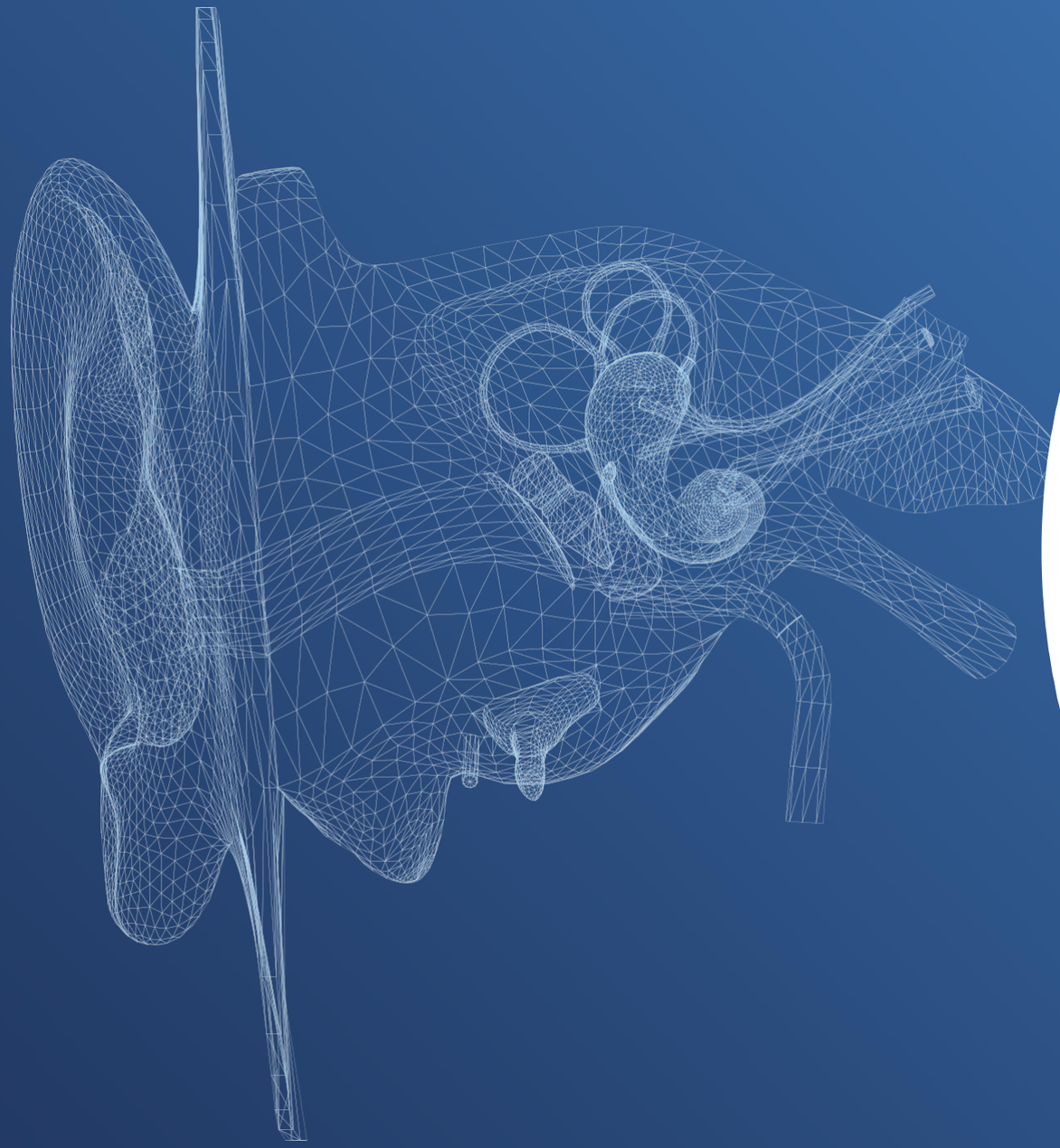

Sensorion

January 2023

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SENSORION

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Sensorion: overview

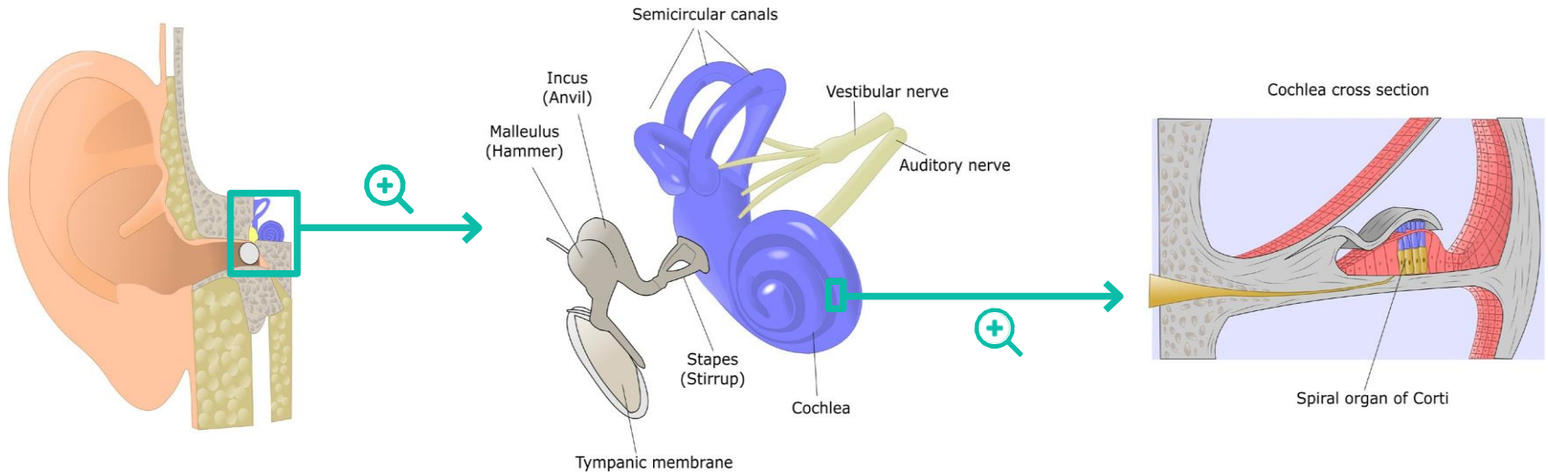
- Sensorion is focused on **innovative treatments** that can **restore**, **treat** and **prevent** **hearing loss**
  - **Oral small molecule asset SENS-401** currently in clinical development in several indications:
    - Sensorion and **Cochlear Ltd.** CTA approved for combo with cochlear implantation
    - **Cisplatin-Induced Ototoxicity** clinical POC study ongoing
    - **Sudden Sensorineural Hearing Loss** positive Phase 2 secondary endpoints
  - **Two Gene Therapy programs, OTOF-GT** and **GJB2-GT,** targeting monogenic forms of deafness in pediatrics:
    - caused by a mutation of the gene encoding for **otoferlin**
    - related to mutation in ***GJB2*** **gene**
    - Prospective natural histories ongoing
- **Exclusive relationship with Institut Pasteur** in the field of hearing genetics
- 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**

