OTONOMY®

Targeted
Medicines
for the **Ear**

Corporate Presentation

May 9, 2018

Forward-Looking Statements

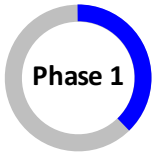
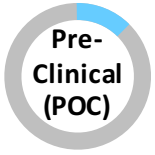
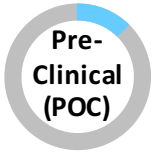
Safe Harbor Statement

These slides and the accompanying oral presentation (the "Presentation") contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements generally relate to future events or future financial or operating performance of Otonomy, Inc. ("Otonomy"). Forward-looking statements in this Presentation include, but are not limited to, timing of the next OTIVIDEX Phase 3 clinical trial, expectations regarding OTIVIDEX clinical trial design, timing of Phase 1/2 clinical trial for OTO-413, timing of Phase 1/2 clinical trial for OTO-313, financial guidance for 2018, timing of candidate selection for OTO-5XX and OTO-6XX programs, ability to fund completion of OTIVIDEX clinical development and having resources to advance our product pipeline, expectations regarding program advancements, milestones and value inflection points, and the ability of and timing for Otonomy to complete a commercial partnership or divestiture of OTIPRIO®. Otonomy's expectations regarding these matters may not materialize, and actual results in future periods are subject to risks and uncertainties. Actual results may differ materially from those indicated by these forward-looking statements as a result of these risks and uncertainties, including but not limited to: Otonomy's limited operating history and its expectation that it will incur significant losses for the foreseeable future; Otonomy's ability to obtain additional financing; Otonomy's dependence on the regulatory success and advancement of product candidates, such as OTIVIDEX, OTO-413 and OTO-313; the uncertainties inherent in the drug development process, including, without limitation, Otonomy's ability to adequately demonstrate the safety and efficacy of its product candidates, the nonclinical and clinical results for its product candidates, which may not support further development, and challenges related to patient enrollment in clinical trials; Otonomy's ability to obtain regulatory approval for its product candidates; side effects or adverse events associated with Otonomy's product candidates; competition in the biopharmaceutical industry; Otonomy's dependence on third parties to conduct nonclinical studies and clinical trials; Otonomy's dependence on third parties for the manufacture of its product candidates; Otonomy's dependence on a small number of suppliers for raw materials; Otonomy's ability to protect its intellectual property related to its product candidates in the United States and throughout the world; expectations regarding potential market size, opportunity and growth; Otonomy's ability to manage operating expenses; implementation of Otonomy's business model and strategic plans for its business, products and technology; and other risks. Information regarding the foregoing and additional risks may be found in the section entitled "Risk Factors" in Otonomy's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (the "SEC") on May 9, 2018, and Otonomy's future reports to be filed with the SEC. This Presentation is dated as of May 9, 2018, and Otonomy undertakes no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

Otonomy: Focus on Innovation in Neurotology

- Proven proprietary technology for targeted drug delivery to the ear
- Pipeline of products in areas of neurotology with high unmet need
- Successful OTIVIDEX™ Phase 3 trial demonstrates treatment benefit for Ménière's Disease; one additional pivotal trial for registration
- Advancing multiple programs for treating hearing loss and tinnitus
- OTIPRIO® now approved for use during ear tube surgery and AOE; evaluating commercial partnering options, including divestiture
- Strong balance sheet and reduced operating costs support advancement of multiple programs to value inflection points

