

Unlocking the potential of  
advanced therapies  
for hearing loss



July 2024



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# SENSORION



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** (for mutations in otoferlin encoding gene – Ph1/2 clinical study approved); **GJB2-GT** (for mutations in GJB2 gene – candidate selected – to enter the clinic in 2025)
- Prospective Natural History Studies ongoing



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

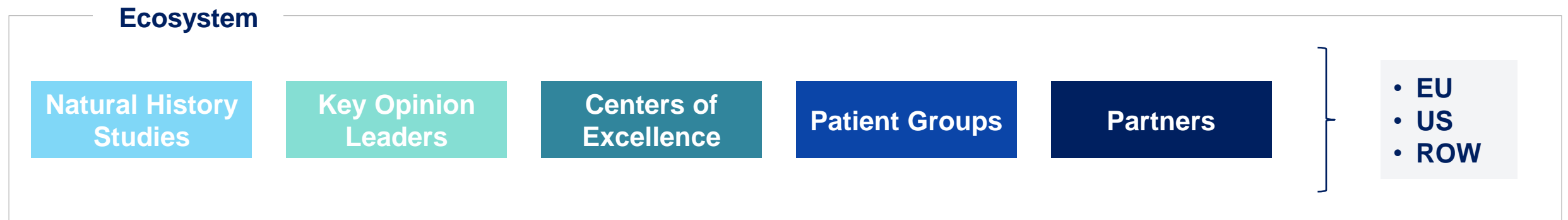
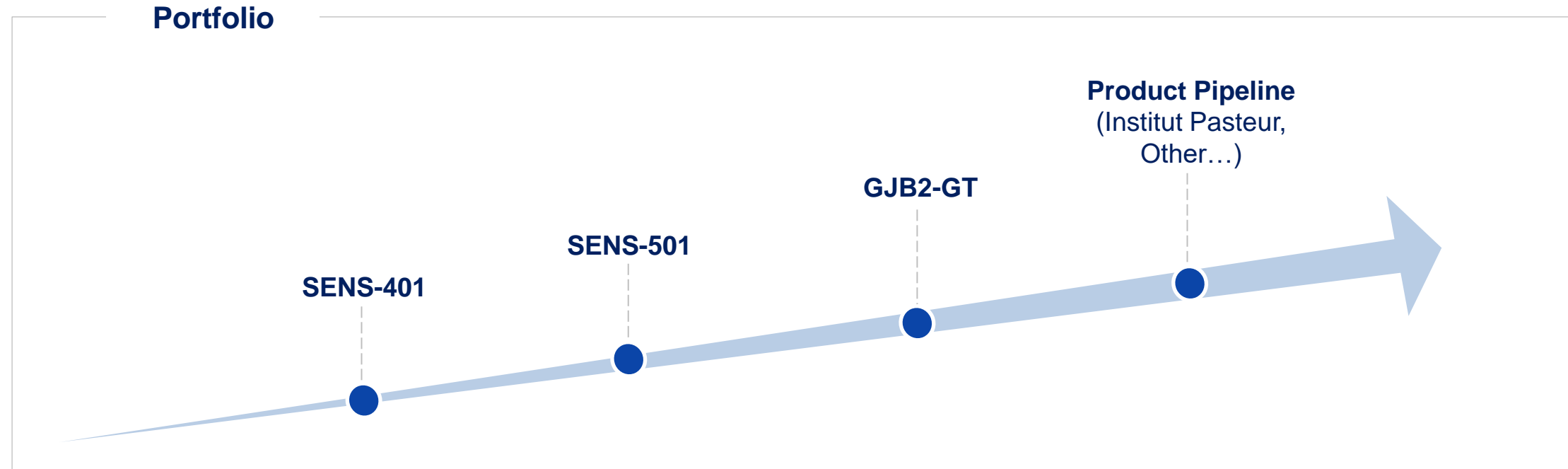


- Multiple **upcoming milestones** across the GT and small molecule pipeline, including the **full Ph 2a data readout for SENS-401 CI** and **first patient communication for the Ph 1/2 GT trial of SENS-501**



- 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

# Our Vision: A Global Franchise Establishing Leadership In The Hearing Space





# 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 initiate Natural History Study in presbycusis



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

# Sensorion Is Well Positioned To Transform the Hearing Landscape

## - Institut Pasteur Partnership Feeds GT Pipeline

### GENE THERAPY

#### Otoferlin deficiency (SENS-501)

**Audiogene Ph1/2 study approved in France;  
First Patient Communication in H2 2024**

- Hearing restoration in DFNB9 pediatric patients aged 6 to 31 months
- Ph1/2 to evaluate safety, tolerability and efficacy of SENS-501

#### Connexin 26 deficiency (GJB2-GT)

**Candidate selected**

#### Considered Indications:

- Hearing restoration in DFNB1 **pediatric patients**
- Hearing restoration in **childhood onset** of hearing loss linked to *GJB2* mutations
- Hearing restoration in early onset severe **presbycusis** linked to *GJB2* mutations

### SMALL MOLECULE: SENS-401

#### Sudden Sensorineural Hearing Loss (SSNHL)

**AUDIBLE-S Ph2 Randomized and Controlled Study Completed**

- Clinically and statistically significant effect on PTA (Pure Tone Audiometry) change over time in a large idiopathic population treated with oral corticosteroids
- Complete PTA recovery in 50% of treated patients

#### Cochlear Implantation (CI)

**Ph2 Randomized and Controlled Study Ongoing  
Primary Endpoint Met**


- Presence of SENS-401 detected in the perilymph of 100% of sampled patients
- Clinically significant difference at 6 and 14 weeks after CI in the residual hearing between SENS-401 and control groups at 500 Hz and in the average of 250-500-750 Hz

#### Cisplatin-Induced Ototoxicity (CIO)

**NOTOXIS Ph2 Randomized and Controlled Study Ongoing  
Positive Preliminary Safety Results**

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

# 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						Communication on First Patient H2 2024
	GJB2-GT*	Adult Onset (presbycusis)							CTA/IND enabling preclinical activities
	GJB2-GT*	Pediatric Progressive							CTA/IND enabling preclinical activities
	GJB2-GT*	Congenital Onset							CTA/IND enabling preclinical activities
PREVENT	SENS-401	Hearing Preservation after CI						 Cochlear™	Final Data Readout Q3 2024
	SENS-401	Cisplatin-Induced Ototoxicity							Preliminary Safety and Efficacy Data Sep 2024 during WCA
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

# Our Team Has Significant Experience In Gene Therapy Clinical Development

The team has been involved in 15+ programs from preclinical to BLA filing...

10

Preclinical

4

Clinical

1

BLA filing

... using different technologies...

15

Gene therapy  
(AAVs / LVs)

1

Cell  
therapy

1

Gene editing

... across different organs and indications...



... with multiple organizations



AUDENTES  
THERAPEUTICS

GENETHON  
CURE THROUGH INNOVATION

rocket  
pharma

SOLID  
BIOSCIENCES

cellectis

ESTEVE  
Advancing health together

GenSight  
BIOLOGICS

Necker  
ENFANTS MALADES  
HÔPITAL UNIVERSITAIRE

SAREPTA  
THERAPEUTICS

Orchard  
therapeutics



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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 ODD, US RPDD

### 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	✓

# Gene Therapy Pediatric Indications Have Blockbuster Sales Potential

## SENS-501 CTA Approved In France

### 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 :
  - ✓ Orphan Drug Designation in the US and EU
  - ✓ Rare Pediatric Disease Designation with eligibility for voucher in the US
  - ✓ Clinical Trial Application approved in France, 1st patient communication H2 2024

