Otonomy, Inc. (OTIC)

Initiating Coverage of Otonomy with a Buy Rating and a $47 PT

Do You Hear What We Hear?

- **Otonomy differentiates via its Sustained Exposure technology.** Otonomy's formulation technology provides sustained drug exposure in the middle/inner ear from a single local administration. The technology is based on a thermo-reversible polymer which transforms from a liquid into a gel at body temperature. The mixture of drug particles and polymers is retained in the middle ear cavity for several weeks until it is excreted. Current treatments are liquids which do not remain at the desired site and require multiple administrations over several days. This technology has the potential to be broadly applied to other otic indications.
- **Technology is de-risked by positive preclinical, PK and human clinical trial data.** Pharmacokinetic (PK) studies of AuriPro and OTO-104 demonstrate an improved drug exposure profile as compared to ear drops or intratympanic injections. The polymer is efficacious and safe as demonstrated in Otonomy's clinical data, and other FDA approved products using the same polymer.
- **Lead asset AuriPro completed Phase III trials successfully and could be approved as early as YE15.** Positive Phase III results were announced in 3Q14 in pediatric patients undergoing tympanostomy tube placement (TTP) surgery. AuriPro achieved the primary efficacy endpoint ($p<0.001$) of cumulative proportion of treatment failures and was well tolerated. Otonomy plans to submit an NDA for AuriPro to the FDA in 1Q15. We believe the likelihood of approval is high and forecast peak WW revenue of ~$200M in the out-year of our model, 2025.
- **Pipeline assets are addressing larger markets.** Otonomy's clinical pipeline includes OTO-104 which is in Phase IIb clinical development for patients with Ménière's disease, and OTO-311 in preclinical development for tinnitus. Both are chronic diseases and potentially represent a greater market potential than the TTP surgical indication. We forecast peak WW revenue of ~$1B for OTO-104 in the out-year of our model, 2025.
- **Our differentiated viewpoint:** we focus on the technology platform as much as the individual pipeline assets; model assumptions consider AuriPro for TTP surgery and OTO-104 for Ménière's disease. OTO-311 for tinnitis and AuriPro label expansion is considered upside and not incorporated in our valuation. An additional $100M to $1B in market potential exists using the delivery technology; we are more bullish than the Street on the commercial

Initiate

Price Target: $47.00

Price (Feb. 3, 2015)	$30.14
52-Wk Range	$40.00-$15.84
Market Cap ($M)	$726
ADTV	170,398
Shares Out (M)	24.1
Short Interest Ratio/% Of Float	2.7%
Dividend/Yield	$0.00/0.0%
TR to Target	55.9%

Cash Per Share	$10.20
Total Debt	$5.7
Long-Term Debt/Total Cap	0%
Cash And Equivalents ($M)	$246.0
Enterprise Value ($M)	$480.0

	2014E	2015E		2016E	
		Curr.	Prior	Curr.	Prior
EPS					
1Q	($0.03)	($0.80)	--	--	NA
2Q	($1.78)	($0.79)	--	--	NA
3Q	($1.23)	($0.79)	--	--	NA
4Q	($0.64)	($0.79)	--	--	NA
FY	($3.63)	($3.17)	--	($2.76)	--
P/E	NM	NM		NM	
Consensus EPS					
FY	($4.24)	($2.91)	--	($3.21)	--
FYE Dec					

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SEE PAGE 54 FOR REQUIRED DISCLOSURE INFORMATION

prospects of OTO-104 as we believe OTO-104 addresses a wide spectrum of disease states for which there are currently no therapeutic options.

- **Upcoming milestones:**
  - NDA submission of AuriPro for middle ear effusion at time of TTP surgery: 1Q15
  - Phase I initiation of AuriPro for possible label expansion: 1H15
  - Phase IIb (potentially pivotal trial) top-line readout of OTO-104 for Ménière's disease: 2Q15
  - Second pivotal trial (Phase III) initiation of OTO-104 for Ménière's disease: 2H15
  - IND submission for OTO-311 in tinnitus: 2015
- **Risks:**
  - AuriPro may not receive FDA approval or approval is delayed
  - AuriPro may not get widely adopted by physicians
  - OTO-104 and OTO-311 may not meet their clinical endpoints in ongoing clinical trials
  - The Sustained Exposure technology may not apply to other ear indications
  - A handful of other companies are developing therapeutics in the otic field and may outpace Otonomy

Otonomy Bull / Bear / STRH Scenarios

Bull Case	Bear Case	STRH case
● Price target $59.98; 29% upside; 15% probability	● Price target $35.68; 23% downside; 15% probability	● Price target $46.57; 70% probability
● AuriPro is widely adopted by physicians and patients alike; it achieves a peak U.S. market penetration of 65% and EU market penetration of 60%	● AuriPro cannot gain significant market share; and it achieves a peak U.S. market penetration of 30% and an EU market penetration of 25%	● AuriPro achieves a peak U.S. and EU market penetration of 55%
● OTO-104 adopts EU pricing that is 90% of its U.S. pricing based on positive physician experience with AuriPro; peak market penetration of OTO-104 in the U.S. is 60% and 60% in the EU	● OTO-104 first Phase Ib does not meet the pre-specified primary endpoints; we subsequently decrease the probability of success to 40%; and the blended success rate of the company to 50%	● OTO-104 EU pricing is 60% of its U.S. pricing
● We attribute a $100MM valuation to Otonomy's Sustained Exposure formulation technology		● We do not include the valuation of OTO-311 for tinnitus in our model, nor do we include any possible label expansions

Source: SunTrust Robinson Humphrey

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OTONOMY, INC.

Otonomy, Inc. is a clinical-stage biopharmaceutical company focusing on disorders of the ear. Its proprietary technology provides sustained exposure of drugs to the middle and inner ear. Otonomy has three product candidates in development. AuriPro is a sustained-exposure antibiotic for which the company has recently completed two identical Phase III clinical trials in 532 pediatric patients with middle ear effusion, or fluid, at the time of tympanostomy tube placement surgery. OTO-104 is a sustained-exposure steroid that is in a Phase IIb clinical trial for patients with Ménière's disease. OTO-311 is in preclinical development as a treatment for tinnitus.

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Senior Management	
David A. Weber, Ph.D.	CEO and President
Paul E. Cayer	CFO and CBO
Carl LeBel, Ph.D.	CSO
Robert Michael Savel, II	Chief Technical Officer
Anthony J. Yost	Chief Commercial Officer

Capitalization	
Long-Term Debt (MM):	$0
Market Value of Equity (MM):	$704
Cash (MM):	$246
Technology Value (MM):	$458

Drug Candidate	Phase	Indication
AuriPro	Pre-NDA	Middle ear effusion at time of TTP surgery
OTO-104	Phase IIb	Ménière's disease
OTO-311	Preclinical	Tinnitus

Note: Cash position is pro forma for the recent financing closed in January 2015
Source: SunTrust Robinson Humphrey

Investment thesis

Otonomy Is Building A Pure Play Ear Focused Company

Otonomy is a clinical-stage biopharmaceutical company focused on the development and commercialization of therapeutics for ear diseases. Otonomy has developed a proprietary technology to deliver retained therapeutics in the ear for an extended period of time, which Otonomy refers to as "sustained-exposure." This technology aims to address the existing issues of delivering drugs to the middle and inner ear.

Based on this technology, Otonomy has three product candidates in clinical and preclinical development. Its lead product candidate, AuriPro, is a sustained-exposure formulation of the antibiotic ciprofloxacin which has recently completed two Phase III clinical trials for middle ear effusion during tympanostomy tube placement (TTP) surgery and is preparing for an NDA filing in 1Q15. The second product candidate, OTO-104, is a sustained-exposure steroid that is in a Phase IIb clinical development for patients with Ménière's disease. Otonomy expects to report results from this trial in 2Q15. Its third product candidate, OTO-311, is in preclinical development for the treatment of tinnitus. There are no FDA approved drugs for the indications Otonomy is currently pursuing, i.e., middle ear effusion at time of TTP surgeries. However, antibiotic ear drops have been approved to be used post-TTP surgeries.

Exhibit 1: Otonomy Clinical And Preclinical Programs

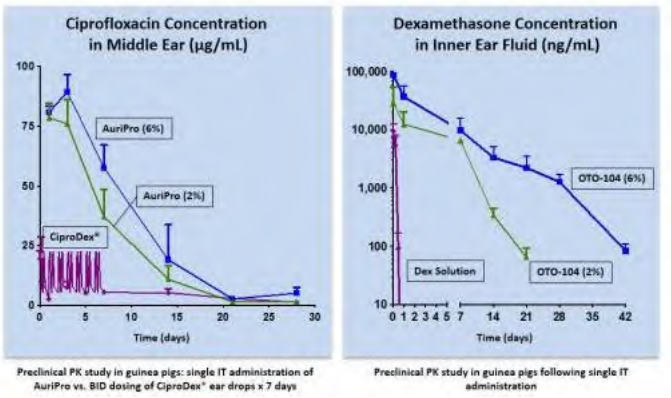
Product Candidate *Lead Indication*	Development Stage Preclinical	Phase I	Phase II	Phase III	Registration	Approval
AuriPro *Middle ear effusion at time of TTP surgery*						
OTO-104 *Ménière's disease*						
OTO-311 *Tinnitus*						

Source: Otonomy

A De-Risked Technology That Could Turn The Street On Its Ear

One of the key differentiations of Otonomy is its formulation technology that provides sustained drug exposure in the middle and inner ear from a single local administration. The foundation of the technology is a thermo-reversible polymer which transforms from a liquid to a gel at body temperature. The mixture of drug particles and polymers are retained in the middle-ear cavity for several weeks until it is excreted. Pharmacokinetic (PK) studies of AuriPro and OTO-104 demonstrated an improved drug exposure profile as compared to delivering therapeutics via ear drops or by intratympanic injection of solutions. The polymer is safe as demonstrated by Otonomy's clinical data and other FDA approved products using the same polymer, such as Sanofi's LeGoo, which we will elaborate more later in this report.

Exhibit 2: Pharmacokinetic Profile of AuriPro and OTO-104



Source: Company presentation

We believe the technology is de-risked according to clinical data generated from AuriPro and OTO-104. We believe the same technology can be used for many other ear indications. To us, Otonomy is reminiscent of other successful biotech stories built around platform delivery technologies, such as Nektar Therapeutics (polymer drug conjugate technology), Immunogen (antibody drug conjugate), and Isis Pharmaceuticals (antisense technology).