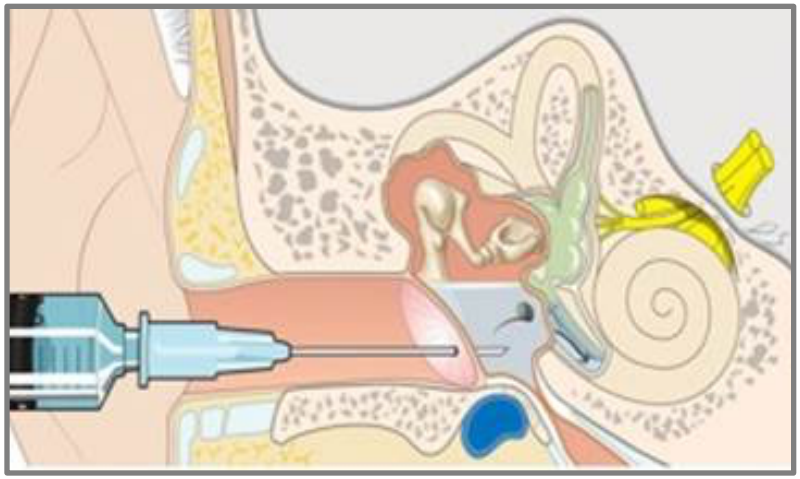
Broad Product Pipeline in Neurotology

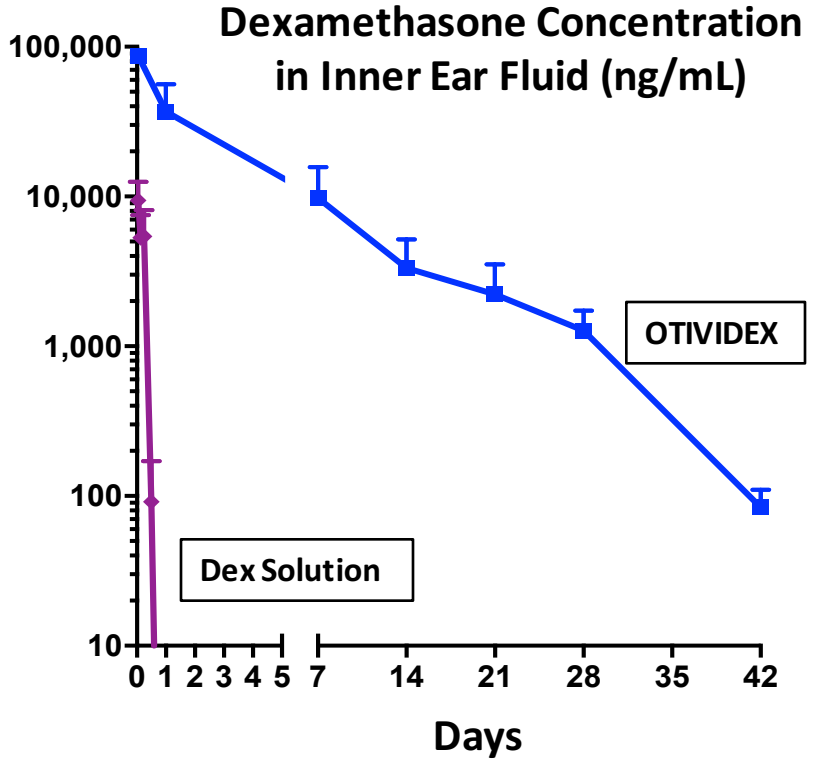
Program	Status	Population	Compound	Next Milestone
OTIPRIO		**Ear Tube Surgery** **Acute Otitis Externa**	Ciprofloxacin	**Commercial Partnership or Divestiture in Mid-2018**
OTIVIDEX		**Ménière's Disease**	Dexamethasone	**Initiate Phase 3 Trial in Mid-2018**
OTO-313		**Tinnitus**	Gacyclidine	**Initiate Phase 1/2 POC Trial in 1H19**
OTO-413		**Synaptopathy Hearing Loss**	Brain-derived Neurotrophic Factor (BDNF)	**Initiate Phase 1/2 Trial in 1H19**
OTO-5XX		**Cisplatin-Induced Hearing Loss**	Otoprotectant	**Candidate Selection in 2H18**
OTO-6XX		**Severe Hearing Loss**	Hair Cell Regeneration	**Candidate Selection in 2H18**

Leader in Otic Drug Delivery

- Pioneered application of targeted, sustained drug delivery to the ear
- Applicable to small molecules, proteins, mAbs and other therapeutics
- Local delivery maximizes otic exposure and minimizes systemic exposure
- Broad patent estate covers otic formulations and target compounds

Intratympanic (IT) Administration for Drug Delivery to the Inner Ear





Overview of Ménière's Disease Opportunity

- Ménière's disease is a chronic disorder characterized primarily by vertigo; also hearing loss, tinnitus and aural fullness
- Population with Ménière's disease diagnosis totals > 850K patients in U.S., with a comparable prevalence in EU-5[1]
- No FDA-approved drugs for treating Ménière's disease
  - First-line therapy is low salt diet and diuretics (plus betahistine in EU)
  - Oral and IT steroids (repeat injections) are used second-line
  - Ablative treatments (IT gentamicin or surgery) for refractory patients
- OTIVIDEX is first product to demonstrate vertigo improvement in robust placebo-controlled clinical trials
- Attractive commercial opportunity based on external assessment