### Sales Potential Illustration

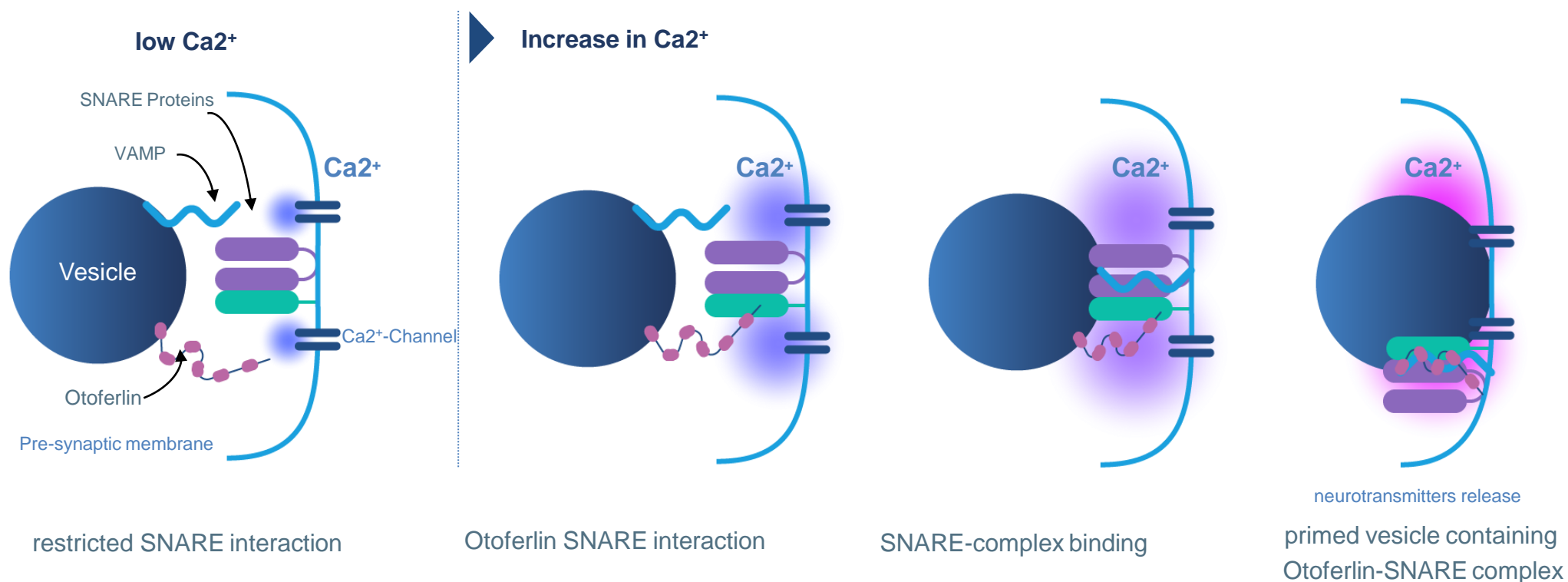
**SENS-501**

**GJB2-GT**

Sources: Sensorion, AT Kearney market research



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



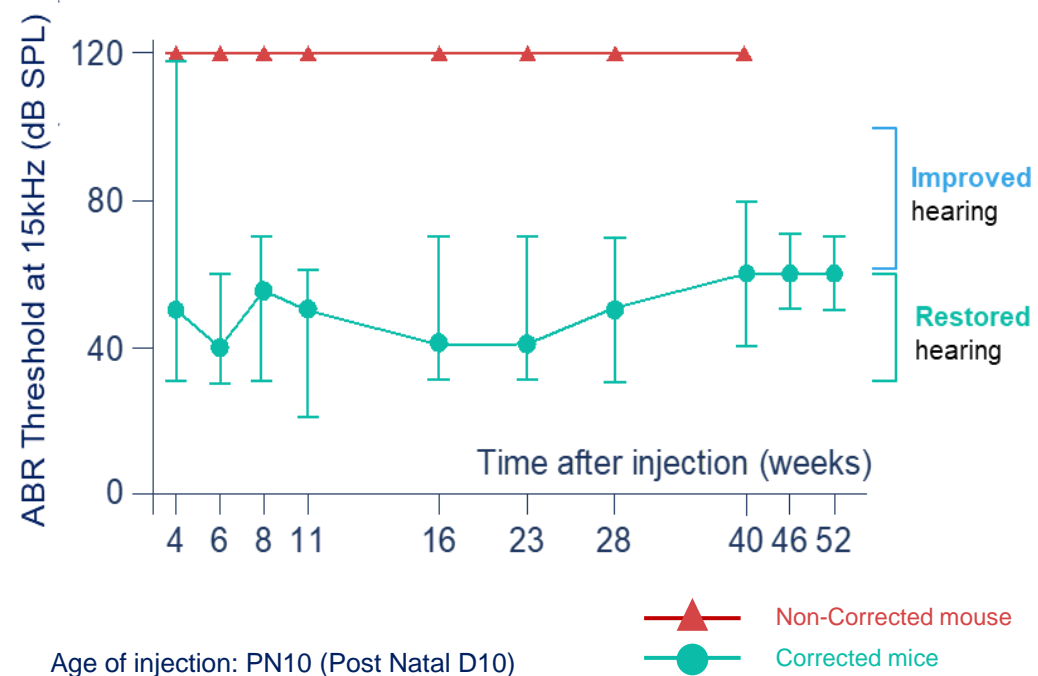
Model illustrating calcium regulation of otoferlin/SNARE interaction in the hair cell – Adapted from Ramakrishnan *et al.* 2014

**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

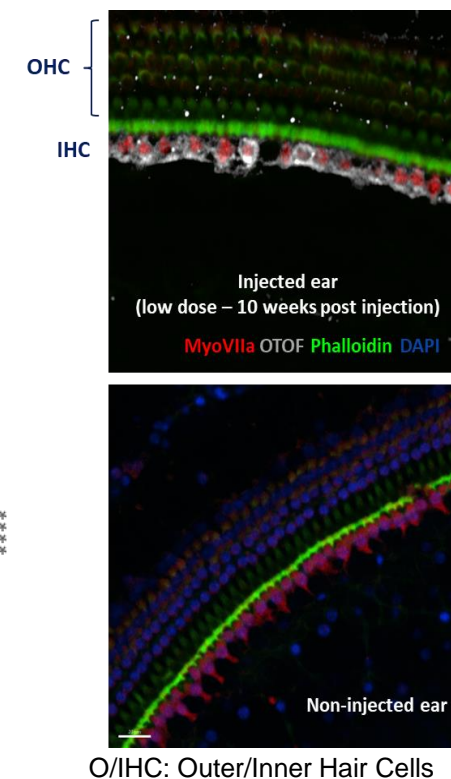
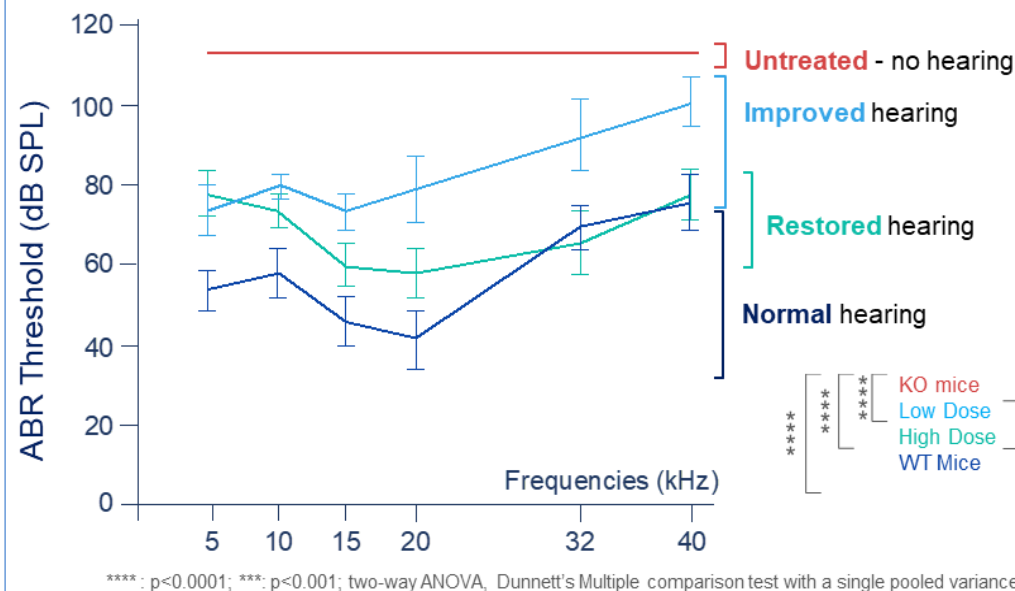
AAV-mOTOF injected in mice before hearing onset



- **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

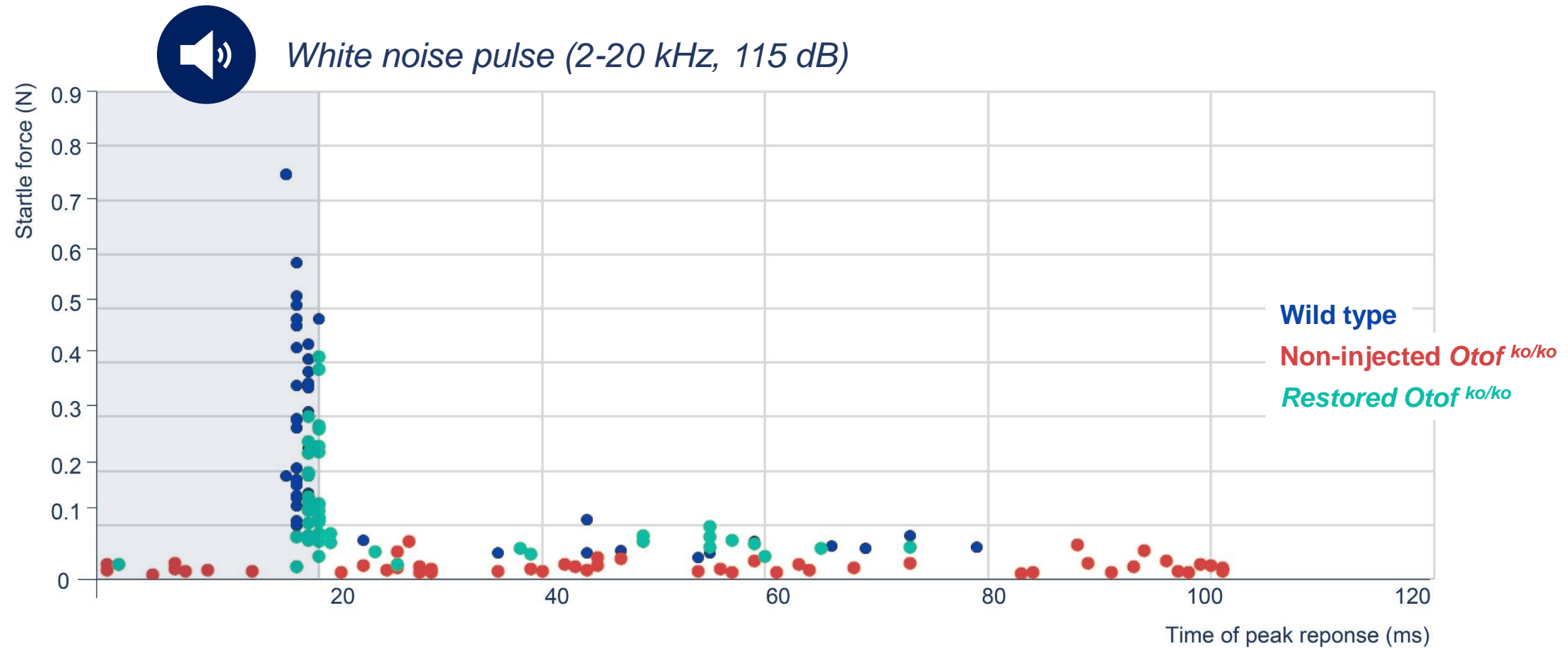
SENS-501 injected in mice after hearing onset  
10 months after injection



- 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

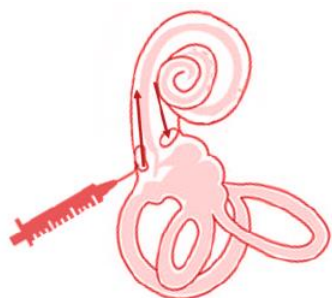


Olivier et al. *ASGCT* 2023 [link](#)

# Dedicated Surgical Approach For Gene Therapy

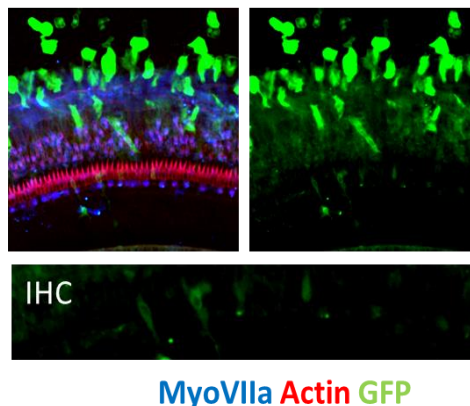
Non-Human Primates injected through the round window membrane (RWI) with or without stapedotomy (stap)

## 1 Fenestration



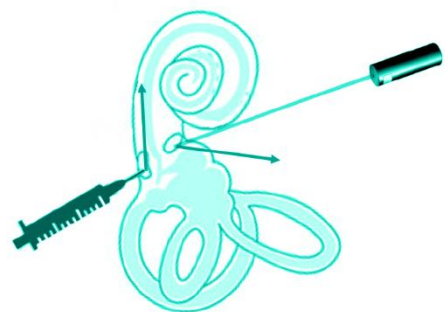
Used for cochlear implant

- Overpressure
- Limited volume
- Backflow
- Irregular transduction rate



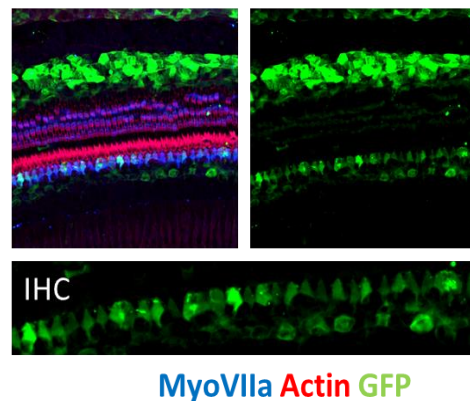
MyoVIIa Actin GFP

## 2 Fenestrations



Combining 2 common surgical techniques: cochlear implant and stapedotomy

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



MyoVIIa Actin GFP

## 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

# Phase 1/2 Audiogene Study (SENS-501) Approved In France

## First Patient Communication Anticipated In H2 2024

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

### Audiogene Study Design



#### Pediatric patients, aged 6 to 31 months at the time of the injection

- Targeting the first years of life 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)