A Hidden Gem – Investors May Hear, But Not All Are Listening

Otology is a branch of medicine which treats abnormalities of the ear. Otology indications are underappreciated by many biotech companies and investors as there has historically been a dearth of otic focused biotechnology companies. Of the 109 biotech companies that went public between January 2012 and December 2014, only two companies, Otonomy (NASDAQ: OTIC) and Auris Medical (NASDAQ: EARS), are developing otology focused therapeutics. This is in contrast to other "hot" spaces such as oncology, where 22 companies went public. Additionally, there have been multiple companies that have worked on and successfully developed therapeutics for eye indications such as wet and dry AMD and CMV retinitis.

Due to the lack of innovations in the otology space, effective treatment options are sparse. For example, there are currently no FDA approved therapies for infections after TTP surgeries. Physicians typically use antibiotic drops off-label, which are inconvenient and possibly ineffective. No FDA approved drugs for tinnitus exist either.

Due to the lack of innovative therapeutics, a well-positioned product that meets the unmet medical need(s) in the otic space has the potential to generate significant revenue for a drug developer. One such example is Ciprodex Otic (ciprofloxacin/dexamethasone) from Novartis (Alcon). Ciprodex is a combination of ciprofloxacin (a fluoroquinolone antibiotic) and dexamethasone (an anti-inflammatory corticosteroid) used to treat bacterial ear infections. According to IMS, Ciprodex has generated more than $300M in revenue per year over the last four years.

There are also many otology specific diseases which offer indication expansion opportunities for a company such as Otonomy. The Company is considering exploring indications such as recurrent otic infections in patients with tympanostomy tubes, acute otitis media with tympanostomy tubes (AOMT), acute otitis externa, chronic suppurative otitis media (a perforated tympanic membrane with persistent drainage from middle ear), and prophylaxis following middle ear surgery, among others. We estimate the approximate U.S. market size of these indications in the following exhibit.

Exhibit 3: Select Indication Expansion Opportunities For Otonomy

Indication	Explanation	Epidemiology	U.S. market size	Current standard of care
Tinnitus	Perception of sound within the human ear ("ringing of the ears") when no external sound is present	~7.7M U.S. population has tinnitus that affect their lives	>$1B	noise suppiression device, off label antidepressants
Acute otitis media with tympanostomy tubes (AOMT)	AOMT is a bacterial infection of the middle ear space in a child who has a well-positioned and patent tympanostomy tube.	83% of children with tympanostomy tubes, 1M TTP surgery per year in the U.S.	>$100M	antibiotic ear drop, Ciprodex
Acute otitis externa	Inflammation of the external auditory canal most often caused by bacterial infection	2.4M healthcare visit per year	~$500M	ear drop to control bacterial growth or kill bacteria
Chronic suppurative otitis media (CSOM)	Perforated tympanic membrane with persistent drainage from the middle ear	~25K per year	$50M-100M	antibiotic ear drop, Ciprodex
Sudden sensorineural hearing loss	A typical patient loses his or her hearing in one ear over a period of one to several days ear.	4,000 cases of SSHL every year in the U.S., most commonly among people aged 30 to 60	<$50M	steorids

Source: SunTrust Robinson Humphrey

A Key Inflection Point For Otonomy Is Within Hearing Distance

Otonomy is approaching a key inflection point with its first regulatory submission of lead clinical candidate AuriPro for pediatric patients during TTP surgery. Positive Phase III results were announced 3Q14, in which AuriPro achieved the primary efficacy endpoint ($p<0.001$) of cumulative proportion of treatment failures (discussed later) and was found to be safe and well tolerated. Otonomy plans to submit an NDA for AuriPro to the FDA in 1Q15. We believe there is a high likelihood of approval based on the clinical trial data seen to date, which would position the drug launch as early as early 2016.

TTP represents a meaningful market opportunity for Otonomy by our analysis. We model peak U.S. revenue for AuriPro in the U.S. at over $100M, which is based on one million TTP surgeries performed annually, with a price of $250 per treatment course. Worldwide revenue is greater than $200M in our financial model.

Of note, it is common to use drugs off label in the otology field, as evidenced in the case of Ciprodex. Should AuriPro be approved for TTP, we believe there is a high likelihood that ears, nose and throat (ENT) physicians may use AuriPro for other similar ear indications, such as AOMT. This represents additional upside potential for AuriPro.

Otonomy's second clinical asset OTO-104 for Ménière's disease completed a Phase Ib trial and demonstrated good tolerability. The drug is now in Phase IIb development which will serve as one of the two FDA required registration trials, according to Otonomy. The Company expects to report topline results from the Phase IIb in 2Q15. We believe OTO-104 could be launched as early as 4Q17. We model peak revenue for OTO-104 at approximately $600M in the U.S. and over $1B worldwide.

Otonomy's third asset, OTO-311 for tinnitus is in preclinical development and to maintain a conservative approach in our modeling and resulting valuation metrics, we do not include it in our financial models.

Exhibit 4: Otonomy Revenue Buildup Model

	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
AuriPro for otitis media patients undergoing TTP surgery											
U.S.											
# of TTP procedures performed annually (000s)	1,000.0	1,010.0	1,020.1	1,030.3	1,040.6	1,051.0	1,061.5	1,072.1	1,082.9	1,093.7	1,104.6
% of patients ≤ 5 yrs of age	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*
# of patients 5 yo or younger with TTP surgeries annually (000s)	667.0	673.7	680.4	687.2	694.1	701.0	708.0	715.1	722.3	729.5	736.8
% of pediatric patients given antibiotic post surgery	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*
# of pediatric patients given antibiotic post surgery (000s)	633.7	640.0	646.4	652.9	659.4	666.0	672.6	679.4	686.2	693.0	699.9
% market penetration by AuriPro	*0.0%*	*10.0%*	*20.0%*	*30.0%*	*40.0%*	*45.0%*	*47.5%*	*50.0%*	*52.5%*	*55.0%*	*55.0%*
# of pediatric patients receiving AuriPro treatment (000s)	0.0	64.0	129.3	195.9	263.8	299.7	319.5	339.7	360.2	381.2	385.0
Cost per course (1 administration) of treatment (AWP)	$250	$188	$250	$255	$260	$265	$271	$276	$282	$287	$293
U.S. Total AuriPro Revenue from TTP Surgery (MM)	**$0.00**	**$12.00**	**$32.32**	**$49.94**	**$68.60**	**$79.51**	**$86.46**	**$93.76**	**$101.42**	**$109.46**	**$112.76**
EU											
# of TTP procedures performed annually (000s)	1,562.5	1,578.1	1,593.9	1,609.8	1,625.9	1,642.2	1,658.6	1,675.2	1,692.0	1,708.9	1,726.0
% of patients ≤ 5 yrs of age	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*	*66.7%*
# of patients 5 yo or younger with TTP surgeries annually (000s)	1042.2	1052.6	1063.1	1073.8	1084.5	1095.3	1106.3	1117.4	1128.5	1139.8	1151.2
% of pediatric patients given antibiotic post surgery	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*	*95.0%*
# of pediatric patients given antibiotic post surgery (000s)	990.1	1000.0	1010.0	1020.1	1030.3	1040.6	1051.0	1061.5	1072.1	1082.8	1093.7
% market penetration by AuriPro	*0.0%*	*5.0%*	*10.0%*	*20.0%*	*30.0%*	*40.0%*	*45.0%*	*47.5%*	*50.0%*	*52.5%*	*55.0%*
# of pediatric patients receiving AuriPro treatment (000s)	0.0	50.0	101.0	204.0	309.1	416.2	472.9	504.2	536.1	568.5	601.5
Cost per course (1 administration) of treatment (AWP)	$150	$38	$150	$153	$156	$159	$162	$166	$169	$172	$176
EU Total AuriPro Revenue from TTP Surgery (MM)	$0.00	$1.87	$15.15	$31.21	$48.24	$66.26	$76.79	$83.50	$90.55	$97.95	$105.72
Royalty of EU Sales of AuriPro Booked by Otonomy (20%) (MM)	**$0.0**	**$0.4**	**$3.0**	**$6.2**	**$9.6**	**$13.3**	**$15.4**	**$16.7**	**$18.1**	**$19.6**	**$21.1**
WW Total AuriPro Revenue During TTP Surgery (MM)	$0.0	$13.9	$47.5	$81.2	$116.8	$145.8	$163.2	$177.3	$192.0	$207.4	$218.5
WW Total AuriPro Revenue Booked by Otonomy (MM)	**$0.0**	**$12.4**	**$35.3**	**$56.2**	**$78.2**	**$92.8**	**$101.8**	**$110.5**	**$119.5**	**$129.0**	**$133.9**
OTO-104 for Ménière's disease											
U.S.											
Prevalence of Ménière's disease (000s)	600.0	640.7	681.1	721.1	760.9	800.3	839.4	878.2	916.6	954.8	992.7
% of patients receiving corticosteroid	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*
# of patients receiving corticosteroid (000s)	120.0	128.1	136.2	144.2	152.2	160.1	167.9	175.6	183.3	191.0	198.5
% market penetration by OTO-104	*0.0%*	*0.0%*	*10.0%*	*25.0%*	*35.0%*	*40.0%*	*42.5%*	*45.0%*	*45.0%*	*45.0%*	*45.0%*
# of patients receiving OTO-104 treatment (000s)	0.0	0.0	13.6	36.1	53.3	64.0	71.3	79.0	82.5	85.9	89.3
Cost per patient per year (AWP)	$6,000	$6,000	$3,000	$6,000	$6,120	$6,242	$6,367	$6,495	$6,624	$6,757	$6,892
U.S. Total OTO-104 Revenue For Ménière's disease	**$0.0**	**$0.0**	**$40.86**	**$216.34**	**$325.95**	**$399.65**	**$454.28**	**$513.29**	**$546.50**	**$580.64**	**$615.73**
EU											
Prevalence of Ménière's disease (000s)	937.5	946.9	956.3	965.9	975.6	985.3	995.2	1,005.1	1,015.2	1,025.3	1,035.6
% of patients receiving corticosteroid	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*
# of patients receiving corticosteroid (000s)	187.5	189.4	191.3	193.2	195.1	197.1	199.0	201.0	203.0	205.1	207.1
% market penetration by OTO-104	*0.0%*	*0.0%*	*5.0%*	*15.0%*	*25.0%*	*30.0%*	*35.0%*	*40.0%*	*42.5%*	*45.0%*	*45.0%*
# of patients receiving OTO-104 treatment (000s)	0.0	0.0	9.6	29.0	48.8	59.1	69.7	80.4	86.3	92.3	93.2
Cost per patient per year (AWP)	$3,600	$3,600	$1,800	$3,600	$3,672	$3,745	$3,820	$3,897	$3,975	$4,054	$4,135
EU Total OTO-104 Revenue For Ménière's disease	$0.0	$0.0	$17.21	$104.32	$179.11	$221.43	$266.13	$313.34	$342.98	$374.12	$385.42
Royalty of EU Sales of OTO-104 Booked by Otonomy (20%) (MM)	**$0.0**	**$0.0**	**$3.4**	**$20.9**	**$35.8**	**$44.3**	**$53.2**	**$62.7**	**$68.6**	**$74.8**	**$77.1**
WW Total OTO-104 Revenue For Ménière's disease	$0.0	$0.0	$58.1	$320.7	$505.1	$621.1	$720.4	$826.6	$889.5	$954.8	$1,001.2
WW Total OTO-104 Booked by Otonomy (MM)	**$0.0**	**$0.0**	**$44.3**	**$237.2**	**$361.8**	**$443.9**	**$507.5**	**$576.0**	**$615.1**	**$655.5**	**$692.8**
WW Total Product Revenues Booked by Otonomy	**$0.0**	**$12.4**	**$79.7**	**$293.4**	**$440.0**	**$536.7**	**$609.3**	**$686.4**	**$734.6**	**$784.5**	**$826.7**

