

Unlocking the potential of  
advanced therapies  
for hearing loss



November 2024



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# SENSORION

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



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# Sensorion: Establishing Global Leadership In Hearing Loss With Strong And Diversified Pipeline



- **Untapped opportunity with 1,5 bn people affected by hearing loss (HL); 0,5 bn suffer from disabling HL**
- **Multiple causes:** genetic, environmental, idiopathic



- **Modality agnostic approach leveraging unparalleled understanding of the inner ear and world-leading, differentiated and exclusive partnerships** (Institut Pasteur, Necker Hospital, Cochlear Ltd, Sonova)



- **Two gene therapies (GT): SENS-501** (OTOF-GT – First patient injected); **GJB2-GT** (preclinical IND/CTA enabling activities)
- Prospective Natural History Studies ongoing



- **Small molecule, SENS-401**, for the treatment and prevention of HL caused by **Cochlear Implantation CI** (POC Ph2a completed), **Cisplatin-Induced Ototoxicity CIO** (POC Ph2a ongoing), and **Sudden Sensorineural HL** (Ph2b completed)



- Multiple **upcoming milestones** across the GT and small molecule pipeline, including completion of patient recruitment of the first cohort in the Ph1/2 GT trial of SENS-501 in H2 2024; the completion of patient recruitment in Ph2a SENS-401 CIO in H1 2025; CTA submission for GJB2-GT in H2 2025



- **Experienced and visionary management team**
- **Strong shareholder base backed by leading blue-chip life sciences investors; €100m raised since Aug 2023 giving cash runway until the end of 2025**



# Together With Best-In-Class Partners We Can Transform The Current Standard of Care



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

TRANSLATIONAL  
RESEARCH

CLINICAL  
RESEARCH

SENSORION

DIAGNOSIS  
&  
PATIENT  
JOURNEY



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



**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



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




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



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

# Sensorion's Portfolio Of Advanced Hearing Loss Therapies

	Product	Indication	Discovery	In-vivo POC	Preclinical	Phase 1	Phase 2	Phase 3	Upcoming Milestones (estimated)
RESTORE	SENS-501*	Otoferlin Deficiency	Phase 1/2						1 <sup>st</sup> cohort completed by end of 2024
	GJB2-GT*	Adult Onset (presbycusis)							Preclinical CTA/IND enabling activities
	GJB2-GT*	Pediatric Progressive							Preclinical CTA/IND enabling activities
	GJB2-GT*	Congenital Onset							Preclinical CTA/IND enabling activities
PREVENT	SENS-401	Hearing Preservation after CI						 Cochlear™	Clinical Study Report completed
	SENS-401	Cisplatin-Induced Ototoxicity							Recruitment Completed H1 2025
TREAT	SENS-401	SSNHL							Exploring Partnering Opportunities

3SBio has a right of first refusal with respect to licensing in Greater China of SENS-401 (except in combination with cochlear implants) and SENS-501 OTOF-GT

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

# We Have Established Internal Capabilities To Ensure Successful Execution



## PRECLINICAL - SMALL MOLECULES & GT PROGRAMS

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



## CLINICAL EXPERIENCE

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



## CMC GENE THERAPY FACILITIES

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



## REGULATORY EXPERTISE

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



## PATIENT ACCESS

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



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# **GENE THERAPY PROGRAMS**

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# Sensorion's Gene Therapy Programs Target Rare Auditory Diseases

## FIRST PROGRAMS RESULTING FROM THE INSTITUT PASTEUR COLLABORATION

### OTOFERLIN DEFICIENCY

- Pediatric 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 Orphan Disease Designation , US Rare Pediatric Disease Designation
- Pediatric Investigational Plan Agreed in EU

### GJB2-RELATED HEARING LOSS

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

- Early onset of severe presbycusis (adult population)
- Childhood onset (pediatric population)
- Congenital onset (pediatric population)
- ~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**

# Aiming To Develop Best-In Class And First-In Class Gene Therapy

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



SENS-501 development has been supported by Audinnove consortium (Institut Pasteur, Hôpital Necker- enfants malades, Fondation pour l'Audition & Sensorion) which is financed by the French State, via the National Research Agency through the "Investing for the future" program (ref: ANR-18-RHUS-0007)

# SENS-501 Gene Therapy Pediatric Indications Have Blockbuster Sales Potential

## SENS-501 (OTOF-GT) is the Perfect Pilot Program

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



- SENS-501 will be the pilot program demonstrating that GT is a relevant medical approach for the inner ear
- SENS-501 will establish understanding of GT in the inner ear by the Regulators and the Payers for future GT programs
- Medical plausibility and target population have been confirmed through :
  - ✓ ODD in the US and EU, RPDD with eligibility for voucher in the US
  - ✓ PIP Agreed in EU
  - ✓ Clinical Trial Application approved in France (FPI injected)

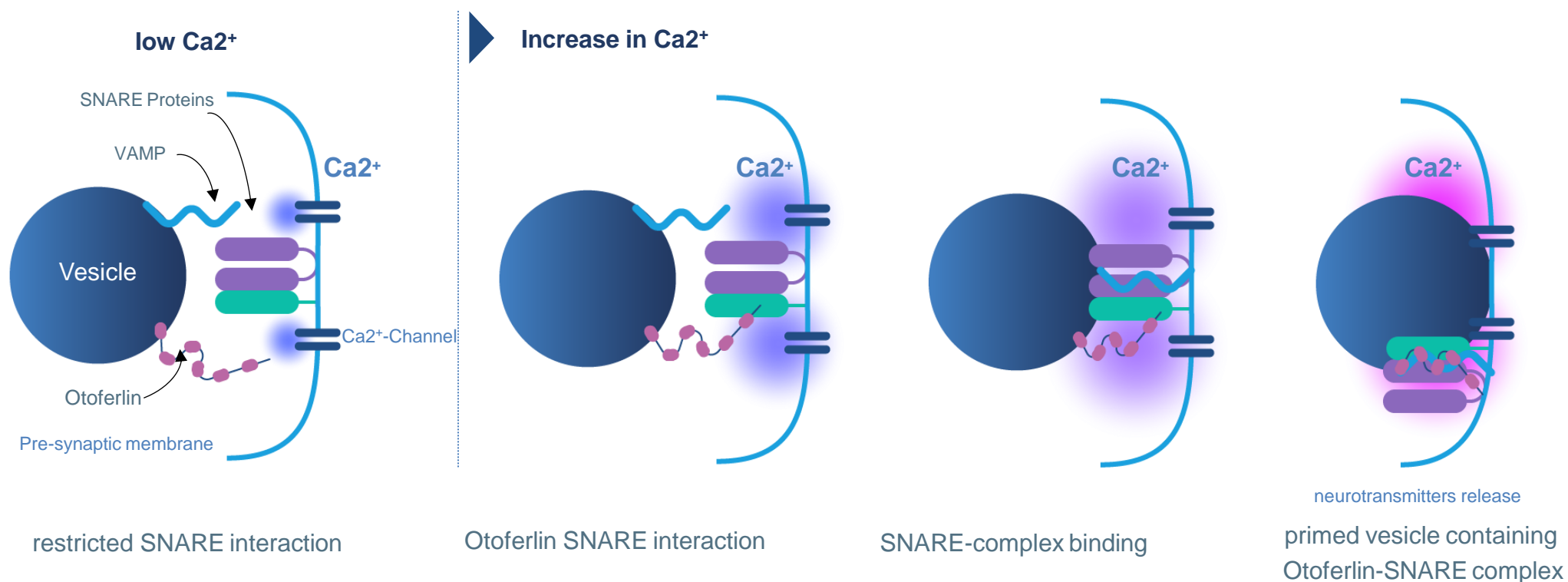
## Sales Potential Illustration

**SENS-501**

**GJB2-GT**

Sources: Sensorion, AT Kearney market research

# OTOF Gene Encodes Otoferlin, A Key $\text{Ca}^{2+}$ Sensor Protein



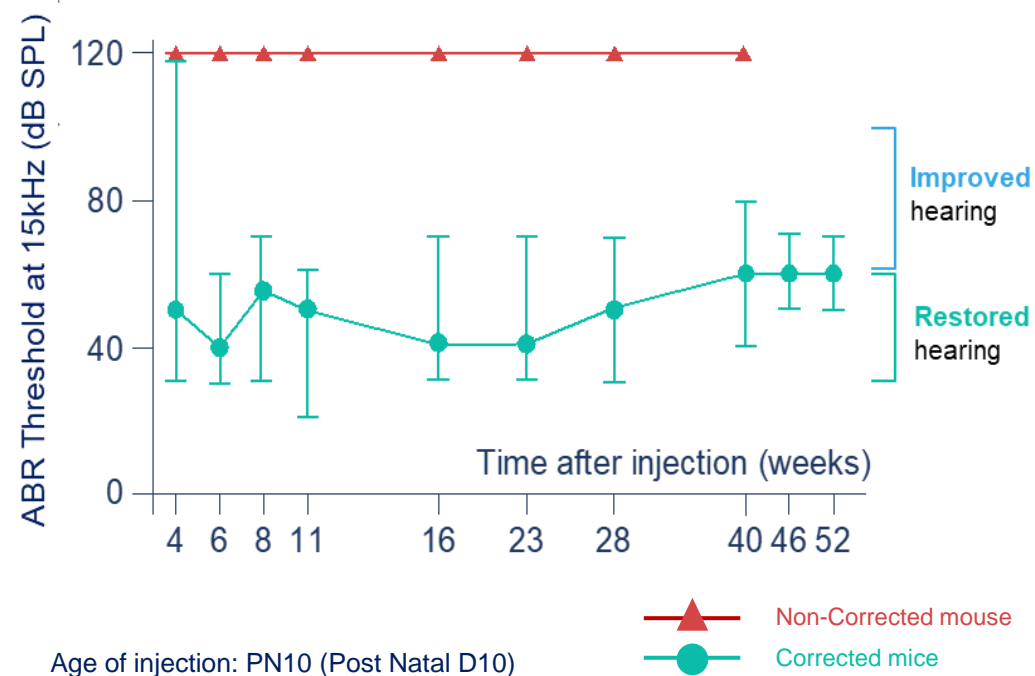
Model illustrating calcium regulation of otoferlin/SNARE interaction in the hair cell – Adapted from Ramakrishnan *et al.* 2014

**OTOF is the gene coding for the otoferlin protein, a  $\text{Ca}^{2+}$  sensor for vesicle fusion and vesicle pool replenishment at auditory hair cell ribbon synapses**