FINANCIAL OVERVIEW

Date Established..... 2009
IPO..... 2015
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

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*:

~ 430m people affected by disabling hearing loss worldwide including 34m children
~ 700m people projected to be affected by 2050

Key Causes of Hearing Loss:

50% of causes are due to genetic causes, 25% are environmental and 25% are idiopathic

World Health Organization, 2021 World report on Hearing

Sensorion is well positioned to capture the opportunity in the hearing field

BY LEVERAGING ITS COMPREHENSIVE PORTFOLIO

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

GENE THERAPY

Otoferlin deficiency (OTOF-GT)

CTA enabling studies

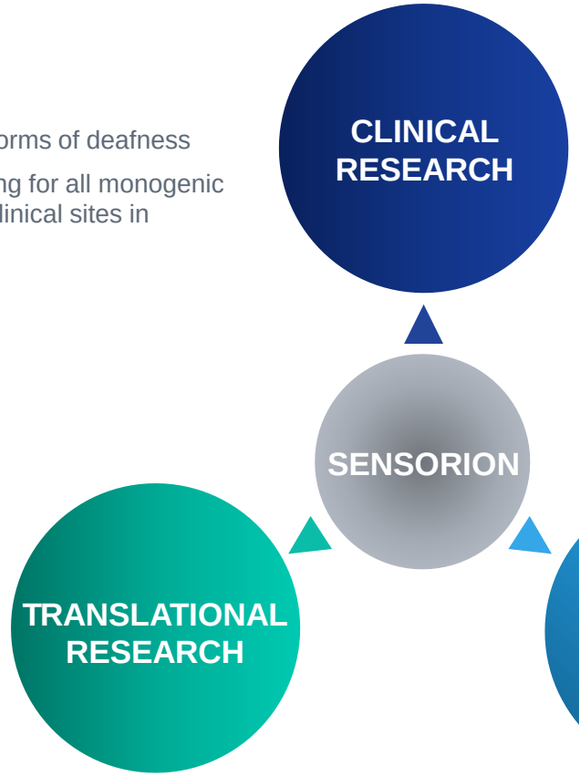
- Hearing restoration in DFNB9 pediatric patients

