OTONOMY®

Targeted
Medicines
for the Ear

Corporate Presentation
November 27, 2017

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, plans to meet with the FDA regarding the clinical development requirements for OTIVIDEX™ and the timing of any such meeting, timing of future pipeline updates from Otonomy, financial guidance for 2017 and ability to fund completion of OTIVIDEX clinical development, and the ability of Otonomy to complete a 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 and OTO-311; 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 November 8, 2017, and Otonomy's future reports to be filed with the SEC. This Presentation is dated as of November 27, 2017, 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.

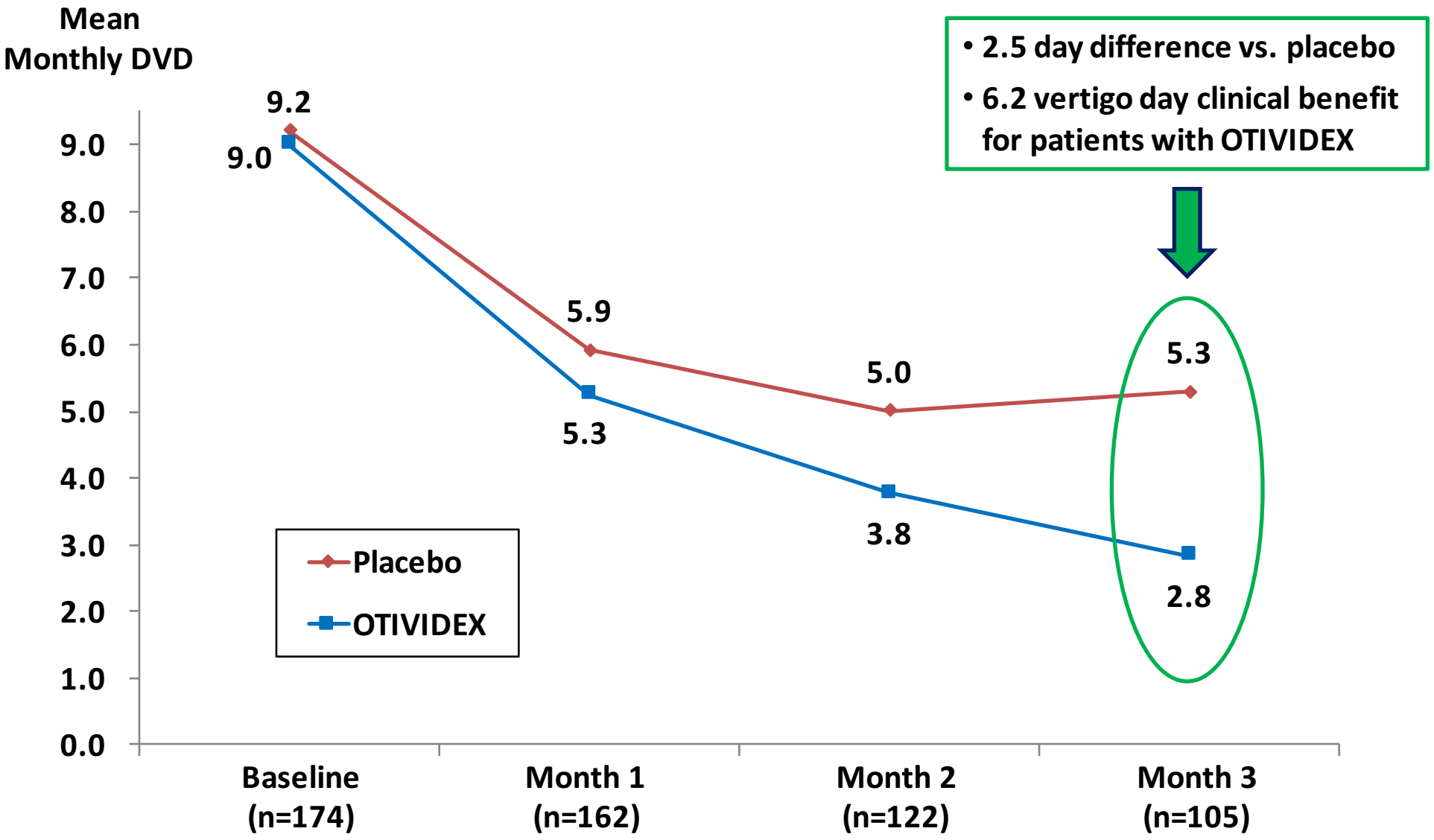
Focusing Resources on Otology Pipeline

- Successful results in AVERTS-2 Phase 3 trial of OTIVIDEX™ in patients with Ménière's disease
- Plan to meet with FDA in 1Q18 to discuss AVERTS results and clinical requirements for U.S. registration
- Advancing multiple programs for sensorineural hearing loss and tinnitus
- Discontinuing OTIPRIO commercial support and discussions underway to divest product
- Strong balance sheet to fund development efforts

