

Equity Research

February 4, 2015

**Price: \$30.14** (02/3/2015)

**Price Target: \$55.00**

**OUTPERFORM (1)**

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**Key Data**

Symbol	NASDAQ: OTIC
52-Week Range:	\$40.45 - 15.19
Market Cap (MM):	\$715.0
Net Debt (MM):	\$(37.3)
Cash/Share:	\$14.07
Dil. Shares Out (MM):	23.7
Enterprise Value (MM):	\$549.9
ROIC:	NA
ROE (LTM):	NA
BV/Share:	\$6.86
Dividend:	NA

FY (Dec)	2014E	2015E	2016E
<b>Earnings Per Share</b>			
Year	\$(5.40)	\$(3.15)	\$(3.05)
P/E	NM	NM	NM
Consensus EPS	(3.88)	(2.85)	(3.31)

Consensus source: Thomson Reuters

<b>Revenue (MM)</b>			
Year	\$0.0	\$0.0	\$10.0
EV/S	-	-	55.0x

Initiating Coverage

# *Initiation: Novel Technology For Ear Disorders Should Create Significant Value*

**The Cowen Insight**

Initiating Otonomy with an Outperform rating and a \$55 price target. Our rating is predicated on the eventual U.S. approval and launch of AuriPro in H1:2016 and successful development of OTO-104. Importantly, our consultants believe the Company's technology is novel, needed, and applicable to numerous additional otic-related disorders and should provide significant value from these levels.

**AuriPro Provides An Attractive Product Profile And Is Targeting An Indication With No Approved Treatments**

Otonomy's lead product is AuriPro (sustained-release ciprofloxacin) for the treatment of middle ear effusion at the time of TTP surgery – an indication with no currently approved treatments. AuriPro provides a full course of treatment with only a single administration as opposed to current off-label drops requiring administration 2-3x times a day for 7-10 days. Beyond the obvious benefits of improved convenience, our consultants found the Phase III efficacy and safety data for AuriPro to be compelling. The AuriPro program has produced positive Phase III results and the Company is expected to file an NDA by the end of this quarter. We estimate that AuriPro could receive approval in Q1:2016 and believe AuriPro could ultimately exceed \$500MM+ in the U.S. and achieve \$300MM+ in the EU.

**OTO-104 Appears To Be A Superior Treatment For Ménière's Disease**

The second clinical development candidate is OTO-104 (sustained-release dexamethasone), which is in Phase II/III studies for the treatment of Ménière's disease, a condition that causes vertigo, tinnitus, and hearing loss. Ménière's has significant unmet need as it is a highly debilitating condition that can eventually lead to permanent hearing loss, and currently has no approved treatment options. OTO-104 is currently being evaluated in an ongoing Phase IIb study, which will be one of two pivotal studies required for approval and should have topline data readout in Q2:2015. Given the significant clinical effects observed in Phase Ib, which had an almost identical design to the ongoing Phase IIb study, we are confident that the study should succeed. Assuming successful development, we believe OTO-104 could be a \$750MM+ product in the U.S., and \$400MM+ in the EU.

**The Valuation Is Attractive Here**

Using the peak sales assumptions noted above and assuming U.S./EU approvals in 2016/2018 for AuriPro and 2018/2020 for OTO-104, we arrive at a base case DCF valuation of \$55 per share, which is the basis of our price target. However, for conservatism, we would note that this assumption still carries a high discount rate, while a normalized discount rate upon approvals would yield a price closer to \$80. We assume an initial hiring of 40 sales reps for the AuriPro launch that will be expanded to 80 reps upon OTO-104 launch and SG&A and R&D costs within the range of normal industry standards. Worth noting, we do not model any of the AuriPro/OTO-104 additional indication expansion opportunities or approvals/partnerships in the rest of the world. We would be buying here.

Please see addendum of this report for important disclosures.

## At A Glance

### Our Investment Thesis

We assume U.S./EU approvals in 2016/2018 for AuriPro along with peak sales estimates of \$500MM+/\$300MM+; for OTO-104, we assume U.S./EU approvals in 2018/2020 and peak sales estimates of \$750MM+/\$400MM+, which puts our base case DCF valuation of \$55 per share, which is the basis of our price target. We assume an initial hiring of 40 sales reps for the AuriPro launch that will be expanded to 80 reps upon OTO-104 launch and SG&A and R&D costs within the range of normal industry standards. Worth noting, we do not model any of the AuriPro/OTO-104 potential additional indication expansion opportunities or approvals/partnerships in the rest of the world. Lastly, our valuation does not attribute any potential sales to OTP-311, the Company's early-stage product candidate. All of these could provide further upside.

### Forthcoming Catalysts

Q1:2015 - AuriPro NDA filing for effusion with TTP surgery  
Q2:2015 - Phase IIb data for OTO-104 in Ménière's disease  
H1:2015 - Initiate AuriPro clinical trial in expansion indications  
H2:2015 - Potential initiation of second pivotal trial for OTO-104 in Ménière's disease  
2015 - IND filing and initiation of a Phase I study for OTO-311 for tinnitus

### Base Case Assumptions

\$55 per share assuming approval of AuriPro and successful development of OTO-104

### Upside Scenario

\$80+ per share including success in additional indications or an acquisition

### Downside Scenario

\$15-20 per share on failure of OTO-104 in the ongoing Phase IIb clinical trial

### Price Performance



Source: Bloomberg

### Company Description

Otonomy is a development-stage specialty pharmaceuticals company focused on bringing to market novel sustained-exposure treatments for otic conditions. The Company has three key products in development and is targeting key addressable markets with considerable unmet need and few – if any – available FDA-approved treatment options.

### Analyst Top Picks

	Ticker	Price (02/3/2015)	Price Target	Rating
Shire Pharmaceutical	SHPG	\$227.41	\$285.00	Outperform
Actavis	ACT	\$268.35	\$350.00	Outperform
Teva Pharmaceutical	TEVA	\$57.01	\$70.00	Outperform

## Investment Thesis: Otonomy's Platform Technology Could Revolutionize The Ear Treatment Paradigm

The AuriPro program has produced positive Phase III results and the company is expected to file an NDA by the end of this quarter. We estimate that AuriPro could receive approval in Q1 of 2016 and be launched in the following quarter.

OTO-104 is currently being evaluated in an ongoing Phase IIb study, which will be one of two pivotal studies for approval and should have topline data readout in Q2 of this year. Given the significant clinical effects observed in Phase Ib, which had an almost identical design to the ongoing Phase IIb study, we are confident that the study should succeed.

AuriPro is a suspension containing microparticles of ciprofloxacin along with a thermosensitive polymer, which is a liquid at or below room temperature and immediately transforms into a gel following administration into the ear and being heated to body temperature. As a result, AuriPro can provide a full course of treatment with only a single administration.

Otonomy is a development-stage company focused on bringing to market novel sustained-exposure treatments for otic conditions. The company has three key products in development and is targeting key addressable markets with considerable unmet need and few – if any – available FDA-approved treatment options. Otonomy's lead product is AuriPro (sustained-release ciprofloxacin) for the treatment of middle ear effusion at the time of TTP surgery. The AuriPro program has produced positive Phase III results and the company is expected to file an NDA by the end of this quarter. We estimate that AuriPro could receive approval in Q1 of 2016 and be launched in the following quarter. The second clinical development candidate is OTO-104 (sustained-release dexamethasone), which is in Phase II/III studies for the treatment of Ménière's disease, a condition that causes vertigo, tinnitus, and hearing loss. Ménière's has significant unmet need as it can eventually lead to permanent hearing loss and currently there are no approved treatments. OTO-104 is currently being evaluated in an ongoing Phase IIb study, which will be one of two pivotal studies required for approval and should have topline data readout in Q2 of this year. Given the significant clinical effects observed in Phase Ib, which had an almost identical design to the ongoing Phase IIb study, we are confident that the study should succeed. Finally, Otonomy is also developing OTO-311 for the treatment of tinnitus, which is ringing in the ear in the absence of an external source. Approximately 16MM patients in the U.S. suffer from tinnitus severe enough to require medical attention. However, like Ménière's, there are no currently approved treatments for this debilitating condition. Otonomy expects to file an IND and initiate a Phase Ib trial for OTO-311 by year-end. Our valuation and \$55 price target is predicated on AuriPro and OTO-104 alone and approval of OTO-311 or any other treatments born by Otonomy's platform technology would simply provide additional – and potentially significant – upside potential.

**AuriPro** is a suspension containing microparticles of ciprofloxacin along with a thermosensitive polymer, which is a liquid at or below room temperature and immediately transforms into a gel following administration into the ear and being heated to body temperature. As a result, AuriPro can provide a full course of treatment with only a single administration. The vast majority of patients receiving ear tubes are young children and our consultants note that about 80% are prescribed antibiotic ear drops after the procedure. These drops require multiple daily drops (2-3x/day) for 7-10 days, and our consultants highlighted that compliance is a major issue that can lead to poor efficacy outcomes and bacterial resistance. Beyond the obvious benefits of improved convenience, our consultants found the Phase III efficacy and safety data for AuriPro to be quite compelling. Importantly, they initially expressed some concern about the possibility of the AuriPro gel clogging the ear tube, but were reassured that there was no increase in clogging the Phase II or Phase III studies in comparison to sham (placebo gel vehicle). If AuriPro is approved – which we believe is likely – it will be the first and only product labeled for the treatment of effusion with TTP surgery. Based on the product's superior product profile and feedback from our consultants, we believe AuriPro could be a \$500MM+ product in the U.S. and \$300MM+ in the EU. Broadening of the label for other indications (acute otitis externa and acute otitis media through tympanostomy tubes [AOMT]) and rest of world approvals and could provide further upside.

**OTO-104** is being developed as a sustained-exposure intratympanic injection for the treatment of Ménière's. The chronic condition affects approximately 600,000 patients in the U.S. and typically occurs in middle-aged (40-50 years of age) patients. It is

Therefore, Otonomy's OTO-104 aims to: (1) provide for an easier method of administration; (2) allow for a high level of drug exposure to the round/oval membrane; and (3) provide sustained-exposure, potentially limiting the overall number of injections for patients. Overall, our consultants strongly agree with the advantage of OTO-104's product profile relative to the current IT steroid injections and believe that the clinical profile is "very compelling."

AuriPro and OTO-104 have significant duration with the IP extending to at least 2030 and 2029, respectively

AuriPro achieved its primary efficacy endpoint along with several secondary endpoints. AuriPro reduced the risk of treatment failure by an average of 49% ( $p < 0.001$ ) and also reduced the proportion of patients that were treatment failures due to otorrhea or use of antibiotics by an average of 62% ( $p \leq 0.004$ ) across both trials.

thought to arise from abnormal fluid and ion homeostasis in the inner ear. The disease is chronic and typically results in symptoms of vertigo and hearing loss – which can eventually become permanent – and can cause a high level of disability. There are currently no FDA-approved treatments for Ménière's disease. Our consultants note that off-label IT steroid injections have shown promise despite their shortcomings and that they see positive responses in 2/3 of patients, but there is still certainly plenty of room for improvement as 10-20% of these patients will eventually still have to undergo invasive surgery as a last resort. Due to the shortcomings of current IT steroid injections (lower drug concentration; not fully retained in inner ear; drug concentration drops to 0 before the end of day 1), Otonomy believes that the therapeutic effect of current off-label IT steroid solution injections is reduced and treatment variability across the general patient population is increased. As such, ENTs will often require patients to remain immobilized for an extended period of time following each IT injection and subsequently return for additional injections. Our consultants suggest that many patients may need up to 10 injections – perhaps every 1-3 months – over several years and potentially a lifetime. Still, drug levels decrease rapidly following each administration and decline away from the round/oval membrane. Therefore, Otonomy's OTO-104 aims to: (1) provide for an easier method of administration; (2) allow for a high level of drug exposure to the round/oval membrane; and (3) provide sustained-exposure, potentially limiting the overall number of injections for patients. Overall, our consultants strongly agree with the advantage of OTO-104's product profile relative to the current IT steroid injections and believe that the clinical profile is "very compelling." Our physician consultants also believe there are several very logical follow-on indication opportunities with OTO-104. With reasonable penetration rates, we believe OTO-104 could be a \$750MM+ product in the U.S., and \$400MM+ in the EU. Once again, expansion into other indications and additional rest of world approvals could provide further upside.

Otonomy's use of FDA approved compounds for all of its pipeline products, in conjunction with the 505(b)(2) regulatory pathway, significantly reduces the overall development risk for the company. Furthermore, our industry checks suggest the improved convenience and compliance with single administration AuriPro could be transformational. They also note that if AuriPro gains traction with ENTs for effusion with TTP, it will easily be used for other indications as the product's label continues to expand – and potentially even before. Our consultants were especially excited about OTO-104, given the lack of treatment options for Ménière's and the debilitating nature of the disease. Importantly, both AuriPro and OTO-104 have significant duration with the IP extending to at least 2030 and 2029, respectively. Assuming clinical success of these products, we arrive at a base valuation of \$55 per share. Of note, this valuation does not factor in any potential upside for additional AuriPro or OTO-104 indications and approvals for both products in markets outside of the U.S. and EU. Furthermore, our valuation also does not factor in the market opportunity of OTO-311 for tinnitus.

### Otonomy Has Generated Compelling Clinical Data

For AuriPro, Otonomy has completed two identical Phase III trials (Study 302 and Study 303) in 532 total pediatric patients across ~60 sites in the U.S. and Canada. Importantly, AuriPro achieved its primary efficacy endpoint along with several secondary endpoints. AuriPro reduced the risk of treatment failure by an average of 49% ( $p < 0.001$ ) and also reduced the proportion of patients that were treatment failures due to otorrhea or use of antibiotics by an average of 62% ( $p \leq 0.004$ ) across both trials. AuriPro was well-tolerated, and there were no notable differences in safety between patients treated with AuriPro or sham. Of note, the AuriPro gel did not cause any increase in the incidence of tube clogging relative to sham in either the Phase II

or Phase III studies. Overall, our consultants found the Phase III data to be impressive and highlighted that in terms of safety, efficacy, and convenience, AuriPro's product profile would provide a superior option relative to current antibiotic ear drops. Otonomy is planning to file an NDA for AuriPro by the end of Q1:2015, and assuming a 12 month review, we estimate that AuriPro could receive approval and launch in H1:2016.

In a Phase Ib clinical trial, OTO-104 demonstrated a significant mean reduction in vertigo frequency (primary endpoint) during month 3 relative to baseline. There was a clear dose response as a 56% and 73% (p-value=0.086) reductions in vertigo frequency in month 3 was observed with the 3mg and 12mg OTO-104 dosing cohorts. The 73% reduction in the 12mg group was equivalent to a reduction in days with vertigo from 8 at baseline to 2 in month 3.

We believe the physician experience with dexamethasone for Ménière's – in conjunction with the existing early clinical data showing an impressive effect – substantially de-risks the program.

Regarding OTO-104, we view the development risk as very low given that IT steroid injections are already used quite frequently in practice and appear to be moderately effective. The goal of OTO-104, is simply to provide higher and sustained concentration of dexamethasone relative to existing injections, which we believe will not adversely affect future clinical trial results. In a Phase Ib clinical trial, OTO-104 demonstrated a significant mean reduction in vertigo frequency (primary endpoint) during month 3 relative to baseline. There was a clear dose response as a 56% and 73% (p-value=0.086) reductions in vertigo frequency in month 3 was observed with the 3mg and 12mg OTO-104 dosing cohorts. The 73% reduction in the 12mg group was equivalent to a reduction in days with vertigo from 8 at baseline to 2 in month 3. A day with vertigo is defined as an episode lasting at least 20 minutes and being completely debilitating. Interestingly, 50% of patients in this study had no vertigo in the third month. Furthermore, 81% of patients in the 1mg OTO-104 arm had at least a 50% improvement in vertigo frequency in month 3 versus baseline. Clearly, the 12mg OTO-104 group was not statistically significant, but we would note that it is due to the study arm only having 16 patients and the fact that it was even close (0.036 off) is impressive. In general, a single injection of OTO-104 was well tolerated and there were no serious adverse events observed during the trial. Moreover, there were no instances of persistent conductive hearing loss associated with OTO-104 injection. We believe the physician experience with dexamethasone for Ménière's – in conjunction with the existing early clinical data showing an impressive effect – substantially de-risks the program. OTO-104 is currently in a Phase IIb clinical trial, which has completed enrollment, and results are expected in Q2:2015. This trial will serve as one of two pivotal efficacy studies. The second pivotal study is expected to start in the second half of 2015 and we estimate final results should come by mid-year 2017 or potentially earlier. Therefore, OTO-104 could be launched in the U.S. by early 2018 and potentially sooner, assuming successful development. It is important to note that OTO-104 has been granted Fast Track Designation, so there is potential to receive an expedited 6-month regulatory review. In the EU, a multiple-dose safety study was initiated in the U.K in October 2014 and is underway and we generally expect a potential European launch at least 1-2 years later as the priority post launching in the U.S. market will be to expand in additional indications.

#### Upcoming Milestones For Otonomy Include:

##### 2015:

- Q1 – NDA filing of AuriPro for effusion with TTP surgery
- Q2 – Phase IIb data for OTO-104 in Ménière's disease
- H1 – Initiate AuriPro clinical trial in expansion indications
- H2 – Potential initiation of second pivotal trial for OTO-104 in Ménière's disease
- IND filing and initiation of Phase I study of OTO-311 for tinnitus

##### 2016:

- Q1 – Potential approval of AuriPro for effusion with TTP surgery
- Q2 – Potential launch of AuriPro for effusion with TTP surgery

##### 2017:

- Potential readout of second pivotal trial for OTO-104 in Ménière's and NDA filing

##### 2018:

- Potential approval and launch of OTO-104 in Ménière's

### The Valuation Is Attractive Here

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Our base case valuation model assumes a U.S. approval and subsequent launch of AuriPro by the second quarter of 2016, and with an estimated net price of \$200 per prescription, we believe U.S. peak sales could reach approximately ~\$500MM for middle ear indications, assuming a penetration of roughly 30% of U.S. antibiotic ear drop prescriptions by 2025. We also assume modest EU sales beginning in 2018 for AuriPro with a peak sales value of \$300MM+. For OTO-104, we assume U.S. approval and launch in 2018 with pricing in the range of \$1,000 per injection, which could be conservative. Assuming a peak 15% penetration of Ménière's patients results in a \$750MM+ U.S. peak sales potential. We also expect approval in the EU in 2020 with peak sales eventually reaching \$400MM+. Worth noting, our estimates for both products could very well be conservative as our consultants suggest each has very logical and viable follow-on indications that the company is exploring. We do not model any of these additional indication expansion opportunities. European approval could also potentially come sooner than we model. Approvals/partnerships in the rest of the world could also provide further upside. We would also note that our valuation does not attribute any potential sales of OTP-311, which like OTO-104, is competing in a market with no currently approved treatments and could potentially have significant pricing flexibility and provide further upside beyond our base case valuation. In terms of operating spend, our base case scenario assumes an initial hiring of 40 sales reps for the AuriPro launch that will be expanded to 80 reps upon OTO-104 launch. We anticipate ultimate margins of ~85% with SG&A and R&D costs within the range of normal industry standards.

