Otonomy, Inc. (OTIC) — Overweight

Opportunity Coming Out Of Its Ears; Initiating With Overweight and $46 PT

CONCLUSION

We are initiating coverage of OTIC with an Overweight rating and $46 PT. OTIC is a top small-cap pick as the company has a derisked lead asset in AuriPro which we believe supports the current valuation and potentially more. AuriPro is a special formulation of ciprofloxacin that confers durable drug delivery to the middle ear and has successfully completed two P3 trials. With commercial launch expected in 2016, we believe AuriPro can support $200M/yr in revenue in the U.S. alone. OTIC also has a P2 candidate, OTO-104, for the treatment of Ménière's syndrome, which we believe is not reflected in the valuation but could offer tremendous upside opportunity with a strong likelihood of success in our view. The commercial opportunity for Ménière's may be upwards of $500M in our estimate. With downside protection and an attractive shot on goal, we see a highly compelling risk/reward profile.

- **AuriPro derisked**: In twin P3 studies, AuriPro demonstrated a compelling benefit for reducing recurrence of infection/effusion in patients undergoing tympanostomy tube placement (TTP) for middle ear effusions. These patients will typically receive antibiotic drops such as Alcon's CiproDex, although the drug is not approved for this specific use. With ~1M TTPs annually, the U.S. market alone is $200M+. Beyond this indication, there are other related indications for which we believe AuriPro can be successfully commercialized. We expect AuriPro to become a market leader based on its convenience and assured compliance compared to drops. ENT specialists with whom we have spoken are also quite enthusiastic for the drug.

- **Ménière's also a compelling opportunity**: Off-label intratympanic steroid injections are part of the care paradigm for Ménière's, a disease characterized by vertigo, tinnitus and hearing loss. These steroid injections require repeated office visits and do not offer durable exposure, but studies do support their clinical benefit for this indication. OTO-104 solves the delivery challenge of steroids by formulating dexamethasone in a gel that provides durable exposure. Consistent with the data for steroids, OTO-104 showed a benefit in vertigo in a placebo-controlled P1 study and also a benefit in tinnitus. With >600K Ménière's patients in the U.S., this is potentially a lucrative opportunity.

- **Not easy to find 'free stuff' these days**: Since we believe the current OTIC valuation is fully supported by AuriPro, we believe the Meniere's program is not reflected in the current stock price. This largely skewed risk/reward profile makes OTIC a top small cap pick with a $400M market cap and $160M in cash.

RISKS TO ACHIEVEMENT OF PRICE TARGET

Development candidates may face clinical, regulatory or commercial setbacks.

COMPANY DESCRIPTION

OTIC is developing drugs to treat a variety of ear conditions.

PRICE: US$18.79
TARGET: US$46.00
DCF thru 2022, 10.5% discount rate, 3.0% terminal growth rate

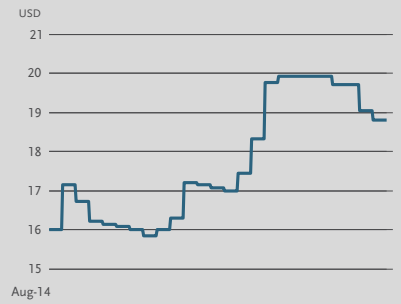
Joshua E. Schimmer, MD
Sr Research Analyst, Piper Jaffray & Co.
212 284-9322, joshua.e.schimmer@pjc.com

Jerry Yang, Ph.D.
Research Analyst, Piper Jaffray & Co.
212 284-9331, jerry.n.yang@pjc.com

Changes	Previous	Current
Rating		Overweight
Price Tgt		US$46.00
FY15E Rev (mil)	—	0.0
FY16E Rev (mil)	—	13.0
FY15E EPS	—	(2.84)
FY16E EPS	—	(3.85)

52-Week High / Low	US$20.45 / US$15.19
Shares Out (mil)	21.3
Market Cap. (mil)	US$400.2
Avg Daily Vol (000)	
Book Value/Share	US$5.26
Net Cash Per Share	US$7.24
Debt to Total Capital	0%
Yield	0.00%
Fiscal Year End	Dec

Price Performance - 1 Year



Source: Bloomberg

YEAR	REVENUE (m)						EARNINGS PER SHARE ( )					
	Mar	Jun	Sep	Dec	FY	FY RM	Mar	Jun	Sep	Dec	FY	FY P/E
2014E	0.0A	0.0A	0.0	0.0	0.0	NA	(3.69)A	(0.67)A	(0.69)	(0.69)	(3.30)	NM
2015E	0.0	0.0	0.0	0.0	0.0	NA	(0.62)	(0.61)	(0.70)	(0.91)	(2.84)	NM
2016E	—	—	—	—	13.0	30.8x	—	—	—	—	(3.85)	NM

Otonomy (OTIC): An Earful of Opportunity And A Top Pick

- OTIC is a biopharmaceutical company currently focused on developing depot-gel formulations of compounds to treat ear-related disorders.
  - Patented thermo-sensitive polymer is liquid at low temperature but transitions to a gel at body temperature.
  - This enables an easy injection into the ear (outer, middle or inner) which then gels for durable presence.
  - OTIC may ultimately venture into other ear programs independent of the gel as opportunities present.

- Lead program, **AuriPro**, is a thermo-sensitive polymer formulation of the antibiotic ciprofloxacin to treat pediatric patients with middle ear infections who require tympanostomy tube placement (TTP; ear tubes) surgery.
  - The company recently reported **positive data for two P3 trials** and plans to file an NDA in 1H 2015 following completion of stability testing.
  - Represents a $200M+ market opportunity in the U.S.

- OTO- 104 (thermo-sensitive polymer formulation of dexamethasone) for Ménière's disease offers significant upside potential in our view.
  - Currently in Phase IIb study, data in 2015.
  - High unmet need, limited treatment options, affects hundreds of thousands of adults in the U.S.; liquid injected steroids are currently used to treat but are cumbersome as they do not provide durable exposure.

- OTO-311 is a thermo-sensitive polymer formulation of an NMDA receptor antagonist (gacyclidine) for treatment of tinnitus (an inner ear disorder).
  - Auris Medical (NASDAQ: EARS; recent IPO, $152M mkt cap, not covered) has positive P2 data for its own NMDA receptor agonist for tinnitus but does not have as attractive a delivery platform as OTIC, we believe.

Overall, we see OTIC as possessing a powerful platform with its thermosensitive polymer technology that is well-suited for developing low-risk, high-reward opportunities in the ear. The ear market is a multi-billion dollar commercial opportunity with features similar to the back-of-the-eye market.

OTIC Investment Thesis

- The lead product, AuriPro, justifies at least the current valuation of the company, if not more, in our view.
  - With P3 trials successfully completed, the company should gain FDA approval to prevent middle ear effusion at the time of TTP surgery with launch expected in 2016.
  - Potential to expand indications to include acute otitis media with TTP (AOMT), acute otitis externa, chronic suppurative otitis media for which topical antibiotics have been proven effective.
  - This product has the potential to achieve >$200M revenue per year in the U.S. across alone across these indicatoins by eliminating the inconvenience and lack of compliance associated with ear drops.
  - With a $400M Mkt cap, $160M cash/equiv, OTIC shares are trading at 1.1x EV multiple on our 2022 AuriPro sales estimates; biotech companies typically trade at 2-3x EV/Rev or higher on 2022 estimates.
- In addition to AuriPro, OTO-104 for Ménière's disease and OTO-311 for tinnitus could each be blockbuster opportunities. Success in either of these programs could offer significant upside for OTIC's valuation.
  - Positive placebo-controlled P1 study for OTO-104 supports activity, and intratympanic steroids are already used for Ménière's but limited by short duration of effect and a cumbersome administration schedule.
- OTIC is scratching the surface of ear drug development.
  - OTIC plans to continue advancing additional drugs to treat ENT conditions. This is a field that has been broadly overlooked by the biopharma industry and as such is 'ripe for the picking'.
  - By establishing close relationships with the ENT physician thought-leaders, OTIC can ultimately build a strong commercial presence that can be leveraged by in-licensing new assets.

OTIC is our top small-cap biopharma pick.

OTIC Valuation: Price Target $46/Share

Our $46 PT represents ~147% potential upside from OTIC's current share price of $18.79 (as of 09/05/2014).

- We arrive at our PT via a DCF analysis of estimated free cash flow (modeled through 2022)
  - Slight premium 10.5% discount rate reflects clinical/commercial risk for OTIC.
  - 3.0% terminal growth (14x terminal multiple with 10.5% discount) reflects a conservative LT outlook for OTIC's current pipeline programs and potential ear therapy additions to the pipeline.

- We assume:
  - For AuriPro
    - OTIC commercializes AuriPro on its own in the US, charging $225/procedure
    - Penetration into "low payor-barrier population" reaches 50%; penetration into "high payor-barrier population" reaches 35%
    - OTIC partners AuriPro ex-US for a royalty which starts at 15%
  - For OTO-104 (Ménière's disease)
    - OTIC commercializes OTO-104 on its own in the US, charging $5,000/yr per patient
    - Penetration rate in the US reaches 7% by 2022 (very conservative)
    - OTIC partners OTO-104 ex-US for a royalty which starts at 15%

By 2022, we model US sales of AuriPro for middle ear effusion reaching $135M, US sales of AuriPro for other indications reaching $65M, and US sales of OTO-104 reaching $380M.

OTIC: Risks

- Clinical trial risks
  - Tinnitus and Ménière's disease programs may fail to generate compelling data.
- Regulatory risk
  - OTIC's therapies may fail to gain regulatory approval.
- Commercialization risks
  - Price sensitive market segments for Auripro.
  - Auris Medical has a tinnitus program further ahead of OTIC's.

We believe AuriPro provides downside protection around current levels, although if our projections are too high and peak sales are below $100M and the entire pipeline fails, a conservative 2x sales could eventually see shares down 50% from current levels-- **but** since we won't know if that bearish commercial outlook is plausible until 2016 launch or beyond, the risk-reward on NT pipeline data readouts is very compelling to us.

OTIC: Expected Upcoming Catalysts That Could Unlock Value

- AuriPro for middle ear effusion at time of TTP surgery
  - Submit an NDA in 1H15 after completion of additional stability testing
  - Commercialize in the US in 2016, pending approval

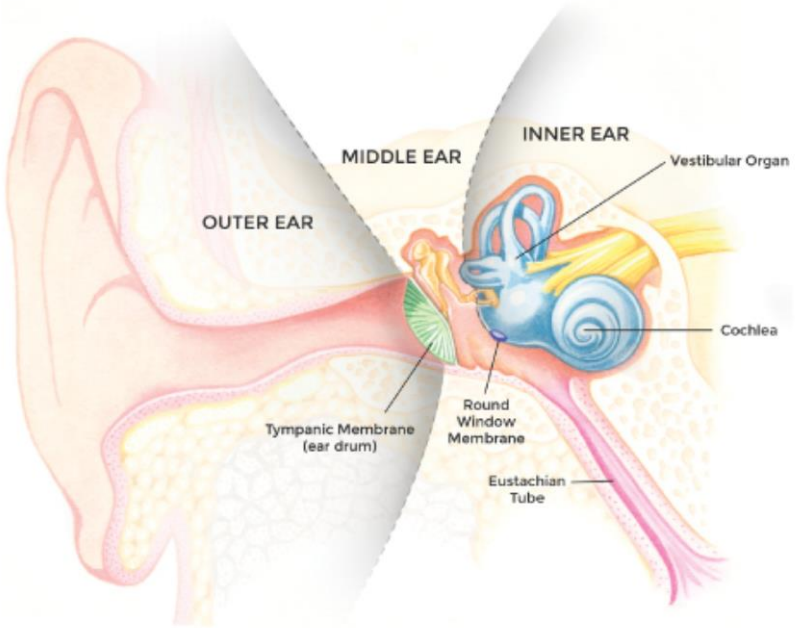
- OTO-104 for Ménière's disease
  - Initiate one or more open-label, multiple-dose safety studies by year end
  - Report results from P2b trial in 1H15
  - Initiate P3 trial in 2015

- OTO-311 for tinnitus
  - Submit an IND application in 2015
  - Initiate clinical development in 2015

We believe the risk-reward profile for OTO-104 (considering the downside protection from AuriPro) represents one of the most attractive binary 2015 events in biotech.

A Quick Overview Of Otology

In the US, around **50M** patients are affected by ear disorders, **20M** of which seek treatment every year. The three major ear segments are outer ear infections, middle ear infections and inner ear disorders.



Source: OTIC S-1 filing

1. **Outer ear infections (e.g., acute otitis externa)**
   - ❑ infection or inflammation in outer ear.
   - ❑ Estimated ~2.5M people are affected each year in the US.
2. **Middle ear infections (e.g., acute otitis media)**
   - ❑ infection or inflammation in middle ear.
   - ❑ Estimated 75% of children are affected before reaching 3 years old.
3. **Diseases of inner ears**
   - ❑ **Tinnitus**
     - ➢ Ringing in the ear ("I hear something you don't"); severe tinnitus could be disabling as patients have trouble hearing, working and sleeping.
     - ➢ Estimated ~16M tinnitus patients require treatment in the US.
   - ❑ **Ménière's disease**
     - ➢ A chronic condition characterized by acute vertigo (dizziness) attacks, nausea, tinnitus, fluctuating hearing loss and a feeling of aural fullness.
     - ➢ Estimated >600,000 patients in the US.
   - ❑ **Hearing loss**
     - ➢ Estimated ~36M patients with some degree of hearing loss in the US.

Source: OTIC S-1 filing; American Hearing Research Foundation; Audiology.org; Medscape; American Academy of Otolaryngology

Current Treatments For Most Common Ear Diseases

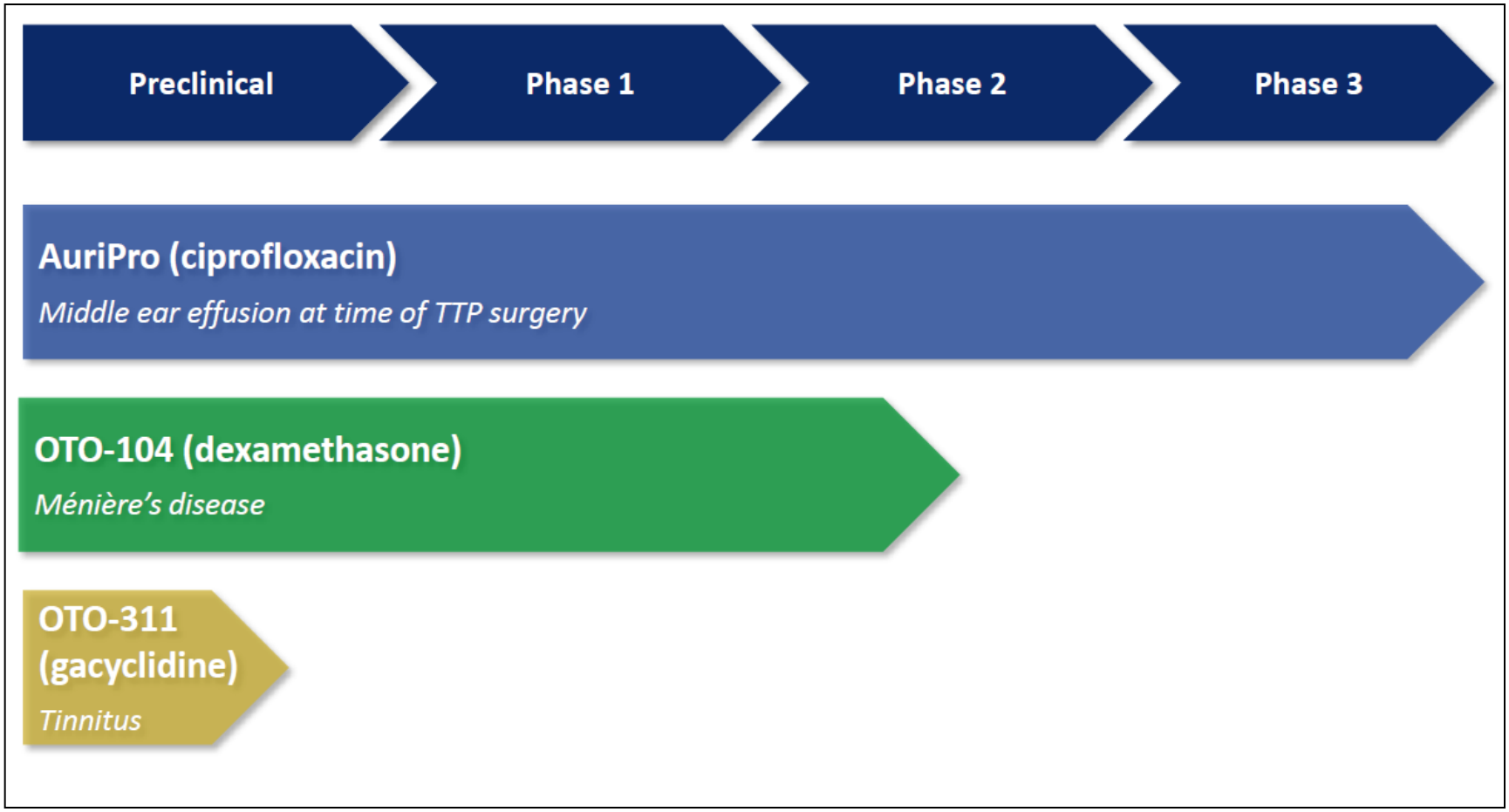
Indications that OTIC is currently targeting

Part of Ear	Disease	Current Treatment	Limitations
Outer ear	Otitis externa	Antibiotic ear drops or oral antibiotics for severe cases	Multi-dose, multi-day regimens
Middle ear	Otitis media	Oral antibiotics or tympanostomy tube placement (TTP) surgery and off-label use of antibiotic ear drops	Systemic side effects and increased risk of bacterial resistance; multi-dose, multi-day regimens particularly for children
Inner ear	Ménière's disease	Low-salt diet, off-label use of diuretics, oral steroid, repeat IT injections of steroid solution, chemical or surgical ablation of vestibular nerve, low-pressure pulse generator (Meniett)	no cure and no FDA approved therapy; off-label use of diuretics is not backed by high-quality evidence; IT injection of steroid solution has short drug exposure and thus dosing regimen is cumbersome; systematic side effects for oral steroid
	Tinnitus	Audio masking devices, hearing aids, cognitive behavioral therapy, off-label administration of antidepressants, anti-anxiety mediations, and steroids	None of these therapies is backed by strong evidence; no FDA approved drugs; no cure
	Hearing loss	Intratympanic injection of steroid for sudden hearing loss	Short drug exposure due to solution-based formulation; pts need to be immobilized for an extended period of time; multi dosing

Source: Piper Jaffray Research

Given the limitation of the current therapies, we believe there is a large unmet need for improved drug delivery with prolonged drug exposure to avoid repeat, cumbersome administration.