# SENS-501 Leads to Long-Term Hearing Recovery in a Translational Model of Otoferlin Deficiency

## Long-Term Hearing Restoration

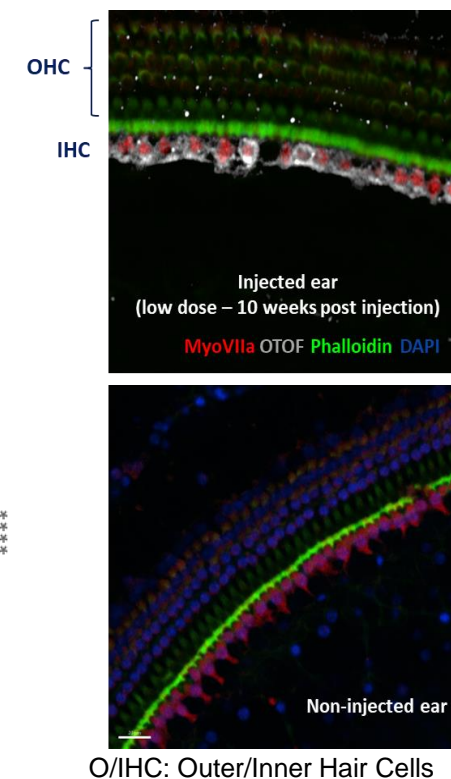
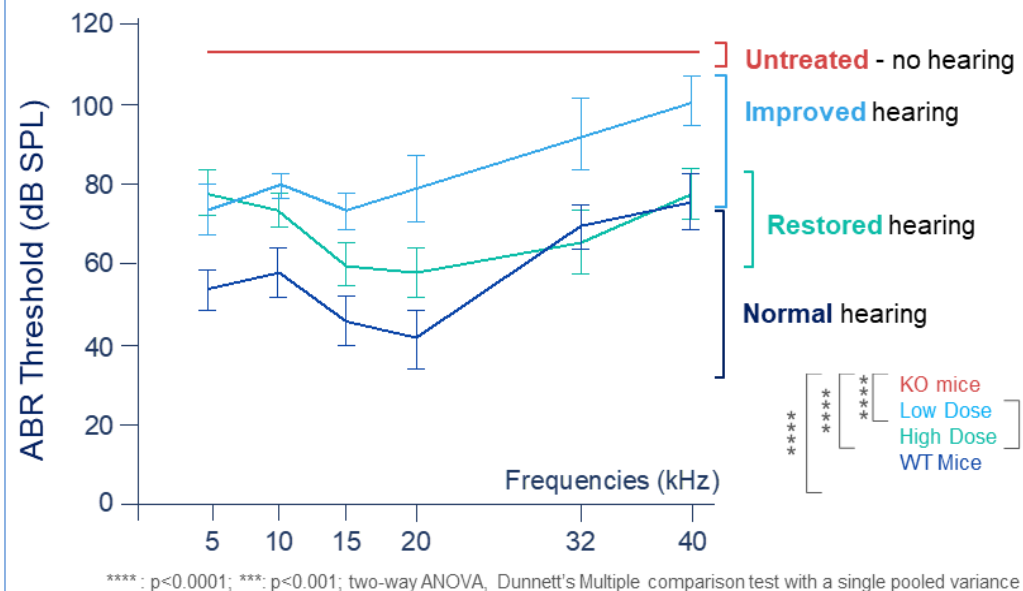
AAV-mOTOF injected in mice before hearing onset



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

## Hearing Restoration Correlates with de novo OTOF Expression

SENS-501 injected in mice after hearing onset  
10 months after injection

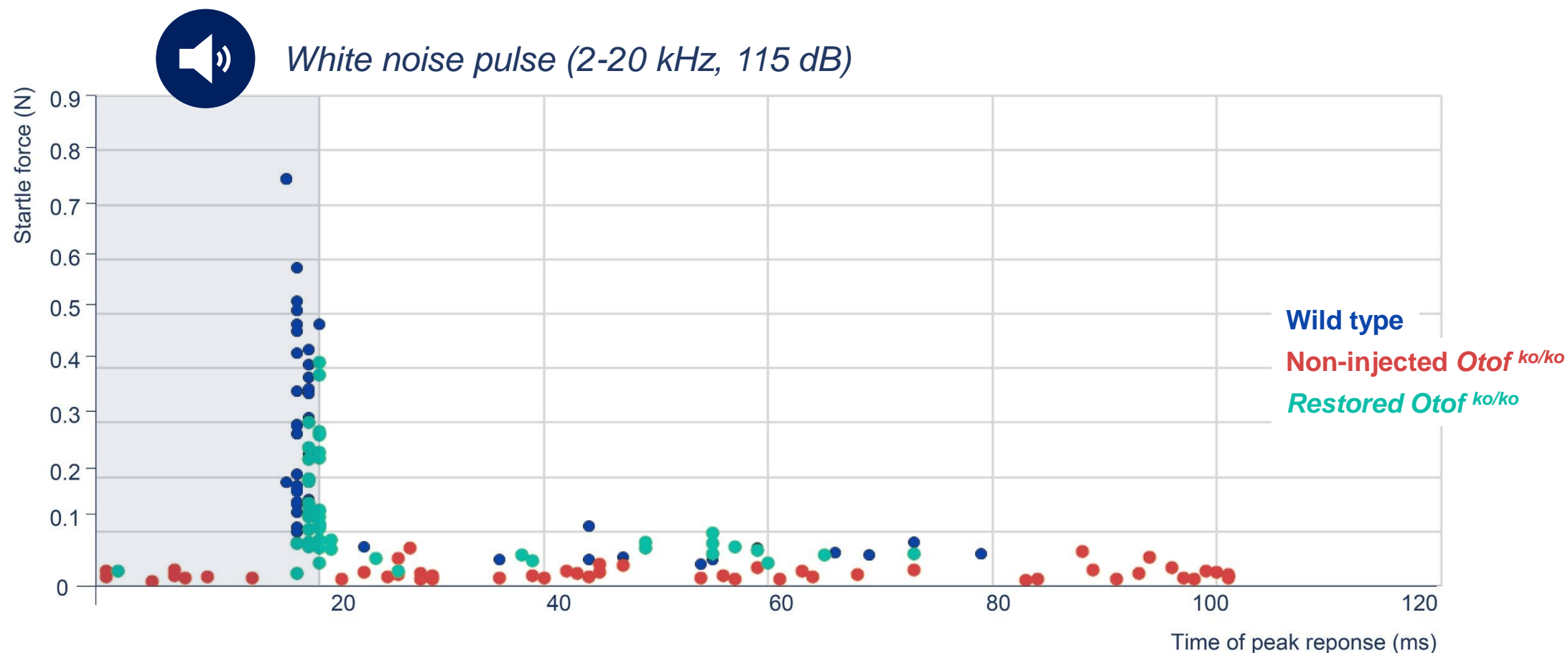


- Both doses of SENS-501 demonstrated efficacy in **improving hearing in KO mice**
- SENS-501 leads to **otoferlin expression in Inner Hair Cells**



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

## Behavior Test Based on Hearing Recovery Implemented in Mouse

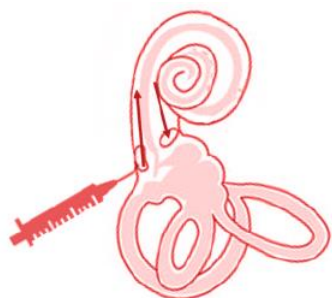


Olivier et al. ASGCT 2023 [link](#)

# Dedicated Surgical Approach for Gene Therapy

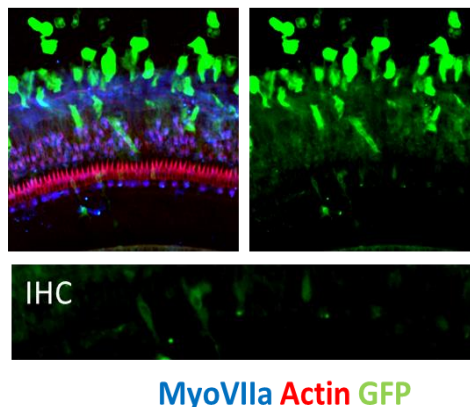
Non-Human Primates injected through the round window membrane (RWI) with or without stapedotomy (stap)

## 1 Fenestration



Used for cochlear implant

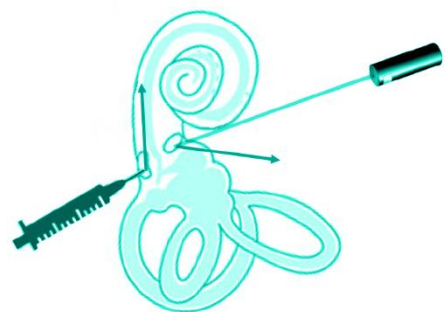
- Overpressure
- Limited volume
- Backflow
- Irregular transduction rate



## Surgical approach

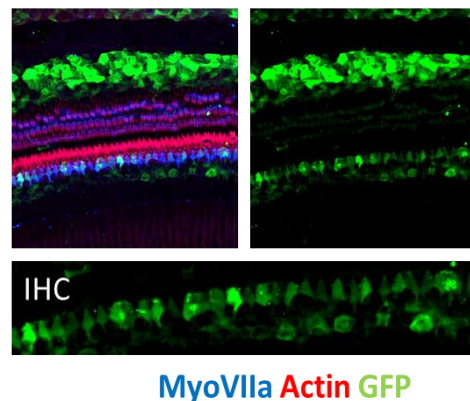
- Surgical procedure is **similar to cochlear implantation and well mastered by ENTs surgeons**
- Optimized surgery uses **stapedotomy procedure** to maximize target cells exposure along the full length of the tonotopic axis
- **Proprietary injection device developed** to inject a defined volume at a controlled flow rate

## 2 Fenestrations

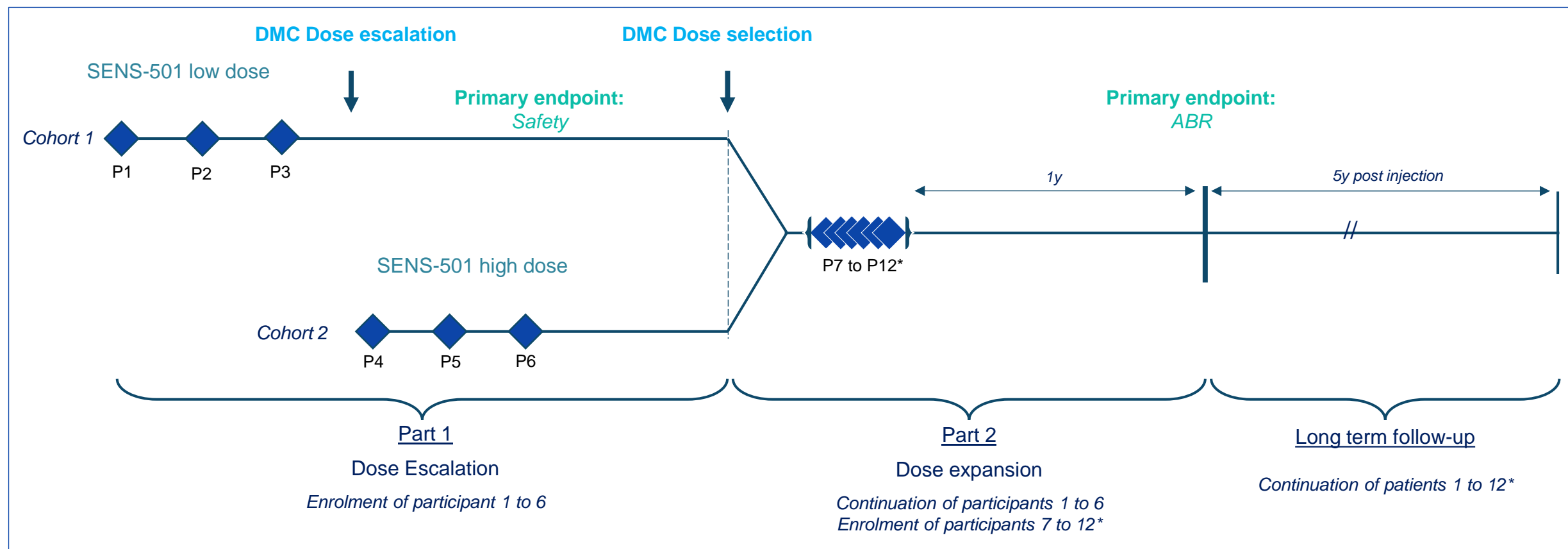


Combining 2 common surgical techniques: cochlear implant and stapedotomy

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



Audiogene, a Phase 1/2 clinical trial in children aged 6 to 31 months to assess safety, tolerability, and efficacy of SENS-501 following unilateral injection into the cochlea



- **Pediatric patients, aged 6 to 31 months at the time of the injection** (to maximize chances of acquiring speech and language)
- **Single intra-cochlear unilateral injection**
- **Dose escalation** (Primary endpoint: safety and tolerability)
- **Dose expansion** (Primary endpoint: efficacy (ABR, Auditory Brainstem Response))

Px = participant number x  
y = year

\*Further participants may be recruited if required, who will be assessed in the same way as P7 to P12.