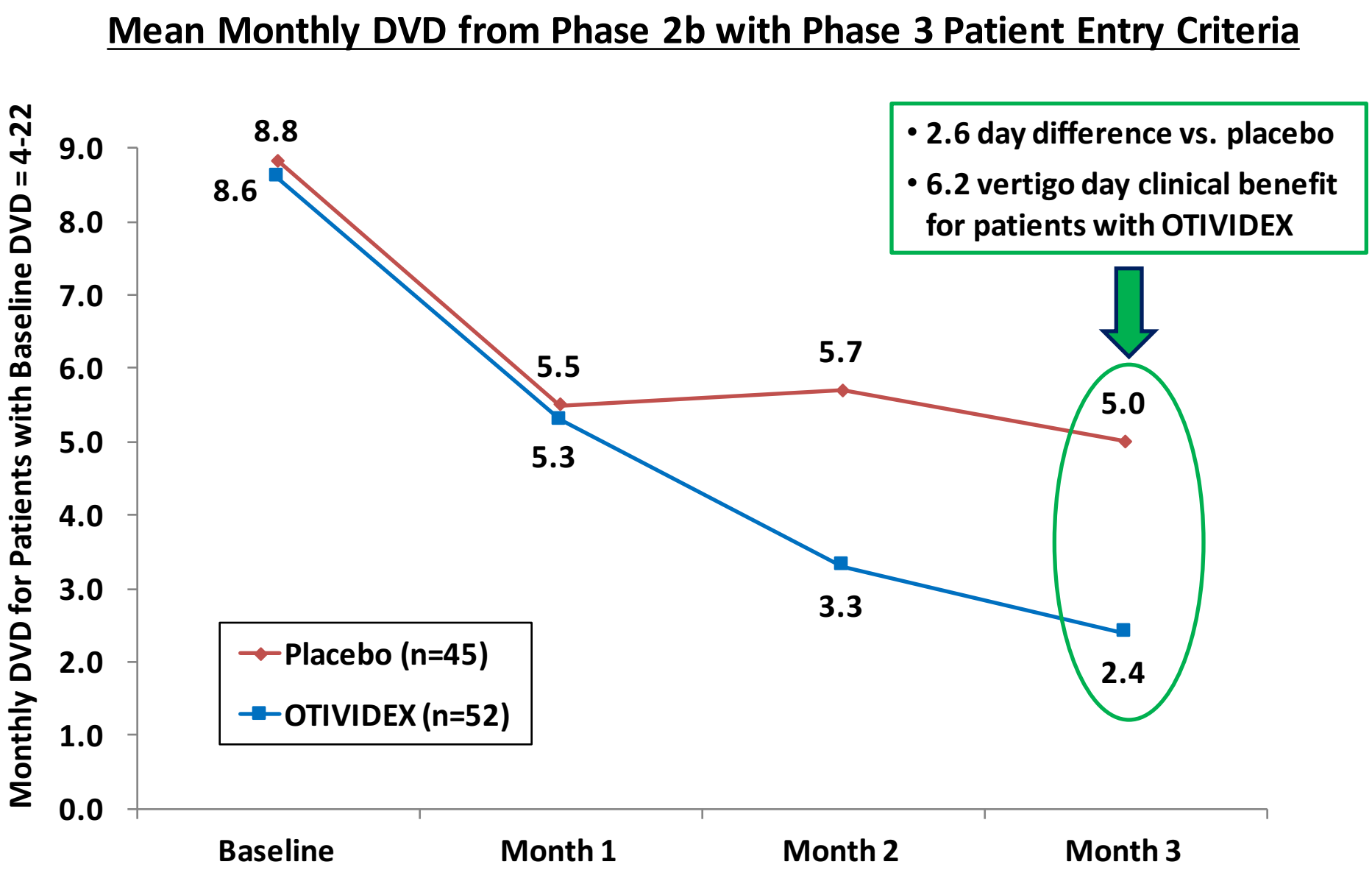
Summary of Results from AVERTS-2 Trial

- Successful result for primary endpoint: statistically significant reduction in count of definitive vertigo days (DVD) by Poisson Regression analysis in Month 3 shown for OTIVIDEX vs. placebo (p value = 0.029)
- Statistical analysis based on all 174 patients enrolled in trial; 105 patients completed daily diaries through Month 3 prior to study termination
- Mean monthly DVD and % reduction from baseline consistent with expectations from Phase 2b trial
- OTIVIDEX was generally well-tolerated with no drug-related serious adverse events