Source: SunTrust Robinson Humphrey

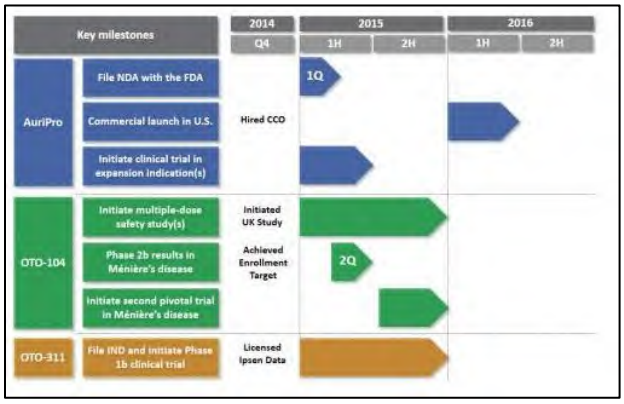
We believe the early success of AuriPro is critical as it serves as validation/confirmation of Otonomy's sustained release technology. A relatively small TTP market requires a smaller sales force (40 specialty reps) and less capital investment to build a successful commercial infrastructure. Follow-on assets, including OTO-104 for Ménière's disease and other label expansion opportunities as discussed above have the potential to fuel the long term growth of the Company.

Multiple Catalysts In 2015

In 2015 there are several catalysts that are expected for all three assets. Among them AuriPro's NDA submission and possible FDA decision, and OTO-104's Phase IIb top-line data readout are the key news events in our opinion. In the table below we summarize the upcoming milestones for Otonomy in 2015 and into 2016.

Exhibit 5: Otonomy Upcoming Milestones

Product	Indication	Timing	Event	Importance
AuriPro	Middle ear effusion at time of TTP surgery	1Q15	NDA submission	++
AuriPro	Middle ear effusion at time of TTP surgery	1H16	FDA approval	+++
AuriPro	Other ear indications expansion	1H15	Ph I initiation	+
OTO-104	Ménière's disease	2Q15	Ph IIb topline readout	+++
OTO-104	Ménière's disease	2H15	Ph III initiation	++
OTO-311	Tinnitus	2015	IND application	++



Source: Company filings, SunTrust Robinson Humphrey

Valuation Summary

We value Otonomy common shares via four different methodologies. In our Discounted Earnings model we discount estimated earnings per share from the first year of meaningful revenue back to 12 months from the current time period after applying a reasonable, market centric, multiple and discount rate which takes into account the competitive landscape and probability of success. We assume profitability in 2018, with a fully diluted estimated EPS of $4.41. We apply a 25x multiple that is in line with the industry average of profitable biotech companies based on 2015E EPS estimates. We discount back by 30%, which takes into consideration the clinical, technological, regulatory, and commercial risks associated with the development and commercial success potential of Otonomy's assets.

Exhibit 6: Otonomy Discounted Earnings Model

Diluted	$4.41
PE	25
Discount Years	3
Discount Rate	30.0%
Valuation	$50.14

Forward P/E Ratio	Discount Rate 55.0%	50.0%	45.0%	40.0%	35.0%	30.0%	25.0%	20.0%
15x	$ 17.75	$ 19.58	$ 21.68	$ 24.09	$ 26.86	$ 30.08	$ 33.84	$ 38.25
20x	23.66	26.11	28.90	32.11	35.82	40.11	45.12	51.00
25x	29.58	32.64	36.13	40.14	44.77	50.14	56.40	63.74
30x	35.50	39.16	43.36	48.17	53.72	60.16	67.68	76.49
35x	41.41	45.69	50.58	56.20	62.68	70.19	78.96	89.24
40x	47.33	52.22	57.81	64.23	71.63	80.22	90.23	101.99
45x	53.24	58.75	65.04	72.26	80.59	90.25	101.51	114.74
50x	59.16	65.27	72.26	80.28	89.54	100.27	112.79	127.49
55x	65.07	71.80	79.49	88.31	98.49	110.30	124.07	140.24

Sources: SunTrust Robinson Humphrey

Next we use a Risk Adjusted Discounted Cash Flow (DCF) model to discount the projected future cash flows to reach a target price of $46.99. From our revenue buildup model, we estimate cash

flow of $343 million to the company in 2025. We employ an industry standard discount rate of 12% and a perpetual growth rate of 0% to be conservative.

Exhibit 7: Otonomy DCF Model

Final year FCF	343
Perpetual Growth Rate	0
Terminal Value	**2,862**
Discount Factor	0.29
Present Value of Terminal Value	**832**
Present Value of Cash Flows	**797**
Enterprise Value	**1,629**
Add: Net cash	165
Market Value	**1,794**
Fully Diluted Shares Outstanding	26.7
Value per Fully Diluted Share	**$67.13**
Average probability of success	*70%*
Risk Adjusted Value per Fully Diluted Share	**$46.99**

Sources: SunTrust Robinson Humphrey

A third methodology we employ, Clinical Net Present Value (NPV), is based on peak revenue for AuriPro and OTO-104 to Otonomy in the out-year of our financial model which is 2025. We estimate 2025 revenue of approximately $134M for AuriPro and $693M for OTO-104 booked to Otonomy. We assign a success probability of 90% for AuriPro and 60% for OTO-104 based on the demonstrated clinical profile and technology validation to date. We assign 100% for the overall economics that Otonomy will realize as all of the revenue in the calculation is booked by Otonomy. Taking into account the number of current shares outstanding, we obtain a clinical NPV of $42.57 for AuriPro and OTO-104.

Exhibit 8: Otonomy Clinical NPV Model

Drug name	Indication	Status	Launch	Success	Peak Sales (US$m)	Economics	Profitability	NPV (US$)
AuriPro	Otitis media patients undergoing TTP surgery	Finished PIII	2016	90%	134	100%	90%	9.57
OTO-104	Ménière's disease	Finished Ph1b	2017	60%	693	100%	90%	33.00
							Total	**42.57**

Sources: SunTrust Robinson Humphrey

We further use a Comparable Company Analysis, which is composed of biotech companies with late-stage clinical assets. As few companies are focused on the otology field as mentioned previously. We choose comparators from diverse therapeutic areas:

- Ophthalmic disorders where formulation technologies are more frequently used
- Anti-infectives to which AuriPro's active ingredient ciprofloxacin belongs
- Platform technology companies

We then compare the mean enterprise value of the comparable universe ($971.3MM) to that of Otonomy ($457.7MM). The comparison demonstrates that Otonomy shares are currently trading at a discount of 53% to the mean value of the comparable universe.

Exhibit 9: Otonomy Comparative Analysis

Group	Company	Ticker	Enterprise Value ($MM)	Price 3-Feb-15	Shares Out (MM)	Market Cap ($MM)	Cash ($MM)	Debt ($MM)	Revenue ($MM)	Indication	Stage of Most AdvancedAsset
ophthalmology	Avalanche Biotechnologies Inc	AAVL	806.0	39.7	24.5	971.4	165.3	0.0	0.5	Wet AMD	Ph I/II
	Aerie Pharmaceuticals, Inc.	AERI	623.7	28.0	24.0	670.6	171.1	124.1	0.0	Glaucoma	Ph III
	Ophthotech Corp.	OPHT	1,484.1	56.3	33.7	1,892.9	408.8	0.0	0.0	Wet AMD	Ph III
Anti-infective	Cempra, Inc.	CEMP	1,106.9	27.7	42.0	1,164.6	74.2	16.5	7.8	Antibiotic	Ph III
	Tetraphase Pharmaceuticals, Inc.	TTPH	1,060.7	36.4	30.7	1,114.7	56.0	2.0	10.5	Antibiotic	Ph III
	Chimerix, Inc.	CMRX	1,275.0	40.1	36.5	1,463.0	188.4	0.4	4.4	Antiviral	Ph III
	Achillion Pharmaceuticals, Inc.	ACHN	1,362.0	14.9	100.2	1,488.7	126.6	0.0	0.0	Antiviral	Ph II
Platform technology	Nektar Therapeutics	NKTR	1,869.6	14.6	128.4	1,880.4	261.6	250.8	148.9	multiple	Approved
	ImmunoGen, Inc.	IMGN	549.1	7.6	85.9	655.7	106.6	0.0	59.9	multiple	Approved
	Average		**971.3**			**1,255.8**					
	Otonomy, Inc.	**OTIC**	**457.7**	$29.20	24.1	**703.7**	246.0	0.0	0	Ear diseases	Ph III

Source: SunTrust Robinson Humphrey, FactSet

Investment Risks

The primary investment risks of Otonomy include the following:

Regulatory risk of AuriPro: While AuriPro's Phase III clinical trials successfully met their clinical endpoints and we believe the drug is likely to be approved, there is no guarantee that the FDA will approve the product. One data point that sticks out is the secondary endpoint that evaluated the cumulative proportion of patients considered treatment failures due to the observation of otorrhea. A significant difference in failure rate was observed between the two sham groups (16% vs. 28%). Although the reduction in the rate of otorrhea in the AuriPro arm was statistically significant in both trials ($p=0.038$ and $p<0.001$), the FDA may have questions regarding the data.

Commercial risk of AuriPro: Otonomy has not previously launched or marketed a commercial product. In order to successfully commercialize AuriPro, Otonomy needs to secure payer coverage and AuriPro needs to be included in the formulary list of hospital outpatient facilities and ambulatory surgery centers. This decision will be based on not only the clinical data, but also on the pricing of AuriPro, which is currently an unknown variable. Should AuriPro fail to be covered, we expect it will significantly diminish AuriPro's commercial prospects.