Below we provide our U.S. and E.U. ear market build for both AuriPro and OTO-104. On the following pages, we provide our Annual P&L and base case DCF.



Figure 1 U.S. And EU Ear Market Build For AuriPro And OTO-104

ESTIMATED UNITED STATES AND EUROPE EAR MARKET BUILD													
UNITED STATES	2014	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	5Y CGR Comments
People affected by disorders of the ear (MM)	50.0	50.5	51.0	51.5	52.0	52.6	53.1	53.6	54.1	54.7	55.2	55.8	- Roughly 1/6 people
% of people currently seeking treatment	40.0%	40.0%	40.0%	40.5%	41.0%	41.5%	42.0%	42.5%	43.0%	43.5%	44.0%	44.5%	- To grow with more products/awareness
# of patients being treated (MM)	20.0	20.2	20.4	20.9	21.3	21.8	22.3	22.8	23.3	23.8	24.3	24.8	+2%
<b>Outer Ear - Acute Otitis Externa</b>													
% of patients affected by acute otitis externa	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	- "Swimmer's Ear," Most of CiproDex sales
# of patients affected by acute otitis externa (MM)	2.5	2.5	2.6	2.6	2.7	2.7	2.8	2.8	2.9	3.0	3.0	3.1	+2% - Potential AuriPro follow-on indication
<b>Middle Ear - Acute Otitis Media Following TTP</b>													
% of patients treated for acute otitis media	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	- "Ear infections"
% of patients treated for acute otitis media (MM)	7.0	7.1	7.1	7.3	7.5	7.6	7.8	8.0	8.1	8.3	8.5	8.7	- ~5.5% per hundred people; ~17MM total pts
# of antibiotic ear drop units administered (MM)	2.3	2.4	2.4	2.5	2.6	2.7	2.7	2.8	2.9	3.0	3.1	3.2	+3% - To increase with promotion of new agents
% of drop units administered due to TTP surgery	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	- Est. 80% of pts get ear drops for 5-7 days
# of drop units administered due to TTP surgery (MM)	1.0	1.0	1.0	1.1	1.1	1.1	1.2	1.2	1.2	1.3	1.3	1.4	
% of drop units administered due to recurrence	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	
# of drop units administered due to recurrence (MM)	0.9	0.9	1.0	1.0	1.0	1.1	1.1	1.1	1.2	1.2	1.2	1.3	
% of drop units admin. due to severe swimmer's ear	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	
# of drop units admin. due to severe swimmer's ear (MM)	0.4	0.4	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.6	
<b>CiproDex</b>													
% penetration of antibiotic ear drops for middle ear	43.5%	43.5%	41.0%	39.0%	35.0%	31.0%	27.0%	25.0%	23.0%	22.0%	21.0%	20.0%	- Made by Alcon; BID dosing for 7 days
# of patients ('000)	1,000.5	1,030.5	1,000.4	980.2	906.0	826.6	741.5	707.2	670.1	660.2	649.1	636.7	- 50% coverage in private practice
Net price per course	\$120.0	\$125.0	\$137.5	\$151.3	\$166.4	\$183.0	\$201.3	\$221.4	\$243.6	\$267.9	\$294.7	\$324.2	- Not indicated for otitis media following TTP
Net sales (MM)	\$120.0	\$130.0	\$140.0	\$150.0	\$150.0	\$150.0	\$150.0	\$155.0	\$165.0	\$175.0	\$190.0	\$205.0	- WAC of \$167.15 per Jan 8, 2015
% Growth		+8%	+8%	+7%	+0%	+0%	+0%	+3%	+6%	+6%	+9%	+8%	- Est. ~30% of sales are from middle ear
<b>Ofloxacin, Tobradex, And Others</b>													
% penetration of antibiotic ear drops for middle ear	56.5%	56.5%	56.5%	56.0%	55.0%	54.0%	53.0%	52.0%	51.0%	50.0%	49.0%	48.0%	- Made by Alcon; BID dosing for 7 days
# of patients ('000)	1,299.5	1,338.5	1,378.6	1,407.4	1,423.8	1,439.8	1,455.5	1,470.9	1,485.9	1,500.5	1,514.6	1,528.2	
Net price per course	\$20.0	\$22.0	\$24.2	\$26.6	\$29.3	\$32.2	\$35.4	\$39.0	\$42.9	\$47.2	\$51.9	\$57.1	- WAC of \$167.15 per Jan 8, 2015
Net sales (MM)	\$25.0	\$30.0	\$35.0	\$40.0	\$45.0	\$50.0	\$55.0	\$60.0	\$65.0	\$70.0	\$80.0	\$85.0	+11% - Est. ~30% of sales are from middle ear
% Growth		+20%	+17%	+0%	+14%	+13%	+11%	+10%	+10%	+8%	+14%	+6%	
<b>AuriPro</b>													
% penetration of antibiotic ear drops for middle ear			2.5%	5.0%	10.0%	15.0%	20.0%	23.0%	26.0%	28.0%	30.0%	32.0%	- Single administration
# of AuriPro patients ('000)			61.0	125.7	258.9	399.9	549.3	650.6	757.5	840.3	927.3	1,018.8	- Penetration including additional indications
Net price per administration			\$200.0	\$220.0	\$242.0	\$266.2	\$292.8	\$322.1	\$354.3	\$389.7	\$428.7	\$471.6	- NDA submission Q1:2015; Q2:2016 launch
													- Priced at premium to CiproDex
<b>Annual U.S. Sales of AuriPro (MM)</b>			\$10.0	\$30.0	\$65.0	\$105.0	\$160.0	\$210.0	\$270.0	\$325.0	\$400.0	\$480.0	+84% - Growth driven by additional indications
% Growth			+200%	+117%	+82%	+52%	+31%	+29%	+20%	+23%	+20%	+20%	
<b>Total Annual U.S. AOM Sales (MM)</b>	\$145.0	\$160.0	\$185.0	\$215.0	\$255.0	\$300.0	\$360.0	\$420.0	\$500.0	\$570.0	\$670.0	\$770.0	+18% - Growth from new agents
% Growth		+10%	+18%	+16%	+19%	+18%	+20%	+17%	+19%	+14%	+18%	+15%	
<b>Inner Ear - Ménière's Disease</b>													
% of patients treated for inner ear disorders	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	
# of patients treated for inner ear disorders (MM)	8.0	8.1	8.2	8.3	8.5	8.7	8.9	9.1	9.3	9.5	9.7	9.9	
% of treated patients affected by Ménière's	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	
# of patients affected by Ménière's (MM)	0.6	0.6	0.6	0.6	0.6	0.7	0.7	0.7	0.7	0.7	0.7	0.7	- No approved agents
% of patients eligible for steroid injections	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	- Low salt diet + diuretics (Diamox) is first line
# of patients eligible for steroid injections (MM)	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.4	
<b>OTO-104</b>													
% penetration of patients eligible for steroid injections					2.5%	5.0%	10.0%	15.0%	20.0%	24.0%	27.0%	30.0%	- Second pivotal trial to be initiated Q2:2015
% penetration of total Ménière's patients					1.3%	2.5%	5.0%	7.5%	10.0%	12.0%	13.5%	15.0%	- Expected early 2018 launch
# of OTO-104 patients ('000)					8.0	16.4	33.4	51.3	69.8	85.6	98.4	111.7	
OTO-104 net price per administration					\$1,000.0	\$1,100.0	\$1,210.0	\$1,331.0	\$1,464.1	\$1,610.5	\$1,771.6	\$1,948.7	- Priced similarly to Wet AMD drugs
Average # of OTO-104 injections per year					3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	- Consultants suggest avg. of 3
Average total annual OTO-104 cost per patient					\$3,000.0	\$3,300.0	\$3,630.0	\$3,993.0	\$4,392.3	\$4,831.5	\$5,314.7	\$5,846.2	
<b>Annual U.S. Sales of OTO-104 (MM)</b>					\$25.0	\$55.0	\$120.0	\$205.0	\$305.0	\$415.0	\$525.0	\$655.0	+75% - Growth driven by additional indications
% Growth					+120%	+118%	+71%	+49%	+36%	+27%	+25%	+25%	
<b>Total Annual U.S. Product Sales (MM)</b>		\$10.0	\$30.0	\$90.0	\$180.0	\$280.0	\$415.0	\$575.0	\$740.0	\$925.0	\$1,135.0	\$1,410.0	+111% - Initially drive by AuriPro
% Growth		+200%	+200%	+75%	+75%	+48%	+39%	+29%	+25%	+23%	+23%	+23%	- Ménière's to contribute significantly
<b>EUROPEAN UNION</b>													
<b>Annual EU Sales of AuriPro (MM)</b>					\$5.0	\$20.0	\$45.0	\$75.0	\$110.0	\$145.0	\$190.0	\$225.0	+98% - Assuming approval two years later
% Growth					+300%	+125%	+87%	+47%	+47%	+32%	+31%	+18%	- Market opportunity slightly smaller
<b>Annual EU Sales of OTO-104 (MM)</b>						\$20.0	\$40.0	\$65.0	\$145.0	\$215.0	\$290.0	\$385.0	+71% - Assuming approval two years later
% Growth						+100%	+113%	+71%	+48%	+35%	+27%	+27%	- Market opportunity slightly smaller
<b>Total Annual EU Product Sales (MM)</b>					\$5.0	\$20.0	\$65.0	\$115.0	\$195.0	\$290.0	\$405.0	\$515.0	+125%
% Growth						+300%	+225%	+77%	+70%	+49%	+40%	+27%	
<b>Total Annual U.S./EU Product Sales (MM)</b>		\$10.0	\$30.0	\$95.0	\$180.0	\$345.0	\$530.0	\$770.0	\$1,090.0	\$1,390.0	\$1,680.0	\$2,000.0	+121% - Significant U.S./EU market opportunities
% Growth		+200%	+217%	+89%	+92%	+54%	+45%	+45%	+34%	+29%	+24%	+24%	

Source: Otonomy; Cowen And Company estimates; PriceRx; Monasta L, Ronfani L, Marchetti F, Montico M, Vecchi Brumatti L, et al. (2012) Burden of Disease Caused by Otitis Media: Systematic Review and Global Estimates. PLoS ONE 7(4): e36226. doi:10.1371/journal.pone.0036226

For our DCF valuation, we assume that Otonomy will develop and commercialize AuriPro and OTO-104 in the U.S. and in the EU. Using the sales estimates provided above and assuming a U.S. launch of AuriPro in 2016 along with the EU in 2018 and a U.S. launch of OTO-104 in 2018 followed with an EU launch in 2020, we arrive at a DCF valuation of \$55 per share, which is the basis of our price target. Label expansion of AuriPro and OTO-104 is likely and should provide further upside. An approval and launch of OTO-311, the company's earlier stage candidate for tinnitus to enter the clinic this year, could provide even further upside.

On the following pages we provide our Annual P&L and base case DCF.

Figure 2 Otonomy Annual P&L

OTONOMY - 2014-2025 ESTIMATED ANNUAL EPS BUILDUP (\$MM)														
	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	5Y CAGR Comments
<b>PRODUCT SALES</b>														
U.S. AuriPro Sales				\$10.0	\$30.0	\$65.0	\$105.0	\$160.0	\$210.0	\$270.0	\$325.0	\$400.0	\$480.0	+84% - Sustained release Cipro for ear infections post TTP surgery
Growth Rate					+200%	+117%	+62%	+52%	+31%	+29%	+20%	+23%	+20%	- Q2:2016 U.S. Launch assumed; IP to 2030
EU AuriPro Sales						\$5.0	\$20.0	\$45.0	\$75.0	\$110.0	\$145.0	\$190.0	\$225.0	+96% - Expected EU launch in 2018
Growth Rate							+300%	+125%	+67%	+47%	+32%	+31%	+18%	
U.S. OTO-104 Sales						\$25.0	\$55.0	\$120.0	\$205.0	\$305.0	\$415.0	\$525.0	\$655.0	+75% - Sustained release dexamethasone for Ménière's
Growth Rate							+120%	+118%	+71%	+49%	+36%	+27%	+25%	- 2018 U.S. launch assumed; IP to 2029
EU OTO-104 Sales								\$20.0	\$40.0	\$85.0	\$145.0	\$215.0	\$290.0	+71% - Expected EU launch in 2020
Growth Rate									+100%	+113%	+71%	+48%	+35%	
<b>Total Otonomy Revenues</b>	<b>\$0.0</b>	<b>\$0.0</b>	<b>\$0.0</b>	<b>\$10.0</b>	<b>\$30.0</b>	<b>\$95.0</b>	<b>\$180.0</b>	<b>\$345.0</b>	<b>\$590.0</b>	<b>\$770.0</b>	<b>\$1,030.0</b>	<b>\$1,380.0</b>	<b>\$1,850.0</b>	<b>+121%</b> - Initial growth driven by AuriPro, then OTO-104 for Ménière's
<b>% Change</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>+200%</b>	<b>+217%</b>	<b>+89%</b>	<b>+92%</b>	<b>+54%</b>	<b>+45%</b>	<b>+34%</b>	<b>+28%</b>	<b>+24%</b>	- To expand into additional indications, then launch ex-US
Cost of Goods	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$10.0	\$20.0	\$45.0	\$65.0	\$95.0	\$130.0	\$165.0	\$205.0	
Gross Profit	\$0.0	\$0.0	\$0.0	\$10.0	\$25.0	\$85.0	\$160.0	\$300.0	\$465.0	\$675.0	\$900.0	\$1,165.0	\$1,445.0	
Gross Margin	100.0%	100.0%	100.0%	85.0%	86.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	- 85% or more gross margins on products
SG&A	\$3.5	\$7.0	\$15.0	\$30.0	\$40.0	\$60.0	\$80.0	\$120.0	\$150.0	\$175.0	\$205.0	\$230.0	\$260.0	+63% - To hire 40 reps for AuriPro U.S. launch and expand to 80 reps for OTO-104
% of Revs	NM	NM	NM	300%	133%	63%	44%	35%	28%	23%	20%	17%	16%	- To develop and commercialize in Europe; partner RoW
R&D	\$16.3	\$33.0	\$55.0	\$90.0	\$90.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	+4%
% of Revs	NM	NM	NM	500%	167%	42%	22%	12%	8%	5%	4%	3%	2%	
Operating Expenses	\$19.9	\$40.0	\$70.0	\$80.0	\$90.0	\$100.0	\$120.0	\$160.0	\$190.0	\$215.0	\$245.0	\$270.0	\$300.0	+25%
% of Revenues	NM	NM	NM	800.0%	300.0%	105.3%	66.7%	46.4%	35.8%	27.9%	23.8%	20.3%	18.2%	
Operating Income	(\$19.9)	(\$40.0)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$40.0	\$140.0	\$275.0	\$460.0	\$655.0	\$895.0	\$1,145.0	NM - Operating profit expected in 2019
% Operating Margin	NM	NM	NM	NM	NM	NM	22%	41%	52%	60%	64%	67%	69%	
Non-Operating Income														
Interest Income	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	
Interest Expense	\$0.0	(\$0.1)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
Other Income	(\$0.2)	(\$3.3)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
Non-Operating Income	(\$0.2)	(\$3.4)	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	
Pretax Income	(\$20.1)	(\$43.4)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$40.0	\$140.0	\$275.0	\$460.0	\$655.0	\$895.0	\$1,145.0	NM
% of Revs	NM	NM	NM	NM	NM	NM	22.2%	40.6%	51.9%	59.7%	63.6%	67.3%	69.4%	
Income Taxes							\$14.0	\$49.0	\$96.3	\$161.0	\$229.3	\$313.3	\$400.8	NM
Income Tax Rate							35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	- Standard U.S. corporate tax rate; assumes no NOLs
Net Income - Operations	(\$20.1)	(\$43.4)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$26.0	\$91.0	\$178.8	\$299.0	\$425.8	\$581.8	\$744.3	NM
% Net Margin	NM	NM	NM	NM	NM	NM	14.4%	26.4%	33.7%	38.8%	41.3%	43.7%	45.1%	
Extraordinary Items	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	
Reported Net Income	(\$20.1)	(\$43.4)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$26.0	\$91.0	\$178.8	\$299.0	\$425.8	\$581.8	\$744.3	NM
Interest Add-Back	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	
<b>EPS (GAAP) - Before Ex. Items</b>	<b>(\$268.80)</b>	<b>(\$5.40)</b>	<b>(\$3.15)</b>	<b>(\$3.05)</b>	<b>(\$2.70)</b>	<b>(\$0.60)</b>	<b>\$0.90</b>	<b>\$3.10</b>	<b>\$5.90</b>	<b>\$8.60</b>	<b>\$13.20</b>	<b>\$17.50</b>	<b>\$21.75</b>	<b>NM</b> - Profitable in 2019 following the launch of AuriPro and OTO-104
<b>Growth Rate</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>+244%</b>	<b>+90%</b>	<b>+63%</b>	<b>+38%</b>	<b>+33%</b>	<b>+24%</b>	
EPS - Extraordinary Items	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	
EPS - Reported	(\$268.80)	(\$5.40)	(\$3.15)	(\$3.05)	(\$2.70)	(\$0.60)	\$0.90	\$3.10	\$5.90	\$8.60	\$13.20	\$17.50	\$21.75	NM
Shares - Fully Diluted (MM)	0.1	8.0	22.1	23.1	24.1	25.1	28.2	29.2	30.2	31.2	32.2	33.2	34.2	- Assuming some onward dilution from options (+2.1MM upon profitability)

Source: Cowen and Company



Figure 3 Otonomy DCF Suggests \$55 Per Share

Assumptions:		Output:	
Increase in WC	5.0%	Equity Value	\$1,370.0
Discount Rate	13.0%	Est. Share Price	\$55.00
Shares Outstanding	24.2	Debt	\$0.0 \$156MM as of Dec 31, 2014
		Cash	\$100.0
		Enterprise Value	\$1,270.0