## First Patient Injected

- **First Patient Injected in Q3 2024**
- **Initial safety data reported at 4 weeks**
  - No dose-limiting toxicities, no Serious Adverse Events
  - Vestibular function remained intact and unchanged from baseline
  - Otoacoustic Emissions (OAEs) remain present
- **Surgical administration procedure was uneventful**
- Medical condition of the child (upper respiratory infection unrelated to SENS-501) at the time of assessment did not allow to get reliable hearing sensitivity. ABR at Month 1 was postponed
  - From early observations, the clinical team and the patient's mother noted a change in the child's behaviour and vocalisations

## Study Update

- **Patient recruitment going as planned:**
  - **1<sup>st</sup> cohort screened; completion expected by year-end 2024**
  - **Initial efficacy data to be reported by year-end 2024**
  - **2<sup>nd</sup> cohort of patients to be recruited in H1 2025**
- **Ongoing Natural History Study Otoconex supports eligible patients' identification**

# SENS-501 (OTOF) Gene Therapy Program Status

CTA Approval in Various Countries ✓

Pediatric Investigational Plan  
agreed in EU ✓

First Patient Communication ✓

1st Cohort Completed  
H2 2024 →

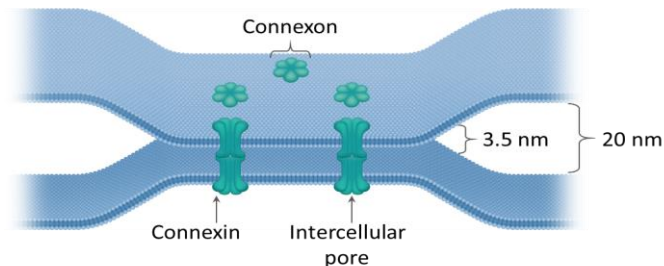
2nd Cohort Completed  
H1 2025 →



# Connexin 26: A Gap-junction Protein Encoded By *GJB2* Gene and Responsible For Tissue Homeostasis

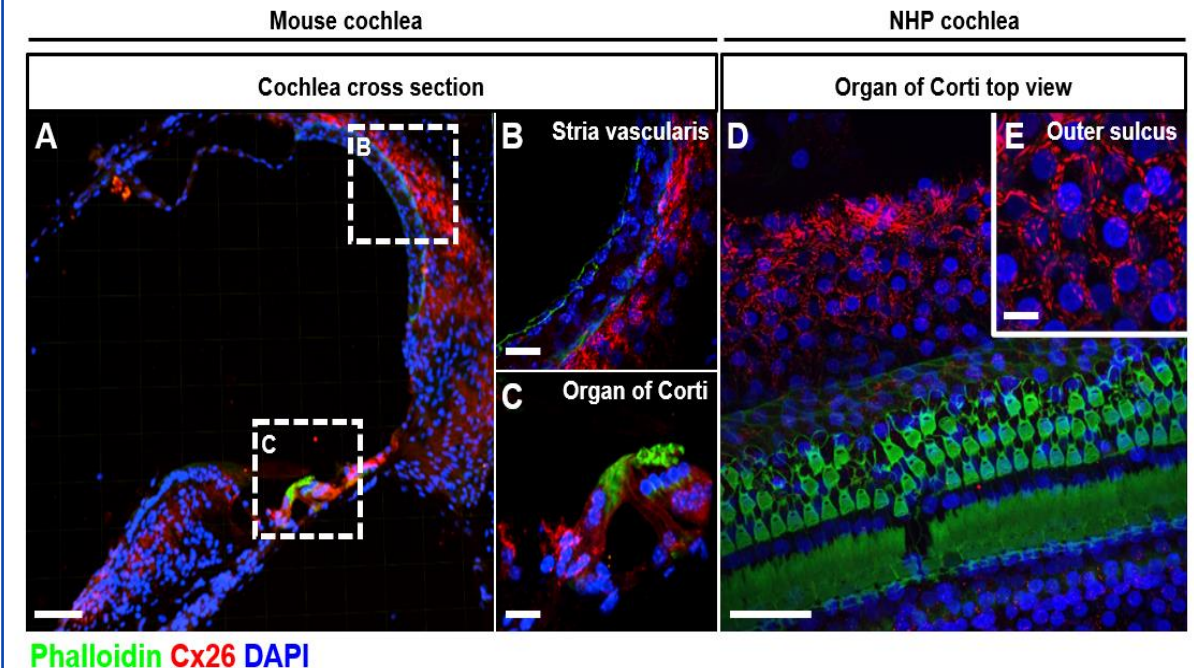
## Mutations in the *GJB2* Lead to Deafness

- *GJB2* is the gene encoding for the Connexin 26 protein; one of 20 known connexins
- Cx26 and Cx30 proteins are the dominating connexins in the cochlea; heteromeric or heterotypic hexamers forming Gap Junctions
- Gap Junctions are key for the intercellular exchange of molecules (miRNA, glucose, ions, etc.) hence responsible for tissue homeostasis
- More than 100 recessive mutations origin Cx26 truncation / deletion leading to non-syndromic hearing loss and deafness, most are addressable via gene replacement
- Severity of hearing loss correlates with degree of loss of GJB2 function








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

## *GJB2* Expression in the Cochlea



- Supporting cells of the organ of Corti
- Fibrocytes of the spiral limbus and the lateral wall
- Intermediate and basal cells of the stria vascularis
- Not expressed in hair cells

# Lead Candidate Was Selected to Answer Specific Developement Criteria

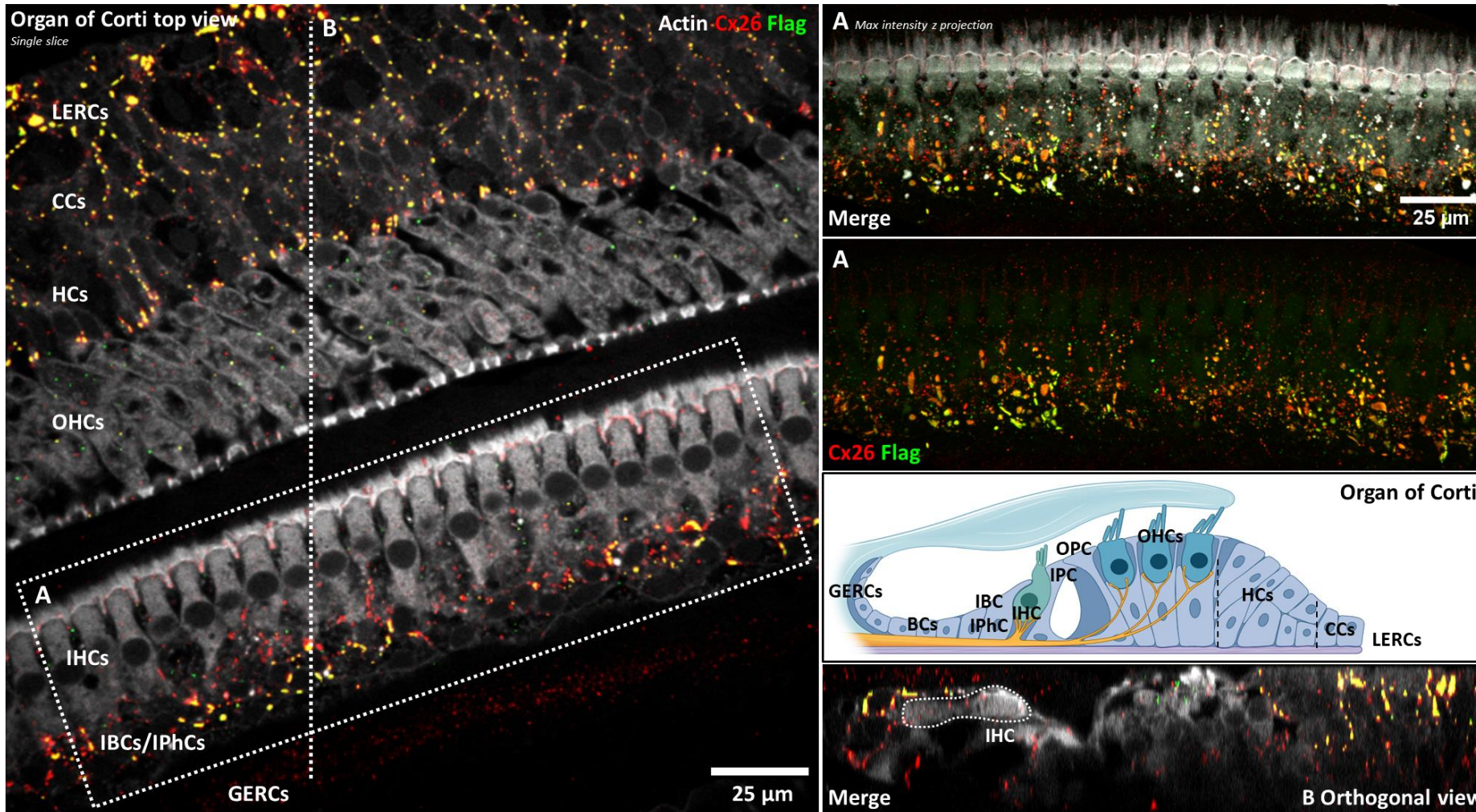
CRITERIA	LEAD CANDIDATE
Natural and synthetic AAV capsid libraries screening for broad coverage of target cells	
Expression cassette design for high-level of target cells transduction, correct cellular localization, active gap-junctions	
Avoiding off-target expression (i.e. hair cells): promoter and regulatory sequences design	
Limited off-target tissue biodistribution	
Surgical approach developed and mastered by ENT surgeons	