[1]IMS patient-centric data

OTIVIDEX (Dexamethasone) for Ménière's Disease

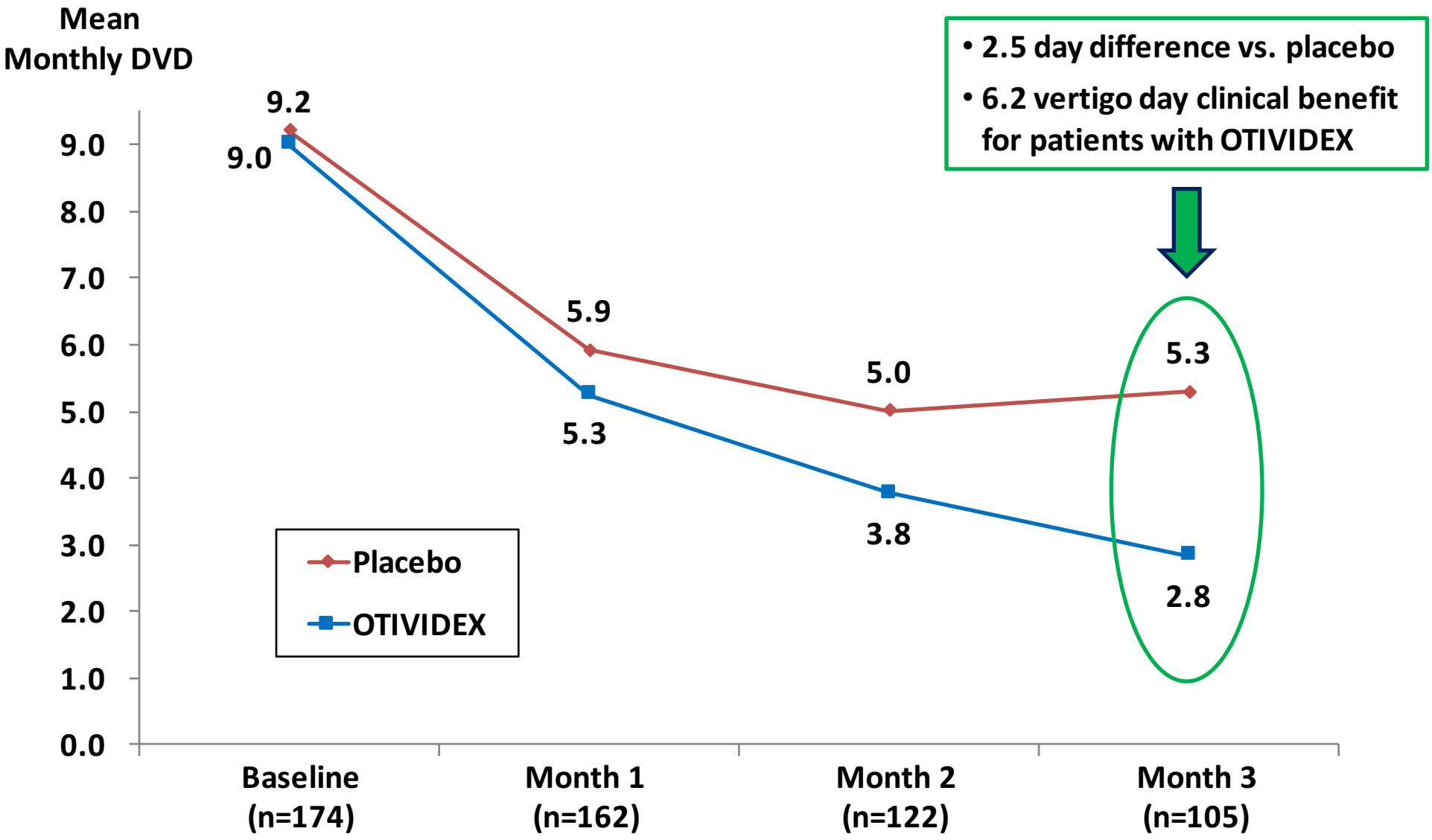
- Positive AVERTS-2 Phase 3 study, demonstrated treatment benefit of OTIVIDEX in patients with Ménière's disease on vertigo primary and secondary endpoints
- Results consistent with Phase 1b and Phase 2 studies
- Parallel AVERTS-1 Phase 3 study in U.S. was negative, primarily due to a higher placebo response
- Successful Type C FDA meeting held - a single additional pivotal study sufficient for NDA filing for U.S. registration
- Study will be initiated mid-2018; design and conduct informed by analysis of AVERTS results
- Registration-ready pending additional successful trial; safety database is sufficient to fulfill FDA registration requirements

AVERTS-2 Phase 3 Study Positive Results

	p value
Primary: Count of Definitive Vertigo Days (DVD) by Poisson Regression Analysis for all 174 Enrolled Patients	0.029
Analysis of Patients who were Enrolled through Month 3 (n = 111)	
Count of DVD by Poisson Regression Analysis	0.014
Mean Vertigo Severity Score	0.030
Change in Vertigo Frequency from Baseline	0.030
Effect of Vertigo on Days Sick at Home or Bed Ridden	0.042

