BRYAN, GARNIER & CO

9th December 2019

SENSORION

CORPORATE initiation of coverage

Fair Value	**EUR2.8**
Share price	EUR0.70
Bloomberg / Reuters	ALSEN FP/ALSEN.PA

Healthcare | **Biotech**

Unique in the hearing loss space

Sensorion is a clinical-stage biotech company focusing on developing novel therapies for hearing loss disorders. Historically focused on small molecules, the company recently announced a transformative world-class partnership with the Institut Pasteur, putting it at the forefront of the gene therapy field.

Gene therapies: The future sounds great. While still at quite an early stage, both of Sensorion's gene therapies seem highly promising and have already drastically transformed the company. Derived from a world-class partnership with the Institut Pasteur, both programmes should reach pre-clinical stage within two years. While there is still a long way to go, we believe that those treatments could generate a significant amount of sales (USD700m of sales at peak for the two programmes) with a strong ramp-up supported by the pool of existing patients. Even with very conservative assumptions (5% PoS and 19.1% WACC), we estimate that Sensorion's gene therapy franchise supports 14% of our valuation.

SENS-401: Our main value driver. Indeed, our valuation is mainly based on SENS-401's strong potential in sudden deafness and cisplatin induced ototoxicity. Combined peak sales of both indications could reach EUR400m at peak, with first sales happening as soon as 2025. Currently in phase II clinical trial in this indication, we are expecting to get results in Q2 2020 and interim safety results by year-end. As for the second promising indication, we are anticipating clinical development to start following results from the ongoing phase II. The whole SENS-401 franchise represents the lion's share of Sensorion's EV (80%) and could further grow if the promising collaboration with Cochlear (not included in our valuation yet) leads to a deal next year.

Finally, we come up with a FV of **EUR2.8/share** representing a significant upside to the current share price.

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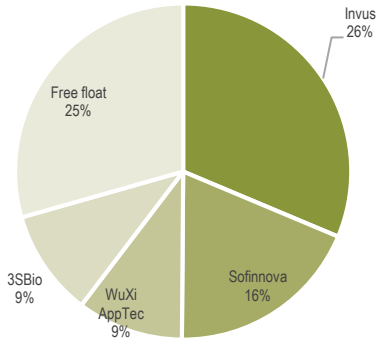
Fair Value	**EUR2.8**
Share price	**EUR0.70**
Market Cap.	**EUR23m**
EPS 3Y CAGR	**NM**

Shareholders



Fiscal year end 31/12	2017	2018	2019e	2020e	2021e	2022e	2023e
Financial Summary							
EPS (EUR)	-1.35	-1.08	-0.41	-0.77	-0.53	-0.65	-0.62
Restated EPS (EUR)	-1.35	-1.08	-0.41	-0.77	-0.53	-0.65	-0.62
% change	-	-19.9%	-62.1%	-88.8%	-30.9%	-22.7%	-4.6%
Net dividend (EUR)	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Average yearly Price	4.80	2.71	-	-	-	-	-
Avg. Number of shares, diluted (m)	7	11	32	32	32	32	32
Historical Entreprise value (EURm)	7.5	2.7	-	-	-	-	-
Profit & Loss Account (EURm)							
Revenues	2.03	2.31	2.61	6.04	3.81	4.80	4.42
Change (%)	-	14.0%	13.0%	131.3%	-36.9%	25.9%	-7.8%
R&D	-7.87	-11.91	-12.00	-27.75	-17.52	-22.05	-20.32
EBIT	-9.52	-12.23	-12.28	-24.89	-17.20	-21.10	-20.13
Change (%)	-	-28.5%	-0.4%	-102.7%	-30.9%	-22.7%	-4.6%
Pre-Tax profits	-9.69	-12.35	-13.19	-24.89	-17.20	-21.10	-20.13
Tax	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Net profit	-9.69	-12.35	-13.19	-24.89	-17.20	-21.10	-20.13
Restated net profit	-9.72	-12.32	-13.19	-24.89	-17.20	-21.10	-20.13
Change (%)	-	-26.8%	-7.0%	-88.8%	-30.9%	-22.7%	-4.6%
Cash Flow Statement (EURm)							
Operating cash flows	-7.78	-12.25	-12.38	-24.09	-16.40	-20.30	-19.33
Change in working capital	-0.03	-0.70	0.00	0.00	0.00	0.00	0.00
Capex, net	-0.17	-0.01	-0.06	-0.06	-0.06	-0.06	-0.06
Free Cash flow	-9.49	-11.63	-13.13	-24.83	-17.14	-21.04	-20.07
Financial investments, net	-0.01	0.00	0.00	0.00	0.00	0.00	0.00
Capital increase	-0.50	-0.37	41.05	0.00	0.00	0.00	0.00
Net debt (+)/cash (-)	7.51	2.63	27.55	3.14	-13.58	-34.20	-53.85
Balance Sheet (EURm)							
Tangible fixed assets	9.9	8.3	36.7	12.2	-4.5	-25.1	-44.7
Intangibles assets	1.2	1.2	0.7	0.2	-0.3	-0.8	-1.2
Cash & equivalents	7.6	2.7	31.1	6.7	-10.1	-30.7	-50.3
current assets	9.9	8.3	36.7	12.2	-4.5	-25.1	-44.7
Other assets	2.3	5.6	5.6	5.6	5.6	5.6	5.6
Total assets	11.2	9.5	37.3	12.4	-4.8	-25.9	-46.0
L & ST Debt	1.4	3.6	23.6	23.6	23.6	23.6	23.6
Provisions	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Others liabilities	0.8	0.8	0.8	0.8	0.8	0.8	0.8
Shareholders' funds	7.3	3.5	11.4	-13.5	-30.7	-51.8	-72.0
Total Liabilities	3.8	6.0	26.0	26.0	26.0	26.0	26.0

Source: Company Data; Bryan, Garnier & Co ests.

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EXECUTIVE SUMMARY

Sensorion is a clinical-stage biotech company focusing on developing novel therapies for hearing loss disorders. Historically focused on small molecules, the company recently announced a transformative world-class partnership with the Institut Pasteur, putting it at the forefront of the gene therapy field.

We are initiating the stock in the aftermath of the phase II failure of SENS-111 in acute unilateral vestibulopathy which has significantly weighted on Sensorion's stock price in the past few days. Considering that SENS-401 is a totally different asset from SENS-111 (fully proprietary whereas SENS-111 has been in-licensed), we do not think there is any negative read-across to be made. Now that the equity story is fully focused on hearing loss (with SENS-401 as well as the promising gene therapies), we think everything is well aligned for Sensorion to deliver.

We are especially excited about Sensorion's gene therapies programmes derived from a world-class partnership with the Institut Pasteur. We think this collaboration has already transformed the company and we are now looking forward for them to reach preclinical stage in the coming months. While there is still a long way to go, we believe that those treatments could generate a significant amount of sales (USD700m of sales at peak for the two programmes) with a strong ramp-up supported by the pool of existing patients. Even with very conservative assumptions (5% PoS and 19.1% WACC), we estimate that Sensorion's gene therapy franchise supports 14% of our valuation.

In the meantime, we are expecting SENS-401's to be one of the main drivers of Sensorion in the coming months. We are expecting results in sudden deafness to be presented before the end of Q2 2020. If positive, we expect Sensorion to start a phase II/III program in cisplatin induced ototoxicity where we believe SENS-401 has a strong potential. Combined peak sales of both indications could reach EUR400m at peak, with first sales happening as soon as 2025. In the end, the whole SENS-401 franchise represents the lion share Sensorion's EV (80%) and could further grow if the promising collaboration with Cochlear (not included in our valuation yet) lead to a deal next year.

Finally, we come up with a FV of **EUR2.8/share** representing a significant upside to the current share price.

Sensorion est une société de biotechnologie spécialisée dans le développement de nouvelles thérapies pour les troubles de l'audition. Historiquement investie dans le développement de petites molécules, la société a récemment annoncé un partenariat de classe mondiale avec l'Institut Pasteur, la plaçant à la pointe de la thérapie génique.

Nous initions le titre à la suite de l'échec de la phase II de SENS-111 qui a eu un impact significatif sur le cours de l'action au cours des derniers jours. Considérant que SENS-401 est un actif totalement différent de SENS-111 (entièrement propriétaire alors que SENS-111 a fait l'objet d'une licence), nous considérons qu'il s'agit d'un actif complètement différent et conservons toute notre confiance dans son avenir clinique. Maintenant que la société est entièrement concentrée sur la perte auditive (avec SENS-401 et les thérapies géniques prometteuses), nous pensons que tout est aligné pour que Sensorion délivre dans les prochains mois.

A commencer par les thérapies géniques développées en partenariat avec l'Institut Pasteur. Nous estimons que cette collaboration a déjà transformé l'entreprise et devrait atteindre le stade préclinique au cours des prochains mois. Bien qu'il reste encore beaucoup de chemin à parcourir, nous pensons que ces traitements pourraient générer un chiffre d'affaires significatif (700 millions de dollars de chiffre d'affaires au plus haut pour les deux programmes) avec une forte montée en puissance soutenue par le pool de patients existants. Même avec des hypothèses très conservatrices (5% de probabilité de succès et 19,1% WACC), nous estimons que la franchise de thérapie génique de Sensorion représente 14% de notre évaluation.

D'ici là, nous estimons que SENS-401 sera l'un des principaux moteurs de Sensorion à court terme. A court terme, la société devrait présenter les résultats de la phase II en SSNL d'ici la fin du Q2 2020. Si ces derniers sont positifs, elle devrait initier une phase II/III en ototoxicité induite par le cisplatine, indication à fort potentiel pour SENS-401. Au pic, nous estimons que les ventes totales du produit devraient atteindre 400 millions d'euros, les premières ventes ayant lieu dès 2025. Au final, l'ensemble de la franchise SENS-401 représente la plus grande part de notre valorisation (80%) et pourrait encore croître si la collaboration prometteuse avec Cochlear (non encore incluse dans notre évaluation) conduit à un accord l'année prochaine.

Enfin, nous arrivons à une Fair Value de 2,8 euros par action, ce qui représente une hausse significative par rapport au cours actuel de l'action.

