Sensorion

The Inner Ear Diseases company

# Corporate Presentation
# February 2018

ALSEN.PA

# Disclaimer

- This document has been prepared by Sensorion (the "Company") and is provided for information purposes only. This document does not purport to contain comprehensive or complete information about the Company and is qualified in its entirety by the business, financial and other information that the Company is required to publish in accordance with the rules, regulations and practices applicable to companies listed on Euronext Paris. No reliance may be placed for any purposes whatsoever on the information or opinions contained in this document or on its accuracy or completeness.
- This presentation does not constitute an offer to sell, a solicitation of, or an invitation to subscribe for or to buy, securities of Sensorion in any jurisdiction
- The information and opinions contained in this document are provided as of the date of this document only and may be updated, supplemented, revised, verified or amended, and thus such information may be subject to significant changes. The Company is not under any obligation to update the information or opinions contained herein which are subject to change without prior notice.
- The information contained in this document has not been subject to independent verification. No representation, warranty or undertaking, express or implied, is made as to the accuracy, completeness or appropriateness of the information and opinions contained in this document. The Company, its subsidiaries, its advisors and representatives accept no responsibility for and shall not, under any circumstance, be held liable for any loss or damage that may arise from the use of this document or the information or opinions contained herein.
- This document contains information on the Company's markets and competitive position, and more specifically, on the size of its markets. This information has been drawn from various sources or from the Company's own estimates which may not be accurate and thus no reliance should be placed on such information.
- This document contains certain forward-looking statements. These statements are not guarantees of the Company's future performance. These forward-looking statements relate to the Company's future prospects, developments and marketing strategy and are based on analyses of earnings forecasts and estimates of amounts not yet determinable. Forward-looking statements are subject to a variety of risks and uncertainties as they relate to future events and are dependent on circumstances that may or may not materialize in the future. Forward-looking statements cannot, under any circumstance, be construed as a guarantee of the Company's future performance and the Company's actual financial position, results and cash flow, as well as the trends in the sector in which the Company operates, may differ materially from those proposed or reflected in the forward-looking statements contained in this document. Important factors that could cause actual results to differ materially from the results anticipated in the forward-looking statements include those discussed or identified in the "Risk Factors" section of our "Document de référence" registration document filed with the Autorité des marchés financiers on July 28, 2016 under n°R.16-069 (a copy of which is available on www.sensorion-pharma.com). Even if the Company's financial position, results, cash-flows and developments in the sector in which the Company operates were to conform to the forward-looking statements contained in this document, such results or developments cannot be construed as a reliable indication of the Company's future results or developments. The Company does not undertake any obligation to update or to confirm projections or estimates made by analysts or to make public any correction to any prospective information in order to reflect an event or circumstance that may occur after the date of this document.
- Certain figures and numbers appearing in this document have been rounded. Consequently, the total amounts and percentages appearing in the tables may not necessarily equal the sum of the individually rounded figures, amounts or percentages.
- All persons accessing this document must agree to the restrictions and limitations set out above.

# Corporate Overview

Sensorion is a clinical-stage biopharmaceutical company focused on developing first-in-class therapies to treat inner ear disorders

| | |
|---|---|
| Company | ○ 20 employees, 16 in R&D (1MD, 7 PhD)<br>○ Headquartered in Montpellier, France<br>○ Spin off of INSERM in 2009 |
| Product Candidates | ○ SENS-111 for Acute Unilateral Vestibulopathy (AUV)<br>○ SENS-401 for hearing disorders |
| Technology Platform | ○ Research and non-regulatory development to support pipeline expansion and attract pharma partners |
| Financial Details | ○ Listed on Euronext Growth Paris since IPO in 2015 (ALSEN)<br>○ €9.2M as of June 30, 2016 |

# Experienced Leadership Team

## Nawal Ouzren

Chief Executive Officer, MSc

- 15+ years at GE, Baxter, Shire
- Solid drug development experience, including global marketing, market access and market development

## Pierre Attali

Chief Medical Officer
MD, MSc, Board certified in HGE

- 30+ years at Synthelabo, Sanofi, BioAlliance Pharma/Onxeo
- 10+ NCE/new formulations registered in EU/US

## Paul Bikard

Administration & Finance Director
MSc Lyon Business school

- 20+ years as auditor (Coopers & Lybrand-PWC, Andersen-E&Y) and CFO (Transgene, Prestwick Chemical)
- Solid Administration & Finance experience of SMEs

## Jonas Dyhrfjeld-Johnsen

Head of Pharmacology, PhD

- 15+ years research in CNS and inner-ear
- PhD in Neuroscience and post-doctoral research (UC Irvine-CA, Harvard Medical School-Boston, USA)

# Investment Highlights

**Deep Pipeline**

"Pure player" industry pioneer focused on inner ear disorders

- U.S. IND/EU voluntary harmonisation procedure (VHP) granted to conduct Phase 2 trial of SENS-111 in AUV
- Received Orphan Drug Designation (ODD) in EU for SENS-401 in Sudden Sensorineural Hearing Loss and Phase 1 completed
- Received Orphan Drug Designation (ODD) in the US for SENS-401 in Platine-Induced Ototoxicity and Phase 1 completed

**Significant Market Opportunities**

- Inner ear disorders represent a global market of $10+ billion
- Millions of patients suffer from vestibular and hearing disorders, representing a huge financial burden on healthcare system (e.g., $122B are spent per year in the US to manage patients suffering from hearing loss)