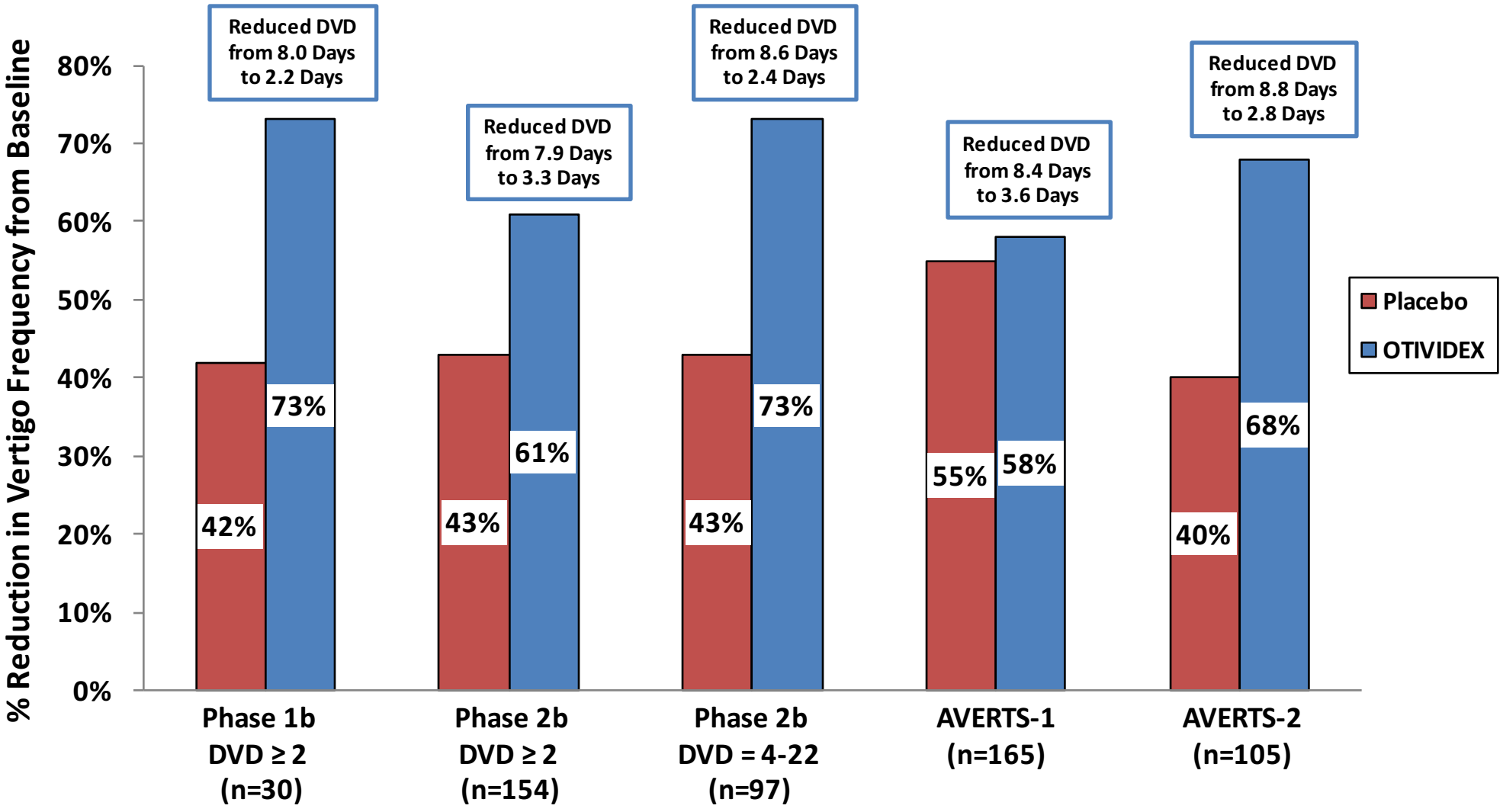
Note: Definitive Vertigo Day is a day with at least one vertigo episode lasting a minimum of 20 minutes

AVERTS-2 Results: Primary Endpoint of Vertigo Days



Note: 111 subjects were enrolled through Month 3; of these, 105 completed their diary entries for Month 3

Reduction in Vertigo Across All OTIVIDEX Trials



Phase 1b Baseline Values: OTIVIDEX (12 mg) = 8.0 Days; Placebo = 8.4 Days
Phase 2b with DVD ≥ 2 Baseline Values: OTIVIDEX = 7.9 Days; Placebo = 7.0 Days
Phase 2b with DVD = 4-22 Baseline Values: OTIVIDEX = 8.6 Days; Placebo = 8.8 Days
AVERTS-1 Baseline Values: OTIVIDEX = 8.4 Days; Placebo = 8.9 Days
AVERTS-2 Baseline Values: OTIVIDEX = 8.8 Days; Placebo = 8.9 Days (for 105 patients completing daily diaries through Month 3 prior to study termination)

Plan for Additional OTIVIDEX Pivotal Trial

- Complete analysis of results supports use of same trial design
  - No change to primary efficacy endpoint or daily diary vertigo scale
  - Continue with one month lead-in and primary analysis at three months
- Will make changes in study implementation to manage patient expectation bias and placebo response
  - Refine site selection criteria; include sites with no OTIVIDEX experience
  - Emphasize recruitment of patients known to investigators
  - Manage investigator communication with study subjects
- Similar sizing to AVERTS trials that each targeted 160 patients; sites will be from U.S. and Europe
- Clinical trial initiation in mid-2018

