Forward-Looking Statements

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Broader Pipeline Targeting Large Market Opportunities

- **Vertigo** ~11 M
  - OTIVIDEX®: successful Phase 3 trial completed, additional Phase 3 trial ongoing; enrollment completed, results in 1Q21; with positive results, expect to submit NDA in 3Q21

- **Tinnitus** ~7.8 M
  - OTO-313: positive top-line Phase 1/2 trial results; advancing to full Phase 2 development

- **Hearing Loss** ~20.5 M
  - OTO-413: positive top-line results in Phase 1/2 trial
  - Preclinical Programs:
    - OTO-510 for cisplatin-induced hearing loss
    - OTO-6XX for severe hearing loss
    - GJB2 gene Tx program for congenital hearing loss

Total Market Potential by Condition: ~39 M in U.S.

Source: ClearView Healthcare Partners (2018): analysis based on patients with moderate to severe symptoms
OTO-413 is first therapeutic to be evaluated for treatment of hearing loss due to cochlear synaptopathy

OTO-413 was well-tolerated across all dose cohorts

Therapeutic activity for OTO-413 demonstrated by subjects achieving a clinically meaningful improvement from baseline across multiple speech-in-noise tests at consecutive timepoints (Days 57 and 85)

No response observed in placebo patients using these stringent criteria

Results support continued clinical development of OTO-413 for hearing loss
Hearing Loss is a Large and Growing Problem Worldwide

Hearing Loss is 4th Leading Cause of Disability Globally\(^1\)

Most prevalent neurologic health issue:

> 360M PEOPLE

have disabling hearing loss\(^2\)

Common causes include:
AGING, NOISE, OTOTOXIC DRUGS AND GENETICS

Leads to Social Isolation, lower QOL, AND HIGHER RATES OF DEMENTIA AND DEPRESSION

NO EFFECTIVE TREATMENTS and no approved drugs for hearing loss

High economic burden:
MEDICAL COSTS + IMPACT of lower work productivity

Cochlear Synaptopathy

- Problem hearing in presence of background noise
- Normal standard hearing test, may have high frequency loss
- U.S. prevalence\(^1\) \(\approx 9M\)

OTO-413 Targets a Broad Hearing Loss Population

Illustrative

Hair Cell Pathology

- Hearing loss detected in standard test (hear tones in quiet setting)

Mixed Pathology

- Speech-in-noise hearing difficulty & hearing threshold deficit
- Significant proportion of 42M in U.S. with hearing threshold deficit\(^2-5\)

OTO-413 Target Patient Population

\(^1\) Tremblay et al., Ear Hear, 2015; \(^2\) Hoffman et al., JAMA Otolaryngol HNS, 2017; \(^3\) Nash et al., Arch Otolaryngol HNS, 2011
\(^4\) Morton et al., N Engl J Med, 2006; \(^5\) Brooke et al., JAMA Otolaryngol HNS, 2017; Analysis by ClearView Healthcare Partners
Description of Cochlear Synaptopathy

- Cochlear synaptopathy is loss of connection between inner hair cells and auditory nerve fibers
- Caused by noise exposure, aging, ototoxic chemicals or combination of these factors
- Evidence suggests that cochlear synaptopathy may occur earlier than hair cell loss
- Patients report speech-in-noise hearing difficulty; may also have high frequency hearing loss

Figure from Moser and Starr, Nature Reviews: Neurology (2016); IHC = inner hair cells; SGN = spiral ganglion neurons
OTO-413: Sustained-Exposure Formulation of BDNF

• Brain-derived neurotrophic factor (BDNF) is an endogenous protein with potent neurotrophic effects on spiral ganglion neurons (auditory nerve fibers)

• OTO-413 is a sustained-exposure formulation of BDNF that provides several weeks of drug exposure from single intratympanic (IT) injection

• Preclinical data support the development of OTO-413 for treating cochlear synaptopathy
Therapeutic Effects of BDNF in the Cochlea

- Promotes SGN Survival
- Increases SGN Neurite Outgrowth
- Reconnects SGNs with Hair Cells after Synaptopathy

Control

Synaptopathy

Synaptopathy + BDNF
OTO-413 Phase 1/2 Clinical Trial Design

Phase 1/2 Ascending Dose Safety and Exploratory Efficacy Study

- All subjects had speech-in-noise (SIN) hearing difficulty (self-reported and by testing)
- Most subjects also had at least moderate hearing loss in quiet setting
- Randomized, controlled trial with 3:1 randomization to OTO-413 or placebo
- Primary objective: assess safety of OTO-413 across four ascending dose cohorts
- Secondary objective: evaluate therapeutic activity of OTO-413 for multiple exploratory endpoints with emphasis on clinically-validated SIN tests