# Otoferlin “Audinove” Consortium Provides Privileged Access To Patients And Surgeons

## Audinove 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)

Audinove 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



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

**OTOCONEX: Natural History Study running across Europe will support identification of DFNB9 patients for Audiogene.**

## AUDINNOVE CONSORTIUM MEMBERS





# SENS-501 (OTOF) Gene Therapy Program Status – Progressing

Preclinical package completed



Injection device system  
development completed



GMP Drug product successfully  
manufactured



CTA Approval in France



Submission European Natural  
History Study OTOCONEX



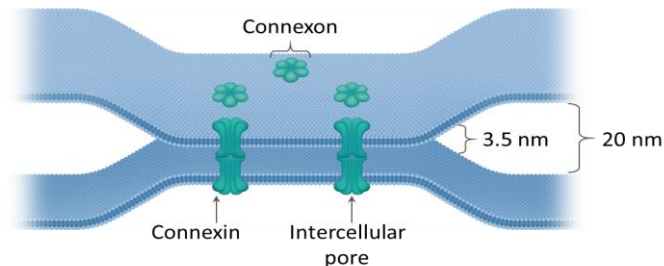
First Patient Communication  
H2 2024



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

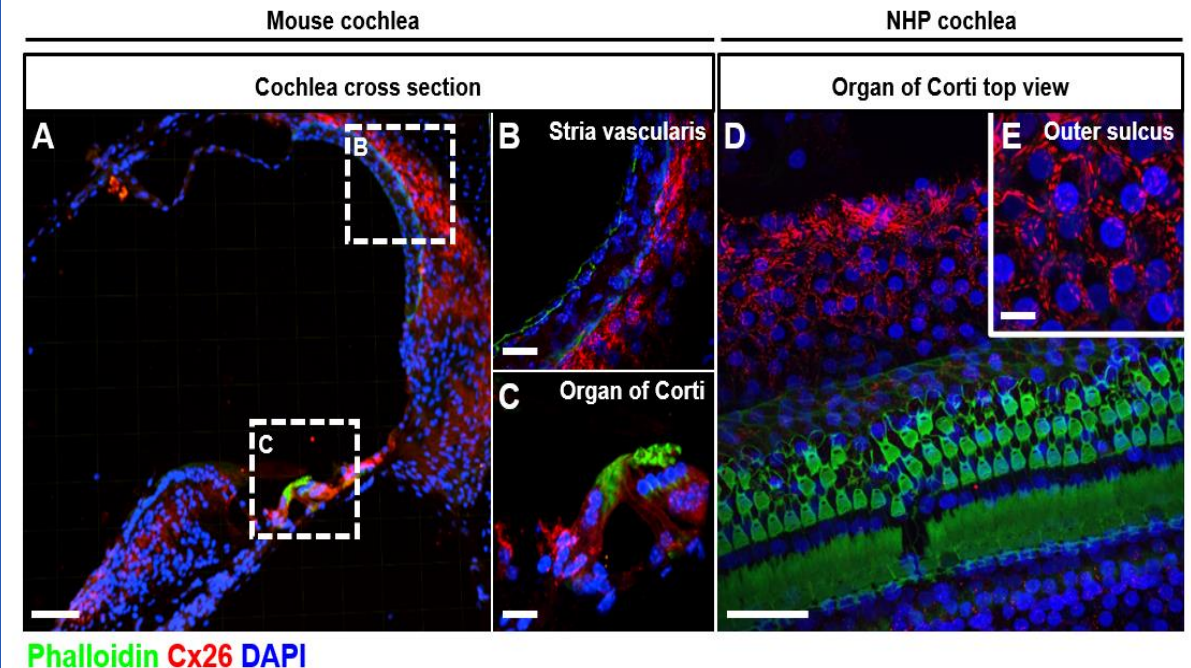
## Mutations in the *GJB2* Lead to Deafness

- *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

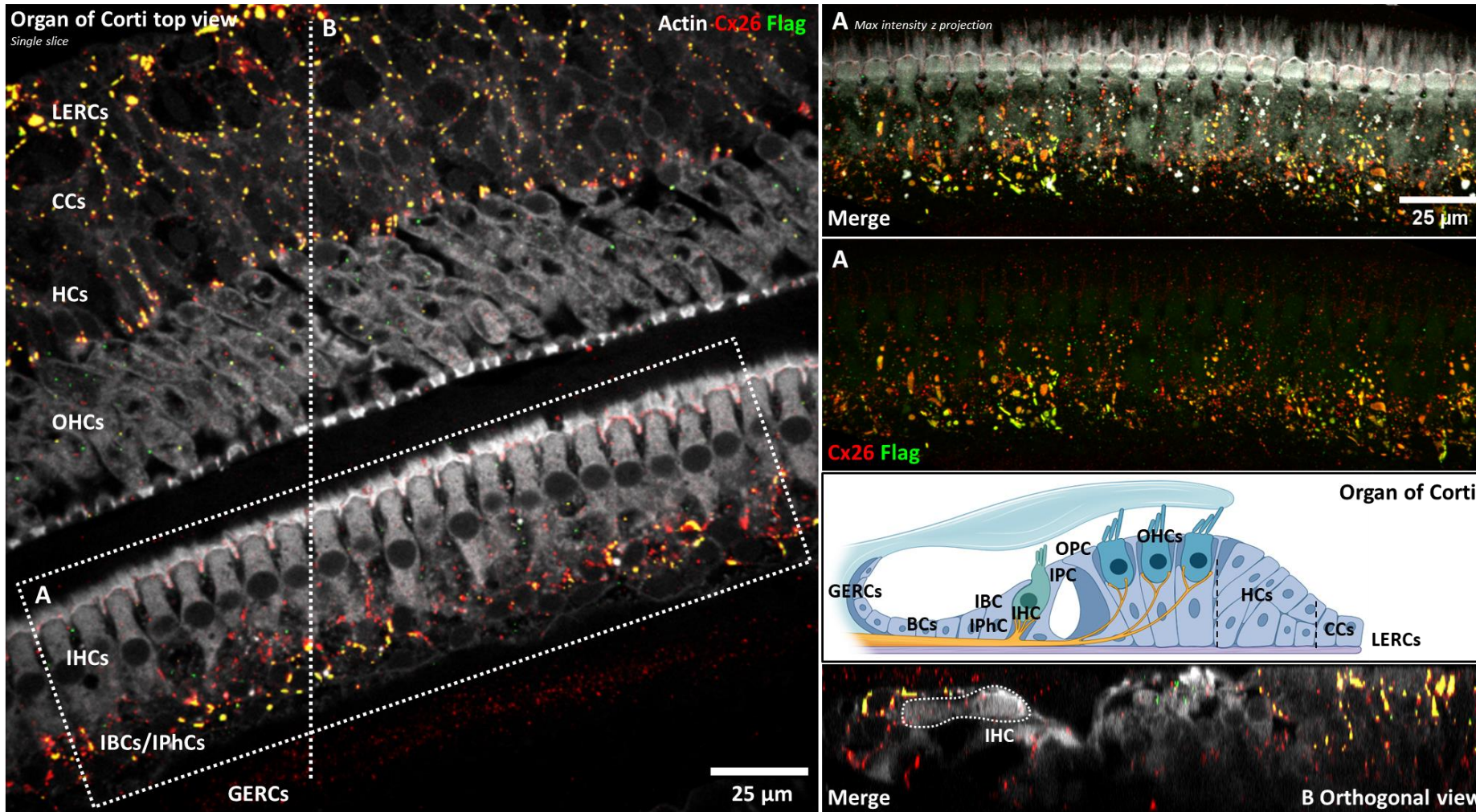
CRITERIA	LEAD CANDIDATE
Natural and synthetic AAV capsid libraries screening for broad coverage of target cells	
Expression cassette design for high-level of target cells transduction, correct cellular localization, active gap-junctions	
Avoiding off-target expression (i.e. hair cells): promoter and 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



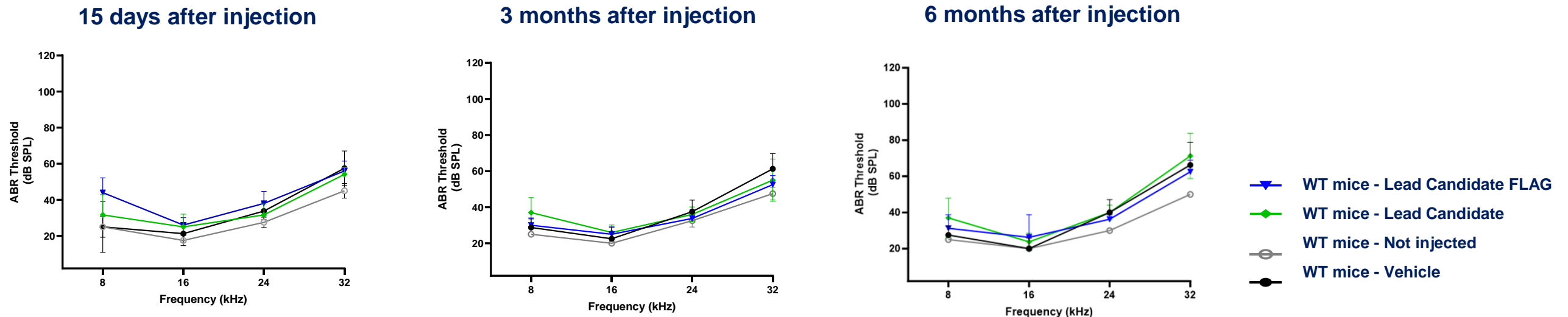
### Cell Types

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

## ABR Thresholds in WT Mice Following Lead Candidate Injection



- No impact on ABR up to 6 months following Lead Candidate injection

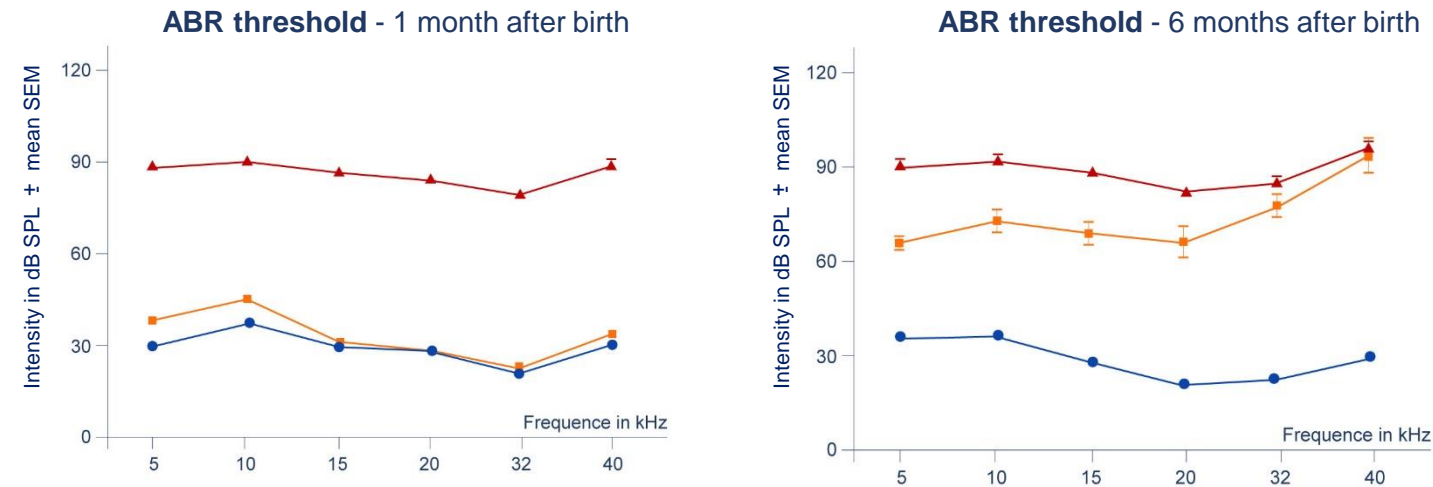
## 3-Month Exploratory Toxicity and Biodistribution in Non-Human Primate