Otonomy needs to build a sales and marketing infrastructure which would include sales reps, medical science liaison (MSL), territory managers, etc., to commercialize AuriPro. According to Otonomy, the Company expects to launch AuriPro with 30 to 40 reps (with a maximum of 80 reps when including reps for OTO-104).

Clinical risk of OTO-104: The OTO-104 Phase Ib study demonstrated some therapeutic signals in reducing vertigo frequencies. However, the study was not designed and powered to do so, and the results may not translate to the current Phase IIb trial.

Technology risk of sustained exposure formulation technology: In theory, the sustained exposure formulation technology should be applicable to other ear indications. Preclinical studies have demonstrated the possibility of co-formulating Poloxamer 407 (P407) with different therapeutic agents. However, different drugs will change the properties of co-polymers, including transition temperature and bioadhesive force, etc., which could make the co-formulation of drugs with P407 more difficult to achieve or even impossible.

Competition risk: A handful of other companies are developing therapeutics in the otology field, with some examples listed in the exhibit that follows. We believe Otonomy's clinical assets with sustained exposure formulation technology offer appealing treatment options to physicians and patients alike. However competing therapeutics may have a first-to-market advantage if they launch products earlier or have competitive pricing/reimbursement coverage.

Exhibit 10: Select Companies Developing Otology Therapeutics

Company	Product	Indication	Stage
Novartis (Alcon)	Ciprodex Otic	Middle ear and outer ear infections	Approved
SALVAT	ciprofloxacin/fluocinolone acetonide	Acute Otitis Media with Tympanostomy tubes (AOMT)	NDA
Synphora AB	latanoprost	Ménière's disease	Phase II/III
Auris	AM-111	Ménière's disease	Pre-IND
Auris	AM-111	Acute inner ear (sensorineural) hearing loss (ASNHL)	Ph III
Auris	AM-101	Tinnitus	Phase III
Autifony	AUT00063	Tinnitus	Phase II
Kyorin Pharmaceuticals	neramexane	Tinnitus	Phase II

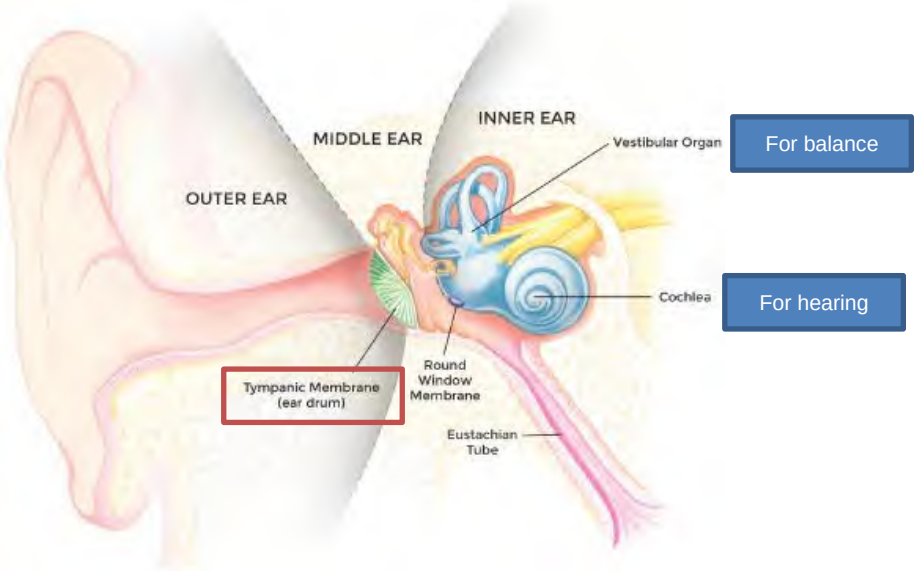
Source: SunTrust Robinson Humphrey

Listen Up: Ear Anatomy And Associated Problems

Ear Structure: Outer, Middle, Inner Ear

The field of otology is a sub-specialty within otolaryngology that focuses on diseases and disorders of the ear. The three main parts of the ear include the outer, middle and inner ear.

Exhibit 11: Ear Structure



Source: Otonomy, SunTrust Robinson Humphrey

Outer Ear

The outer ear is the external region up to the tympanic membrane (a.k.a., ear drum). Infection or inflammation in this region includes acute otitis externa, or swimmer's ear.

Middle Ear

The middle ear is the portion of the ear internal out to the eardrum, and external to the oval window of the inner ear. The middle ear contains three ossicles (bones) transferring vibrations from the eardrum into waves in the fluid and membranes of the inner ear. Infection or inflammation in this area, known as otitis media, is common in young children due to the immaturity of their immune systems.

Inner Ear

The inner ear is the most inner part of the ear, which contains sensory organs for hearing and balance. Disorders associated with this region include balance disorders, such as Ménière's disease, as well as tinnitus and hearing loss.

Exhibit 12: Common Ear Indications

Ear Indication	Cause	Symptom
Otitis Media	an infection of the middle ear	experience pain deep in the ear and/or fluid draining from the ear
Ménière's Disease	not well understood; may due to abnormal volume or composition of fluid in the inner ear	mainly spontaneous episodes of vertigo
Serious Ear Infection	an infection in ear canal, outer ear and the skin around ears	redness and swelling of the outer ear and the surrounding skin
Mastoiditis	an infection of the bone behind the ear, or from an enlarged lymph node.	have a headache-type pain and redness behind ears or tenderness when touching the bone behind ears
Ruptured Eardrum	an infection of the middle ear	thick pus-filled or bloody drainage from the ear canal that started after a sharp, sudden pain
Otitis Externa	an infection of the ear canal that is also called swimmer's ear	ear swollen, and does it itch or hurt when pulingl on ear or earlobe
Temporomandibular Joint (TMJ) Syndrome	a disorder that affects the jaw joint	jaw joint "crack" when chewing or openning mouth, or feel tenderness in the jaw
Blocked Eustachian Tube	colds and the flu often lead to this condition	hear fluid in ear, and feel pressure or stuffiness that can't be cleared with coughing, yawning or swallowing, and have cold
Ear Pain Due To Tooth Problem	a tooth problem can radiate pain to the ear on the same side	have tooth pain on the same side as the ear pain when bite down
Barotrauma	also called airplane ear, which is caused by changes in altitude and air pressure	ear pain start during an airplane flight or right after traveled on an airplane
Serous Otitis	a buildup of fluid in the ear canal	the affected person is a child who doesn't have ear pain or redness but is having problems hearing
Ceruminosis	a buildup of wax in the ear canal	the affected person is a child who doesn't have ear pain or redness but is having problems hearing

Source: FamilyDoctors.org, SunTrust Robinson Humphrey

It is estimated that more than 50 million people in the U.S. are affected by otic disorders and that approximately 20 million patients each year seek treatments for the most common conditions including ear infections, balance disorders, tinnitus and hearing loss. Therefore, ear indications represent a sizable market opportunity from a therapeutics development standpoint.

- The American Academy of Otolaryngology – Head and Neck Surgeons reports that approximately 2.5 million people in the U.S. are affected by acute otitis externa each year.
- The National Institute on Deafness and Other Communications Disorders (NIDCD) reports that three out of every four children experience otitis media before three years of age.
- According to the NIDCD, approximately 615,000 individuals in the U.S. are currently diagnosed with Ménière's disease and that 45,500 cases are newly diagnosed each year.

- According to the American Tinnitus Association, approximately 16 million patients in the U.S. have severe tinnitus symptoms and seek medical attention, and about two million patients cannot function on a normal day-to-day basis.
- According to the NIDCD, approximately 36 million adults report some degree of hearing loss. According to Hearing Loss Association of America, about 20% of adults in the U.S, or 48 million people, report some degree of hearing loss.

Current Treatment Options Include Anti-Infectives And Devices

Outer Ear

Outer ear infections are typically treated with antibiotic ear drops and, in more severe cases, oral antibiotics. For most cases of otitis externa (swimmer's ear), doctors will prescribe eardrops that have some combination of the following ingredients, depending on the type and seriousness of the infection:

- Acidic solution to help restore ear's normal antibacterial environment
- Steroid to reduce inflammation
- Antibiotic to fight bacteria
- Antifungal medication to fight an infection caused by a fungus

In general, antibiotic ear drops are effective in resolving infections of the outer ear. However, treatment involves burdensome multi-dose, multi-day regimens, and non-compliance with such regimens may lead to treatment failure and antibiotic resistance.

Middle Ear

Middle ear infections are typically treated with oral antibiotics. However, this approach may lead to an increased risk of antibiotic resistance.

Patients with persistent effusion or recurrent infections may be referred to an ENT physician for TTP surgery, during which a small tympanostomy tube is inserted through the eardrum to ventilate the middle-ear cavity to prevent the accumulation of fluid in the middle ear.

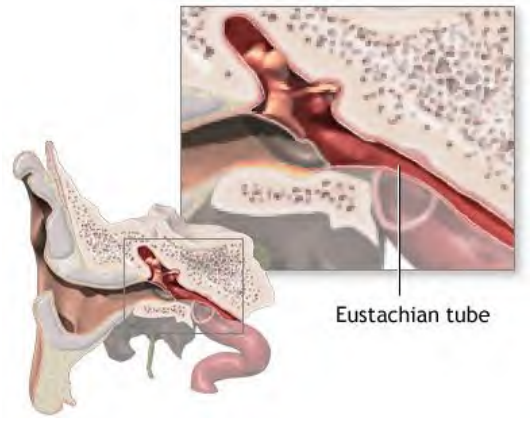
Tympanostomy tubes are frequently insufficient to treat the middle-ear effusion, therefore antibiotic ear drops are routinely used off-label during and following the procedure. Similar to the outer ear antibiotic treatment, such ear drop treatments involve multi-dose, multi-day regimens. This can be more difficult to comply with especially among pediatric patients who represent the bulk of the TTP patient population (two-thirds of patients are at or under five years of age).

Inner Ear

Inner ear disorders, such as Ménière’s disease, acoustic neuroma, drug-induced ototoxicity, purulent labyrinthitis, vestibular neuronitis, etc., are an emerging field for drug development. Local drug (e.g., antibiotics or steroids) delivery via direct injection through the ear drum (intra-tympanic [IT] injection) has been demonstrated as a viable approach to address many inner ear disorders. Relatively high drug concentrations can be achieved in the inner ear and systemic drug exposure is low through IT injections.