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Contents

Part 1: Valuation

Fair Value of EUR2.8 per share (BGe)

Our valuation is based on a sum of the parts i.e. dedicated DCF model for each asset, with estimates out to 2036 to capture the full value of the portfolio until the patent expires. We derive a Fair Value of EUR2.8 per share. Our WACC stands at 15.6% for the SENS-401 franchise and 19.1% for the gene therapy programmes expected to reach pre-clinical stage within two years, assuming a beta of 2.0 (our common approach at clinical stage small-cap biotech companies) and 2.5 respectively to reflect the earlier stage of development of the gene therapy programmes. We are assuming a risk-free rate of 1.6% and a risk premium of 7.0% based on Bryan, Garnier & Co's Equity Research assumptions. Since Sensorion is not paying any coupon on the EUR20m convertible bonds issued in June 2019, its WACC equals the cost of equity.

Fig. 1: WACC assumptions (BGe)

Cost of debt before tax	0,0%	Cost of debt before tax	0,0%
Risk free rate	1,6%	Risk free rate	1,6%
Equity risk premium	7,0%	Equity risk premium	7,0%
Beta	2,00	Beta	2,50
Cost of Equity	15,6%	Cost of Equity	19,1%
WACC	**15,6%**	**WACC**	**19,1%**

Source: Bryan, Garnier & Co ests.

Taking into account the EUR20m convertible bond issued in June 2019, as well as the recent EUR18.1m capital increase announced in late September 2019, we estimate Sensorion's cash position at EUR31.1m and EUR6.7m at the end of 2019 and 2020 respectively. This gives Sensorion financial runway to Q1 2021. Note that we took the cash situation at the end of 2020 in our sum-of-the-parts valuation, and we already rolled over our model into 2020 as well.

As mentioned above, our valuation of Sensorion works out to EUR2.8 per share (based on 32.2m shares on a fully-diluted basis). It mainly relies on SENS-401 both in Sudden Sensorineural Hearing Loss (SSNHL) and in Cisplatin Induced Ototoxicity (CIO) representing 79% of our valuation. We are expecting results from the ongoing phase II trial in SSNHL to be presented in Q2 2020 preceded by a safety interim before the end of this year. While we have attached a 30% PoS to the SSNHL programme, we modelled only a 20% PoS for CIO. Although we consider CIO to be a very promising indication for SENS401, we are awaiting its clinical start through a registrational phase II/III trial, which should lead us to increase our PoS.

While being early stage, we have included both gene therapy programmes (Usher 1G and Otoferlin) in our scenario with a conservative PoS (5%) and a 19.8% WACC based on a 2.5 beta to reflect their clinical stage of development. As of now, this only represents 14% of our valuation, but we believe they have already put the company at the forefront of the gene therapy movement.

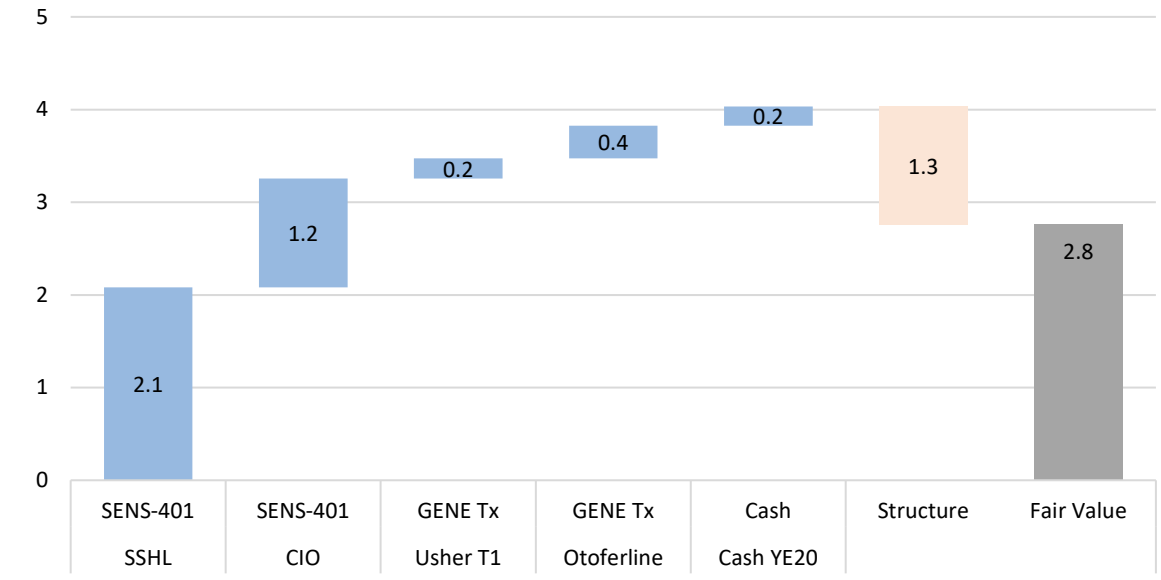
Following the failure of SENS-111's phase IIb trial in acute unilateral vestibulopathy, Sensorion has announced that no further activities related to this asset will be pursued and intends to now focus on advancing their promising pipeline in hearing loss disorders. Afterwards, we believe that investors have been overly harsh given that 1/ the stock has already been heavily impacted one year ago when the company announced a re-design of the study to address slower than expected patient recruitment and 2/ even when the result were approaching we did not see it as a key asset for Sensorion in terms of valuation.

Fig. 2: Sensorion's valuation (BGe)

Product	Indication	Market Share	Peak Sales	Status	PoS	EV	/Share	% of EV (Structure /Product)
SENS-401	Sudden Sensorineural Hearing Loss (SSHL)	30%	230	Ph II	30%	67	2.1	50%
SENS-401	Cisplatin Induced Ototoxicity (CIO)	30%	183	Ph II	20%	38	1.2	28%
GENE Tx	Usher T1 Syndrome	80%	227	Preclinic	5%	7	0.2	5%
GENE Tx	Otoferline deficiency	50%	395	Preclinic	5%	11	0.4	9%
Cash	Year-end 2020					7	0.2	7%
Structure Costs					23%	-41	-1.3	
Fair Value						**89**	**2.8**	**100%**

Source: Bryan, Garnier & Co ests.

Fig. 3: SOTP *waterfall*



Source: Bryan, Garnier & Co ests.

Part 2: At the forefront of the hearing loss space

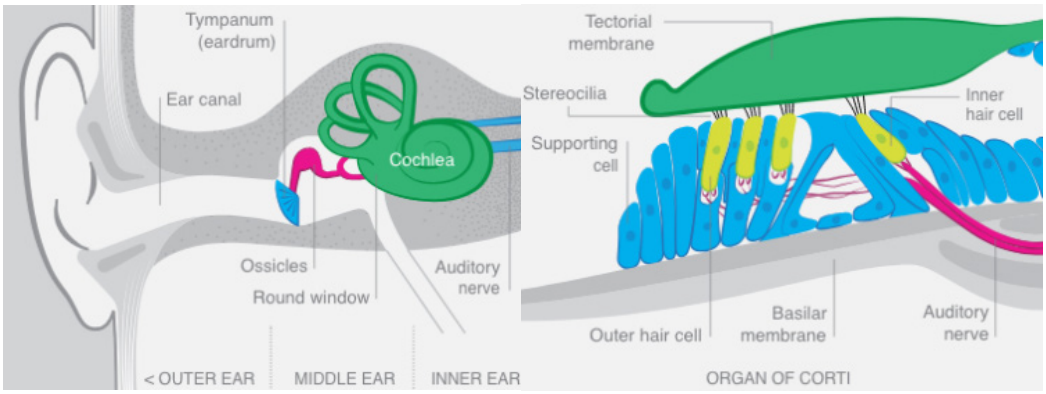
A vast therapeutic area with huge unmet needs

Hearing impairment is one of the most common human disabilities. According to the World Health Organization (WHO), five percent of the world's population (~360 million people) suffers from disabling hearing loss. That number is expected to grow to one billion by 2050. There are currently no approved therapeutics for the treatment of hearing loss. Hearing aids and cochlear implants may offer benefits, but they **fall short of replicating** normal hearing function.

HOW HEARING WORKS?

Sound waves travel into the out-ear canal and cause the eardrum to vibrate. It leads to the vibration of a series of small bones causing the fluid inside the cochlea to move back and forth. A part of the cochlea is known as the organ of corti (as shown in Fig.4) which contains the hair cells that convert this fluid movement into what our brain perceives as sound.

Fig. 4: Anatomy of the ear



Source: Decibel Therapeutics

There are two types of hair cells: inner hair cells and outer hair cells, both of which are important for detection and processing of auditory information. Damage or dysfunction within any of these cells and cell structures can lead to symptoms of hearing loss, tinnitus or hyperacusis.

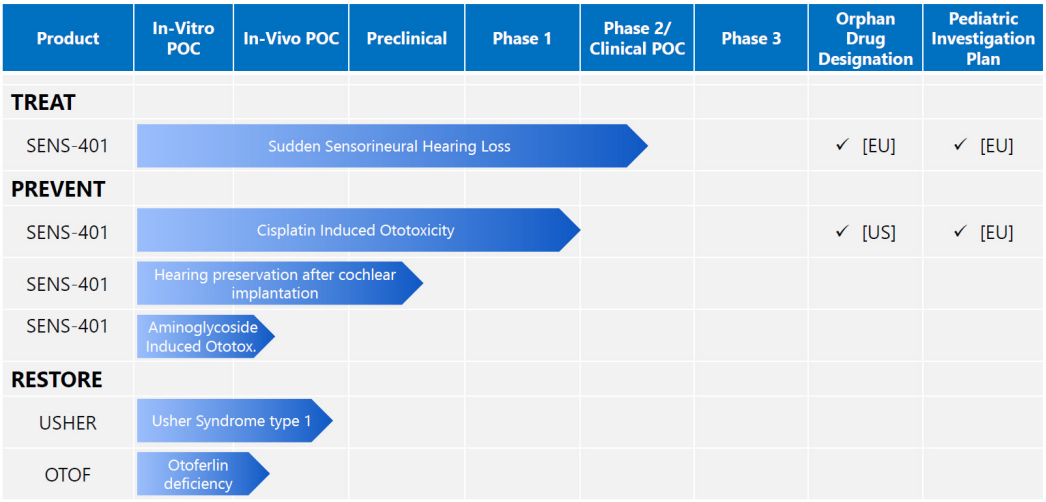
HOW DO THOSE CELLS BECOME DYSFONCTIONAL?