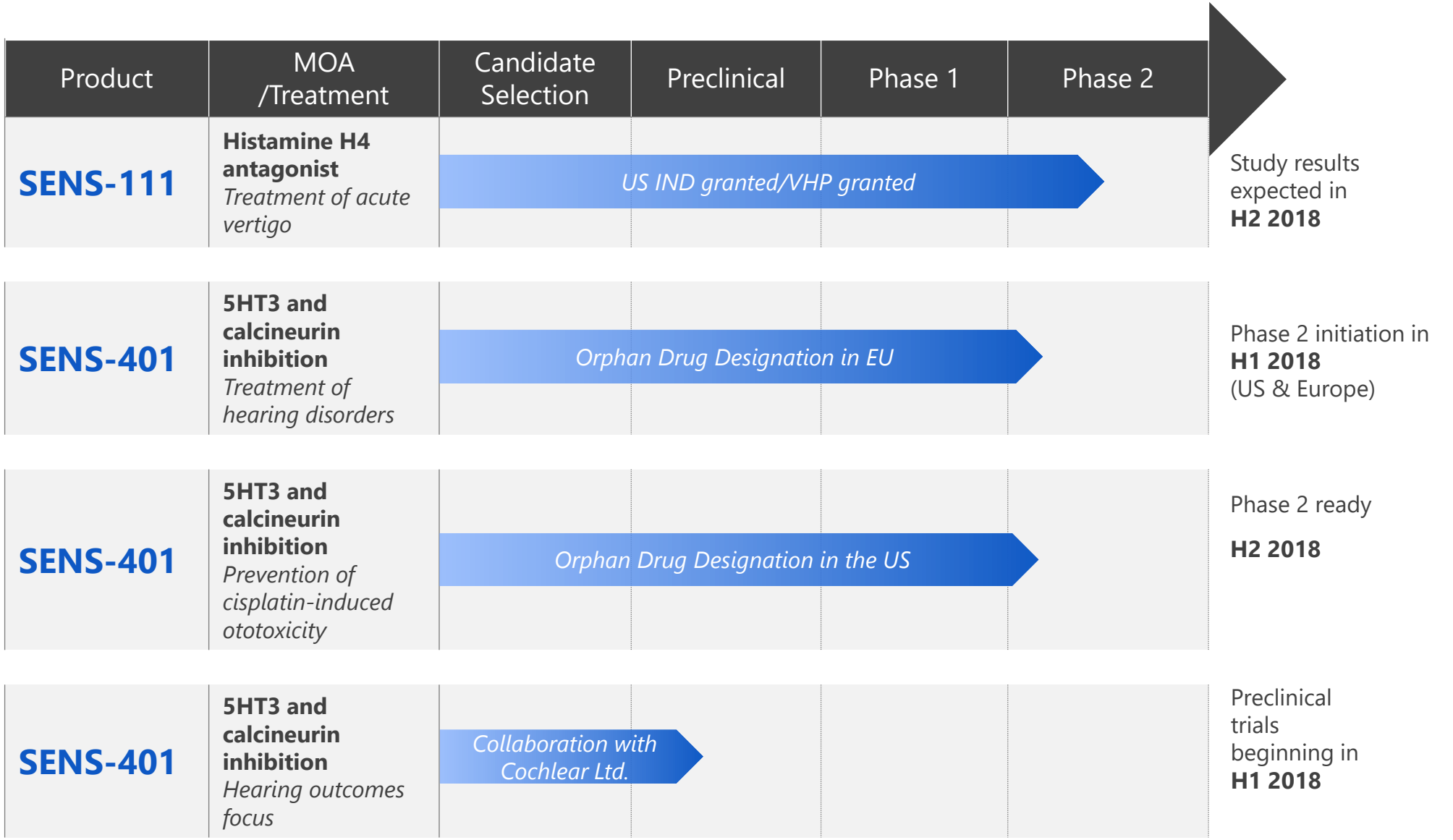
**Strong IP Protection**

- Pipeline covered by 7 patent families, including composition-of-matter and use patents in inner ear disorders