**Our Lead Candidate Was Designed to Ensure Broad Coverage of Relevant Cochlear Cells While Detargeting Hair Cells**



# Lead Candidate Can Deliver Cx26 in the Appropriate Target Cells

## Correct Delivery of Cx26 Using Lead Candidate Flag in Non-Human Primate Cochlea



### Cell Types

Claudian Cells	✓
Deiters Cells	✓
Great Epithelial Ridge Cells	✓
Hensen Cells	✓
Inner Border Cells	✓
Inner Hair Cells	—
Inner Phalangeal Cells	✓
Pilar Cells	✓
Lateral Epithelial Ridge Cells	✓
Outer Hair Cells	—
Fibrocytes	✓
Stria Vasularis	✓

- No expression in Hair Cells confirmed
- No morphological defects observed 3 and 9 weeks after intracochlear administration

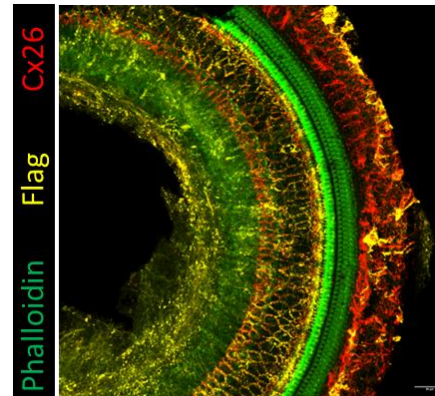
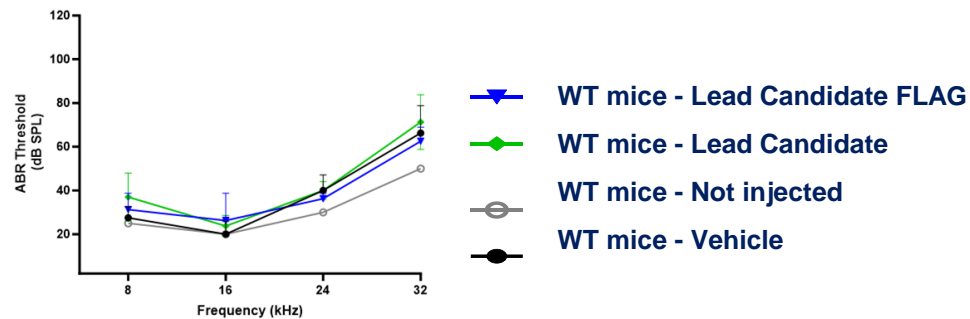
# Lead Candidate Demonstrates Adequate Safety and Biodistribution Profile - Including Long-Term Local Tolerability in Mice and NHP

## Acute toxicity in WT Mice - High dose IV injection

- Study performed in preparation of upcoming GLP-toxicity in mice after IV injection
- GT-GJB2 does not interfere with normal growth and don't elicit elevated transaminase levels 4 and 8 weeks after injection
- Behavioral evaluation (Functional Observation Battery, exploratory behavior (videotracking) 3 and 7 weeks after injection: no findings

## 6-Month Exploratory Safety and Transgene Expression in WT Mice – Intracochlear injection

### 6 months after injection



GT-GJB2-Flag imaging – 6 months post intracochlear injection in mice

- No impact on ABR up to 6 months following Lead Candidate injection
- Normal histology maintained, transgene expression persistence
- Hair cells detargeted
- Clinical pathology: no findings

## 3-Month Exploratory Toxicity and Biodistribution in Non-Human Primate – Intracochlear injection

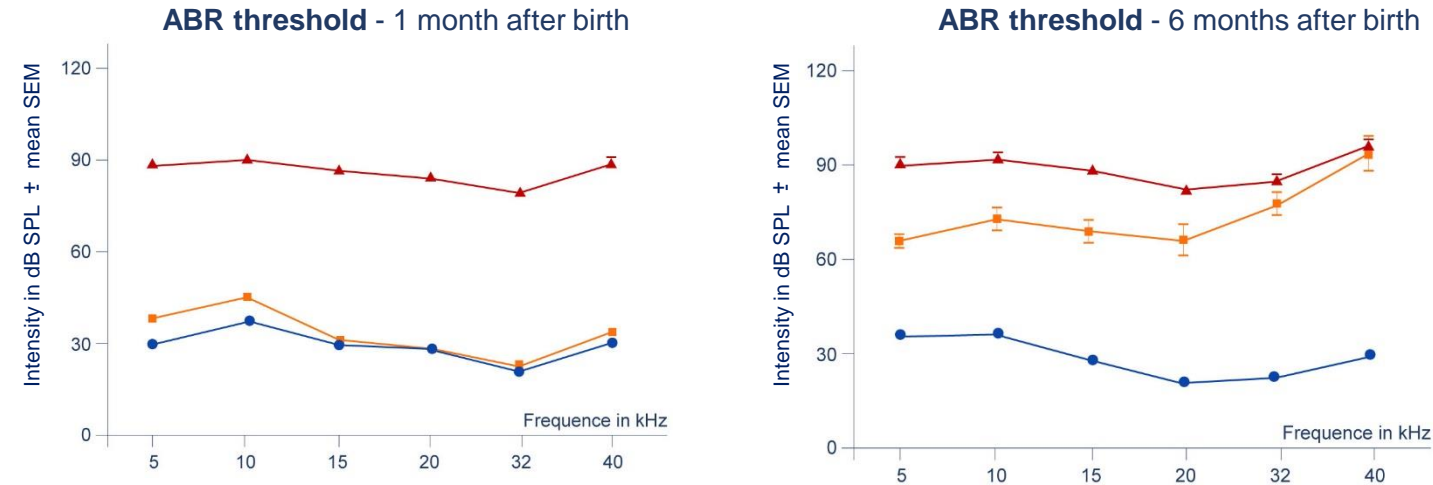
- Lead Candidate is well tolerated and did not induce any macroscopic/organ weight changes or local/systemic microscopic findings
- Normal cochlear histology
- No lab and clinical findings
- Biodistribution: the vast majority of the vector remains in injected ears, no dissemination observed in gonads, main organs, dorsal root ganglion (DRG)



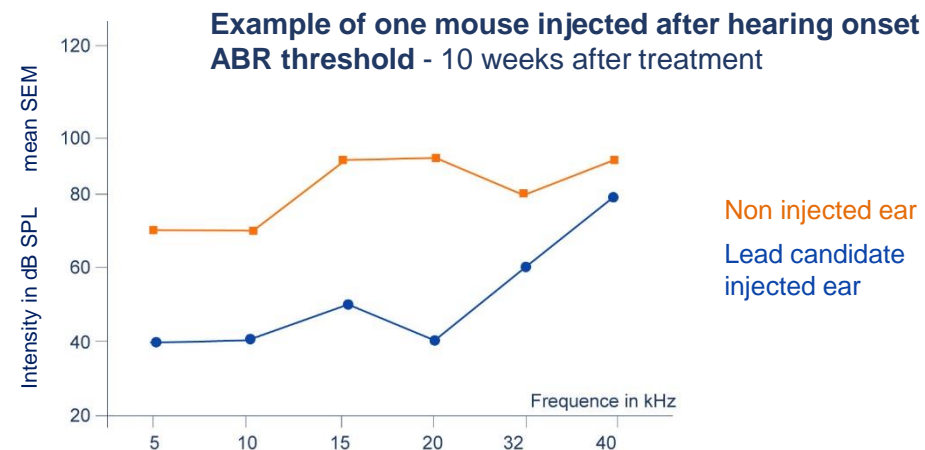
# Lead Candidate Prevents Hearing Loss in Relevant Mouse Model

## Proof Of Concept In Progressive Mouse Model

Conditional knock-out mouse model leading to 2 phenotypes



Control mice    Congenital-like Profound Cx26 ↓ ↓ ↓    Progressive Cx26 ↓

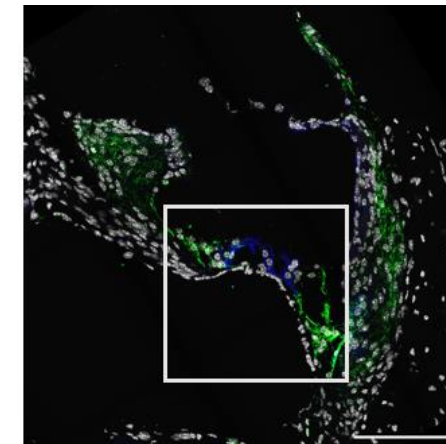


Non injected ear  
Lead candidate injected ear

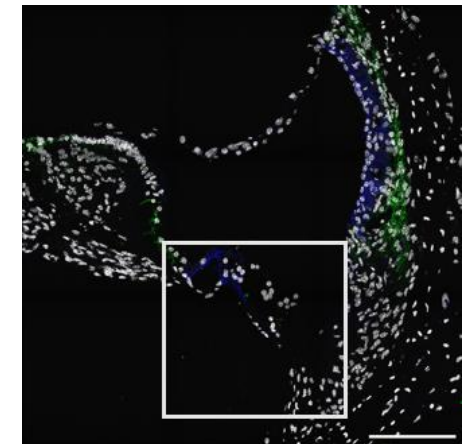
## Hearing Loss Prevention Correlates With Connexin 26 Expression

Example of one mouse injected after hearing onset  
Connexin 26 expression in the cochlea  
- 10 weeks after treatment

Lead candidate injected ear



Non injected ear



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



# GJB2 Gene Therapy Program Status

Ongoing European Natural History  
Study OTOCONEX 

Ongoing Natural History Study  
in Collaboration with Sonova 

Preclinical IND/CTA Enabling  
Studies 

Update on Additional PoC Efficacy  
and Safety Data Oct 2024 (ESGCT) 

Clinical Trial Applications  
H2 2025 



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# **SENS-401 PROGRAMS**

**Multiple Indications To Treat And Prevent Hearing Loss**

# 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



Cognitive decline



Isolation



Depression



Ability to work



Falls



Loss of independence

Source: Cochlear® 2018 investor day ([link](#))

### KEY FIGURES

**36,450**

Implants sold by Cochlear® globally in 2021<sup>1</sup>  
(representing ~60% of global market share)

**\$1.5bn**

Cochlear implant market in 2020<sup>2</sup>

**80%**

Market penetration in children in developed  
markets<sup>1</sup>  
and 3% in adults<sup>1</sup>

<sup>1</sup>Cochlear® FY21 Result Presentation ([link](#))