- Environmental factors: Hair cells are commonly impacted by **noise exposure**, aging, certain viral infections or **exposure to ototoxic drugs**, resulting in hearing loss. That's the focus of **SENS-401** aiming to reduce cellular stress induced by a hearing trauma.
- Genetic factors: In developed countries, severe or profound hearing loss is mostly caused by genetic mutations. These forms are generally "monogenic", meaning that they can be attributed to a single deficient gene producing atypical proteins. That's when **Sensorion's gene therapies** come into play. They are aiming to deliver a healthy piece of DNA cells in the cochlea, enabling them to produce functional protein and restore hearing.

Sensorion's pipeline covers the whole hearing loss space

Sensorion has one of the most exciting pipelines for **hearing loss disorders** starting with SENS-401, a small molecule with strong potential in both sudden hearing loss (phase II ongoing) and cisplatin induced ototoxicity. At the other end of the spectrum, the company is developing **breakthrough gene therapies** for hereditary hearing loss (Usher Syndrome and Otoferlin deficiency) in collaboration with world-renowned Institut Pasteur.

Fig. 5: Sensorion's pipeline



Source: Company

GENE THERAPIES: SENSORION'S LONG SHOT IN PRECISION MEDICINE

While there is still a long way to go, we believe that Sensorion's move into gene therapy is already paying off. Indeed, the collaboration with the Institut Pasteur already puts Sensorion at the forefront of the gene therapy space for hearing loss.

If proven successful, we believe that those treatments could generate significant amount of sales based on a **premium pricing** (USD400k) in line with the expected benefits which should allow patients to avoid costly cochlear implants (which are gold standard for the most severe patients).

On top of that, they should benefit from a pool of existing patients which should drive sales' ramp-up from the very beginning. While being still early stage, we believe that those assets should not be overlooked as they represent Sensorion's take in a highly attractive market.

SENS-401: NEXT SIGNIFICANT CATALYST FOR SENSORION

With results of the ongoing phase II study in SSNHL expected for the end of Q2 2020, SENS-401 will be the main focus of attention in the coming months. This asset is a selective 5-HT3 receptor antagonist which reduce cellular stress induced by a hearing trauma. It has potential in sudden hearing loss (BGe: c.EUR230m of sales at peak) and cisplatin-induced ototoxicity which could add EUR180m in sales at peak.

On top of promising preliminary results in terms of efficacy, one of the key strengths of SENS-401 lies in its extended otoprotection, which is still significant even after an initiation delay of up to four days post trauma. We are equally excited by its potential for cisplatin-induced ototoxicity where unmet needs are still strong.

Last but not least, we are expecting preliminary data from the collaboration with Cochlear to be disclosed in the first half of next year. If positive, we are anticipating a deal to be signed between the two companies, allowing us to include this opportunity in our valuation.

Newsflow

Sensorion's newsflow should be dense in the upcoming months with key readouts for assets that are in clinical trials, as well as strengthening of the company's early-stage pipeline of products addressing inner ear diseases.

- **Clinical readouts**

By the end of the year, Sensorion is expected to report the interim safety readout for SENS-401 in Sudden Sensorineural Hearing Loss (SSHL). In Q2 2020, we are anticipating top line results from this study to presented. If positive, it should lead Sensorion to start a phase II/III clinical study to assess SENS-401's potential in Cisplatin-induced Ototoxicity.

- **Broadening the portfolio of products in hearing loss**

Meanwhile, Sensorion should also strengthen its early-stage pipeline of products addressing hearing loss disorders with the follow-up from preclinical trials carried out by Cochlear and the beginning of preclinical in-vivo studies for the gene therapy programme.

Fig. 6: Sensorion 2019-2020 expected newsflow

PERIOD	EVENT	PRODUCT	INDICATION	COMMENTS
H2 2019	Ph II results	SENS-401	Sudden Sensorineural Hearing Loss	Interim safety readout
H1 2020	Start Preclin	Cochlear partnership	Undisclosed	Led by Cochlear
Q2 2020	Ph II results	SENS-401	Sudden Sensorineural Hearing Loss	Efficacy results
2020	Start Ph II/III	SENS-401	Cisplatin Induced Ototoxicity	US+EU trial in paediatric pop.
2020	Start Preclin.	Gene Therapy	Usher T1 syndrome	

Source: Company data; Bryan, Garnier & Co ests.

Part 3: Pasteur partnership makes future sounds great

A transformative world-class partnership in gene therapy

A UNIQUE OPPORTUNITY TO ESTABLISH ITSELF AS A GENE THERAPY PLAYER

Back in May, Sensorion announced the signature of a research partnership framework agreement with the Genetics and Physiology of the Hearing Unit of the Institut Pasteur. In detail, this collaboration grants Sensorion an option to obtain exclusive licenses to develop and market drug candidates in gene therapy from collaborative projects in the hearing disorders space.

Before diving in the two programmes covered by this agreement, it is worth highlighting that the team led by Pr. Christine Petit (also chairman of the scientific advisory board of Sensorion) at the Institut Pasteur has developed world-class expertise over the last 25 years in the molecular physiology and physiopathology of the hearing system. Their most recent works have led to the development of a breakthrough gene therapy programme which restored hearing in a mouse model of DFNB9 (otoferlin) deafness[1].

Other recent advances include the pathophysiology of hearing loss associated with mutations of the gene encoding clarin-1, a protein playing an essential role in the auditory system. It has been identified as one of the genes associated with Usher Syndrome type III. While the otoferlin programme is covered by the current terms of the agreement, this programme could provide an option for Sensorion to further strengthen its gene therapy pipeline in the future.

In a nutshell, we believe that it is a unique opportunity for Sensorion to enter the highly promising gene therapy space while taking advantage of Institut Pasteur's expertise.

GENE THERAPY: ONE OF THE HOTTEST AREAS OF DEVELOPMENT IN THE BIOTECH INDUSTRY

Gene therapy development has taken a drastic turn in the past few years. Following strong investment by venture investors and Big Pharma, the volume of active gene therapies has increased very strongly. It ultimately led to the approval of drugs such as Luxturna or Zolgensma, a gene therapy for children with spinal muscular atrophy priced at USD2.1m. Its strong commercial performance (USD175m) since its US FDA approval in May is particularly promising for the commercial outlook of the whole field, and thus for Sensorion's early gene therapy programmes for hearing loss.

These successes have generated a lot of interest for gene-therapy companies, leading to more than USD10bn being spent for the first 9 months of 2019 in M&A in this field (including Roche's planned acquisition of Spark Therapeutics, expected to close by year's end). Most recent transaction is Audentes' acquisition by Astellas for USD3.0bn, as shown in Fig. 7.

[1] Akil O et al.Dual AAV-mediated gene therapy restores hearing in a DFNB9 mouse model. Proc Natl Acad Sci U S A.

Fig. 7: Selected gene therapy acquisitions and partnerships in 2019

Date	Buyer	Target company	Type of deal	Comments
January	Neurocrine	Voyager	Collaboration	USD **165m** (upfront), up to USD **1.7bn** in milestones
January	Janssen	MeiraGTx	Collaboration	USD **100m** (upfront), up to USD **340m** in milestones
February	Roche	Spark	Acquisition	USD **4.3Bn**
February	AbbVie	Voyager	Collaboration	USD **65m** (upfront), up to USD **245m** in milestones
March	Biogen	Nighstar	Acquisition	USD **800m**
March	Pfizer	Vivet	15% Equity stake	USD **51m** with a USD **636m** option to acquire
May	Amicus	Upenn	Collaboration	Up to USD **50m**
September	Castle Creek	Fibrocell	Acquisition	USD **63m**
December	Astellas	Audentes	Acquisition	USD **3.0Bn**

Source: Bryan, Garnier & Co

Several other companies are following Sensorion's move in hereditary hearing loss with gene therapies targeting congenital hearing disorders, such as Akouos or Otonomy. Little information has been disclosed so far by Akouos, but it appears that the company is also developing a dual-AVV candidate for otoferlin deficiency, further validating Sensorion's approach in our view. On the other hand, Otonomy recently announced a collaboration with AGTC (a US company listed on the NASDAQ) to develop an AAV-based gene therapy for patients with a GJB2 (Gap Junction protein Beta 2 gene) hearing loss.

Sensorion's pipeline gains two promising gene therapies

HEREDITARY MONOGENIC HEARING LOSS: A PERFECT MATCH FOR GENE THERAPY

The inner ear is a good candidate for gene therapy for several reasons: (1) it is reasonably self-contained anatomically, allowing easy and direct delivery of gene therapy; (2) it is a fluid-filled organ, which allows for widespread diffusion of the delivered gene; (3) a vast majority of hearing loss are monogenic and (4) hair cells have the advantage of not dividing themselves, avoiding the loss of the newly integrated gene.

Gene therapy for hearing loss is all the more interesting because half of the cases of non-syndromic profound congenital deafness have a genetic cause, and most (c. 80%) are autosomal recessive forms. Prosthetic cochlear implants are currently used for rehabilitation, but hearing recovery is far from perfect, particularly for the perception of speech in a noisy environment or of music, highlighting a need for more targeted curative treatments possibly including gene therapy[2]. Gene- and cell-based therapies may potentially preserve or restore hearing with more natural sound perception, since their theoretical frequency resolution power is much higher than that of cochlear implants.

[2] Akil O et al. Dual AAV-mediated gene therapy restores hearing in a DFNB9 mouse model. Proc Natl Acad Sci

USHER SYNDROME TYPE 1 & OTOFERLIN: TWO PROMISING PROGRAMMES TO BEGIN WITH

For now, the terms of the agreement cover two specific programmes aiming to correct hereditary monogenic forms of deafness: **Usher Type 1** and a type of deafness caused by a mutation of the gene encoding **Otoferlin**. Both have reported very promising results and should start their respective preclinical studies before the end of the year.