**Technology Platform**

- To facilitate pipeline expansion and attract pharma partners

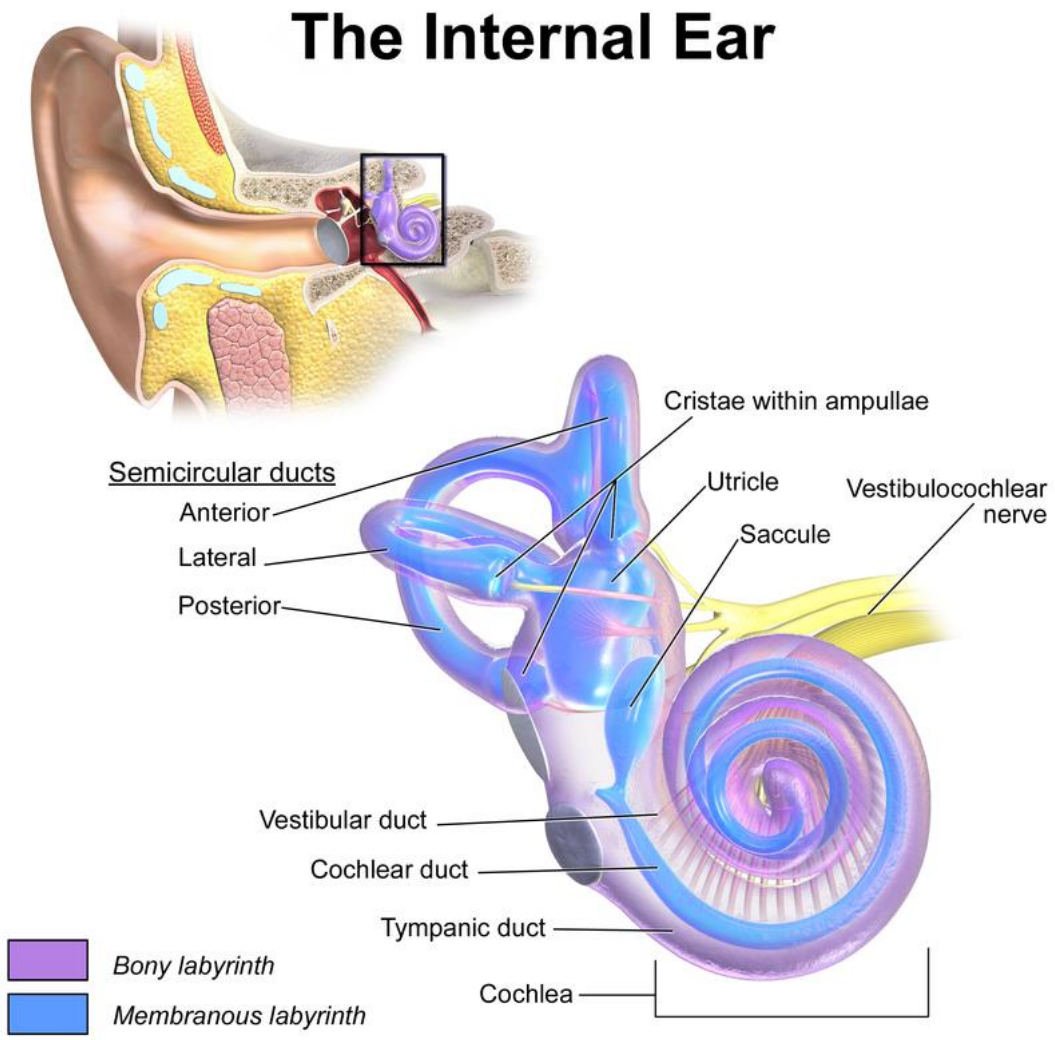
# Pipeline of Novel Drug Therapies

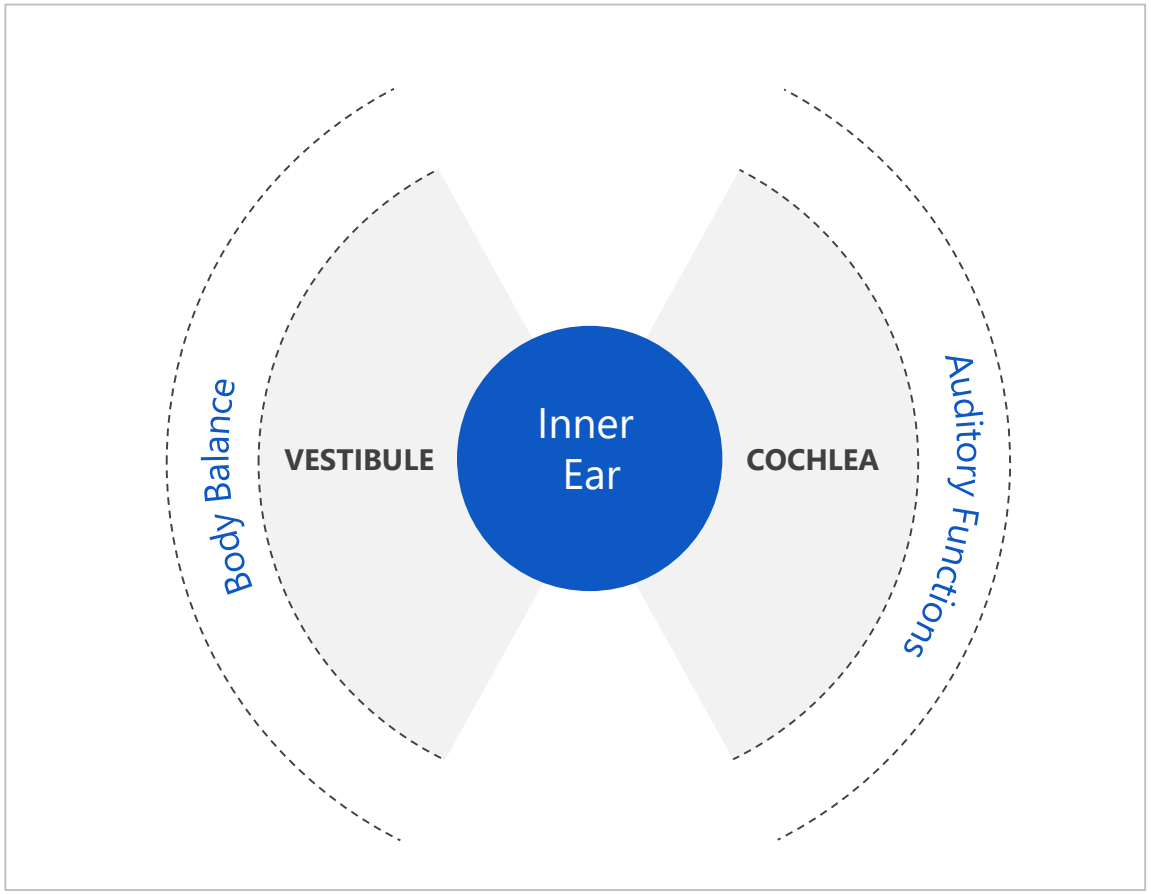





Sensorion
The Inner Ear Diseases company

# Inner Ear Biology



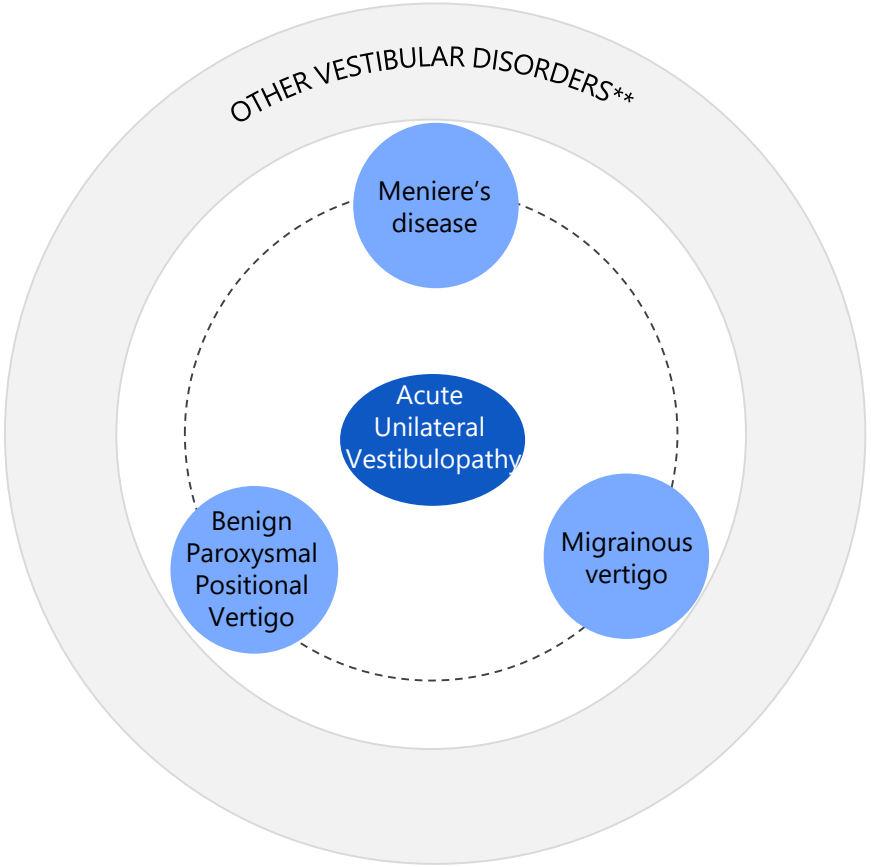





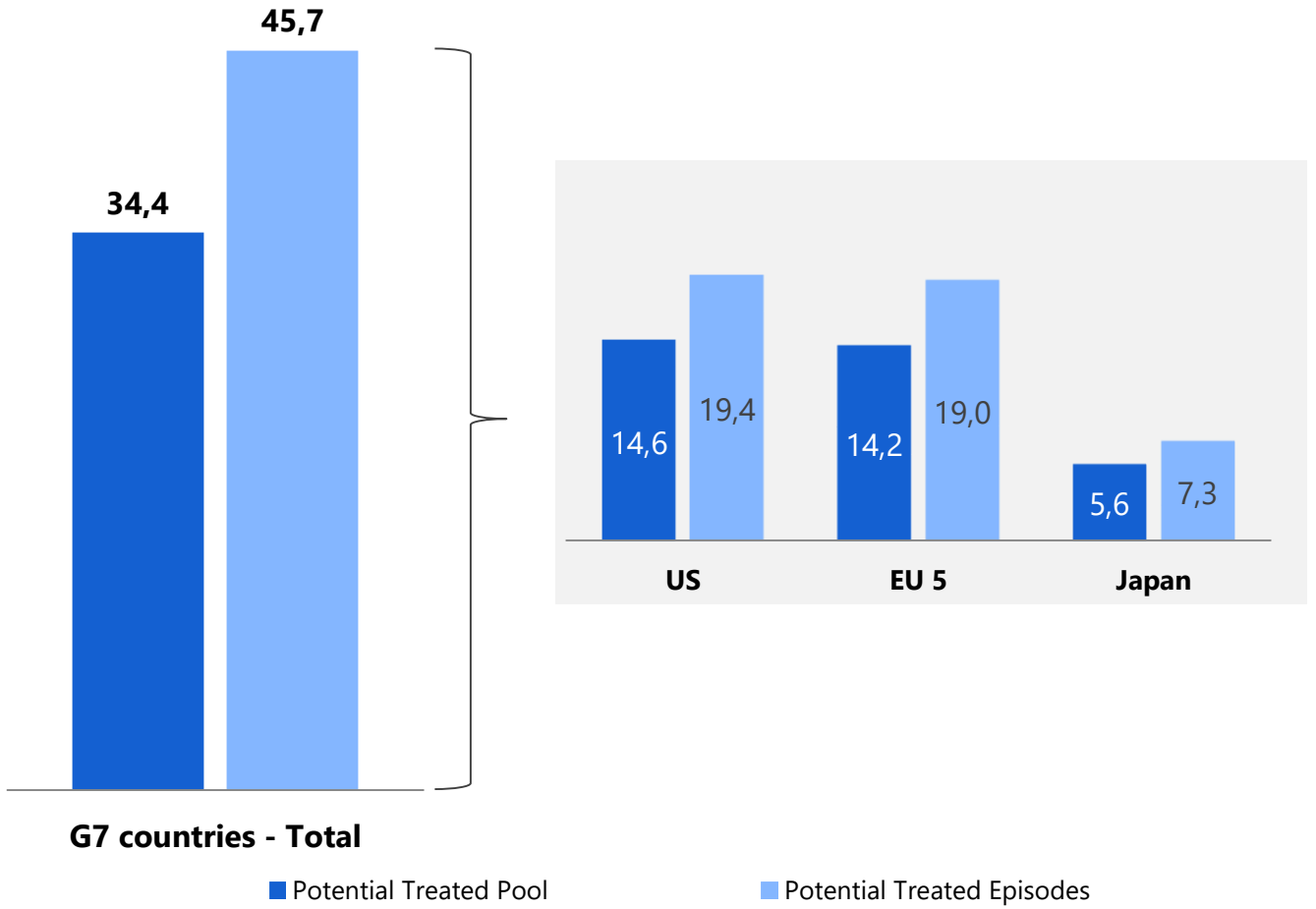

Sensorion
The Inner Ear Diseases company

# Vestibular Disorders: Etiology & Epidemiology

## ETIOLOGY




## Number of patients suffering from vestibular disorders (in millions, in 2017)




Source: Vestibular disorders association, Curr Opin Neurol 20:40-46 (2007), Strupp & Brandt (2009) Semin Neurol, J Neurol Neurosurg Psych 78:710-715 (2007), Neurology 67:1028-1033 (2006); [1] Primary research estimate USA - [2] Frankel group estimate; * Diagnosed and undiagnosed; **other vestibular disorders include Wallenberg's syndrome, perilymph fistula or acoustic neurinoma, otitis media, perilymph fistula, motion sickness and others.



Sensorion
The Inner Ear Diseases company

# Vestibular Disorder: Acute Unilateral Vestibulopathy (AUV)

**What is AUV:**

Acute, severe unilateral vestibular dysfunction giving the sensation that you or your surroundings are moving (spinning, whirling or moving vertically or horizontally)

**Incidence:**

Between 3.5 to 15.5 per 100,000 people

(68,000 patients in 2017 in G7 countries)[1]

**Sudden occurrence of AUV:**

Crisis lasts between 4 and 7 days

**Complications:**

The AUV crisis can lead to long-term complications in ~50% of the cases

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

- Dizziness, imbalance, abnormal gait, unsteadiness increasing the risk of severe fall by 12
- Psychological handicaps and disabilities

**Acute need for safe, effective drugs is clear**

> "AUV is assumed to be an ideal model for vestibular diseases. If this trial shows a benefit, the drug is assumed to work in other diseases leading to dizziness and vertigo."