A limitation of IT injection of solution-based therapeutics is the rapid elimination from the middle ear cavity down the Eustachian tube (see exhibit below) when patients move their ears when talking or swallowing. In general, injections need to be conducted in a physicians' office and require anesthesia, which can be burdensome to patients and physicians.

Exhibit 13: Inner-Ear Structure



Source: U.S. National Library of Medicine

Overall, we believe there is a significant unmet medical need for improved otic drug delivery, given the compliance challenges of multi-dose and multi-day ear drop regimens, and the issue of rapid drug elimination in the inner ear via an IT injection of therapeutic solutions.

Exhibit 14: Pros And Cons Of Current Ear Disease Treatments

Area	Indication	Treatment	Examples	Pros	Cons
Outer ear	Infection	Antibiotic ear drops	CIPRODEX, Cirpo HC, Cortisporin	Inexpensive	multi-dose, multi-day regimens
Middle ear	Infection	oral antibiotics	Amoxicillin	Convenient	antibiotic resistance
	Otitis media, etc.	TTP surgery	/	physically prevent the accumulation of fluid	frequently insufficent treatment; less convenient than other
Inner ear	Meniere's Disease, etc.	Intratympanic injection of therapeutic	Gentamicin, steroid	High drug concentration achievable locally	Rapid elimination of drugs, less convenient

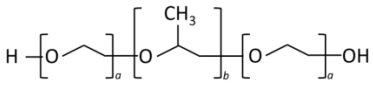
Source: SunTrust Robinson Humphrey

Otonomy Differentiates With A Sustained-Exposure Formulation Technology

Otonomy has developed a proprietary formulation technology that provides sustained drug exposure in the middle or inner ear from a single local administration. The technology utilizes a thermo-sensitive polymer, poloxamer 407 (P407), which is able to transform from a liquid to a gel at body temperature. P407 is mixed with drug microparticles to form a suspension/solution that is retained in the middle ear cavity for an extended period of time. The polymer is ultimately excreted via the body fluid. This prolonged residence time provides a high and sustained drug exposure in the middle and inner ear.

What Is Poloxamer 407?

Exhibit 15: Poloxamer 407 Structure



Source: SunTrust Robinson Humphrey

P407 is a hydrophilic non-ionic surfactant belonging to the general class of copolymers known as poloxamers. P407 is a triblock (three blocks) copolymer consisting of a central hydrophobic block of polypropylene glycol (PPG) flanked by two hydrophilic blocks of polyethylene glycol (PEG). The approximate length of the two PEG blocks is 101 repeat units while the approximate length of the PPG block is 56 repeat units. The solution-to-gel transition temperature increases when Poloxamer 407 concentration decreases.

What Is The Purpose Of Poloxamer 407?

Most of the common uses of poloxamer 407 are related to its surfactant properties. It is widely used in cosmetics for dissolving oily ingredients in water. It can also be found in multi-purpose contact lens cleaning solutions, where its purpose there is to help remove lipid films from the lens. It can also be found in some mouthwashes.

In therapeutics, P407 is mostly used as an excipient. Many *in vitro* release studies have been conducted to deliver various therapeutic agents with P407 via different routes of administration including topical, rectal, ophthalmic, subcutaneous, etc.

Exhibit 16: *In Vitro* Release Studies Conducted with Poloxamer 407 (P407)

Drug	Concentration of P407	Route of Administration
Diclofenac, P407	15%	Rectal
Flurbiprofen P407	20-30%	Topical
Human epithelial growth factor included in cyclodextrin complex, P407	16%	Ophthalmic
Ibuprofen (or ketoprofen), P407	25%	Topical
Ibuprofen included in a liposomal formulation, P407	25%	Epidural
Insulin included in nanoparticles, P407	20-30%	Subcutaneous
Insuline + enhancers, P407	20%	Sublingual
Interleukin-2, P407	30/35%	Intraperitoneal
Ketoprofen, P407	20/25/30%	Topical
Lidocaine microparticle, P407	25%	Intra-sciatic nerve
Lidocaine P407	20/25/30%	Injectable
Melanotan-I, P407	25%	Peritoneal
Mitomycin C, P407	20/25/30%	Intraperitoneal
Oligonucleotide pdT 16 within liposomes, P407	20/27%	Ophthalmic
Paclitaxel, P407	20%	Intratumoral
Pilocarpine, P407	25%	Ophthalmic
Pilocarpine, P407	25%	Ophthalmic
Piroxicam + enhancers, P407	10-25%	Topical
Propanolol , P407	15%	Rectal
Quinine, P407	18%	Rectal
Short-chain fatty acids, P407	17-20%	Rectal
Timolol, P407	15/20/25%	Ophthalmic
Triamcinolone acetonide P407	20%	Sublingual
Vancomycin P407	25%	Injectable

Source: SunTrust Robinson Humphrey, revised from Pharm Res. 2006 Dec;23(12):2709-28

In October 2011, the FDA approved Sanofi's LeGoo, a P407-based gel that allows surgeons to temporarily stop blood flow during surgery so that they can join blood vessels without clamps or elastic loops.

LeGoo is comprised 20% (weight percent in saline) of purified P407 which dissolves in blood and is excreted in urine. At room temperature it is a viscous but injectable liquid, and it transitions to a temporary self-forming polymeric plug at body temperature. We believe this change from solution to gel is similar to what is observed in AuriPro.

In support of approval of the pre-marketing application, the FDA reviewed studies showing that LeGoo is biocompatible and non-toxic. The FDA also looked at data from a clinical trial of 110 patients undergoing bypass surgery without stopping the heart (off pump coronary artery bypass). Investigators found that LeGoo is as safe and effective as vessel loops, devices commonly used to stop blood flow during coronary bypass surgery.

Is P407 Safe?

P407 is generally considered a safe product. Below is a summary of adverse events of LeGoo's pivotal trial comparing LeGoo with conventional vessel loops for temporary coronary artery occlusion during off-pump coronary artery bypass surgery. Although LeGoo was approved as a medical device, we believe these data can provide evidence to increase our confidence in P407's overall safety profile.

Exhibit 17: LeGoo's Adverse Events As Reported In The Pivotal Study By Sanofi

System Organ Class	LeGoo (N=56)		Control (N=54)	
	Events	Patients with Events	Events	Patients with Events
No Adverse Events	-	13 (23.2%)	-	21 (38.9%)
At Least One Adverse Event	139	43 (76.8%)	115	33 (61.1%)
Blood and lymphatic system disorders	5	5 (8.9%)	3	3 (5.6%)
Cardiac disorders	37	29 (51.8%)	21	19 (35.2%)
Endocrine disorders	0	0 (0%)	1	1 (1.9%)
Gastrointestinal disorders	13	9 (16.1%)	6	5 (9.3%)
General disorders and administration site conditions	16	11 (19.6%)	10	9 (16.7%)
Infections and infestations	8	7 (12.5%)	5	5 (9.3%)
Injury, poisoning and procedural complications	11	10 (17.9%)	14	11 (20.4%)
Investigations	2	2 (3.6%)	5	5 (9.3%)
Metabolism and nutrition disorders	4	3 (5.4%)	7	5 (9.3%)
Musculoskeletal and connective tissue disorders	2	2 (3.6%)	0	0 (0%)
Nervous system disorders	5	4 (7.1%)	1	1 (1.9%)
Psychiatric disorders	7	6 (10.7%)	6	6 (11.1%)
Renal and urinary disorders	3	3 (5.4%)	6	4 (7.4%)
Respiratory, thoracic and mediastinal disorders	20	14 (25%)	21	14 (25.9%)
Skin and subcutaneous tissue disorders	3	3 (5.4%)	1	1 (1.9%)
Surgical and medical procedures	0	0 (0%)	1	1 (1.9%)
Vascular disorders	3	2 (3.6%)	7	5 (9.3%)

Source: LeGoo U.S. website

Exhibit 18: Serious Adverse Events Of LeGoo Reported In The Pivotal Study

System Organ Class	LeGoo (N=56)		Control (N=54)	
	Events	Subjects with Events	Events	Subjects with Events
At Least One Serious Adverse Event	19	16 (28.6%)	11	8 (14.8%)
No Adverse Events	0	40 (71.4%)	0	46 (85.2%)
Cardiac disorders	9	9 (16.1%)	3	2 (3.7%)
General disorders and administration site conditions	3	3 (5.4%)	1	1 (1.9%)
Infections and infestations	0	0 (0%)	2	2 (3.7%)
Injury, poisoning and procedural complications	7	6 (10.7%)	3	3 (5.6%)
Investigations	0	0 (0%)	1	1 (1.9%)
Respiratory, thoracic and mediastinal disorders	0	0 (0%)	1	1 (1.9%)

Source: LeGoo U.S. website

What Are The Benefits Of Using P407 For Otic Diseases?

Compared to conventional ear drops and other injection therapeutics, Otonomy's sustained-exposure technology offers potential benefits that include:

- Convenient dosing regimen
  - Provides full course of treatment via a single local administration
  - Increases patient compliance by avoiding multi-dose, multi-day treatment regimens
  - Permits simple office-based administration by ENTs
- Local delivery
  - Achieves higher drug concentrations and drug exposure in the target location and minimizes systemic exposure
  - Provides sustained drug levels in the middle ear compared to the pulsatile drug levels observed with antibiotic ear drops

Is Seeing Really Believing? Listen Hear For More About The Ear

There has been a rapid growth and advancement of intravitreal treatments for the eyes (an injection into the vitreous, the jelly-like substance inside the eye), which, similar to the ears, are a protected sensory organ. Ophthalmologists have demonstrated that intravitreal injection is a safe and efficacious way of treating visual disorders, such as age-related macular degeneration (AMD). Intravitreal medications used to treat wet AMD include bevacizumab (Avastin), ranibizumab (Lucentis), pegaptanib (Macugen), and aflibercept (Eylea). The AMD space is a multi-billion dollar market.

Prior to 2001, the number of intravitreal injections (CPT code 67028) was relatively stable at approximately 4,500 per year, primarily for the treatment of end-ophthalmitis. In 2002, the number of injections tripled to 15,000 (largely triamcinolone) and by 2004 it was 83,000. The breakthrough year was 2005 with growth to 252,000 following the first reports on pegaptanib (Macugen), bevacizumab (Avastin) and ranibizumab (Lucentis). By 2008, more than 1,000,000 injections were performed. In 2011, aflibercept became available and total intravitreal injections reached 2,000,000. In 2012, 2,354,753 were reported.