OTIC Pipeline



Source: OTIC company presentation

OTIC also plans to develop AuriPro for other indications including acute otitis media with tympanostomy tube in place (AOMT), acute otitis externa, chronic suppurative otitis media, and prophylaxis following middle ear surgeries, which could provide meaningful upside for AuriPro sales if approved.

Competitors In Otology Space

Indications	Company	Stock Ticker	Lead Program	Mechanims	Formulation and Administration	Status
Otitis Media, Externa	Novartis	NVS	AL-60371	Ciprofloxacin/ Dexamethasone	Suspension	In P2 and P3 trials
Ménière's disease	Auris Medical	EARS	AM-111	Synthetic peptide D-JNKI-1	Gel	Plan to initiate P2 (open-label)
	Synphora AB	Private	Latanoprost	Prostaglandin $F_{2\alpha}$ receptor agonist	Single or repeated IT injection?	in P2/3 trial
Tinnitus	Auris Medical	EARS	AM-101	NMDA receptor antagonist	Gel; triple intratympanic injection on 3 consecutive days	in P3 trial
	Autifony Therapeutics	Private	AUT00063	Kv3 modulator	N/A	Finished P1
	Merz Pharma/Kyorin Pharma	Private	Neramexane	NMDA receptor antagonist	Oral	Merz suspended development for chronic tinnitus while Kyorin continues with a P2 trial for tinnitus
	Novartis	NVS	BGG492A	Active AMPA/kainate antagonist	Oral	Finished P2
Hearing loss	Auris Medical	EARS	AM-111	Synthetic peptide D-JNKI-1	Gel; single or multiple doses	Finished P2; planning to initiate a single-dose P3 study and a multiple-dose P2 study
	AudioCure Pharma	Private	AC002	Beta-carboline	Gel	N/A
	Otologic Pharma	Private	NHPN1010	N-acetylcysteine plus HPN-07 neuroprotectant	Oral	Preclinical
	Sound Pharma	Private	SPI-1005	Anti-oxidant; neuroprotectant	Oral	Reported positive P2 data in the preventation and treatment of temporary inner ear hearing loss from listening to loud music

Source: Piper Jaffray Research and OTIC S-1

We view OTIC as a leader in developing therapies in the otology space and may eventually become a consolidator (or a target) of other players in the field.

Our Quick Thoughts On Ear Space

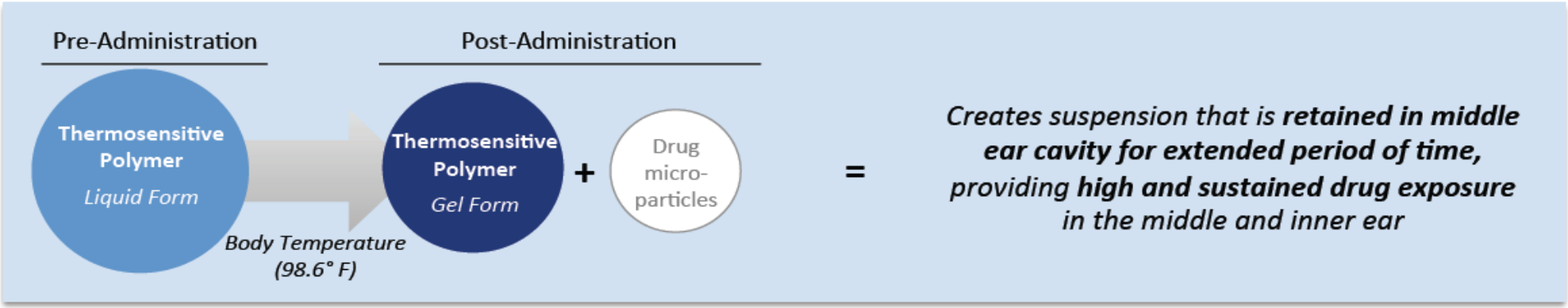
- Large market with unmet need
  - ~20M patients in the US seek treatment each year for conditions like ear infections, Ménière's disease, tinnitus and hearing loss.
  - There are no cures for diseases like Ménière's disease and tinnitus. Additionally, there are no FDA-approved therapies for these diseases. As a result, patients who seek treatment are often inadequately treated and there remains a large population of untreated patients.
  - Challenges accessing the space behind the tympanic membrane to treat various diseases is reminiscent of the back-of-the-eye opportunity.

- Lack of innovation in treating ear diseases for many years
  - Difficulty of delivering drug to the middle and inner ears has made the field challenging to many drug developers.
  - Diseases like Ménière's disease and tinnitus are still not fully understood.

- Why OTIC is a top pick
  - Best-in-class ear delivery technology in our view.
  - Derisked lead asset after P3 data with AuriPro.
  - Meaningful potential upside opportunity from the Ménière's program.
  - There are only a handful of companies focused on ear disease. Lack of competition in the space enables OTIC to emerge as a leader in this underserved market.

OTIC's Proprietary Drug Delivery Technology

Provides sustained drug exposure in the middle or inner ear from a single local administration:



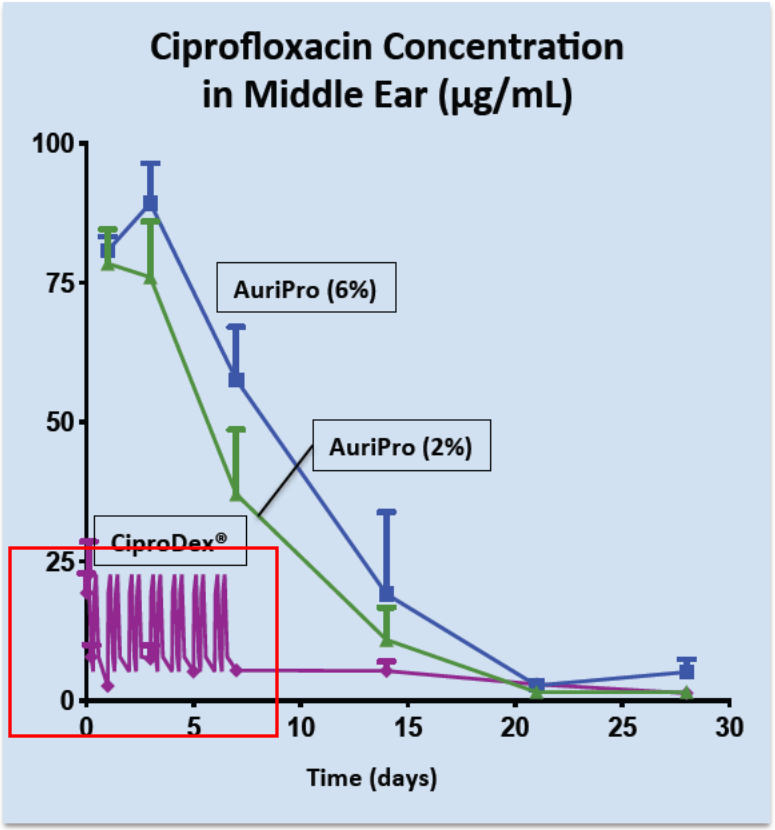
Source: OTIC Company Presentation

- ❑ OTIC has developed a proprietary formulation technology that utilizes a thermo-reversible polymer, poloxamer 407, which is in liquid form at room temperature but transitions to a gel at body temperature.

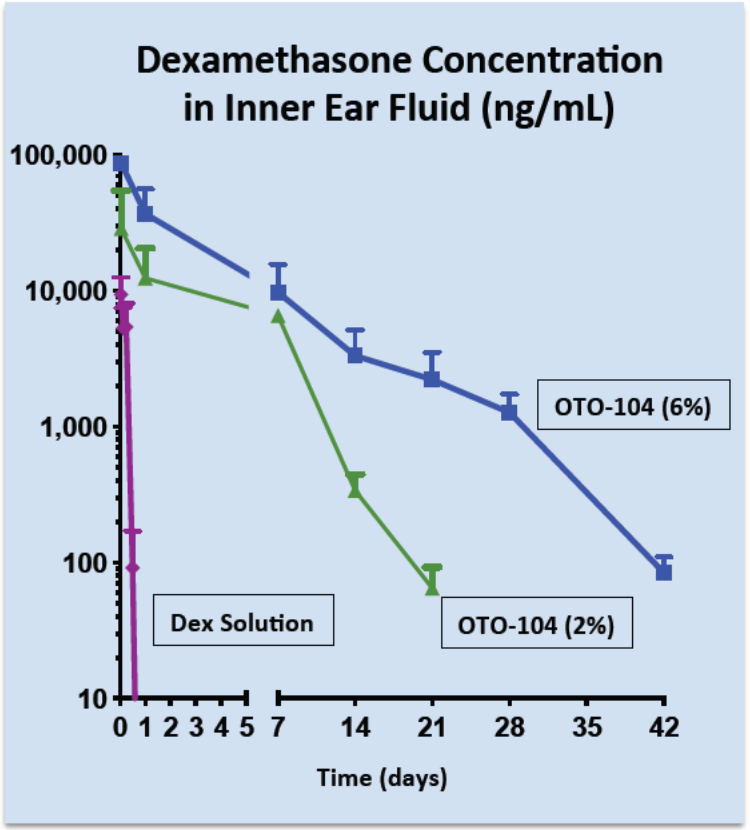
- ❑ The polymer is mixed with drug microparticles to create suspensions that allows for prolonged residence time in the middle ear and prevents the loss of fluid down the eustachian tube (found in current ear drop treatment).

There are 'depot' formulations for sustained drug delivery in various difficult-to-access settings such as the eye, where a long lasting drug exposure helps avoid repeat cumbersome administration. OTIC borrowed this concept to apply to the ear.

AuriPro's Drug Release Kinetics



Preclinical PK study in guinea pigs: single IT administration of AuriPro vs. BID dosing of CiproDex* ear drops x 7 days



Preclinical PK study in guinea pigs following single IT administration

*CiproDex is a registered trademark of Alcon

Source: OTIC Company Presentation

OTIC's polymer formulation provides sustained drug exposure with a single administration. What is more attractive is that this platform technology is enabling the company to mix the polymer with many well-studied molecules to treat many ear diseases.

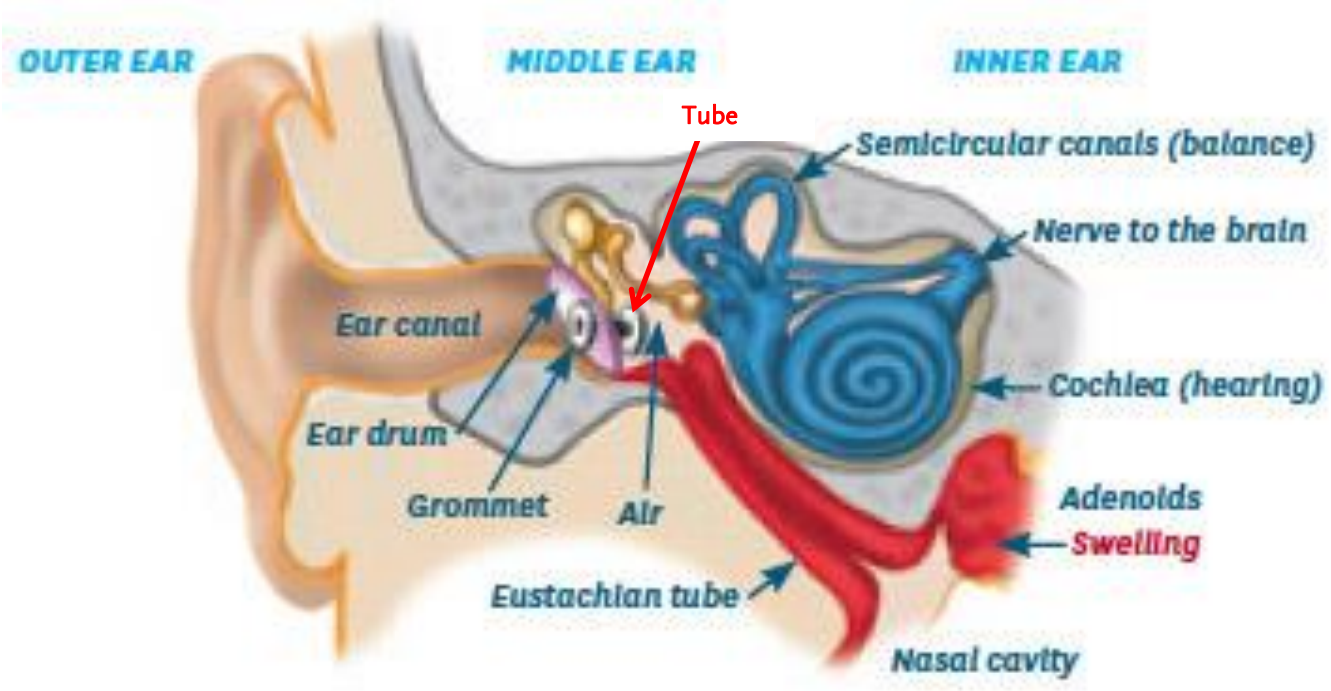
Safety Profile Of Poloxamer 407

- Poloxamer 407 is made up of 70% polyoxyethylene and 30% polyoxypropylene.

- It has been extensively used at low concentrations in permanent waves, mouthwashes and breath fresheners, oral hygiene products, underarm deodorants, skin care preparations, etc. Also used at higher concentration in LeGoo endovascular occlusion gel for vascular surgery.

- Singh-Joy and McLain reported extensive safety profiles of poloxamers including 407 (International Journal of Toxicology 2008) and concluded that poloxamers are largely nontoxic to animals.

Focus On AuriPro: Tympanostomy Tube Placement (TTP)



Source: www.healthed.govt.nz

The Eustacian tube drains fluid (and clear infection) from the middle ear space, but its function can be impaired if the passageway is blocked by swelling of the adenoids or other structures around the nasal cavity.

TTP is a surgical procedure which involves insertion of a tube across the eardrum to ventilate the middle ear space. The tympanostomy tube is approximately 1/20th of an inch in width. Most tympanostomy tubes stay in the ear for **12-14** months but can be reinserted if problems persist.

Usage Of TTP

- TTP has been used extensively to treat otitis media, or middle ear inflammation, with persistent middle ear fluid and/or frequent ear infections.

- Otitis media is the 2nd most common illness diagnosed in children after acute upper respiratory infection. Children younger than 7 years have a high risk of developing otitis media as a result of immature immune systems (and frequent swelling of the adenoid glands) which can confound limited function/patency of the eustachian tube.

- Without being properly treated, children with chronic/recurrent otitis media can develop irreversible hearing loss, delays in speech, language and learning development.

- There are about 1M TTP surgeries performed in the US every year, a majority of which are performed on children (OTIC S-1; Rosenfeld, R.M. 2013).
  - Approximately 667,000 children (< 15 years) receive TTP every year.
  - By year 3, ~7% children receive TTP.
  - TTP is the most common ambulatory surgery performed on children in the US.

Guidelines For TTP Use

Recommendation	Chronic bilateral OME with hearing difficulty
	Recurrent AOM with EE
Option	Chronic OME with symptoms
	Children with recurrent AOM or with OME of any duration at risk of speech, language, or learning problems
Recommendation (against)	OME of short duration
	Recurrent AOM without EE

AOM: acute otitis media

EE: ear effusion

OME: otitis media with effusion

Source: Rosenfeld, R.M. 2013

TTP is not recommended for children with a single epsiode of OME of less than a 3-month duration or recurrent AOM without EE.

Benefits And Risks Of TTP

❑ Benefits of TTP

- Severe or persistent acute otitis media
  - Allow drainage of fluid from the middle ear.
  - Provide a direct delivery route for topical antibiotic eardrops.
  - Avoid the AEs of systemic therapy.
  - Minimize the risk of bacterial resistance.
- Chronic otitis media (Rosenfeld, R.M. 2013)
  - Reduce the prevalence of middle ear effusion by 32% in the 1st year in children.
  - Improve average hearing level by 5 to 12 dB .
  - For children with development delays, TTP might also help improve speech, language, or cognitive outcomes.

❑ Risks and adverse events of TTP

- Anesthesia typically required for young children (office procedure for older children/adults).
- Otorrhea (drainage from ear)
  - The most common sequela of TTP .
- Visible changes in the appearance of the tympanic membrane.
  - Tympanosclerosis (calcification of tissues in the middle ear): does not affect hearing or future chance of ear infection.
  - Persistent perforation: seen in **1-6%** of ears after TTP; surgical closure might be required (if persists) with **80%-90%** success rates through a single outpatient procedure (Rosenfeld, R.M. 2013).
- Hearing worsening is trivial for most patients; however, there is a possibility of measurable LT hearing loss (although prevention of hearing loss from resolving effusions should outweigh this risk).

Tube Otorrhea Treatment

- Otorrhea is the most common consequence of TTP. During the first 18 months after TTP, the proportion of patients who had one or more episodes of otorrhea reached 74.8% after 12 months and 83.0% after 18 months (Ah-Tye, C. 2001).

- Otorrhea may be categorized as four types depending on the timing of occurrence (Rosenfeld, R.M. 2013):
  - Early postoperative otorrhea (within first 4 weeks after TTP)
  - Delayed otorrhea (> 4 weeks after TTP)
  - Chronic otorrhea (persisting >= 3 months)
  - Recurrent otorrhea (3 or more discrete episodes)

- Most otorrhea is acute, with only **7%** of children experiencing recurrent otorrhea (Rosenfeld, R.M. 2013).

- For acute tube otorrhea, prescription of topical antibiotic eardrops is strongly recommended (Rosenfeld, R.M. 2013), though no eardrops have been approved to treat middle ear effusion at or after TTP.

Otorrhea is used as a marker for presence of infection, but it is insensitive and non-specific. Because of this, the FDA does not require microbial eradication as an endpoint in clinical trials.

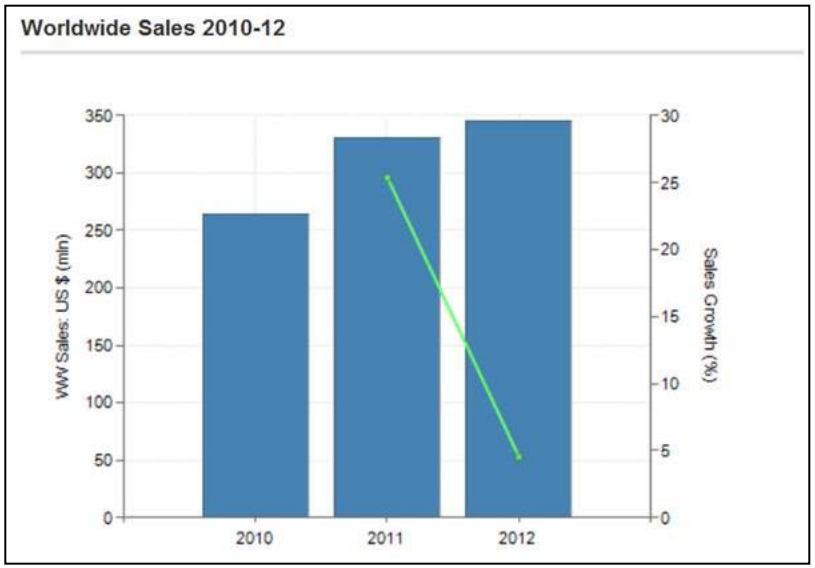
Ciprodex: Leading Branded Antibiotic Ear Drop Used After TTP

- Ciprodex is the leading branded antibiotic ear drop from Alcon, a division of NVS. It is a sterile otic suspension of ciprofloxacin and dexamethasone (although evidence suggests the dexamethasone component doesn't add activity).