OTONOMY DCF																								
	2013	2014P	2015P	2016P	2017P	2018P	2019P	2020P	2021P	2022P	2023P	2024P	2025P	2026P	2027P	2028P	2029P	2030P	2031P	2032P	2033P	2034P	2035P	
Total Revenues	\$0.0	\$0.0	\$0.0	\$10.0	\$30.0	\$95.0	\$180.0	\$345.0	\$530.0	\$770.0	\$1,030.0	\$1,330.0	\$1,650.0	\$1,900.0	\$2,075.0	\$2,250.0	\$1,525.0	\$800.0	\$400.0	\$200.0	\$125.0	\$100.0	\$100.0	
% Change					+200%	+217%	+89%	+92%	+54%	+45%	+34%	+29%	+24%	+15%	+9%	+8%	-32%	-48%	-50%	-50%	-38%	-20%	+0%	
Cost of Goods	\$0.0	\$0.0	\$0.0	\$0.0	\$5.0	\$10.0	\$20.0	\$45.0	\$65.0	\$95.0	\$130.0	\$165.0	\$205.0	\$235.0	\$260.0	\$280.0	\$190.0	\$100.0	\$50.0	\$25.0	\$15.0	\$10.0	\$10.0	
Gross Profit	\$0.0	\$0.0	\$0.0	\$10.0	\$25.0	\$85.0	\$160.0	\$300.0	\$465.0	\$675.0	\$900.0	\$1,165.0	\$1,445.0	\$1,665.0	\$1,815.0	\$1,970.0	\$1,335.0	\$700.0	\$350.0	\$175.0	\$110.0	\$90.0	\$90.0	
Gross Margin - Total	NM	100.0%	100.0%	85.0%	86.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	
SG&A	\$3.5	\$7.0	\$15.0	\$30.0	\$40.0	\$60.0	\$80.0	\$120.0	\$150.0	\$175.0	\$205.0	\$230.0	\$260.0	\$300.0	\$330.0	\$330.0	\$280.0	\$200.0	\$100.0	\$75.0	\$65.0	\$55.0	\$50.0	
% of Revs	NM	NM	NM	300.0%	133.3%	63.2%	44.4%	34.8%	28.3%	22.7%	19.9%	17.3%	15.8%	15.8%	15.9%	14.7%	18.4%	25.0%	25.0%	37.5%	52.0%	55.0%	50.0%	
R&D	\$16.3	\$33.0	\$55.0	\$50.0	\$50.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$30.0	\$20.0	\$20.0	\$10.0	\$5.0	\$5.0	\$5.0	
% of Revs	NM	NM	NM	500.0%	166.7%	42.1%	22.2%	11.6%	7.5%	5.2%	3.9%	3.0%	2.4%	2.1%	1.9%	1.8%	2.0%	2.5%	5.0%	5.0%	4.0%	5.0%	5.0%	
Operating Expenses	\$19.9	\$40.0	\$70.0	\$80.0	\$90.0	\$100.0	\$120.0	\$160.0	\$190.0	\$215.0	\$245.0	\$270.0	\$300.0	\$340.0	\$370.0	\$370.0	\$310.0	\$220.0	\$120.0	\$85.0	\$70.0	\$60.0	\$55.0	
% of Revenues	NM	NM	NM	800.0%	300.0%	105.3%	66.7%	46.4%	35.8%	27.9%	23.8%	20.3%	18.2%	17.9%	17.8%	16.4%	20.3%	27.5%	30.0%	42.5%	56.0%	60.0%	55.0%	
Operating Income	(\$19.9)	(\$40.0)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$40.0	\$140.0	\$275.0	\$460.0	\$655.0	\$895.0	\$1,145.0	\$1,325.0	\$1,445.0	\$1,600.0	\$1,025.0	\$480.0	\$230.0	\$90.0	\$40.0	\$30.0	\$35.0	
% Operating Margin	NM	NM	NM	NM	NM	-15.8%	22.2%	40.6%	51.9%	59.7%	63.6%	67.3%	69.4%	69.7%	69.6%	71.1%	67.2%	60.0%	57.5%	45.0%	32.0%	30.0%	35.0%	
Other Income	(\$0.248)	(\$3.3)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
Adjusted EBIT	(\$20.1)	(\$43.3)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$40.0	\$140.0	\$275.0	\$460.0	\$655.0	\$895.0	\$1,145.0	\$1,325.0	\$1,445.0	\$1,600.0	\$1,025.0	\$480.0	\$230.0	\$90.0	\$40.0	\$30.0	\$35.0	
% of Revs	NM	NM	NM	NM	NM	-15.8%	22.2%	40.6%	51.9%	59.7%	63.6%	67.3%	69.4%	69.7%	69.6%	71.1%	67.2%	60.0%	57.5%	45.0%	32.0%	30.0%	35.0%	
Taxes						\$14.0	\$49.0	\$96.3	\$161.0	\$229.3	\$313.3	\$400.8	\$463.8	\$505.8	\$560.0	\$358.8	\$168.0	\$80.5	\$31.5	\$14.0	\$10.5	\$12.3		
Income Tax Rate						35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	
NOPAT	(\$20.1)	(\$43.3)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$26.0	\$91.0	\$178.8	\$299.0	\$425.8	\$581.8	\$744.3	\$861.3	\$893.3	\$1,040.0	\$666.3	\$312.0	\$149.5	\$58.5	\$26.0	\$19.5	\$22.8	
Adjustments:																							Terminal	
Capex	(\$0.5)	\$0.5	(\$0.5)	(\$1.0)	(\$5.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$5.0)	(\$3.0)	(\$2.0)	(\$1.0)	\$0.0	\$0.0	
Depreciation & Amortization	\$0.3	\$0.2	\$0.3	\$0.3	\$0.3	\$1.0	\$2.0	\$3.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	
Change In Working Capital	\$32.6	(\$5.0)	(\$5.3)	(\$5.5)	(\$5.8)	(\$6.1)	(\$6.4)	(\$6.7)	(\$7.0)	(\$7.4)	(\$7.8)	(\$8.1)	(\$8.6)	(\$9.0)	(\$9.4)	(\$9.9)	(\$10.4)	(\$10.9)	(\$11.5)	(\$12.0)	(\$12.6)	(\$13.3)	(\$13.9)	
Free Cash Flow	\$12.2	(\$48.8)	(\$76.5)	(\$76.5)	(\$76.5)	(\$56.1)	\$11.6	\$77.3	\$168.7	\$288.8	\$419.0	\$568.8	\$730.7	\$847.3	\$924.8	\$1,026.1	\$860.8	\$301.1	\$140.0	\$49.5	\$17.4	\$11.2	\$13.8	\$106.8

Source: Cowen and Company

## Otonomy Is Targeting Diseases And Disorders Of The Ear

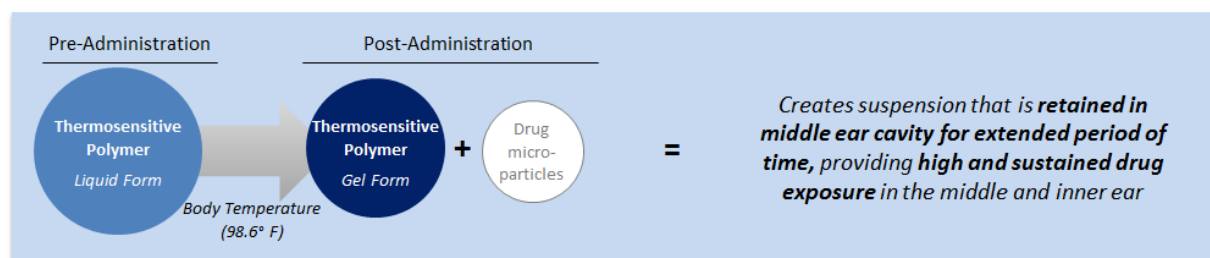
Otonomy has developed a proprietary formulation technology that provides sustained drug exposure in the ear from a single local administration. The novel technology utilizes a thermosensitive polymer, Poloxamer 407 (P407), which is a liquid at or below room temperature and immediately transforms into a gel at body temperature. As a gel, P407 avoids elimination down the Eustachian tube as seen with other ear drops formulations. The polymer can be combined with drug microparticles to create a suspension that is retained in the ear cavity for an extended period of time and provides sustained drug exposure. As a result, Otonomy's lead product AuriPro could potentially provide a full course of treatment from a single local administration and would eliminate the need for repeat dosing that is seen with current ear drop solutions.

Our consultants note that Otonomy's novel technology is indeed interesting and offers a unique product profile when compared to the lack of treatment options available today. This is a space in need of innovation.

Along with added convenience and potential improvement in compliance, the sustained-exposure approach would virtually eliminate the pulsatile drug levels seen with current daily ear drops. The Otonomy products would still provide high drug levels at the target location and provide distribution throughout the inner ear compartment, but should help minimize systemic exposure and reduce any unwanted side effects. Our consultants note that Otonomy's novel technology is indeed interesting and offers a unique product profile when compared to the lack of treatment options available today. This is a space in need of innovation.

Figure 4 Otonomy's Proprietary Otic Technology

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

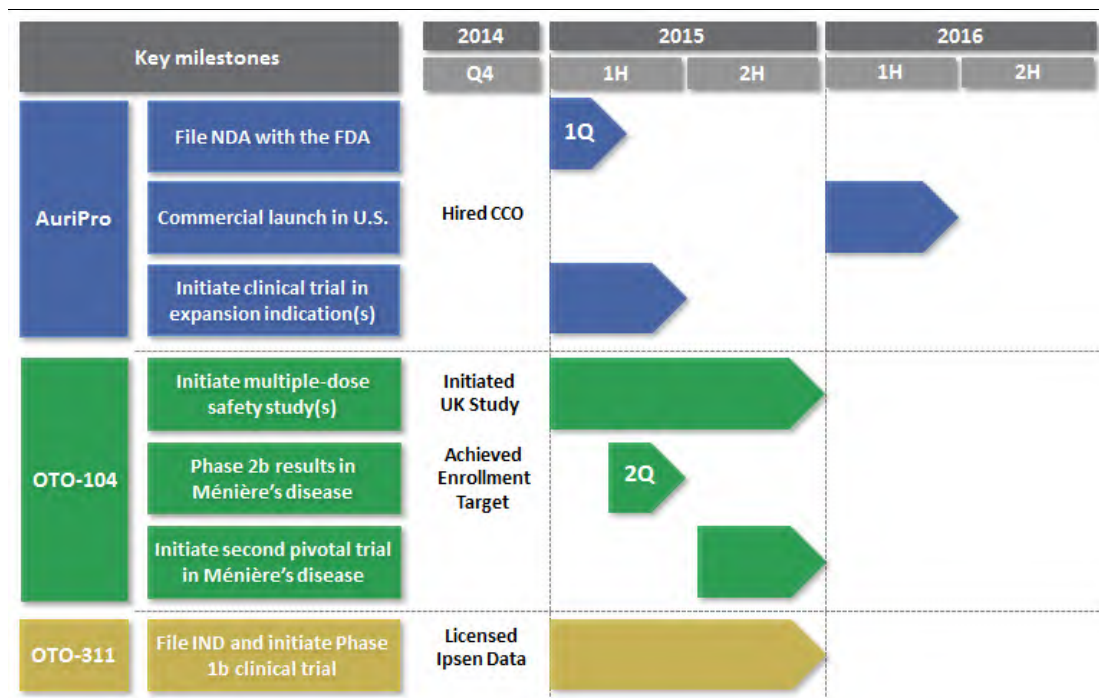


Source: Otonomy

The AuriPro program has produced positive Phase III results and the company is expected to file an NDA by the end of this quarter. We estimate that AuriPro could receive approval in Q1 of 2016 and be launched in the following quarter.

Otonomy's lead product in development is AuriPro for the treatment of middle ear effusion at the time of tympanostomy tube placement (TTP), for people with recurrent otitis media, commonly known as an ear infection. The AuriPro program has produced positive Phase III results and the company is expected to file an NDA by the end of this quarter. We estimate that AuriPro could receive approval in Q1 of 2016 and be launched in the following quarter. Otonomy will also initiate a trial in an additional indication during the first half of this year. The second clinical development candidate is OTO-104, which is in Phase II/III for the treatment of Ménière's disease, a debilitating condition that causes vertigo, tinnitus, and hearing loss. Ménière's is a disease with substantial unmet need as there are currently no approved treatments and patients can eventually permanently lose their hearing. OTO-104 is currently in an ongoing Phase IIb study, which will be one of two pivotal studies for approval and should have data readout in Q2 of this year. Finally, Otonomy is also developing OTO-311 for the treatment of tinnitus, which is ringing in the ear in the absence of an external source of noise. The company expects to file an IND and initiate a Phase Ib trial for OTO-311 by year-end.

Figure 5 Otonomy Has Several Near-Term Milestones



Source: Otonomy

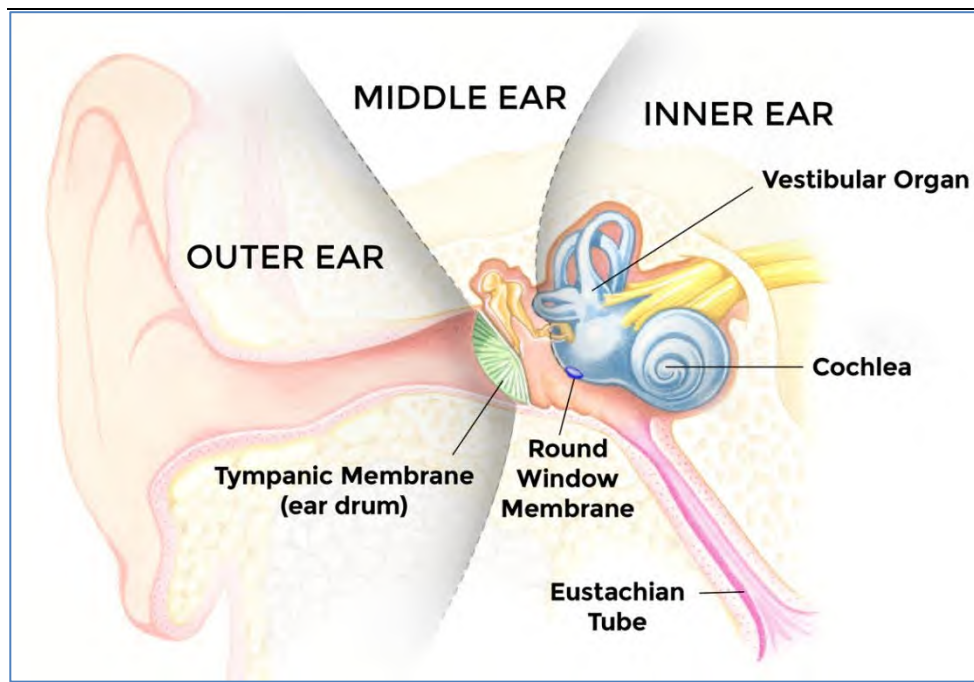
## Ear Anatomy Overview

The ear is comprised of three main compartments: the outer, middle, and inner ear. All three compartments work together and are necessary for detecting sound as it travels from the outer ear, through the middle, and finally to the inner part of the ear. A secondary function of the ear is to maintain balance.

Diseases and disorders of ear result from various complications that are segmented depending upon the part of the ear that they affect. The ear is comprised of three main compartments: the outer, middle, and inner ear. All three compartments work together and are necessary for detecting sound as it travels from the outer ear, through the middle, and finally to the inner part of the ear. A secondary function of the ear is to maintain balance. The **outer ear**, or the auricle, is the cartilage covered by skin placed on both sides of the head that we most commonly refer to. The auricle helps collect sound and guides it as it travels through the auditory/ear canal and reaches the outer layer of the eardrum, also called the tympanic membrane. This is where sound reaches the **middle ear**. The middle ear contains the eardrum, the tympanic cavity, and ossicles, which are 3 tiny bones that are attached. The 3 ossicle bones are: (1) the malleus of hammer, which is the long handle attached to the ear drum; (2) the incus or anvil, which is the bridge bone between the malleus and: (3) the stapes or stirrup, which is the footplate and the smallest bone in the body attached to the cochlea in the inner ear. Once sound is in the middle ear, it causes the eardrum and ossicles to vibrate, which in turn amplifies the sound and changes from air to liquid. The **inner ear** includes: (1) the oval window that connects the middle ear with the inner ear; (2) the semicircular ducts that are filled with fluid and attached to the cochlea and nerves that send information on balance and head position to the brain; (3) the cochlea, which is the spiral-shaped organ of hearing and transforms sound into signals that get sent to the brain; and (4) the auditory tube that drains fluid from the middle ear into the throat behind the nose. When the stapes in the middle ear moves, it pushes the oval window that moves the cochlea, which then takes the fluid vibration of sounds from the surrounding semicircular ducts and translates them into

signals that are sent to the brain by nerves – primarily the vestibular and cochlear nerve.

Figure 6 Ear Anatomy Schematic



Source: Otonomy

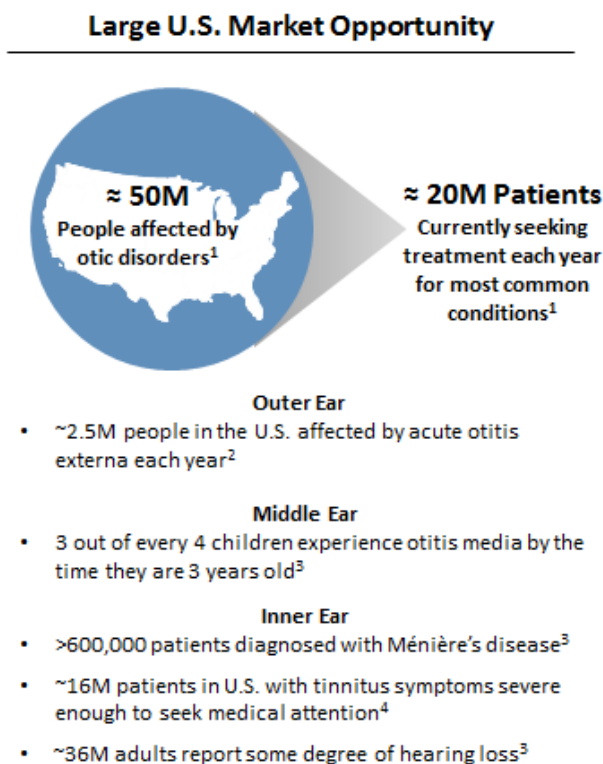
### Common Ear Diseases/Disorders

Nearly 50MM people in the U.S. are affected by conditions of the ear, with approximately 20MM annually seeking treatment. The most common disease of the outer ear is acute otitis externa, which is commonly referred to as swimmer's ear and can be exceptionally painful. With respect to the middle ear, the most common disease is otitis media, which primarily occurs in young children and is also commonly referred to as an ear infection. For the inner ear, related disorders are balance disorders, such as Ménière's disease that causes vertigo-like symptoms, tinnitus, and hearing loss.

For illustrative purposes, Otonomy's approach has been likened to current injectable anti-VEGF treatments for retina disorders. If one agrees and considers the performance of intravitreal treatments for the eye over the past decade, it would suggest that Otonomy's product could achieve significant commercial success.

For illustrative purposes, Otonomy's approach has been likened to current injectable anti-VEGF treatments for retina disorders. If one agrees and considers the performance of intravitreal treatments for the eye over the past decade, it would suggest that Otonomy's product could achieve significant commercial success. Similar to the eye, the ear is a protected sensory organ and over the last two decades, ophthalmologists have demonstrated that injecting drugs into the eye can be done safely to treat debilitating visual disorders. Otolaryngologists are increasingly using locally administered drugs to treat middle and inner ear conditions demonstrating the potential for multiple, significant new market opportunities for otic drug developers and it appears that Otonomy will be one of the first to capitalize.

Figure 7 Targeting The Otic Market Is An Attractive Opportunity



Source: <sup>1</sup>Otonomy; <sup>2</sup>American Academy of Otolaryngology; <sup>3</sup>National Institute on Deafness and Other Communications Disorders (NIDCD); <sup>4</sup>The American Tinnitus Association

## AuriPro, An Attractive Product Profile In An Area With Undifferentiated Treatments

AuriPro has been formulated to provide a sustained-exposure of ciprofloxacin so that a single administration provides a full course of treatment.

Utilizing its proprietary technology, Otonomy's lead product candidate is AuriPro, a sustained-exposure antibiotic for middle ear effusion (fluid), at the time of tympanostomy tube placement (TTP). AuriPro has been formulated to provide a sustained-exposure of ciprofloxacin so that a single administration provides a full course of treatment. Otonomy has completed two identical Phase III studies in 532 total pediatric patients across ~60 sites in the U.S. and Canada. AuriPro was well-tolerated and achieved its primary endpoint with a 49% reduction ( $p < 0.001$ ) in treatment failures relative to sham. Based on the study findings, and positive discussions with the FDA during a pre-NDA meeting, Otonomy plans to submit an NDA for AuriPro in Q1:2015. If approved with a standard 12-month review, a potential U.S. launch for AuriPro could take place in the first half of 2016.