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

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

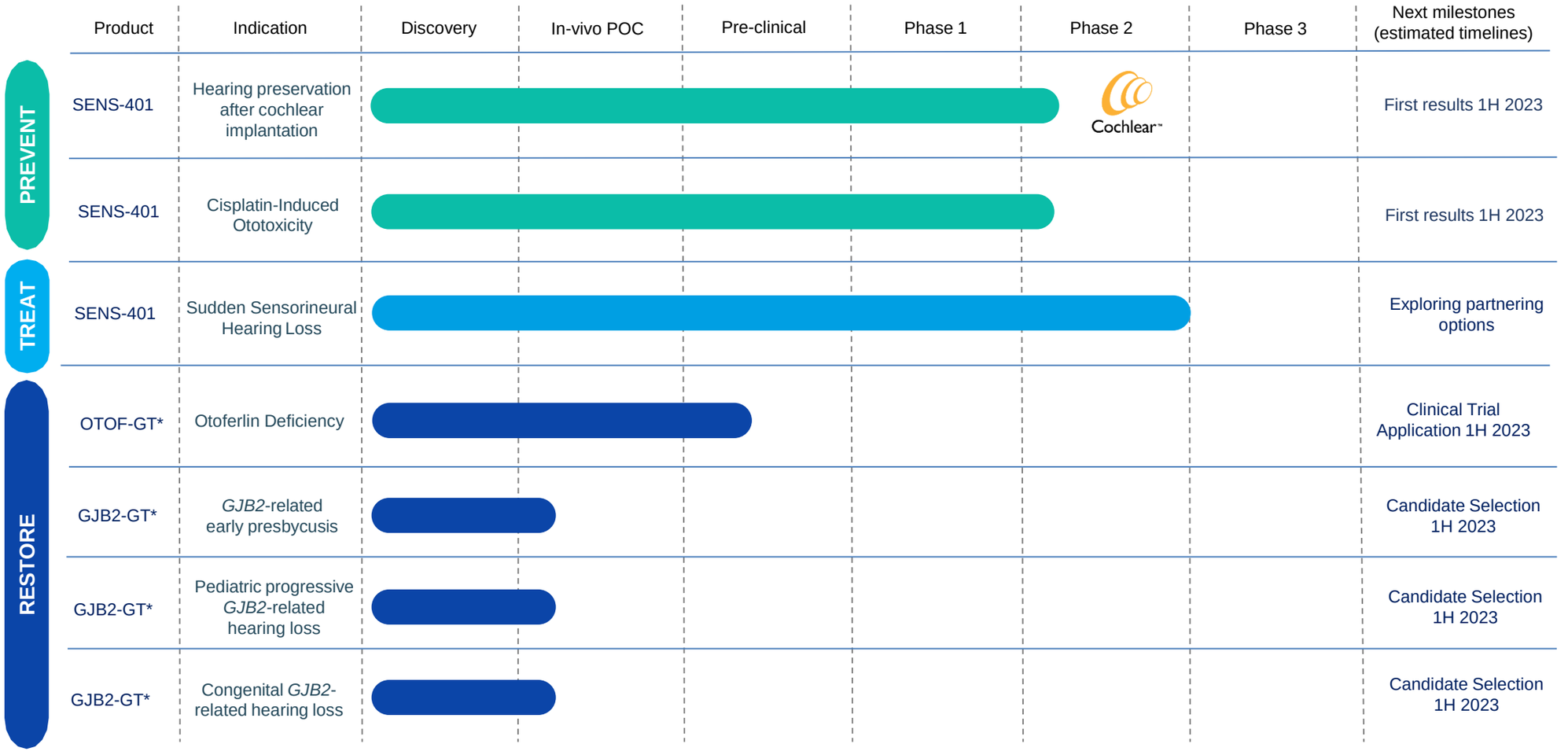
sonova HEAR THE WORLD

- 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 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

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
Preclinical Development Director

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)*

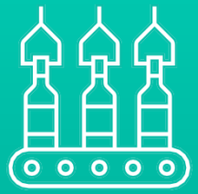
We have established internal capabilities to ensure successful execution

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

SENS-401

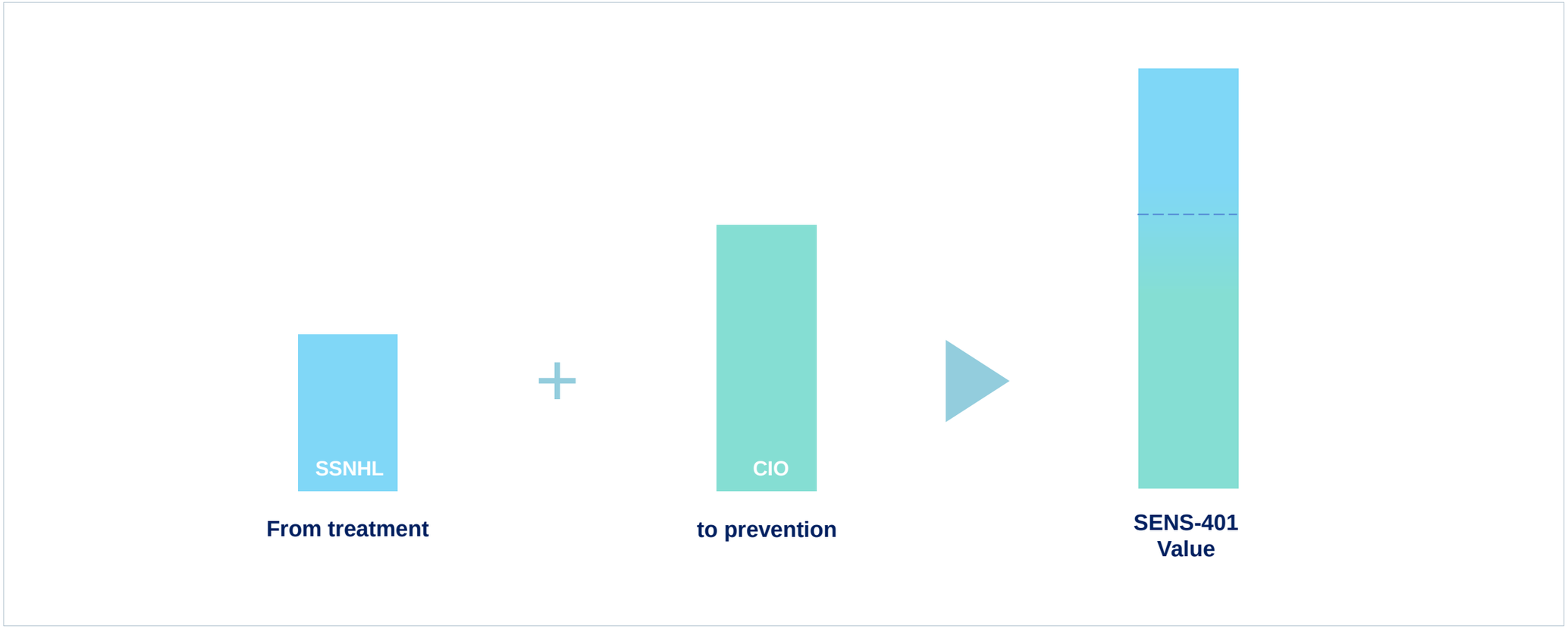
TREAT
AND
PREVENT

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™	
PREVENT	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*