Similar to ophthalmologists, ENTs are increasingly using locally administered drugs to treat middle- and inner-ear conditions. We believe intra-tympanic injections can become widely adopted in the

future, similar to intravitreal injections to eyes. In our opinion, Otonomy's sustained exposure technology makes it a more powerful tool to treat otic diseases.

Can Otonomy Use The Polymer Freely?

P407 is a generic chemical reagent and as such has no composition of matter patent protection surrounding its use. This is analogous to using pharmaceutical excipients, such as sugars (e.g., cellulose, corn starch, xylitol), amino acids (e.g., glycine), or other organic or inorganic reagents.

Otonomy exclusively licensed patents from the University of California for the composition and therapeutic use in current clinical candidates and future ones. Otonomy also has solely owned patents covering composition of matter and methods of use. Below is a summary of all the patents owned or co-owned by Otonomy in the U.S. We will discuss the Otonomy's intellectual property estate in more detail later in this report.

Exhibit 19: Otonomy Patents In The U.S.

Title	Patnet Or Application Number	Type	Filed	Issued	Assignees
Controlled Release Corticosteroid Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8030297	Grant	5/14/2009	10/4/2011	Otonomy, Inc., The Regents of the University of California
Controlled Release Immunomodulator Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8648119	Grant	5/26/2009	2/11/2014	Otonomy, Inc., The Regents of the University of California
Controlled Release Aural Pressure Modulator Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8846770	Grant	6/17/2009	9/30/2014	Otonomy, Inc., The Regents of the University of California
Colloidal Suspensions Comprising A Therapeutic Agent And Squalene	Patent number: 8771746	Grant	6/18/2009	7/8/2014	Otonomy, Inc.
Controlled Release Cytotoxic Agent Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8349353	Grant	6/29/2009	1/8/2013	Otonomy, Inc., The Regents of the University of California
Controlled Release Auris Sensory Cell Modulator Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8496957	Grant	7/16/2009	7/30/2013	Otonomy, Inc, The Regents of the University of California
Controlled Release Antimicrobial Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8318817	Grant	7/20/2009	11/27/2012	Otonomy, Inc., The Regents of the University of California
Controlled Release Compositions For Modulating Free-Radical Induced Damage And Methods Of Use Thereof	Patent number: 8784870	Grant	7/21/2009	7/22/2014	Otonomy, Inc., The Regents of the University of California
Controlled Release Ion Channel Modulator Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8399018	Grant	7/21/2009	3/19/2013	Otonomy, Inc., The Regents of The University of California
Controlled Release Auris Sensory Cell Modulator Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8575122	Grant	4/26/2010	11/5/2013	Otonomy, Inc.
Controlled Release Corticosteroid Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8546363	Grant	7/15/2010	10/1/2013	Otonomy, Inc.
Controlled Release Corticosteroid Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8828980	Grant	7/25/2011	9/9/2014	Otonomy, Inc., The Regents of the University of California
Controlled Release Corticosteroid Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8680083	Grant	7/25/2011	3/25/2014	Otonomy, Inc., The Regents of the University of California
Controlled Release Corticosteroid Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8680082	Grant	7/25/2011	3/25/2014	Otonomy, Inc., The Regents of the University of California
Controlled Release Corticosteroid Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8658626	Grant	7/25/2011	2/25/2014	Otonomy, Inc., The Regents of the Univeristy of California
Controlled-Release Cns Modulating Compositions And Methods For The Treatment Of Otic Disorders	Patent number: 8852626	Grant	3/20/2012	10/7/2014	Otonomy, Inc., The Regents of the University of California
Auris Formulations For Treating Otic Diseases And Conditions	Application number: 20090306225	Application	4/21/2009	12/10/2009	Otonomy, Inc., The Regents of the University of California
Controlled Release Corticosteroid Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20100009952	Application	5/14/2009	1/14/2010	Otonomy, Inc., The Regents of the University of California
Controlled Release Immunomodulator Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20090297533	Application	5/26/2009	12/3/2009	Otonomy, Inc., The Regents of the Univeristy of California
Controlled Release Aural Pressure Modulator Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20100004225	Application	6/17/2009	1/7/2010	Otonomy, Inc., The Regents of the Univeristy of California
Controlled-Release Cns Modulating Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20090325938	Application	6/29/2009	12/31/2009	Otonomy, Inc., The Regents of the Univeristy of California
Controlled Release Cytotoxic Agent Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20090324552	Application	6/29/2009	12/31/2009	Otonomy, Inc., The Regents of the Univeristy of California
Controlled-Release Apoptosis Modulating Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20100016218	Application	7/9/2009	1/21/2010	Otonomy, Inc., The Regents of the Univeristy of California
Controlled Release Auris Sensory Cell Modulator Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20100015263	Application	7/16/2009	1/21/2010	Otonomy, Inc., The Regents of the Univeristy of California
Controlled Release Antimicrobial Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20100036000	Application	7/20/2009	2/11/2010	Otonomy, Inc., The Regents of the Univeristy of California
Controlled-Release Otic Structure Modulating And Innate Immune System Modulating Compositions And Methods For	Application number: 20100021416	Application	7/20/2009	1/28/2010	Otonomy, Inc., The Regents of the Univeristy of California
Controlled Release Compositions For Modulating Free-Radical Induced Damage And Methods Of Use Thereof	Application number: 20100022661	Application	7/21/2009	1/28/2010	Otonomy, Inc., The Regents of the Univeristy of California
Controlled Release Delivery Devices For The Treatment Of Otic Disorders	Application number: 20100016450	Application	7/21/2009	1/21/2010	Otonomy, Inc., The Regents of the Univeristy of California
Controlled Release Ion Channel Modulator Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20100015228	Application	7/21/2009	1/21/2010	Otonomy, Inc., The Regents of the Univeristy of California
Controlled Release Auris Sensory Cell Modulator Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20100273864	Application	4/26/2010	10/28/2010	Otonomy, Inc.
Controlled Release Corticosteroid Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20110008456	Application	7/15/2010	1/13/2011	Otonomy, Inc.
Modulation Of Gel Temperature Of Poloxamer-Containing Formulations	Application number: 20120277199	Application	10/19/2010	11/1/2012	Otonomy, Inc.
Controlled Release Corticosteroid Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20110319377	Application	7/25/2011	12/29/2011	Otonomy, Inc., The Regents of the Univeristy of California
Controlled Release Corticosteroid Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20110319375	Application	7/25/2011	12/29/2011	Otonomy, Inc., The Regents of the University of California
Controlled Release Corticosteroid Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20110319374	Application	7/25/2011	12/29/2011	Otonomy, Inc., The Regents of the University of California
Controlled Release Corticosteroid Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20110319373	Application	7/25/2011	12/29/2011	Otonomy, Inc., The Regents of the University of California
Prevention Of And Recovery From Drug-Induced Ototoxicity	Application number: 20130045957	Application	2/16/2012	2/21/2013	Otonomy, Inc.
Controlled-Release Cns Modulating Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20120190671	Application	3/20/2012	7/26/2012	Otonomy, Inc., The Regents of the Univeristy of California
Controlled Release Antimicrobial Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20130116210	Application	10/4/2012	5/9/2013	Otonomy, Inc., The Regents of the Univeristy of California
Controlled Release Ion Channel Modulator Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20130150410	Application	2/7/2013	6/13/2013	Otonomy, Inc., The Regents of the Univeristy of California
Controlled Release Antimicrobial Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20130216609	Application	3/21/2013	8/22/2013	Otonomy, Inc., The Regents of the Univeristy of California
Controlled Release Auris Sensory Cell Modulator Compositions And Methods For The Treatment Of Otic Disorders	Application number: 20140018395	Application	6/26/2013	1/16/2014	The Regents of the University of California, Otonomy, Inc.
Controlled Release Compositions For Modulating Free-Radical Induced Damage And Methods Of Use Thereof	Application number: 20140243425	Application	5/1/2014	8/28/2014	Otonomy, Inc., The Regents of the University of California

Source: USPTO, SunTrust Robinson Humphrey

AuriPro During TTP Surgery – The Lead Indication

Tympanostomy Tube Placement (TTP) Surgery Is Common For Children

Tympanostomy tube placement (TTP), also known as ear tube insertion, is a surgery that places a pressure equalizer tube into the tympanic membrane. This surgical procedure drains middle ear fluid to prevent hearing loss and reduce the risk of ear infections. In the U.S., ear tube insertion is the most frequently performed otologic surgical procedure in children: approximately one million TTP surgeries are performed each year in the U.S., of which more than 50% of the patients are age three and under, and 75% are five and under.

Various sizes and shapes of ear tubes are available which are determined by the surgeon on the basis of the underlying pathophysiology, the tube's specific characteristics, the number of previous sets of tubes placed, and the surgeon's preference. Alternatives to ear tube insertion are myringotomy (a surgery to create a tiny incision in the eardrum) and tympanocentesis (a surgery where a doctor uses a special needle with a tube attached to remove fluid from the middle ear).

The most common indication for ear tube insertion is persistent otitis media with effusion (OME), or serous otitis media (SOM), that does not resolve after three months of clinical observation or does not improve with antibiotic therapy. TTP promotes the drainage of the middle ear fluid, which can cause speech and language delay and also predisposes the patient to recurrent infections.

Another indication for ear tube insertion is acute otitis media (AOM) that is refractory to antibiotic therapy. TTP permits easy delivery of topical antibiotic drops to the middle ear space. Additional indications requiring ear tube insertion include complications of AOM, such as meningitis, facial nerve palsy, and otomastoiditis.

Antibiotic ear drops are generally prescribed for three to seven days to treat middle ear inflammation and maintain ear tube patency post-surgery. Children who undergo TTP are followed every six to twelve months until the tubes have extruded and the episodes of otitis media have resolved.

Currently No FDA Approved Drugs For Effusions During TTP Surgery

Antibiotics are frequently used to treat otic infections. According to Otonomy, the estimated annual volume of antibiotics used to treat otic infections is approximately 21 million units in the U.S., of which 13 million units are oral antibiotics. The remaining eight million units consist of antibiotic ear drops. FDA-approved indications for antibiotic ear drops include acute otitis externa and AOMT. Antibiotic ear drops are also used off-label during and following TTP surgery and for various other middle ear conditions. In total, it is estimated that approximately 2.3 million antibiotic ear drop units are used each year for the middle ear.

There are approximately one million TTP surgeries performed each year in the U.S. and antibiotic ear drops are used in nearly all cases. Despite their routine use, no antibiotic ear drop has received FDA approval for this indication. Current antibiotic ear drop products are used off-label and require multi-dose, multi-day regimens. For example, Ciprodex Otic’s treatment regimen is twice daily dosing for seven days and ofloxacin, a generic antibiotic, is administered three-times daily for ten days. Compliance of this regimen, especially among young children, is challenging.