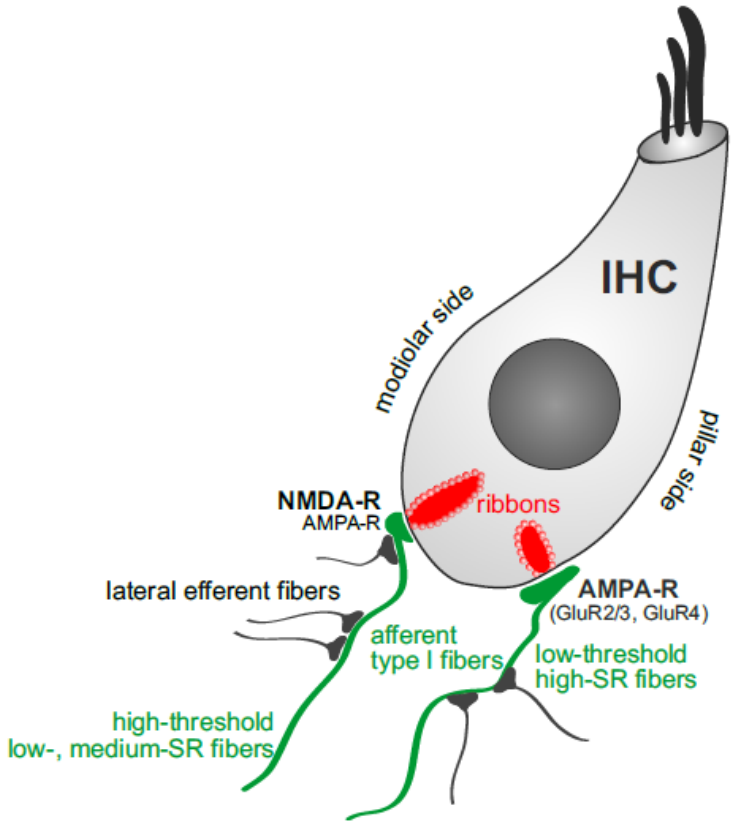
Overview of Tinnitus Opportunity

- Tinnitus is the perception of sound without external acoustic stimulation
- Approximately 20 million people in U.S. struggle with burdensome chronic tinnitus[1]; also most prevalent service-related disability in military[2]
- Tinnitus may seriously impact the ability to sleep or relax, leads to tiredness, irritation, anxiety, and depression
- No accepted standard of care for tinnitus or approved drug
- Completed Phase 1 study of OTO-311 - no safety or tolerability concerns
- Proof-of-concept trial of OTO-313 (improved formulation) in tinnitus patients ready to initiate 1H19

[1]American Tinnitus Association based on 2011-2012 National Health and Nutrition Examination Survey
[2]U.S. Department of Defense

Mechanism of Action of OTO-313 in Tinnitus

- NMDA receptors play a key role in mediating neurotransmission within the inner hair cell synaptic complex
- Injury leads to NMDA receptor-mediated aberrant excitation of auditory nerve & deafferentation of inner hair cell ribbons → tinnitus trigger
- OTO-313 (otic formulation of gacyclidine) locally blocks NMDA receptors to normalize aberrant activation and protect from further deafferentation



Bing et al (2015), Cell Physiol Biochem, 35:1905

Best-in-Class Profile of OTO-313

- Gacyclidine is a potent and selective NMDA-R antagonist
- OTO-313 formulation provides targeted and sustained delivery to the cochlea
- Comparison with Auris' AM-101 indicates overall superior profile

Parameter	OTO-313 (Gacyclidine)	AM-101 (S-Ketamine)	Comparison
NMDA Receptor Potency	6.5 nM	320 nM	Gacyclidine is ~50x more potent than S-Ketamine
Receptor Selectivity[1]	600x Preference for NMDA Receptor	40x Preference for NMDA Receptor	Gacyclidine is ~15x more selective for NMDA-R than S-Ketamine
NMDA Receptor Association[2]/ Dissociation[3]	On rate: 5.05 x 10^6 Off rate: 6.9	On rate: 0.79 x 10^6 Off rate: 1.1	Gacyclidine's ligand binding is ~ 40x more potent than S-Ketamine
Inner Ear Pharmacokinetics	AUC: 1404 ng.h/ml Duration of exposure: weeks	AUC: 71 ng.h/ml Duration of exposure: < 1 day	Gacyclidine's inner ear exposure is ~ 70x greater than S-Ketamine

[1]Receptor selectivity based on binding profile for 80 receptor targets including NMDA receptor
[2]Binding association rate (M^{-1} min^{-1})
[3]Binding dissociation value $T_{1/2}$ (min)

Source: testing performed by an independent contract research laboratory and internal Otonomy data

Clinical Support and Plan for OTO-313 Program

- Safety profile with gacyclidine systemic dosing established by Ipsen in trials with > 300 neuro-trauma patients (Otonomy licensed data)
- Two pilot clinical studies conducted with locally delivered gacyclidine in tinnitus patients[1]
- Completed Phase 1 study using OTO-311: no safety or tolerability concerns and predictable pharmacokinetics
- Phase 1/2 POC study in tinnitus patients to be initiated in 1H19
  - Proof-of-Concept study designed with KOL input
  - Powered for POC clinical efficacy on 'registration-enabling' tinnitus primary endpoint; will also include additional tinnitus and QOL secondary endpoints
  - Clear clinical development path to registration – substantial work by tinnitus investigators characterizing disease and endpoints

[1]Wenzel et al., Eur Arch Otorhinolaryngol (2009)

Hearing Loss: Large and Growing Unmet Need

Hearing Loss is 4th Leading Cause of Disability Globally[1]

[1]Lancet, July 2017

Review

Global hearing health care: new findings and perspectives

Blake S Wilson, Debara L Tucci, Michael H Merson, Gerard M O'Donoghue

In 2015, approximately half a billion people had disabling hearing loss, about 6·8% of the world's population. These numbers are substantially higher than estimates published before 2013, and point to the growing importance of hearing loss and global hearing health care. In this Review, we describe the burden of hearing loss and offer our and others' recommendations for halting and then reversing the continuing increases in this burden. Low-cost possibilities exist for prevention of hearing loss, as do unprecedented opportunities to reduce the generally high treatment costs. These possibilities and opportunities could and should be exploited. Additionally, a comprehensive worldwide initiative like VISION 2020 but for hearing could provide a focus for support and also enable and facilitate the increased efforts that are needed to reduce the burden. Success would produce major personal and societal gains, including gains that would help to fulfil the "healthy lives" and "disability inclusive" goals in the UN's new 2030 Agenda for Sustainable Development.