**Pr. Michael Strupp**
Ludwig-Maximilians-University Munich, Germany (KOL event, *Nov. 29, 2016)*

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



Sensorion
The Inner Ear Diseases company

# SENS-111 for Acute Unilateral Vestibulopathy

## SENS-111

### AUV is a significant unmet medical need

- Current standard of care is suboptimal: no direct effect on vertigo, sedative effects
- 50% of patients complain of chronic dizziness/imbalance post-AUV

### First-in-class treatment

- First-in-class oral H4 receptor antagonist
- Mechanism of action well-defined and understood (H4R antagonist)
- SENS-111 acts through modulation of vestibular neuron excitability. It is not sedative.

### IP protection

- 3 composition of matter and use patent families
- IP issued in all major markets

### SENS-111 demonstrated activity in phase 1b

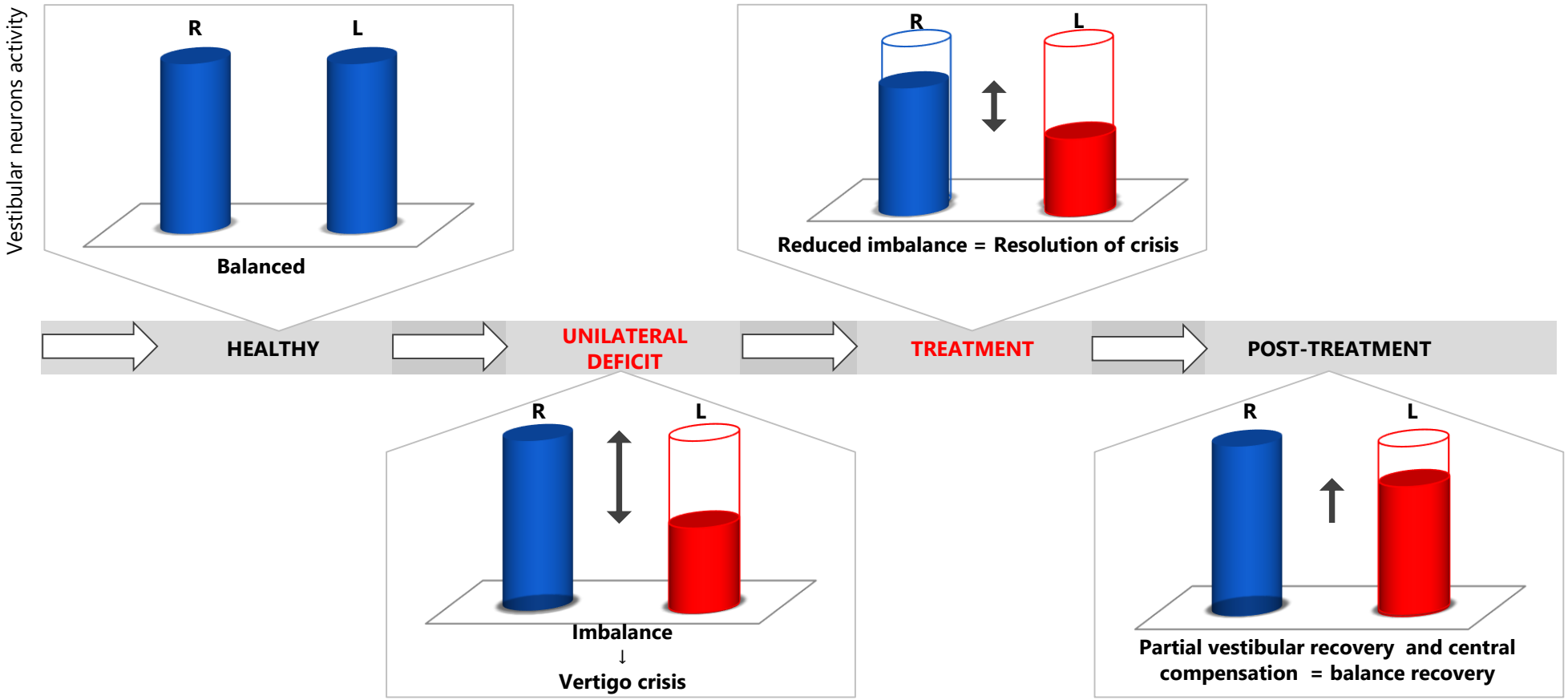
- 100 healthy volunteers enrolled
- Reduced vertigo symptoms from doses of 50 mg/day to 200 mg/day using caloric induction
- No sedation and significant adverse events reported

### A phase 2 trial underway

- Enrollment of 207 patients planned
- Final phase 2 read-out in H2 2018
- Trial being conducted in the US, Europe and South Korea

# Pathophysiology of Vertigo of Peripheral Origin

## Imbalance of neuronal activity between contralateral vestibules leads to vertigo




**Treatment goal to restore balance by reversibly reducing neuronal activity in vestibules**



Sensorion
The Inner Ear Diseases company

# SENS-111: Phase 1b Study Demonstrated Safety

## Phase 1 study design

Randomized placebo controlled in 100 healthy volunteers

**PART A**

Single oral dosing from 100 mg to 500 mg

- 5 cohorts of 8 HV (6 SENS-111, 2 placebo)

**PART B**

4 to 7 days of daily oral dosing from 50 mg to 250 mg

- 5 cohorts of 12 HV (9 SENS-111, 3 placebo)

## Study endpoints

PRIMARY

- Evaluate the safety of single and repeated ascending doses of SENS-111
- Determine the pharmacokinetic profile of SENS-111

SECONDARY

- Document the effect of a routine vestibular stress test (caloric induction) and activity of SENS-111 on part B

1. SENS-111 is well-tolerated
2. Pharmacokinetics of SENS-111 is linear with doses up to 200 mg/day, slightly over proportional at higher doses and **allows for once-a-day dosing**
3. SENS-111 demonstrated an activity related to plasma concentrations ranging between 0 and 500-700 ng/mL in vertigo induced by a caloric test
4. Clinical data are consistent with data obtained in preclinical testing
5. Valuable data available to guide phase 2 study design and selection of doses to be tested

# SENS-111 Phase 2 Program: 100 and 200 mg vs. Placebo

**25**
CLINICAL SITES
In Europe, US, Korea

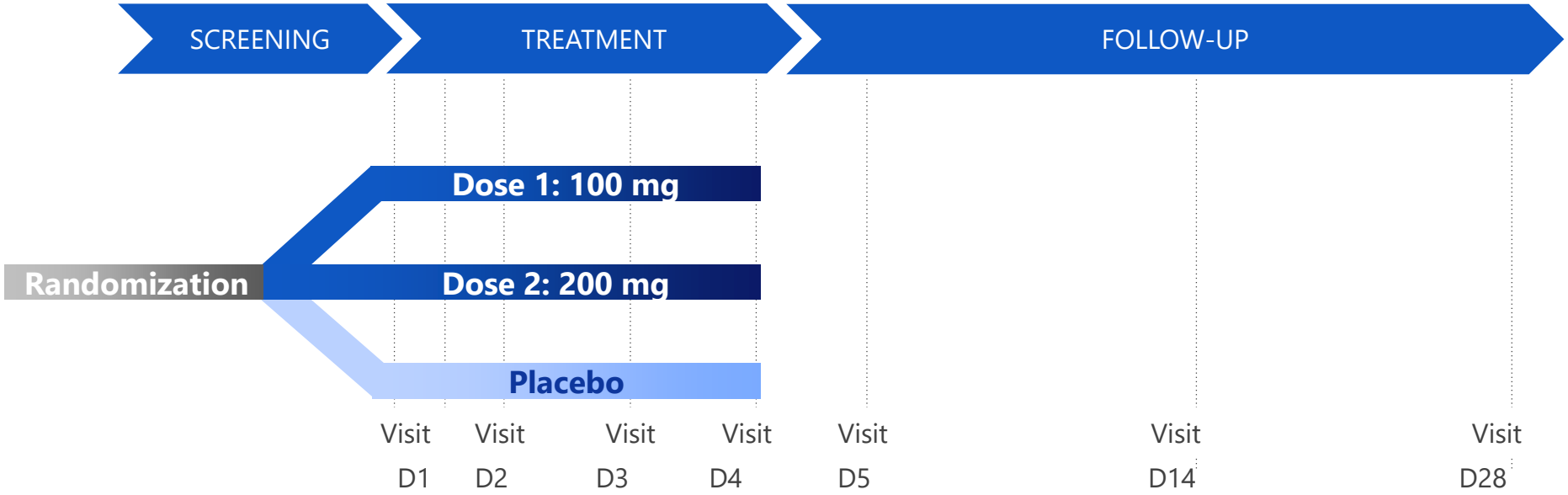
**1**
PRIMARY ENDPOINT
Vertigo intensity (visual analogic scale)