Beyond these two, Sensorion has negotiated preferential access to any other assets in the field of genetic inner ear diseases coming from the Institut Pasteur, making it a rich source of programmes that will feed Sensorion's pipeline in the future. In the light of the Institut Pasteur's reputation in the field, we believe that this partnership already puts Sensorion at the forefront of the highly attractive gene-therapy space.

Usher syndrome: the most advanced programme of the collaboration

A RARE GENETIC CONDITION WITH NO CURE

Usher syndrome (USH) is the **leading genetic cause** of combined hearing and vision loss. It is a rare genetic condition that affects 16,000–20,000 people in the United States alone, and is responsible for 3–6% of early childhood deafness. It is defined by a bilateral sensorineural deafness that originates in the cochlea (the auditory sensory organ) and a loss of vision due to retinitis pigmentosa which can be explained by the fact that retinal and cochlear sensory cells present similarities in terms of development and functionality.

As shown in Fig. 8, there are three clinical types (USH1, USH2 and USH3) classified according to the severity and early onset of the attack auditory, presence or not of an achievement of balance, and the age of onset of the retinal disease. USH1 and USH2 are the most common forms, accounting respectively for c.45% and c.55% of all Usher cases.

Fig. 8: Comparison of the three Usher Syndrome subtypes

	Type 1	Type 2	Type 3
Hearing	Profound hearing loss or deafness at birth.	Moderate to severe hearing loss at birth.	Progressive hearing loss in childhood or early teens.
Vision	Decreased night vision by age 10, progressing to severe vision loss by midlife.	Decreased night vision by adolescence, progressing to severe vision loss by midlife.	Varies in severity and age of onset; night vision problems often begin in teens and progress to severe vision loss by midlife.
Balance (vestibular function)	Balance problems from birth.	Normal balance.	Normal to near-normal balance in childhood; chance of later problems.

Source: NIDCD (NIH)

Of three subtypes, Usher type I (USH1) is the **most severe form**. USH1 patients suffer profound sensorineural hearing loss, balance deficiency and progressive blindness. To date, 12 loci are known for Usher syndrome, and for 10 of these loci, the genes involved have been identified. Eight loci are known for Usher syndrome type I, and the six causative genes are *MYO7A*, *CDH23*, *USH1C*, *PCDH15*, ***USH1G***, and *CIB2*.

Patients affected by both sensorineuronal hearing impairment and balance disorders due to inner ear defects are currently fitted with auditory prostheses, but outcomes remain variable from one patient to another. **Therefore, scientists at Institut Pasteur tested local gene replacement as an alternative approach to cure deafness and balance disorders in a mouse model of Usher syndrome type 1G.**

THE ONLY GENE THERAPY IN DEVELOPMENT FOR USHER TYPE 1G

Pasteur's scientists have been focusing on the *USH1G* mutation

Among all the genes involved in USH1 (as shown in Fig. 9), scientists from the Institut Pasteur have focused their efforts on one of the most severe forms: **Usher type 1G**. It is associated with mutations in the *SANS* gene, encoding the same name (Sans, scaffold ankyrin and sterile alpha motif-containing protein). While epidemiology data are sparse regarding this specific subtype, discussions with KOLs led us to believe that it could represent around **2,000 patients in the US** and **1,500 patients in Europe**.

Fig. 9: Usher type 1: phenotypes, genes and associated proteins

	Surdité	Phénotype Atteinte vestibulaire	Rétinite pigmentaire	Locus	Gène	Protéine	Fonction	Localisation
Usher de type 1	Congénitale profonde	Aréflexie vestibulaire bilatérale congénitale	Début pré-pubertaire	USH1B	MYO7A	myosine VIIa	Protéine motrice : transport des autres protéines USH le long des filaments d'actine du stéréocil	Autour de l'extrémité intracellulaire du lien apical Plaque cuticulaire
				USH1C	USH1C	harmonine	Protéine d'échafaudage : lien entre les protéines du lien apical et le cytosquelette d'actine	Autour de l'extrémité intracellulaire du lien apical
				USH1D	CDH23	cadhérine 23	Protéine d'adhérence intercellulaire constitutive du lien apical	Partie supérieure du lien apical
				USH1F	PCDH15	protocadhérine 15	Protéine d'adhérence intercellulaire constitutive du lien apical	Partie inférieure du lien apical
				USH1G	USH1G	Sans	Protéine d'échafaudage : lien entre les protéines du lien apical et le cytosquelette d'actine	Autour de l'extrémité intracellulaire du lien apical
				USH1J	CIB2	CIB2	Protéine de liaison au Ca^{2+} et à l'intégrine	Autour de l'extrémité intracellulaire du lien apical

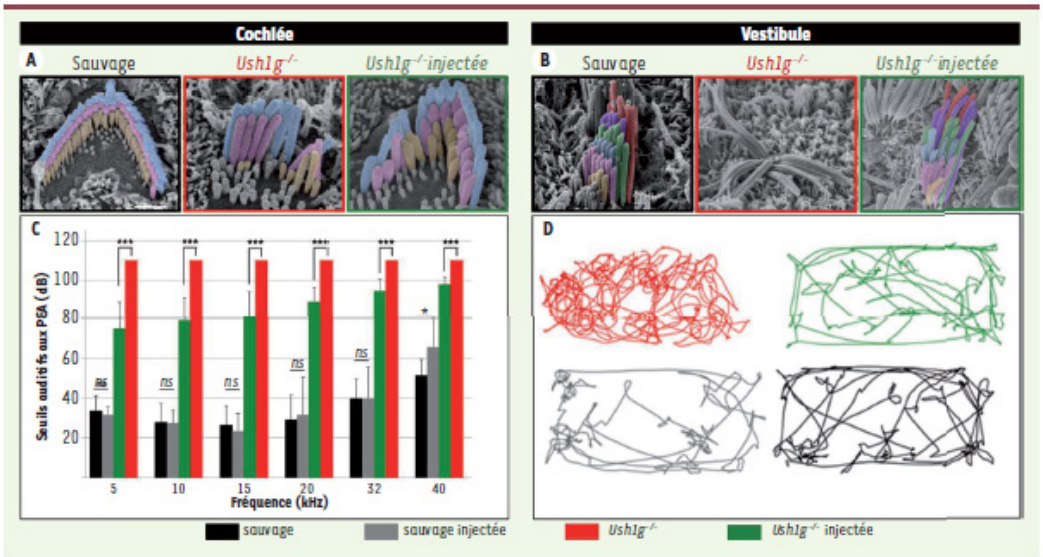
Source: Calvet C. et al, Progrès de la thérapie génique

USH1G patients are born with **profound deafness** associated with **severe imbalance disorders** that are followed by progressive retinal damage **progressing to blindness**. This visual loss hinders lip reading and limits compensation for vestibular disorders, thus aggravating the disability of these patients. While **no curative treatment** is available for those patients, scientists from the Institut Pasteur have developed a gene therapy that has shown promising results in mice so far, providing a basis for future clinical trials in humans.

First results in mice are promising

To treat those patients, scientists came up with a gene therapy based on an adenoassociated virus 8 (AAV8) which deliver the *SANS* complementary DNA (cDNA) directly to the inner ear hair cells. In a mouse model of Usher Syndrome type 1G, this therapy has demonstrated a long-term restoration of inner ear functions. The gene replacement therapy efficiently restored the structure and function of inner ear hair cells in *Ush1g*$^{-/-}$ mice and **prevented** the balance deficit, while **limiting** the hearing impairment for low sound frequencies (as shown in Fig. 10).

Fig. 10: Both restoration of the structure and function of sensory cells in the inner ear



Source: Calvet C. et al, Progrès de la thérapie génique

Indeed, video-tracking in an open-field chamber (part D of Fig.10) showed that injected *Ush1g*$^{-/-}$ mice explored the field in a manner similar to control mice, without circling behaviour (which is a key symptom of *Ush1g*$^{-/-}$ mutant mice), highlighting the **almost complete restoration of vestibular functions**.

On the other hand, the only partial hearing restoration reported by mice injected with *Ush1g*$^{-/-}$ is still very promising given that: 1/ *Ush1g*$^{-/-}$ mice are profoundly deaf and did not show any response to sounds of intensities of up to 110 dB; and 2/ higher rates of hair cell transduction in the vestibular end organs than in the cochlea raise the **hope of a full restoration of hearing** by increasing the transduction rates in the cochlear hair cells in the future.

Finally, one of the most important findings of this study is that the time window for treating deafness and balance disorders by gene transfer in patients with USH1 **may be larger** than initially thought, given that mutant mice already have severe structural abnormalities in the sensory cells of the inner ear at birth that have been corrected by gene therapy. If proven clinically, it should expand the therapeutic window of such therapies to older patients.

EUR300M OF SALES AT PEAK

Large addressable patient pool should drive sales from day one

We are expecting sales of the Usher type 1G gene therapy to come from two distinct pools of patients (existing Usher 1G patients and new cases from births). While Usher syndrome is seen as one of the major causes of genetic deafness and blindness, and the type 1 is believed to represent around 45% of all User cases[3], epidemiological data regarding the specific 1G subtype remain sparse.

Following a review of several published studies and multiple contacts with the company, we believe that there are around **3,500 existing patients with Usher 1G** (1,500 in the US and 2,000 in Europe) and 200 new births on each side of the Atlantic per year.

Firstly, we believe that around 50% of existing patients with Usher type 1G will benefit from this therapy and that Sensorion's gene therapy will capture 10% of these patients from the very first year of commercialisation. This pool of patients should drive sales in the first years of marketing and be quickly drained. The second source of revenues will come from the **400 new cases** each year of type 1G worldwide.