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NEJM, Dec 2017

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REVIEW ARTICLE

Allan H. Ropper, M.D., *Editor*

Hearing Loss in Adults

Lisa L. Cunningham, Ph.D., and Debara L. Tucci, M.D., M.B.A.

HEARING LOSS IN ADULTS IS ENCOUNTERED IN ALL MEDICAL SETTINGS and frequently influences medical encounters. This disorder constitutes a substantial burden on the adult population in the United States, yet screening for hearing loss is not routine,[1] and treatments are often inaccessible because of the high cost or perceived ineffectiveness.

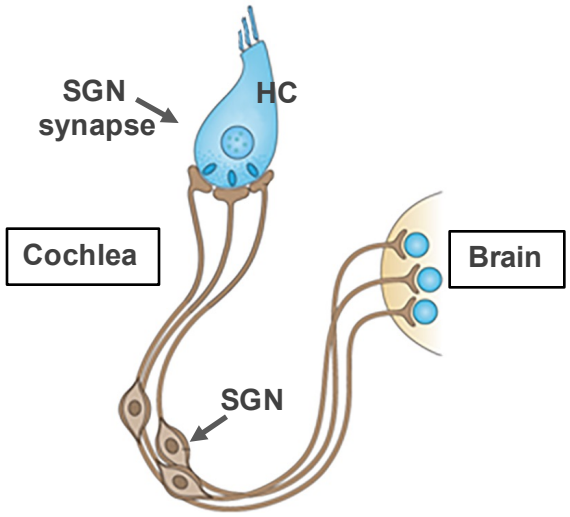
From the Section on Sensory Cell Biology, National Institute on Deafness and Other Communication Disorders, Bethesda, MD (L.L.C.); and the Division of Head and Neck Surgery and Communication Sciences, Duke University Medical Center, Durham, NC (D.L.T.). Address reprint requests to Dr. Tucci at the Division of

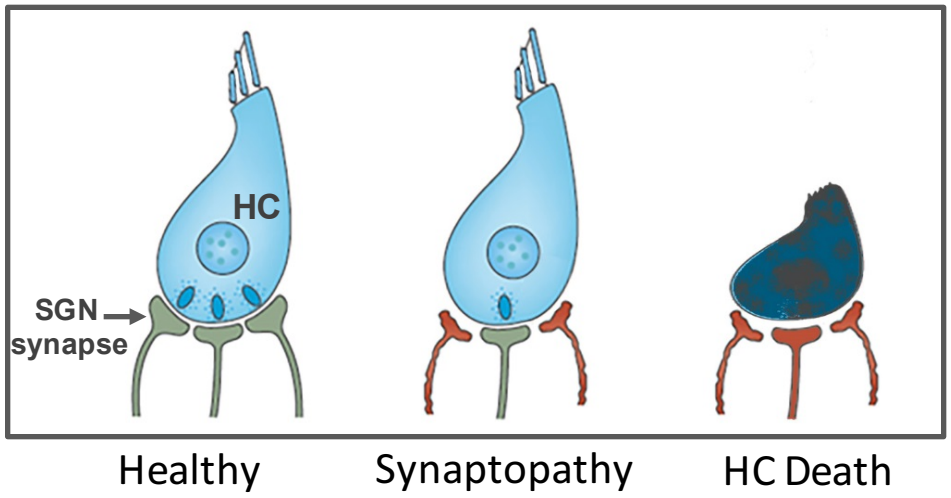
- Most prevalent neurologic health issue: > 360M people have disabling hearing loss[2]
- High economic burden: medical costs + impact of lower work productivity
- Leads to social isolation, lower QoL, and higher rates of dementia and depression
- Common causes: aging, noise, ototoxic drugs and genetics
- Established clinical outcome measures that are objective patients assessments

[2]World Health Organization, Global Estimates on Prevalence of Hearing Loss, 2012.

Addressing Multiple Hearing Loss Pathologies

Hearing loss may result from damage to hair cells (HC) and/or spiral ganglion neurons (SGN) in the inner ear





Otonomy's Three Distinct Hearing Loss Programs:

- OTO-413: Synapse Repair → Speech-in-Noise Hearing Loss
- OTO-5XX: Otoprotection → Cisplatin-Induced Hearing Loss
- OTO-6XX: Hair Cell Regeneration → Severe Hearing Loss

Figure modified from Moser and Starr, Nature Reviews: Neurology (2016)