- Ciprodex is indicated to treat acute otitis media in pediatric patients with tympanostomy tubes and also treatment of acute otitis externa. However, it has been used routinely off-label during and shortly after the TTP surgery for patients with acute otitis media, as often TTP is not sufficient to treat middle ear effusion.

- The treatment regimen is four drops instilled into the affected ear twice daily for seven days.

- In 2012, the global sales of Ciprodex reached ~$350M, with IMS data suggesting most of the sales are derived in the U.S. Ciprodex patents are expected to expire around ~2020.



Source: EvaluatePharma.com

Limitations Of Ciprodex

Although effective, Ciprodex has several limitations:

- Its twice-daily, seven-day regimen poses a significant compliance/convenience challenge for patients. Failure to comply with the regimen may promote selection and proliferation of resistant pathogens.

- Difficulty in injecting liquid drops through the tympanostomy tube could lead to limited and variable exposure, and thus inconsistent efficacy among different patients.

- Liquid drops, once administered, tend not to stay in the middle ear compartment for long, and as a result, provide limited exposure and short lasting relief.

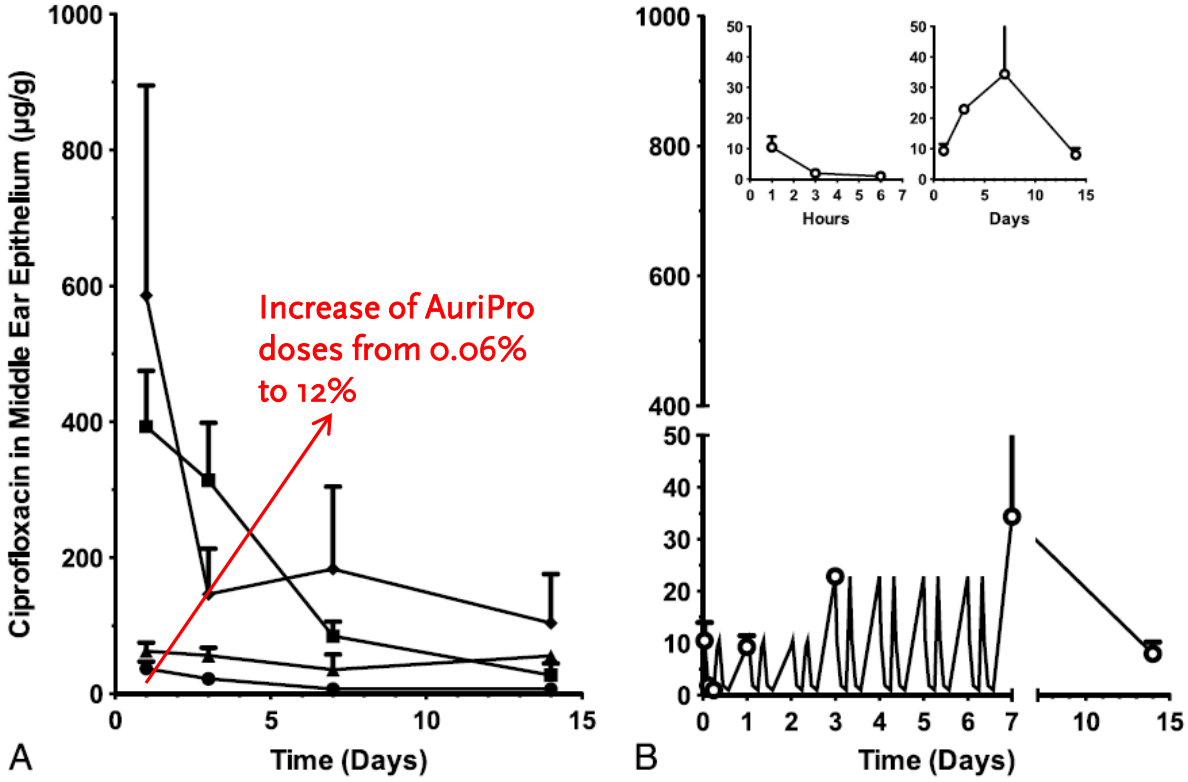
There is an important unmet need for a sustained-release antibiotic therapy with prolonged drug exposure to avoid repeat cumbersome administration for young children (which we believe most parents can relate to).

OTIC's Leading Program: AuriPro For Middle Ear Effusion At The Time Of TTP

- OTIC's leading program, AuriPro, is a sustained formulation of antibiotic ciprofloxacin. It is being developed to treat middle ear effusion in pediatric patients who requires TTP surgery.

- AuriPro provides sustained release to the middle ear and thus can effectively treat otitis media, when compared to FDA-approved ciprofloxacin otic drop formulations (Ciprodex).

Middle ear free ciprofloxacin levels after administration of AuriPor (A) or Ciprodex (B) in guinea pigs



Source: Wang, X. et al. Otology & Neurotology 2014

A single IT injection of AuriPro provides high C_{max} and steady dose, with gradual decline over time. In contrast, administration of Ciprodex results in a pulsatile profile with sharp declines within hours of each administration.

Potential Benefits Of AuriPro Relative To Ciprodex And Oral Antibiotics

Otonomy technology	Solution and oral based treatments
✓ Full course of treatment from a single administration	✗ Repeat dosing (both)
✓ High and sustained drug levels in the middle ear	✗ Pulsatile drug levels with antibiotics (both)
✓ Drug distribution throughout the inner ear compartment	✗ Declining drug levels away from the round window membrane (solution)
✓ Local delivery minimizes systemic exposure	✗ Systemic exposure and side effects (oral)
✓ Gelation occurs immediately upon administration	✗ Patients must remain in prone position for an extended period (solution)
✓ Improved patient compliance by enabling simple office-based administration by the ENT	✗ Compliance issues with multi-dose, multi-day regimens (both)

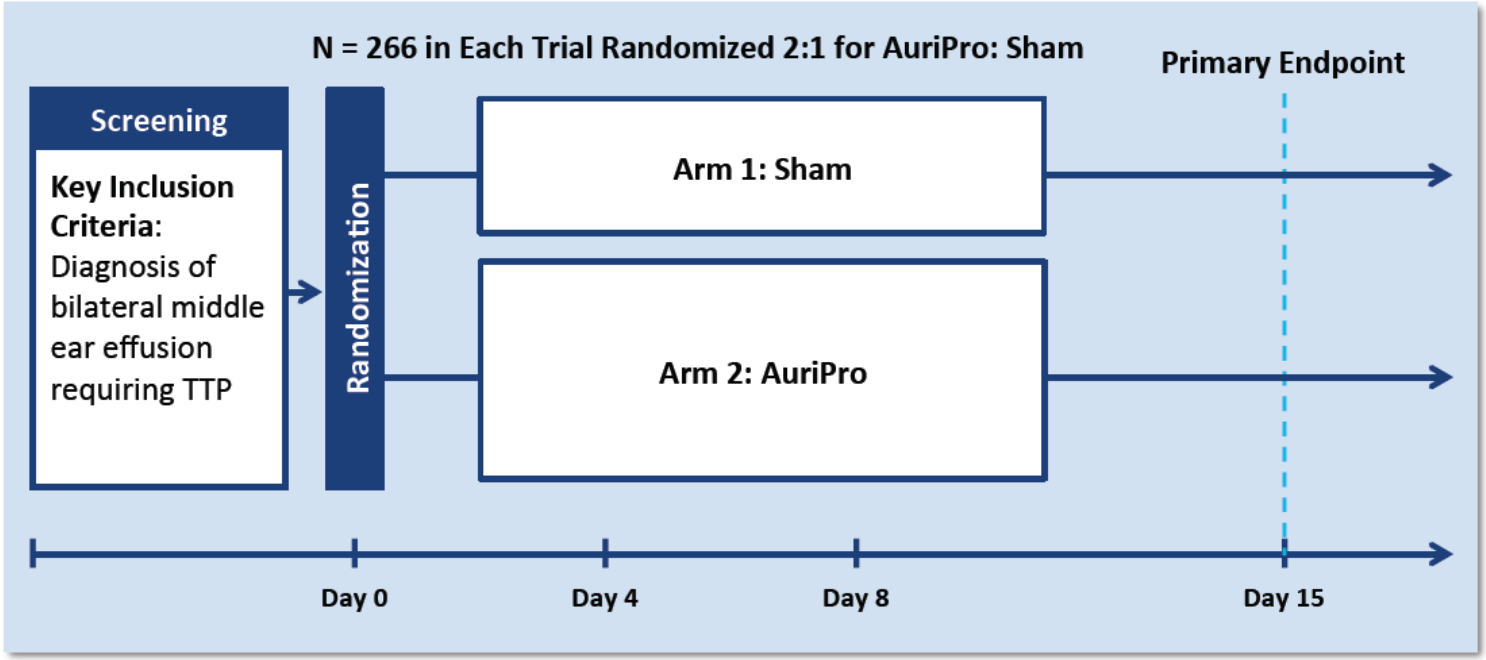
Source: OTIC presentation

AuriPro P3 Trial Design

- OTIC recently completed 2 identical P3 studies of AuriPro with 532 pediatric patients (6 months to 17 years of age) enrolled from 60 sites in the US and Canada.

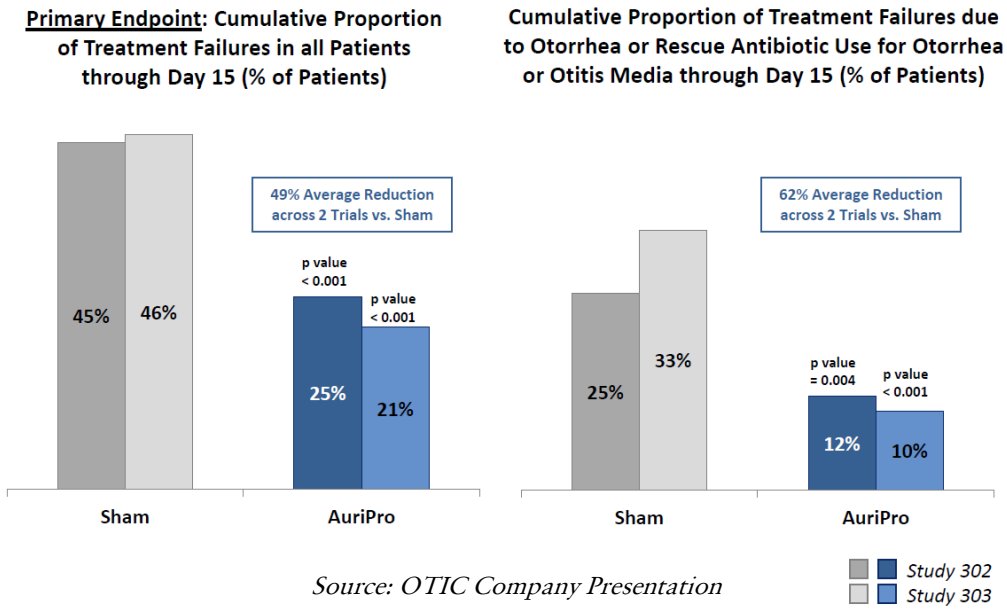
- In each trial, patients undergoing TTP for bilateral middle ear effusions were randomized 2:1 to receive a single intra-operative IT injection of AuriPro or a stimulated single IT injection (Sham).

- Primary endpoint is % of "treatment failures", defined as presence of otorrhea (observed by a blinded assessor) from Day 4 to Day 15 or use of rescue antibiotics (determined by treating physicians) from Day 1 through Day 15, whichever occurred first.



Source: OTIC Company Presentation

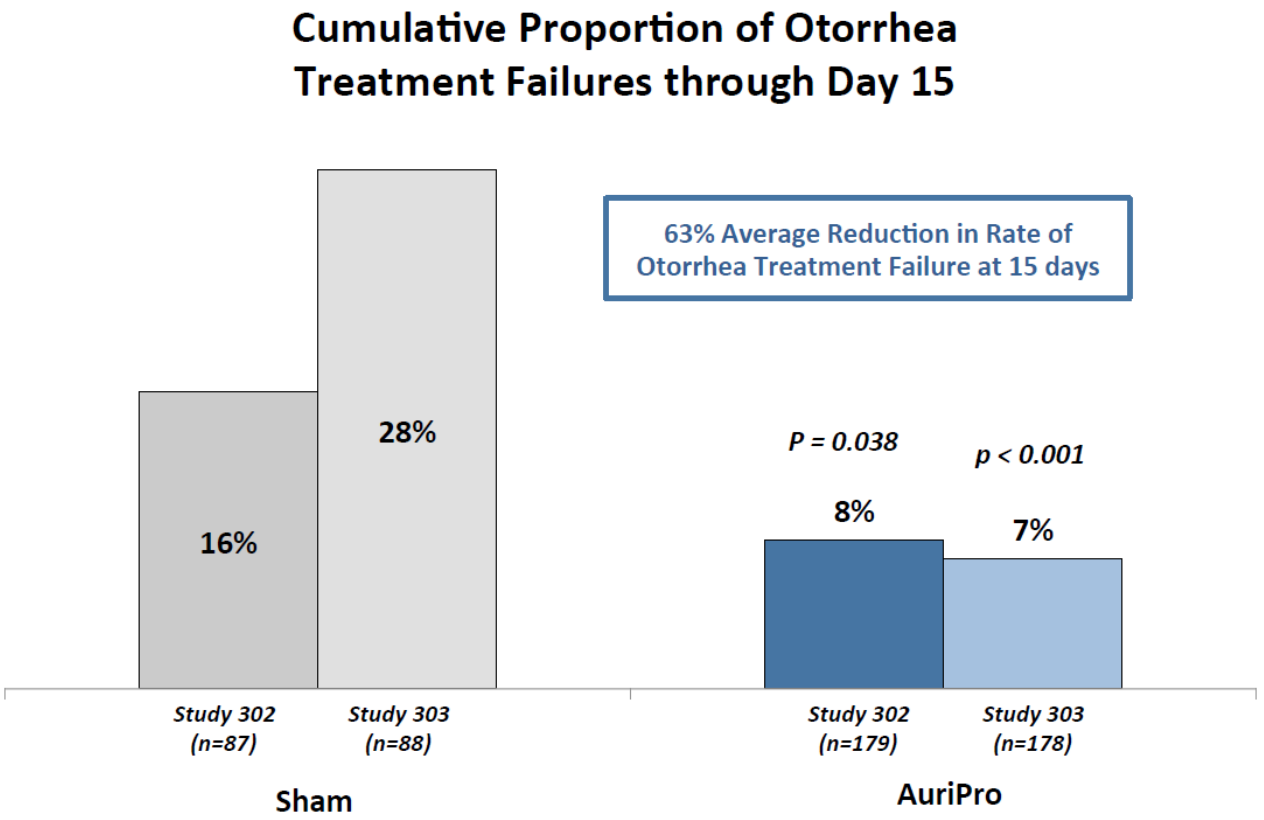
AuriPro P3 Trial Data: Primary Endpoint



Source: OTIC Company Presentation

- AuriPro demonstrated ~49% reduction in treatment failure across the two trials when compared to sham.
- OTIC later conducted a comprehensive patient-by-patient analysis to determine the incidence of treatment failure due to otorrhea or rescue antibiotic use for otorrhea or otitis media through Day 15. AuriPro reduced the failure rate by 62% compared to control.
- Patients who were treatment failures on AuriPro may have been non-bacterial effusions or with pathogens resistant to Cipro. Additional data from the trials will be informative and may identify new opportunities for OTIC.
- Longer-term follow-up data may identify a role for subsequent re-administration of AuriPro which would expand the commercial opportunity.

AuriPro P3 Trial Data: Secondary Endpoint



Source: OTIC Company Presentation

- A secondary endpoint in the P3 trials evaluated treatment failure due to otorrhea observed by blinded observer through Day 15.
- AuriPro reduced otorrhea rate by 63% across the two trials as opposed to sham.

AuriPro P3 Trial Data: Safety

No Difference in Treatment Emergent Adverse Events (TEAE)

(Patients from Combined 302 and 303 Studies)

System Organ Class: Number of Patients (%)	Sham (N=174)	AuriPro (N=356)
Total Patients with at least one TEAE Reported	**95 (54%)**	**189 (53%)**
Infections and infestations	40 (23%)	85 (24%)
General disorders and administration site conditions	30 (17%)	62 (17%)
Gastrointestinal disorders	17 (10%)	41 (11%)
Respiratory, thoracic and mediastinal disorders	23 (13%)	38 (11%)
Injury, poisoning and procedural complications	20 (11%)	26 (7%)
Ear and labyrinth disorders	11 (6%)	25 (7%)
Skin and subcutaneous tissue disorders	4 (2%)	13 (4%)
All others	≤2%	≤2%

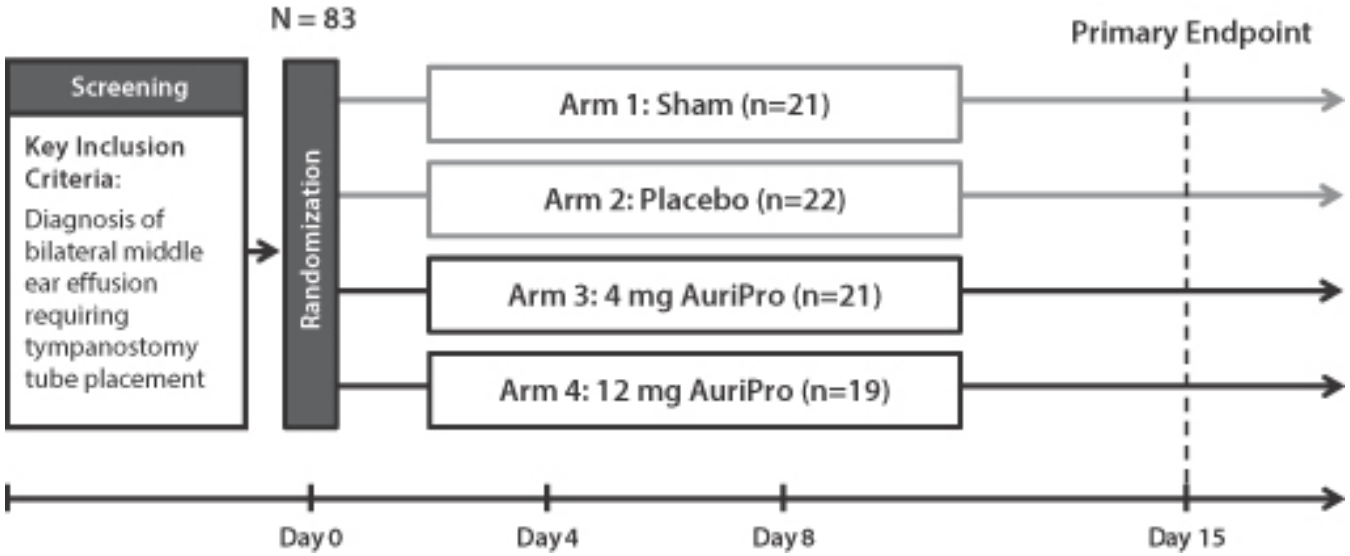
Note: 2 patients were randomized on the day of surgery but not treated (1 patient in the sham group and 1 in the AuriPro group)

Source: OTIC Company Presentation

Drug was very well tolerated. No increase in AE. One of the cleanest Phase III datasets we've seen.