AuriPro Is A Sustained-Exposure Formulation Of A Generic Antibiotic

AuriPro is a sustained-exposure formulation of the generic antibiotic ciprofloxacin for the treatment of middle ear effusion in pediatric patients requiring TTP surgery. It is expected that a single administration provides a full course of treatment. There are two components to AuriPro: thermosensitive polymer P407 and ciprofloxacin microparticles. Immediately following injection the P407 gels to avoid elimination through the eustachian tube as occurs with solution-based formulations. The gel provides sustained-exposure of ciprofloxacin for one to two weeks while solution based antibiotics are excreted daily.

Ciprofloxacin is a second-generation fluoroquinolone antibiotic for the treatment of bacterial infections. Ciprofloxacin, approved by the U.S. FDA in 1987 is the most widely used of the second-generation quinolone antibiotics that came into clinical use in the late 1980s and early 1990s. Ciprofloxacin is used to treat a wide variety of infections, including infections of bones and joints, endocarditis, gastroenteritis, malignant otitis externa, respiratory tract infections, cellulitis, urinary tract infections, prostatitis, anthrax, and chancroid.

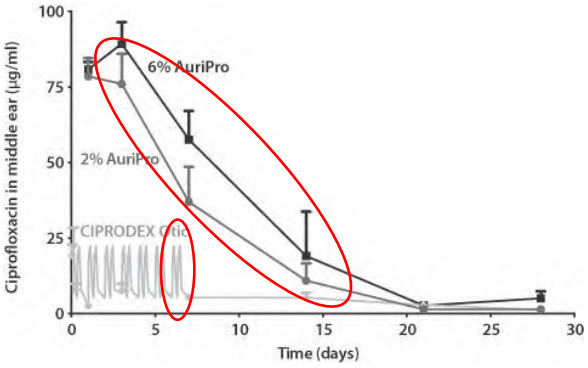
Ciprofloxacin for systemic administration is available as immediate-release tablets, extended-release tablets, an oral suspension, and as a solution for intravenous infusion. It is also available for local administration as eye drops and tear drops. According to a report published by the CDC in 2014, resistance to ciprofloxacin increase significantly from almost absent in 1991 to as high as 25% in 2006 in some cities in the U.S.

AuriPro Preclinical And Clinical Trial Data

Preclinical PK studies

Preclinical pharmacokinetic studies in guinea pigs demonstrated that a single administration of AuriPro provided sustained-exposure of ciprofloxacin in the middle ear for approximately one to two weeks. And for more than one week, local ciprofloxacin concentrations were higher for AuriPro than with Ciprodex Otic treatment. The data were published in March 2014 in Otology & Neurotology. Twice daily administration of Ciprodex Otic ear drops through a tympanostomy tube resulted in drug levels that fluctuated considerably. These data suggest that a single administration of AuriPro provides higher cumulative drug exposure in the middle ear than a multi-dose, multi-day regimen of antibiotic ear drops.

Exhibit 20: Ciprofloxacin Drug Concentration Measured in Middle Ear Following Single Administration of AuriPro vs. Twice Daily Dosing of Ear Drops for 7 Days through Ear Tube



Source: Otonomy

The pharmacological profile of AuriPro was compared to antibiotic ear drops in a standard preclinical model of otitis media. This study demonstrated that a single administration of AuriPro reduced effusion volume and bacterial count to a level comparable to a multi-dose, multi-day regimen with antibiotic ear drops administered through a tympanostomy tube. In a subsequent study, AuriPro demonstrated a reduction in effusion volume and bacterial count even without the placement of a

tube thereby highlighting the potential for AuriPro to address new clinical indications where multi-dose, multi-day antibiotic ear drops are not utilized currently.

The preclinical safety program for AuriPro focused on ototoxicity and middle ear histology compared to multi-dose, multi-day antibiotic ear drops. In general, AuriPro's profile compared favorably to antibiotic ear drop products already approved by the FDA for other otic indications.

Otonomy submitted an IND to the FDA in August 2011 to begin clinical development of AuriPro for the treatment of middle ear effusion in pediatric patients requiring TTP. The company's clinical development strategy was originally presented to the FDA during pre-IND discussions in November 2010. Following Otonomy's Phase Ib clinical trial, Otonomy met with the FDA in September 2013 to review the results from the Phase Ib clinical trial and the Company's development strategy to progress directly from Phase Ib to Phase III, and to discuss the remaining requirements for submission of an NDA under Section 505(b)(2). Based on this meeting, Otonomy concluded that it did not anticipate that the FDA would require conducting additional studies to support a registration filing. However, Otonomy mentioned that it had no assurances from the FDA that additional studies or additional information would not be required to support a registrational filing. Section 505(b)(2) permits the submission of an NDA where some or all of the data required for approval comes from studies not conducted by the applicant and for which the applicant has not obtained a right of reference. This regulatory approval pathway differs from submission of an NDA under Section 505(b)(1) where the data required for approval comes from studies conducted by or for the applicant or for which the applicant has obtained a right of reference.

A summary of AuriPro's Phase III and Phase Ib human clinical studies is shown below. Of note, OTO-201 is the clinical-study name of AuriPro.

Exhibit 21: AuriPro Clinical Study Results

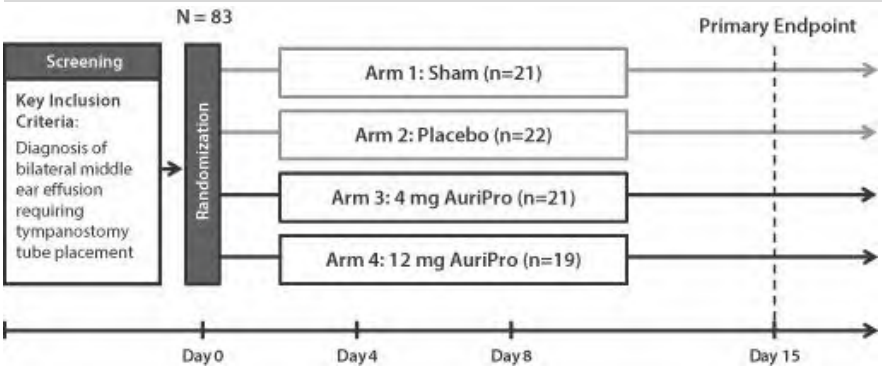
Study	201-201302 and 201-201303			
	OTO-201 for the Treatment of Middle Ear Effusion in Pediatric Subjects Requiring Tympanostomy Tube Placement			
Phase	**III**			
Patient Number	Total 530 (266 for study 302, 264 for study 303)			
Inclusion Criteria	Aged 6 months to 17 years			
Treatment Cohorts	Single, intratympanic injection of 6mg OTO-201			
	Sham (no treatment)			
Primary Endpoint	Efficacy: Cumulative proportion of treatment failures			
Secondary Endpoint	Safety: Evaluation of adverse events, otoscopic exams, audiometry, and tympanometry			
	Efficacy: Microbiological response through end of therapy and study			
Efficacy Data		Sham	AuriPro	Treatment Diff (p value)
	Cumulative proportion of failure	45.1% (79/175)	22.7% (81/357)	-22.4% (p<0.001)
	Per-protocal analysis	38.9% (56/144)	14% (43/307)	-24.9% (p<0.001)
	Otorrhea rate	22.3% (39/175)	7.3% (26/357)	-15% (p<0.05)
Safety Data		Sham (N=174)	AuriPro (N=356)	Treatment Diff
	Total patients with at least one TEAE reported	95 (54%)	189 (53%)	-1%
	Infections and infestations	40 (23%)	85 (24%)	1%
	General disorders and administration site	30 (17%)	62 (17%)	0
	Gastrointestinal disorders	17 (10%)	41 (11%)	1%
	Respiratory, thoracic and mediastinal disorders	23 (13%)	38 (11%)	-2%
	Injury, poisoning and procedural complications	20 (11%)	26 (7%)	-4%
	Ear and labyrinth disorders	11 (6%)	25 (7%)	1%
	Skin and subcutaneous tissue disorders	4 (2%)	13 (4%)	2%
	All others	≤2%	≤2%	/
Study	201-201101			
	OTO-201 for Middle Ear Effusion in Pediatric Subjects Requiring Tympanostomy Tube Placement			
Phase	**Ib**			
Patient Number	83			
Inclusion Criteria	Aged 6 months to 12 years			
Treatment Cohorts	Single intra-operative injection of 4mg OTO-201			
	Single intra-operative injection of 12mg OTO-201			
	Placebo: Single intratympanic injection of vehicle for OTO-201			
	Sham: Simulated single intratympanic injection			
Primary Endpoint	Safety: Evaluation of adverse events, otoscopic exams, audiometry, and tympanometry			
Secondary Endpoint	Efficacy: Clinical Activity, evaluation of physician reported and caregiver reported otorrhea			
	Efficacy: Microbiological eradication of pretherapy bacteria			
Efficacy Data		Sham/Placebo	4mg AuriPro	12mg AuriPro
	Cumulative proportion of failure	47% (20/43)	14% (3/21) (p=0.02)	16% (3/19) (p=0.04)

Source: Company filings, CliniTrials.gov, SunTrust Robinson Humphrey

Phase Ib

In the single Phase Ib clinical trial, two doses (4mg and 12mg) of AuriPro were evaluated compared to P407 vehicle (placebo) and no treatment (sham). A total of 83 patients were enrolled in the clinical trial (21 in the sham group, 22 in the placebo group, 21 in the 4mg AuriPro group, and 19 in the 12mg AuriPro group). According to Otonomy, baseline demographics were balanced with no notable differences between treatment groups. All enrolled patients completed the study, except one patient who was considered lost to follow-up because the patient did not return to the trial site for the final visit.

Exhibit 22: Design of AuriPro Phase Ib Clinical Trial in Pediatric Patients

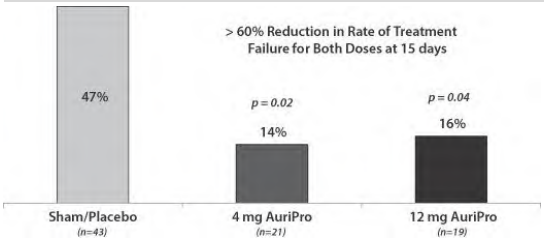


Source: Otonomy

Patients between six months to 12 years of age were eligible for the clinical trial if they presented with effusion in both ears at the time of TTP surgery. Similar to the Phase III trial, treatment was administered in the operating room following the myringotomy and suctioning, and before the placement of the tube. All patients were treated and received tubes in both ears. Follow-up visits occurred on day four, eight, 15 and 29 post surgery.