OTO-413: Synaptopathy-related Hearing Loss

Indication

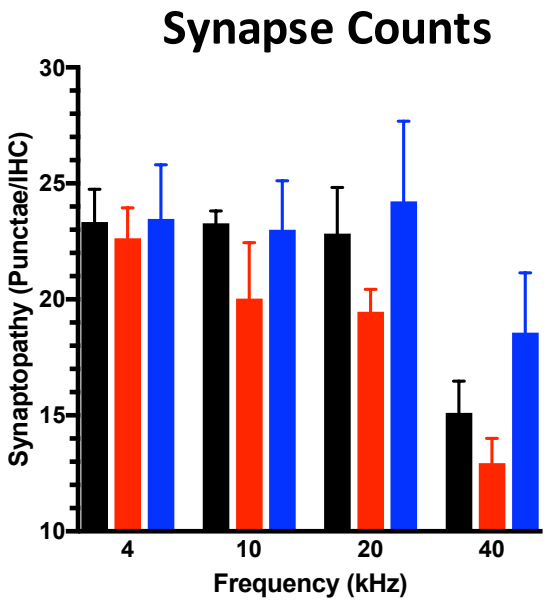
- Speech-in-Noise Hearing Impairment: primary complaint is inability to hear against background noise despite a normal audiogram
- Contributes to impaired social, psychological and cognitive function
- Estimated overall prevalence of at least 3% in U.S. population; even higher in the elderly[1]
- Results from disruption of spiral ganglion neuron function, specifically a loss of afferent fibers and ribbon synapses in cochlea[2]

Otonomy Program / Status

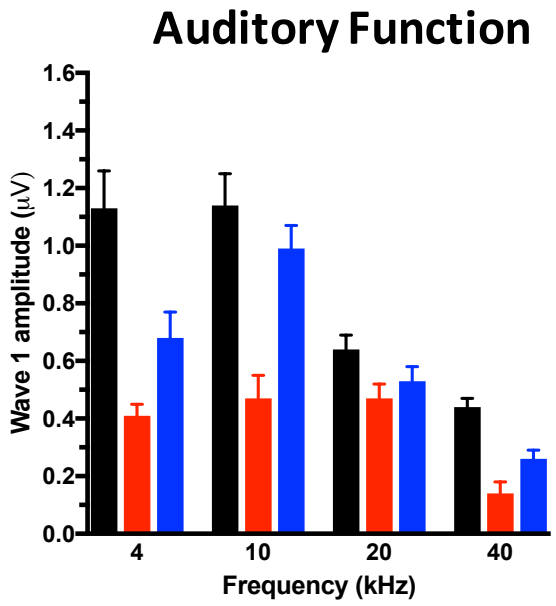
- OTO-413 is a sustained exposure formulation of brain-derived neurotrophic factor (BDNF)
- BDNF is a neurotrophin critical for establishing afferent synapses in development[3] and treatment with BDNF restores afferent synapses and hearing function[4]
- IND-enabling activities ongoing
- Expect to initiate Phase 1/2 study in hearing loss patients in 1H19

[1]Tremblay et al. 2015
[2]Liberman, 2015
[3]Fritzsch et al, 2004; Green et al, 2012
[4]Wang et al, 2004; Suzuki et al, 2016; Sly et al, 2016

OTO-413: POC in Synaptopathy Animal Model



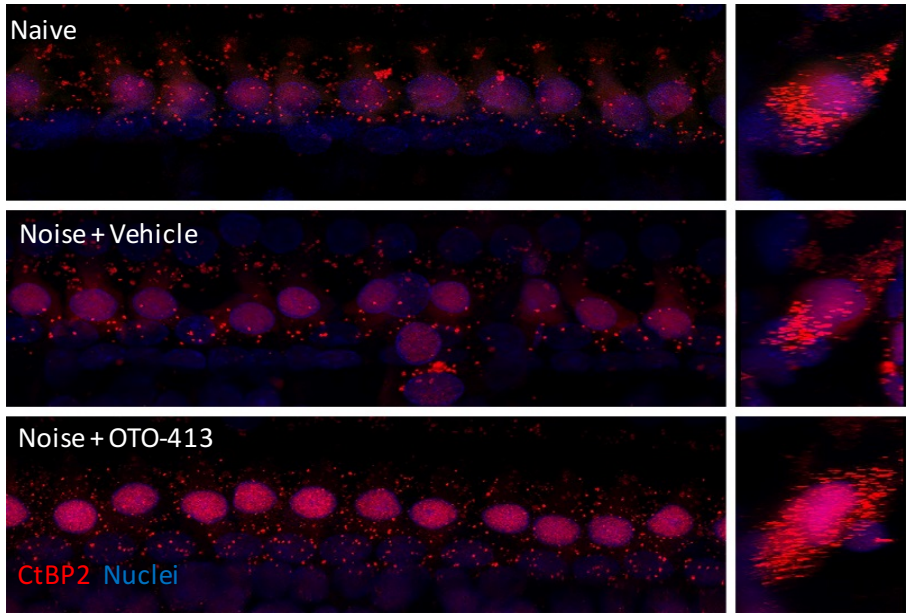
Naïve
Noise + Vehicle
Noise + OTO-413



Synaptopathy POC Animal Model

- 'Middle-aged' rats exposed to noise
- Recovery of both synapse numbers as well as auditory function with OTO-413