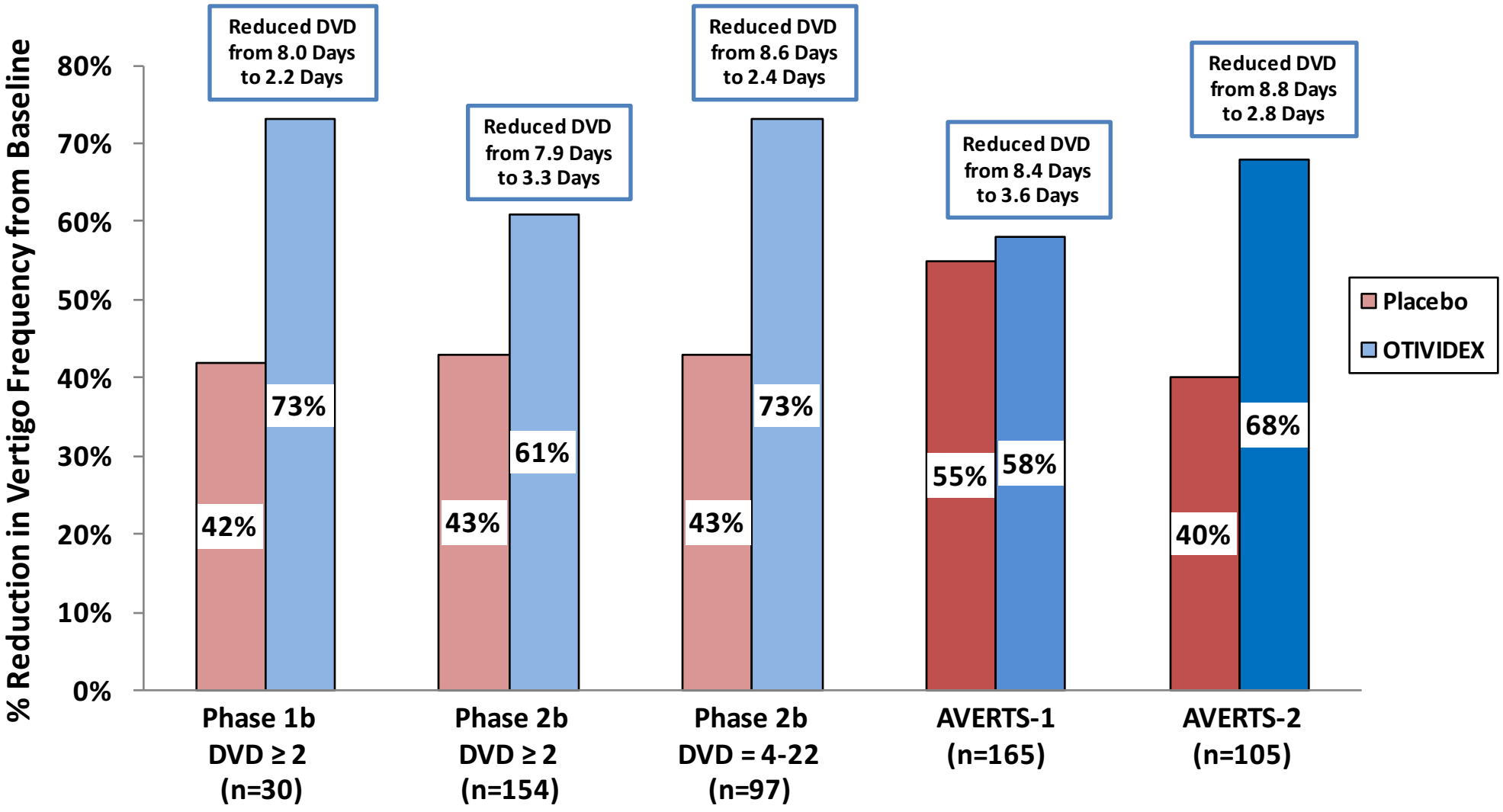
AVERTS-2 Results: Mean Monthly DVD



Results Consistent with Expectations from Phase 2b



% Reduction in Vertigo Frequency Across 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)