AuriPro is a suspension containing microparticles of ciprofloxacin along with a thermosensitive polymer called Poloxamer 407 (P407), which is a liquid at or below room temperature and immediately transforms into a gel following administration into the ear and being heated to body temperature.

AuriPro is a suspension containing microparticles of ciprofloxacin along with a thermosensitive polymer called Poloxamer 407 (P407), which is a liquid at or below room temperature and immediately transforms into a gel following administration into the ear and being heated to body temperature. As a gel, P407 avoids elimination down the Eustachian tube as seen with other ear drop formulations. The P407 gel remains in the middle ear for about a week. This increased residence time in the middle ear enables the localization and adherence of ciprofloxacin microparticles, which provide

If approved, AuriPro will be the first and only product labeled for the treatment of effusion with TTP surgery. Despite the lack of approved products, our consultants note that about 80% of patients are still treated with antibiotic ear drops after the procedure. Our consultants believe a single-use, physician-administered product has significant advantages over current treatment options in terms of convenience and compliance.

Approximately 1MM TTP procedures are performed every year. Our consultants state that it is the most common outpatient procedure performed in kids besides circumcision. In the majority of cases – our consultants suggest 80% of the time – antibiotic ear drops such as CiproDex and ofloxacin are used off-label during and following the procedure.

sustained-exposure for approximately 1-2 weeks. Ciprofloxacin is commonly used for otic infections and is present in several FDA-approved antibiotic ear drop products, thereby inherently reducing the regulatory risk of this program.

If approved, AuriPro will be the first and only product labeled for the treatment of effusion with TTP surgery. Despite the lack of approved products, our consultants note that about 80% of patients are still treated with antibiotic ear drops after the procedure. Our consultants believe a single-use, physician-administered product has significant advantages over current treatment options in terms of convenience and compliance. For example, Ciprodex is administered twice daily for 7 days and ofloxacin is administered 3x daily for 10 days. Furthermore, approximately 75% of TTP procedures are done in patients that are 5 years of age or younger. Our consultants note that compliance in this patient population can be a major challenge as it can be difficult for caretakers to effectively administer drops over a course of 7-10 days in young children. They also highlighted that missed doses can often compromise treatment efficacy and increase the potential for bacterial resistance.

### Otitis Media (Ear Infection): A Common Affliction And Nuisance For Caregivers

Otitis media (OM) is most commonly known as an ear infection. OM, by far, occurs most frequently in young children and can result in significant ear pain (otalgia), pressure, and distortion of hearing. The National Institute on Deafness and Other Communication Disorders (NIDCD) reports that three out of every four children experience otitis media by the time they are three years old and a systemic literature review by Monasta L. et al. (Burden of Disease Caused by Otitis Media: Systematic Review and Global Estimates. PLoS ONE 7(4): e36226.) suggests that just over 17MM people get ear infections annually. Ear infections are typically treated with oral antibiotics – particularly when treated by primary care specialists – however, this approach can result in systemic side effects and increased risk of bacterial resistance. Patients with persistent effusion (leakage from the ear) or recurrent infections may be referred to an otolaryngologist, more commonly known as an ear, nose, and throat (ENT) specialist for tympanostomy tube placement (TTP) surgery. During a TTP procedure, a tympanostomy tube is inserted through the eardrum to ventilate and dry out the middle ear cavity. Approximately 1MM TTP procedures are performed every year. Our consultants state that it is the most common outpatient procedure performed in kids besides circumcision. In the majority of cases – our consultants suggest 80% of the time – antibiotic ear drops such as CiproDex and ofloxacin are used off-label during and following the procedure. These drops are approved for recurrent infections in patients with tympanostomy tubes, but not for the indication that AuriPro is being developed for. Our consultants estimate that only 10-15% of children who undergo the TTP procedure have recurrent ear infections. Unfortunately, current ear drop treatments involve regimens that require administration 2-3 times per day for 7-10 days. The parent or physician typically needs to hold the child down in order to place the ear drops and there is never assurance that it was properly administered or has reached the middle ear. These ear drop regimens are clearly inconvenient, especially in children under the age of 5 (75% of patients), and a nuisance for parents and caregivers.

### AuriPro Clinical Development Program Has Demonstrated Success Through Phase III

Otonomy originally presented to the FDA regarding the development of AuriPro during pre-IND discussions in November 2010. Subsequently they submitted an IND in August 2011 to begin clinical development. Following the Phase Ib clinical trial,



Following approval, Otonomy plans to develop AuriPro in additional indications such as acute otitis externa (swimmer's ear), chronic suppurative otitis media, and prophylaxis following middle ear surgeries – all of which our consultants agree make sense. An initial trial in one of these additional indications will begin during the first half of this year.

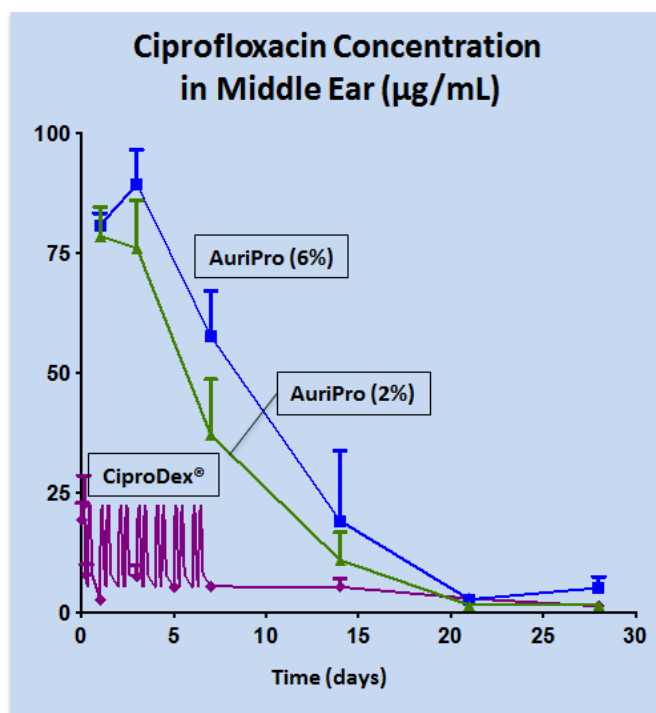
Otonomy met with the FDA in September 2013, which was designated as an End-of-Phase II meeting by the Agency, to review the findings from the Phase Ib study and to discuss the remaining requirements for submission of an NDA under the 505(b)(2) pathway. After completing the Phase III trials, Otonomy had pre-NDA discussions with the FDA regarding the filing and CMC matters. The company is expected to submit its NDA during Q1 of 2015 and does not anticipate that the FDA will require additional studies or that an advisory committee meeting will be convened for the approval of AuriPro. In December 2014, Otonomy commenced one year stability testing for AuriPro, which they believe is supportive of regulatory approval. Following approval, Otonomy plans to develop AuriPro in additional indications such as acute otitis externa (swimmer's ear), chronic suppurative otitis media, and prophylaxis following middle ear surgeries – all of which our consultants agree make sense. An initial trial in one of these additional indications will begin during the first half of this year. Otonomy has global commercial rights for AuriPro and issued patents through 2030 with potential extensions. Once launched in the U.S., the company plans to develop and commercialize AuriPro in Europe and partner the product for the remaining global market opportunities.

#### Preclinical Studies Show That AuriPro Provides Superior Exposure To Ciprofloxacin

Preclinical PK studies of AuriPro demonstrated that a single administration provides sustained-exposure of ciprofloxacin in the middle ear for 1-2 weeks. In contrast, repeat administration with Alcon's Ciprodex, a leading antibiotic ear drop, resulted in drug levels that fluctuated considerably – with significantly lower middle ear concentrations and shorter duration.

As seen in the figure below, preclinical PK studies of AuriPro demonstrated that a single administration provides sustained-exposure of ciprofloxacin in the middle ear for 1-2 weeks. In contrast, repeat administration with Alcon's Ciprodex, a leading antibiotic ear drop, resulted in drug levels that fluctuated considerably – with significantly lower middle ear concentrations and shorter duration. Thus, early preclinical PK data suggests that a single administration of AuriPro provides higher cumulative drug exposure in the middle ear than multiple daily doses over several treatment days of antibiotic ear drops.

Figure 8 Preclinical PK Studies Demonstrate Sustained Ciprofloxacin Release



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

Source: Otonomy

### AuriPro Phase Ib Study Demonstrated Early Proof Of Concept

Both the 4mg and 12mg AuriPro doses demonstrated a reduction in the incidence of treatment failures at Day 15 by greater than 60% ( $p < 0.05$ ).

The Phase Ib clinical trial for AuriPro had the same basic study design as the Phase III studies, which we describe later in this report. 83 patients in total were enrolled across 4 arms: (1) 21 received 4mg AuriPro; (2) 19 received 12mg AuriPro; (3) 21 in the sham group (no treatment); and (4) 22 in the placebo group (P407 gel vehicle). Treatment was administered in the operating room after making a small incision in the ear drum (myringotomy) and suctioning, and before the placement of the tube. All patients were under general anesthesia for the procedure, which is standard for TTP surgery, and received tubes in both ears. Follow-up visits took place on Days 4, 8, 15 and 29 after surgery. The primary endpoint was the cumulative proportion of treatment failures, which was defined as: (1) the presence of otorrhea (fluid draining through the tube as observed by a blinded assessor) between Days 4 through 15; or (2) use of rescue antibiotics from Days 1 through 15. Since the proportion of treatment failures was similar between the sham and placebo groups, these groups were combined into a single control group for the statistical analysis. Both the 4mg and 12mg AuriPro doses demonstrated a reduction in the incidence of treatment failures at Day 15 by greater than 60% ( $p < 0.05$ ).

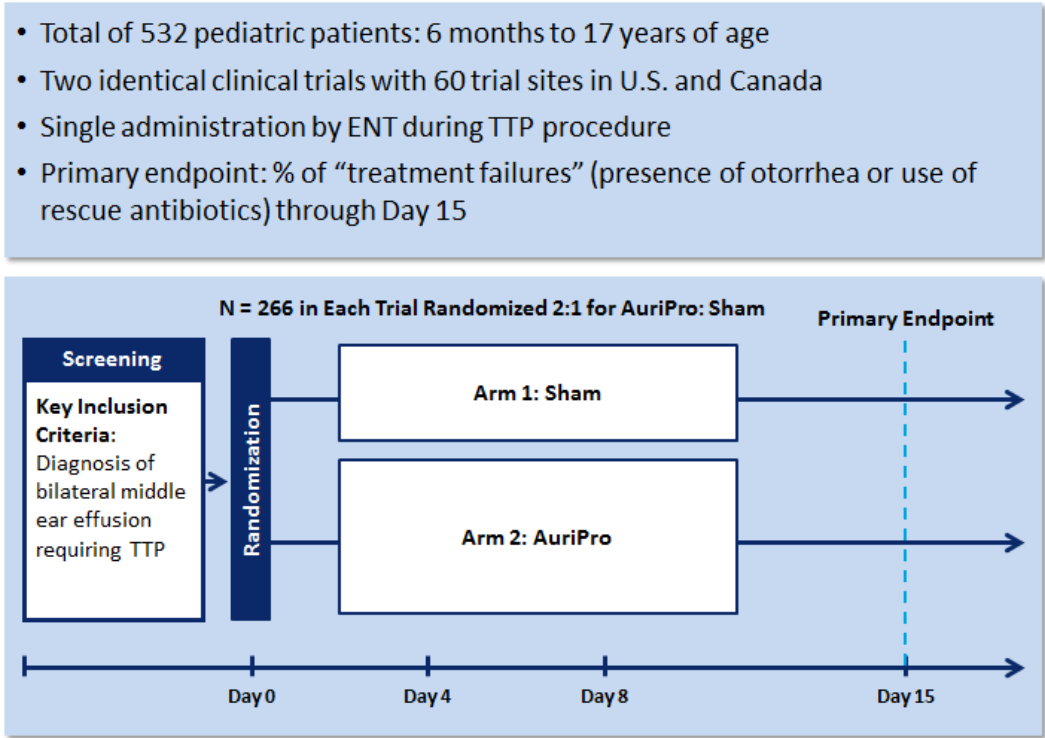
Patients enrolled in the Phase Ib study were between ages six months to 12 years and presented with effusion in both ears at the time of TTP surgery. There was no notable difference in the baseline demographics of the patients in each arm. All enrolled patients completed the clinical trial except one that did not return to the trial site for the final visit. AuriPro was well tolerated with no serious adverse events or

discontinuations due to adverse events. Most adverse events were mild or moderate in severity. Additionally, AuriPro did not have a negative impact on hearing, tympanometry or on general examination of the ear with otoscopy. Importantly, as we discuss in greater detail below, the AuriPro gel did not increase clogging of the tube.

**AuriPro Phase III Clinical Studies Successful And Provide The Basis Of The NDA Submission**

In April 2014, Otonomy completed two identical Phase III trials (Study 302 and Study 303) in 532 total pediatric patients across ~60 sites in the U.S. and Canada. In each trial, patients randomized 2:1 to either 6 mg AuriPro or sham (no treatment). The primary endpoint was the cumulative proportion of treatment failures (same as Phase 1b), which was defined as (1) the presence of otorrhea (fluid draining through the tube as observed by a blinded assessor) between Days 4 through 15; or (2) use of rescue antibiotics from Days 1 through 15. Treatment was administered in the operating room after myringotomy and suctioning, and before the placement of the tube. All patients were under general anesthesia for the procedure and received tubes in both ears. Follow-up visits took place on Days 4, 8, 15 and 29 after surgery. All enrolled patients completed the Day 15 visit (primary endpoint), except for a single patient in the sham group and the AuriPro group, who were both randomized but not treated. Patients enrolled in the Phase III studies were between ages 6 months to 17 years and presented with effusion in both ears at the time of TTP surgery. Analysis of the baseline patient demographics from both trials suggests good balance with no notable differences between the treatment groups.

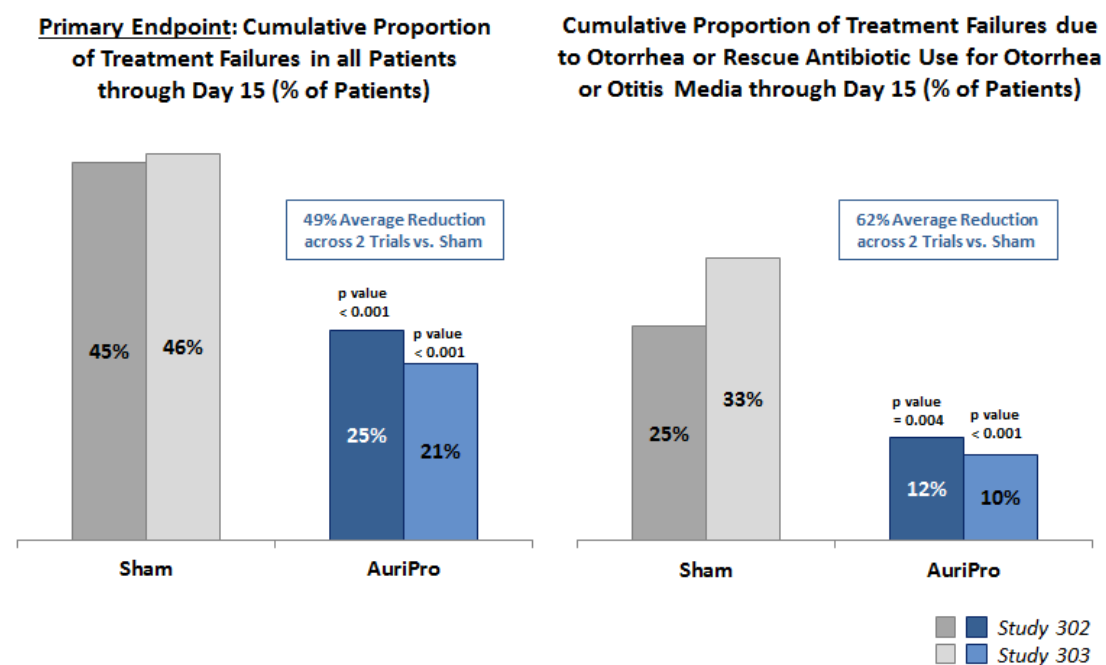
Figure 9 AuriPro Phase III Study Design



In July 2014, Otonomy announced that AuriPro achieved its primary efficacy endpoint along several secondary endpoints. As indicated in the figure below, AuriPro reduced the risk of treatment failure by an average of 49% ( $p < 0.001$ ) relative to sham for all patients randomized across both trials.

In July 2014, Otonomy announced that AuriPro achieved its primary efficacy endpoint along several secondary endpoints. As indicated in the figure below, AuriPro reduced the risk of treatment failure by an average of 49% ( $p < 0.001$ ) relative to sham for all patients randomized across both trials. Furthermore, a post-hoc analysis found that the cumulative proportion of patients in the Phase III trials considered to be treatment failures due to otorrhea or use of otic/systemic antibiotics with documented otorrhea or otitis media (through Day 15) was reduced by an average of 62% ( $p \leq 0.004$ ) across both trials.

Figure 10 AuriPro Phase III Data Was Highly Statistically Significant



Source: Otonomy

Importantly, our consultants initially expressed some concern that the AuriPro gel could cause some clogging of the ear tubes, but were reassured by the Phase III data, which showed no increase in the incidence of tube clogging relative to sham.

In terms of safety, there were no notable differences between patients treated with AuriPro or sham. AuriPro was well tolerated with no serious adverse events or discontinuations due to adverse events. Most adverse events were mild or moderate in severity. Additionally, AuriPro did not have a negative impact on hearing, tympanometry or on general examination of the ear with otoscopy. Importantly, our consultants initially expressed some concern that the AuriPro gel could cause some clogging of the ear tubes, but were reassured by the Phase III data, which showed no increase in the incidence of tube clogging relative to sham.

Figure 11 AuriPro Phase III Safety Was In-Line With Sham

**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)
<b>Total Patients with at least one TEAE Reported</b>	<b>95 (54%)</b>	<b>189 (53%)</b>
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: Otonomy

Overall, our consultants found the Phase III data to be impressive and highlighted that in terms of safety, efficacy, and convenience, AuriPro's product profile would provide a superior option relative to current antibiotic ear drops.