**20%**
IMPROVEMENT
vs PLACEBO
207 patients

PLANNING

| **Q1 2017** Centers opening | | **Q4 2018** readout |
|---|---|---|

## A multicenter, randomized, double-blind, placebo-controlled study

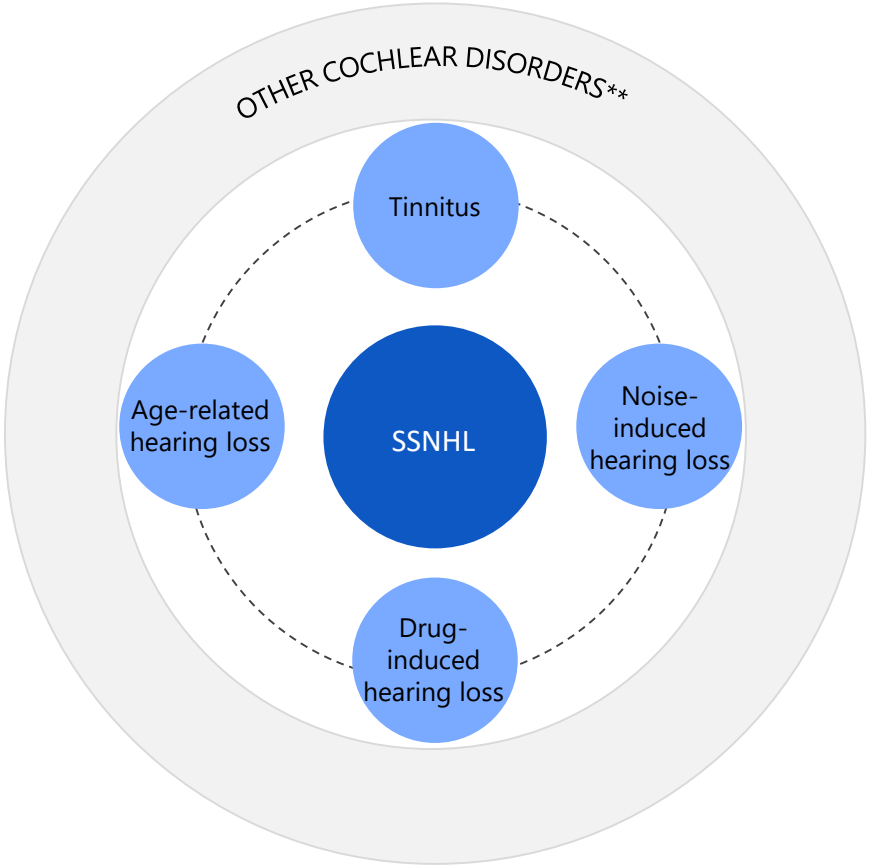




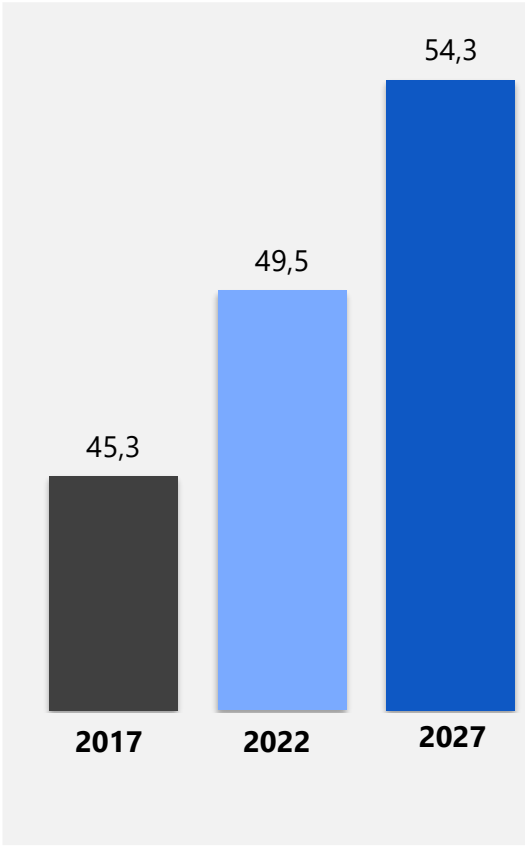

Sensorion
The Inner Ear Diseases company

# Cochlear diseases: Etiology & Epidemiology

## ETIOLOGY




## Number of patients suffering from cochlear disorders (in millions)




**The number of cochlear disease patients in the US is currently estimated at approximately 45 million**

Source: Phamax market research study**other cochlear disorders include congenital hearing loss (Usher syndrome, Pendred syndrome, Cogan syndrome...), otitis media/externa, loss of residual hearing after cochlear implant surgery, ototoxicity from drugs other than cisplatin.



Sensorion
The Inner Ear Diseases company

# SENS-401 for Sudden Sensorineural Hearing Loss

## SENS-401

### SSNHL is a significant unmet medical need

- No current effective treatment recommended in clinical practice guidelines
- More than 50% of patients suffer from permanent, disabling hearing loss, mostly those with severe to profound hearing loss
- Tinnitus, often disabling, is almost always associated with hearing loss

### First-in-class treatment

- First-in-class oral $5HT_3$ receptor antagonist & other undisclosed mechanism of action (MoA)
- The MoA is well-defined and understood (5HT3 antagonism, calcineurin inhibition)
- SENS-401 acts through reduction of cochlear cell death and neurodegeneration

### IP protection

- 2 patent families filed
- Orphan Drug Designation from EMA

### SENS-401 demonstrated safety and PK in phase 1

- 36 healthy volunteers enrolled in a double-blind, randomized, multiple ascending dose design (7 days)
- No serious or significant adverse events reported, safety profile comparable to placebo
- Pharmacokinetics match effective systemic exposures in preclinical model

### Phase 2 trial planned for 2018

- Trial to be conducted in the US and Europe
- Principal investigator and first centers identified

### Collaborative trial with Cochlear Ltd.

- Collaboration signed December 2017
- Cochlear invested €1.6 million in shares of Sensorion
- Will study SENS-401 in combination with cochlear implants
- Preclinical studies to begin in H1 2018
- Mid-stage clinical studies may start in 2019

# Sensorion And Cochlear Collaborate To Improve Hearing Outcomes Of Patients Recieving Cochlear Implants with SENS-401

Cement LEADERSHIP in Inner Ear Disorders

Invest in COMPLEMENTARY EXPERTISE

Identify Opportunities to IMPROVE PATIENTS' OUTCOMES

## Strategic Rationale For A Complementary Partnership

- Collaboration signed in December 2017
  - Cochlear invested €1.6 million in shares of Sensorion
  - In exchange, Cochlear received a right of first negotiation for a global license to use SENS-401 in patients with certain implantable devices
- Sensorion and Cochlear to study SENS-401 in combination with cochlear implants
- Preclinical studies to begin in 2018
- Mid-stage clinical studies may start in 2019

# Cochlear Disorder: Sudden Sensorineural Hearing Loss (SSNHL)

**What is SSNHL:**

The sudden onset of a significant hearing loss due to dysfunction of the cells of the cochlea and central auditory structures

**Incidence:**

Between 27 to 35 per 100,000 people (218,000 patients in 2017 in G7 countries)[1]. >70% cases are idiopathic, known causes include noise/head trauma, ischemia and infection

**Sudden occurrence of SSNHL:**

Hearing loss develops over less than 72 hrs, hearing sensitivity is reduced by at least 1,000 fold in the affected ear(s)

**Complications:**

More than 50% suffer from permanent, disabling hearing loss, mostly those with initial severe to profound hearing loss

Complications significantly impact patients' quality of life due to:

- Difficulty communicating, social isolation, cognitive decline
- Accompanying tinnitus

**Acute need for safe, effective drugs is clear**

> "Sudden sensorineural hearing loss (SSNHL) is considered an otological emergency. It may present as an isolated condition or be the presenting feature of a systemic disease process. Idiopathic sudden sensorineural hearing loss (ISSNHL) is diagnosed when an underlying cause or condition cannot be identified."