In addition, AuriPro did NOT affect hearing, tympanometry or otoscopy (examination of the ear) and did not cause tube clogging.

AuriPro P1b Trial

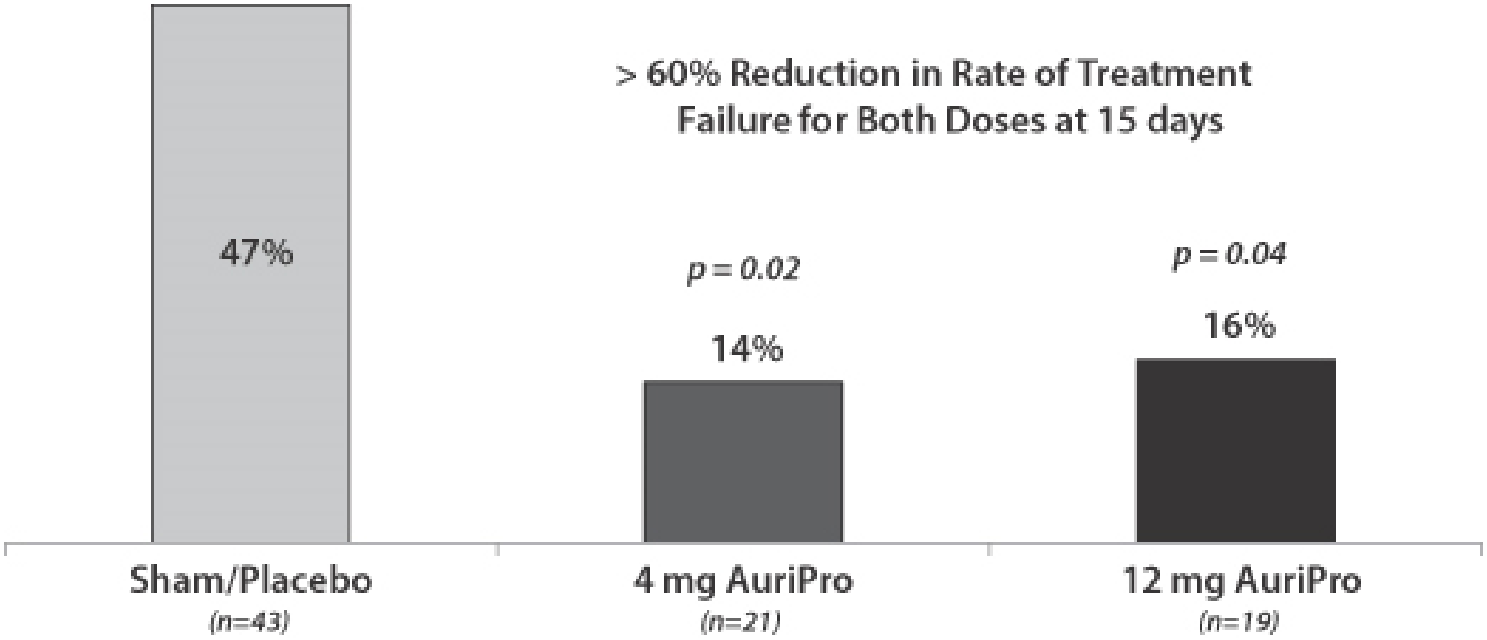


Source: OTIC S-1

- OTIC conducted a P1b trial of AuriPro before the 2 P3 trials. Two dose levels of AuriPro, 4 mg and 12 mg, were compared to P407 gel vehicle (placebo) and no treatment (sham). Patients were examined on Day 4, 8, 15 and 29 after surgery.

- Primary endpoint of the trial was treatment failure due to otorrhea (from Day 4 to Day 15) or use of rescue antibiotics (from Day1 to Day 15).

AuriPro P1b Trial Data



Source: OTIC Company Presentation

- Both 4 mg arm and 12 mg arm demonstrated significant reductions (> 60%) in treatment failure when compared to control, in line with P3 results.
- 12 mg of AuriPro led to slightly higher reduction than 4 mg of AuriPro, consistent with preclinical pharmacokinetic profile.
- No serious AEs were found in AuriPro arms.

AuriPro Data Compared To Antibiotic Ear Drops

- To compare the efficacy of AuriPro and antibiotic ear drop, we conducted an extensive literature search and assembled clinical trials of antibiotics in treating infection after TTP surgery (see next slide for details). Overall, there are big variations in trial protocol designs especially with regard to selection of primary endpoints.

- We identified 3 trials of ciprodex or ciprofloxacin (highlighted in orange) for intra- or post-operative treatment of early middle ear effusion, all of which used otorrhea rate as the primary endpoint. Not surprisingly, otorrhea rate the in control arm varies widely among the trials probably due to different patient selection criteria, different timing for otorrhea examination, and/or different definitions of otorrhea.

- In the AuriPro P3 trials, otorrhea rates in control arms were 16% and 28% for studies 302 and 303, respectively, which are more in line with the study published by Nawasreh, O.O. et al. (16.5% in control arm) versus other studies. Thus Nawasreh's study may be the optimal comparator for AuriPro P3 trials. Otorrhea rate after ciprofloxacin treatment was ~8% in Nawasreh's study, which is in line with the AuriPro treatment effect (8% for 302 and 7% for 303).

- It is difficult to compare AuriPro data to Ciprodex data published by Giles, W. et al, given the big difference in otorrhea rate between the control arms. In addition, Giles's study was a single-center study, which could be naturally biased. Moreover, there is lack of evidence that the addition of dexamethasone to ciprofloxacin improves clinical outcome for patients experiencing TTP.

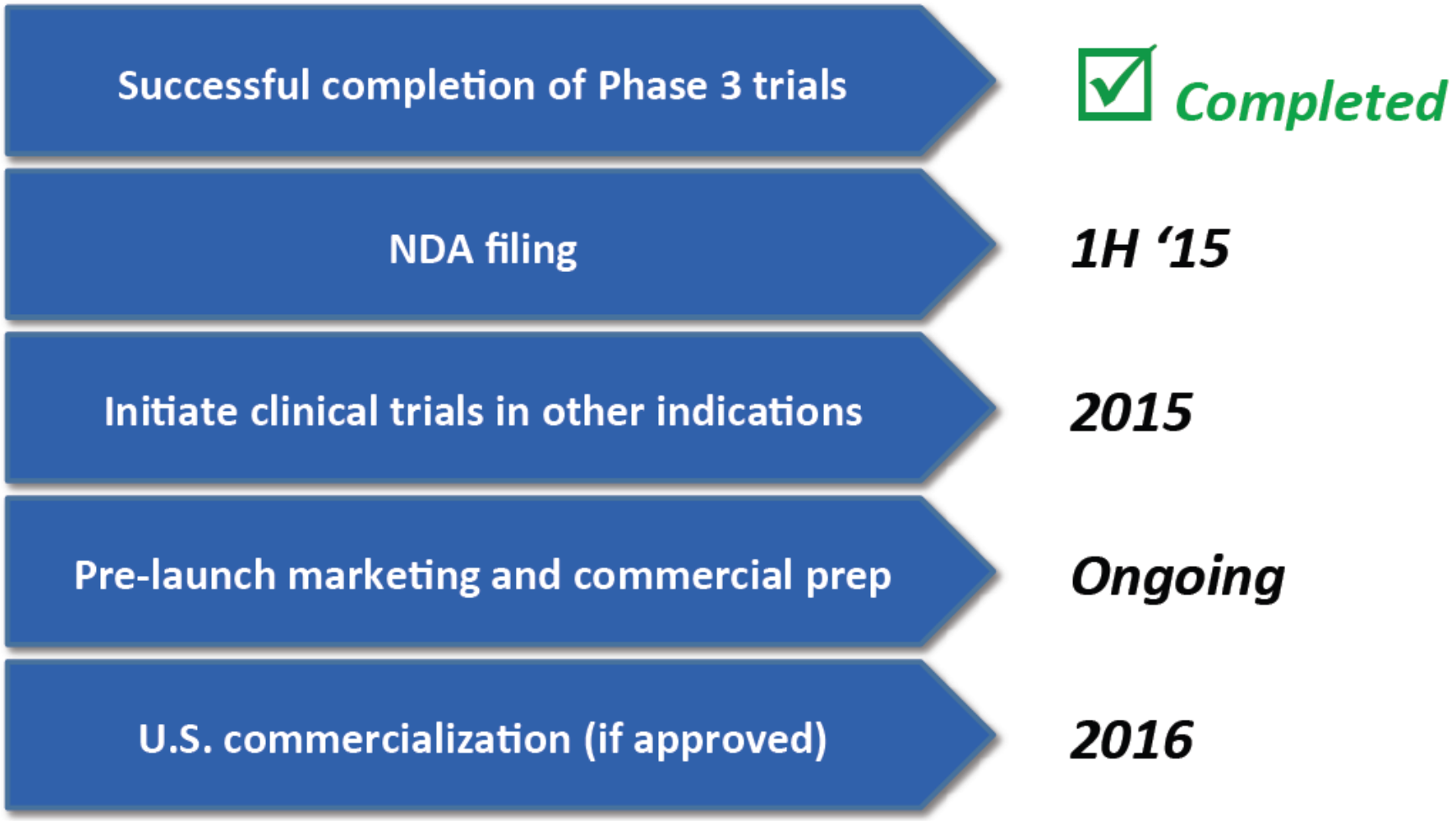
- In summary, we think that AuriPro is at least as effective as ciprofloxacin ear drops in treating otorrhea after TTP surgery, but offers significant advantages in compliance and convenience.

Data Summary For AuriPro Vs. Antibiotic Drops For TTP

Study Design	Settings	Dosing	Patient #	Age	Endpoints	Results	Reference
2 identical P3, multi-center, randomized, placebo-controlled	Intra-operative treatment of middle ear effusion	1st arm: single dose of **AuriPro** during TTP procedure; 2nd arm: sham	532	6 months - 17 years	% of otorrhea treatment failures through Day 15 (secondary endpoint of the study)	8% vs. 16% (p = 0.038); 7% vs. 28% (p < 0.001)	OTIC S-1
Randomized, 3-arm	Intra-operative treatment of middle ear effusion	1st arm: no treatment; 2nd arm: a single dose of **ciprofloxacin** drops intraoperatively; 3rd arm: received a single dose followed by 5-day postoperative course	155	3-14 years	Otorrhea incidence	16.5% vs. 8.4% vs. 8.2% (p = 0.011 between treated and untreated)	Nawasreh, O.O. et al. Saudi Med J 2004
Single-center, randomized, evaluator-blinded, parallel-group	Post-operative treatment of early middle ear effusion after TTP surgery	1st arm: receive **Ciprodex** trentment (4 drops twice daily) for 5 days; 2nd arm: no treatment	200	<6 months to 4 years	Otorrhea incidence at 2 weeks after TTP surgery	4.95% vs. 39.39%	Giles, W. et al. International Journal of Pediatric Otorhinolaryngology, 2007
Single-blind, randomized	Intra-operative treatment of middle ear effusion	One ear received **topical ciprofloxacin**, while the contralateral ear served as a control	154	6 months to 14 years	Postoperative otorrhea between 24 hours and 2 weeks after TTP surgery	3.9% vs. 9.1% (p = 0.029)	Zipfel, T.E. et al. The American Journal Of Otology 1999
Randomized, 3-arm	Post-operative treatment of early middle ear effusion after TTP surgery	1st arm: no treatment; 2nd arm: received **gentamicin** otic drops immediately after TTP surgery; 3rd arm: received additional 48 hours of drops (4 drops in each ear, 3 times a day)	N/A	N/A	Otorrhea incidence within 2 weeks post-operation	12% vs. 8.8% vs. 5.6% (p = 0. 62)	Scott, B.A. et al. Otolaryngology - Head and Neck Surgery 1992
Randomized, 3-arm	Intra-operative treatment of middle ear effusion	1st arm: no treatment; 2nd arm: a single dose of **polymyxin B-neomycin-hydrocortisone** intraoperatively; 3rd arm: an intraoperative dose followed by a 5-day course	300	Mean age of 43 months	Otorrhea incidence	16.4% vs. 8.3% vs. 8.1% (p = 0.011 between treated and untreated; no difference between single dose and multiple doses)	Hester, T.O. et al. Arch Otolaryngol Head Neck Surg 1995
Prospective analysis	Intra-operative treatment of middle ear effusion	Received **ciprofloxacin** drops or **oxymetazoline** drops	488	6 months to 14 years	2-4 weeks postoperative otorrhea and tube occlusion	otorrhea rate: 7% vs. 10% (p = 0.32);	Kumar, V.V. et al. The Laryngoscope 2005
Blinded, randomized, 3-arm	Post-operative treatment of early middle ear effusion after TTP surgery	1st arm: no treatment; 2nd arm: **ofloxacin** drops; 3rd arm: **neomycin sulfate-polymyxin B sulfate-hydrocortisone**	306	Mean age of ~22 months	Treatment failure defined as presence of otorrhea or plugged tube	29.9% vs. 12.1% vs. 7.7% (P < 0.05 between treated and untreated)	Poetker, D.M. et al. Arch Otolaryngol Head Neck Surg 2006

Source: Piper Jaffray Research

Next Catalysts For AuriPro For TTP Indication



Source: OTIC Company Presentation

AuriPro Expansion Into New Indications

❑ Acute Otitis Media With TTP (AOMT)

- ➢Treatment of infection that develops after TT are inserted.
- ➢Ciprodex drops approved for this indication already.
- ➢Obvious add-on given similar setting and indication as for TTP with effusion.
- ➢Additional trial will increase comfort in injecting the drug through the TT.
- ➢P3b study will likely be non-inferiority vs approved drops, to start in 2015 (see data summary of Ciprodex for AOMT indication in next slide).

❑ Chronic Suppurative Otitis Media

- ➢Less frequent in the U.S.; condition with fluid build-up in the middle ear with spontaneous rupture of TM.
- ➢Equivalent scenario to having a TT in place considering access to the middle ear.
- ➢This indication may be combined with AOMT.

❑ Middle Ear Surgery Prophylaxis

- ➢Procedures for mastoiditis, etc to ensure prophylaxis around the time of the intervention.

❑ Acute Otitis Externa

- ➢Infection of the outer year ("Swimmer's Ear").
- ➢Very advanced condition by the time it gets to the ENT specialist.
- ➢Will need to identify delivery strategy to treat the external ear canal but the premise is otherwise similar.

Data Summary Of Antibiotic Drops For AOMT

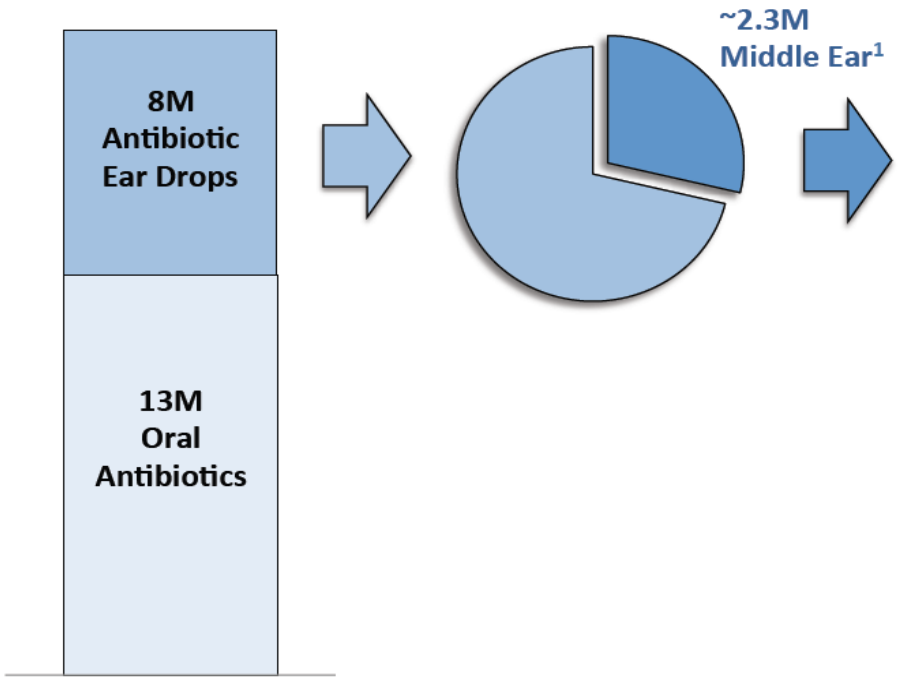
Study Design	Settings	Dosing	Patient #	Age	Primary Endpoints	Results	Reference
Nonrandomized, open-label	AOMT	Each patient received 3 drops of **ciprofloxacin** each time, 3 times a day, for 14 days	10	3 to 8 years	Cure/improvement rates at days 7 and 14	10 of 11 infected ears were improved or cured at day 7; 10 of 11 ears were completely cured at days 14 and 44.	Force, R.W. et al. Arch Otolaryngol Head Neck Surg 1995
Randomized, double-blind, controlled, 3-arm	AOMT	1st arm: saline; 2nd arm: 4 **ciprofloxacin** drops twice daily for 1 wk; 3rd arm: **amoxicillin** 3 daily doses for 1 wk	68	Mean age of 22 months	Treatment failure defined as presence of otorrhea in at least one ear after 7 days of treatment	58% vs. 23% vs. 70% ($p < 0.05$ compared to saline; $p < 0.005$ compared to amoxicillin)	Heslop, A. et al. The Laryngoscope 2010
Randomized,multicenter, controlled, 2-arm	AOMT	1st arm: dosed **Ciprodex** drops 2 times per day for 7 days; 2nd arm: **ofloxacin** drops. Only AOMT patients were recruited in the study.	N/A	N/A	Clinical cure; microbiological eradication rate	Clinical cure rate among culture positive patients: 90% vs. 79%; microbiological eradiation rate: 91% vs. 82%	Ciprodex label
Randomized, observer-masked, parallel-group, multicenter	AOMT	1st arm: 4 drops of **Ciprodex** twice daily for 7 years; 2nd arm: 600mg of amoxicillin/42.9mg of clavulanic acid oral suspension every 12 hours for 10 days	80	6 months - 12 years	Clinical cure rate	85% vs. 59%	Dohar, J. et al. Pediatrics 2006
AOMT: acute otitis media in patients with tympanostomy tubes							