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

TREAT

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

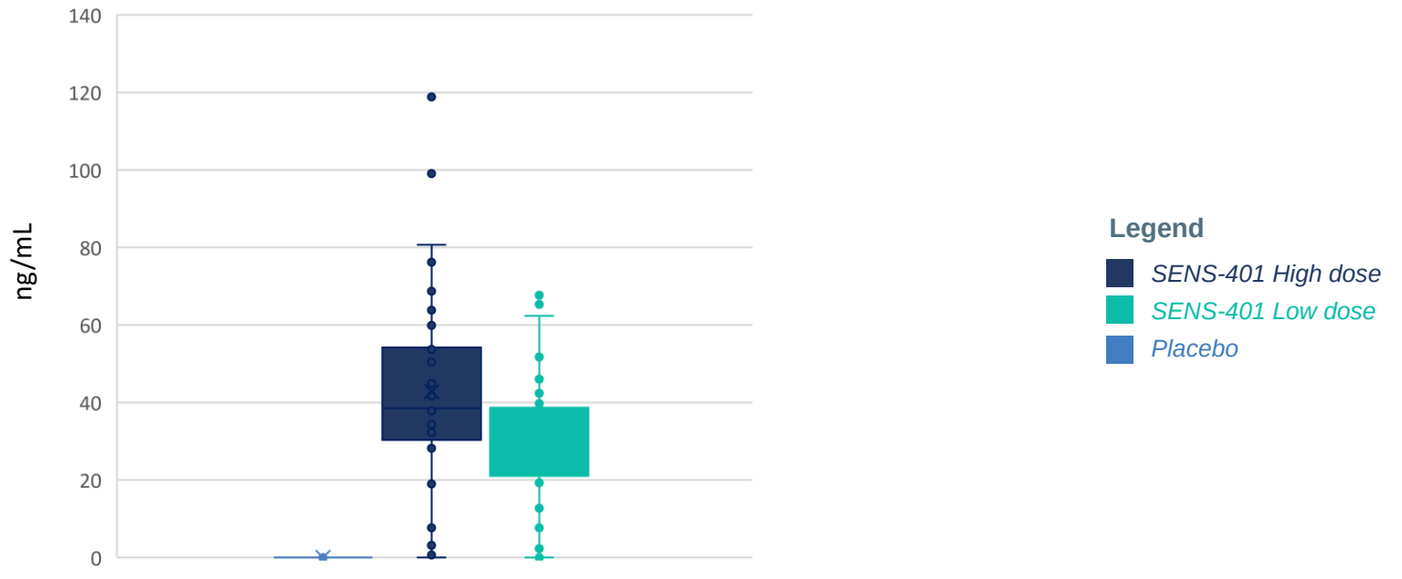
Incidence: 27-35 per 100,000 (218,000 patients in 2017 in G7 countries)[1]

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

TREAT

SENS-401 plasmatic exposure

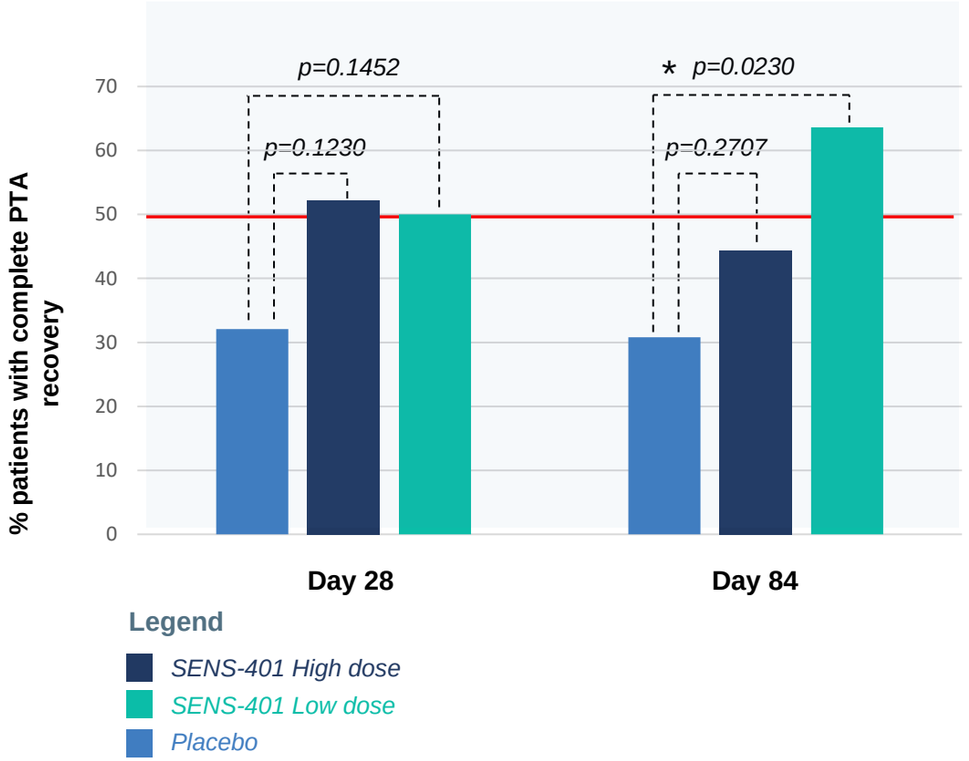
Plasmatic concentration (Pre-dose at Day 14 and Day 28)



TREAT

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

Complete PTA recovery



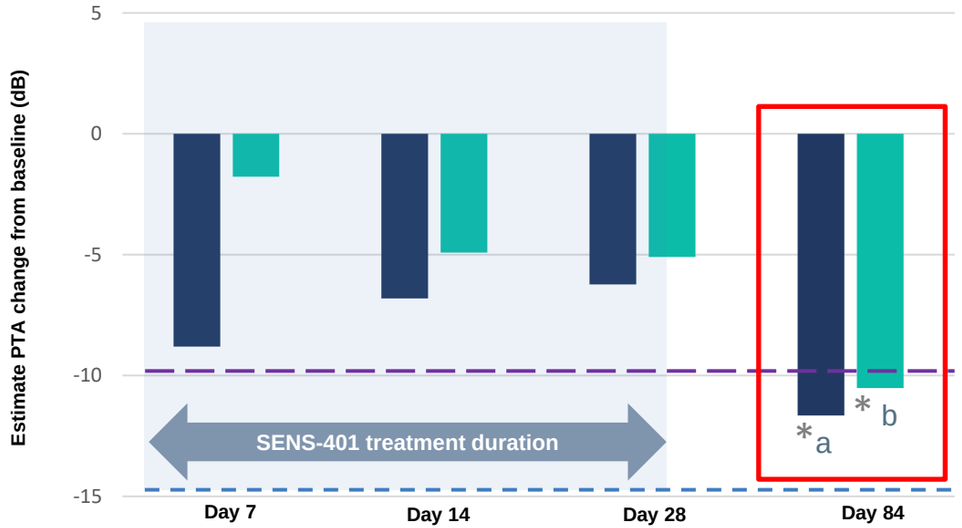
Complete PTA recovery (n/n total)	Placebo	High Dose	Low Dose
Day 28	9/28	12/23	13/26
Day 84	8/26	8/18	14/22

- **Complete hearing recovery** is defined as patients with hearing loss at baseline who will **revert to PTA < 20 dB,** considered as *"normal"* hearing.