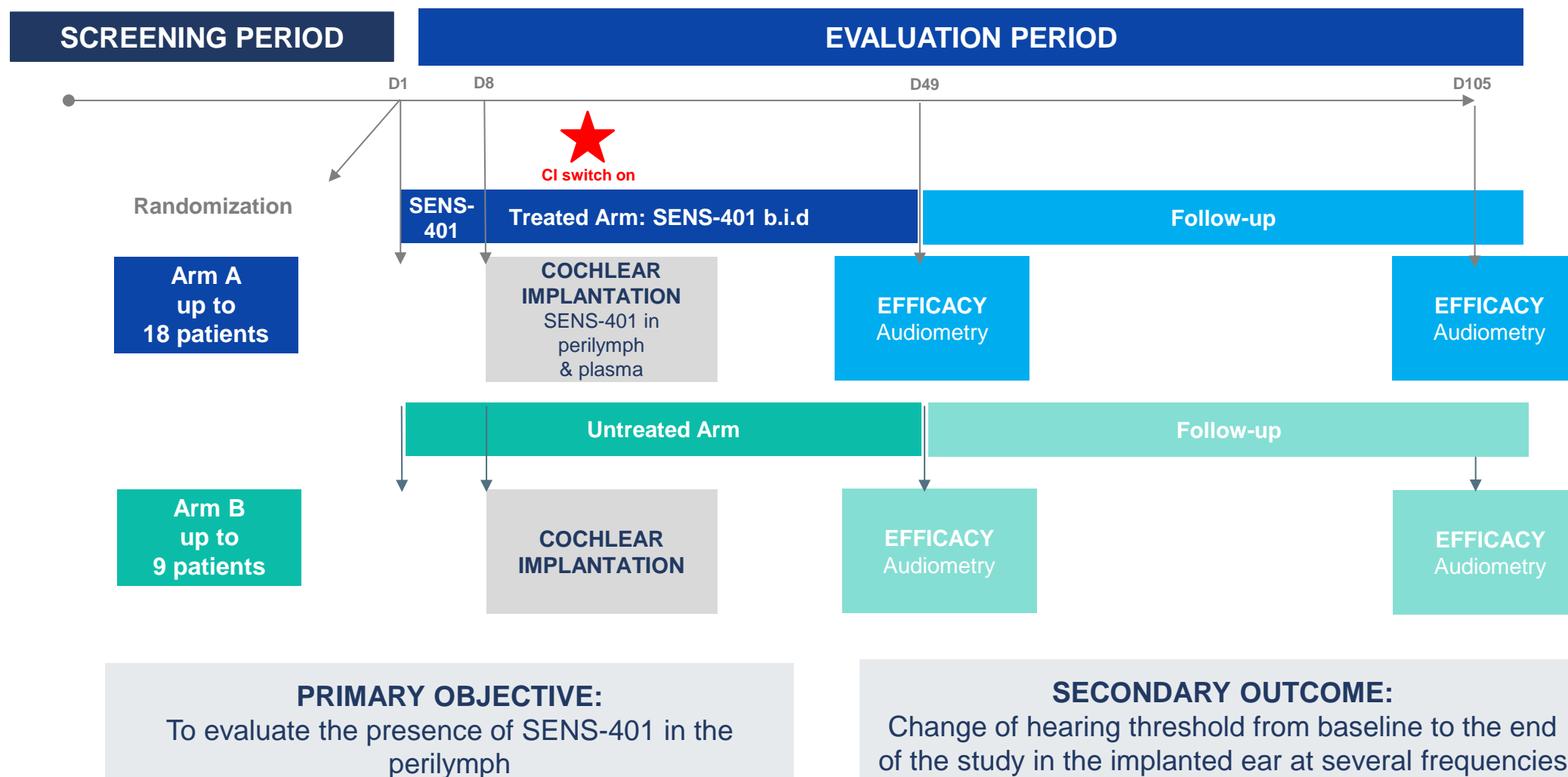
<sup>2</sup>Market estimates ([link](#))

# SENS-401 CI Study Design

## Study completed



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



# Primary Endpoint of the Phase 2a Clinical Study for Residual Hearing Preservation Has Been Met

## Perilymph Concentrations Data

	Treated with SENS-401 (n=16) n (%)
SENS-401 levels $\leq$ LLOQ	0
SENS-401 levels $>$ LLOQ	14*(100)

*\*Among the 16 participants who underwent surgery, 15 have a perilymph samples and 14 samples were analyzable*

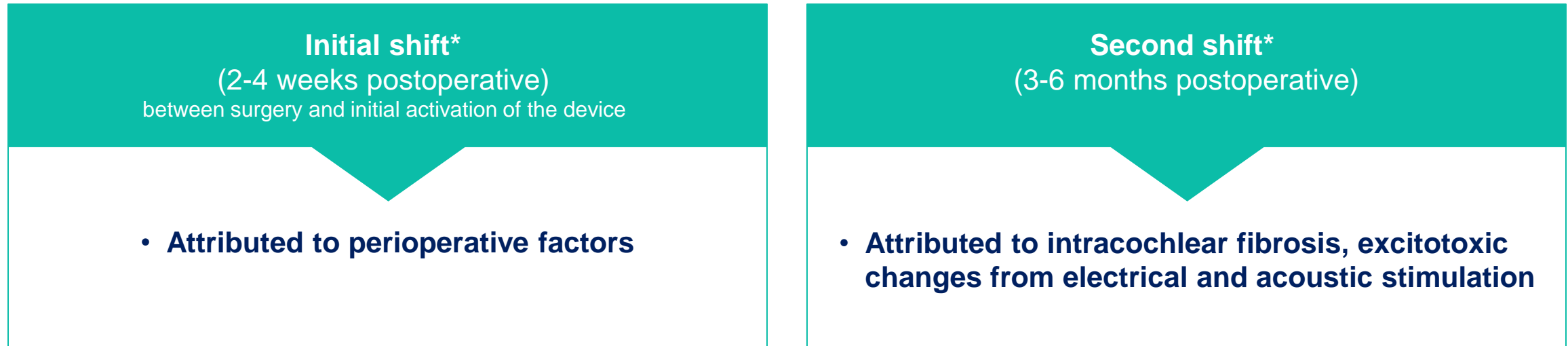
*\*LLOQ define by a specific method developed for SENS-401*

*\*\* The sampling times for SENS-401 levels in the perilymph were standardized in relation to the last oral dose of treatment*

- **Presence of SENS-401 in the perilymph is confirmed in 100% of the patients** sampled following cochlear implantation
- These results confirm that SENS-401 administered orally **crosses the labyrinth barrier**



# Residual Low Frequency Hearing Benefits for Cochlear Implant Users

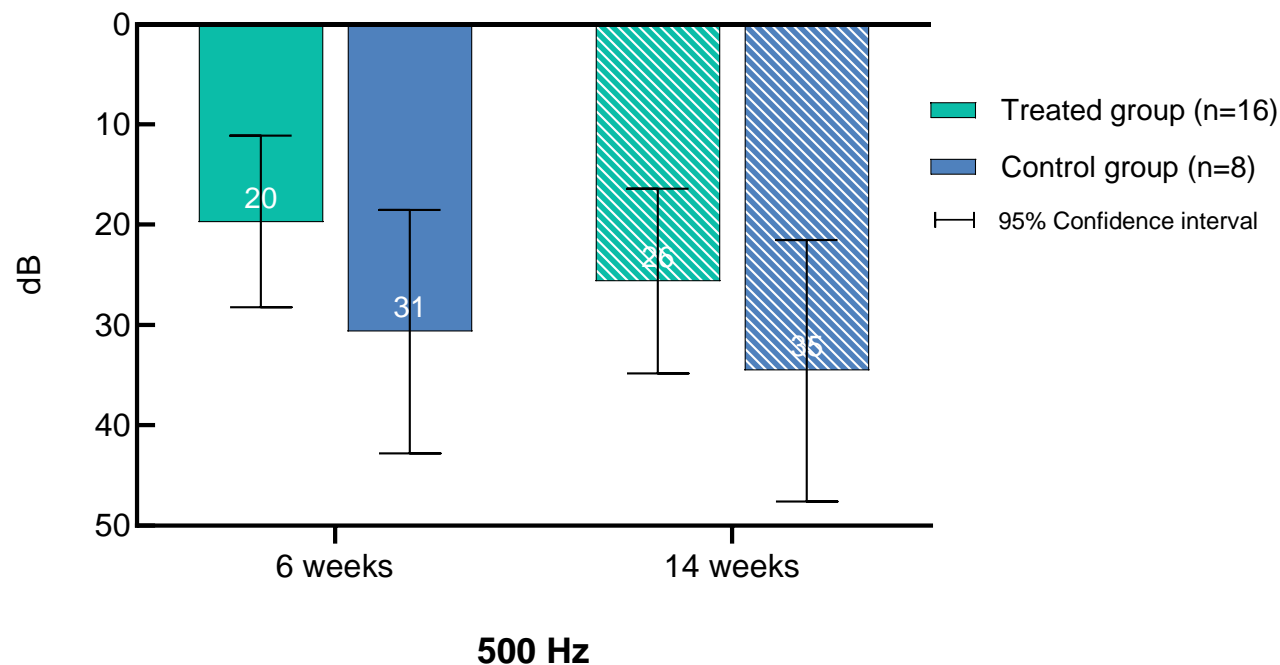


**Postoperative hearing preservation** defined as:  
unaided air-conduction **thresholds < 85 dB HL** at 125, 250, and 500 Hz

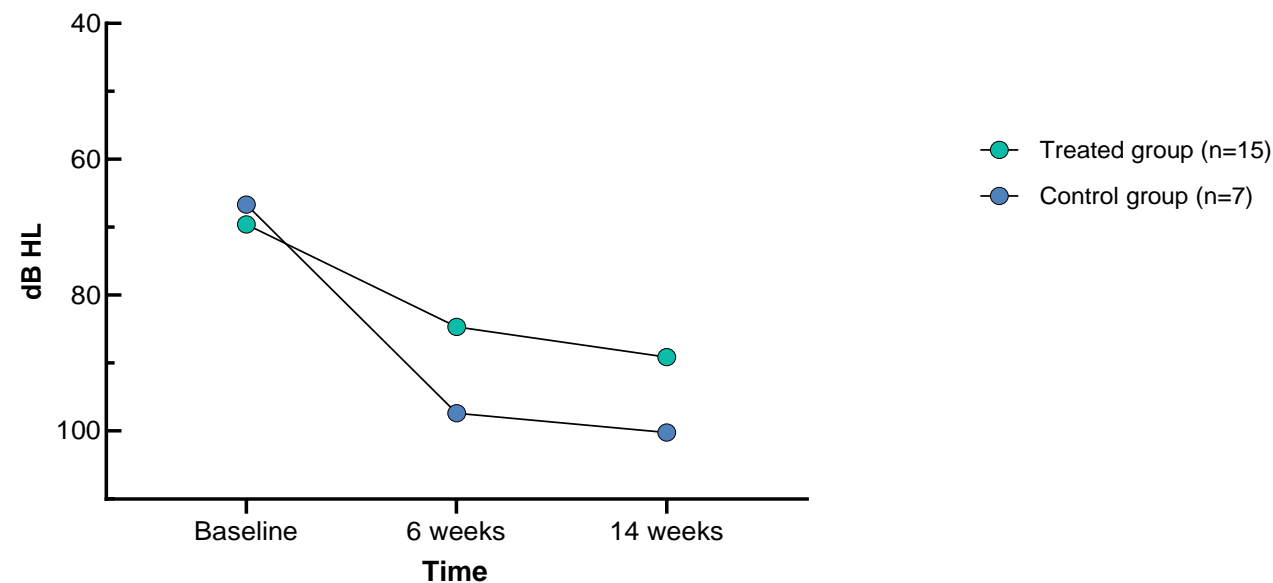
*\*Jensen et al., Hearing Preservation After Cochlear Implantation, 2021*