Source: Piper Jaffray Research

Market Opportunities For AuriPro

> 20M Antibiotic Units for Otic Uses

> 2M Ear Drop Units for Middle Ear Uses[1]



Rationale for TTP as Lead Indication

- 1 million TTP procedures per year
- Antibiotic ear drops are used routinely during and post TTP surgery
- Ear drops not approved for use
- ~75% of patients are ≤ 5 years of age
- Compliance with multi-dose, multi-day regimen is challenging
- Single-use treatment by ENT in OR eliminates patient compliance risk

+

Expansion Indications

- AOMT
- Chronic suppurative otitis media
- Middle ear surgery prophylaxis
- Acute otitis externa

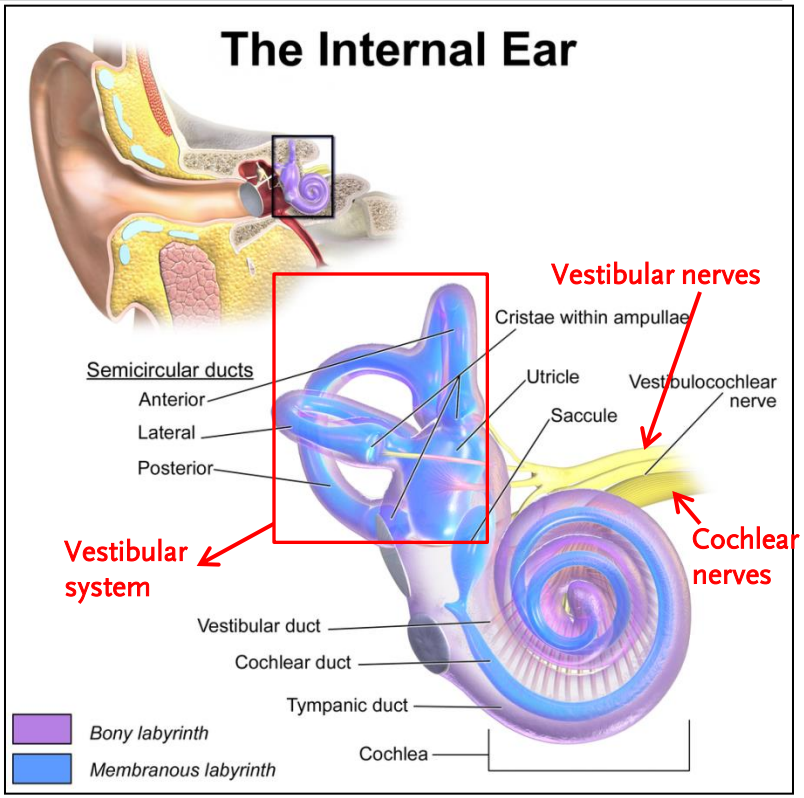
[1]Company estimates

Source: OTIC Company Presentation

Across all indications, we believe AuriPro peak U.S. sales could be between $200M to $400M assuming a conservative net price point of ~$225/dose. **Specialists with whom we have spoken are very enthusiastic for the product** and parents can well appreciate the challenges of having to chase children around to put drops in their ears. Compliance advantage is also significant.

Next Program: OTO-104 For Ménière's Disease

- Before we dive into Ménière's disease (a disease of inner ear), it is useful to have a quick review of inner ear anatomy.
- The inner ear is the innermost part of the ear which comprises two major functional parts responsible for hearing and balance:
  - **Cochlea** (dedicated to hearing): converts sound pressure waves from the outer ear into electrochemical impulses which are passed on to the brain via the cochlear nerves
  - **Vestibular system** (dedicated to balance): collect balance information and pass it on to the brain via the vestibular nerves
- The cochlea and the vestibular system constitute the bony labyrinth, a hollow cavity with a system of fluid-filled canals.
- Inside the bony labyrinth is a collection of fluid-filled tubes and chambers known as the membranous labyrinth.
- The membranous labyrinth contains fluid named endolymph and is separated from the bony labyrinth by fluid called perilymph.
- The level of inner ear fluid is maintained by a small organ called the endolymphatic sac (not shown in the diagram).



Source: http://en.wikipedia.org/

What Is Ménière's Disease?

- Ménière's disease is a chronic disease of the inner ear that mainly affects adults aged 40-60 years. The disease is characterized by intermittent episodes of vertigo attacks (lasting from minutes to hours), nausea, fluctuating hearing loss, tinnitus and aural fullness.

- Vertigo attacks are often preceded by aura (visual, sensory or language disturbance), similar to migraine attacks.

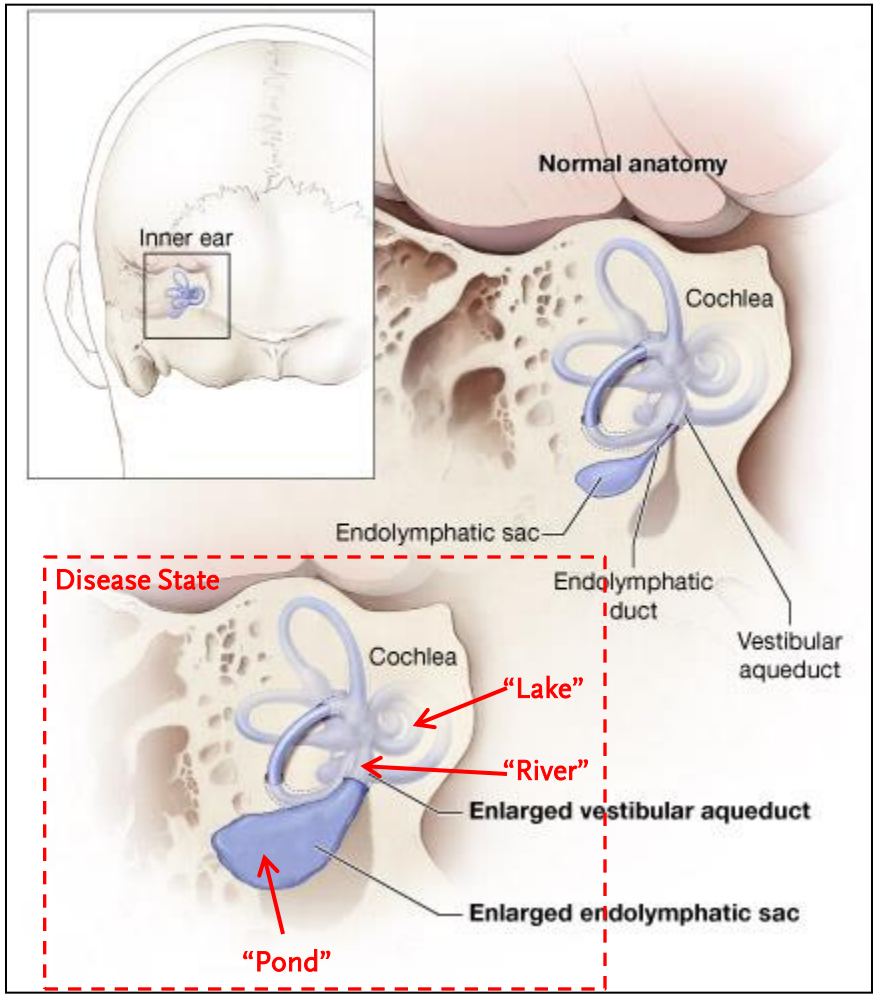
- Ménière's disease is difficult to diagnose, especially in early stages when true vertigo may not present.

- According to the NIDCD (National Institute on Deafness and Other Communication Disorders), there are 615,000 patients with Ménière's disease in the US alone, with 45,500 new cases diagnosed per year. 20% of the patients develop bilateral disease (Coelho, D. H. et al. Laryngoscope 2008).

Source: http://www.dallasspinalcare.com/

Pathophysiology Of Ménière's Disease: Endolymphatic Hydrops?

- Ménière's disease is a disease of inner ear. The mechanism behind Ménière's disease is not well understood and no theories have been 100% accepted.
- Many researchers believe that Ménière's disease symptoms are a result of endolymphatic hydrops (excess endolymphatic fluid) that interfere with normal balance and hearing signals between the inner ear and the brain.
- Paparella, M.M. (Acta Otolaryngol Suppl 1984) developed a "lake, river, and pond" notion to explain the occurrence of inadequate absorption (or maybe too much production?) of endolymph leading to hydrops. He described the endolymphatic sac as a "pond", the vestibular aqueduct as a "river", and the endolymphatic fluid space as a "lake". Hydrops are created when there is an obstruction near the endolymphatic sac or duct. This model is somewhat akin to the etiology of glaucoma in the eye.
- A potential problem with the hydrops theory is that all patients with Ménière's disease have hydrops, but not all patients with hydrops have Ménière's disease. Thus hydrops may not tell the whole story.



Source: http://www.nidcd.nih.gov/

Ménière's Disease: Other Theories

- Schuknecht attributed the attacks of vertigo and temporary hearing loss to periodic ruptures of the membranous labyrinth which allows high potassium endolymph to enter the perilymphatic space:
  - Nerve cells depolarize and become deactivated
  - Acute hearing loss and vestibular disfunction
  - Recovery as membrane heals
  - Repeated insults cause permanent dysfunction
- Autoimmune process?
- Viral infection?
- Allergy?
- Ischemia/vascular mechanism?
- Multifactorial?
- Common endpoint for a variety of mechanisms/insults?

Source: Mills, J. and Bien, A. 2012

Diagnosis Of Ménière's Disease

- The American Academy of Otolaryngology – Head And Neck Surgery (AAO-HNS) criteria for diagnosis of Ménière's disease (1995) includes:
  - Recurrent spontaneous and episodic vertigo (lasting ≥ 20 mins; accompanied by disequilibrium that can last several days; usually nausea and/or vomiting)
  - Hearing loss (not necessarily fluctuating)
  - Either aural fullness or tinnitus or both

- Episodic vertigo without hearing loss, tinnitus or aural fullness does NOT constitute Ménière's disease.

Certain Ménière's disease	Definitive Ménière's disease	Probable Ménière's disease	Possible Ménière's disease
Definite disease with histopathological confirmation	Two or more definitive episodes of spontaneous vertigo lasting > 20 mins with hearing loss, plus tinnitus and/or aural fullness	Only one definitive episode of vertigo and the other symptoms and signs	Definitive vertigo with no associated hearing loss or hearing loss with non-definitive disequilibrium

Adopted From 1995 AAO-HNS Guidelines

Ménière's Disease – Management Principles

- Ménière's disease is a chronic disease that cannot be effectively treated due to poor understanding of the disease. There is no cure for the disease. The disease is managed with aims limited to:
  - Reducing the number and severity of acute vertigo attacks
  - Aborting or alleviating hearing loss and tinnitus associated with such attacks
  - Alleviating any chronic symptoms (e.g. tinnitus and imbalance)
  - Preventing progression of the disease
- No known treatment adequately addresses all four of the above aims. In particular, no treatment seems to result in LT preservation of hearing.
- Typically, the main goal of current therapies is to reduce/alleviate vertigo attacks which are the most troubling for patients since they disrupt daily activities and are difficult to anticipate and manage.

Overview Of Medical Management Options

Absence of robust prospective, randomized, placebo-controlled studies has led to a variety of medical and surgical therapeutic interventions of uncertain benefits.

- **Acute management**
  - Vestibular suppressants
  - Anti-emetics
  - Rehydration
  - Electrolyte adjustment

- **Chronic management**
  - Lifestyle adjustment
    - Trigger avoidance
    - Salt restriction
  - Pharmacology
    - Diuretics
    - Vasodilators
    - Corticosteroids
    - Aminoglycoside ablation (gentamicin)
  - Complementary and alternative medicine
  - Devices
    - Meniett (marketed by MDT)
    - P-100 (marketed by enttex, Germany)
  - Rehabilitation therapy
    - Vestibular
    - Tinnitus
    - Hearing

Typical first-line treatment for Ménière's disease in the US is observance of a low-salt diet and off-label use of diuretics. A subset of patients with persistent or severe symptoms are treated by oral or IT steroids. Patients who do NOT respond to steroids may seek surgical or chemical ablation, which can cause irreversible hearing loss.

Source: Coelho, D.H. et al. Laryngoscope 2008

Diuretics

- Diuretics are often used along with dietary salt restrictions to reduce body salt and consequently total body fluid. Decreasing fluid volume is believed to reduce the enolymphatic pressure and volume or hydrops of the inner ear.

- Although diuretics are commonly used, a recent review by Thirlwall, A.S. et al. (Cochrane Database of Syst Rev 2006) found no high-quality studies to support its use, though lower quality research tends to support use.

- Santos, P.M. et al. (Otolaryngol Head Neck Surg 1993) evaluated 54 patients after 24-month treatment of diuretics and low-salt diet in a retrospective study:
  - Complete or substantial vertigo control in 79%, limited or insignificant control in 19%, worse in 2%
  - Stabilization of low-mid frequency HL (average 0 dB loss at 74 months)
    - HL improved in 35%, unchanged in 29%, worse in 22%

- Patients can be slowly tapered off their particular regimen when symptom-free for 6-12 months.

Corticosteroids

- Corticosteroids are potentially useful in treating Ménière's disease because of their anti-inflammatory properties. Many believe Ménière's disease has an auto-immune component - although it could be related to fluid or other effects.

- Side effects like adrenal suppression limit the amount of steroids that can be administered systemically. Thus, IT (intra-tympanic) injections of steroids offers a way to deliver a high concentration of steroids to the perilymph without causing systemic side effects.

- Dexamethasone appears to be effective in treating vertigo, as shown in a 2-year, randomized, double-blind, placebo-controlled study of IT dexamethasone (5 consecutive daily IT injections) conducted by Garduno-Anaya, M.A. et al. (Otolaryngology – Head and Neck Surgery 2005):
  - 82% with complete vertigo control vs. 57% in placebo
  - 35% with subjective hearing improvement vs. 10% for placebo
    - No difference for pure tone audiogram (PTA) or speech discrimination
  - 48% with tinnitus improvement vs. 20% for placebo

- IT injection of dexamethasone shown no benefit over placebo for the treatment of hearing loss and tinnitus in Ménière's disease (Silverstein, H. et al. 1998).

Other Treatment Options For Ménière's Disease

- IT gentamycin
  - Effective in reducing vertigo attacks
  - Annihilates hearing & balance in the treated ear
- Vasodilators
  - Not much evidence to support its use
- Complementary and alternative medicines (CAM)
  - Ginger root, acupuncture, Tai Chi, et al.
  - No evidence exists to support efficacy
  - 42% of patients have used or are using CAM (Eisenberg, et al. 1997); 75% of them do not tell their physicians
- Meniett device – approved in the US since 2000
  - Alternating low-density pressure generator, which provides low-pressure air pulses to the middle ear to displace the excess inner ear fluid, normalize the pressure within the ear and help to relieve the symptoms
  - Requires insertion of a LT tympanostomy tube
  - Inconvenient; patients need to receive treatment 2-3 times per day, ~10 mins per treatment
  - Amount of data to support its use is thin; in a small follow up study of 58 patients, 67% achieved either complete control or satisfactory control of vertigo (Gates et al. 2006)
  - No benefit for hearing
  - Expensive and rarely covered by insurance ($3500) given the fairly limited clinical dataset.
- P-100 device – not approved in the US
  - Positive pressure pulse generator
  - Requires insertion of a LT tympanostomy tube
  - Amount of data to support its use is thin; appears to be comparable to Meniett in reducing vertigo (Franz, B. et al. International Tinnitus Journal 2005)
  - Cheaper than Meniett
- Surgery
  - Endolymphatic sac surgery
  - Vestibular nerve section
  - Labyrinthectomy

Source: Coelho, D.H. et al. Laryngoscope 2008

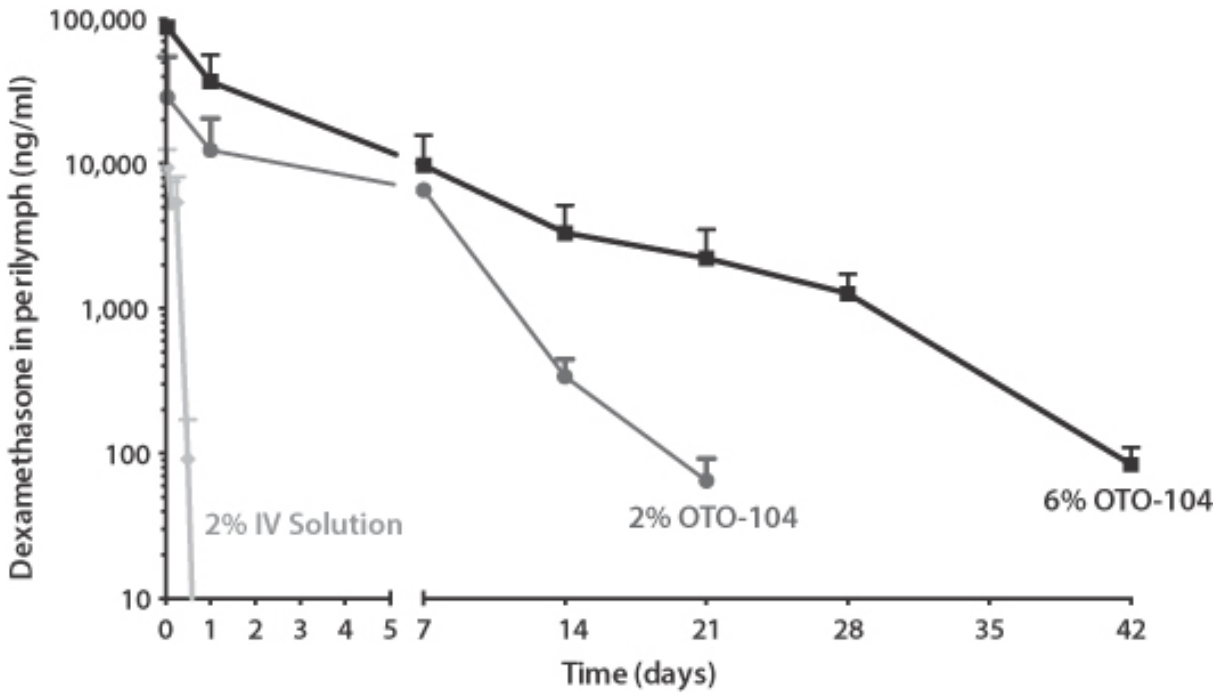
IT gentamycin and surgery should be considered as last resort due to their destructive nature.

Our Quick Thoughts On Ménière's Disease

- Sizeable market with meaningful unmet need
  - Disease is not well understood.
  - > 600,000 patients in the US.
  - No cure for the disease.
  - No FDA-approved drugs for the disease.

- Many treatment options, most of which are backed by little evidence
  - Most therapies focus on vertigo reduction.
  - Off-label use of diuretics is NOT well supported.
  - IT injection of steroids works for vertigo, though dosing regimen is cumbersome.
  - Chemical or surgical ablation are disruptive and could cause permanent hearing loss.
  - Approved device in the U.S. not supported by robust data.