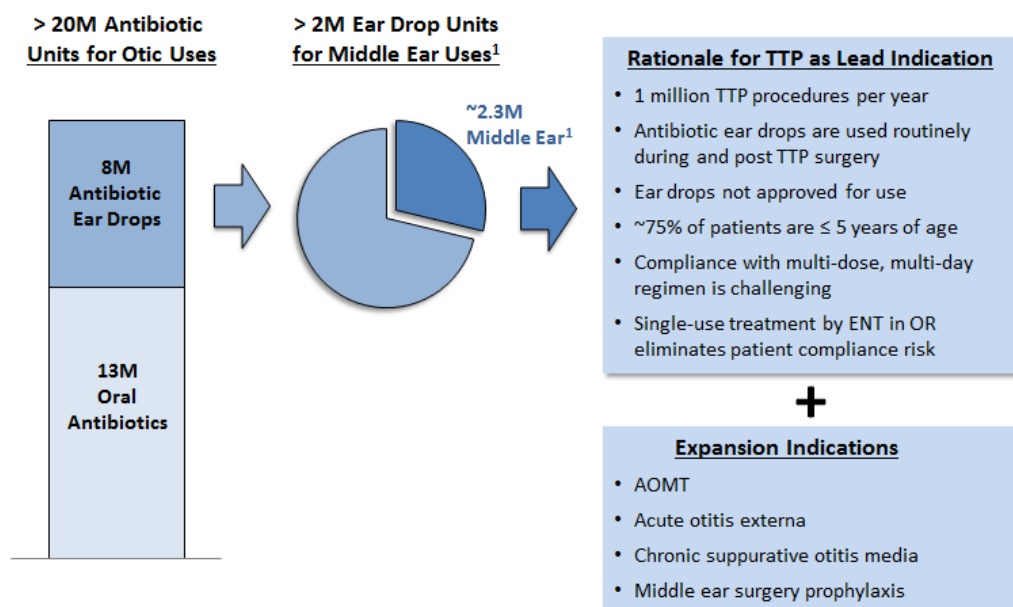
Overall, our consultants found the Phase III data to be impressive and highlighted that in terms of safety, efficacy, and convenience, AuriPro's product profile would provide a superior option relative to current antibiotic ear drops.

**AuriPro Is Expected To Expand The Branded Market**

There are roughly 1MM TTP surgeries performed each year in the U.S., and antibiotic ear drops are used in about 80% of all cases. Despite the routine use, there still remains significant unmet need as there is no antibiotic ear drop actually approved for this indication. Otonomy estimates that the U.S. annual volume of antibiotics to treat otic infections is approximately 21MM units, of which roughly 13MM are oral antibiotics and 8MM are antibiotic ear drops. FDA-approved indications for antibiotic ear drops include acute otitis externa and acute otitis media through tympanostomy tubes (AOMT). As noted above, antibiotic ear drops are also used off-label for TTP surgery and other middle ear conditions. Otonomy estimates that of the 8MM units of antibiotic ear drops prescribed in the U.S., approximately 2.3MM are for the treatment of the middle ear. As discussed previously, Otonomy plans to also assess AuriPro in potential additional indications including acute otitis externa, recurrent ear infections in patients with tympanostomy tubes, chronic suppurative otitis media (a perforated tympanic membrane with persistent drainage from the middle ear), and infection prophylaxis following middle ear surgeries. Of note, the U.S. market for recurrent ear infections for patients with ear tubes already in place is comparable to the market for new TTP procedures (~1MM annually for both). The company plans to initiate clinical trials in one or more of these indications during H1:2015.

Along with the already approved antibiotic ear drops (Ciprodex, ofloxacin), AuriPro will likely face competition from other products in development. Alcon recently received FDA approval for Xtoro (finafloxacin) for the treatment of acute otitis externa and may evaluate the product in additional indications. Otic Pharma also has a foam-based formulation of ciprofloxacin in clinical development for otic indications.

Figure 12 AuriPro (Ciprofloxacin) U.S. Commercial Opportunity



Source: Otonomy

As highlighted in the figure below, survey feedback suggests that more than 80% of respondents expect AuriPro to be better than antibiotic ear drops in terms of compliance/adherence; approximately 50% expect better drug exposure and tolerability; and 43% expect a lower incidence of post-operative otorrhea. Importantly, nearly 70% of surveyed physicians expressed strong interest in using AuriPro if it was available.

In 2014, Otonomy commissioned third-party market research to better understand the market potential of AuriPro. A survey of 100 otolaryngologists that regularly conduct TTP surgeries suggests that AuriPro would garner significant interest from physicians. As highlighted in the figure below, survey feedback suggests that more than 80% of respondents expect AuriPro to be better than antibiotic ear drops in terms of compliance/adherence; approximately 50% expect better drug exposure and tolerability; and 43% expect a lower incidence of post-operative otorrhea. Importantly, nearly 70% of surveyed physicians expressed strong interest in using AuriPro if it was available.

In terms of coverage, AuriPro will likely be reimbursed as a physician-administered drug. Otonomy's initial estimates are to price the drug in the range of \$200-250 per unit, which would be sufficient for treating both ears of a single patient. This price range is at a premium to current branded antibiotic ear drops, but can likely be justified given AuriPro's promising product profile. For reference, Alcon's Ciprodex, which is the leading branded antibiotic ear drop, has a current WAC price of \$167 for a full course of treatment. The company expects to conduct formal pricing research prior to finalizing any pricing for AuriPro.

Otonomy plans to make AuriPro available at hospital outpatient facilities and ambulatory surgery centers (ASC), where most TTP procedures are conducted. This

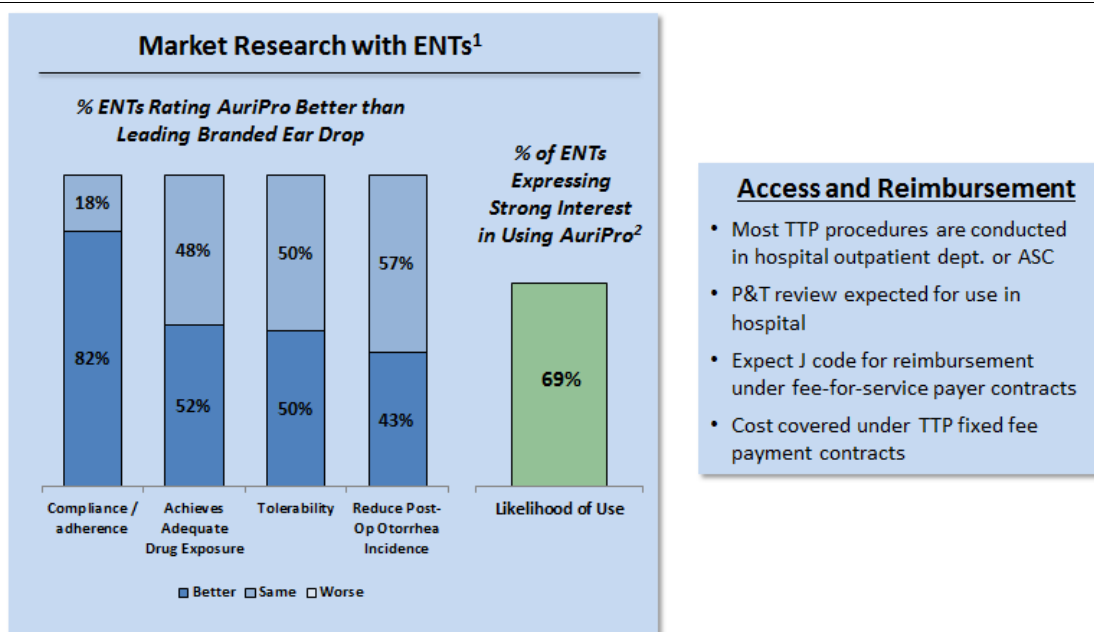


The reimbursement structure for AuriPro should help incentivize physicians to use the product in favor of antibiotic ear drops which do not provide any type of fee for administration.

will require approval from hospital pharmacy committees and ASC administrators, which generally entails an assessment of the product's profile, safety and efficacy, level of interest by physicians, and the cost impact on the facility.

As a physician-administered medication, AuriPro should be assigned a unique J-Code. As a result, facilities that contract with insurers on a fee for service basis should receive reimbursement on a cost plus basis. For facilities that are reimbursed a fixed amount for TTP surgery, the cost of the drug product should be covered depending on the specific contract terms. AuriPro already has a CPT code for the tube placement procedure. The reimbursement structure for AuriPro should help incentivize physicians to use the product in favor of antibiotic ear drops which do not provide any type of fee for administration.

Figure 13 AuriPro Market Research And Reimbursement



Source: Otonomy, <sup>1</sup>Third-party market research firm commissioned in 2014 with 100 ENTs surveyed; <sup>2</sup>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.

## OTO-104 (Sustained-Exposure Dexamethasone) For Ménière's Disease: Our Consultants Believe The Product Profile Is "Very Compelling"

Otonomy's OTO-104 uses the same platform technology as AuriPro as described previously in this report, but includes a different active ingredient. As opposed to having a gel releasing an antibiotic over a sustained period of time, OTO-104 releases a commonly used steroid, dexamethasone.

Otonomy's OTO-104 uses the same platform technology as AuriPro as described previously in this report, but includes a different active ingredient. As opposed to having a gel releasing an antibiotic over a sustained period of time, OTO-104 releases a commonly used steroid, dexamethasone. OTO-104 has been granted Fast Track Designation by the FDA and has completed a 44 patient Phase Ib trial with positive clinical results. OTO-104 is currently in a Phase IIb clinical trial, which has completed enrollment, and results are expected in Q2:2015. This trial will serve as one of two pivotal efficacy studies. The second pivotal study is expected to start in the second half of 2015 and we estimate final results should come by mid-year 2017 or potentially earlier. Therefore, OTO-104 could be launched in the U.S. by early 2018 and potentially sooner, assuming successful development. In the EU, a multiple-dose safety study is under way and we generally expect a potential European launch 1-2 years later as the

Our consultants agree that sensorineural hearing loss and tinnitus are obvious potential follow-on indications. Otonomy has global commercial right for OTO-104 and issued patents through 2029 with potential extensions. We expect Otonomy to develop and commercialize OTO-104 in the U.S. and Europe and pursue a partnering strategy for the rest of the world.

Despite this, our consultants note that they see positive responses with IT steroid injections in 2/3 of patients, but there is still certainly plenty of room for improvement as 10-20% of these patients will eventually still have to undergo invasive surgery as a last resort.

priority after launching in the U.S. market will be to expand in additional indications. This makes sense to us as some of the follow-on indications for OTO-104 may actually be more prominent in the various European markets. Therefore, Otonomy will be able to pick and choose specifically what indications they want to target in the various EU countries.

Currently, while IT steroid injections are used off-label for Ménière's as described below, there are no FDA-approved drugs indicated for the disease and other inner ear disorders, which result in a cumulative 8MM+ treated patients per year. Therefore, while the initial Ménière's indication is only about 5-10% of the total number of patients with inner ear disorders, potential viable expansion indications could be significant including sudden sensorineural hearing loss, other types of sensorineural hearing loss, other balance disorders, and tinnitus. Indeed, positive results on the tinnitus handicap endpoint, TH-25, were observed in Phase Ib. Additionally, in preclinical studies, OTO-104 has been shown to provide a protective effect when given before exposure to loud noise or ototoxic chemotherapeutic agents and administration of OTO-104 within two to three days following exposure to acoustic trauma promotes hearing recovery (sensorineural hearing loss). Our consultants agree that sensorineural hearing loss and tinnitus are obvious potential follow-on indications. Otonomy has global commercial right for OTO-104 and issued patents through 2029 with potential extensions. We expect Otonomy to develop and commercialize OTO-104 in the U.S. and Europe and pursue a partnering strategy for the rest of the world.

#### Ménière's Disease: Available Treatment Options Are Limited And Not Optimal

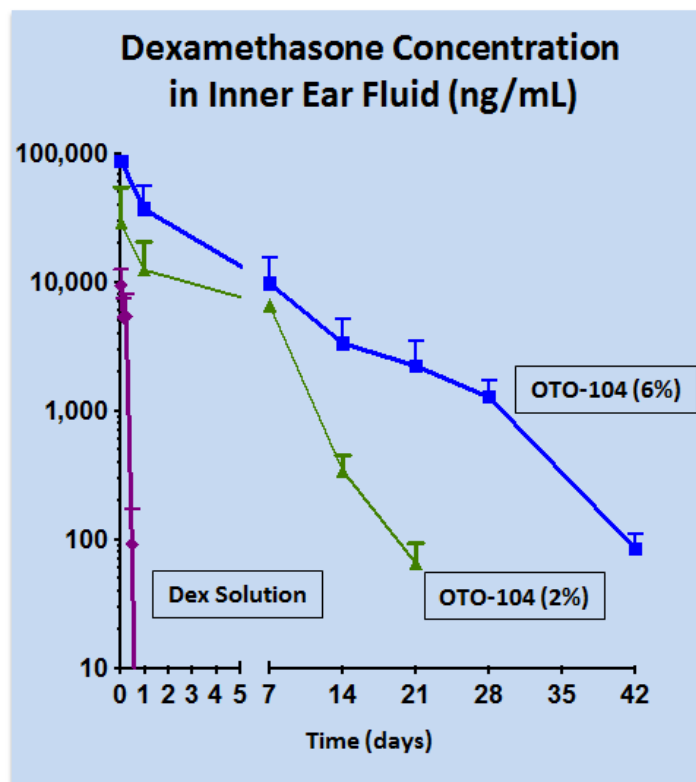
Ménière's is a disease of the inner ear that affects approximately 600,000 patients in the United States. It is a chronic condition and typically occurs in middle-aged (40-50 years of age) patients. Ménière's is thought to arise from abnormal fluid and ion homeostasis in the inner ear. The disease is chronic and typically results in symptoms of vertigo, tinnitus, and hearing loss – which can eventually become permanent – and can cause a high level of disability. The quality of life appears to be horrendous. For patients who have tried a low salt diet plus diuretics (i.e. Diamox) and/or oral steroids and symptoms are not well controlled, the next and only option for treatment is local drug delivery via a direct steroid injection through the ear drum. This is called an intratympanic (IT) injection and it allows for delivery of drugs to the middle ear cavity through the ear drum and eventually to the inner ear compartment via passage through to oval/round window membrane. This allows for high drug levels in the inner ear and low systemic drug exposure, which is especially important in the case of steroids. Our consultants suggest that about half of their treated Ménière's patients receive IT steroid injections. Clinical trials of IT steroid injections have shown promising results for treating Ménière's and sudden sensorineural hearing loss. However, a major issue with solution-based IT steroid injections is that they are eliminated rapidly down the Eustachian tube when the patient talks, swallows, or sits up. The short time that the solution remains in contact with the round/oval window membrane limits the amount of drug exposure that passes into the inner ear. This also reduces the duration that the drug is retained in the inner ear. Despite this, our consultants note that they see positive responses with IT steroid injections in 2/3 of patients, but there is still certainly plenty of room for improvement as 10-20% of these patients will eventually still have to undergo invasive surgery as a last resort. Often high dose oral steroids are added to account for the shortcomings of current IT steroid injections.

## OTO-104 Appears To Be A Meaningful Improvement Over Current IT Steroid Options

In stark contrast, preclinical studies of 6% OTO-104 resulted in an initial inner ear fluid concentration almost 10x higher with a much more gradual decline all the way through day 42 (note: it still does not reach 0 by day 42). Thus, Otonomy's OTO-104 aims to: (1) provide for an easier method of administration; (2) allow for a high level of drug exposure to the round/oval membrane; and (3) provide sustained-exposure, potentially limiting the overall number of injections for patients. Overall, our consultants strongly agree with the advantage of OTO-104's product profile relative to the current IT steroid injections and believe that the clinical profile is "very compelling."

Per the discussion above, Otonomy believes that the therapeutic effect of current off-label IT steroid solution injections is reduced and treatment variability across the general patient population is increased. As such, ENTs will often require patients to remain immobilized for an extended period of time following each IT injection and subsequently return for additional injections. Our consultants suggest that many patients may need up to 10 injections – perhaps every 1-3 months – over several years and potentially a lifetime. Still, drug levels decrease rapidly following each administration and decline away from the round/oval membrane. Preclinical PK studies have shown that current solutions of dexamethasone for IT injection drop rapidly from a 10,000 ng/mL concentration in the inner ear fluid to 0 in less than a day. In stark contrast, preclinical studies of 6% OTO-104 resulted in an initial inner ear fluid concentration almost 10x higher with a much more gradual decline all the way through day 42 (note: it still does not reach 0 by day 42). Thus, Otonomy's OTO-104 aims to: (1) provide for an easier method of administration; (2) allow for a high level of drug exposure to the round/oval membrane; and (3) provide sustained-exposure, potentially limiting the overall number of injections for patients. Overall, our consultants strongly agree with the advantage of OTO-104's product profile relative to the current IT steroid injections and believe that the clinical profile is "very compelling." Our physician consultants also believe the follow-on indications mentioned above are very logical opportunities.

Figure 14 Preclinical PK Studies Demonstrate Sustained Dexamethasone Release



Preclinical PK study in guinea pigs following single IT administration

Source: Otonomy

The goal of OTO-104, as already discussed, is simply to provide higher and sustained concentration of dexamethasone relative to existing injections, which we believe will not adversely affect future clinical trial results. We believe this – in conjunction with the impressive early clinical data – substantially de-risks the program.

Interestingly, 50% of patients in this study had no vertigo in the third month. Furthermore, 81% of patients in the 1mg OTO-104 arm had at least a 50% improvement in vertigo frequency in month 3 versus baseline.

## OTO-104 Early Clinical Trial Results Demonstrate Strong Proof Of Concept

In general, we view the development of OTO-104 in Ménière's as very low risk given that IT steroid injections are already used quite frequently in practice and appear to be moderately effective. The goal of OTO-104, as already discussed, is simply to provide higher and sustained concentration of dexamethasone relative to existing injections, which we believe will not adversely affect future clinical trial results. We believe this – in conjunction with the impressive early clinical data – substantially de-risks the program. OTO-104 has completed a 44 patient Phase Ib trial with positive clinical results. The product is currently in a Phase IIb clinical trial, which has completed enrollment, and results are expected in Q2:2015. This trial will serve as one of two pivotal efficacy studies. The second pivotal study is expected to start in the second half of 2015 and we estimate final results should come by mid-year 2017 or potentially earlier. Therefore, OTO-104 could be launched in the U.S. by early 2018 and potentially sooner, assuming successful development. It is important to note that OTO-104 has been granted Fast Track Designation, so there is potential to receive an expedited 6-month regulatory review.

In the EU, a multiple-dose safety study was initiated in the UK in October 2014 and is under way and we generally expect a potential European launch at least 1-2 years later as the priority after launching in the U.S. market will be to expand in additional indications.