A USD400k pricing seems coherent with the expected benefits

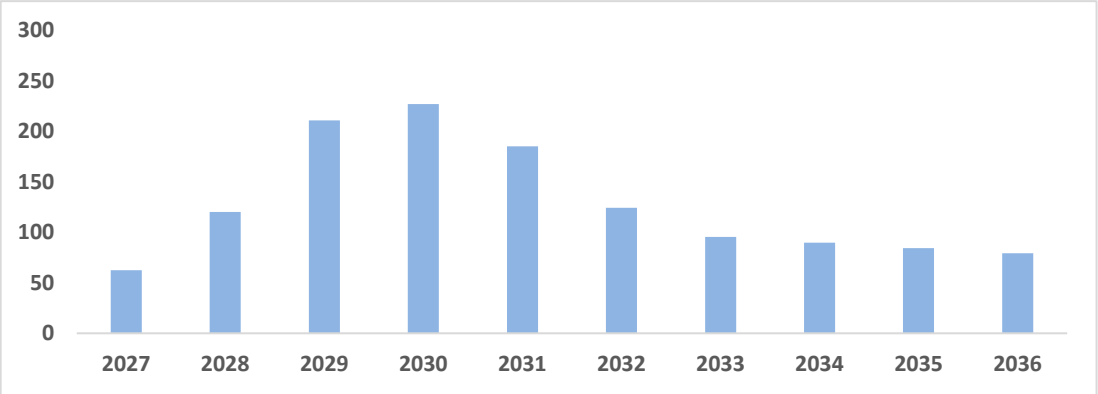
We have based our estimation on the lifetime cost of cochlear implants, which remains today the **standard-of-care therapy** for those patients. Given that the company is aiming to reduce deafness' severity from profound to severe hearing loss (requiring only hearing aids), we believe that the cost of such therapy (if proven effective) should reflect the cost savings achieved by avoiding cochlear implants in favour of cheaper hearing aids.

Indeed, cochlear implants are a significantly more expensive option, costing USD60k each, and have to be replaced four times representing a total cost of USD480k over a lifetime. On the other hand, hearing aids only cost USD5k a pair lasting between 5 to 8 years. Assuming an 80-year implant life, a lifetime treatment with hearing aids should represent only c.USD33k.

Therefore, it is fair to assume that a treatment allowing patients to avoid expensive cochlear implants in favour of cheaper hearing aids could be priced **around USD400k**, thus accounting for our price assumption.

[3] Petit C. Usher syndrome: from genetics to pathogenesis. Annu Rev Genomics Hum Genet.

Fig. 11: Estimates of Usher type 1G gene therapy sales (EURm)



Source: Bryan, Garnier & Co ests.

Luxturna's clinical development pathway as a proxy suggesting first sales in 2027

In terms of clinical development, we base our assumptions on Luxturna's clinical development, the first gene therapy for a genetic disease approved by the FDA. Therefore, we are anticipating one phase I/II trial in 12 patients lasting two years, followed by a three-year confirmatory phase III study in 30 patients allowing to file on the basis of the one-year follow-up data.

Otoferlin: a second gene therapy supported by public funding

FUNDED UNTIL CLINICAL STAGE THROUGH THE AUDINNOVE PROJECT

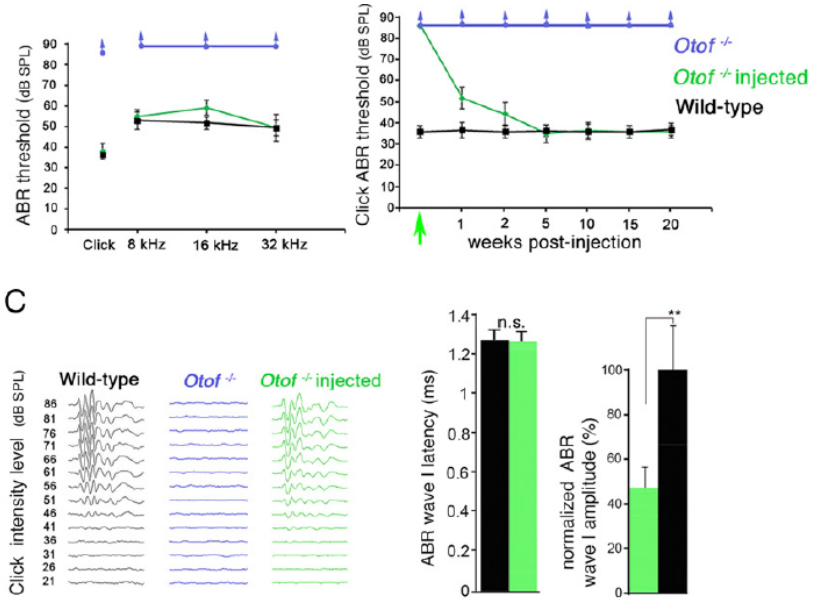
Following the Usher 1G programme, Sensorion's second gene therapy programme aims to correct an inherited monogenic form of deafness caused by a mutation in the gene encoding for the Otoferlin protein (DNBF9). It is supported by funding from the public investment programme "Avenir" in the form of the AUDINNOVE project. With a EUR9.7m funding grant, this project gathers world-class actors with a single objective: **to develop a gene therapy programme for otoferlin deficiency up to the clinical stage.**

PRELIMINARY FINDINGS RAISE HOPE FOR A GENE THERAPY FOR DFNB9 PATIENTS

DFNB9 deafness is a hearing disorder that represents one of the most frequent cases of congenital genetic deafness. Individuals with DFNB9 deafness are **profoundly deaf** as they are deficient in the gene coding for **otoferlin**, a protein that plays a key role in transmitting sound information at the inner hair cell synapses. Indeed, it enables the sensory cells of the ear (hair cells) to release neurotransmitter in response to stimulation by sound to activate auditory neurons. Without functional otoferlin protein, auditory signals received by the ear cannot be transmitted to the brain.

To tackle this condition, scientists of the Institut Pasteur used an adeno-associated viral (AAV) vector to deliver a healthy copy of the OTOF gene to cochlear hair cells, with the goal of restoring long-term physiologic hearing following a single administration to the inner ear. Initial findings in Otof$^{-/-}$mutant mice are promising and have fueled confidence to further investigate it.

Fig. 12: Otoferlin gene therapy in Otof$^{-/-}$ mice on postnatal day 17



Source: Dual AAV-mediated gene therapy restores hearing in a DFNB9 mouse model

Indeed, scientists have reported that their DFNB9 gene therapy can effectively restore production of the full-length protein, resulting in a **long-lasting correction of the profound deafness** phenotype of these mice. It's worth highlighting that this gene therapy not only prevented deafness in Otof$^{-/-}$ when administered before hearing onset, but also **reversed the deafness phenotype** in a sustained manner when administered well after hearing onset.

A MUCH BIGGER OPPORTUNITY THAN USHER 1G WITH EUR400M AT PEAK

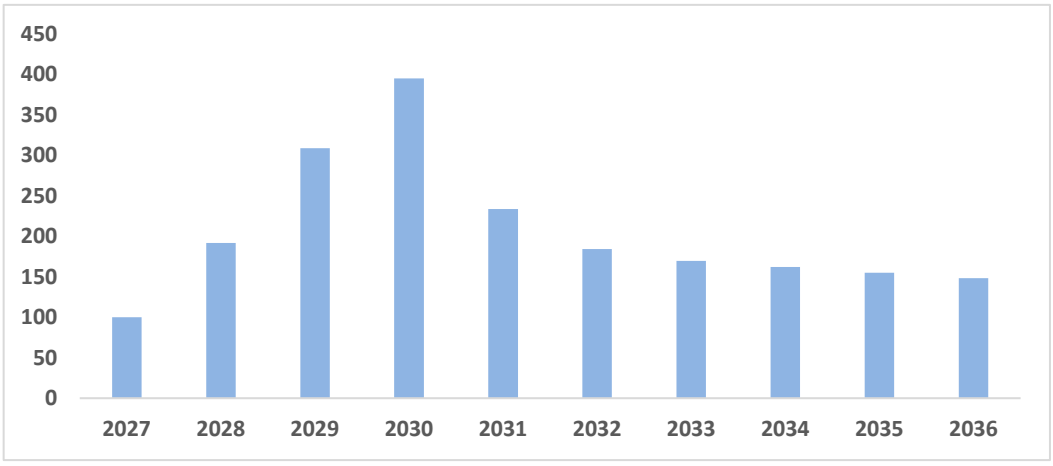
As seen before in Usher 1G, we are also expecting that this gene therapy will both address existing patients and newborns affected by this disorder. However, in this case epidemiological data regarding DNFB9 are more common.

Firstly, regarding the incidence of Otoferlin deficiency, the company estimates that it represents up to **8%** of all prelingual non-syndromic hereditary hearing loss. Given that it represents between 15k and 20k new cases per year, we believe that it could translate into more than **1,100 births per year** in the US and in Europe. In this case, we anticipate Sensorion to only capture at peak 50% of the market due to potential competition from Akouos, a privately-owned US company currently developing an Otoferlin gene therapy in very early stages of development.

Therefore, we have estimated that the pool of pre-existing patients with Otoferlin deficiency between 0 to 4 years should represent **4,400 patients** derived from the 1,100 births/year number mentioned above. From this pool of patients, we also estimate that considering Akouos potential competition, Sensorion could treat 50% of those patients at peak.

Finally, given the parallels with Usher 1G, we have taken the same pricing assumption (EUR360k in the US and EUR252k in Europe), as well as a similar clinical development pathway allowing first sales as of 2027.

Fig. 13: Estimates of Otoferlin gene therapy sales (EURm)



Source: Bryan, Garnier & Co ests.