OTIC's OTO-104 For Ménière's disease



Source: OTIC S-1

- OTO-104 is a sustained formulation of dexamethasone in the thermosensitive polymer P407. It exists as a liquid at room temperature and is transformed to gel immediately following an IT injection into the ear.

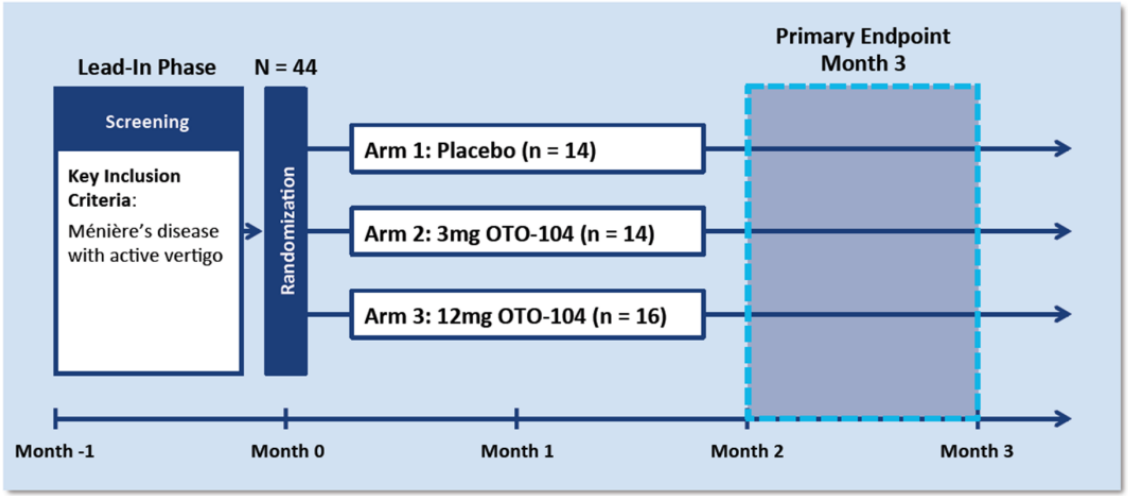
- Preclinical studies (Piu, F. et al. Otology & Neurology 2010) indicated that measurable dexamethasone levels in the inner ear fluid, perilymph (between bony labyrinth and membranous labyrinth), lasted for > 1 month after a single IT injection, as opposed to < 1 day after a single IT injection of dexamethasone solution. This unique property makes OTO-104 desirable to treat both acute and chronic intermittent otic disease like Ménière's disease.

Mechanism Of Action Of Dexamethasone Within The Inner Ear

- The mechanism of Dexamethasone to treat Ménière's disease is not fully understood.
- Dexamethasone likely plays multiple roles within the inner ear (Lambert, et al. 2012):
  - Corticosteroids bind to glucocorticoid receptors on the cell surface, which leads to initiation or modulation of gene transcriptions and alteration of intracellular signaling pathways.
  - Corticosteroids may modulate ion homeostasis vis sodium channels, which drives caption and water transport in the vestibular labyrinth.
  - Corticosteroids also reduces the production of free radicals in the inner ear and protect against proinflammatory cytokines such as tumor necrosis factor α.

Even though the mechanism of action is not fully clear, IT injections of dexamethasone solution have shown good efficacy in clinical trials to treat vertigo in Ménière's disease (we will discuss this shortly) and has been used off-label in the ENT community. This gives us reasonably high conviction that OTO-104 should work for reducing vertigo in Ménière's disease, as shown in P1b trial (presented in next few slides).

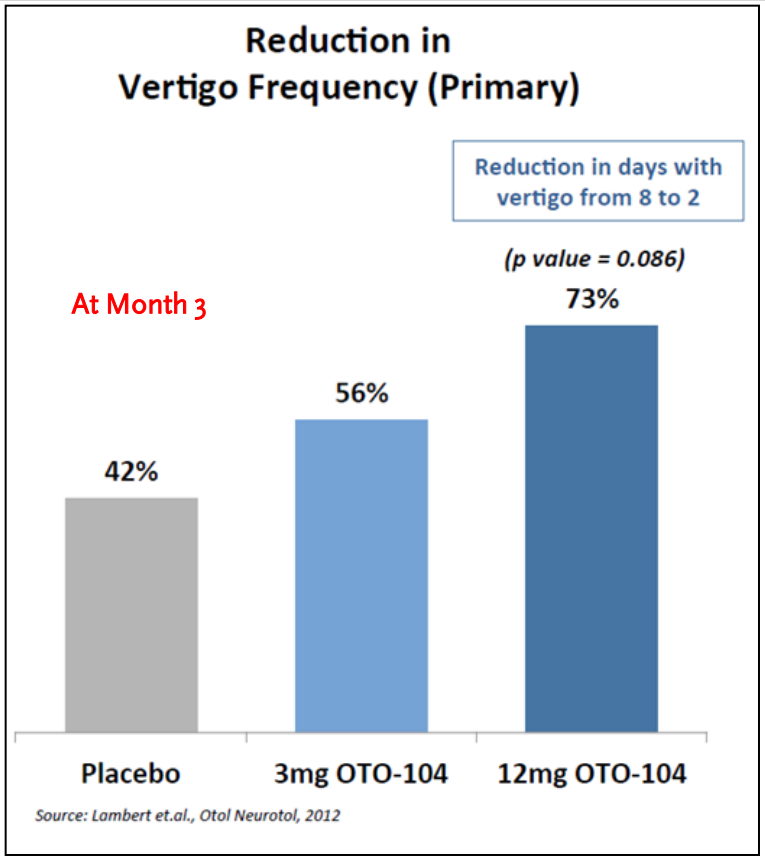
OTO-104 P1b Trial Design



Source: OTIC Company Presentation

- OTIC completed a randomized, double-blind, placebo-controlled, P1b trial of a single IT injection of OTO-104 in patients with Ménière's disease.
- A total of 44 patients were randomized roughly 1:1:1 to placebo, 3 mg OTO-104, and 12 mg OTO-104.
- Primary endpoint was vertigo frequency during Month 3 compared to baseline (vertigo frequency during 4-week lead-in period). A definitive vertigo episode was defined as one lasting ≥ 20 mins (equivalent to a vertigo score ≥ 2). If multiple attacks occurred on the same day, only the worst was recorded.
- Secondary endpoints included Tinnitus Handicap Inventory (THI 25-item questionnaire), the Ménière's Disease Patient-Oriented Symptom-Severity Index (MDPOSI), and the severity of vertigo episodes as measured by Gates' vertigo score.

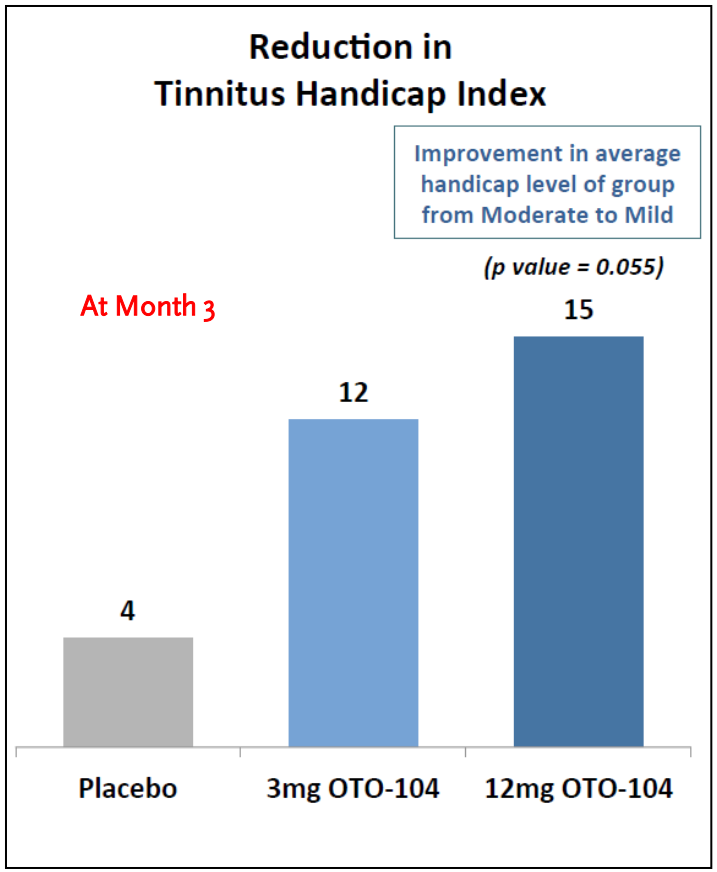
Change In Vertigo Frequency



Source: OTIC Company presentation

In the placebo and OTO-104 3mg arms, the greatest reduction in vertigo was noted at Month 1, and the effects seemed to plateau afterwards. In the OTO-104 12mg arm, vertigo frequency decreased steadily month-over-month, and the trend seemed to continue after Month 3, though no data were available beyond this timepoint. The 3-month OTO-104 data, though, were statistically insignificant compared to placebo presumably because the study was underpowered.

Change In Tinnitus Handicap Index



Source: OTIC presentation

A significant decrease in the THI-25 total score was observed for both OTO-104 groups, whereas the score was relatively flat for placebo.

Safety Of OTO-104

	OTO-104, n(%)		Pooled placebo
No. patients adverse event preferred term	**3 mg (n = 14)**	**12 mg (n=16)**	**(n = 14), n (%)**
Patients with serious AEs	0	0	0
Patients with AEs	9 (64.3)	12 (75.0)	8 (57.1)
Ear pain	2 (14.3)	1 (6.3)	0
Tympanic membrane perforation	2 (14.3)	6 (37.5)	0
Sinusitis	0	2 (12.5)	0
Migraine	2 (14.3)	0	0

Adopted from Lambert, P.R. Otology & Neurology 2012

- No deaths or discontinuation from the study. No clinically meaningful changes observed in hearing at all frequencies, pure-tone averages, or speech discrimination.
- Tympanic membrane perforation and transient ear pain were the most frequently reported AEs. At the end of the study, the incidence of tympanic membrane perforation was 3% in OTO-104 groups. It is worth noting that tympanic membrane perforation has been observed in other IT injection studies (Rauch, S.D. et al. JAMA 2011; Herraiz, C. et al. Otol Neurotol 2010).

OTO-104 Comparison With IT/Oral Steroids

- To put the OTO-104 P1b data in perspective, we conducted an extensive literature search for clinical data of steroids for treating Ménière's disease. Overall, there is lack of high-quality randomized, double-blind, placebo-controlled trials of steroids in Ménière's disease, although the studies do support a benefit with this approach.

- Nevertheless, we assembled 5 trials of IT injections of dexamethasone and 1 trial of oral prednisone shown in the next slide. All retrospective studies were excluded due to selection bias.

- Here are some key takeaways from these trials:
  - Overall, both IT and oral steroids appear to be effective in reducing vertigo, though % of vertigo control varies widely from trial to trial.
  - The placebo effect appears to be strong and long lasting, as indicated in Garduno-Anaya's study (2005) and OTO-104 P1b study.
  - There are a variety of primary endpoints used in the studies (e.g. complete control of vertigo, satisfactory control of vertigo , et al.). As a result, it is difficult to compare efficacy across the trials.
    - Control of vertigo is defined as (X/Y) x 100, rounded to the nearest whole number, where X is the average number of definitive spells per month for the 6 months interval spanning 18 to 24 months after therapy and Y is the average number of definitive spells per month for the 6 months before therapy.
    - **Complete control of vertigo** is equivalent to AAO-HNS 1995 Class A with (X/Y) x 100 = 0.
    - **Substantial control of vertigo** is equivalent to AAO-HNS 1995 Class B with (X/Y) x 100 = 1-40.
    - OTIC used vertigo days rather than vertigo episodes for the primary endpoint, and thus it is difficult to compare OTO-104 P1b trial data to others, though numerically OTO-104 data is superior to placebo and its dose-dependent efficacy profile is assuring.
  - Impact of baseline vertigo on the trial outcomes is unknown.

Data Summary

Targeted Indication	Study Design	Dosing	Patient #	Mean Age	Primary Endpoints	Time of Measurement	Results	Reference
Unilateral Ménière's disease	P1b, Randomized, double-blind, placebo-controlled, 15-center	3 mg or 12 mg of **OTO-104** or placebo	44	~53	Change from baseline in vertigo frequency (vertigo days per month) at month 3	3 months	56% (low dose) vs. **73%** (high dose) vs. 42% (insignificant)	Lambert 2012
Unilateral Ménière's disease (without any previous treatment with steroids or surgery)	Randomized, double-blind, placebo-controlled	5 consecutive daily IT of **dexamethasone** or placebo	22	50	Complete control of vertigo	2 years	**82%** vs. 57%	Garduno-Anaya 2005
Intractable vertigo in Ménière's disease	3-arm	IT **dexamethasone** (5 drops every another day for 3 months) vs. IT **gentamicin** vs. **decompression of the ESD**	65	~36	Satisfactory control of vertigo (includes complete and substantial)	18 months	**72%** vs. 75% vs. 52%	Sennaroglu 2001
Intractable unilateral Ménière's disease	Randomized, controlled	IT injection of **dexamethasone** (4 mg/mL, 3 injections at intervals of 1 every 3 days) or **gentamicin** (<=2 injections)	60	54.2	Complete control of vertigo	2 years	**43%** vs. 81%	Casani 2012
Ménière's disease	Prospective, single arm	2 mg (0.5 ml) injection of dexamethasone for a total of 4 or 5 times at intervals of 1 or 2 wks	61	49.4	Response for vertigo (AAO-HNS 1985)	N/A	**80%**	Itoh 1991
Ménière's disease (includes unilateral and bilateral)	Prospective, single arm	3 0.2- to 0.4-ml injections of IT dexamethasone hyaluronate (16 mg/ml) during a week and with initial intramuscular injection of 15 mg	17	48	Sufficient vertigo control	1 year	**76%**	Hirvonen 2000
Refactory vertigo in Ménière's disease	Blinded, randomized, controlled	**oral** diphenidol (25 mg/d) + acetazolamide (250 mg / 48 h) or same treatment + oral prednisone (0.35 mg/kg) daily for 18 weeks	16	~40	Change from baseline in vertigo frequency	18 weeks	11% (control) vs. **64%** (prednisone arm)	Morales-Luckie 2005

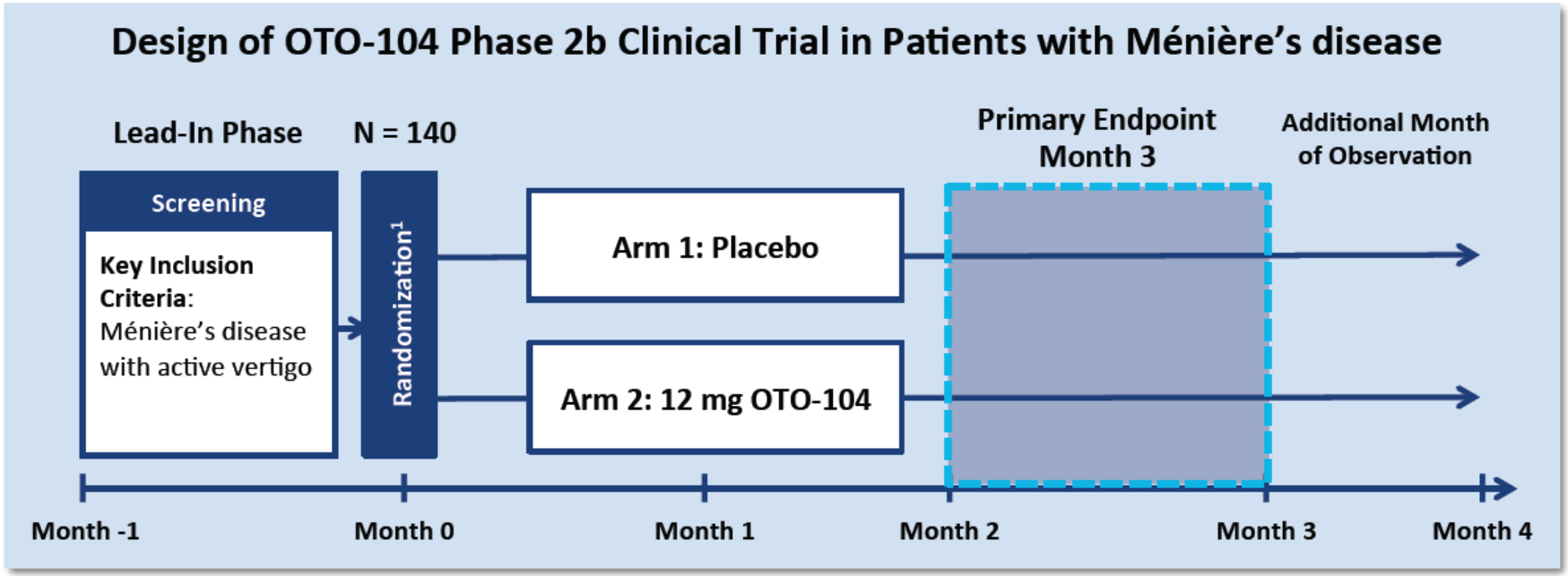
Source: Piper Jaffray Research

Both Full And Partial Clinical Holds Were Cleared

- Following the completion of P1b trial, OTO-104 program was put on full clinical hold due to some ototoxicity observed in a particular animal study. Not knowing whether the tox was from dexamethasone or P407 or both, OTIC voluntarily placed AuriPro on full clinical hold.

- Eventually, the ototoxicity was found to be non-product related. As a result, full clinical hold for AuriPro was removed in Nov 2012. Subsequently, OTO-104 was cleared from full clinical hold and placed on partial clinical hold in July 2013, allowing initiation of a single-dose P2b study (will discuss in next slides). The partial clinical hold was cleared in June 2014, permitting OTIC to conduct multi-dose study in the future.

OTO-104 Being Evaluated In A Phase IIb Study



Source: OTIC Company Presentation

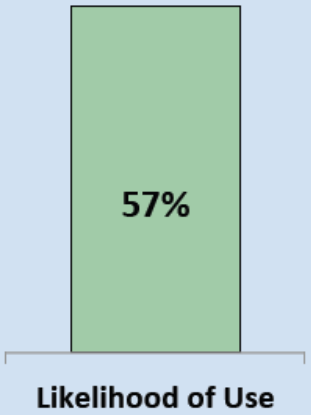
- ❑ OTIC is conducting a P2b trial of OTO-104 in Ménière's disease with data readout due 1H 2015.
- ❑ The primary endpoint is reduction in vertigo frequency during Month3 vs. baseline.
- ❑ If the results are positive, the company plans to start a P3 trial in 2H 2015. One or more open-label safety studies are also expected to be initiated in 4Q 2014.
- ❑ OTO-104 received Fast Track Designation from the FDA.

Commercial Opportunities For OTO-104

Lead Indication: Ménière's disease

- > 600,000 patients diagnosed
- High level of patient disability – serious unmet medical need
- No FDA-approved drug treatment for indication
- Chronic disorder – need for retreatment
- Expect J code for reimbursement
- Potential for market expansion with education, awareness, approved treatment, etc.