Next Steps for OTIVIDEX Program

- Complete analysis of AVERTS-2
- Further assess AVERTS-1 trial and identify factors that might explain high placebo response
- Meet with FDA to discuss results and clinical requirements for registration
- Expect to provide program update in 1Q18 including plan to complete clinical development required to file NDA

Multiple Programs for Hearing Loss

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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See Online for appendix

Introduction

Results from the most recent Global Burden of Disease (GBD) Studies[1–3] indicate a growing, and now alarmingly high, burden of hearing loss. Analyses of the results to enable direct comparisons across the studies show that hearing loss was the 11th leading cause of years lived with disability (YLDs) in 2010 and the fourth leading cause in both 2013 and 2015 (appendix pp 2–3). Moreover, the prevalence of disabling hearing loss is far greater today than in 1985 when the first estimates for all world regions were published.[4] As noted in a recent editorial in *The Lancet*,[5] hearing loss has become a major concern for global health.

In this Review we aim to provide the detailed information that decision makers need to position hearing loss optimally among health-care priorities; present best practices for hearing health care; indicate the many additional changing conditions for hearing health care worldwide; and offer our and others' recommendations for first halting the growth in the burden of hearing loss, and then reducing it.

Although awareness of hearing loss and its sequelae is increasing, prevention and treatment are still not regarded as urgent needs in many countries, especially in low-income and middle-income countries (LMICs) where scarce resources force difficult choices. Hearing loss has been and remains in some places the "invisible disability" that can all too easily be set aside in favour of attention to other health problems.[6] And yet, new and earlier data indicate that the consequences of not allocating resources for at least targeted prevention and treatment of hearing loss are dire, both in personal and societal terms. Therefore, in this Review we also consider choices to maximise benefit-to-cost ratios for fixed budgets and for budgets that might be increased with changing priorities or the rapidly improving economies in many LMICs.

Global burden of hearing loss

Impact of losses in hearing

The reach of hearing loss extends far beyond sensory impairment.[7–9] The absence or substantial attenuation of auditory input to the brain alters brain connectivity and processing,[8–12] especially before about age 3 years[9] and perhaps again after about age 60 years.[13,14] Hearing loss in those early years precludes or delays the acquisition of spoken language.[10,15] Children with severe or worse losses in hearing have lower literacy than do their normally hearing peers,[16] and their educational attainments are greatly compromised.[17,18] Most adults with disabling hearing loss have a sense of profound isolation (appendix p 4), and they typically withdraw from society and even family interactions.[7,19–21] Furthermore, relations within couples are often severely tested when one person in the couple has normal