# SENS-401 Provides Hearing Protection 6 & 14 Weeks Post-Cochlear Implantation

LS Mean change from baseline of hearing threshold values at 6 and 14 weeks post CI



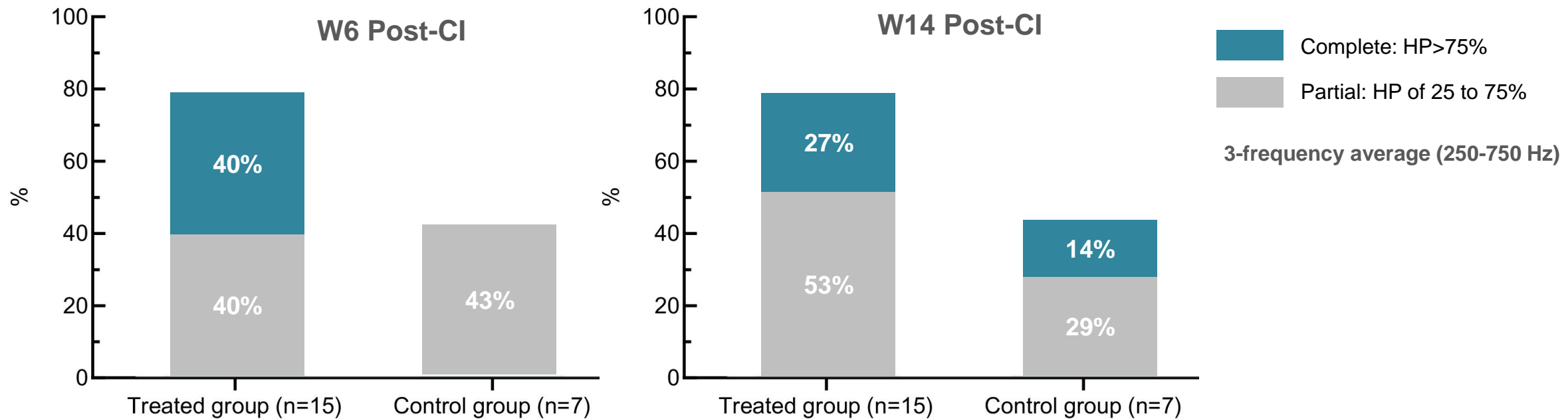
Mean of the 3-frequency average (250-750 Hz) hearing threshold values at baseline, 6 weeks and 14 weeks post CI



ANCOVA analysis and descriptive statistics used  
p-value of 0.0567 for the PTA (250-750 Hz) suggested  
a trend towards statistical significance

- Residual hearing loss is lower in patients treated with SENS-401 compared to control group 6 weeks after cochlear implantation
- This preservation effect is maintained 8 weeks after SENS-401 discontinuation (14 weeks post-CI)

# SENS-401 Provides Residual Hearing Preservation\* 6 & 14 Weeks Post-Cochlear Implantation



- Patients in the SENS-401 treated group are **twice as likely to show complete or partial hearing preservation** compared to control group after 7 weeks of continuous treatment
- Only SENS-401 treated group show a **complete hearing preservation with 40%** of treated patients compared to 0% in the control group at 6 weeks post-CI
- **These results are maintained 8 weeks** after SENS-401 discontinuation (14 weeks post-CI)

\*Skarzynski H, van de Heyning P, Agrawal S, Arauz SL, Atlas M, Baumgartner W, et al. Towards a consensus on a hearing preservation classification system. Acta Otolaryngol Suppl. 2013(564):3-13.

# SENS-401 CI Final Results - Conclusion



**SENS-401 can cross the labyrinthine barrier to target cochlear hair cells in all patients sampled, confirming primary endpoint is met. SENS-401, present in the perilymph fluid, reaches concentrations that are pharmacologically active.**



A **complete hearing preservation** is exclusively observed in 40% of patients treated with SENS-401 at 6 weeks post cochlear implantation



Eight weeks after discontinuation of SENS-401, the **hearing protective effect is maintained**



**Residual hearing loss is reduced in the SENS-401 treated group** compared to the untreated group at 6 weeks post-cochlear implantation



SENS-401 taken for 8 weeks confirms it has a **good safety profile**



**SENS- 401 has the potential to modify the outcome of CI while preserving residual hearing by improving speech perception in quiet and noise, music perception, spatial localization and maintaining more natural sound quality**



These results support the SSNHL phase 2 data and further development of SENS-401

# Cisplatin Administration For Chemotherapies Damages The Inner Ear And Leads To Hearing Loss, Tinnitus And Dizziness

## WHAT IS CIO?

**Hearing loss caused by cisplatin administration as chemotherapeutic treatment.**

Risk factors include young age as well as individual and cumulative cisplatin doses.

CIO leads to permanent inner ear problems in 50-60% of adult cases and in 90% of pediatric cases.

**These complications significantly impact patients' quality of life due to:**

- Hearing loss, tinnitus and dizziness impacting daily life activities
- Problems in language acquisition and learning for pediatric patients
- Difficulties in communicating, social isolation, cognitive decline

Potential treatments must not interfere with cisplatin efficacy.

**Incidence of cisplatin treated patients:** 500,000 patients in 2025 in G7 countries<sup>1</sup>



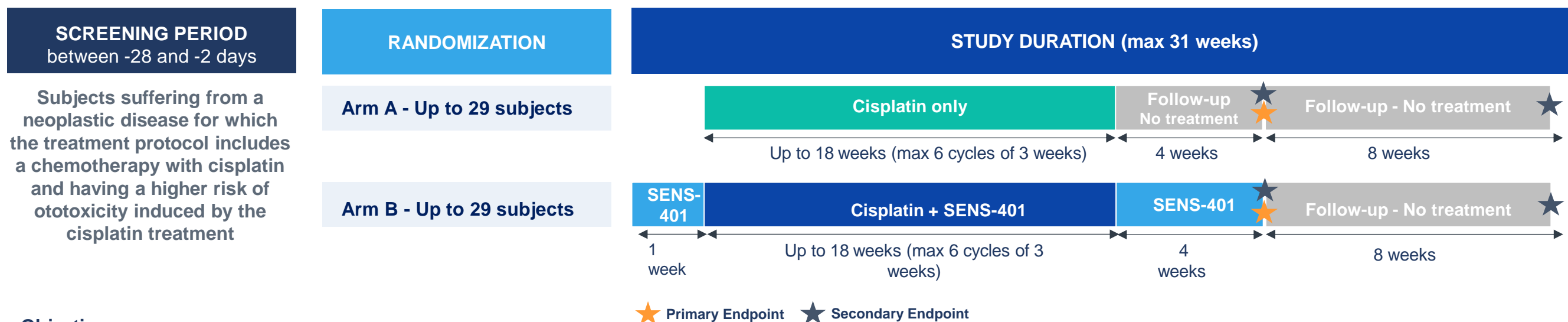
<sup>1</sup> Company/ estimates based on publicly available data (in the US, Japan, Germany, France, the UK, Italy and Spain)



# SENS-401 Phase 2a Proof-Of-Concept Study NOTOXIS

## Positive Preliminary Safety Data

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



### Objectives:

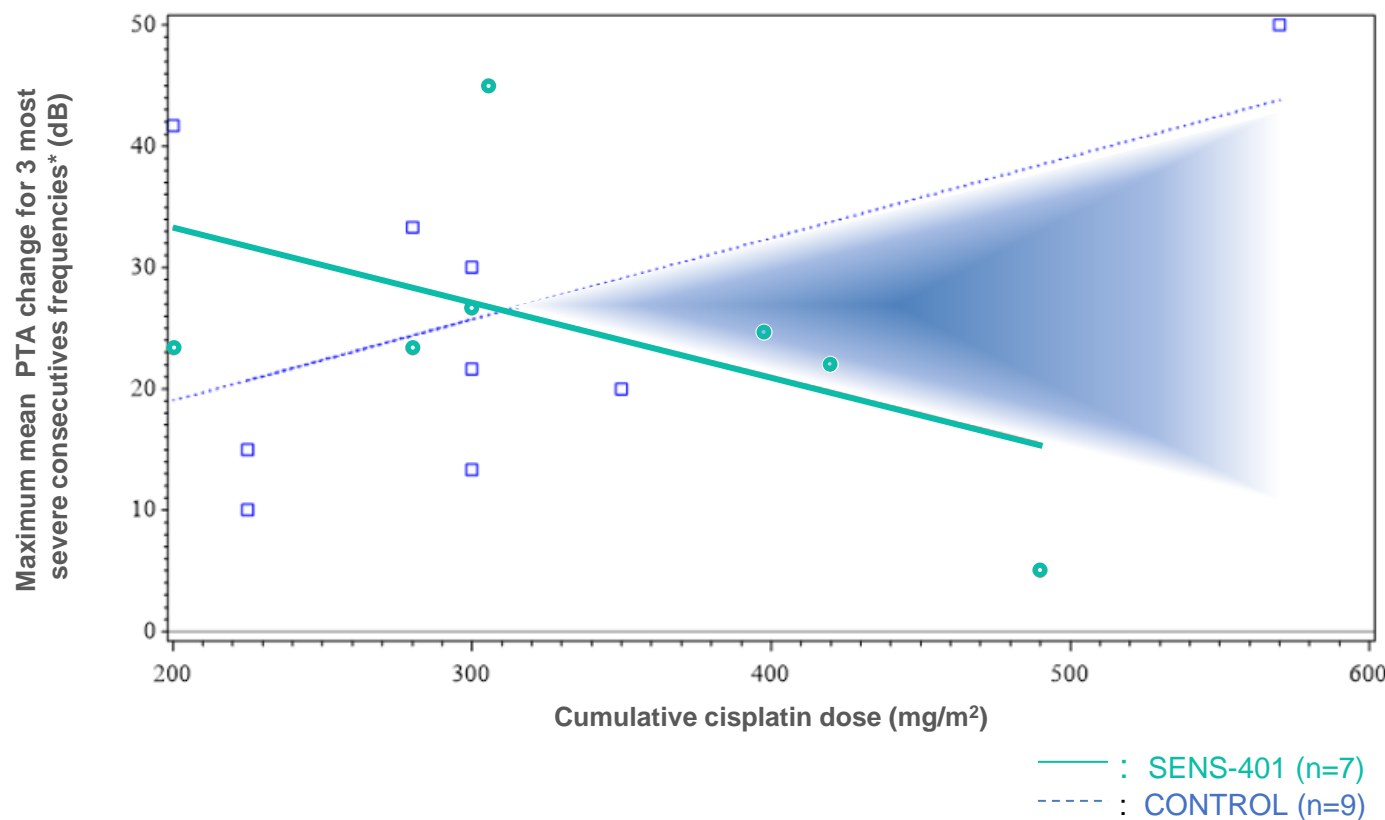
#### Efficacy

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

#### Safety

- AEs & SAEs incidence

# Preliminary Results Show Patients with High Exposure to Cisplatin May Benefit the Most from SENS-401's Otoprotective Effects