% of ENTs Expressing Strong Interest in Using OTO-104[1,2]



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Potential Expansion Indications

- >8 million patients treated each year in U.S. for inner ear disorders[3]
- Steroids used in subset of patients:
  - Sensorineural hearing loss including sudden hearing loss
  - Non-Ménière's balance disorders
  - Tinnitus

[1]Source: third-party market research firm commissioned in 2014 by Otonomy with 100 ENTs surveyed
[2]On a scale of 1 to 10, where 10 means "extremely likely" and 1 means "not at all likely," strong interest considered a ranking of 8, 9 or 10
[3]Company estimate

Source: OTIC Company Presentation

Indication Expansion: Sudden Hearing Loss

- Of all potential indication expansions for OTO-104, clinicians were particularly enthusiastic for use in sudden hearing loss and, if approved, it could meaningfully drive sales growth for OTO-104.

- The estimated incidence of idiopathic sudden sensorineural hearing loss is between 5-20 per 100,000 persons per year, which translates into a patient population between ~16,000 to ~62,780 per year (Byl, F.M. Jr. 1984). This is likely an underestimate because many patients may not seek treatment due to quick recovery.

- The current standard of care for sudden hearing loss is a tapering course of oral corticosteroid (prednisone or methylprednisolone).

- IT treatment, however, is more beneficial (at least theoretically) due to reduced systemic steroid exposure and associated systemic AEs.

- In a prospective, randomized, non-inferiority trial of 250 patients with unilateral sensorineural hearing loss (Rauch, S.D. et al. JAMA 2011), hearing level 2 months after IT treatment (4 IT injections over 14 days of methylprednisolone) was not inferior to oral prednisone treatment (14-day regimen with a 5-day taper).

- Dexamethasone has favorable pharmacokinetics for IT administration over methylprednisolone, and thus potentially can be dosed at a much lower level. OTO-104, therefore, should be an ideal treatment option for sudden hearing loss given its prolonged drug exposure and superior pharmacokinetics.

Shifting Focus To OTO-311 For Tinnitus

- Tinnitus is the perception of ringing in the ears when no external sound is present. Tinnitus can significantly impair quality of life and affect normal day-to-day activities.

- Tinnitus is categorized as acute and chronic depending on persistence of the disease. Acute tinnitus lasts for < 3 months, while chronic tinnitus persists much longer.
  - As acute tinnitus progresses, the likelihood of spontaneous recovery declines exponentially. For chronic tinnitus, cure is unlikely and therapeutic focus shifts from curing to managing the disorder (like in Ménière's disease).

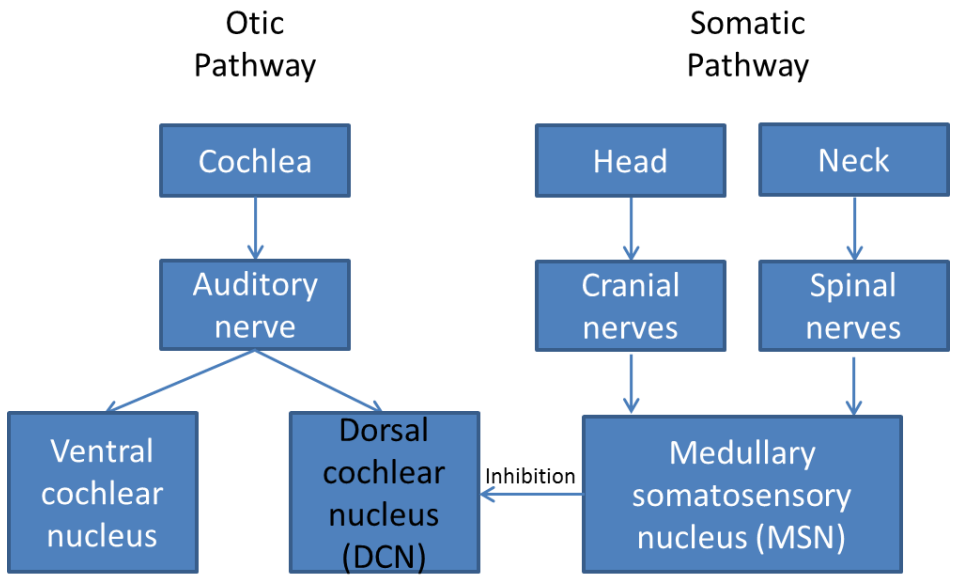
- Approximately 16M patients in the US have symptoms severe enough to seek medical attention (American Tinnitus Association), about 2M of which cannot function on a normal day-to-day basis due to having trouble hearing, working, and sleeping.
  - Tinnitus is the most prevalent service-related disability in the US military with estimated cost of ~$2.26B by 2014 (United States Department of Defense).

- At this time, there is no cure for tinnitus and no FDA-approved drug for the condition.

Adopted from Wikipedia

Pathophysiology Of Tinnitus

- Tinnitus is a highly heterogeneous condition that can arise from pathological changes along the entire auditory pathway.
- Tinnitus is often triggered by cochlear impairment as a consequence of exposure to loud noise, administration of ototoxic drugs, etc. The impairment results in abnormal neuronal activity in central auditory pathways that can eventually be perceived as tinnitus. Tinnitus can also be triggered by abnormal changes to the auditory nerve.
- In addition, abnormal somatosensory afferent input from the neck and head regions can affect activity in central auditory pathways, which might contribute to tinnitus.



Adopted from Levine, R.A. 2001

DCN is important for the induction of tinnitus.

Current Treatments

Currently there is no cure and no FDA-approved therapies for tinnitus. We summarized commonly used strategies to manage tinnitus as shown below, none of which are backed by high level of evidence (Langguth, B. 2013).

- ❑ Psychological treatments
  - Counseling and psychoeducation
  - Tinnitus retraining therapy
  - Cognitive-behavioral therapy
- ❑ Auditory stimulation
  - Sound therapy
  - Hearing aids
  - Cochlear implants
  - Individualized sound stimulation
  - Auditory perceptual training
- ❑ Pharmacological treatment
  - No drug has been approved by the FDA or EMA
- ❑ Brain stimulation

OTO-311 – Intratympanic Treatment For Tinnitus

- OTO-311 is a sustained gel formulation of NMDA receptor antagonist gacyclidine in treating tinnitus.
  - NMDA receptor antagonists act on NMDA receptors in the cochlea and the nervous system and can prevent apoptosis of traumatized neurons.

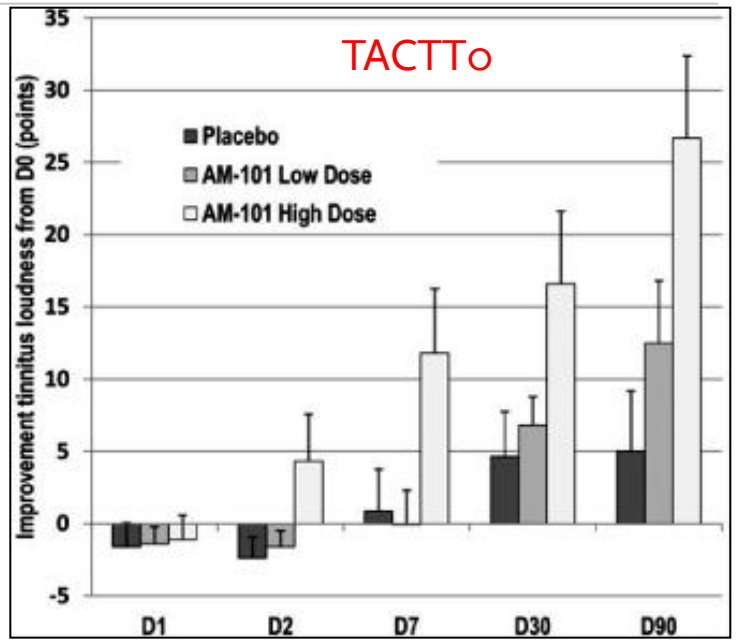
- Historical clinical data of NMDA in treating tinnitus have yielded mixed results, probably due in part to the heterogeneity of the disease. However, results from Auris Medical (EARS – not covered) using the same mechanism but a less robust delivery/platform (see next page) are encouraging.
  - A open-label study of flupirtine (a functional NMDA receptor antagonist) appeared NOT to be efficacious in treating 24 patients with continuous subjective tinnitus (Salembier, L. et al. 2006).
  - Acamprosate, a mixed NMDA receptor antagonist and GABA-A agonist, appeared to significantly reduce tinnitus levels in two independent, double-blind, placebo-controlled trials (Azevedo, A.A. et al. 2005; Sharma, D.K. et al. 2012), though Azevedo's study did NOT employ a standardized tinnitus evaluation instrument nor did it obtain objective measures of tinnitus loudness.
  - A compassionate use of gacyclidine (40-63h constant perfusion) yielded temporary tinnitus relief in 4 out of 6 patients with unilateral deafness associated with tinnitus (Wenzel, G. I. et al. 2010).
  - EARS reported an improvement in tinnitus loudness and tinnitus severity for a subset of tinnitus patients after receiving repeated IT injection of AM-101, a NMDA receptor antagonist in a P2 trial (we will review data in more details in next slide).
  - Merz Pharma reported an improvement in the tinnitus handicap index after receiving oral NMDA receptor antagonist neramexane in a P2 trial (OTIC S-1).

- OTO-311 is currently in preclinical development. OTIC plans to file IND and start clinical development in 2015.

- Given that the program is in a very early stage of development, we do not ascribe any value to OTO-311 in our model.

Auris's Tinnitus Program: AM-101 (I)

- AM-101 is a gel formulation of Esketamine hydrochloride, a small molecule non-competitive NMDA receptor antagonist.
- Auris conducted 2 multi-center P2 trials of AM-101 - one in Europe (TACTT0) and one in Europe and the US (TACTT1).
- In TACTT0 trial, AM-101 failed to show improvement in psychoacoustic measure, minimum masking level (MML) when compared to placebo due to high data variability. However, a subgroup of patients with tinnitus caused by acute acoustic trauma (AAT) or otitis media (OM) had a statistically significant improvement 90 days post-treatment in subjective tinnitus loudness and annoyance as well as in tinnitus-related sleep difficulties and overall tinnitus impact compared with placebo. AAT and OM patients have well-established cochlear origin of tinnitus.

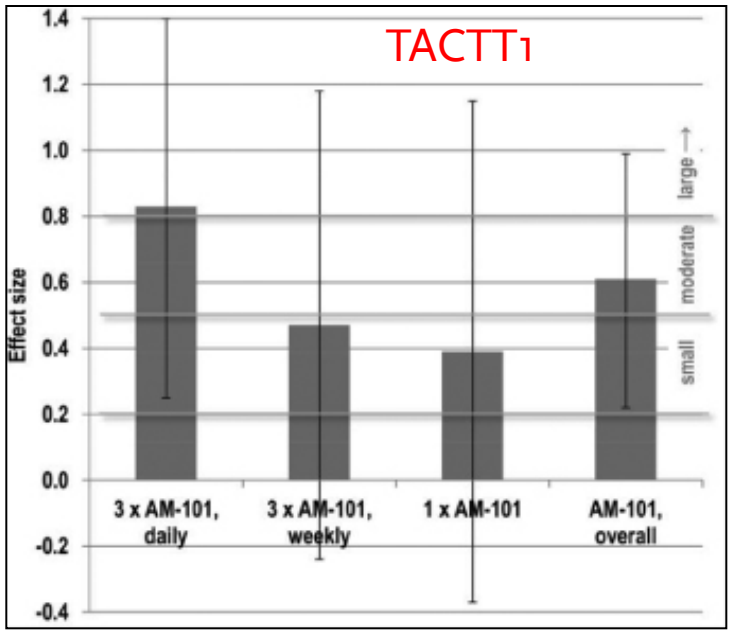


Source: Auris S-1

Auris's Tinnitus Program: AM-101(II)

- TACTT1 trial was designed to evaluate whether repeated doses of AM-101 improved efficacy in attenuating tinnitus versus a single dose. 3x AM-101 daily dosing regimen demonstrated the best efficacy.

- Auris is currently conducting 2 P3 trials of AM-101 in acute and/or post-acute tinnitus. The same subgroup of patients identified in the P2 trials will be recruited for the P3 trials, with data readout due early 2016. **Patients will receive 3 injections of AM-101 or placebo at max dose over 3-5 days and will be followed for 84 days**. Auris and the FDA/EMA have agreed on using patient reported score (PRO) measures of tinnitus loudness and tinnitus annoyance as primary endpoints.

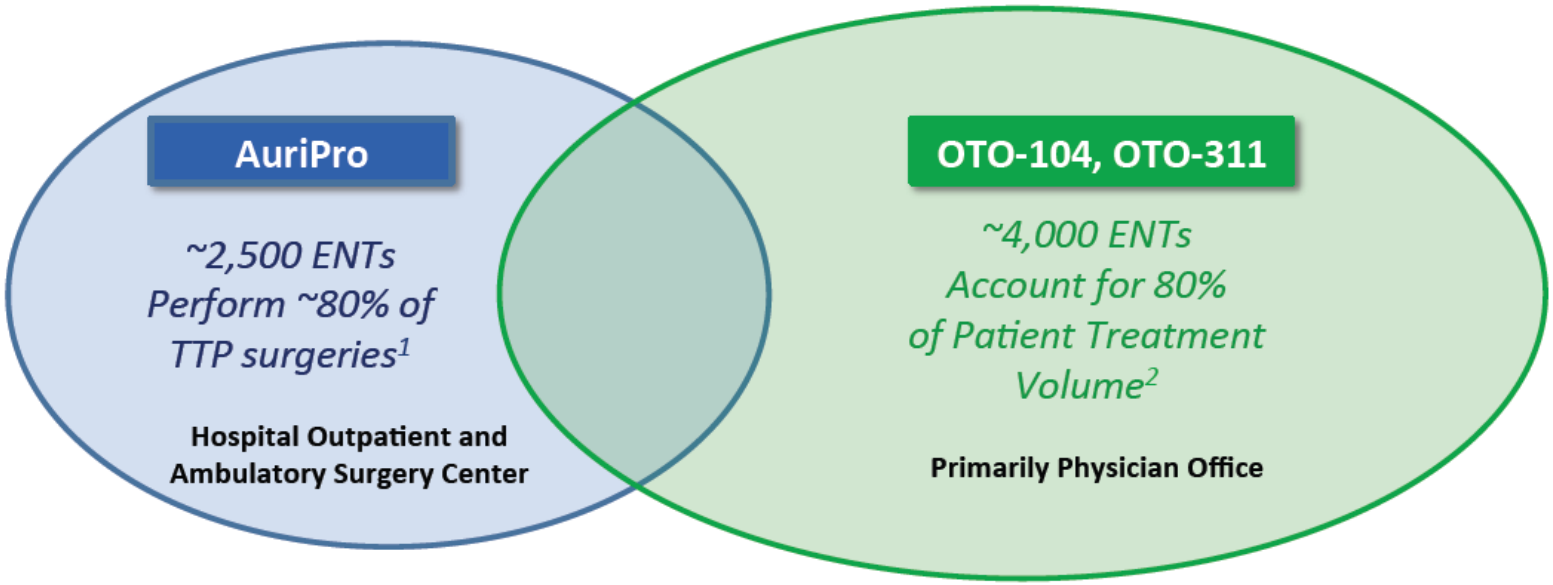


Source: Auris S-1

OTIC's platform may offer formulation advantages over EARS' platform

OTIC's Commercialization Strategy

Expect to commercialize approved products in the U.S. with focused, specialized sales force targeting ~5,000 ENTs



Evaluating whether to develop and commercialize product candidates outside U.S. ourselves or with partners

[1]Based on procedure data for tympanostomy tube placement (TTP) surgery
[2]Based on prescription data for product category most commonly prescribed by ENTs

Source: OTIC Company Presentation

OTIC has global commercialization rights for all 3 programs (AuriPro, OTO-104, OTO-311).

OTIC: Thoughts/Questions From The Roadshow #1

We had an opportunity to speak with a significant number of investors around the time of the IPO roadshow. These are some of the most common questions/comments that arose (or did not):

❑ Question Asked: How big is the market for AuriPro for TTP?

- The value proposition of AuriPro vs. the minimal price/procedure ($200-250) plus physician enthusiasm suggests meaningful penetration into a sizeable market.
- While some segments of the market fall under a global payment for TTP placement, the value proposition and modest price point should still carry the day to drive meaningful adoption.
- We believe AuriPro can generate peak U.S. sales >$150M for the lead TTP indication.

❑ Question NOT Asked: What are the opportunities for AuriPro beyond TTP?

- Very little discussion about high-probability label expansion opportunities for AuriPro.
- Few investors approached the stock by asking what minimum AuriPro sales level did they think was needed to justify the current valuation.
- Few questions on the delay to NDA submission, which is a result of the very rapid clinical development that has meaningfully outpaced stability testing. No reason to believe stability will emerge as an issue.

OTIC: Thoughts/Questions From The Roadshow #2

We had an opportunity to speak with a significant number of investors around the time of the IPO roadshow. These are some of the most common questions/comments that arose (or did not):

❑ Question Asked: What about Auris Medical (EARS – not covered)?

- Many investors confused (and still have difficulty differentiating) OTIC with EARS given both are recent IPOs with drugs in development for ear conditions.
- Those who spent time with both companies appreciated the key differentiating features for OTIC, including its unique proprietary delivery platform and the derisked post-P3 lead asset.

❑ Question Not Asked: How do we think about relative valuation?

- EARS mkt cap is $152M with cash of $68M for a $84M EV; OTIC is $400M mkt cap, cash of $160M, $240M EV. Given the similar nature of the earlier stage pipelines, there is only an incremental ~$150M EV ascribed to the derisked P3 AuriPro asset for OTIC and to the differentiated delivery platform. We believe this is a marked under-ascription of value.

OTIC: Thoughts/Questions From The Roadshow #3

We had an opportunity to speak with a significant number of investors around the time of the IPO roadshow. These are some of the most common questions/comments that arose (or did not):

❑ Question Asked: What about the pipeline?

- Some investors moved beyond AuriPro to consider the incremental value of the pipeline. Those who were most enthusiastic were comfortable that AuriPro established a base value at (or above) the current valuation and that the Ménière's program (and possibly tinnitus program) represented potentially large upside with a fairly high probability of success.

❑ Question Not Asked: What's the up/down on the Ménière's indication?

- Considering that we believe AuriPro alone represents possible upside to the current valuation, we see little downside to shares if the Ménière's program fails.
- If Ménière's succeeds however, this could represent a very leveragable incremental revenue opportunity of $500M+. Assuming a conservative 2x peak sales on this effort, it could represent an incremental 250% from current levels.

OTIC met with a fairly equal mix of biotech and spec pharma investors. Interestingly, the biotech investors were more likely to take a risk/reward approach to the Ménière's indication and were more enthusiastic for the stock. Spec pharma investors were less likely to consider assets beyond AuriPro.

OTIC: Thoughts/Questions From The Roadshow #4

We had an opportunity to speak with a significant number of investors around the time of the IPO roadshow. These are some of the most common questions/comments that arose (or did not):

❑ Question Asked: What do you think about the management team?