Part 4: SENS 401: Our main value driver

From sudden deafness to drug-induced ototoxicity

A SELECTIVE 5-HT3 RECEPTOR ANTAGONIST PREVENTING INNER EAR'S LESIONS

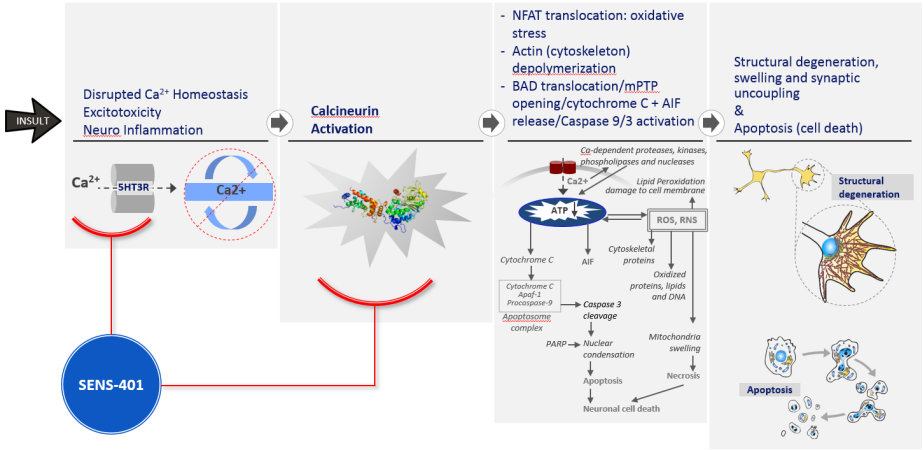
SENS-401 (R-azasetron besylate) is an enantiomer of the R-S azasetron chlorydrate, **a marketed selective 5-HT3 receptor antagonist** in Japan in the mid-1990s, but never approved in the EU or the US, for its antiemetic capacity in chemotherapy patients. Sensorion initially based its SSNHL programme on this asset, until the moment they discovered that its enantiomer (SENS-401) demonstrated a better pharmacokinetic profile, making it an **even more attractive candidate** for further development.

It was also an opportunity to strengthen Sensorion's intellectual property by using a proprietary asset. Sensorion received ODD (orphan drug designation) for SENS-401 in Europe for the treatment of SSNHL and in the US for the treatment of platine-induced ototoxicity.

A NEUROPROTECTIVE EFFECT THROUGH CALCINEURIN INHIBITION

In the 1990s, 5-HT3 receptors have revolutionized the treatment of chemotherapy-induced emesis. Nonetheless, other therapeutic potentials of this class were neglected for years until recent investigations demonstrated that these compounds could alleviate the pathology of certain neurodegenerative and neuropsychiatric disorders. Starting with inner ear diseases where multiple studies suggested that those therapies could be of interest.

Fig. 14: SENS-401's MoA through calcineurin inhibition and 5-HTR3 antagonism



Source: Sensorion

Before clarifying SENS-401 mechanism of action, it's worth recalling that it has been proved that a cellular stress (such as a hearing trauma) activate the **calcineurin pathway** leading to death of cells through inflammation, structural degeneration and oxidative stress, making it a potential therapeutic target. Since then, several publications have demonstrated that calcineurin inhibition reduce hearing loss in pre-clinical models of noise-induced hearing loss and clinical cases of Sudden Sensorineural Hearing Loss (SSNHL), **further validating SENS-401's potential**.

SSNHL: SENS-401 main opportunity

ANY IMPROVEMENT IN HEARING WILL BE WELCOMED BY PATIENTS AND PHYSICIANS

Sensorineural hearing loss is principally caused by damage or death of sensory hair cells in the cochlea. While it is widespread, Sudden Sensorineural Hearing Loss (SSNHL) is a rarer condition affecting 27 per 100,000 individuals (c.60k in the US) annually characterized by:

- A hearing reduction of **at least 30 dB** over at least three contiguous frequencies;
- **Rapid onset** (within 72h) of a subjective sensation of hearing impairment;
- No identifiable cause in more than **70% of all cases**;
- **Permanent, disabling hearing loss** in more than 50% of cases.

While being mostly idiopathic, it may be the result of **multiple etiologies**. The leading ones being vascular events, viral infection, and autoimmune disorders. Even if some patients recover spontaneously, more than **half of them** remains impacted by hearing loss for the rest of their lives. Even if it is typically unilateral, this hearing loss can have a significant impact on cognitive and auditory function, substantially **reducing their quality of life**.

Unfortunately, there are **no approved treatments** that improve hearing recovery for those patients, and the ones currently used remain somewhat **controversial**. It appears that both oral and intratympanic corticosteroids have *de facto* established themselves as an accepted off-label standard of care while there is no firm evidence to support their efficacy and they are not actively recommended (as shown in Fig. 15).

Fig. 15: Management of Patients with SSNHL

Treatment	2006 (%)	2007 (%)
Systemic corticosteroids alone	41.08	40.45
IT injection alone	1.19	1.24
Systemic corticosteroids and IT injection	2.24	4.32
Other or no treatment	55.49	53.99
	100.00	100.00

Source: Incidence of sudden sensorineural hearing loss

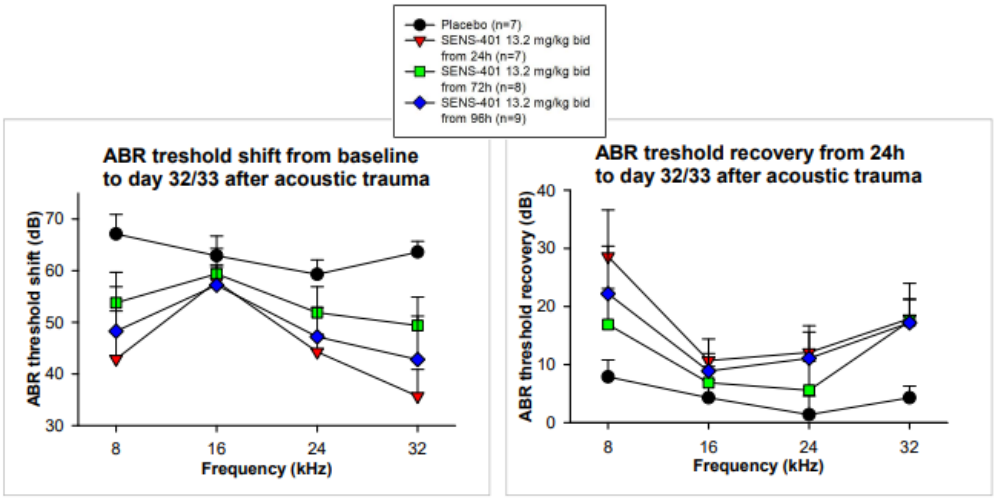
According to the clinical practice, steroids are an option since "even a small possibility of hearing improvement makes this a reasonable treatment to offer patients, considering the profound impact on quality of life a hearing improvement may offer".

At the end of the day, a majority of patients remains untreated, highlighting the fact that SSNHL remains a challenging condition and, at the same time, the main unmet need for effective treatment options. Therefore, **any treatment that improves hearing and/or reduces the risk of persistent hearing loss will be warmly welcomed by patients and physicians.**

SENS-401 SHOWED PROMISING DATA IN NOISE-INDUCED COCHLEAR LESIONS

In a *peer-reviewed* article published in Otology & Neurology, SENS-401's potential has been assessed in a male rat model of acute acoustic trauma-induced hearing loss. Following the induced trauma, rats received either twice daily placebo or SENS-401 *per os* for 28 days (which is the length of follow-up required by the EMA, 91 days for the FDA). Authors have reported both *in vivo* and histological evidence of **significant improvements in hearing loss**.

Fig. 16: Effect of delaying initiation by 24-, 72- and 96-hours post-trauma

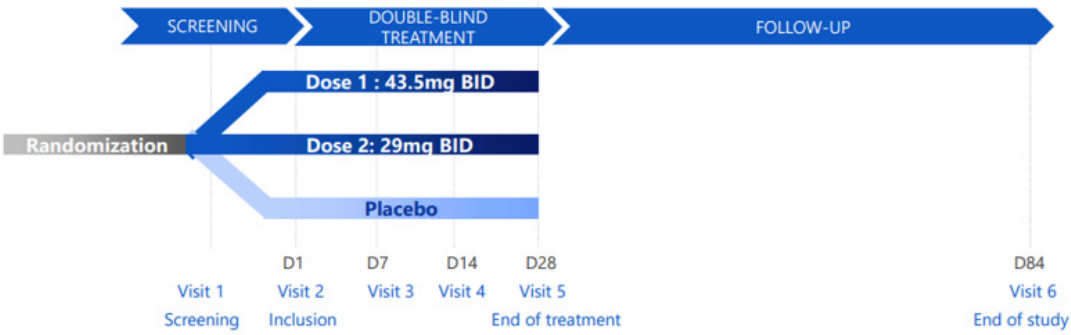


Source: Otology & Neurology; ABR: Auditory Brainstem Responses

As a whole, it has been showed that SENS-401 led to a reduction of auditory deficit, an improvement in terms of recovery and a reduction in hair cell loss. Two of the main findings of the study are: 1/ **earlier intervention** with SENS-401 has been associated with the greatest treatment benefits; and 2/ it offered significant otoprotection **even after an initiation delay of up to four days** post trauma.

Following this study, a phase I clinical trial in 35 healthy volunteers has been completed allowing selection of the doses to be used in phase 2 testing: 29mg and 43.5mg twice a day for 28 days. The primary endpoint is the **10dB hearing improvement** on three frequencies versus placebo which is considered meaningful by both the FDA and the EMA.

Fig. 17: SENS-401 phase 2 clinical trial



Source: Sensorion

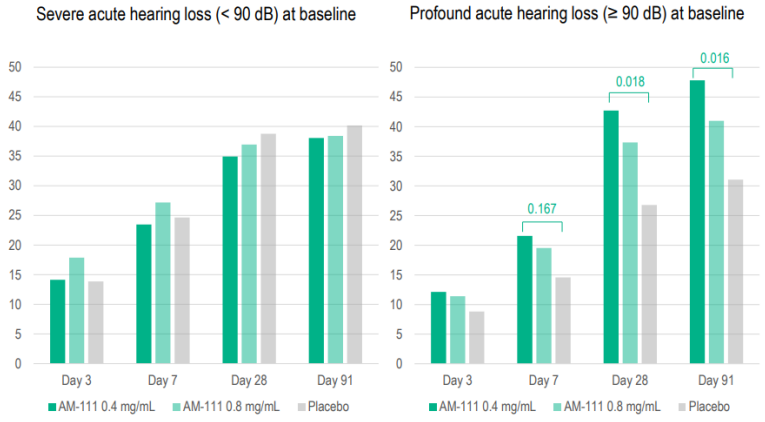
While interim safety results will be presented before the end of the year, top line results should be disclosed before the end of Q2 2020. Even if Auris Medical's recent setbacks illustrated the difficulty to develop drugs in SSNHL, **we believe that SENS-401 is a better product in every way**.

