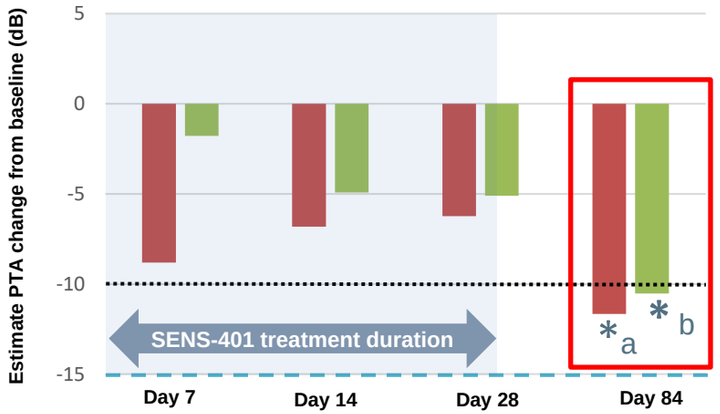


Primary endpoint definition:
"…change in pure tone audiometry (PTA); average of the hearing threshold of 3 contiguous most affected hearing frequencies in decibels in the affected ear from baseline to the end of treatment visit (Visit 5/D28±3)"

TREAT

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



Legend

- *SENS-401 High dose vs Placebo*
- *SENS-401 Low dose vs Placebo*

**a : p < 0,05* **b : p = 0.0566*

	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

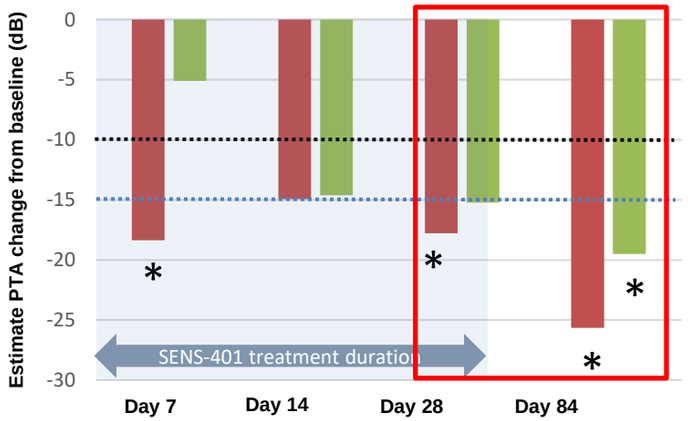
Sub-population
Homogeneous idiopathic population of patients treated with corticosteroids

- **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

TREAT

SENS-401 effect is more pronounced in a profound hearing loss sub-group (PTA ≥ 80 dB)

PTA improvement from baseline compared to placebo



	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

Legend

- ***SENS-401 High dose vs Placebo***
- ***SENS-401 Low dose vs Placebo***

* *p < 0,05*

_ _ _ 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

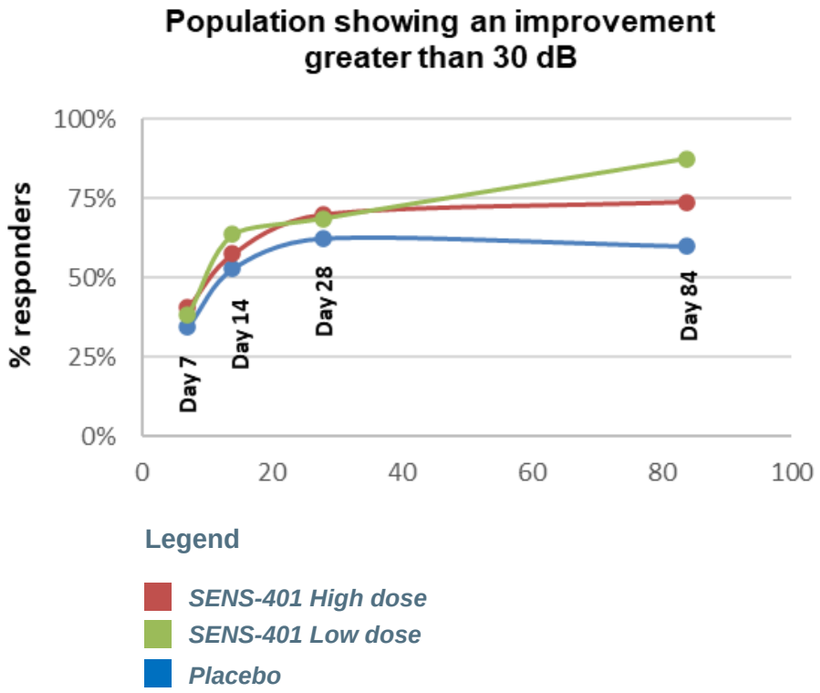
Sub-population
Homogeneous idiopathic population of patients with profound hearing loss (PTA ≥ 80 dB) treated with corticosteroids