Visualization of Synapses on Hair Cells



OTO-5XX: Otoprotection

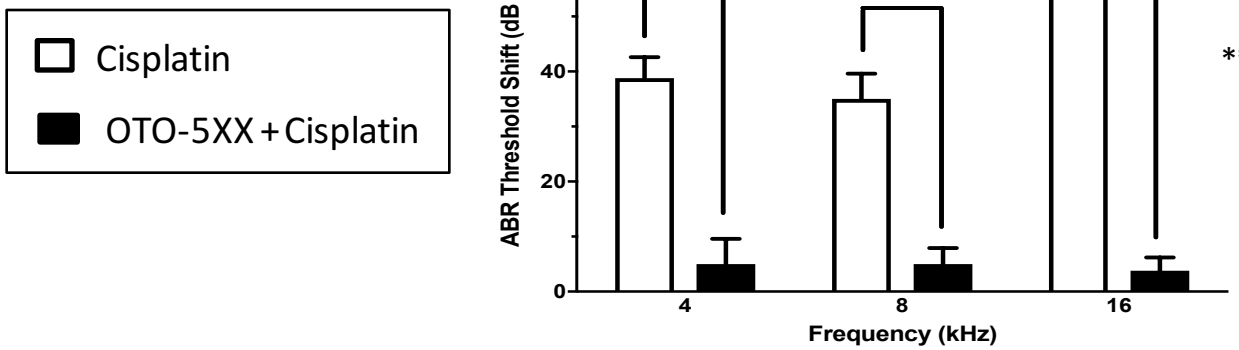
Indication

- Prevent death of hair cells due to ototoxic compounds
- Cisplatin-induced hearing loss (CIHL) is well-documented; in children, also adversely affects speech, language development and socialization
- ~ 500,000 patients treated with platinum-based chemotherapies each year in U.S.

Otonomy Program / Status

- Established clinical feasibility of indication/delivery in pilot study
- Identified therapeutic target with POC demonstrated in CIHL animal model
- Selecting final candidate for development by end of 2018

CIHL POC Animal Model



*** p < 0.001

OTO-6XX: Hair Cell Regeneration

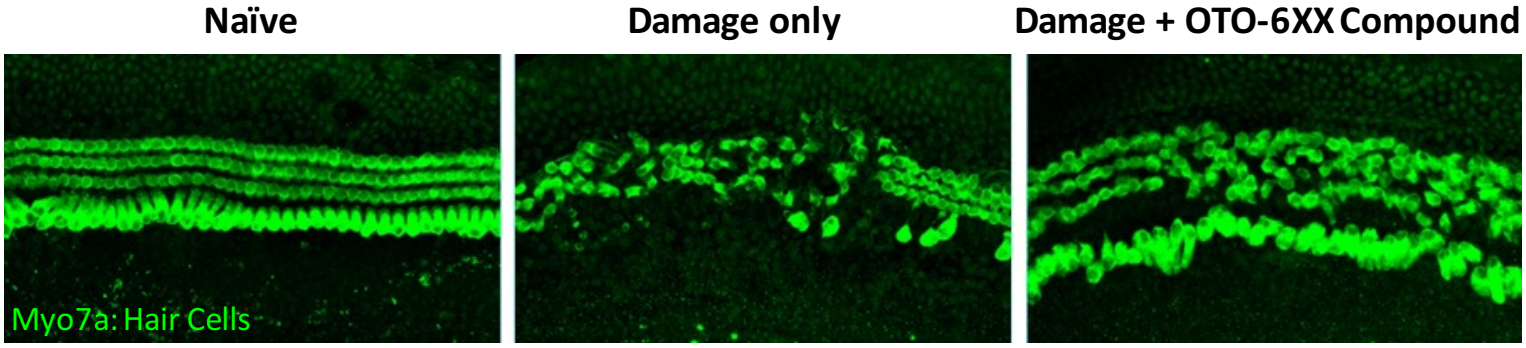
Indication

- Multiple possible indications in which severe hearing loss is due to hair cell death
- May result from a variety of insults and significantly affects ability to communicate
- Estimated 6.6 million patients with severe hearing loss in U.S.[1]

Otonomy Program / Status

- Non-mammalian species able to regenerate hair cells; knowledge of pathways involved provides targets
- POC in hair cell regeneration model
- Selecting final candidate for development by end of 2018

Hair Cell Regeneration Model



[1]Goman and Lin, 2016

Financial Update and 2018 Guidance

- Cash and equivalents as of March 31, 2018 = $110M
- 1Q18 GAAP operating expenses totaled $11.8M and Non-GAAP operating expenses totaled $9.1M*
- 2018 Financial Guidance: GAAP operating expenses of $52-$57M; Non-GAAP operating expenses of $40-45M
- Expect current cash balance will fund completion of clinical development for OTIVIDEX registration and advance other programs to value inflection milestones

*Primary adjustment from GAAP to Non-GAAP is stock-based compensation expense

Upcoming Otonomy Milestones

Mid-2018	OTIVIDEX: clinical trial initiation in Ménière's Disease
Mid-2018	OTIPRIO: commercial partnership or divestiture
2H18	OTO-5XX: select candidate for development
2H18	OTO-6XX: select candidate for development
1H19	OTO-313: initiate Phase 1/2 POC in tinnitus patients
1H19	OTO-413: initiate Phase 1/2 in hearing loss patients