TREAT

Although primary endpoint not met, data supports further clinical development

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



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

Legend

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

	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.

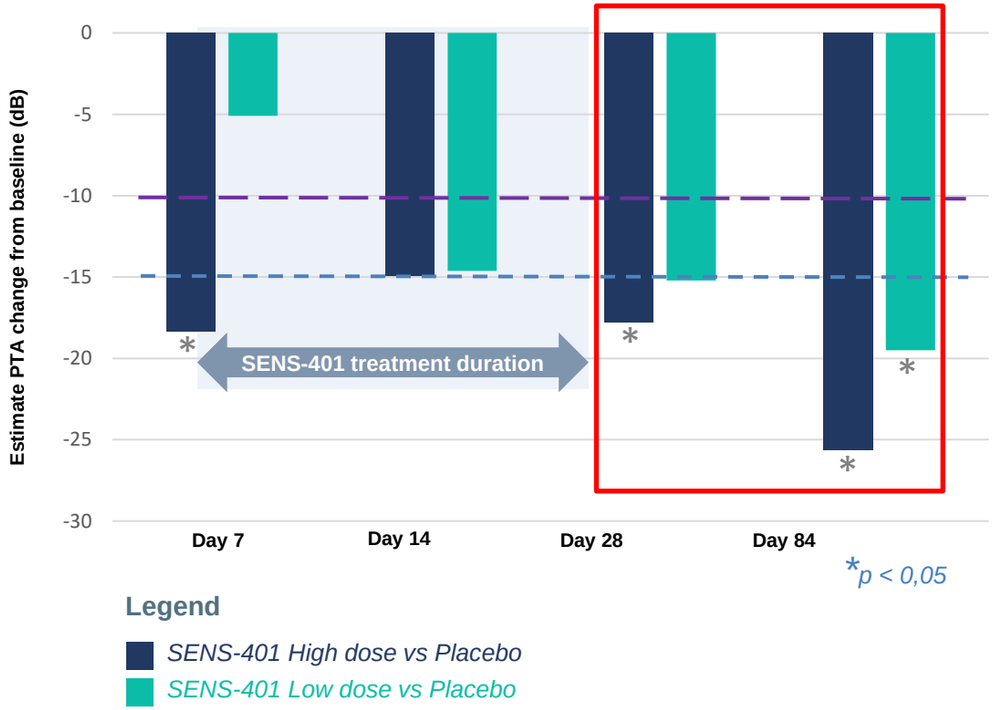
Sub-population
Homogeneous idiopathic population of patients treated with corticosteroids.

- **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



Legend

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

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

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

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

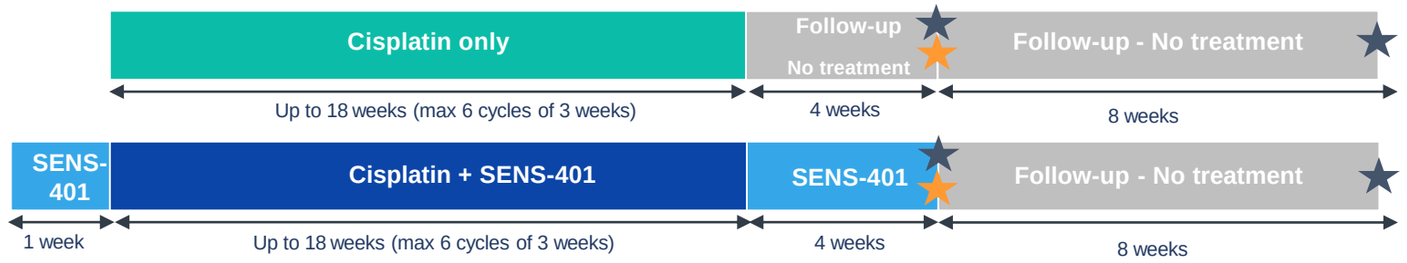
SENS-401 Phase 2a proof-of-concept study; first data expected 1H 2023

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) | **RANDOMIZATION** | **STUDY DURATION (max 31 weeks)**

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 78 subjects)



Objectives:

Efficacy

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

Safety

- AEs & SAEs incidence

Primary Endpoint

Secondary Endpoint

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

HEALTHY AGEING

Growing understanding of the link between healthy hearing and healthy ageing

Source: Cochlear® 2018 investor day (link)

KEY FIGURES

36,450
Implants sold by Cochlear® globally in 2021[1]
(representing ~60% of global market share

$1.5bn
Cochlear implant market in 2020[2]