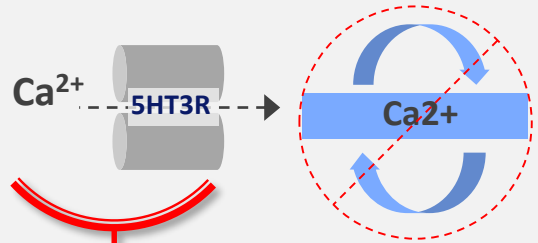
**Lawrence & Thevasagayam**
Clinical Otolaryngology
June 2015, 40(3):176-82

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

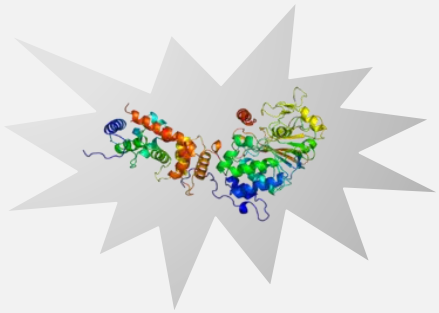
# SENS-401: Reduces Hair Cells Apoptosis By Inhibiting The Calcineurin Activation

INSULT

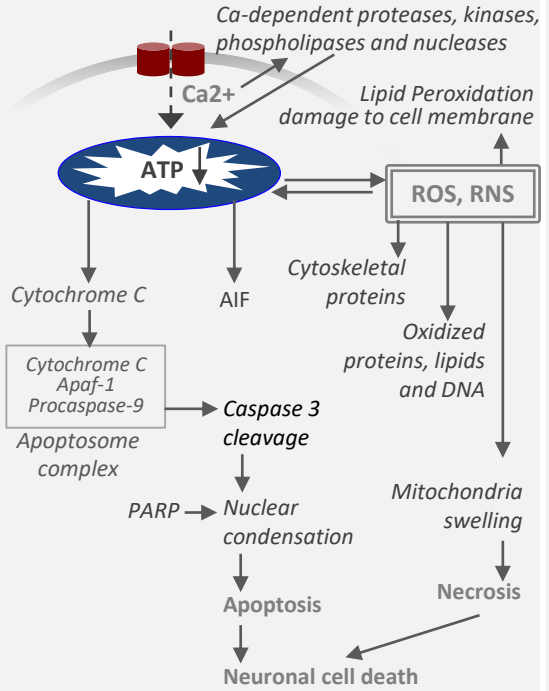
Disrupted $Ca^{2+}$ Homeostatis
Neuro Inflammation



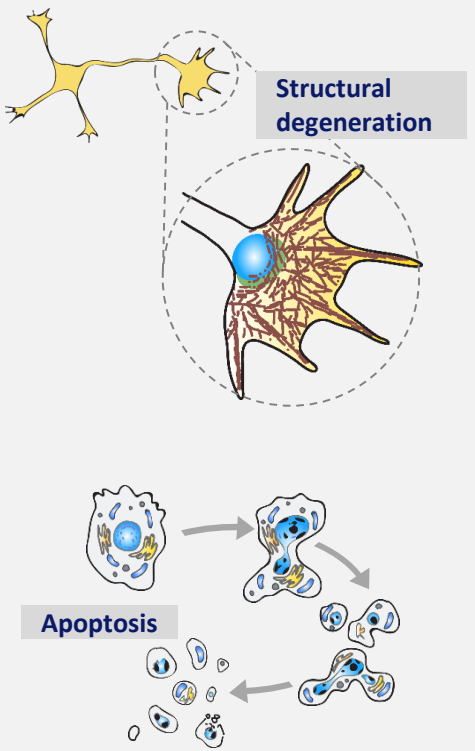

**Calcineurin Activation**



- NFAT translocation: oxid stress
- Actin (cytoskeleton) depolymerization
- BAD translocation/mPTP opening/cytochromeC + AIF release/Caspase 9/3 activation




Structural degeneration, swelling and synaptic uncoupling
&
Apoptosis (Cell Death)




SENS-401



Sensorion
The Inner Ear Diseases company

# SENS-401: Preclinical Data in Noise-Induced Cochlear Lesions

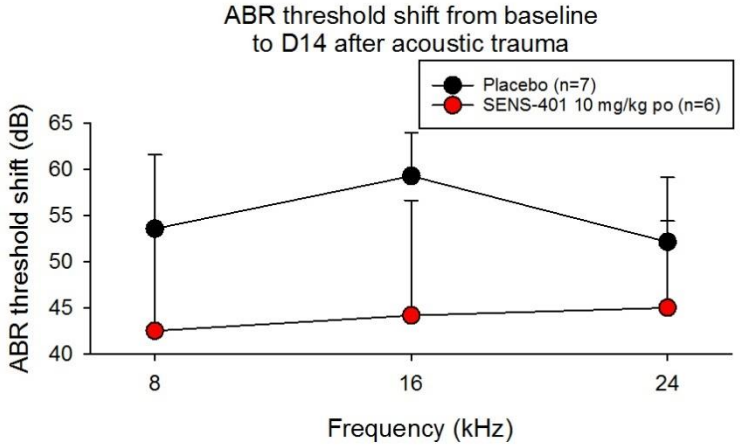
## A daily oral administration of SENS-401 reduces auditory deficit, improves recovery and reduces hair cell loss

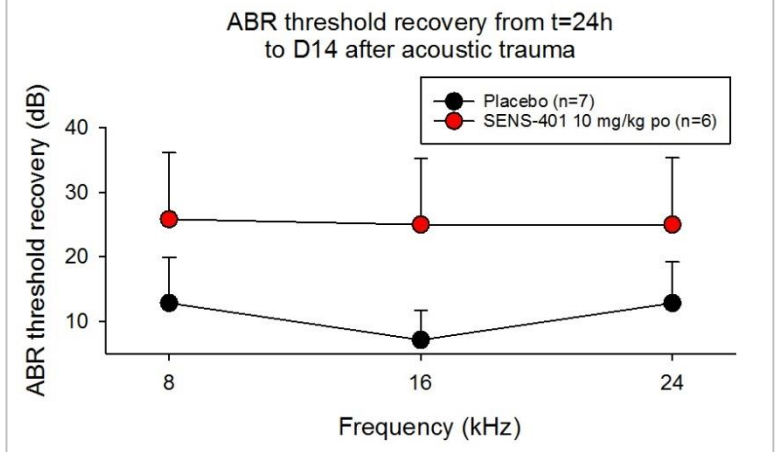
MODEL

- Randomized treatment post-noise induced trauma (2h exposure at 120 dB) in rats receiving either placebo or SENS-401 PO for 14 days

BENEFIT

- Regulatory threshold for efficacy (>10 dB improvement)



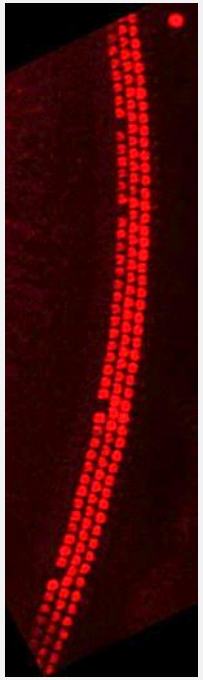




## Histology of hair cell layers

Significant hair cell loss

Limited hair cell loss

*Cochleograms*



Placebo

SENS-401



Sensorion
The Inner Ear Diseases company

# SENS-401: Phase 1b Study Demonstrated Very Good Clinical Tolerance

## Phase 1 study design

Randomized placebo controlled in 36 healthy volunteers

**Cohort 1** (12 subjects)
29 mg SENS-401 or placebo once daily for 7 days

**Cohort 2** (12 subjects)
29 mg SENS-401 or placebo twice daily for 6 days and a single dose of SENS-401 or placebo on day 7