Screening & Baseline Testing

Single IT injection: OTO-413 or placebo

Three Month Follow-up with Testing at Day 15, 29, 57 and 85
OTO-413 Phase 1/2 Ascending Dose Trial Subject Disposition

Cohort 1 (0.01 mg)
- 6 OTO-413
- 2 Placebo

Cohort 2 (0.03 mg)
- 6 OTO-413
- 2 Placebo

Cohort 3 (0.10 mg)
- 6 OTO-413
- 2 Placebo

Cohort 4 (0.30 mg)
- 11 OTO-413
- 4 Placebo

Safety Evaluation
- 29 OTO-413
- 10 Placebo

Top-Line Assessment of Therapeutic Activity
- OTO-413: 9 evaluable subjects from high dose cohort (1 subject with no Day 57 visit and 1 early term not related to AE)
- Placebo: 8 subjects pooled from Cohort 2, 3 and 4

Sub-therapeutic dose
Start-up and technical challenges with large battery of tests
**Review of Speech-in-Noise (SIN) Tests**

**Digits-in-Noise Test (DIN)**
- 3 spoken numbers presented at varying sound intensities
- 23 digit-triplets (e.g., 9-2-5)
- Continuous, synchronous background noise at fixed level

**Words-in-Noise Test (WIN)**
- Word recognition test with multi-talker babble as background
- 35 words (5 words each at 7 varying signal-to-noise ratios)

**American English Matrix Test**
- 20 five-word sentences
- Fixed background noise
- Test uses grammatically correct but unpredictable sentences to minimize learning effect
- Example: “Rachel wants for pretty chairs”

**SIN tests conducted at screening, baseline (pre-dose), Day 15, 29, 57 and 85**

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Figure from Cowen & Company Equity Research
OTO-413 Efficacy Signal Demonstrated on Responder Analysis

<table>
<thead>
<tr>
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<th>OTO-413</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>≥ 1 SIN Test at Both Day 57 and 85</td>
<td>67% (6 of 9)</td>
<td>0% (0 of 8)</td>
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<tr>
<td>≥ 2 SIN Tests at Both Day 57 and 85</td>
<td>33% (3 of 9)</td>
<td>0% (0 of 8)</td>
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<tr>
<td>Response on American English Matrix Test: OTO-413 at Both Day 57 and 85 vs. Any Visit for Placebo</td>
<td>44% (4 of 9)</td>
<td>0% (0 of 7)</td>
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Notes: SIN = speech-in-noise test; one OTO-413 subject did not complete Day 57 visit but had clinically meaningful improvement at Day 85 for two SIN tests; one placebo subject did not complete Matrix test.
Response for Subset with Moderate-to-Severe Hearing Loss

Notes: SIN = speech-in-noise test; one OTO-413 patient did not complete the Day 57 visit but had a clinically meaningful improvement at Day 85 for two SIN tests
SIN Test Improvement in Context of “Real-World” Hearing

Small Improvement in SIN Test Can Mean Significant Improvement in Speech Intelligibility

Ability to Understand Someone in Noisy Setting

Source: adapted from Victoria Sanchez, Au.D., Ph.D., University of South Florida
OTO-413 Was Well-Tolerated Across All Dose Cohorts

- Safety assessment: 29 subjects treated with OTO-413 and 10 placebo
- 52% of OTO-413 vs. 70% of placebo subjects reported an adverse event (AE)
- No apparent impact of dose on AE incidence across OTO-413 cohorts
- No serious adverse events and no discontinued patients due to an AE
- OTO-413 AE severity was mild 28/37 (76%) or moderate 8/37 (22%)
  - Most ear-related AE’s occurred on same day as injection or immediately following
  - Single severe AE (intermittent diarrhea) related to COVID-19 and not OTO-413
Positive Top-Line Clinical Trial Results for OTO-413

• OTO-413 therapeutic activity demonstrated by subjects achieving a clinically meaningful improvement from baseline across multiple speech-in-noise tests at consecutive timepoints (Days 57 and 85)

• No response observed in placebo subjects using these stringent criteria

• Top-line results focus on high dose cohort and speech-in-noise endpoints, however activity also observed for other exploratory endpoints and doses

• OTO-413 was well-tolerated across all dose cohorts

• Results support continued clinical development of OTO-413 in patients with hearing loss
## Review of OTIC’s Multiple Clinical Trial Catalysts

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<tr>
<th>Expected Timing</th>
<th>Program Milestone</th>
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<tbody>
<tr>
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<td>OTO-313 Phase 1/2 trial results</td>
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<tr>
<td>1Q21</td>
<td>OTIVIDEX Phase 3 trial results</td>
</tr>
<tr>
<td>1Q21</td>
<td>Initiate OTO-313 Phase 2 trial</td>
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