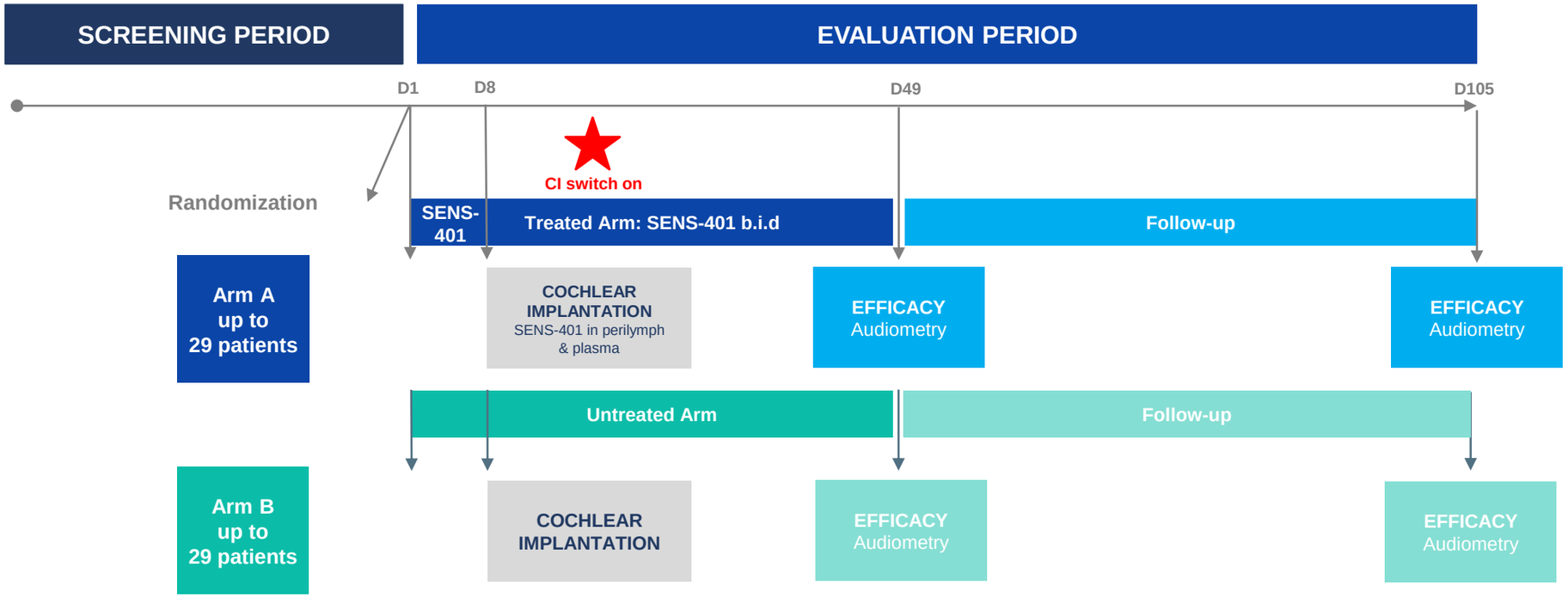
80%
Market penetration in children in developed markets[1] and 3% in adults [1]

[1]Cochlear® FY21 Result Presentation (link)
[2]Market estimates (link)

PREVENT

SENS-401 study commenced in Sept. 2022; first data expected 1H 2023

A Phase 2a, 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

SENS-401 program key milestones, data readouts in Q2 2023

SENS-401 CIO NOTOXIS CTA amendment approved Oct 2022

First patient enrolled in SENS-401 CIO NOTOXIS Dec 2022

SENS-401 combo with cochlear implants - first results 1H 2023

SENS-401 CIO NOTOXIS - first results 1H 2023

3

GENE THERAPY

RESTORE

Sensorion

RESTORE

Sensorion's Gene Therapy programs aim 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 ~1,100 per year in USA + EU
- EU and US ODD
- US FDA has granted RPDD

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

Aiming to develop best-in class and first-in class Gene Therapy

CRITERIA	SENSORION
AAV capsid selected fo high-level of target cells specificity	✓
GT product showing high level of target cells transduction	✓
Biodistribution in favor of good safety profile	✓
Surgical approach developed and mastered by ENTs surgeons	✓
Natural History Study preparing execution of the clinical trial	✓
Regular engagement with regulatory agencies	✓

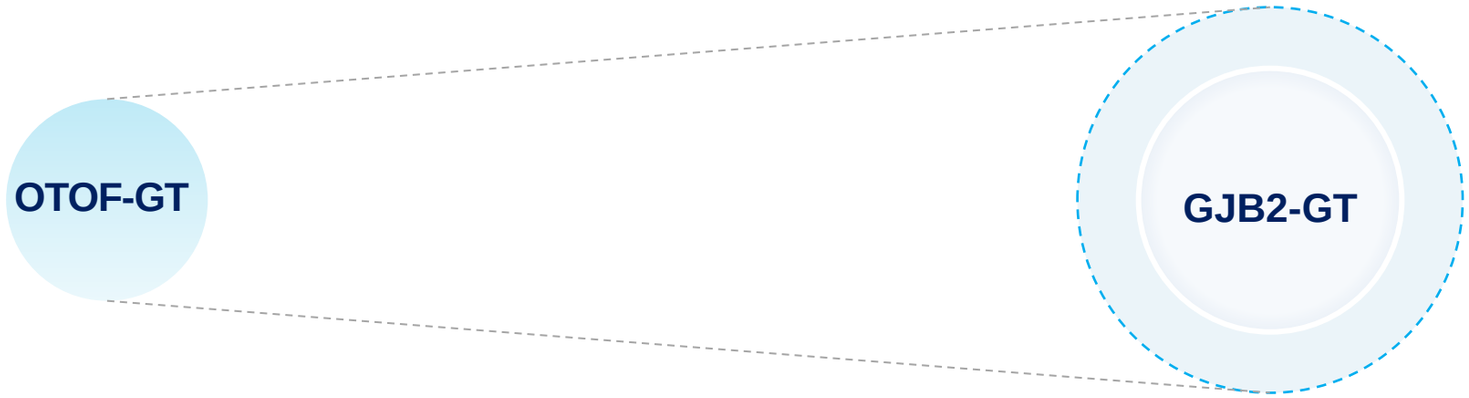
The GT pediatric indications have blockbuster sales potential

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 demonstrating that GT is a relevant medical approach for the inner ear
- It will test the regulatory pathway in the US and EU
- Orphan Drug Designation in the US and EU
- Rare Pediatric Disease Designation Voucher is a development incentive