**Cohort 3** (12 subjects)
43.5 mg SENS-401 or placebo twice daily for 6 days and a single dose of SENS-401 or placebo on day 7

## Study endpoints

PRIMARY
- Evaluate the safety of single and repeated ascending doses of SENS-401

SECONDARY
- Determine the pharmacokinetic profile of SENS-401

## Study results

- Very good clinical tolerance of SENS-401
- Plasma concentrations corresponding to those observed in animal models that showed the effect of SENS-401
- Pharmacokinetic data enabling Sensorion to select the doses for phase 2 testing

# Cochlear Disorder: Cisplatin-Induced Ototoxicity (CIO)

**What is CIO:**

Cisplatin administration for chemotherapeutic treatment of cancer damages the inner-ear and leads to hearing loss, tinnitus and dizziness

**Incidence:**

Between 350 to 450 per 100,000 people (~500,000 patients in 2017 in G7 countries)[1]

**Risk factors for CIO:**

Young age, individual and cumulative cisplatin doses during chemotherapy

**Complications:**

CIO leads to permanent inner ear problems in 50-60% of 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
- Difficulty communicating, social isolation, cognitive decline

Potential treatments must not interfere with cisplatin efficacy

**Acute need for safe, effective and non-interfering drugs is clear**

> "Ototoxicity is a well-established toxicity associated with a subgroup of antineoplastic therapies that includes platinum chemotherapy… The impact of ototoxicity on subsequent health-related and psychosocial outcomes in these patients can be substantial, and the burden of morbidity related to ototoxic agents is particularly high in very young children."

***Landier***
Cancer
February 2016, 122:1647-58

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

# SENS-401 for Cisplatin-Induced Ototoxicity

## SENS-401

### CIO is a significant unmet medical need

- No current effective treatment recommended in clinical practice guidelines
- More than 50-60% of pediatric patients suffer from permanent, disabling hearing loss, mostly those with severe to profound hearing loss
- Cisplatin treatment might be reduced or stopped because of hearing loss
- Severe social and learning disabilities

### First-in-class treatment

- First-in-class oral $5HT_3$ receptor antagonist & other undisclosed mechanism of action (MoA)
- The MoA is well-defined and understood (5HT3 antagonism, undisclosed MoA)
- SENS-401 acts through reduction of cochlear cell death and neurodegeneration

### IP protection

- 2 patent families filed
- Orphan Drug Designation for pediatric patients from US FDA

### SENS-401 demonstrated safety and PK in phase 1

- 36 healthy volunteers enrolled in a double-blind, randomized, multiple ascending dose design (7 days)
- No serious or significant adverse events reported, safety profile comparable to placebo
- Pharmacokinetics match effective systemic exposures in preclinical model

### Phase 2 ready by end of 2018

- Trial to be conducted in the US and Europe

# SENS-401 Significantly Reduces Cisplatin-Induced Hearing Loss and Outer Hair Cell Death

## Treatment

Placebo and SENS-401 at 6.6 mg/kg, 13.2 mg/kg or placebo once daily before and for 13 consecutive days after cisplatin infusion

## Results: ABR Threshold Shift at Day 14

Significant improvement versus placebo

- **23-29 dB, up to 65% reduction with 6.6 mg/kg**
- **22-29 dB, up to 73% reduction with 13.2 mg/kg**

## Results: DPOAE Amplitude Loss

Significant improvement versus placebo

- **1.5-19 dB, up to 78% reduction with 6.6 mg/kg**
- -1.2-14.6 dB up to 58% reduction with 13.2 mg/kg (p:0.08)

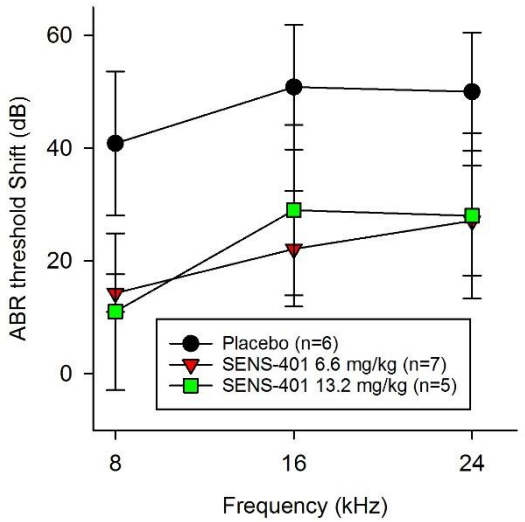
## Cochleograms

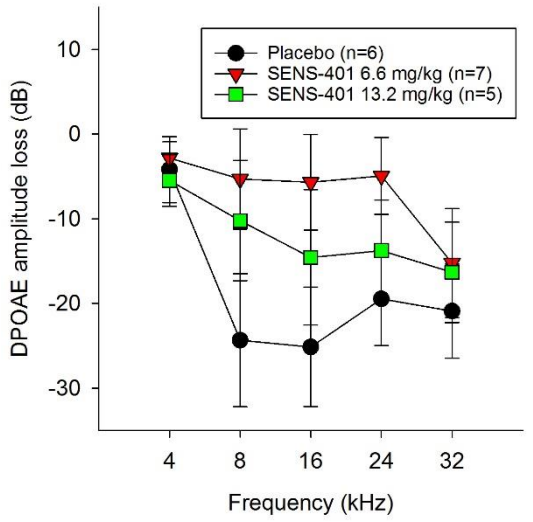
Significant **enhancement of OHC survival 22-264% for both doses**

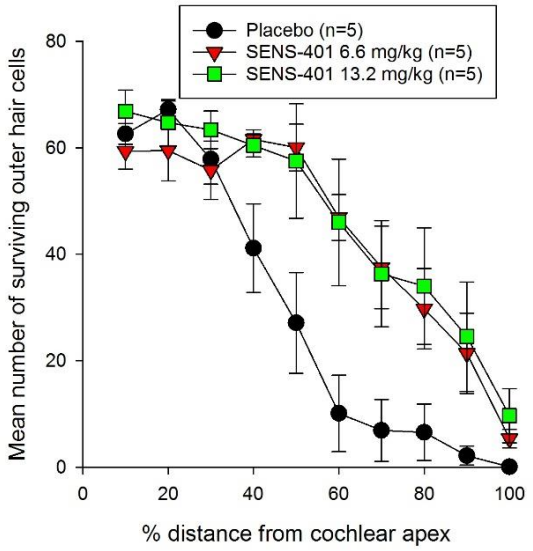
## Pharmacokinetics

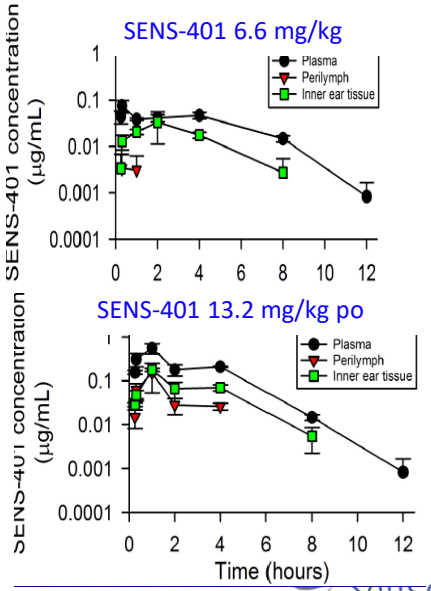
- Dose dependent plasma concentrations and PK profile
- Inner ear exposure: about 50% plasma exposure
- Perilymph exposure: about 30%  plasma exposure

**Conclusions:SENS-401 effective in models of CIO on ABR, DPOAE and OHC preservation. Concentrations are higher than $IC_{50}$ calcineurin inhibition**