AURIS MEDICAL'S SETBACK SHOULD NOT OVERSHADOW SENS-401 POTENTIAL

Among the few assets currently in clinical development in Hearing Loss, AM-111 is by far the most advanced of all. It is an inhibitor of the JNK stress kinase, formulated as a gel to be administered in a single dose intratympanic injection into the middle ear. This drug binds to JNK, an enzyme activated following cochlear stress that could lead to SSNHL. By inhibiting it, AM-111 was believed to prevent SSNHL to mediate apoptosis and inflammatory response which could result in irreversible loss of hair cells and cochlear neurons.

Back in January 2018, the company announced that it failed to meet the primary endpoint of its HEALOS phase III clinical study. While it has naturally weighed on Auris Medical's share price, we believe it has also **unfairly impacted** Sensorion since then. As we approach SENS-401's phase II results, it's worth looking at those results.

Fig. 18: Hearing recovery from baseline (dB) from HEALOS phase III



Source: Auris Medical

While it failed to prove its efficacy in the overall population, a *post-hoc* analysis showed that it was clinically meaningful in the subpopulation of patients with profound acute sudden deafness (≥90dB), as shown in Fig.18. After an extended review of their data, we believe that this trial failed for two reasons that are specific to this asset:

- Firstly, we believe that it can be explained by AM-111's biological effect which only come into play if the injury is **severe enough** to trigger activation of the JNK pathway. If it does not get activated, the drug has no target. But it turns out that only very loud noise (around 110-120dB) resulted in activation of JNK in mice while sound exposure at 90dB only caused temporary hearing loss, preventing AM-111 to be effective in this less traumatic condition.
- Secondly, preclinical data of AM-111 have suggested that its therapeutic window after hearing loss was only about six hours, whereas clinical trials included patients up to 48h (phase II) and 72h (phase III) after onset. It's worth mentioning that a Finnish research group has independently demonstrated peak activity of JNK at six hours (in line with AM-111's preclinical data) and no activity after 22 hours in a model of SSNHL. By enlarging the window treatment, they exposed themselves to patients **less likely to respond** properly.

Unfortunately, this set of data was not enough to convince the FDA, which asked the company to launch a novel phase III trial in this population of more severe patients. Since then, the company is actively looking for a partner to conduct such study, without success so far.

While it has been considered as a negative read-across back then, we believe that in fact it gave hope regarding this very challenging indication and in the meantime, it has **excluded** a potential competitor.

UP TO EUR230M IN SSNHL ALONE

Following the ongoing phase II clinical trial assessing SENS-401's potential in 276 patients with SSNHL (results anticipated by end of Q2 2020), we are expecting the company to start a **registrational phase III clinical trial in 300 patients** before the end of next year (to be confirmed by an end of phase II meeting).

We believe that a premium pricing is achievable as suggested by a health economic model for novel therapeutics for hearing loss. Indeed, this study showed that novel therapeutics for SSNHL should lead to an **incremental net monetary benefit of £39k** over current standard-of-care.

Therefore, we believe that our pricing assumption are conservative (US: EUR15,000 and EU: EUR7,500). With a market share of 30% at peak, up to EUR230m in sales is achievable, from which we deduct a 3% royalty rate in favour of INSERM. We anticipate a launch as of 2025, following a phase III study expected to enroll around 300 patients (to be confirmed after end of phase II meeting if 2 pivotal studies are required for the US).

Cisplatin-induced ototoxicity: SENS-401's second indication

HIGHLY BURDENSOME SIDE EFFECTS OF CHEMOTHERAPIES

Cisplatin is one of the main chemotherapeutic agents used for children with solid tumour (especially in neuroblastoma and hepatoblastoma). Although the application of cisplatin has produced a **significant increase of overall survival**, many paediatric survivors suffer from serious side effects, such as **ototoxicity**. In children, the reported incidence of hearing loss ranges from 4% to 80% following cisplatin administration. This side effect is all the more **detrimental to young children** given that it will affect language and social development[4].

In the US, it is estimated that approximately **5,000 children** receive platinum-based chemotherapy annually, and up to 10,000 globally. Of these, 40% to 90% develop profound and irreversible ototoxicity. Age at the time of diagnosis and treatment is a significant risk factor for treatment induced ototoxicity. Children five years of age and under are at a **21-times greater** risk of developing hearing loss compared to adolescents.

Unfortunately, existing strategies for mitigating ototoxicity are unsatisfactory, requiring many children to use lifelong hearing aids and cochlear implants. It's worth mentioning that the average cost for hearing aids is **USD4,600** and they have an expected lifespan of 5 to 8 years.

Therefore, there is an urgent need to find less toxic alternative cancer therapies, as well **as novel treatments to mitigate and compensate the effects of hearing loss.**

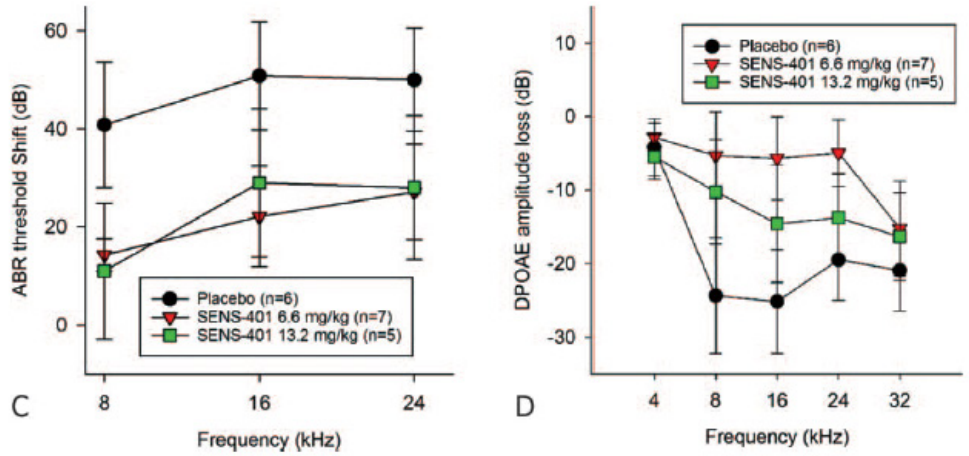
SENS-401 SHOWED POTENTIAL IN CISPLATIN-INDUCED HEARING LOSS MODEL

Back in 2017, Sensorion reported *in vivo* and histological evidence that daily oral treatment with SENS-401 significantly reduced cisplatin-induced hearing loss in rats treated with SENS-401 for 14 consecutive days after a severe acoustic trauma. Although early-stage, those data are promising in many respects.

- Firstly, when combined with cisplatin, SENS-401 does not impact its cytotoxicity which was one of the hurdles met by sodium thiosulfate (from Fennec Pharma) during its clinical development.
- Secondly, initial efficacy data in mice on well validated endpoints are very encouraging. As shown in Fig. 19, treatment with 6.6 and 13.2mg/kg SENS-401 for 14 days significantly reduced the ABR (auditory brainstem response) threshold shifts and the DPOAE (distortion product otoacoustic emission) amplitude losses. ABR is considered an accurate clinical indicator to predict the extent and form of hearing loss, whereas DPOAE is used in the clinic to identify early changes to auditory function and is considered appropriate for monitoring cisplatin ototoxicity.

[4] Wei M, Yuan X. Cisplatin-induced Ototoxicity in Children With Solid Tumor.

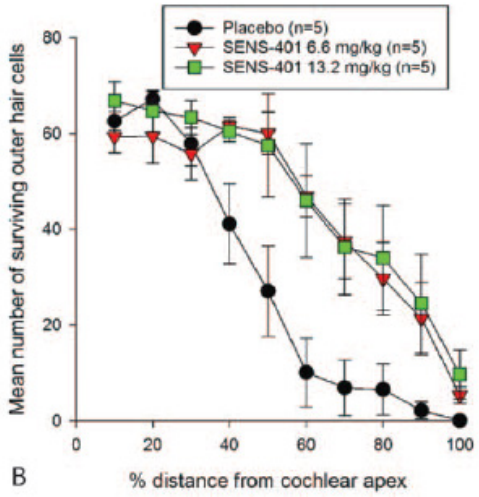
Fig. 19: Effect of SENS-401 on cisplatin-induced hearing loss in rats



Source: Oral Administration of Clinical Stage Drug Candidate SENS-401 Effectively Reduces Cisplatin-induced Hearing Loss in Rats.

Finally, the number of surviving OHCs (outer hair cell) was significantly higher in animals having received 14 days of treatment.

Fig. 20: Outer hair cell survival



Source: Oral Administration of Clinical Stage Drug Candidate SENS-401 Effectively Reduces Cisplatin-induced Hearing Loss in Rats.

All in all, we believe that those data support a phase II trial that should be initiated after the results in SSNHL expected for Q2 2020.

IS PEDMARK (FENNEC PHARMA) A THREAT FOR SENS-401?

Among the companies currently developing a drug candidate for cisplatin ototoxicity, US-based biopharmaceutical company Fennec Pharma is the most advanced, with a ready-to-file drug candidate.

PEDMARK (sodium thiosulfate) has reported positive clinical results from SIOPEL 6 pivotal study, a randomized, controlled trial of sodium thiosulfate for protection from cisplatin-induced hearing loss in children with **localized** hepatoblastoma. While it showed efficacy without compromising survival in this specific population of patients, it was not the case in its prior proof-of-concept ACCL0431 trial.

In that study, completed back in 2014, PEDMARK's potential was assessed in a broader population of children including multiple cancer types at any stage. While being effective in all patients, a *post hoc* analysis showed that participants with **disseminated disease** reported a **lower overall survival** for patients treated with sodium thiosulfate than for patients in the control group.

That is why the company initiated the SIOPEL 6 pivotal study in a more homogenous population of patients (**non-metastatic** hepatoblastoma patients) which did not compromise survival this time.

On top of that, it's worth mentioning that this treatment can only be given **six hours after the last dose of cisplatin,** whereas SENS-401 could be given during the infusion of cisplatin. Therefore, we believe that the SENS-401's otoprotective effect should be **higher** given that the ototoxicity of Cisplatin is already present in the lag period of six hours after the infusion. On the other hand, it could allow physicians to increase the doses of cisplatin and increase overall survival.