Groups	n	Variables	Mean	SD
Control	9	Cisplatin dose	305	110.0
		PTA change	26	13.6
SENS-401	7	Cisplatin dose	342	98.7
		PTA change	24	11.7

- Hearing loss is similar between SENS-401 and control group
- SENS-401 subjects were exposed to significantly more cisplatin than control

- As the cumulative dose of cisplatin increases, severity of ototoxicity observed in the control group escalates  $r=0.42$
- **Benefit of SENS-401 increases with higher cisplatin doses**
- **SENS-401 treatment group outperforms the control group at cisplatin doses > 300 mg/m²**

# Key Takeaways from Preliminary Study Data



**Cumulative dose** of cisplatin is a **key factor** of ototoxicity severity



SENS-401 has a **favorable safety profile** when administered continuously for up to **23 weeks** in adult patients undergoing cisplatin-based chemotherapy



Recruitment is progressing well



Based on preliminary data, **no significant difference** observed on ototoxicity measured by **PTA change** or CTCAE grading, **however SENS-401 treated group received higher cumulative dose of cisplatin compared to control**



Patients with **higher exposure to cisplatin** may **benefit the most** from SENS-401's otoprotective effect



The preliminary results suggest a trend toward an otoprotective effect of SENS-401 beyond a cisplatin dose of 300 mg/m<sup>2</sup>

# SENS-401 Programs Status

SENS-401 with cochlear implants –  
Full Data Readout Sept 20, 2024



SENS-401 CIO NOTOXIS  
- Preliminary Results S2 2023



SENS-401 CIO NOTOXIS  
- Preliminary Safety and Efficacy Data  
Sep 20, 2024



SENS-401 with cochlear implants –  
Final Results



SENS-401 NOTOXIS – Completion of  
Enrollment H1 2025



# Sensorion Newsflow [Estimated Timelines]

## **SENS-501 Gene Therapy Program**

H2 2024 – Audiogene Initial efficacy data to be reported by year end  
Audiogene enrollment completion of the first cohort

H1 2025 – Audiogene enrollment completion of the second cohort

## **GJB2-GT Program**

H2 2025 – Clinical Trial Applications

## **SENS-401 Program**

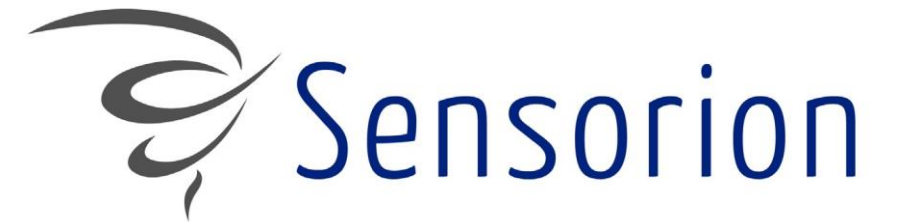
H1 2025 – CIO NOTOXIS: Patient recruitment completion



# THANK YOU



[E: contact@sensorion-pharma.com](mailto:contact@sensorion-pharma.com)



# Hearing Loss



# Access And Clarity Are Mandatory For Optimal Outcomes

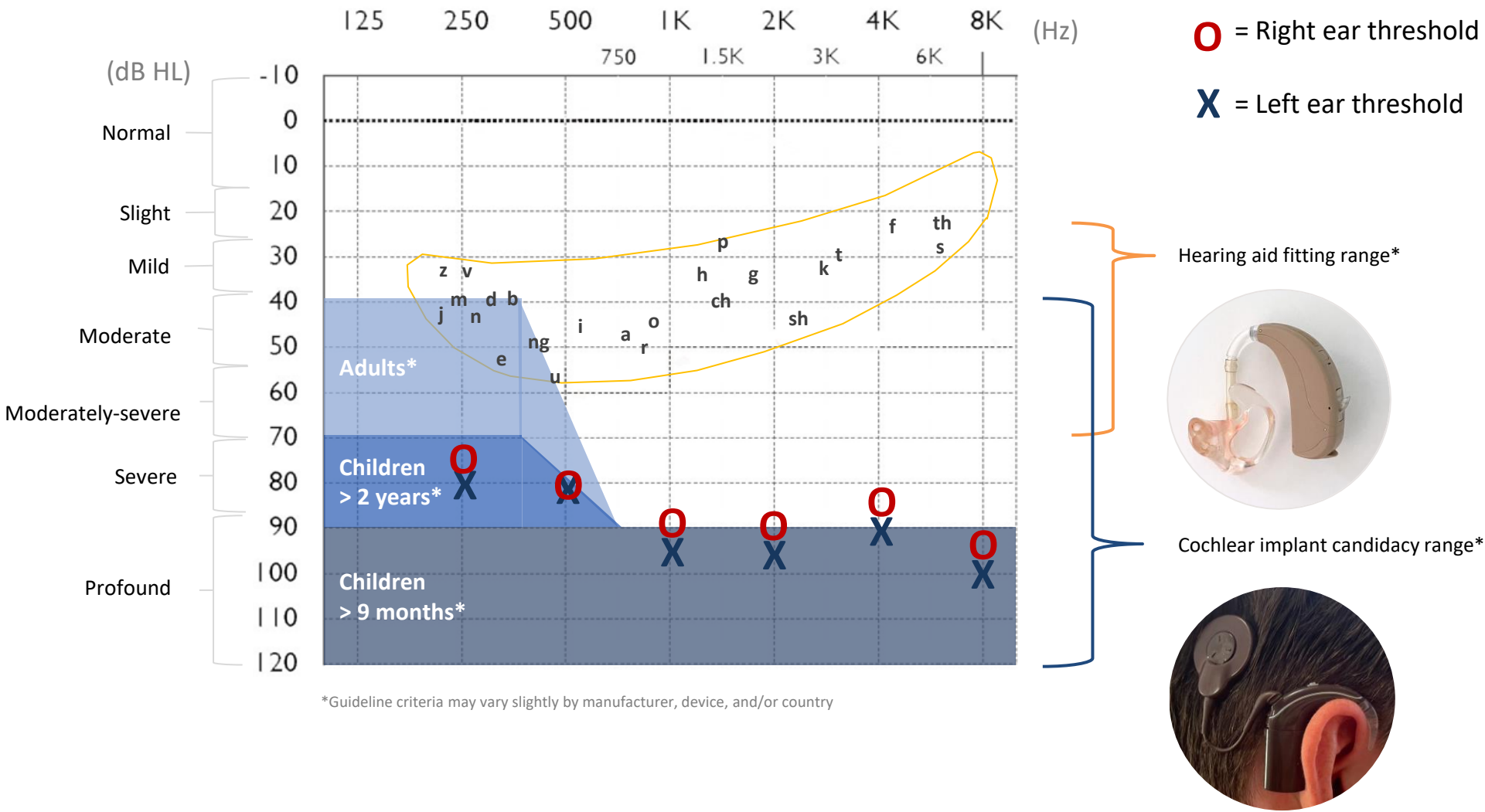


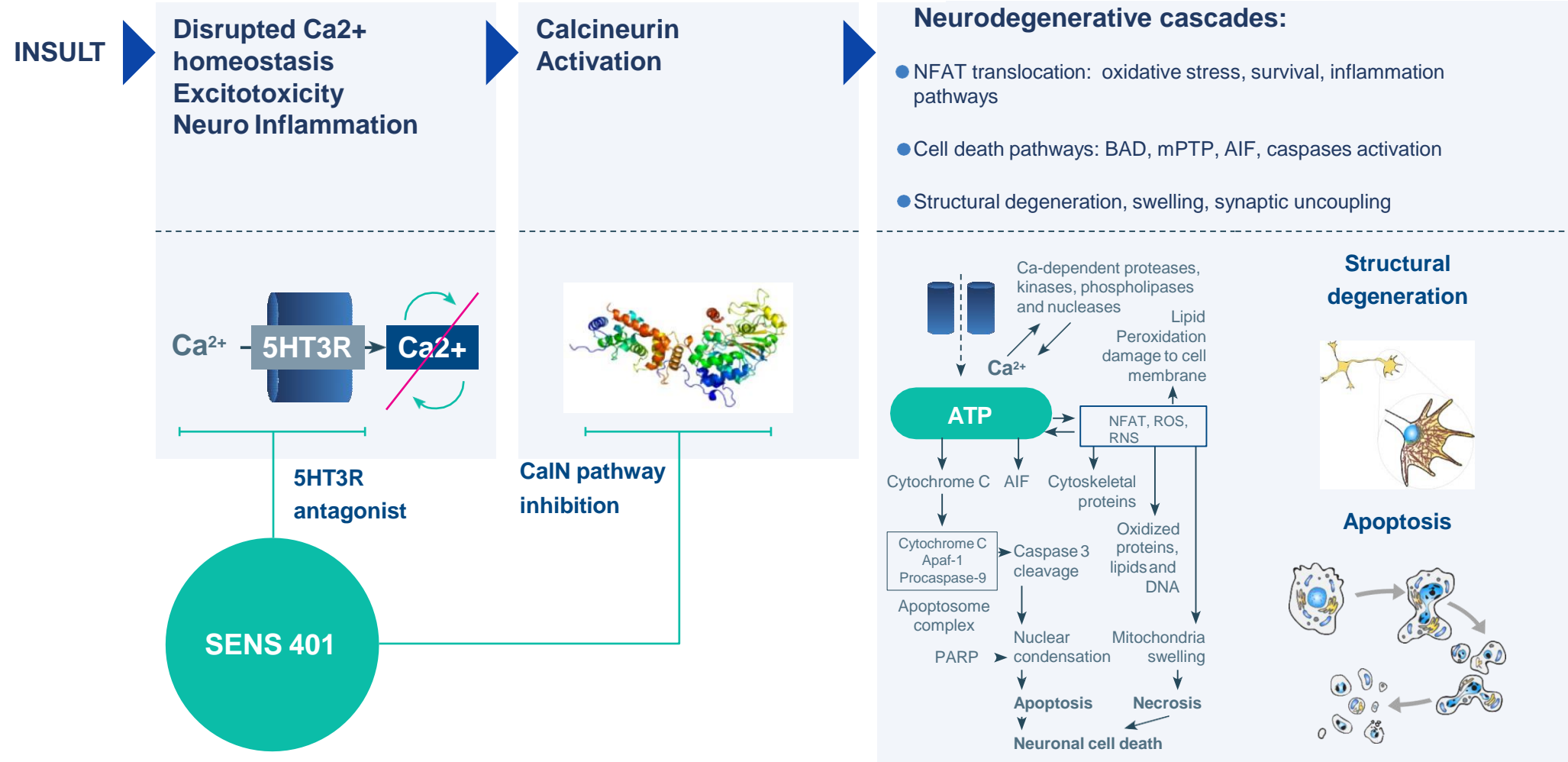
Image of hearing aid: [https://commons.wikimedia.org/wiki/File:Unitron\\_Ziel\\_photo\\_2.jpg](https://commons.wikimedia.org/wiki/File:Unitron_Ziel_photo_2.jpg)  
Image of cochlear implant sound processor on ear: [https://commons.wikimedia.org/wiki/File:Cochlear\\_Nucleus%20AE\\_7\\_Sound\\_Processor.jpg](https://commons.wikimedia.org/wiki/File:Cochlear_Nucleus%20AE_7_Sound_Processor.jpg)