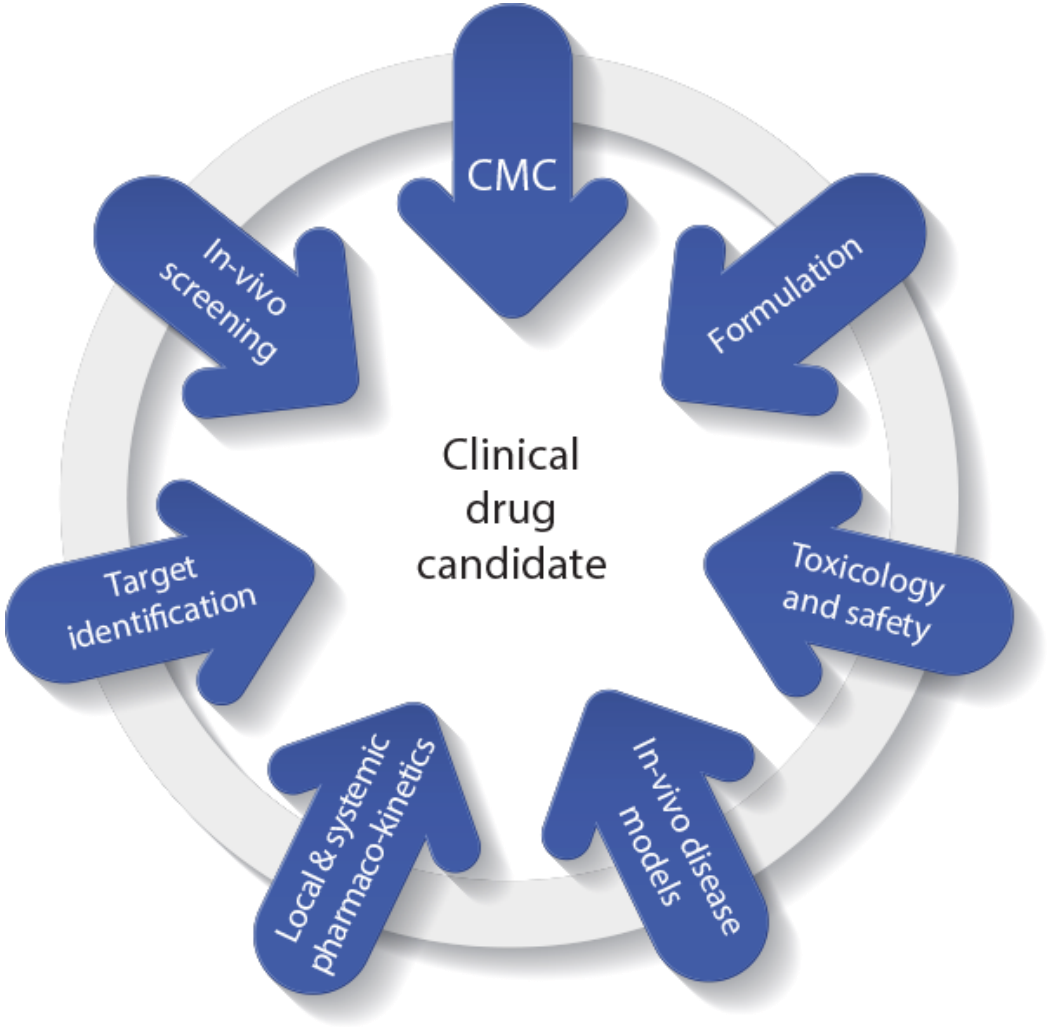

Sensorion
The Inner Ear Diseases company

# Our In-House Screening Platform is Dedicated to Inner Ear Disorders

**15+ YEARS** Academic & Pharma know-how

**COMPREHENSIVE TOOLBOX** To explore vestibular & cochlear applications

**AAALAC CERTIFIED** In-house platform



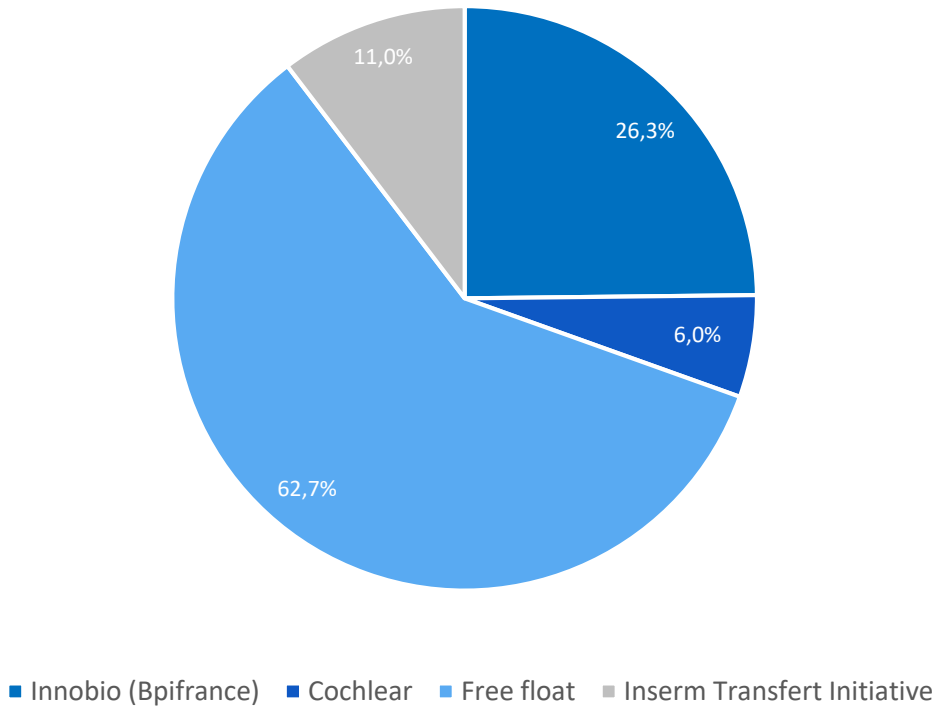

* Outsourced



Sensorion
The Inner Ear Diseases company

# Financial Update

## Shareholding structure at December 30, 2017




| Cash position | |
|---|---|
| €9.2m | Cash as of 30/06/2017 |
| up to €9.0m | Flexibility with Convertible Notes from Yorkville |
| €7.7m | 2016 cash used for operations |
| **Share information** | |
| IPO in 2015 | Euronext Growth Paris: ALSEN |
| 8,919,476 | Number of outstanding shares (31 December 2017) |
| €3.28 | Current share price (16 February 2018) |
| €30.0m | Market capitalization (16 February 2018) |

# Catalysts Over Next 18 Months

| Catalyst | Expected Timeline |
|---|---|
| Initiate SENS-401 phase 2 clinical trial in Europe and USA in SSNHL | H1 2018 |
| Initiate preclinical studies in collaboration with COCHLEAR | H1 2018 |
| SENS-111 AUV phase 2 study results | H2 2018 |
| SENS-401 phase 2 ready in Cisplatin-Induced Ototoxicity in pediatric population | H2 2018 |

# Investment Highlights

**Deep Pipeline**

"Pure player" industry pioneer focused on inner-ear disorders

- U.S. IND/EU voluntary harmonisation procedure (VHP) granted to conduct Phase 2 trial of SENS-111 in AUV
- Received Orphan Drug Designation (ODD) in EU for SENS-401 in Sudden Sensorineural Hearing Loss and Phase 1 completed
- Received Orphan Drug Designation (ODD) in the US for SENS-401 in Platine-Induced Ototoxicity and Phase 1 completed

**Significant Market Opportunities**

- Inner ear disorders represent a global market of $10+ billion
- Millions of patients suffer from vestibular and hearing disorders, representing a huge financial burden on healthcare system (e.g., $122B are spent per year in the US to manage patients suffering from hearing loss)

**Strong IP Protection**

- Pipeline covered by 7 patent families, including composition-of-matter and use patents in inner ear disorders

**Technology Platform**

- To facilitate pipeline expansion and attract pharma partners

Sensorion

The Inner Ear Diseases company

Caring for Inner Ear Disability

# Thank You