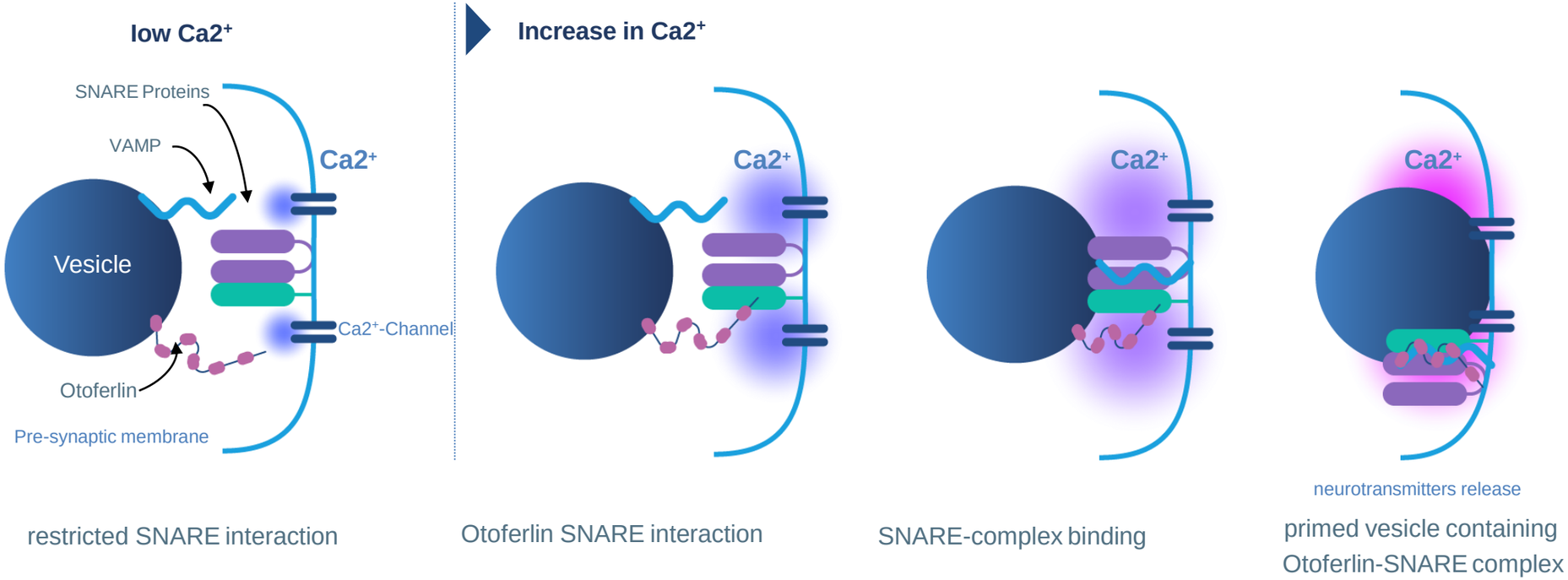
Sales potential illustration



Sources: Sensorion, AT Kearney market research

RESTORE

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



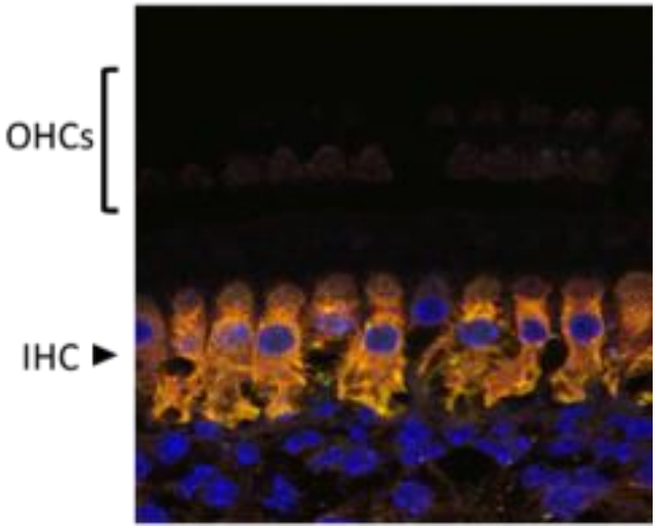
Model illustrating calcium regulation of otoferlin/SNARE interaction in the hair cell – Adapted from Ramakrishnan *et al.* 2014

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

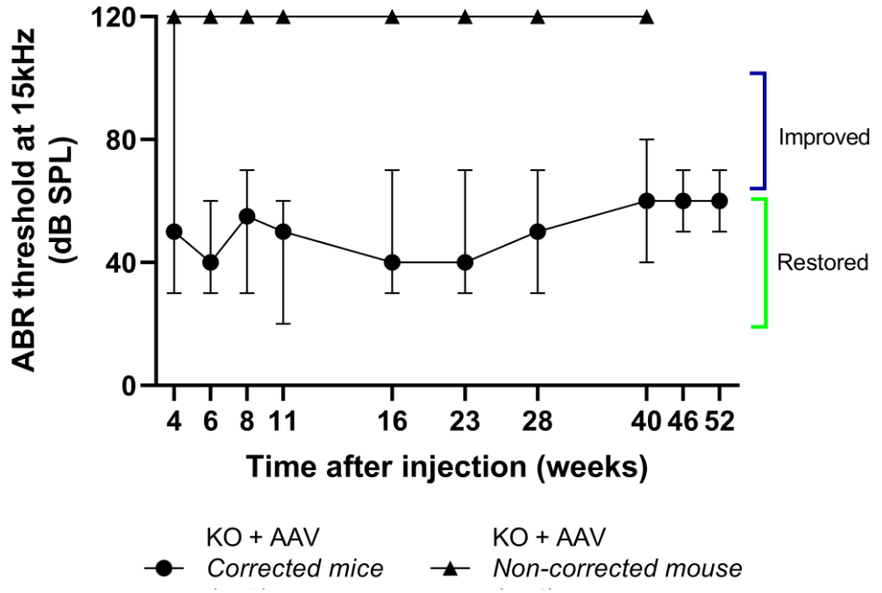
Dual AAV-OTOF resulted in IHCs specific expression and hearing restoration in DFNB9 mice