- 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**

TREAT

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

Responder analysis on ITT population



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

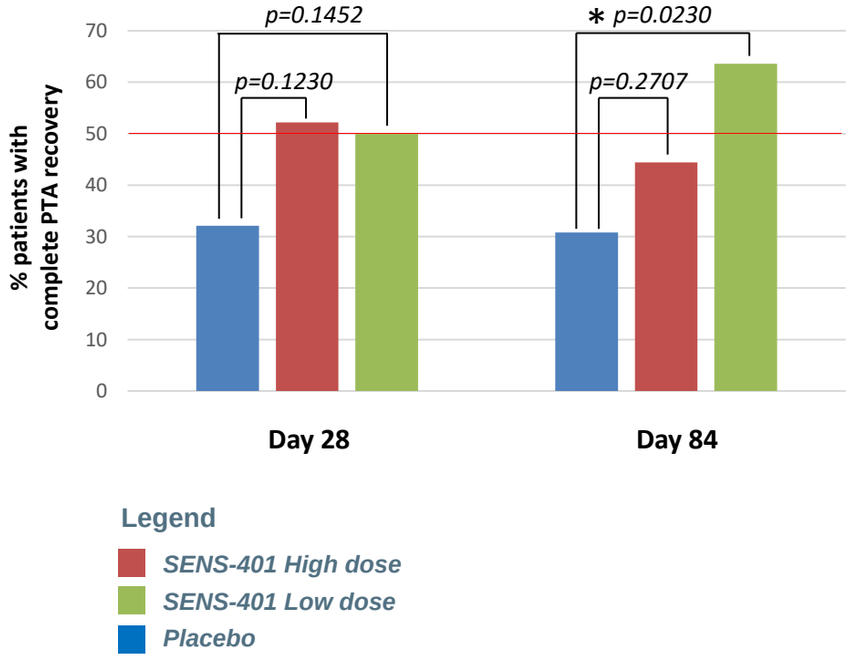
Responder rate
Calculated with the data available at each visit

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

TREAT

SENS-401 induces complete PTA recovery in 50% of patients

Complete PTA recovery



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

TREAT

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 19dB 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 clinical study submission to preserve residual hearing post cochlear implementation

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

HEALTHY AGEING

Growing understanding of the link between healthy hearing and healthy ageing

Source: Cochlear® 2018 investor day (link)

36,450
Implants sold by Cochlear® globally in 2021[1]

$1.5bn
Cochlear implant market in 2020[2]

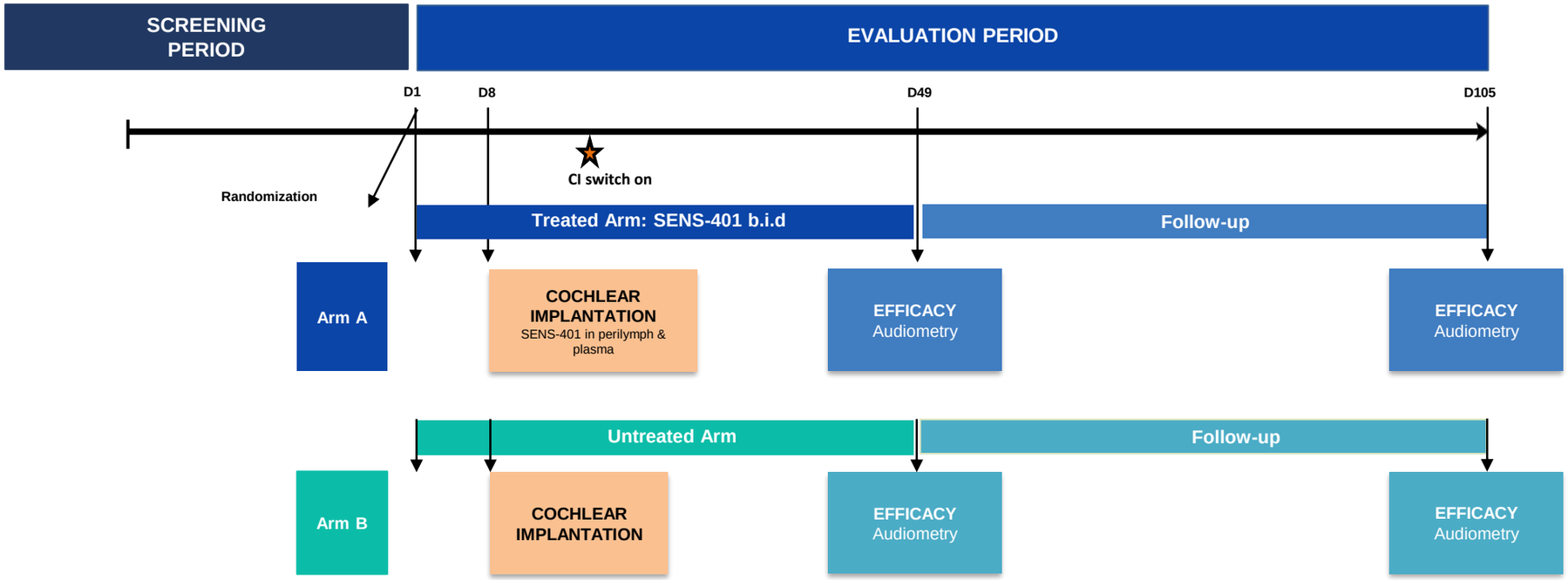
- In Q4 2017 Sensorion and Cochlear® entered into an agreement to evaluate whether SENS-401 in combination with Cochlear's cochlear implants can reduce cell-death from the implant procedure
- Cochlear® invested €1.6m in Sensorion equity. In exchange, Cochlear® received a right of first negotiation for a global license to use SENS-401 in combination with its implantable devices
- The two companies are progressing with a trial of SENS-401 for hearing preservation in patients scheduled for cochlear implantation. In June 2022, the proposed trial design for SENS-401 was approved by the regulatory authorities in France