For all these reasons, we believe that SENS-401 has the potential to be **superior** to PEDMARK in all aspects. If approved, it should even benefit from the awareness created around the marketing of PEDMARK.

THE OTOTOXICITY OPPORTUNITY COULD ADD EUR C.180M AT PEAK

Unlike Pedmark, we believe that SENS-401 should be effective in all patients, even those with disseminated disease, allowing it to address a pool of new patients of more than 10k per year. Considering that it could capture up to 30% of this market at peak and that the pricing power is more significant in this indication than in the previous one (BGe: EUR65k US/EUR39k EU[5]), we believe that sales could reach almost EUR180m at peak. In terms of clinical development, we expect the company to start a registrational phase II/III next year, following results of the ongoing phase II in SSNHL. In line with Fennec Pharma's phase III, we believe that this trial will enrol 100 to 150 patients with timing to be confirmed after end of phase II meeting and a commercial launch as soon as 2025 upon approval.

[5] DionneF et *al*. Economic impact of a genetic test for cisplatin-induced ototoxicity.

An innovative collaboration with Cochlear further validating SENS-401

A POTENTIAL TREATMENT AGAINST HEARING LOSS AFTER COCHLEAR IMPLANT SURGERY

At the end of 2017, Cochlear (a global leader in implantable hearing solutions) and Sensorion announced a collaboration to improve hearing outcomes in patients **with cochlear implants**. The idea behind this partnership is to evaluate the combination of SENS-401 with cochlear implants.

A cochlear implant is a small, complex electronic device that can help to provide a sense of sound to a person who is profoundly deaf or severely hard-of-hearing. Unlike hearing aids — which amplify sound — a cochlear implant **bypasses damaged portions of the ear** to deliver sound signals to the auditory (hearing) nerve. However, in some cases, the surgery can be associated with the loss of residual hearing, damaging any remaining ability to hear.

Indeed, the surgery can be associated with mechanical trauma and other perturbations leading to **loss of sensitive outer hair cells**. This can translate in an acute loss of residual hearing of more than 30dB in about 20% of patients, and report late onset loss in up to 30% of patients.

With its **otoprotectant profile** and its demonstrated capacity to enhance hearing and outer hair cell survival in animal models, SENS-401 sounds like a perfect candidate to prevent hearing loss after implant surgery and support long-term functional stability of the implant. The company is currently carrying out additional studies to further assess its potential in this indication. **We expect a decision regarding the continuation of this collaboration in the first half of next year.**

Part 5: Executive management and capital structure

Executive management and Board of Directors

Nawal Ouzren - CEO

Nawal has over 15 years' experience in the pharmaceutical industry. She held various roles at Baxter including VP of the BioSimilars business unit before joining Baxalta in 2014 to lead the Haemophilia franchise. Following the acquisition of Baxalta by Shire in 2016, she headed the Genetic Diseases franchise of Shire where she supervised all marketing, business and strategy operations of the franchise which generated 25% of the group's turnover (c.USD2.7bn in sales 2016). In April 2017, Nawal took the reins of Sensorion as CEO.

Juergen Heitmann – Chief Business Officer

Juergen is a biologist by training with a PhD from the University of Tübingen where he already worked in the inner ear field. Juergen started his professional career in the medical device industry at Biotronik and as a Senior Consultant at McKinsey & Co. He then spent more than 20 years in the pharmaceutical industry in various Business Development roles at Novartis, Nycomed and Takeda. More recently he advised Venture Capital and Biotech companies on Corporate Development and Strategy topics. He started working for Sensorion in 2017 first as a consultant and since September 2019 as their Chief Business Officer.

Judith Laredo – Head of Clinical Development

Judith is PhD by training with extensive experience in Clinical Development and Alliance Management, gained over 20 years in pharmaceutical industry. She has worked on Proof of Concept Studies, Phase I in patient studies, Phase 2, through to global Phase 3 studies in Neuro-psychiatry as well as several alliance programmes in Oncology (CAR-T cells, Immunotherapy) at Servier Laboratory. She started working for Sensorion in 2016.

Jonas Dyhrfjeld-Johnsen – VP Research and Translational Development

Jonas has over 15 years of experience in CNS and inner ear research and development. He joined Sensorion in 2010, first as consultant, then as project leader responsible for the identification of targets and development of the company's in-vivo research platform in 2010 and head of pharmacology in 2015 before taking the lead of Research & Translational Development in 2018. Jonas is also a member of the company's board of directors. Before joining Sensorion he spent nearly two years at the INSERM. Jonas was a post-doctoral researcher at UCI (CA, USA) and research fellow at the Massachusetts General Hospital, the largest teaching hospital of Harvard Medical School.

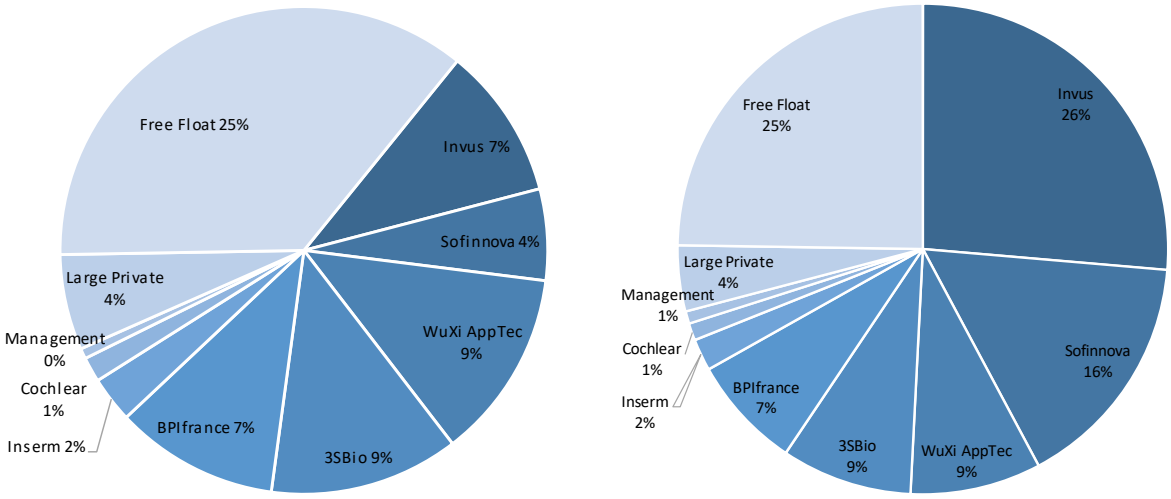
John Furey – Independent Board Member

John joined the board of directors in August 2019. He brings to Sensorion over 20 years of experience in the pharmaceutical industry at Pfizer, Baxter and Baxalta. We believe that his experience in gene therapy as COO of Spark Therapeutics before the company was bought by Roche for USD4.3bn should benefit Sensorion.

Capital Structure

On a fully diluted basis (assuming that Invus and Sofinnova OCs shall be converted at EUR1,3662 per share), Invus is the largest shareholder of Sensorion, with 26% of the capital. Invus has two seats on the board of directors of the company and is represented by Julien Miara and Khalil Barrage. Sofinnova, which has 16% of the capital, is represented by Cedric Moreau. Both Invus and Sofinnova structured the convertible bond issued in June, raised their stake in Sensorion in September and are locked until June 2020. During the later WuXi AppTec and 3SBIO, two Chinese pharmaceutical companies also entered the capital of Sensorion, but are not represented on the Board of Directors. BPIfrance is represented by Jean-François Morin and Chahra Louafi. We note that Cochlear took a stake in the company when the collaboration agreement was announced in late 2017. 4% of the Sensorion's capital is owned by three private individuals. Lastly, management has a 1% stake in the company.

Fig. 21: Sensorion capital structure (not diluted and fully diluted basis)



Source: Company data.

Part 6: Appendices

Historical milestones

Based in Montpellier (France), Sensorion was founded in 2009 as a spin-off from the Neuroscience Institute of Montpellier (INSERM) which still holds 2% of the company's capital. As of 30th June 2019 (latest available report), Sensorion had 35 employees including 30 dedicated to R&D activities. Since inception, Sensorion raised c.EUR94.8m of which 88% or EUR83.1m through various equity rounds.

- EUR83.1m in equity including EUR8m at IPO in 2015.
- EUR11.7m in non-dilutive funding (e.g. 0% rate loan from BPI or grant).

Fig. 22: Selected historical milestones

YEAR	MILESTONE
2019	Appointment of John Furey (former COO of Spark) as independent board member
'	positive DSMB for SENS-111 in AUV
	Deal with Pasteur in Gene Therapy
2018	Re-design of SENS-111 Ph II trial in AUV to accelerate recruitment
2017	Collaboration with Cochlear
'	ODD for SENS-401 in CIO
'	SENS-111 Ph II start in Acute Vertigo
2016	ODD for SENS-401 in SSHL
'	Positive Ph Ib results for SENS-111 in AUV
2015	IPO on Alternext Paris
2012	Option agreement with Palau Pharma for SENS-111
2009	Spin-off from INSERM

Source: Company data.

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Stock rating

BUY — Positive opinion for a stock where we expect a favourable performance in absolute terms over a period of 6 months from the publication of a recommendation. This opinion is based not only on the FV (the potential upside based on valuation), but also takes into account a number of elements that could include a SWOT analysis, momentum, technical aspects or the sector backdrop. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

NEUTRAL — Opinion recommending not to trade in a stock short-term, neither as a BUYER or a SELLER, due to a specific set of factors. This view is intended to be temporary. It may reflect different situations, but in particular those where a fair value shows no significant potential or where an upcoming binary event constitutes a high-risk that is difficult to quantify. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

SELL — Negative opinion for a stock where we expect an unfavourable performance in absolute terms over a period of 6 months from the publication of a recommendation. This opinion is based not only on the FV (the potential downside based on valuation), but also takes into account a number of elements that could include a SWOT analysis, momentum, technical aspects or the sector backdrop. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

Distribution of stock ratings

BUY ratings 48.5% NEUTRAL ratings 43.6% SELL ratings 7.9%

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