Search strategy and selection criteria

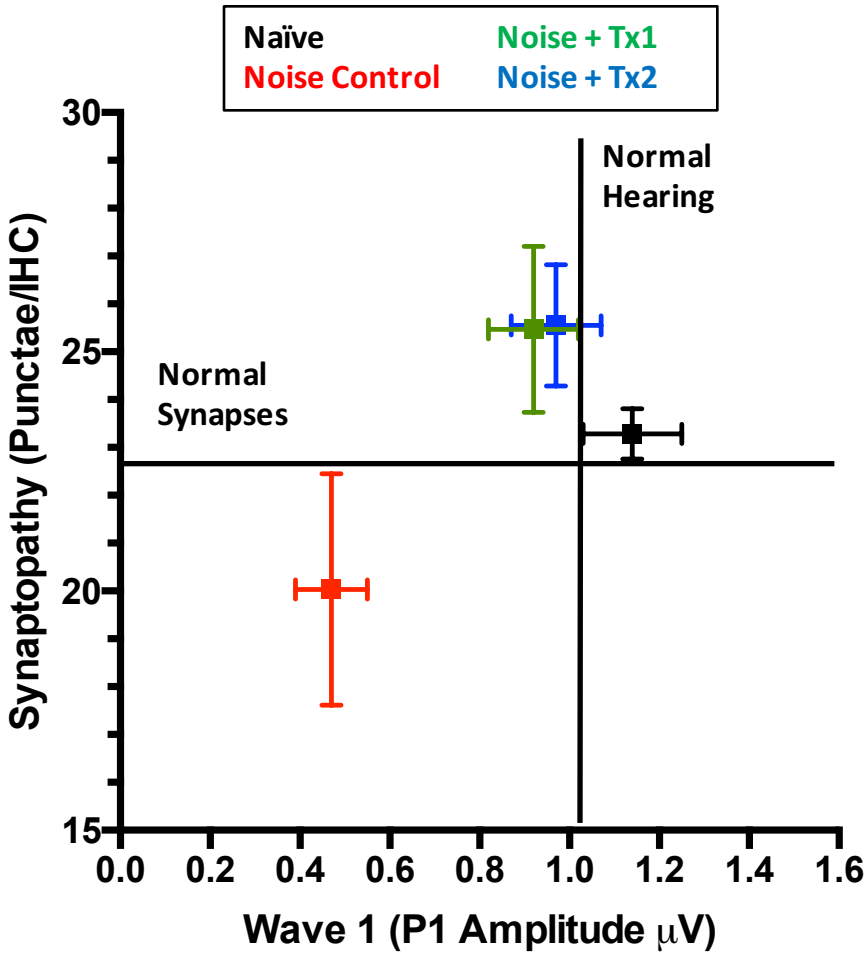
We searched the Cochrane Library, PubMed, and Embase for relevant and high-quality references (eg, references that reported results from worldwide surveys). The start dates for the searches were 2004, 1988, and 1973, respectively, and the end dates all were in September, 2014, with supplemental searches of PubMed up to Oct 8, 2016. For the Cochrane search, we used the following logical combination of search terms: ("hearing loss" OR "deafness" OR "hearing health" OR "hearing aids" OR "audiology" OR "otolaryngology" OR "cochlear implant") AND ("education" OR "research" OR "early detection") AND ("developing countries" OR "global health"). The same terms were used for the PubMed searches except for the term "developing countries". For Embase, we used a similar search strategy but substituted the appropriate Emtree terms. With one important exception (WHO's resolution WHA48.9 from 1995), we selected publications from the past 15 years with a high emphasis on publications from the past 3 years. We also searched the reference lists in the identified publications for further potentially relevant references, and we remained vigilant to new publications in the specialty journals in the fields indicated by the search terms and in the broad-audience journals such as *The Lancet* that frequently publish papers in the field of global health. Suggestions for additional references from outside world experts (see Acknowledgments) were incorporated into our set of selected references for careful study.

- Largest otology disorder: estimate that 1.3 billion people worldwide have hearing loss
- Pursuing several approaches for protection and treatment:
  - Repair of ribbon synapses
  - Protect against chemotoxicity
  - Regenerate hair cells
- Leading edge capabilities in research and development

POC for Repair of Ribbon Synapses

- Targeting neurotrophic pathways
- Formulate for sustained drug exposure from single IT injection
- *In vivo* proof of concept shown in noise injury model
- Additional program details including timeline in 1Q18

Proof-of-Concept Preclinical Study



OTO-311 for Tinnitus

- Tinnitus = hearing noise when there is no sound
- Debilitating condition; no FDA-approved drug treatment
- 16 million patients in the U.S. have severe symptoms[1]
- Most prevalent service-related disability in U.S. military[2]
- Gacyclidine is potent and selective NMDA receptor antagonist
- Sustained drug exposure provides additional advantage
- Completed Phase 1 trial in healthy subjects
- Timing of Phase 2 initiation to be determined

[1]Source: American Tinnitus Association
[2]Source: United States Department of Defense

Discussions Underway to Divest OTIPRIO

- Decision to focus resources on product pipeline
- Discontinuing commercial support which will significantly reduce future operating expenses
- Cash savings expected to total more than $20M for 2018
- OTIPRIO is available for purchase by customers during process

Financial Update and 2017 Guidance

- Cash and equivalents as of Sept 30, 2017 = $134.3M
- GAAP operating expenses for 3Q17 totaled $21.3M (R&D = $10.8M, SG&A = $10.5M)
- Non-GAAP operating expenses for 3Q17 = $17.4M
- Financial Guidance: cash balance at end of 2017 expected to total $118-$123M; will fund completion of OTIVIDEX clinical development for registration

Summary of Otonomy Opportunity

- Otology market is large and untapped
- Otonomy's product pipeline targets large patient populations with important unmet medical needs
- Focusing resources on pipeline development including OTIVIDEX for Ménière's disease
- Strong balance sheet and cost reductions support program advancement to value inflection points
- Program timelines to be presented in 1Q18