- We're big fans. Thoughtful, conservative, credible, articulate. We believe the company could have pushed for an IPO prior to P3 AuriPro data, but that would have exposed them and investors to meaningful binary risk. Waiting for the data earned the team high marks, in our view.

❑ Question Not Asked: What do you think about the team's long-term strategy?

- Investors understandably spent the most time on the lead asset(s) but did not ask about the company's strategic views.
- OTIC has the opportunity to emerge as a partner of choice for new assets in the ENT space and will actively pursue new in-licensing or acquisition opportunities.
- Once the company can establish a dominant position in this very underserved physician base, we believe they can emerge as having core "domain influence" to better identify emerging target programs and to influence prescribing.
- We believe this strategy is an unappreciated long-term strength of the company.

We like the 'big picture' opportunity to create a dominant ENT franchise with potential value well beyond the core current assets.

IP And Manufacturing Overview

INTELLECTUAL PROPERTY

- **Broad patent portfolio in major global markets**
- **~50 issued patents and allowed patent applications**
- **85+ pending patent applications**
  - — Composition of matter, therapeutic use, novel discoveries and manufacturing process patents
  - — Coverage through at least 2029
- **Additional patent filings** planned
- **Trademark registrations**

MANUFACTURING

- **Contract with third parties** for manufacture, testing and storage
- **Cost effective** – minimizes investment in manufacturing equipment and facilities
- **Experienced personnel** to manage and oversee contract manufacturing

IP protections:

- ❑ AuriPro: until +2030
- ❑ OTO-104: 2029
- ❑ OTO-311: until +2031

Source: OTIC presentation

High-Caliber Management Team

Executive	Position	Prior Experience
David A. Weber, Ph.D.	CEO President and Board Member	CEO of MacuSight
		Acting CEO and executive vice president of Oculex
		Ph.D. in medical microbiology
Paul E. Cayer	CFO	Senior VP for Verus Pharma
		CFO of Targeted Molecules Corporation
		Master's degree in business from Harvard University
Carl LeBel, Ph.D.	CSO	Executive director of Amgen
		Ph.D. in biomedical sciences from Northeastern University
Robert Michael Savel, II	CTO	GM and SVP of operation for Optimer Pharmaceuticals
		SVP and CTO for Inspire Pharmaceuticals
		BS in mechanical engineering

Source: OTIC

We find the OTIC management team to be very thoughtful, conservative, forward-thinking and well-prepared. High caliber team overall.

OTIC: Comparable Valuations

OTIC COMP TABLE							
Ticker	**Company**	**Description**		**Mkt Cap ($M)**	**Cash ($M)**	**Shares (M)**	**EV ($M)**
OPHT	Ophthotech	P3 program for wet AMD	$37.56	1,258	270	24	988
RLYP	Relypsa	Positive P3 for hyperkalemia	$23.06	784	80	30	704
ZSPH	ZS Pharma	P3 program for hyperkalemia	$38.97	811	135	20	676
NKTR	Nektar	Pegylation based platform	$13.90	1,770	159	125	1,611
ACAD	Acadia	Positive P3 for parkinson's/psychosis	$26.96	2,681	369	93	2,312
ANAC	Anacor	Drug approved for onycho	$21.92	921	156	42	765
KERX	Keryx	Positive P3 for hyperphosphatemia	$17.01	1,562	155	89	1,407
Average				**1,398**			**1,209**
OTIC	Otonomy	Positive P3 for AuriPro	$18.79	400	160	21	240

Sources: Company Reports, FactSet, Piper Jaffray analyst. Priced as of market close, 9/5/14

Our comps focus on late-stage, derisked assets addressing broader market opportunities. OTIC's market cap and EV are well below the peer average of comparable companies.

Key Events For OTIC				
Program	**Disorder**	Type	Event	Expected Timing
AuriPro	TTP	Regulatory	File NDA with the FDA	1H 2015
		Commercial	Commercial launch in US	2016
OTO-104	Ménière's disease	Clinical	Initiate open-label studies	Q4 2014
		Clinical	P2 readouts	1H 2015
		Clinical	Initiate pivotal trial	2H 2015
OTO-311	Tinnitus	Preclinical	File IND and initiate P1b study	2015
		Competitive/ validating	Auris Medical P3 data for AM-101	1H16

Source: Company reports and Piper Jaffray

OTIC Discounted Cash Flow (DCF) and Equity Valuation ($ M):	
Assumed Discount Rate (%)	10.5%
Discounted Net Cash Flow (2014-'20)	884
Terminal Growth Rate (%)	3.0%
Implied Terminal Year FCF Multiple	**13.7x**
NPV of FCFF	$1,167
Terminal Value as % of total	24.3%
Add: Net Cash	160
Shares Outstanding 2017E (million)	29
Price Target	**$46**

Source: Company Reports and Piper Jaffray.

	OTIC DCF Valuation Analysis				
	Discount Rate				
Terminal Growth		10.0%	10.5%	11.0%	11.5%
	2.0%	$45	$41	$37	$34
	3.0%	$52	**$46**	$42	$38
	4.0%	$61	$54	$48	$44
	5.0%	$73	$64	$57	$51
	6.0%	$92	$79	$69	$61

Source: Company Reports and Piper Jaffray.

	OTIC Potential Upside Vs Current				
Terminal Growth		10.0%	10.5%	11.0%	11.5%
	2.0%	138%	116%	97%	80%
	3.0%	174%	147%	124%	103%
	4.0%	223%	188%	158%	133%
	5.0%	290%	243%	204%	171%
	6.0%	392%	323%	268%	223%

Source: Company Reports and Piper Jaffray.

OTIC Annual P&L	2013A	Q1 14A	Q2 14A	Q3 14E	Q4 14E	2014E	Q1 15E	Q2 15E	Q3 15E	Q4 15E	2015E
Total U.S. Product Sales (000s)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
ex-US royalty	$0	0.0	0.0	0.0	0.0	$0	0.0	0.0	0.0	0.0	$0
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
Costs & Expenses:											
Cost of Goods Sold	$0	0.0	0.0	0.0	0.0	$0	0.0	0.0	0.0	0.0	$0
% Product sales	0	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%
R&D	$16	9.0	8.3	12.0	12.0	$41	11.0	11.0	11.0	12.0	$45
% Revenue	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
SG&A	$4	1.6	1.6	3.0	3.0	$9	3.0	3.0	5.0	9.0	$20
% Revenue	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total Operating Expenses	$20	10.6	9.8	15.0	15.0	$50	14.0	14.0	16.0	21.0	$65
Operating Income (loss)	**($20)**	**(10.6)**	**(9.8)**	**(15.0)**	**(15.0)**	**($50)**	**(14.0)**	**(14.0)**	**(16.0)**	**(21.0)**	**($65)**
Interest and Other Income, Net	$0	(0.3)	(0.3)	(0.3)	(0.3)	($1)	0.1	0.1	0.1	0.1	$1
Accretion, convertible preferred	($1)	(0.0)	(0.0)	0.0	0.0	($0)	0.0	0.0	0.0	0.0	$0
Pretax Income (Loss)	($20)	**($11)**	**($10)**	**($15)**	**($15)**	**($52)**	**($14)**	**($14)**	**($16)**	**($21)**	**($64)**
Income Taxes (Benefit)	$0	0.0	0.0	0.0	0.0	$0	0.0	0.0	0.0	0.0	$0
Tax rate	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Net Income, adjusted (GAAP)	**($20)**	**(10.8)**	**(10.2)**	**(15.3)**	**(15.3)**	**($52)**	**(13.9)**	**(13.9)**	**(15.9)**	**(20.9)**	**($65)**
Stock option expenses	0	0.3	0.3	0.3	0.3	1	1	1	1	1	2
% Revenue	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Net Income, non-GAAP	($20)	(11.1)	(10.4)	(15.6)	(15.6)	($53)	(14.4)	(14.4)	(16.4)	(21.4)	($67)
Diluted EPS (Non-GAAP)	($4.51)	($3.77)	($0.69)	($0.70)	($0.70)	($3.36)	($0.64)	($0.64)	($0.72)	($0.93)	($2.93)
Diluted EPS, GAAP	**($4.47)**	**($3.69)**	**($0.67)**	**($0.69)**	**($0.69)**	**($3.30)**	**($0.62)**	**($0.61)**	**($0.70)**	**($0.91)**	**($2.84)**
Diluted Shares Outstanding (MM)	4.5	2.9	15.1	22.3	22.4	16	22.5	22.7	22.8	23.0	23

Source: Company Reports and Piper Jaffray.

Joshua Schimmer: 212-284-9322
Joshua.E.Schimmer@pjc.com

OTIC Product Model	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
TTP Procedures/Yr, U.S. (000s)	1,000	1,000	1,000	1,005	1,010	1,015	1,020	1,025	1,030	1,036	1,041
% children	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*
# children TTP procedures/yr, U.S. (000s)	900	900	900	905	909	914	918	923	927	932	937
% of market without payor obstacles	*55%*	*55%*	*55%*	*55%*	*55%*	*55%*	*55%*	*55%*	*55%*	*55%*	*55%*
% penetration, low barrier population	*0%*	*0%*	*0%*	*0%*	*10%*	*20%*	*30%*	*35%*	*40%*	*45%*	*50%*
% penetration, high barrier population	*0%*	*0%*	*0%*	*0%*	*2%*	*5%*	*15%*	*20%*	*25%*	*30%*	*35%*
# adult TTP procedures/yr, U.S. (000s)	100	100	100	101	101	102	102	103	103	104	104
% penetration, adults	*0%*	*0%*	*0%*	*0%*	*1%*	*5%*	*15%*	*35%*	*40%*	*50%*	*50%*
AuriPro treatments/yr, U.S. (000s)	$0	$0	$0	$0	$59	126	229	297	350	408	457
Cost/treatment	$225	$225	$225	$225	$225	234	243	253	263	274	285
Total AuriPro revenue, U.S. (mm) For TTP	**$0**	**$0**	**$0**	**$0**	**$13**	**$30**	**$56**	**$75**	**$92**	**$112**	**$135**
AuriPro revenue, Other (mm)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$10**	**$25**	**$40**	**$55**	**$65**
Total AuriPro revenue, U.S. (mm)	**$0**	**$0**	**$0**	**$0**	**$13**	**$30**	**$66**	**$100**	**$132**	**$167**	**$200**
Meniere's patients, U.S. (000s)	650	650	650	663	676	697	717	746	776	807	839
% OTO-104 penetration	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*1%*	*3%*	*5%*	*6%*	*7%*
OTO-104 ears treated, U.S. (000s)	0	0	0	0	0	0	4	19	39	48	59
Cost/yr	$5,000	$5,000	$5,000	$5,000	$5,150	$5,305	$5,517	$5,737	$5,967	$6,206	$6,454
OTO-104 revenue/yr, U.S. (mm)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$20**	**$107**	**$232**	**$300**	**$380**

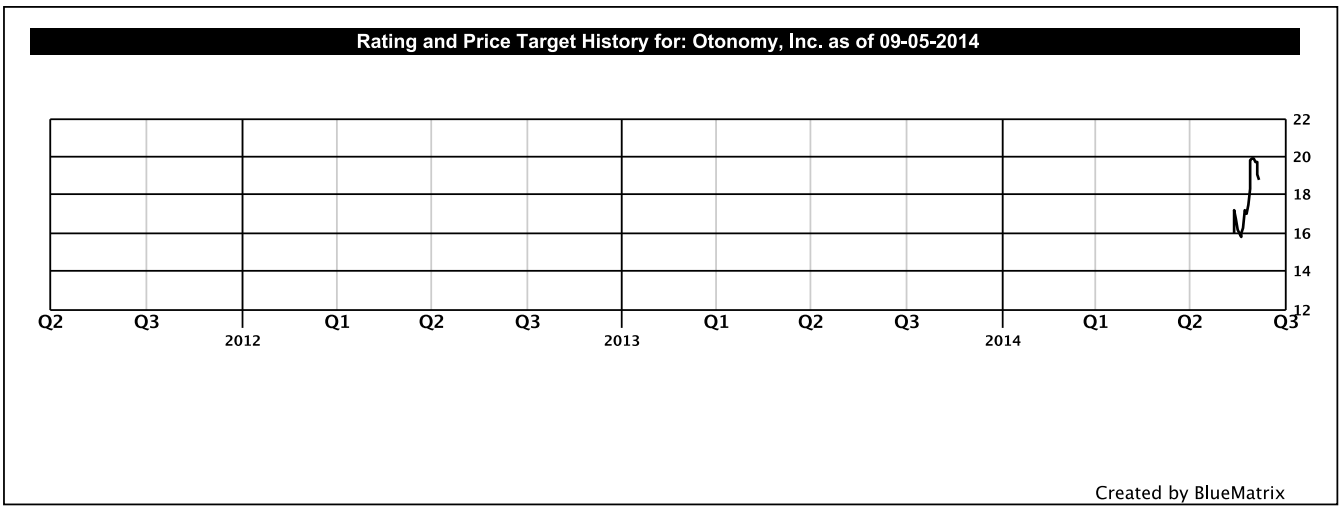
Source: Company reports, PJC estimates

OTIC Annual P&L	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
Total U.S. Product Sales (000s)	**$0**	**$0**	**$0**	**$0**	**$13**	**$30**	**$85**	**$207**	**$364**	**$467**	**$580**
ex-US royalty	$0	$0	$0	$0	$0	$5	$15	$25	$30	$35	$50
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$13**	**$35**	**$100**	**$232**	**$394**	**$502**	**$630**
Cost of Goods Sold	$0	$0	$0	$0	$1	$3	$9	$21	$36	$47	$58
% Product sales	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%
R&D	$8.5	$16.3	$41	$45	$50	$50	$65	$70	$75	$75	$80
% Revenue	N/A	N/A	N/A	N/A	N/A	N/A	64.7%	30.2%	19.1%	14.9%	12.7%
SG&A	$2.4	$3.5	$9	$20	$70	$85	$100	$120	$150	$165	$165
% Revenue	N/A	N/A	N/A	N/A	N/A	N/A	99.5%	51.7%	38.1%	32.9%	26.2%
Total Operating Expenses	$10.9	$19.9	$50	$65	$121	$138	$174	$211	$261	$287	$303
Operating Income (loss)	**(10.9)**	**(19.9)**	**($50)**	**($65)**	**($108)**	**($103)**	**($73)**	**$21**	**$132**	**$216**	**$327**
Interest and Other Income, Net	$3.4	$0.3	($1)	$1	$1	$1	$1	$1	$1	$1	$1
Accretion, convertible preferred	(0.8)	(0.5)	($0)	$0	$0	$0	$0	$0	$0	$0	$0
Pretax Income (Loss)	**($8)**	**($20)**	**($52)**	**($64)**	**($107)**	**($102)**	**($72)**	**$22**	**$133**	**$217**	**$328**
Income Taxes (Benefit)	0.0	0.0	$0	$0	$0	$0	$0	$7	$40	$65	$98
Tax rate	0%	0%	0%	0%	0%	0%	0%	30%	30%	30%	30%
Net Income, adjusted (GAAP)	**(8.37)**	**(20.1)**	**($52)**	**($65)**	**($107)**	**($102)**	**($72)**	**$16**	**$93**	**$152**	**$230**
Stock option expenses	0	0	1	2	2	3	4	5	8	10	13
% Revenue	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2%	2%	2%	2%
Net Income, non-GAAP	($8.6)	($20.3)	($51)	($63)	($105)	($99)	($69)	$20	$101	$162	$242
Diluted EPS (Non-GAAP)	($3.46)	($4.51)	($3.23)	($2.75)	($3.78)	($3.48)	($2.19)	$0.63	$3.01	$4.64	$6.69
Diluted EPS, GAAP	**($3.38)**	**($4.47)**	**($3.30)**	**($2.84)**	**($3.85)**	**($3.58)**	**($2.31)**	**$0.48**	**$2.78**	**$4.35**	**$6.34**
Diluted Shares Outstanding (MM)	2.5	4.5	15.7	22.7	27.8	28.6	31.3	32.4	33.6	34.9	36.3

Source: Company Reports and Piper Jaffray.

Cash Flow Statement	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
Net Income (Loss)	-8.4	-20.1	-51.7	-64.6	-107.0	-102.4	-72.1	15.7	93.2	151.6	229.8
Accretion to RV of convert	0.8	0.5	(0.0)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Depreciation and amortization	0.2	0.3	0.2	0.5	1.0	1.2	1.3	1.4	2.0	2.5	3.0
Stock-based compensation	0.2	0.2	1.0	2.0	2.0	3.0	3.5	4.6	7.9	10.0	12.6
Non cash interest exp	0.4	2.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Change in FV of convert	(3.8)	(2.8)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Deferred rent	0.3	(0.0)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Changes in operating assets and liability	(0.6)	(0.0)	0.5	1.2	(1.7)	(5.4)	(17.4)	(36.0)	(41.2)	(27.8)	(32.9)
Cash From Operations	**(10.8)**	**(19.5)**	**(50.0)**	**(60.9)**	**(105.7)**	**(103.7)**	**(84.7)**	**(14.3)**	**61.9**	**136.3**	**212.5**
Capex	(0.2)	(0.5)	(0.5)	(2.0)	(2.5)	(3.0)	(3.5)	(3.5)	(5.9)	(7.5)	(9.5)
FCF	(11.0)	(20.0)	(50.5)	(62.9)	(108.2)	(106.7)	(88.2)	(17.8)	56.0	128.8	203.0
Proceeds from convertible notes	8.0	7.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Proceeds from issuance of conv pref stocks	0.0	45.6	49.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Proceeds from issuance of common stocks	0.0	0.0	104.0	0.0	200.0	0.0	100.0	0.0	0.0	0.0	0.0
Other	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Cash From Financing	**8.0**	**52.6**	**153.0**	**0.0**	**200.0**	**0.0**	**100.0**	**0.0**	**0.0**	**0.0**	**0.0**
Net increase in cash and cash equivalents	(3.0)	32.6	102.5	(62.9)	91.8	(106.7)	11.8	(17.8)	56.0	128.8	203.0
Cash/equivalents at beginning	7.7	4.7	37.3	139.8	76.9	168.7	62.0	73.8	56.1	112.1	240.9
Cash/equivalents at end	4.7	37.3	139.8	76.9	168.7	62.0	73.8	56.1	112.1	240.9	443.9

IMPORTANT RESEARCH DISCLOSURES



Notes: The boxes on the Rating and Price Target History chart above indicate the date of the Research Note, the rating, and the price target. Each box represents a date on which an analyst made a change to a rating or price target, except for the first box, which may only represent the first Note written during the past three years.

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T: Transferring Coverage
D: Discontinuing Coverage
S: Suspending Coverage
OW: Overweight
N: Neutral
UW: Underweight
NA: Not Available
UR: Under Review

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Piper Jaffray

			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OW]	359	61.16	99	27.58
HOLD [N]	217	36.97	24	11.06
SELL [UW]	11	1.87	0	0.00

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