- 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 the injected ear, no dissemination observed in gonads, main organs, DRG

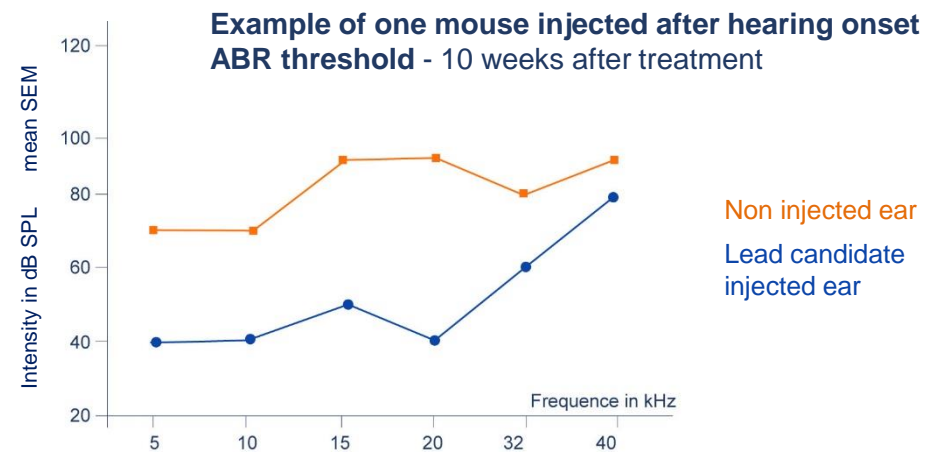
# Lead Candidate Prevents Hearing Loss In Relevant Mouse Model

## Proof Of Concept In Progressive Mouse Model

Conditional knock-out mouse model leading to 2 phenotypes



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

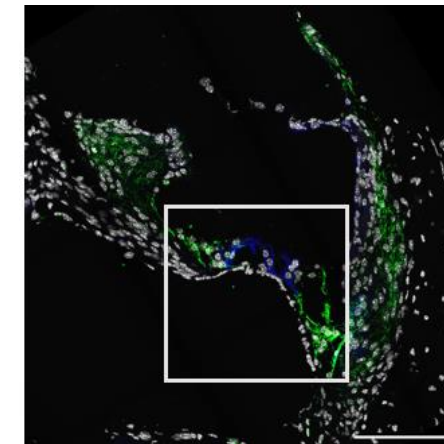


Non injected ear  
Lead candidate injected ear

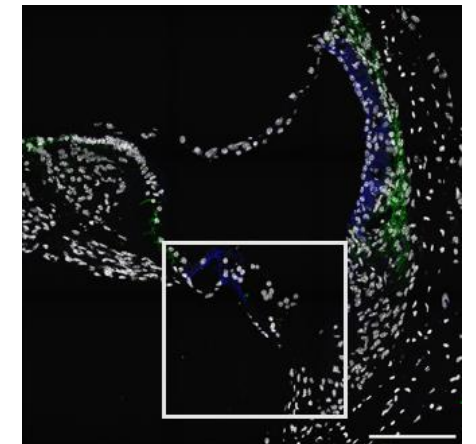
## Hearing Loss Prevention Correlates With Connexin 26 Expression

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 Next Steps

Submission of European Natural  
History Study OTOCONEX



Submission of Natural History Study  
in collaboration with Sonova



Candidate selection Q2 2023



Preclinical IND enabling studies



Clinical Trial Applications  
Mid-Year 2025



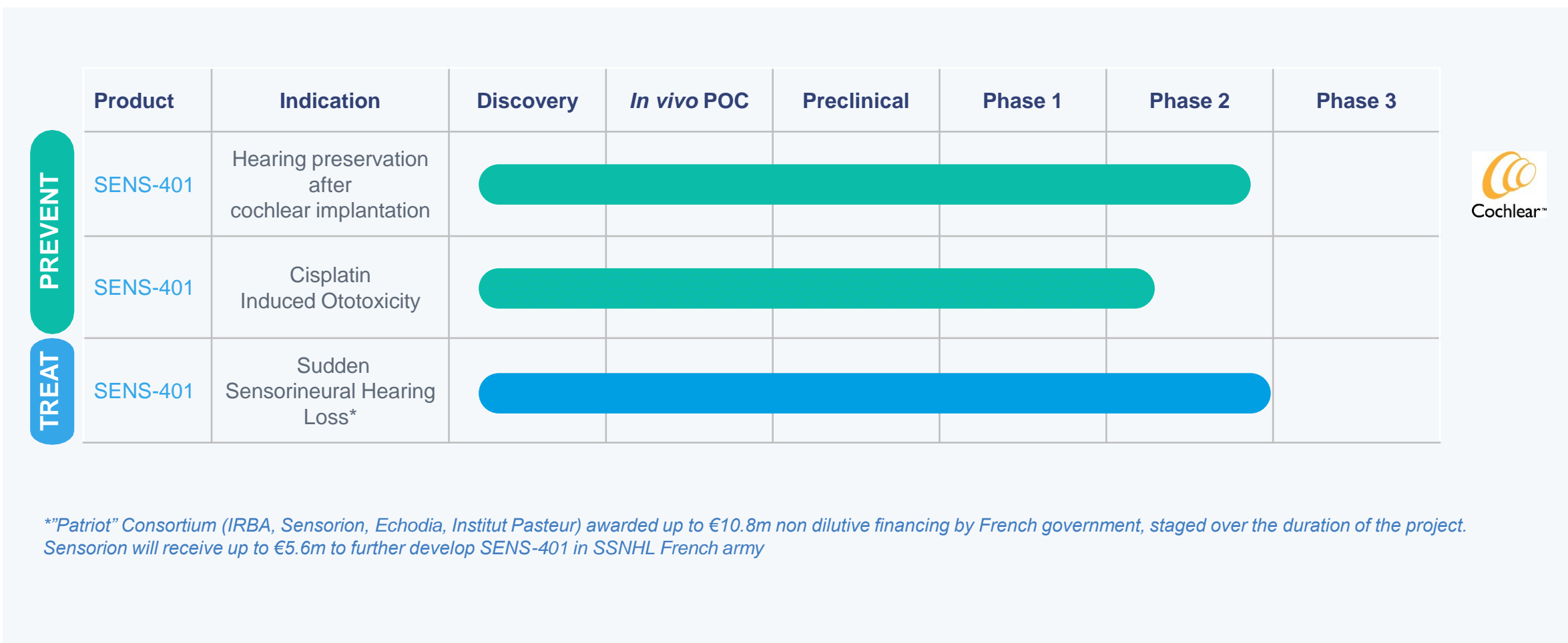


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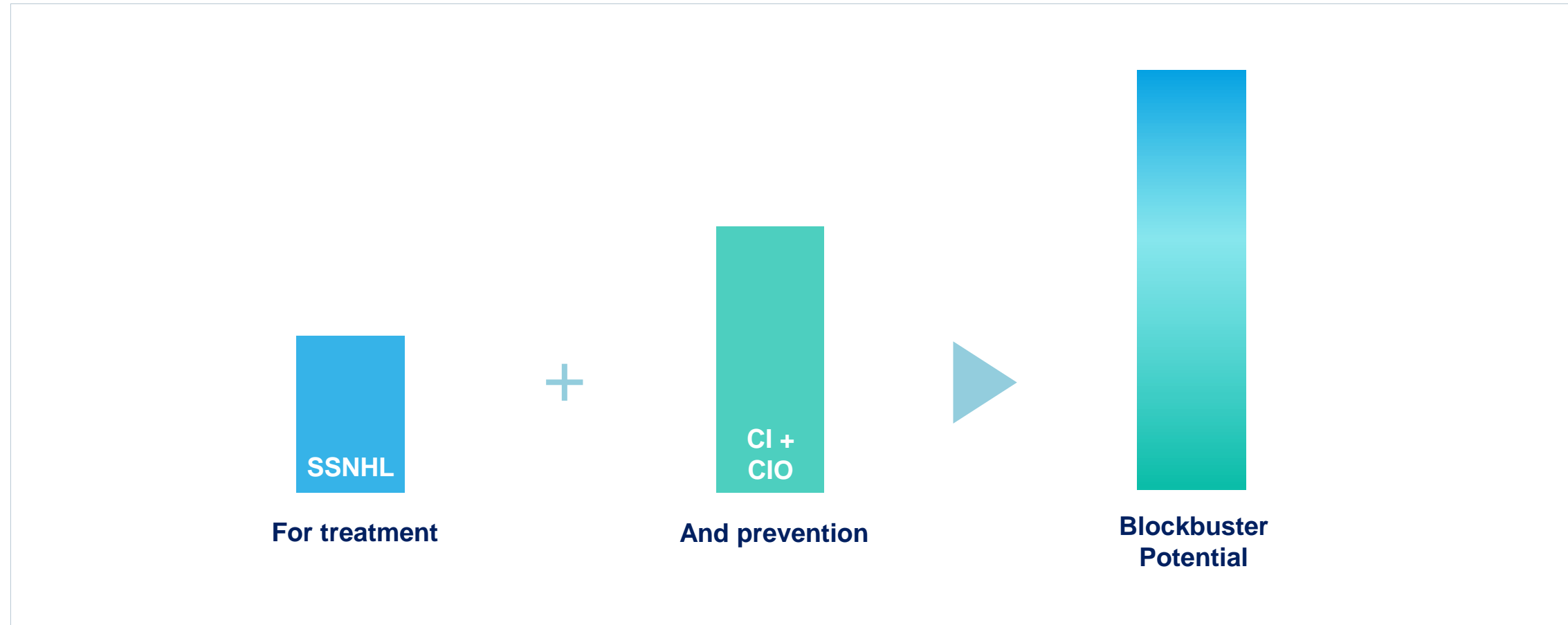
# **SMALL MOLECULE PROGRAMS**

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



# SENS-401 - A Portfolio With Potential Blockbuster Value



SENS-401 SSNHL clinical data and insight **derisk** further development of SENS-401 in other indications