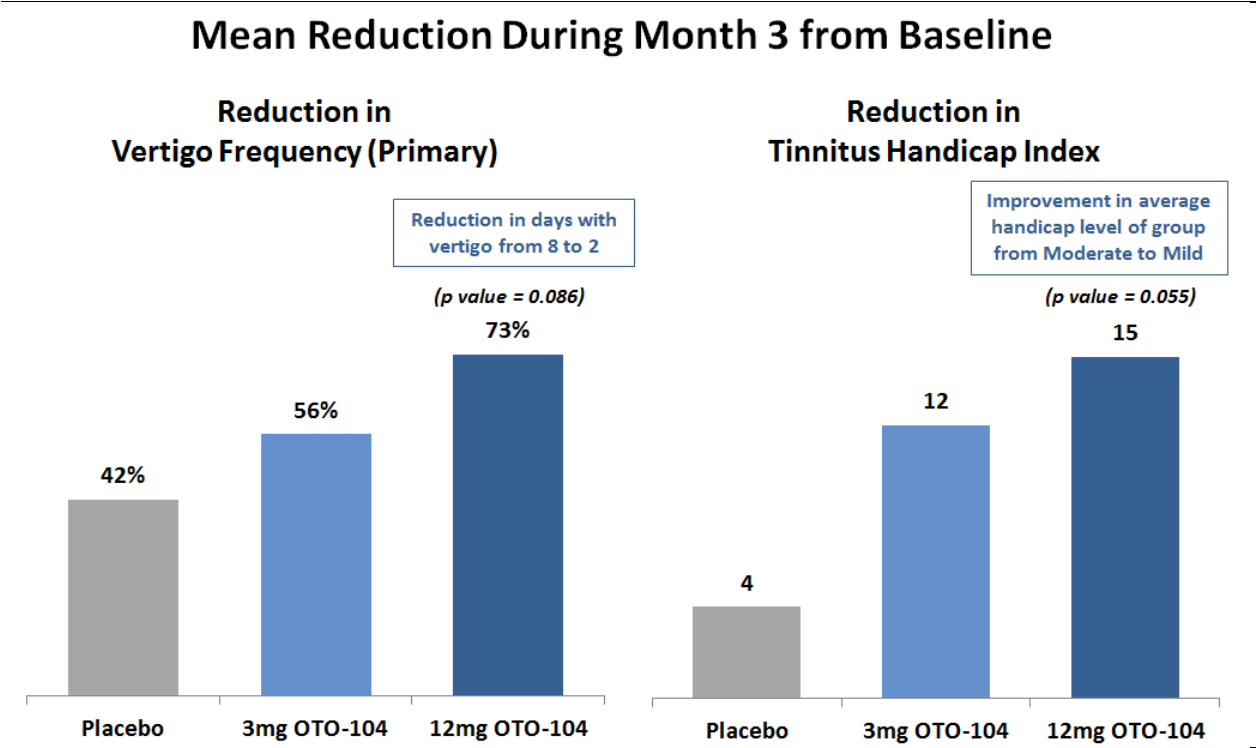
## Phase Ib Trial Results Demonstrate A Significant Reduction In Vertigo Frequency

In a Phase Ib clinical trial, OTO-104 demonstrated a significant mean reduction in vertigo frequency (primary endpoint) during month 3 relative to baseline. There was a clear dose response as a 56% and 73% (p-value=0.086) reduction in vertigo frequency in month 3 was observed with the 3mg and 12mg OTO-104 dosing cohorts, respectively. The 73% reduction in the 12mg group was equivalent to a reduction in days with vertigo from 8 at baseline to 2 in month 3. A day with vertigo is defined as an episode lasting at least 20 minutes and being completely debilitating. Interestingly, 50% of patients in this study had no vertigo in the third month. Furthermore, 81% of patients in the 1mg OTO-104 arm had at least a 50% improvement in vertigo frequency in month 3 versus baseline. Clearly, the 12mg OTO-104 group was not statistically significant, but we would note that it is due to the study arm only having 16 patients and the fact that it was even close (0.036 off) is impressive. In general, a single injection of OTO-104 was well tolerated and there were no serious adverse events observed during the trial. Moreover, there were no instances of persistent conductive hearing loss associated with OTO-104 injection. A single 12mg patient reported vertigo during the procedure, and a single placebo patient reported serious otitis media. The only adverse event reported in more than one patient was injection site perforation of the tympanic membrane, which were predominantly described as pinhole perforations observed following injections – most of these resolved spontaneously and all but one resolved by the end of the clinical trial. Importantly, safety events were consistent with those reported in published clinical trials with the use of IT steroid injections. We believe these results bode very well for the outcome of the first pivotal trial to readout next quarter, which has a very similar design.

Additionally, meaningful, dose-dependent reductions in the tinnitus handicap index (TH-25) were observed in the trial. At the 12mg dose, the improvement in the average handicap level of the group resulted in an increase to mild status at month 3 (-15 points on TH-25 with 12mg OTO-104) from moderate status (52-58 on TH-25) at baseline. The tinnitus handicap inventory index, or TH-25, will be assessed as an

exploratory endpoint in the Phase IIb study. This initial data also provides proof of concept for the potential future tinnitus follow-on indication.

Figure 15 OTO-104 Phase Ib Study Showed Meaningful Improvements In Vertigo And Tinnitus

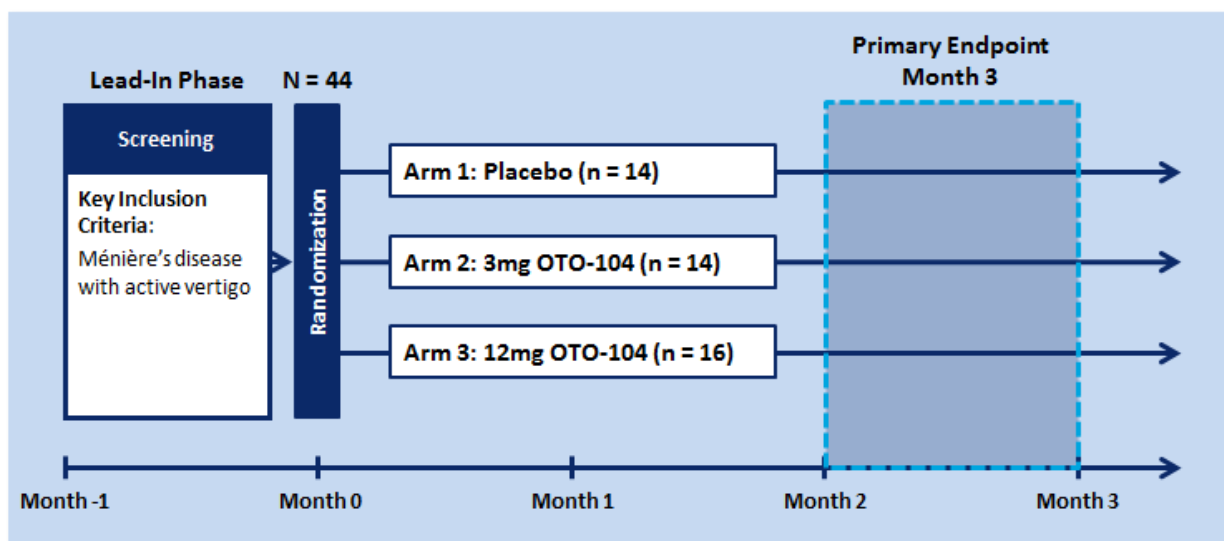


Source: Otonomy; Lambert et.al., Otol Neurotol, 2012

As for the design of the Phase Ib study that aimed to assess the safety and tolerability of OTO-104, the primary endpoint was the reduction in vertigo frequency as recorded via daily diaries during month 3 versus baseline. The trial began with a month-long lead-in/screening phase with the key inclusion criteria being that patients must have Meniere’s with active vertigo. Once the patients were screened, they were randomized at baseline to three arms: (1) P407 gel vehicle placebo, n=14; (2) 3mg OTO-104, n=14; (3) 12mg OTO-104, n=16. Finally, over the third month of the study from randomization, the primary endpoint, or reduction in vertigo frequency was measured.

Figure 16 OTO-104 Phase Ib Study Design

- Ménière's disease patients experiencing recurrent vertigo episodes
- Single IT injection by ENT in office setting
- Designed to assess safety and tolerability
- Primary endpoint: reduction in vertigo frequency (recorded via daily diaries) during Month 3 vs. baseline



Source: Otonomy

### Ongoing Phase IIb Pivotal Clinical Trial Likely To Produce Positive Results

The primary endpoint is the reduction in vertigo frequency at 3 months versus baseline – the same endpoint studied in Phase Ib. Worth noting, the trial size was determined to provide 90% power to achieve statistical significance ( $p < 0.05$ ) for a 30% treatment effect, which was the level observed in Phase 1b per above. Overall, the design is almost identical to the Phase Ib study that produced positive results. The only difference is that it is much larger (154 vs. 44 patients) thereby having sufficient power to produce statistically significant results and patients are randomized to two arms instead of three.

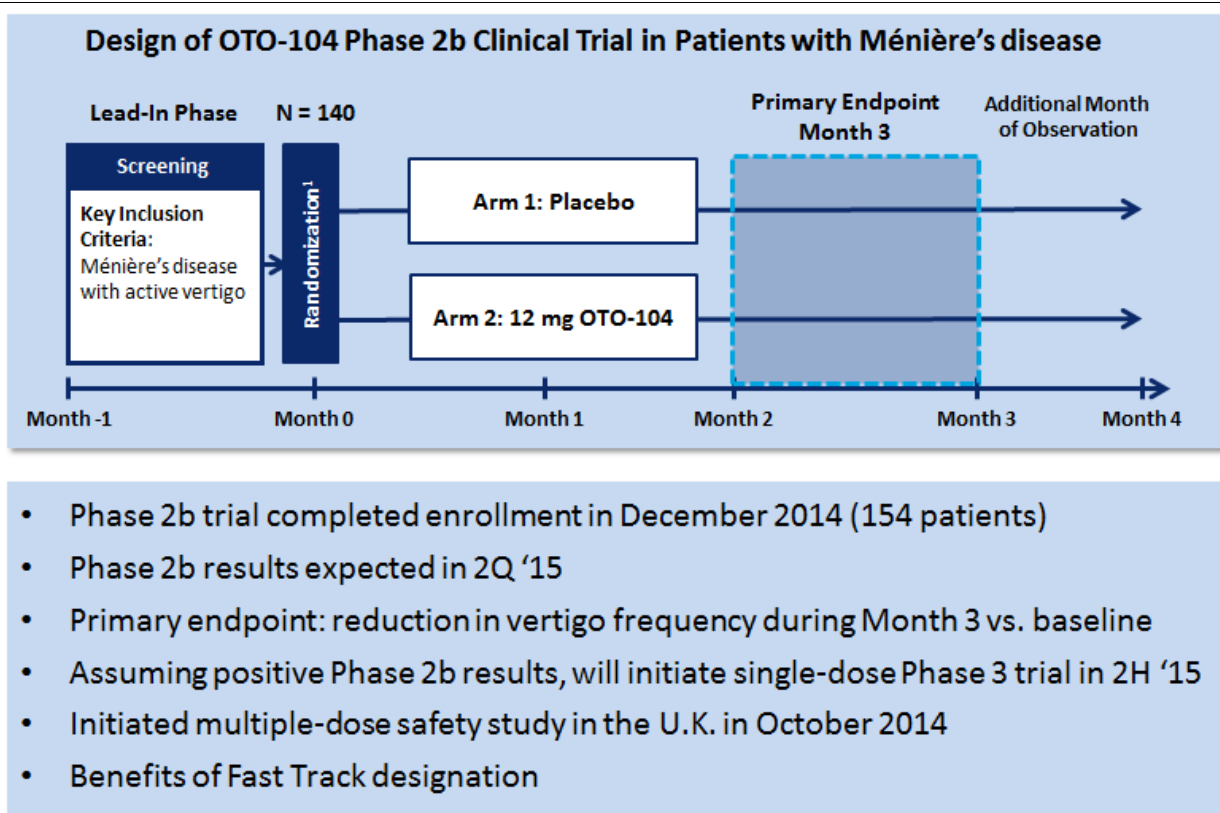
The ongoing Phase IIb pivotal (first of two) clinical trial completed enrollment of 154 patients last December and results are expected in the second quarter of this year. The study has enrolled patients at more than 50 centers in the U.S. and Canada. The primary endpoint is the reduction in vertigo frequency at 3 months versus baseline – the same endpoint studied in Phase Ib. Worth noting, the trial size was determined to provide 90% power to achieve statistical significance ( $p < 0.05$ ) for a 30% treatment effect, which was the level observed in Phase 1b per above. Overall, the design is almost identical to the Phase Ib study that produced positive results. The only difference is that it is much larger (154 vs. 44 patients) thereby having sufficient power to produce statistically significant results and patients are randomized to two arms instead of three. Patients were randomized to either P407 gel vehicle placebo or 12mg OTO-104. Assuming positive results, which we believe will occur based upon the Phase Ib data and our knowledge of IT steroid injections currently used off-label in practice, the company will initiate the second pivotal, single-dose, Phase III trial for Ménière's in the second half of this year. These two single dose efficacy studies should be sufficient for approval, but the FDA also wants to see retreatment safety data, which the company plans to collect in the ongoing multiple dose safety study. This, in addition to the multiple dose UK study described below, should satisfy the U.S. FDA safety requirements.



Worth adding, while only initial conversations with the European regulatory authorities have been conducted (safety discussions with MHRA, but not efficacy), it is possible that these two pivotal U.S. registration studies could be sufficient for EU approval as it appears the EMA will approve a new drug for Ménière's based upon a single dose efficacy study with a single drug administration and 3 month follow-up. The ongoing UK-based study of 125 patients should satisfy the one-year safety requirements by the EMA. This study will administer 12mg OTO-104 or placebo at three month intervals.

In terms of potential competition, Synphora AB is conducting a Phase II/III clinical trial with a formulation of latanoprost administered via single or repeat IT injections, and Auris Medical intends to evaluate AM-111 in an open-label study of Ménière's patients.

Figure 17 OTO-104 Phase IIb Study Is Fully Enrolled And Data Expected In Q2:2015



Source: Otonomy

### Marketing OTO-104 For Ménière's Overlaps With The AuriPro And Potential Future OTO-311 Commercial Efforts

Upon approval, which we believe could occur in early 2018 (and potentially earlier given the Fast Track Designation), OTO-104 will be launched and marketed to ~4,000 ENTs targeted by the company that account for approximately 80% of the treatment volume. These ENTs are primarily based in a physician's office versus a hospital outpatient and ambulatory surgery center that houses the physicians targeted for AuriPro. Interestingly, the earlier product candidate, OTO-311 (described in greater detail below), would be marketed to the same physicians and there is also some level of overlap with AuriPro. Hence, we expect some sales/revenue synergies to occur

Our consultants described the procedure as “not hard” and “super, super easy.” Moreover, the company is expecting to receive a J-code (\$100 reimbursement like wet AMD) and CPT code for OTO-104, which would clearly give doctors a financial incentive to administer the product over the currently-used off-label steroids. We expect AuriPro to be priced at least around \$1,000 per injection and potentially more – which is similar to the pricing strategy for wet AMD drugs. Our consultants suggest that the average patient may receive 3 injections per year putting the total annual average treatment cost at \$3,000.

For AuriPro, Otonomy estimates that less than 2,500 otolaryngologists perform 80% of all TTP surgeries. For OTO-104 and OTO-311, roughly 4,000 ENTs account for approximately 80% of the prescription volume, of which a subset will also be targets for AuriPro. This suggests that a small, targeted sales force could be highly effective for promoting Otonomy's product portfolio. Approximately 40 sales reps are expected to be hired for the launch of AuriPro and an additional 40 for the launch of OTO-104. Otonomy estimates that an even smaller sales force will be needed for the EU launches.

between AuriPro and OTO-104 as the sales force will already be launched and promoting AuriPro to some doctors that would prescribe OTO-104 upon approval and subsequent launch. In early market research conducted by a third party for Otonomy, 57% of ENTs surveyed expressed strong interest and a high likelihood of using OTO-104.

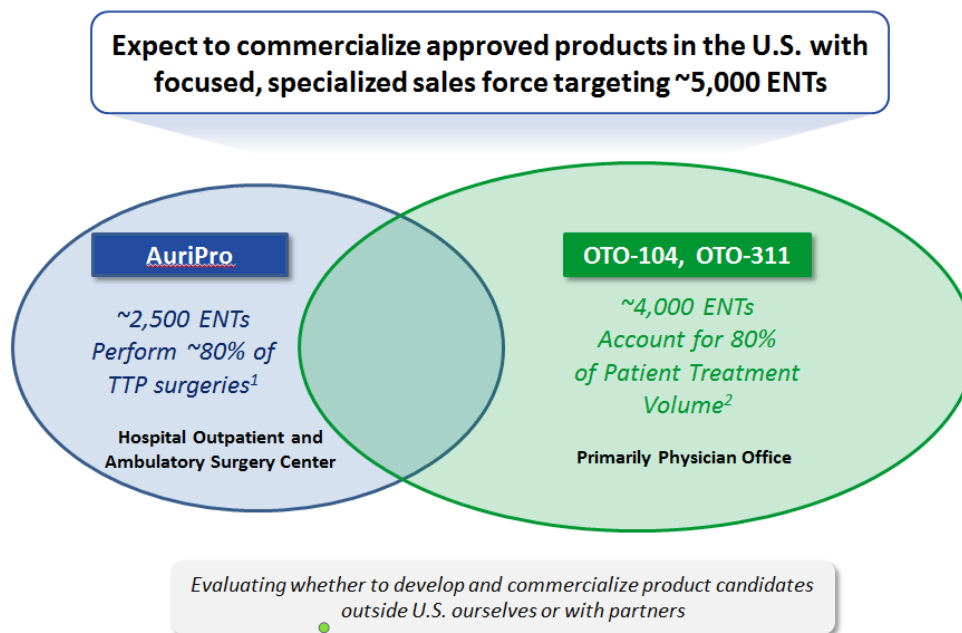
In terms of actually administering the drug, it appears that most otolaryngologists that have completed their medical training in the last one or two decades are very familiar using IT steroid injections. Thus, we are unconcerned about onerous training required upon launch, which could potentially limit the product's uptake. In-line with these thoughts, our consultants described the procedure as “not hard” and “super, super easy.” Moreover, the company is expecting to receive a J-code (\$100 reimbursement like wet AMD) and CPT code for OTO-104, which would clearly give doctors a financial incentive to administer the product over the currently-used off-label steroids. We expect AuriPro to be priced at least around \$1,000 per injection and potentially more – which is similar to the pricing strategy for wet AMD drugs. Our consultants suggest that the average patient may receive 3 injections per year putting the total annual average treatment cost at \$3,000. We think this is a reasonable approach as the unmet need for an approved treatment for Ménière's is significant and OTO-104 appears to have a very differentiated profile relative to current off-label IT steroid injections – both in terms of efficacy and reduced number of injections. Finally, the company believes that there is further opportunity for expanding the market through education, increased awareness, and of course providing the first FDA approved treatment for Ménière's.

## We Expect Otonomy's Commercial Strategy To Deliver Significant Revenue Synergies

Otonomy has the worldwide commercial rights to all of its products in development. Assuming approval of their development products, Otonomy plans to commercialize AuriPro, OTO-104, and OTO-311 in the U.S. using a targeted specialty sales force. In total, the company estimates that approximately 5,000 otolaryngologists perform the majority of TTP surgeries and manage patients with Ménière's disease, hearing loss, and tinnitus. For AuriPro, Otonomy estimates that less than 2,500 otolaryngologists perform 80% of all TTP surgeries. For OTO-104 and OTO-311, roughly 4,000 ENTs account for approximately 80% of the prescription volume, of which a subset will also be targets for AuriPro. This suggests that a small, targeted sales force could be highly effective for promoting Otonomy's product portfolio. Approximately 40 sales reps are expected to be hired for the launch of AuriPro and an additional 40 for the launch of OTO-104. Otonomy estimates that an even smaller sales force will be needed for the EU launches.