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

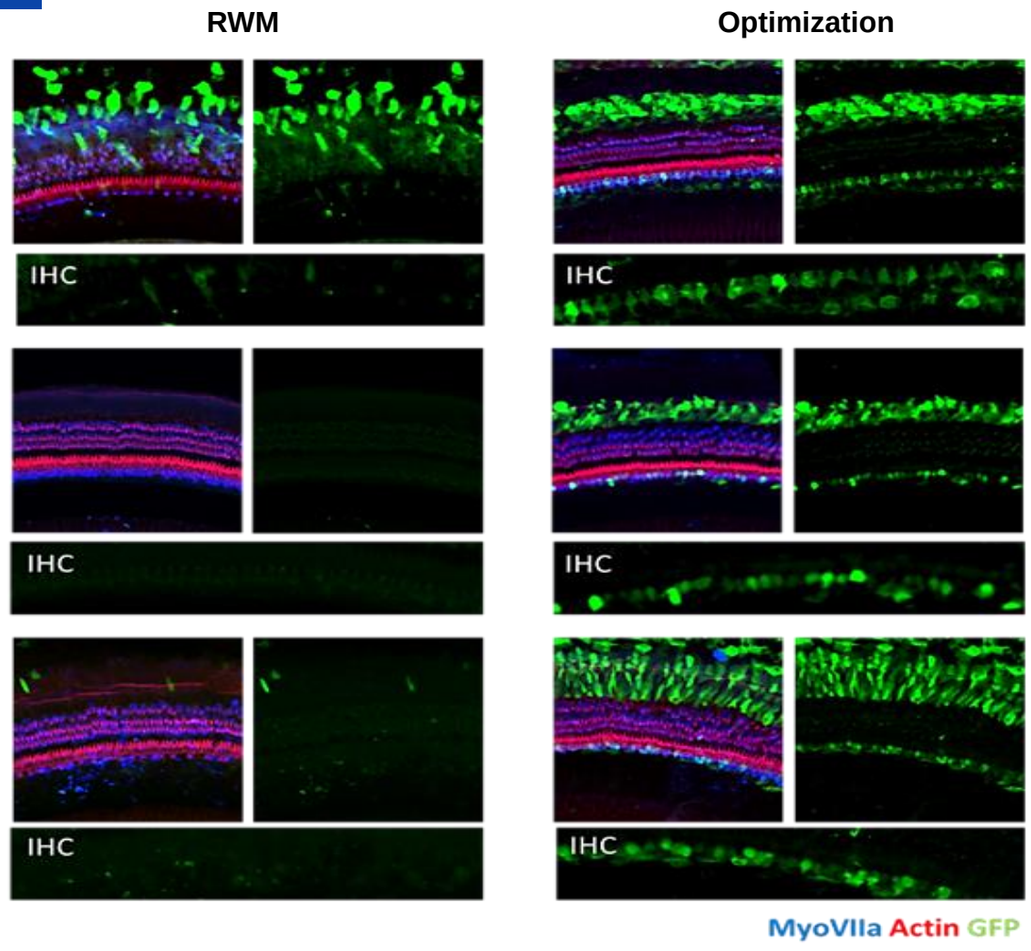
Lahlou et al. ARO 2022 link

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

RESTORE

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

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OTOF Gene Therapy program status

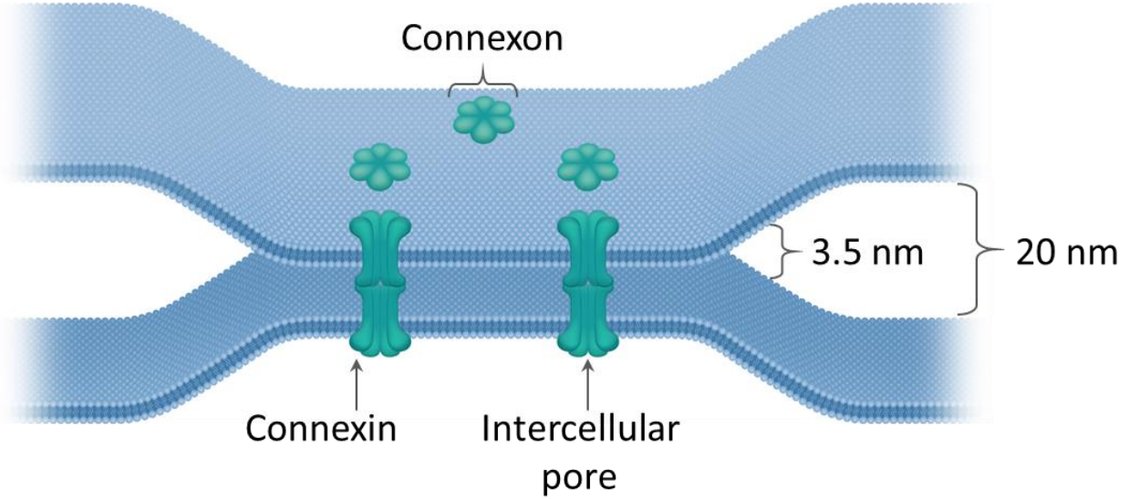
- POC data in mouse & POC preliminary data in NHPs ✓
- Product development and manufacturing agreement ✓
- Advice from regulatory authorities ✓
- Submission of European Natural History Study OTOCONEX ✓
- Delivery of batches for toxicology study mid-2022 ✓
- Clinical Trial Application mid year 2023 →

RESTORE

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]

[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

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GJB2 Gene Therapy program next steps

Submission of European Natural History Study OTOCONEX

Submission of Natural History Study in collaboration with Sonova

Candidate selection 1H 2023

Preclinical IND enabling studies

Sensorion potential newsflow [estimated timelines]

- Mid-2022 – OTOF-GT: delivery of batches for toxicology study
- 2H 2022 – OTOF-GT: EMA’s positive opinion for ODD
- 2H 2022 – SENS-401 CIO: NOTOXIS CTA study amendment approval
- 2H 2022 – OTOF-GT: FDA approval for RPDD
- 2H 2022 – OTOF-GT: FDA approval for US ODD
- 1H 2023 – GJB2-GT: candidate selection
- 1H 2023 – SENS-401 in combination with cochlear implantation: first results
- 1H 2023 – SENS-401 CIO: NOTOXIS first results
- 1H 2023 – OTOF-GT: submission of the Clinical Trial Application (CTA)

THANK YOU

E: contact@sensorion-pharma.com

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