# 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](#))

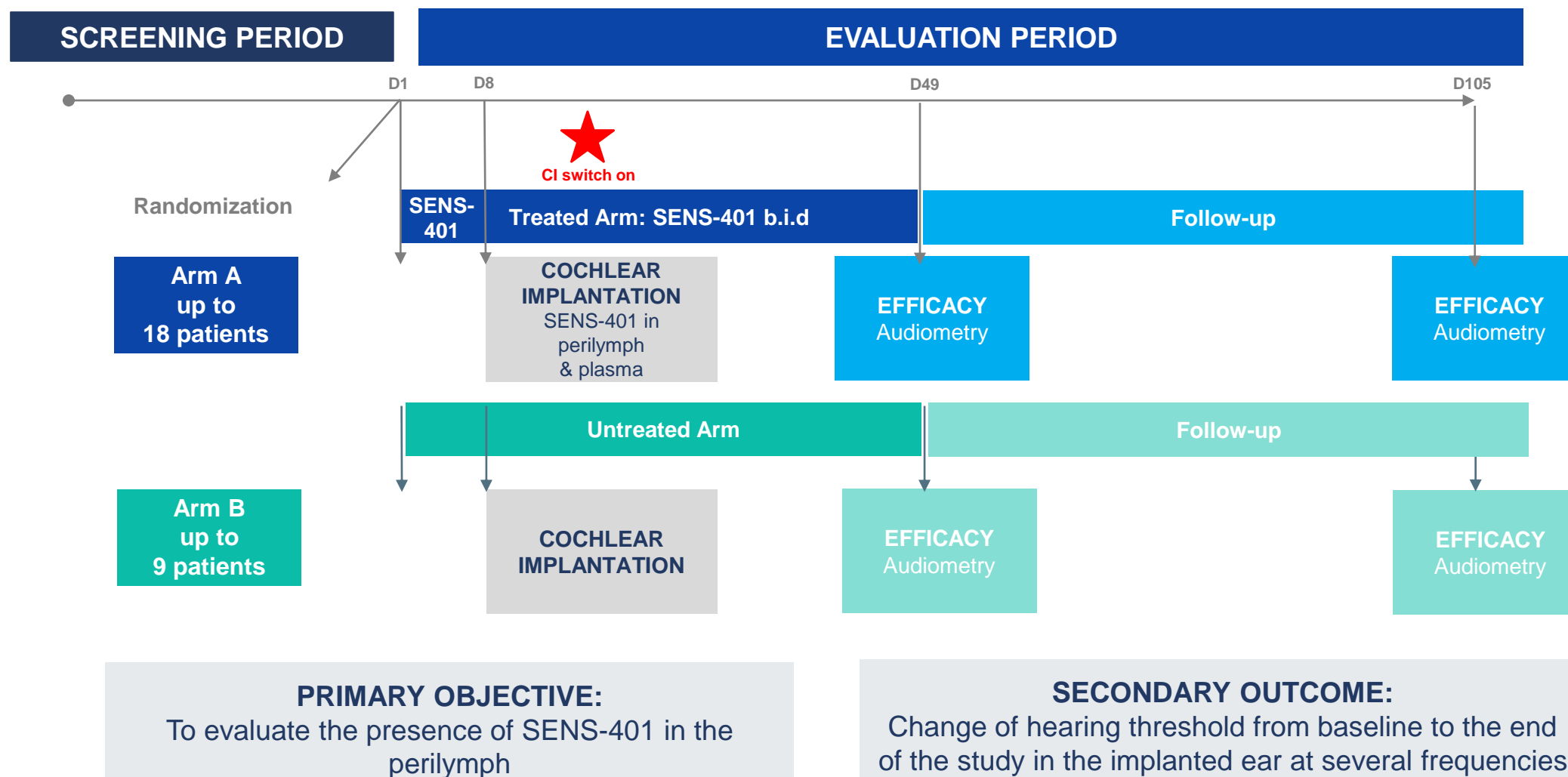
<sup>2</sup>Market estimates ([link](#))

# SENS-401 CI Study Design

## Primary Endpoint Met



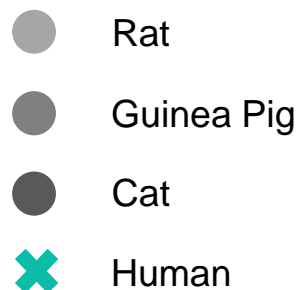
A Phase 2a, Multicenter, Randomized, Controlled, Open-label Study



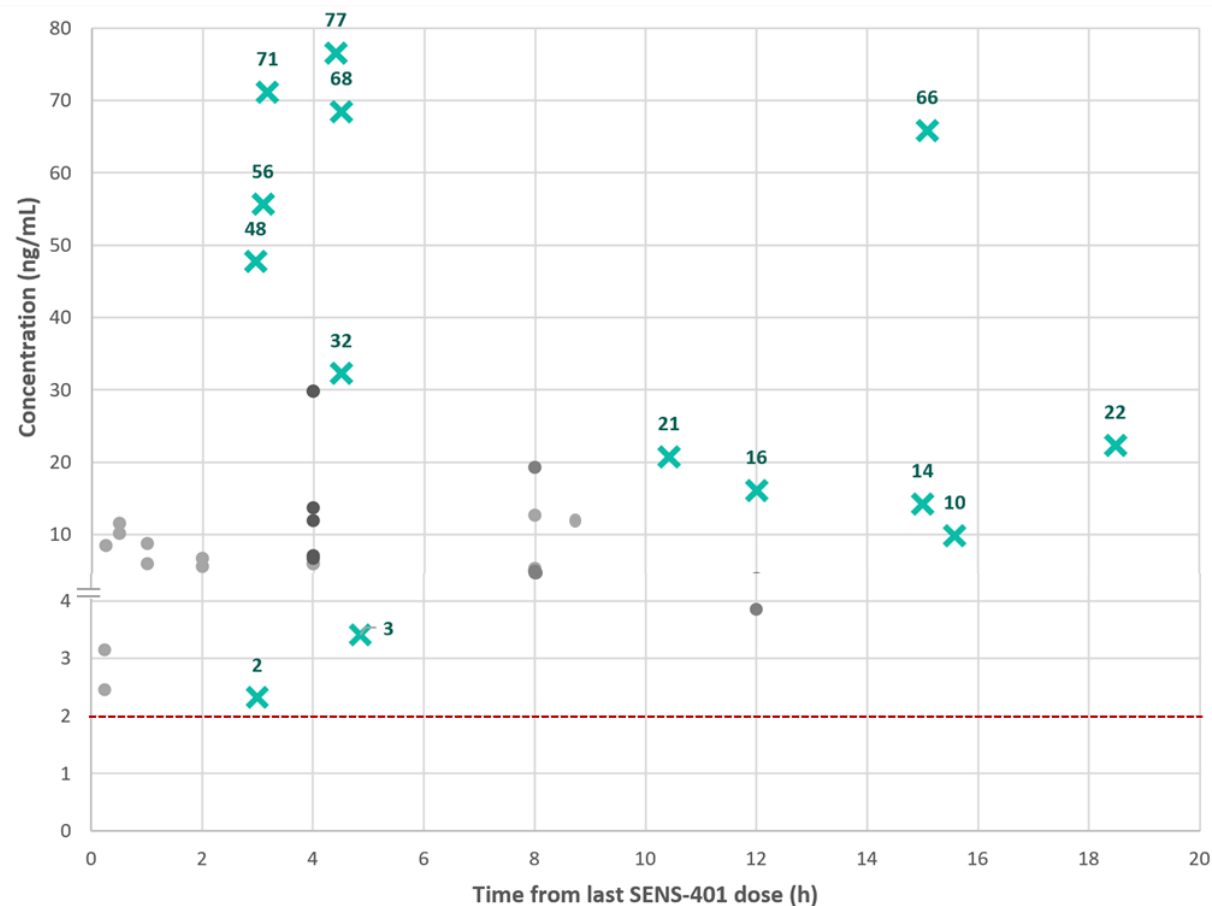


# Primary Endpoint Of The Phase 2a Clinical Study For Residual Hearing Preservation Has Been Met

## Perilymph Concentrations Data



-- Minimal perilymph concentration in animals



- 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

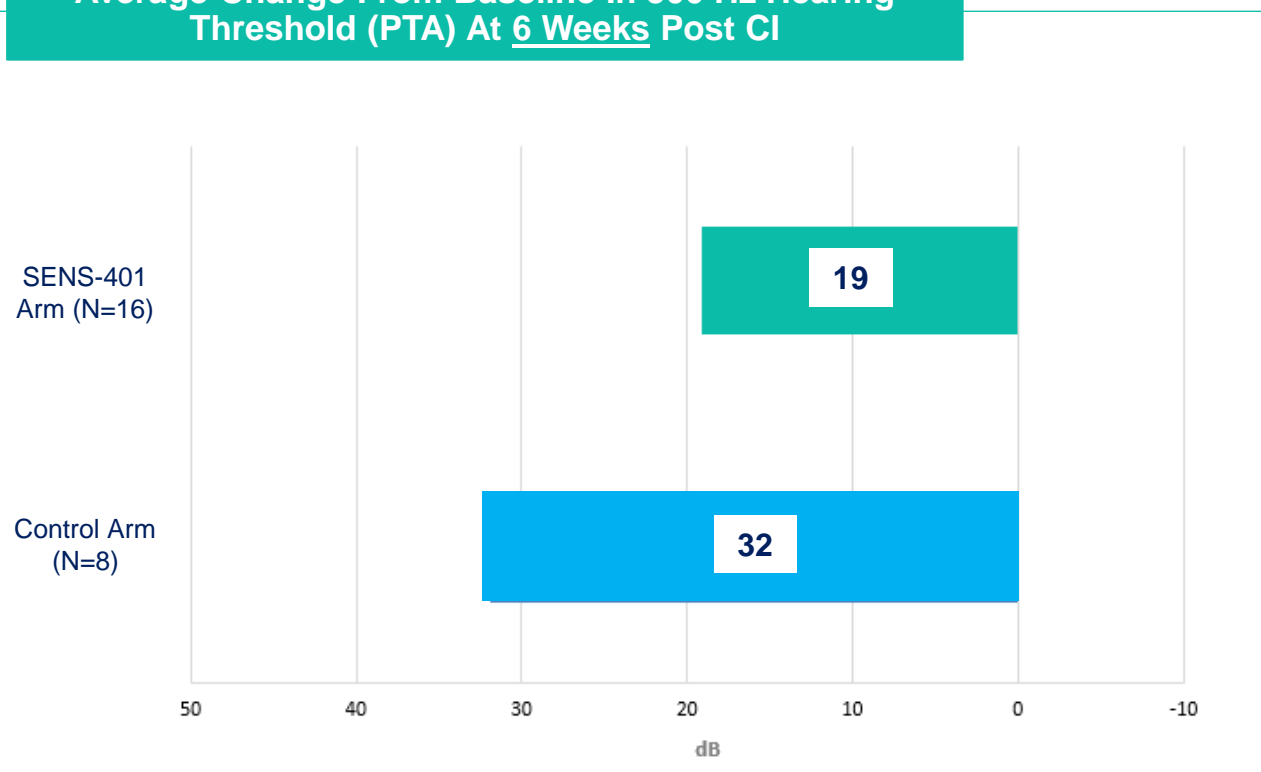


**Postoperative hearing preservation** defined as:  
unaided air-conduction **thresholds < 85 dB HL** at 125, 250, and 500 Hz