**SENS-401**



# SENS-401 Mechanism Of Action







**SSNHL**



# 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:**

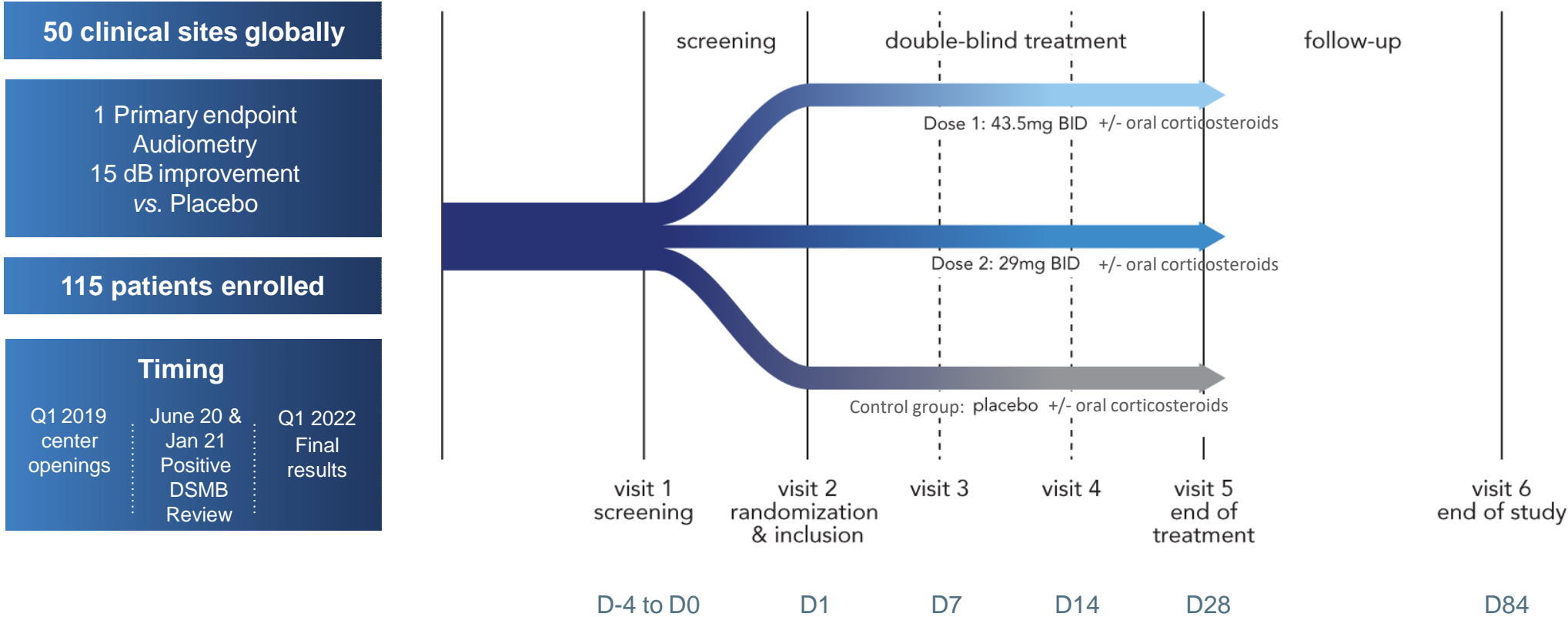
- Difficulties in communicating, social isolation, cognitive decline
- Accompanying tinnitus

**Incidence:** 27-35 per 100,000 (218,000 patients in 2017 in G7 countries)<sup>1</sup>

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

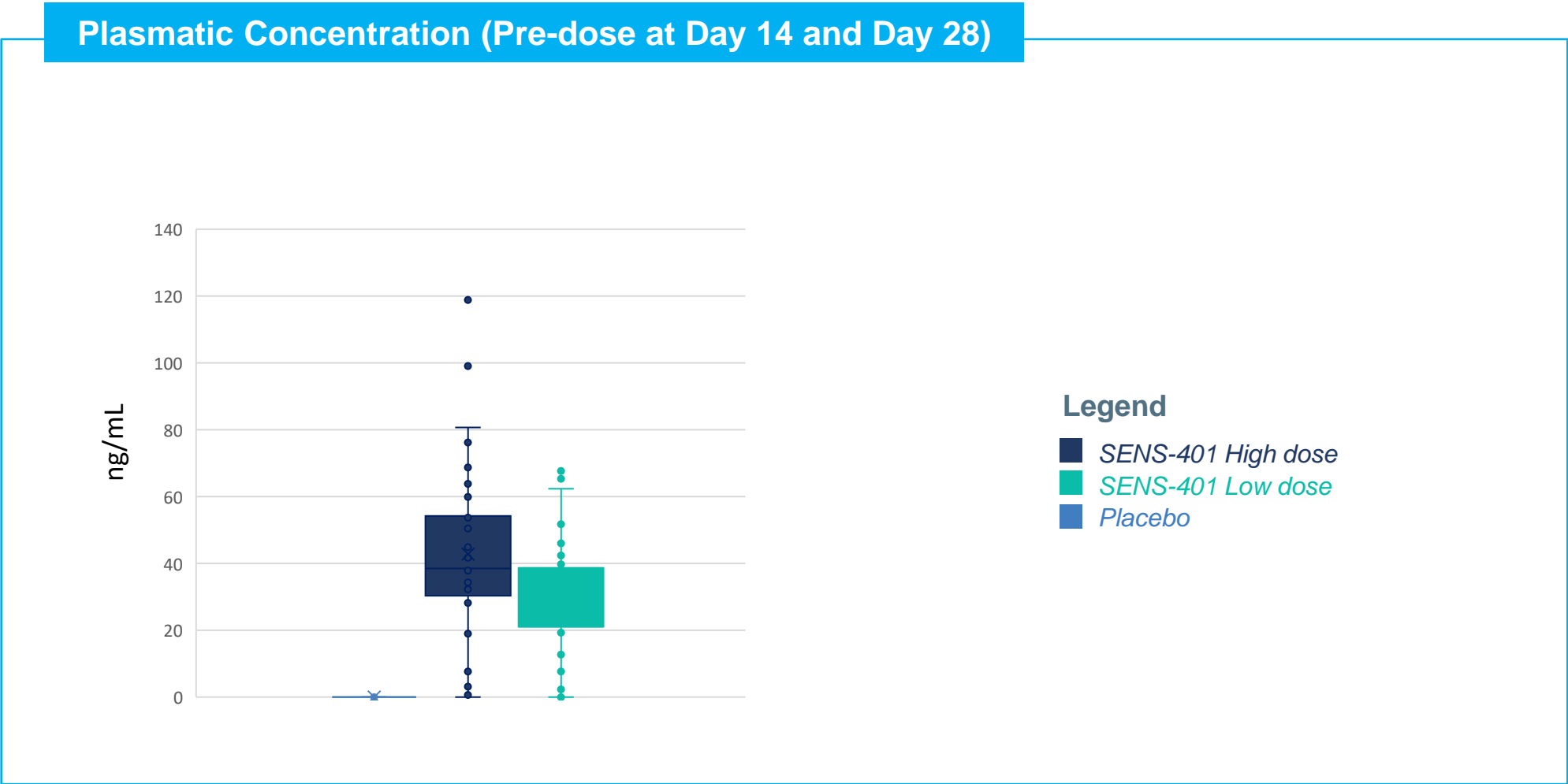
# SENS-401 SSNHL Program: AUDIBLE-S Phase 2 Design

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



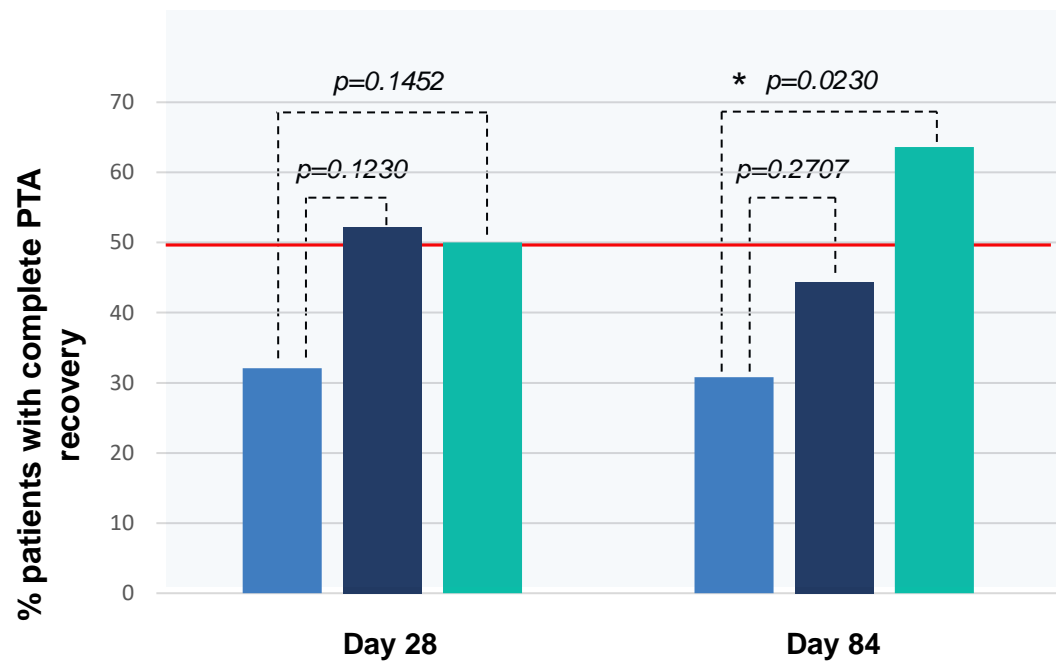
**Primary endpoint definition:**  
“...change in pure tone audiometry (PTA); average of the hearing threshold of 3 contiguous most affected hearing frequencies in decibels in the affected ear from baseline to the end of treatment visit (Visit 5/D28±3)”

# SENS-401 Plasmatic Exposure



# 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

- Legend
- SENS-401 High dose
  - SENS-401 Low dose
  - Placebo

- 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

## *Seeking Partners For Late-Stage Development And Commercialization*

### AUDIBLE-S SECONDARY ENDPOINT RESULTS

- Complete PTA recovery is achieved in 50% of the SENS-401 treated patients
- SENS-401 shows a **clinically meaningful and statistically significant effect on PTA change** (at least 10 dB) over time in a **large homogeneous idiopathic population of patients treated with corticosteroids**
- SENS-401 induces a **significant PTA change of at least 19 dB at day 28 and up to 25 dB at Day 84 allowing a reduction of the hearing loss degree from profound to mild, in large profound hearing loss sub-group**
- A better response was observed in both treatment groups with a **continuous improvement between Day 28 and Day 84**
- **The change in PTA translates into functional improvement evidenced with speech audiometry tests**
- Safe and well tolerated in 115-patient SSNHL study; although primary endpoint not met data supports and informs further clinical development
- **Responder rate is always better in the treated group** compared to Placebo and difference with Placebo increases over time