[1] *Cochlear® 2021 financial report (link)*
[2] *Market estimates (link)*

PREVENT

SENS-401 study design approved in France

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



PRIMARY OBJECTIVE:
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 countries[1]

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

PREVENT

SENS-401 CIO NOTOXIS
Working on CTA amendment submission

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

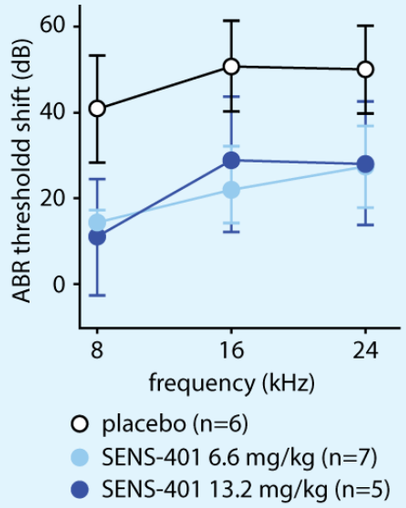
Significant improvement *versus* placebo
23-28 dB with 6.6 mg/kg (p<0.010)
22-30 dB with 13.2 mg/kg (p<0.013)

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

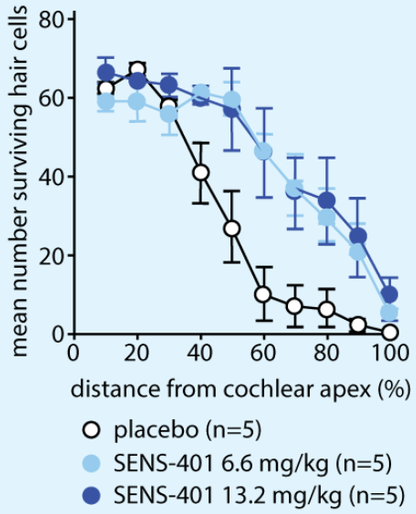
TREATMENT PROTOCOL

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



Cochleograms 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 H1 2022

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

SENS-401 CIO NOTOXIS CTA amendment submission H2 2022

SENS-401 SSNHL exploring potential partners for further developments

Sensorion potential newsflow [estimated timelines]

- H1 2022 – CTA approval for SENS-401 study to preserve residual hearing post cochlear implantation in France
- Mid-2022 – First patient in for SENS-401 study to preserve residual hearing post cochlear implantation
- Mid-2022 – Delivery of toxicological batches for OTOF-GT
- Mid-2022 – GJB2-GT candidate selection
- H2 2022 – SENS-401 CIO (Cisplatin-Induced Ototoxicity) NOTOXIS CTA amendment submission
- October 31, 2022 – H1 Results
- H1 2023 – Submission of the Clinical Trial Application for the OTOF-GT program (CTA/IND)

THANK YOU

Nawal Ouzren
Chief Executive Officer
E: contact@sensorion-pharma.com

Sensorion