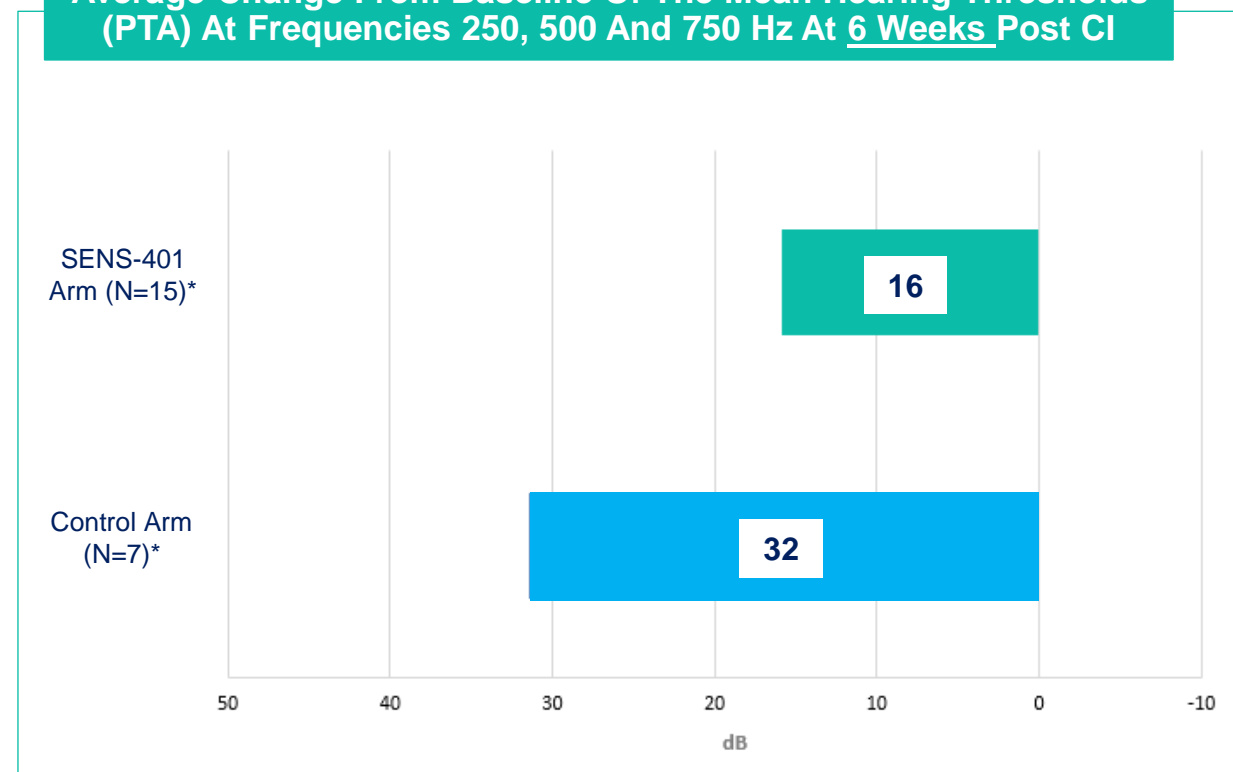
*\*Jensen et al., Hearing Preservation After Cochlear Implantation, 2021*

# SENS-401 Provides Medically Significant Hearing Protection 6 Weeks Post-Cochlear Implantation

Average Change From Baseline In 500 Hz Hearing Threshold (PTA) At 6 Weeks Post CI



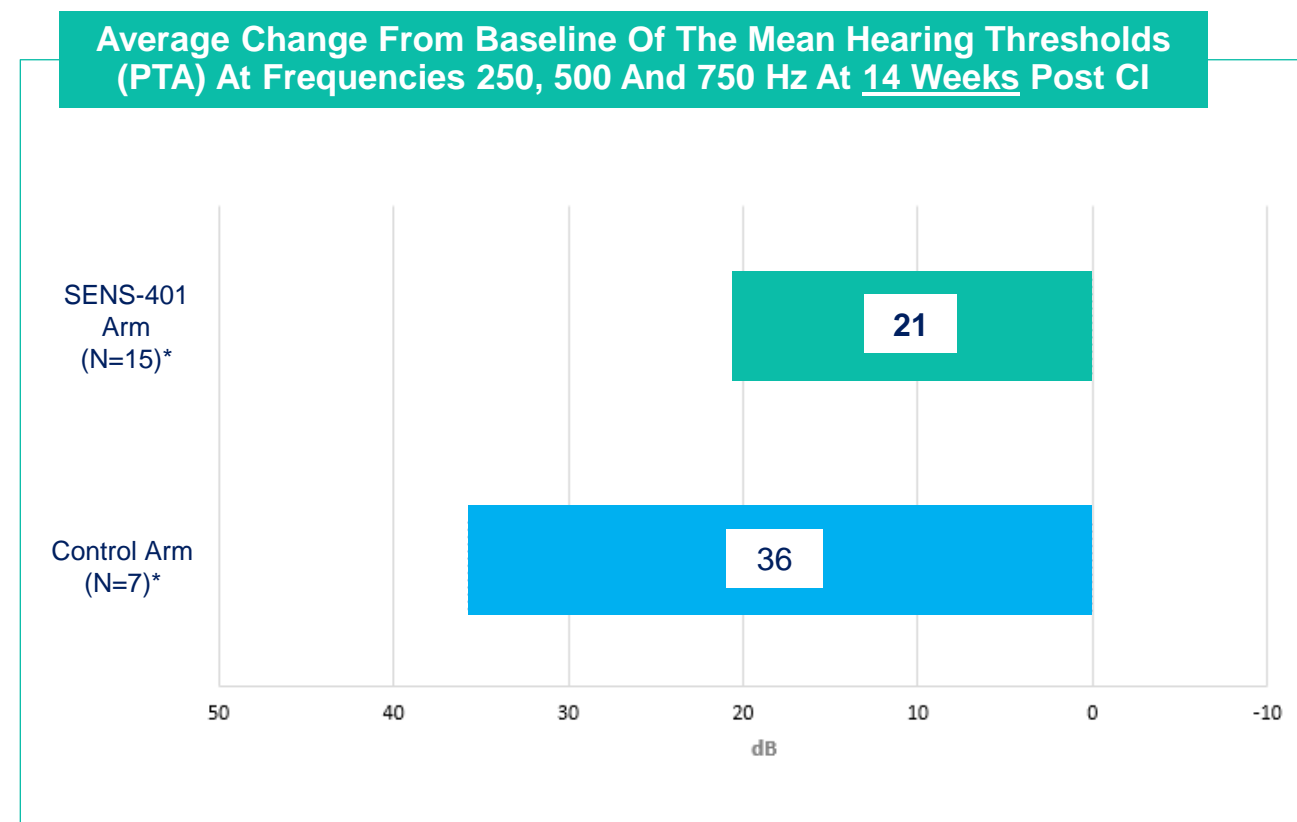
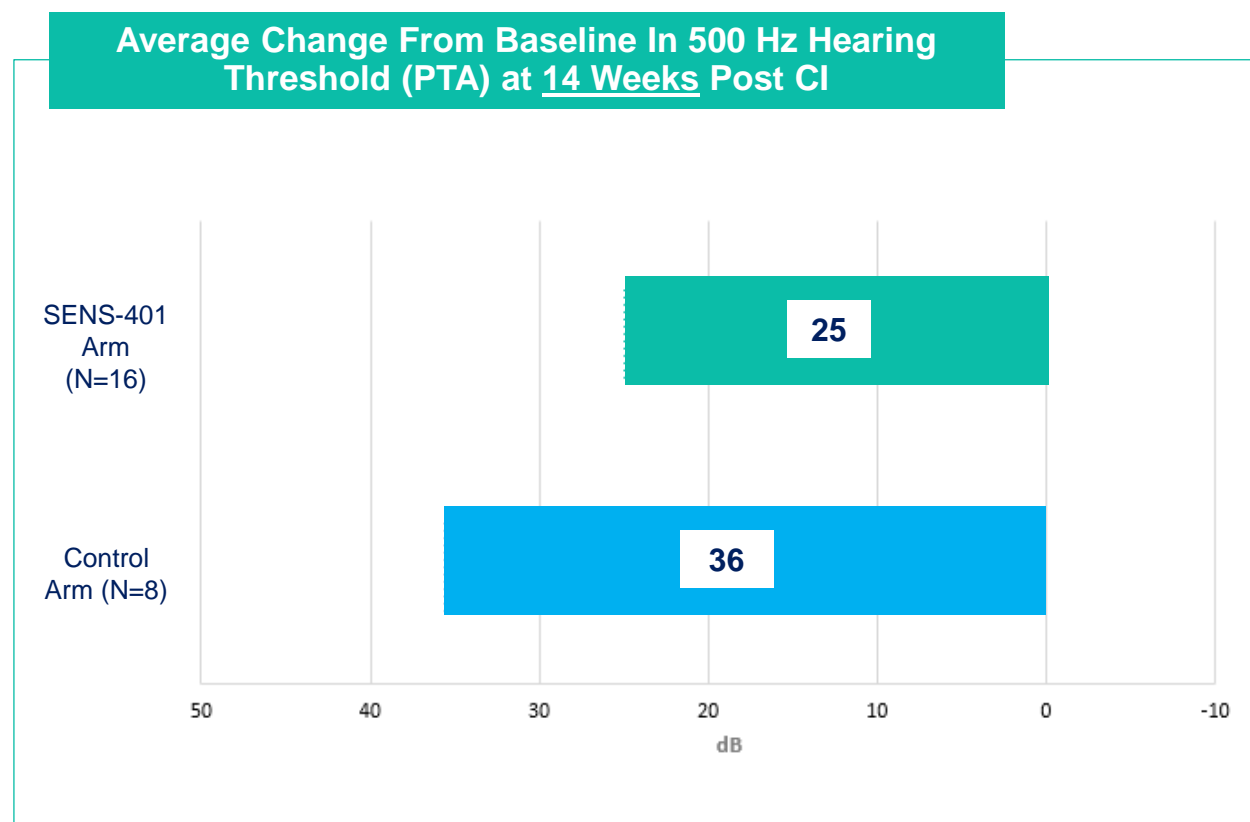
Average Change From Baseline Of The Mean Hearing Thresholds (PTA) At Frequencies 250, 500 And 750 Hz At 6 Weeks Post CI



- SENS-401 administered one week before and six weeks after cochlear implantation leads to a lower loss of residual hearing (19 dB and 16 dB), as measured by hearing thresholds at the 500 Hz frequency and the average of three contiguous frequencies ranging from 250 to 750 Hz, compared to 32 dB in the control group.**

\* One participant in each group had a missing hearing threshold at the frequency 750 Hz at the baseline.

# The Hearing Protection Provided By SENS-401 Post-Cochlear Implantation Continues For Up To 8 Weeks After End Of Treatment



- Residual hearing loss is lower** on average in patients treated with SENS-401 (25dB) compared to untreated patients with SENS-401 (36 dB) 8 weeks after the end of the treatment period.

\* One participant in each group had a missing hearing threshold at the frequency 750 Hz at the baseline.