Similar to the U.S., there is significant unmet need for the treatment of otic conditions in the ex-U.S. markets. Otonomy will likely commercialize a few key countries in the EU and partner for the remaining territories. Timing of the MAA filings will likely take place roughly 1-2 years after the initial U.S. NDA filings. As noted in the section below, Otonomy has aggressively pursued patent protection both in and outside the U.S. to facilitate its worldwide commercial efforts.

Figure 18 Schematic Of Otonomy's Commercial Strategy



Source: Otonomy

## OTO-311 (Gacyclidine) For Tinnitus

Preclinical studies of gacyclidine have demonstrated biological activity for tinnitus along with a broad neuroprotective therapeutic window. Additionally, recent pilot clinical trials of gacyclidine delivered using a micro-pump and indwelling catheter have shown evidence of modulating aspects of tinnitus for symptomatic patients.

Otonomy's NMDA antagonist in development is OTO-311, a sustained-exposure formulation of gacyclidine that could – similar to AuriPro – potentially provide a full course of treatment from a single IT injection. Gacyclidine is a potent and selective NMDA antagonist, and receptor binding studies have demonstrated selectivity for the receptor subtype believed to be relevant for tinnitus. Binding studies also indicate that gacyclidine's dissociation kinetics are slower than other NMDA antagonists and may be effective in a sustained-exposure formulation. Preclinical studies of gacyclidine have demonstrated biological activity for tinnitus along with a broad neuroprotective therapeutic window. Additionally, recent pilot clinical trials of gacyclidine delivered using a micro-pump and indwelling catheter have shown evidence of modulating aspects of tinnitus for symptomatic patients.

In November 2014, Otonomy announced the completion of an exclusive license agreement with Ipsen that enables use of clinical and non-clinical gacyclidine data to support worldwide development and regulatory filings for OTO-311. Otonomy plans to file an IND for OTO-311 and initiate a Phase I clinical trial sometime in 2015. While gacyclidine has never been approved or commercialized, gacyclidine has been evaluated in clinical trials by Ipsen for the treatment of traumatic brain and spinal cord injury in the late 1990's. These studies evaluated gacyclidine in more than 300 patients, which has helped establish a maximum tolerated dose with systemic exposure. While OTO-311 is being developed as an IT injection and systemic exposure should be limited, these previous studies nonetheless provide guidance on potential dose selection.

## Tinnitus Disease Background

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Tinnitus is the clinical term for hearing noise when there is no outside source of the sound. It is often described as a ringing in the ear but can also sound like buzzing, clicking, or hissing. The most common cause of tinnitus is exposure to loud noise, but it is a multifactorial condition, and a number of other factors can be involved including cardiac health, hormonal changes, infections, thyroid dysfunction, and certain medications.

Tinnitus is a large, addressable market opportunity with the American Tinnitus Association reporting that approximately 16MM patients in the U.S. have tinnitus symptoms severe enough to seek medical assessment, and roughly 2MM patients with symptoms severe enough that they cannot function on a normal day-to-day basis. The United States Department of Defense reports that tinnitus accounts for the most prevalent service-connected disability among veterans and that the costs of service-related tinnitus exceed \$2B annually. Furthermore, there is significant unmet need as there are currently no approved drugs for the treatment of this debilitating condition.

## Strong Rationale Exists For Employing NMDA Antagonists For The Treatment Of Tinnitus

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For example, in a Phase II study, Auris Medical reported improvement in tinnitus loudness and severity in a subset of patients with repeat IT injections of AM-101, a formulation of the NMDA antagonist esketamine. Furthermore, in a Phase II study, Merz Pharmaceuticals reported an improvement in the tinnitus handicap index with the oral NMDA antagonist neramexane.

Historic and new clinical data support the use of NMDA receptor antagonists for the treatment of tinnitus. Mechanistically, NMDA antagonists may reduce dysfunctional activity resulting from injury to the cochlea. For example, in a Phase II study, Auris Medical reported improvement in tinnitus loudness and severity in a subset of patients with repeat IT injections of AM-101, a formulation of the NMDA antagonist esketamine. Furthermore, in a Phase II study, Merz Pharmaceuticals reported an improvement in the tinnitus handicap index with the oral NMDA antagonist neramexane.

Regarding competition for OTO-311, there are no drugs currently approved for tinnitus as mentioned above, but there are a few other products in development. Auris Medical is developing AM-101 (esketamine) mentioned above, and is currently in Phase III trials evaluating repeat IT injections in patients with acute and post-acute inner ear tinnitus. Autifony Therapeutics is developing AUT00063, an oral product candidate for tinnitus, which is being evaluated in a Phase II study in the UK. Merz Pharmaceuticals has suspended development of neramexane, an oral treatment for chronic tinnitus, but its partner in Japan, Kyorin Pharmaceuticals, is continuing with a Phase II trial. Finally, Novartis is developing BGG492, which is currently in Phase II of clinical development for chronic tinnitus.

## Otonomy's Intellectual Property Estate Provides Substantial Duration

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Otonomy's patent estate includes patents and applications related to AuriPro, OTO-104 and OTO-311. On a worldwide basis, this includes approximately 60 issued patents and allowed patent applications, and at least 85 pending patent applications. The patent estate also provides patents and applications with claims for a broad range of additional active agents as potential future product candidates.

**For AuriPro**, Otonomy co-owns a patent family with the University of California that is related to the composition and therapeutic use of AuriPro. Through an exclusive

Through an exclusive license agreement, Otonomy has acquired the University of California's rights, which includes one issued AuriPro U.S. patent, which extends until April 2030

license agreement, Otonomy has acquired the University of California's rights, which includes one issued U.S. patent, which extends until April 2030, and two pending U.S. applications. This patent family also includes issued patents or allowed applications in Australia, Canada, Israel, Korea, Philippines, Russia, South Africa and Taiwan; and pending applications in Argentina, Brazil, China, Europe, India, Japan, Jordan, Mexico, Pakistan, Singapore, Thailand, Uruguay and Venezuela. Additionally, Otonomy owns a patent family directed to certain therapeutic uses of AuriPro and has filed a U.S. application related to the manufacturing methods for the product.

**This OTO-104 patent family includes five issued U.S. patents and one pending application, with expiry dates that range from May 2029 to September 2029**

**Regarding OTO-104,** Otonomy has acquired exclusive rights from the University of California to a patent family related to the composition and therapeutic use of the product. This family includes five issued U.S. patents and one pending application, with expiry dates that range from May 2029 to September 2029. This OTO-104 patent family also includes issued patents or allowed applications in Australia, Canada, China, Hong Kong, Japan, Korea, Mexico, Peru, Russia, Singapore, South Africa, Taiwan and the UK; and pending applications in Argentina, Brazil, Chile, Europe, India, Indonesia, Israel, Jordan, Malaysia, Pakistan, Philippines, Thailand, Uruguay, Venezuela and Vietnam. Otonomy also owns an issued U.S. patent related to the manufacturing of OTO-104, which will expire in April 2030. Finally, the company solely owns a patent family directed to additional therapeutic uses of the product.

**The OTO-311 families include one issued U.S. patents, which expires in April 2031, and one pending application.**

**Regarding OTO-311,** Otonomy has acquired exclusive rights from the University of California to two patent families related to the composition and therapeutic use of the product. The families include one issued U.S. patents, which expires in April 2031, and one pending application. These families also include issued patents or allowed applications in Australia, Canada, China, Korea, Mexico, Russia, South Africa, Taiwan and UK; and pending applications in Argentina, Brazil, Chile, Europe, India, Israel, Japan, Jordan, Pakistan, Thailand, Uruguay and Venezuela. Finally, Otonomy has licensed a patent family from Durect related to the therapeutic use of OTO-311. This family includes one issued U.S. patent, which expires in June 2024, and one issued Japanese patent.

For future product candidates, Otonomy co-owns and has exclusive rights to eight other patent families from the University of California directed to a broad range of other active agents. Furthermore, to strengthen protection against potential design-around, the company solely owns a patent family directed to alternative formulations. Finally, Otonomy has also acquired from IncuMed patent families directed to formulations or devices that deliver active agents into the ear for treatment of otic diseases.

Figure 19 U.S. And EU Ear Market Build For AuriPro And OTO-104

ESTIMATED UNITED STATES AND EUROPE EAR MARKET BUILD													
UNITED STATES	2014	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	5Y CGR Comments
People affected by disorders of the ear (MM)	50.0	50.5	51.0	51.5	52.0	52.6	53.1	53.6	54.1	54.7	55.2	55.8	- Roughly 1/6 people
% of people currently seeking treatment	40.0%	40.0%	40.0%	40.5%	41.0%	41.5%	42.0%	42.5%	43.0%	43.5%	44.0%	44.5%	- To grow with more products/awareness
# of patients being treated (MM)	20.0	20.2	20.4	20.9	21.3	21.8	22.3	22.8	23.3	23.8	24.3	24.8	+2%
<b>Outer Ear - Acute Otitis Externa</b>													
% of patients affected by acute otitis externa	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	- "Swimmer's Ear;" Most of CiproDex sales
# of patients affected by acute otitis externa (MM)	2.5	2.5	2.6	2.6	2.7	2.7	2.8	2.8	2.9	3.0	3.0	3.1	+2% - Potential AuriPro follow-on indication
<b>Middle Ear - Acute Otitis Media Following TTP</b>													
% of patients treated for acute otitis media	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	- "Ear infections"
# of patients treated for acute otitis media (MM)	7.0	7.1	7.1	7.3	7.5	7.6	7.8	8.0	8.1	8.3	8.5	8.7	- ~5.5% per hundred people; ~17MM total pts
# of antibiotic ear drop units administered (MM)	2.3	2.4	2.4	2.5	2.6	2.7	2.7	2.8	2.9	3.0	3.1	3.2	+3% - To increase with promotion of new agents
% of drop units administered due to TTP surgery	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	- Est. 80% of pts get ear drops for 5-7 days
# of drop units administered due to TTP surgery (MM)	1.0	1.0	1.0	1.1	1.1	1.1	1.2	1.2	1.2	1.3	1.3	1.4	
% of drop units administered due to recurrence	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	
# of drop units administered due to recurrence (MM)	0.9	0.9	1.0	1.0	1.0	1.1	1.1	1.1	1.2	1.2	1.2	1.3	
% of drop units admin. due to severe swimmer's ear	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	
# of drop units admin. due to severe swimmer's ear (MM)	0.4	0.4	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.6	
<b>CiproDex</b>													
% penetration of antibiotic ear drops for middle ear	43.5%	43.5%	41.0%	39.0%	35.0%	31.0%	27.0%	25.0%	23.0%	22.0%	21.0%	20.0%	- Made by Alcon; BID dosing for 7 days
# of patients ('000)	1,000.5	1,030.5	1,000.4	980.2	906.0	826.6	741.5	707.2	670.1	660.2	649.1	636.7	- 50% coverage in private practice
Net price per course	\$120.0	\$125.0	\$137.5	\$151.3	\$166.4	\$183.0	\$201.3	\$221.4	\$243.6	\$267.9	\$294.7	\$324.2	- WAC of \$167.15 per Jan 8, 2015
Net sales (MM)	\$120.0	\$130.0	\$140.0	\$150.0	\$150.0	\$150.0	\$150.0	\$155.0	\$165.0	\$175.0	\$190.0	\$205.0	+3% - Est. ~30% of sales are from middle ear
% Growth		+8%	+8%	+7%	+0%	+0%	+0%	+3%	+6%	+6%	+9%	+8%	
<b>Ofloxacin, Tobradex, And Others</b>													
% penetration of antibiotic ear drops for middle ear	56.5%	56.5%	56.5%	56.0%	55.0%	54.0%	53.0%	52.0%	51.0%	50.0%	49.0%	48.0%	- Made by Alcon; BID dosing for 7 days
# of patients ('000)	1,299.5	1,338.5	1,378.6	1,407.4	1,423.8	1,439.8	1,455.5	1,470.9	1,485.9	1,500.5	1,514.6	1,528.2	
Net price per course	\$20.0	\$22.0	\$24.2	\$26.6	\$29.3	\$32.2	\$35.4	\$39.0	\$42.9	\$47.2	\$51.9	\$57.1	- WAC of \$167.15 per Jan 8, 2015
Net sales (MM)	\$25.0	\$30.0	\$35.0	\$35.0	\$40.0	\$45.0	\$50.0	\$55.0	\$65.0	\$70.0	\$80.0	\$85.0	+11% - Est. ~30% of sales are from middle ear
% Growth		+20%	+17%	+0%	+14%	+13%	+11%	+10%	+18%	+14%	+14%	+6%	
<b>AuriPro</b>													
% penetration of antibiotic ear drops for middle ear			2.5%	5.0%	10.0%	15.0%	20.0%	23.0%	26.0%	28.0%	30.0%	32.0%	- Single administration
# of AuriPro patients ('000)			61.0	125.7	258.9	399.9	549.3	650.6	757.5	840.3	927.3	1,018.8	- Penetration including additional indications
Net price per administration			\$200.0	\$220.0	\$242.0	\$266.2	\$292.8	\$322.1	\$354.3	\$389.7	\$428.7	\$471.6	- NDA submission Q1:2015; Q2:2016 launch
													- Priced at premium to CiproDex
<b>Annual U.S. Sales of AuriPro (MM)</b>		<b>\$10.0</b>	<b>\$30.0</b>	<b>\$85.0</b>	<b>\$105.0</b>	<b>\$180.0</b>	<b>\$210.0</b>	<b>\$270.0</b>	<b>\$325.0</b>	<b>\$400.0</b>	<b>\$480.0</b>	<b>\$580.0</b>	<b>+84% - Growth driven by additional indications</b>
<b>% Growth</b>			<b>+200%</b>	<b>+117%</b>	<b>+82%</b>	<b>+52%</b>	<b>+31%</b>	<b>+29%</b>	<b>+20%</b>	<b>+23%</b>	<b>+20%</b>	<b>+20%</b>	
<b>Total Annual U.S. AOM Sales (MM)</b>	<b>\$145.0</b>	<b>\$160.0</b>	<b>\$185.0</b>	<b>\$215.0</b>	<b>\$255.0</b>	<b>\$300.0</b>	<b>\$360.0</b>	<b>\$420.0</b>	<b>\$500.0</b>	<b>\$570.0</b>	<b>\$670.0</b>	<b>\$770.0</b>	<b>+18% - Growth from new agents</b>
<b>% Growth</b>		<b>+10%</b>	<b>+18%</b>	<b>+16%</b>	<b>+19%</b>	<b>+18%</b>	<b>+20%</b>	<b>+17%</b>	<b>+19%</b>	<b>+14%</b>	<b>+18%</b>	<b>+15%</b>	
<b>Inner Ear - Ménière's Disease</b>													
% of patients treated for inner ear disorders	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	
# of patients treated for inner ear disorders (MM)	8.0	8.1	8.2	8.3	8.5	8.7	8.9	9.1	9.3	9.5	9.7	9.9	
% of treated patients affected by Ménière's	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	
# of patients affected by Ménière's (MM)	0.6	0.6	0.6	0.6	0.6	0.7	0.7	0.7	0.7	0.7	0.7	0.7	- No approved agents
% of patients eligible for steroid injections	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	- Low salt diet + diuretics (Diamox) is first line
# of patients eligible for steroid injections (MM)	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.4	
<b>OTO-104</b>													
% penetration of patients eligible for steroid injections					2.5%	5.0%	10.0%	15.0%	20.0%	24.0%	27.0%	30.0%	- Second pivotal trial to be initiated Q2:2015
% penetration of total Ménière's patients					1.3%	2.5%	5.0%	7.5%	10.0%	12.0%	13.5%	15.0%	- Expected early 2018 launch
# of OTO-104 patients ('000)					8.0	16.4	33.4	51.3	69.8	85.6	98.4	111.7	
OTO-104 net price per administration					\$1,000.0	\$1,100.0	\$1,210.0	\$1,331.0	\$1,464.1	\$1,610.5	\$1,771.6	\$1,948.7	- Priced similarly to Wet AMD drugs
Average # of OTO-104 injections per year					3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	- Consultants suggest avg. of 3
Average total annual OTO-104 cost per patient					\$3,000.0	\$3,300.0	\$3,630.0	\$3,993.0	\$4,392.3	\$4,831.5	\$5,314.7	\$5,846.2	
<b>Annual U.S. Sales of OTO-104 (MM)</b>					<b>\$25.0</b>	<b>\$55.0</b>	<b>\$120.0</b>	<b>\$205.0</b>	<b>\$305.0</b>	<b>\$415.0</b>	<b>\$525.0</b>	<b>\$655.0</b>	<b>+75% - Growth driven by additional indications</b>
<b>% Growth</b>						<b>+120%</b>	<b>+118%</b>	<b>+71%</b>	<b>+49%</b>	<b>+36%</b>	<b>+27%</b>	<b>+25%</b>	
<b>Total Annual U.S. Product Sales (MM)</b>		<b>\$10.0</b>	<b>\$90.0</b>	<b>\$90.0</b>	<b>\$180.0</b>	<b>\$280.0</b>	<b>\$415.0</b>	<b>\$575.0</b>	<b>\$740.0</b>	<b>\$925.0</b>	<b>\$1,135.0</b>	<b>\$1,415.0</b>	<b>+111% - Initially drive by AuriPro</b>
<b>% Growth</b>			<b>+200%</b>	<b>+200%</b>	<b>+78%</b>	<b>+75%</b>	<b>+48%</b>	<b>+39%</b>	<b>+29%</b>	<b>+25%</b>	<b>+23%</b>	<b>+23%</b>	<b>- Meniere's to contribute significantly</b>
<b>EUROPEAN UNION</b>													
<b>Annual EU Sales of AuriPro (MM)</b>					<b>\$5.0</b>	<b>\$20.0</b>	<b>\$45.0</b>	<b>\$75.0</b>	<b>\$110.0</b>	<b>\$145.0</b>	<b>\$190.0</b>	<b>\$225.0</b>	<b>+98% - Assuming approval two years later</b>
<b>% Growth</b>						<b>+300%</b>	<b>+125%</b>	<b>+87%</b>	<b>+47%</b>	<b>+32%</b>	<b>+31%</b>	<b>+18%</b>	<b>- Market opportunity slightly smaller</b>
<b>Annual EU Sales of OTO-104 (MM)</b>							<b>\$20.0</b>	<b>\$40.0</b>	<b>\$65.0</b>	<b>\$145.0</b>	<b>\$215.0</b>	<b>\$290.0</b>	<b>+71% - Assuming approval two years later</b>
<b>% Growth</b>								<b>+100%</b>	<b>+113%</b>	<b>+71%</b>	<b>+48%</b>	<b>+35%</b>	<b>- Market opportunity slightly smaller</b>
<b>Total Annual EU Product Sales (MM)</b>					<b>\$5.0</b>	<b>\$20.0</b>	<b>\$65.0</b>	<b>\$115.0</b>	<b>\$195.0</b>	<b>\$290.0</b>	<b>\$405.0</b>	<b>\$515.0</b>	<b>+125%</b>
<b>% Growth</b>						<b>+300%</b>	<b>+225%</b>	<b>+77%</b>	<b>+70%</b>	<b>+49%</b>	<b>+40%</b>	<b>+27%</b>	
<b>Total Annual U.S./EU Product Sales (MM)</b>		<b>\$10.0</b>	<b>\$90.0</b>	<b>\$95.0</b>	<b>\$180.0</b>	<b>\$345.0</b>	<b>\$530.0</b>	<b>\$770.0</b>	<b>\$1,090.0</b>	<b>\$1,390.0</b>	<b>\$1,850.0</b>	<b>\$2,230.0</b>	<b>+121% - Significant U.S./EU market opportunities</b>
<b>% Growth</b>			<b>+200%</b>	<b>+217%</b>	<b>+89%</b>	<b>+92%</b>	<b>+54%</b>	<b>+45%</b>	<b>+34%</b>	<b>+29%</b>	<b>+24%</b>	<b>+24%</b>	