# SENS-401 CI Conclusion

## Primary Endpoint Met



SENS-401 can cross the labyrinthine barrier to target cochlear hair cells in all patients sampled, confirming primary endpoint is met.



**Six and Fourteen weeks post-cochlear implantation**, the **residual hearing loss** whether assessed at 500 Hz or across an average of 3 consecutive frequencies **exhibited a clinically significant difference for the treated group (19-dB), in comparison to the untreated group (32dB). This difference is maintained up to 14 weeks with 25 dB in the treated group vs 36 dB in the untreated group.**



This supports the assumption that **SENS-401, present in the perilymph fluid, reaches concentrations that are pharmacologically active.**



SENS-401 taken for 6 weeks confirms it has a **good safety profile.**



These encouraging trends necessitate further validation across the full study participant group.



**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>



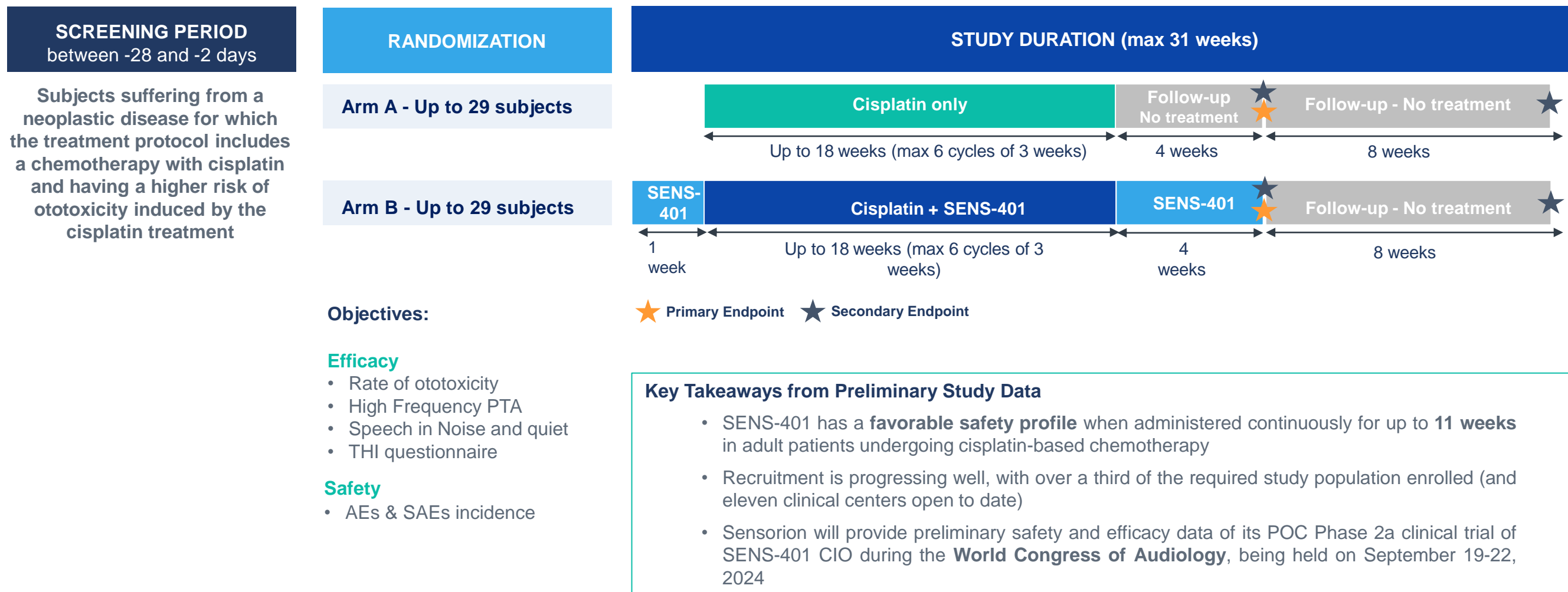
<sup>1</sup> Company/ estimates based on publicly available data (in the US, Japan, Germany, France, the UK, Italy and Spain)



# 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**



# SENS-401 Program Key Milestones, Data Readouts in 2024

SENS-401 with cochlear implants (CI)  
- Positive Preliminary Results Reported



SENS-401 with cochlear implants (CI)  
- Primary Endpoint Readout H1 2024



SENS-401 CIO NOTOXIS  
- Preliminary Results S2 2023



SENS-401 CIO NOTOXIS  
- Preliminary Safety and Efficacy Data  
Sep. 2024 during WCA



SENS-401 with cochlear implants (CI) –  
Full Data Readout Q3 2024



# Sensorion Newsflow [Estimated Timelines]

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

H2 2024 - First Patient Communication

H1 2025 – Enrollment completion of the first two cohorts

## **GJB2 Gene Therapy Program**

Ongoing – Preclinical IND/CTA enabling studies

Mid-Year 2025 – Clinical Trial Applications

## **SENS-401 Program**

Sept 2024, during WCA – CIO NOTOXIS: preliminary safety and efficacy data

Q3 2024 – Cochlear Implantation: full data readout

# THANK YOU



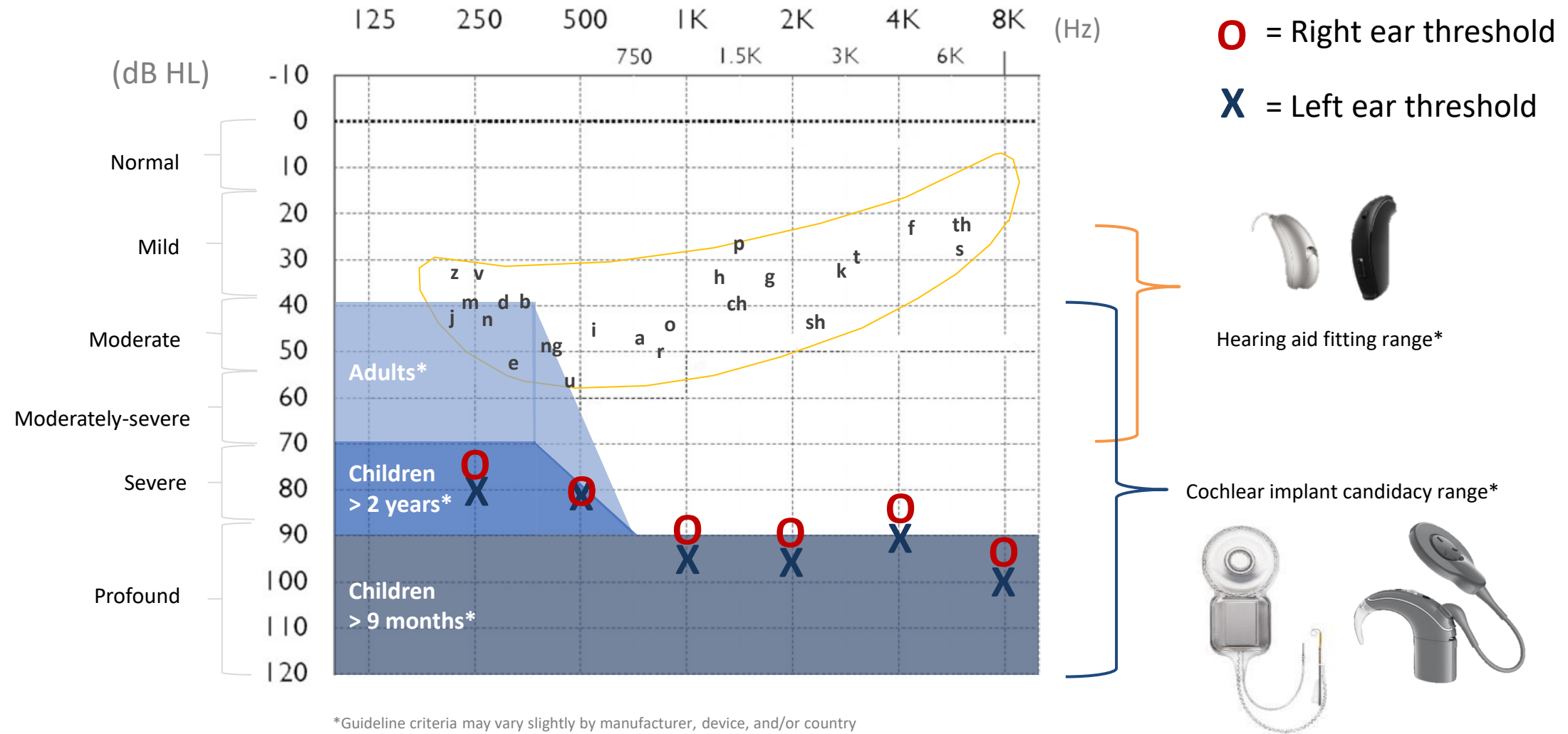
[E: contact@sensorion-pharma.com](mailto:contact@sensorion-pharma.com)



# Hearing Loss



# Access And Clarity Are Mandatory For Optimal Outcomes



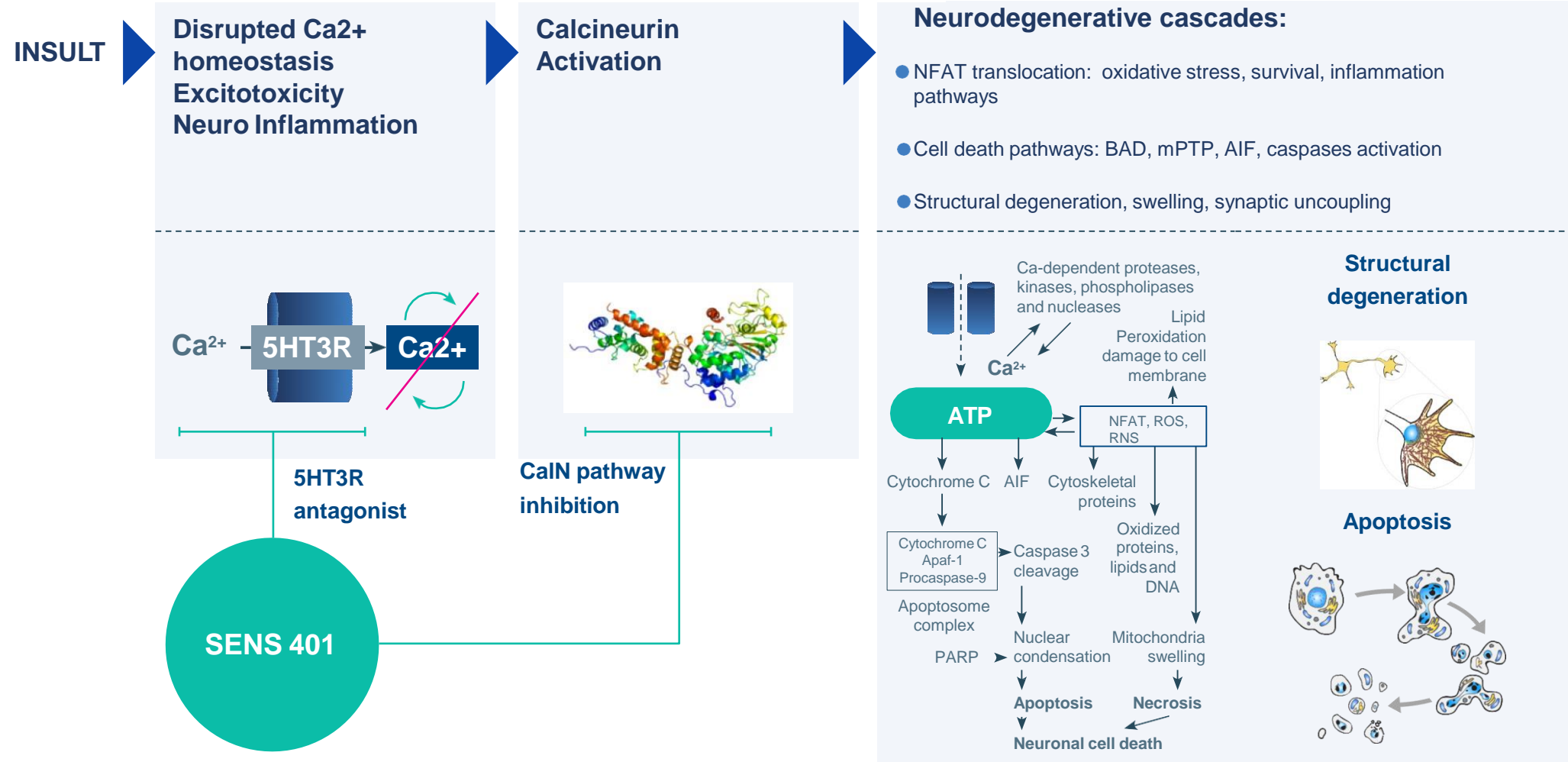




**SENS-401**



# SENS-401 Mechanism Of Action





**SSNHL**

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# 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:**

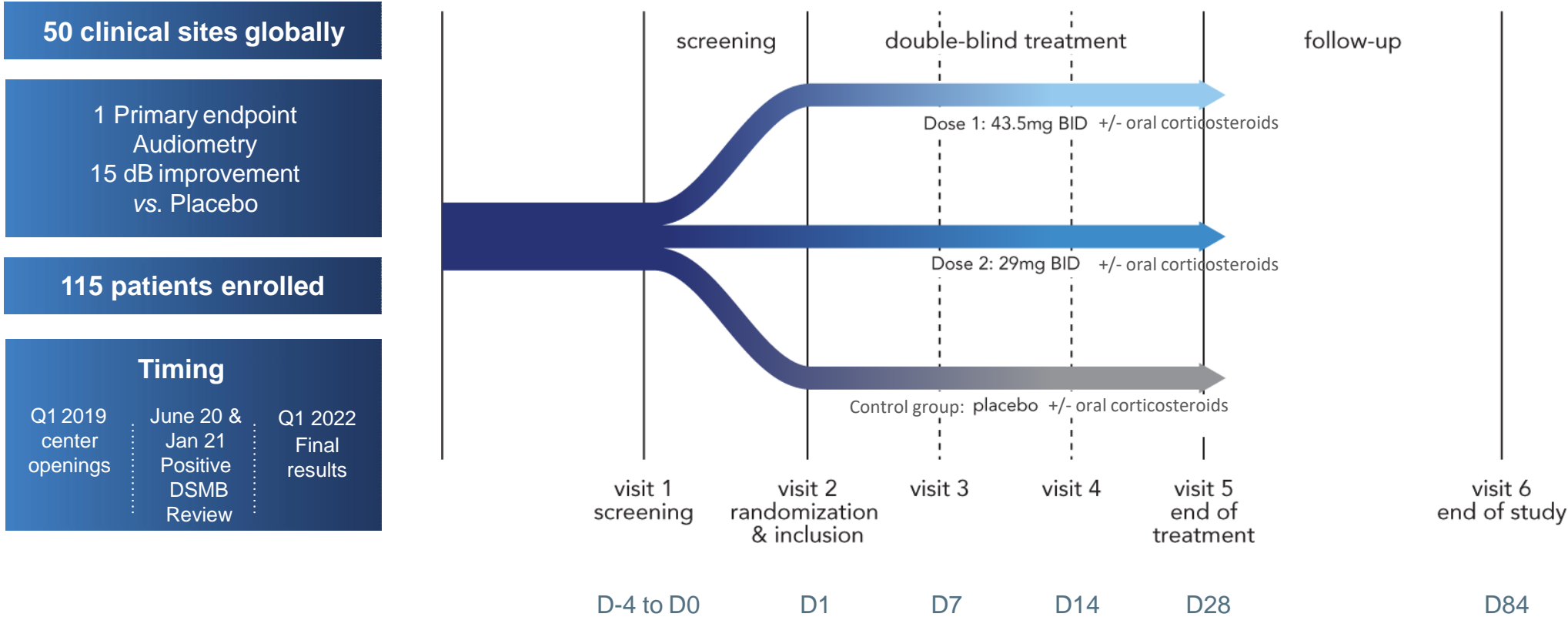
- Difficulties in communicating, social isolation, cognitive decline
- Accompanying tinnitus

**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)

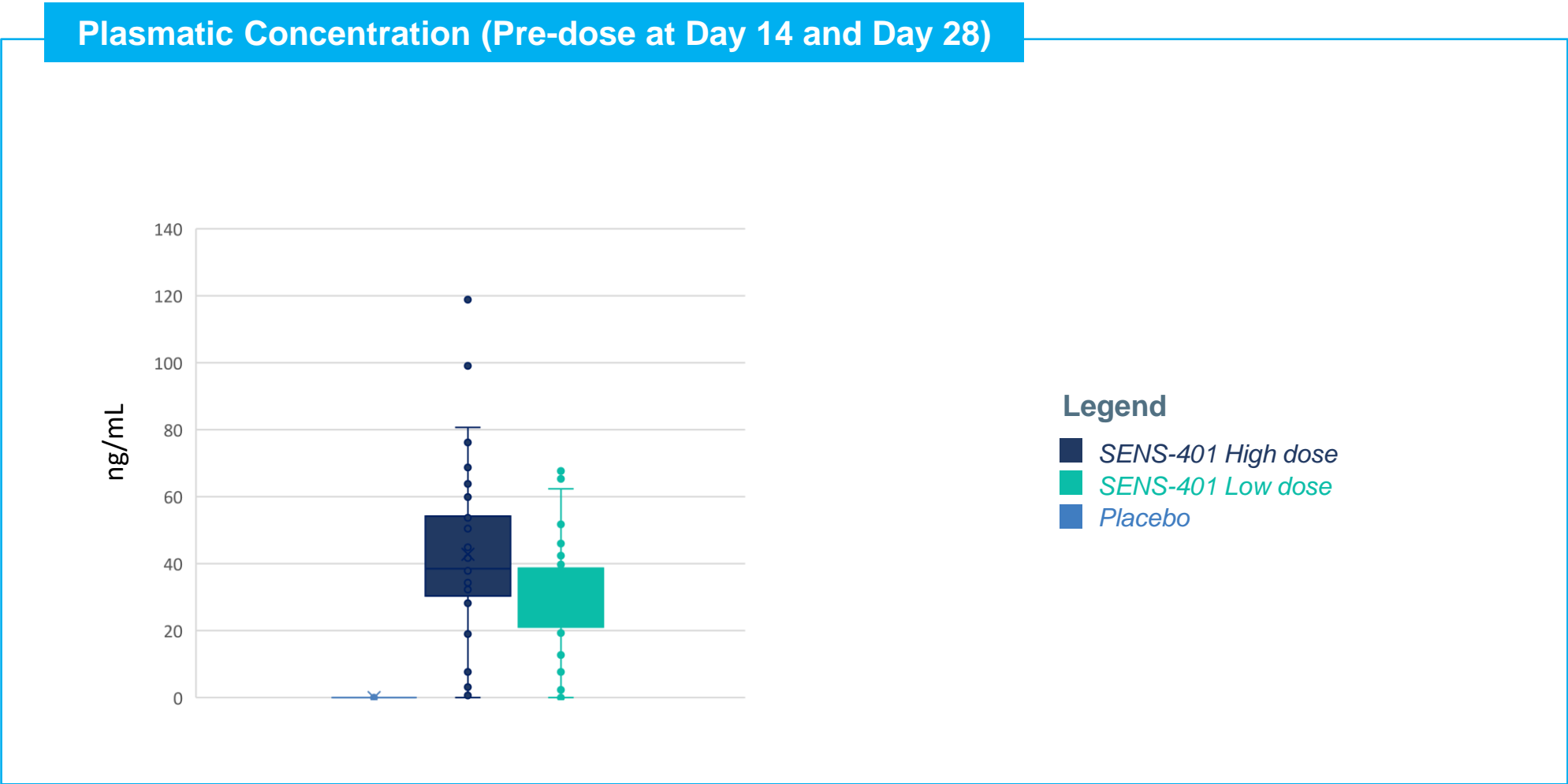
# SENS-401 SSNHL Program: AUDIBLE-S Phase 2 Design

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)”

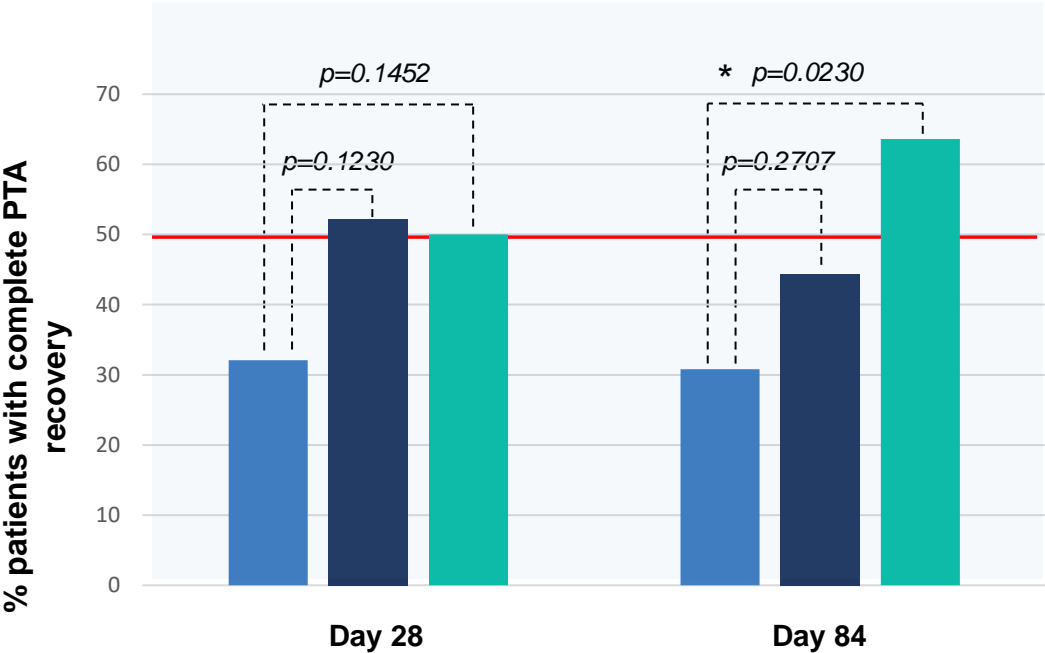
# SENS-401 Plasmatic Exposure





# 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