Source: Otonomy; Cowen And Company estimates; PriceRx; Monasta L, Ronfani L, Marchetti F, Montico M, Vecchi Brumatti L, et al. (2012) Burden of Disease Caused by Otitis Media: Systematic Review and Global Estimates. PLoS ONE 7(4): e36226. doi:10.1371/journal.pone.0036226



Figure 20 Otonomy Annual P&L

OTONOMY - 2014-2025 ESTIMATED ANNUAL EPS BUILDUP (\$MM)														
	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	5Y CAGR Comments
<b>PRODUCT SALES</b>														
U.S. AuriPro Sales				\$10.0	\$30.0	\$65.0	\$105.0	\$160.0	\$210.0	\$270.0	\$325.0	\$400.0	\$480.0	+84% - Sustained release Cipro for ear infections post TTP surgery
Growth Rate					+200%	+117%	+62%	+52%	+31%	+29%	+20%	+23%	+20%	- Q2:2016 U.S. Launch assumed; IP to 2030
EU AuriPro Sales						\$5.0	\$20.0	\$45.0	\$75.0	\$110.0	\$145.0	\$190.0	\$225.0	+96% - Expected EU launch in 2018
Growth Rate							+300%	+125%	+67%	+47%	+32%	+31%	+18%	
U.S. OTO-104 Sales						\$25.0	\$55.0	\$120.0	\$205.0	\$305.0	\$415.0	\$525.0	\$655.0	+75% - Sustained release dexamethasone for Ménière's
Growth Rate							+120%	+118%	+71%	+49%	+36%	+27%	+25%	- 2018 U.S. launch assumed; IP to 2029
EU OTO-104 Sales								\$20.0	\$40.0	\$85.0	\$145.0	\$215.0	\$290.0	+71% - Expected EU launch in 2020
Growth Rate									+100%	+113%	+71%	+48%	+35%	
<b>Total Otonomy Revenues</b>	<b>\$0.0</b>	<b>\$0.0</b>	<b>\$0.0</b>	<b>\$10.0</b>	<b>\$30.0</b>	<b>\$95.0</b>	<b>\$180.0</b>	<b>\$345.0</b>	<b>\$590.0</b>	<b>\$770.0</b>	<b>\$1,030.0</b>	<b>\$1,380.0</b>	<b>\$1,850.0</b>	<b>+121%</b> - Initial growth driven by AuriPro, then OTO-104 for Ménière's
<b>% Change</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>+200%</b>	<b>+217%</b>	<b>+89%</b>	<b>+92%</b>	<b>+54%</b>	<b>+45%</b>	<b>+34%</b>	<b>+28%</b>	<b>+24%</b>	- To expand into additional indications, then launch ex-US
Cost of Goods	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$10.0	\$20.0	\$45.0	\$65.0	\$95.0	\$130.0	\$165.0	\$205.0	
Gross Profit	\$0.0	\$0.0	\$0.0	\$10.0	\$25.0	\$85.0	\$160.0	\$300.0	\$465.0	\$675.0	\$900.0	\$1,165.0	\$1,445.0	
Gross Margin	100.0%	100.0%	100.0%	85.0%	86.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	- 85% or more gross margins on products
SG&A	\$3.5	\$7.0	\$15.0	\$30.0	\$40.0	\$60.0	\$80.0	\$120.0	\$150.0	\$175.0	\$205.0	\$230.0	\$260.0	+63% - To hire 40 reps for AuriPro U.S. launch and expand to 80 reps for OTO-104
% of Revs	NM	NM	NM	300%	133%	63%	44%	35%	28%	23%	20%	17%	16%	- To develop and commercialize in Europe; partner RoW
R&D	\$16.3	\$33.0	\$55.0	\$90.0	\$50.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	+4%
% of Revs	NM	NM	NM	500%	167%	42%	22%	12%	8%	5%	4%	3%	2%	
Operating Expenses	\$19.9	\$40.0	\$70.0	\$80.0	\$90.0	\$100.0	\$120.0	\$160.0	\$190.0	\$215.0	\$245.0	\$270.0	\$300.0	+25%
% of Revenues	NM	NM	NM	800.0%	300.0%	105.3%	66.7%	46.4%	35.8%	27.9%	23.8%	20.3%	18.2%	
Operating Income	(\$19.9)	(\$40.0)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$40.0	\$140.0	\$275.0	\$460.0	\$655.0	\$895.0	\$1,145.0	NM - Operating profit expected in 2019
% Operating Margin	NM	NM	NM	NM	NM	NM	22%	41%	52%	60%	64%	67%	69%	
Non-Operating Income														
Interest Income	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	
Interest Expense	\$0.0	(\$0.1)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
Other Income	(\$0.2)	(\$3.3)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
Non-Operating Income	(\$0.2)	(\$3.4)	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	
Pretax Income	(\$20.1)	(\$43.4)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$40.0	\$140.0	\$275.0	\$460.0	\$655.0	\$895.0	\$1,145.0	NM
% of Revs	NM	NM	NM	NM	NM	NM	22.2%	40.6%	51.9%	59.7%	63.6%	67.3%	69.4%	
Income Taxes							\$14.0	\$49.0	\$96.3	\$161.0	\$229.3	\$313.3	\$400.8	NM
Income Tax Rate							35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	- Standard U.S. corporate tax rate; assumes no NOLs
Net Income - Operations	(\$20.1)	(\$43.4)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$26.0	\$91.0	\$178.8	\$299.0	\$425.8	\$581.8	\$744.3	NM
% Net Margin	NM	NM	NM	NM	NM	NM	14.4%	26.4%	33.7%	38.8%	41.3%	43.7%	45.1%	
Extraordinary Items	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	
Reported Net Income	(\$20.1)	(\$43.4)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$26.0	\$91.0	\$178.8	\$299.0	\$425.8	\$581.8	\$744.3	NM
Interest Add-Back	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	
<b>EPS (GAAP) - Before Ex. Items</b>	<b>(\$268.80)</b>	<b>(\$5.40)</b>	<b>(\$3.15)</b>	<b>(\$3.05)</b>	<b>(\$2.70)</b>	<b>(\$0.60)</b>	<b>\$0.90</b>	<b>\$3.10</b>	<b>\$5.90</b>	<b>\$8.60</b>	<b>\$13.20</b>	<b>\$17.50</b>	<b>\$21.75</b>	<b>NM</b> - Profitable in 2019 following the launch of AuriPro and OTO-104
<b>Growth Rate</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>NM</b>	<b>+244%</b>	<b>+90%</b>	<b>+63%</b>	<b>+38%</b>	<b>+33%</b>	<b>+24%</b>	
EPS - Extraordinary Items	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	
EPS - Reported	(\$268.80)	(\$5.40)	(\$3.15)	(\$3.05)	(\$2.70)	(\$0.60)	\$0.90	\$3.10	\$5.90	\$8.60	\$13.20	\$17.50	\$21.75	NM
Shares - Fully Diluted (MM)	0.1	8.0	22.1	23.1	24.1	25.1	28.2	29.2	30.2	31.2	32.2	33.2	34.2	- Assuming some onward dilution from options (+2.1MM upon profitability)

Source: Cowen and Company

Figure 21 Otonomy DCF Suggests \$55 Per Share

Assumptions:		Output:	
Increase in WC	5.0%	Equity Value	\$1,370.0
Discount Rate	13.0%	Est. Share Price	\$55.00
Shares Outstanding	24.2	Debt	\$0.0 \$156MM as of Dec 31, 2014
		Cash	\$100.0
		Enterprise Value	\$1,270.0

OTONOMY DCF																								
	2013	2014P	2015P	2016P	2017P	2018P	2019P	2020P	2021P	2022P	2023P	2024P	2025P	2026P	2027P	2028P	2029P	2030P	2031P	2032P	2033P	2034P	2035P	
Total Revenues	\$0.0	\$0.0	\$0.0	\$10.0	\$30.0	\$95.0	\$180.0	\$345.0	\$530.0	\$770.0	\$1,030.0	\$1,330.0	\$1,650.0	\$1,900.0	\$2,075.0	\$2,250.0	\$1,525.0	\$800.0	\$400.0	\$200.0	\$125.0	\$100.0	\$100.0	
% Change					+200%	+217%	+89%	+92%	+54%	+45%	+34%	+29%	+24%	+15%	+9%	+8%	-32%	-48%	-50%	-50%	-38%	-20%	+0%	
Cost of Goods	\$0.0	\$0.0	\$0.0	\$0.0	\$5.0	\$10.0	\$20.0	\$45.0	\$65.0	\$95.0	\$130.0	\$165.0	\$205.0	\$235.0	\$260.0	\$280.0	\$190.0	\$100.0	\$50.0	\$25.0	\$15.0	\$10.0	\$10.0	
Gross Profit	\$0.0	\$0.0	\$0.0	\$10.0	\$25.0	\$85.0	\$160.0	\$300.0	\$465.0	\$675.0	\$900.0	\$1,165.0	\$1,445.0	\$1,665.0	\$1,815.0	\$1,970.0	\$1,335.0	\$700.0	\$350.0	\$175.0	\$110.0	\$90.0	\$90.0	
Gross Margin - Total	NM	100.0%	100.0%	85.0%	86.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	87.5%	
SG&A	\$3.5	\$7.0	\$15.0	\$30.0	\$40.0	\$60.0	\$80.0	\$120.0	\$150.0	\$175.0	\$205.0	\$230.0	\$260.0	\$300.0	\$330.0	\$330.0	\$280.0	\$200.0	\$100.0	\$75.0	\$65.0	\$55.0	\$50.0	
% of Revs	NM	NM	NM	300.0%	133.3%	63.2%	44.4%	34.8%	28.3%	22.7%	19.9%	17.3%	15.8%	15.8%	15.9%	14.7%	18.4%	25.0%	25.0%	37.5%	52.0%	55.0%	50.0%	
R&D	\$16.3	\$33.0	\$55.0	\$50.0	\$50.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$40.0	\$30.0	\$20.0	\$20.0	\$10.0	\$5.0	\$5.0	\$5.0	
% of Revs	NM	NM	NM	500.0%	166.7%	42.1%	22.2%	11.6%	7.5%	5.2%	3.9%	3.0%	2.4%	2.1%	1.9%	1.8%	2.0%	2.5%	5.0%	5.0%	4.0%	5.0%	5.0%	
Operating Expenses	\$19.9	\$40.0	\$70.0	\$80.0	\$90.0	\$100.0	\$120.0	\$160.0	\$190.0	\$215.0	\$245.0	\$270.0	\$300.0	\$340.0	\$370.0	\$370.0	\$310.0	\$220.0	\$120.0	\$85.0	\$70.0	\$60.0	\$55.0	
% of Revenues	NM	NM	NM	800.0%	300.0%	105.3%	66.7%	46.4%	35.8%	27.9%	23.8%	20.3%	18.2%	17.9%	17.8%	16.4%	20.3%	27.5%	30.0%	42.5%	56.0%	60.0%	55.0%	
Operating Income	(\$19.9)	(\$40.0)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$40.0	\$140.0	\$275.0	\$460.0	\$655.0	\$895.0	\$1,145.0	\$1,325.0	\$1,445.0	\$1,600.0	\$1,025.0	\$480.0	\$230.0	\$90.0	\$40.0	\$30.0	\$35.0	
% Operating Margin	NM	NM	NM	NM	NM	-15.8%	22.2%	40.6%	51.9%	59.7%	63.6%	67.3%	69.4%	69.7%	69.6%	71.1%	67.2%	60.0%	57.5%	45.0%	32.0%	30.0%	35.0%	
Other Income	(\$0.248)	(\$3.3)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
Adjusted EBIT	(\$20.1)	(\$43.3)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$40.0	\$140.0	\$275.0	\$460.0	\$655.0	\$895.0	\$1,145.0	\$1,325.0	\$1,445.0	\$1,600.0	\$1,025.0	\$480.0	\$230.0	\$90.0	\$40.0	\$30.0	\$35.0	
% of Revs	NM	NM	NM	NM	NM	-15.8%	22.2%	40.6%	51.9%	59.7%	63.6%	67.3%	69.4%	69.7%	69.6%	71.1%	67.2%	60.0%	57.5%	45.0%	32.0%	30.0%	35.0%	
Taxes						\$14.0	\$49.0	\$96.3	\$161.0	\$229.3	\$313.3	\$400.8	\$463.8	\$505.8	\$560.0	\$358.8	\$168.0	\$80.5	\$31.5	\$14.0	\$10.5	\$12.3		
Income Tax Rate						35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	
NOPAT	(\$20.1)	(\$43.3)	(\$70.0)	(\$70.0)	(\$65.0)	(\$15.0)	\$26.0	\$91.0	\$178.8	\$299.0	\$425.8	\$581.8	\$744.3	\$861.3	\$939.3	\$1,040.0	\$666.3	\$312.0	\$149.5	\$58.5	\$26.0	\$19.5	\$22.8	
Adjustments:																							Terminal	
Capex	(\$0.5)	\$0.5	(\$0.5)	(\$1.0)	(\$5.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$10.0)	(\$5.0)	(\$3.0)	(\$2.0)	(\$1.0)	\$0.0	\$0.0	
Depreciation & Amortization	\$0.3	\$0.2	\$0.3	\$0.3	\$0.3	\$1.0	\$2.0	\$3.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	\$5.0	
Change In Working Capital	\$32.6	(\$5.0)	(\$5.3)	(\$5.5)	(\$5.8)	(\$6.1)	(\$6.4)	(\$6.7)	(\$7.0)	(\$7.4)	(\$7.8)	(\$8.1)	(\$8.5)	(\$9.0)	(\$9.4)	(\$9.9)	(\$10.4)	(\$10.9)	(\$11.5)	(\$12.0)	(\$12.6)	(\$13.3)	(\$13.9)	
Free Cash Flow	\$12.2	(\$48.8)	(\$76.5)	(\$76.5)	(\$76.5)	(\$56.1)	\$11.6	\$77.3	\$168.7	\$288.8	\$419.0	\$568.8	\$780.7	\$847.3	\$924.8	\$1,025.1	\$660.8	\$301.1	\$140.0	\$49.5	\$17.4	\$11.2	\$13.8	\$108.8

Source: Cowen and Company

## *Valuation Methodology And Risks*

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### **Valuation Methodology**

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#### **Pharmaceuticals/Specialty**

For our valuation methodology, we arrive at fair value utilizing a discounted cash flow (DCF) approach to derive our 12-month price target.

### **Investment Risks**

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#### **Pharmaceuticals/Specialty**

**Risks include:** (1) growing competitive dynamics in the specialty pharmaceuticals space; (2) the ability of management to execute on external growth by successfully acquiring new strategic, accretive products; (3) the ability to grow organically and keep the product pipeline robust; (4) potential regulatory delays, rejections, or failures of pipeline products; (5) economic sensitivity of any self-pay products or weakening consumer demand; (6) domestic or international pricing pressures for marketed products; and (7) failure to execute on new product launches.

#### **Risks To The Price Target**

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Otonomy is a development-stage company and with that carries risk. We believe the clinical risk is mitigated as Otonomy's products employ active ingredients that have been approved in other indications. However, failure for AuriPro to receive FDA approval in 2016 and for OTO-104 to achieve success in Phase IIb could result in significant downside to our valuation.

# Addendum

## Stocks Mentioned In Important Disclosures

Ticker	Company Name
ACT	Actavis
OTIC	Otonomy
SHPG	Shire Pharmaceutical
TEVA	Teva Pharmaceutical

## Analyst Certification

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#### Cowen and Company Rating System effective May 25, 2013

**Outperform (1):** The stock is expected to achieve a total positive return of at least 15% over the next 12 months

**Market Perform (2):** The stock is expected to have a total return that falls between the parameters of an Outperform and Underperform over the next 12 months

**Underperform (3):** Stock is expected to achieve a total negative return of at least 10% over the next 12 months

**Assumption:** The expected total return calculation includes anticipated dividend yield

#### Cowen and Company Rating System until May 25, 2013

**Outperform (1):** Stock expected to outperform the S&P 500

**Neutral (2):** Stock expected to perform in line with the S&P 500

**Underperform (3):** Stock expected to underperform the S&P 500

**Assumptions:** Time horizon is 12 months; S&P 500 is flat over forecast period

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**Hold** – The fundamentals/valuations of the subject company are neither improving nor deteriorating and the investment return is expected to be in line with the general market return

**Cowen And Company Rating Definitions**

**Distribution of Ratings/Investment Banking Services (IB) as of 12/31/14**

Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	461	60.50%	109	23.64%
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Sell (c)	13	1.71%	0	0.00%

(a) Corresponds to "Outperform" rated stocks as defined in Cowen and Company, LLC's rating definitions. (b) Corresponds to "Market Perform" as defined in Cowen and Company, LLC's ratings definitions. (c) Corresponds to "Underperform" as defined in Cowen and Company, LLC's ratings definitions.

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**Actavis Rating History as of 02/03/2015**

powered by: BlueMatrix



**Otonomy Rating History as of 02/03/2015**

powered by: BlueMatrix



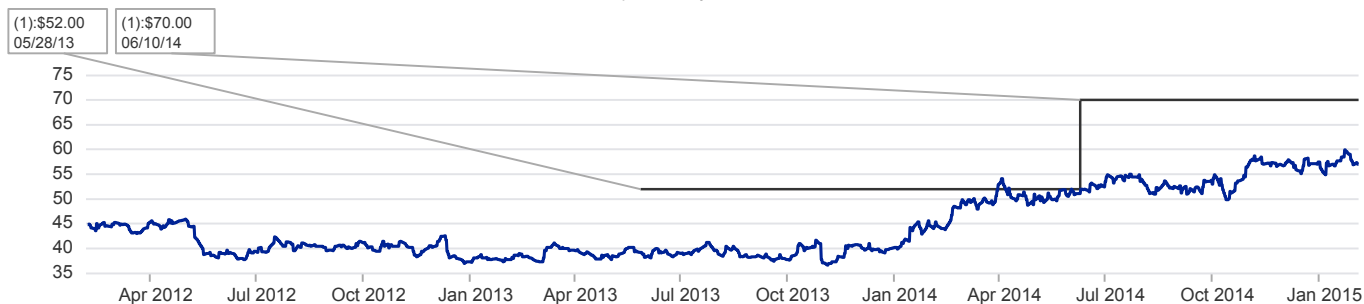
### Shire Pharmaceutical Rating History as of 02/03/2015

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### Teva Pharmaceutical Rating History as of 02/03/2015

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#### Legend for Price Chart:

I = Initiation | 1 = Outperform | 2 = Market Perform | 3 = Underperform | UR = Price Target Under Review | T = Terminated Coverage | \$xx = Price Target | NA = Not Available | S=Suspended



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