The primary endpoint for assessing clinical activity of AuriPro was the cumulative proportion of treatment failures defined as otorrhea observed by a blinded assessor from day four through the day 15 visit or use of rescue antibiotics from day one through the day 15 visit, whichever occurred first. Otonomy combined the sham and placebo groups into a single control group (sham/placebo) according to the pre-specified statistical analysis plan since the proportion of treatment failures was similar between the sham and placebo groups. Both 4mg and 12mg doses demonstrated a statistically significant reduction (70.0% for 4mg and 66.0% for 12mg) in the incidence of treatment failures through day 15. However, there was no dose-dependent response between the two AuriPro dosage levels. According to Otonomy, this is expected based on the preclinical pharmacokinetic profile.

Exhibit 23: Phase Ib Clinical Trial Results for AuriPro vs. Sham/Placebo: Cumulative Proportion of Treatment Failures through Day 15



Source: Otonomy

AuriPro was well tolerated in the Phase Ib clinical trial. There were no deaths in the clinical trial and no serious adverse events that were related to AuriPro treatment. Most adverse events were mild or moderate in severity. Treatment with AuriPro was not found to have a negative impact on hearing, tympanometry, or otoscopy (general examination of the ear) and there was no evidence of tube clogging with AuriPro.

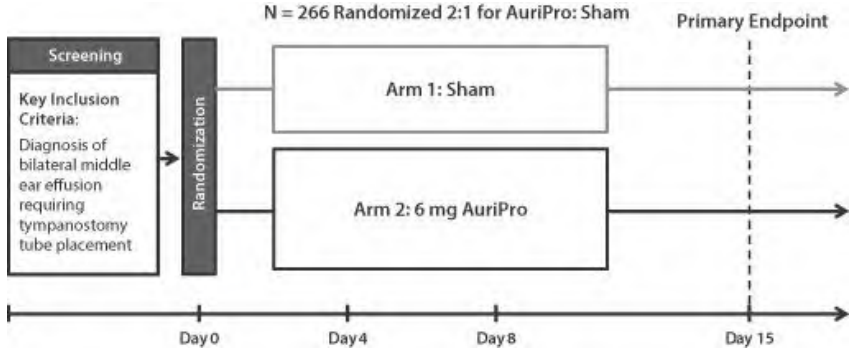
Phase III Clinical Trials (Study 302 and Study 303)

Otonomy has completed two randomized, prospective, double-blind, sham-controlled Phase III clinical trials with identical protocols that enrolled a total of 532 pediatric patients. Data were announced 3Q14: AuriPro met the primary efficacy endpoint, which was reduction in the incidence of treatment failures ($p<0.001$), and AuriPro was well tolerated.

AuriPro reduced the risk of treatment failure, as measured by the occurrence of post-operative otorrhea (drainage) or use of rescue antibiotics (regardless of causes), by an average of 50% across the two trials and the risk of post-operative otorrhea alone by an average of more than 60% across the two trials, in each case as compared to sham. Based on these results, Otonomy plans to submit an NDA for AuriPro to the FDA in 1Q15. If approved, Otonomy plan to commercialize AuriPro in the U.S. beginning in 2016.

In both studies AuriPro was administered as a single IT injection for intra-operative treatment of middle ear effusion in pediatric patients requiring TTP surgery. Each trial consisted of two treatment arms, 6 mg AuriPro and no treatment (sham), with patients randomized 2:1, respectively.

Exhibit 24: Design of AuriPro Phase III Clinical Trials in Pediatric Patients (Two Identical Trials)



Source: Otonomy

The primary endpoint is identical the one in the Phase Ib: the cumulative proportion of treatment failures, which is defined as otorrhea (fluid draining through the tube) observed by a blinded assessor from day four through the day 15 visit, or in the case of using rescue antibiotics from day one through the day 15 visit, whichever occurred first.

Patients between six months and 17 years of age (Phase Ib was six months to 12 years of age) were eligible for the clinical trial if they presented with effusion (fluid) in both ears (bilateral) at the time of TTP surgery.

Enrollment in the AuriPro Phase III clinical trials was initiated in November 2013 and was completed in April 2014. Approximately 60 trial sites in the U.S. and Canada participated, and a total of 532 pediatric patients were enrolled across the two clinical trials. According to Otonomy, baseline patient demographics were reasonably balanced. All enrolled patients completed the day 15 study visit, except for one patient in a sham group and one patient in an AuriPro group who were randomized but not treated.

Exhibit 25: AuriPro Phase III Study Design

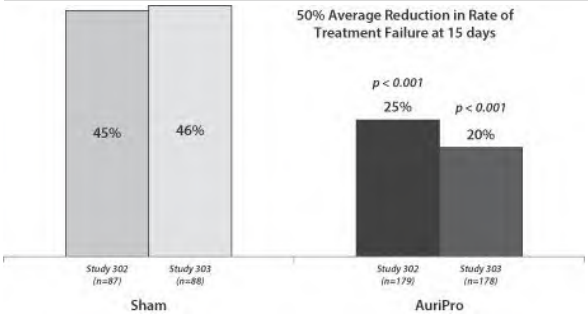
Study	201-201302 and 201-201303 OTO-201 for the Treatment of Middle Ear Effusion in Pediatric Subjects Requiring Tympanostomy Tube Placement
Phase	III
Patient Number	Total 530 (266 for study 302, 264 for study 303)
Inclusion Criteria	Aged 6 months to 17 years Has a clinical diagnosis of bilateral middle ear effusion requiring TTP Subject's caregiver is willing to comply with the protocol and attend all study visits
Exclusion Criteria	Has a history of prior ear or mastoid surgery, not including myringotomy or myringotomy with TTP Has a history of sensorineural hearing loss Has a history of chronic or recurrent bacterial infections other than otitis media that likely will require treatment with
Treatment Cohorts	Single, intratympanic injection of 6mg OTO-201 Sham (no treatment)
Primary Endpoint	Efficacy: Cumulative proportion of treatment failures
Secondary Endpoint	Safety: Evaluation of adverse events, otoscopic exams, audiometry, and tympanometry Efficacy: Microbiological response through end of therapy and study

Source: CliniTrials.gov, SunTrust Robinson Humphrey

On July 8th 2014, Otonomy announced that the Phase III clinical trials had demonstrated that AuriPro achieved its primary efficacy endpoint as well as several secondary endpoints and was well tolerated.

AuriPro demonstrated an average of 50% reduction for the primary efficacy endpoint which was statistically significant (p<0.001) for both trials.

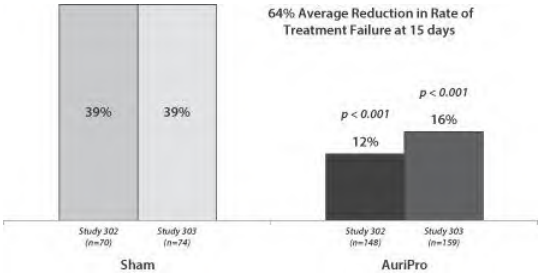
Exhibit 26:Phase III Results for AuriPro vs. Sham (All Patients): Cumulative Proportion of Treatment Failures through Day 15



Source: Otonomy

Otonomy conducted a per-protocol analysis, a sensitivity analysis on the primary endpoint, to evaluate the incidence of treatment failures in all enrolled patients who did not have a major protocol deviation, in which >80% of patients in each arm were qualified. AuriPro demonstrated a reduction in the rate of treatment failure through day 15 in the per-protocol population averaging 64% across the two trials.

Exhibit 27: Phase III Results for AuriPro vs. Sham (Per-Protocol Analysis): Cumulative Proportion of Treatment Failures through Day 15

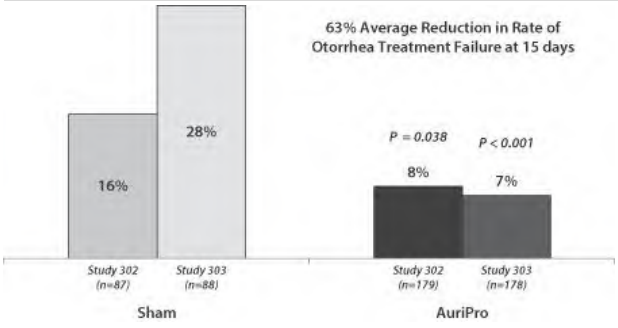


Source: Otonomy

The secondary endpoint evaluated the cumulative proportion of patients considered treatment failures due to observation of otorrhea by the blinded observer through day 15. AuriPro reduced the rate of otorrhea by 63% when averaged across both trials. The rate of otorrhea is comparable (8% and 7%) for AuriPro in both trials. However, there is variation in the rate of otorrhea in the sham group (16% vs 28%). This could be due to randomization issues.

Despite this difference in the sham groups, the reduction in the rate of otorrhea demonstrated by AuriPro was statistically significant (p=0.038 and p<0.001) and meaningful (50% and 75% reduction) in both trials

Exhibit 28: Phase III Results for AuriPro vs. Placebo (All Patients): Cumulative Proportion of Otorrhea Treatment Failures through Day 15



Source: Otonomy

AuriPro was generally well tolerated in the Phase III clinical trials. There were no deaths or serious adverse events related to AuriPro, or discontinuation due to adverse events. Most adverse events were mild or moderate. Safety assessments included treatment-emergent adverse events, or TEAEs, hearing function testing and tympanometry (middle ear function).

Exhibit 29: Phase III Results: Treatment-Emergent Adverse Events (Patients from Combined 302 and 303 Studies)

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

Source: Otonomy, SunTrust Robinson Humphrey

Major Competitors Are Antibiotic Ear Drops

Antibiotic ear drops are currently the primary treatment option for middle ear effusion during TTP surgery. The leading branded antibiotic ear drop is Ciprodex Otic (ciprofloxacin 0.3% and dexamethasone 0.1%) from Alcon. However, no antibiotic ear drop has been approved by the FDA for the specific indication of middle ear effusion during TTP surgery.

Ciprodex Otic was approved in the U.S. in July 2003 and the EU in July 2012. It is indicated for the treatment of infections caused by susceptible isolates of the designated microorganisms involved in the specific conditions listed below:

- Acute Otitis Media in pediatric patients (age six months and older) with tympanostomy tubes due to *Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis*, and *Pseudomonas aeruginosa*.
- Acute Otitis Externa in pediatric (age six months and older), adult and elderly patients due to *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

Ciprodex Otic is contraindicated in patients with a history of hypersensitivity to ciprofloxacin, to other quinolones, or to any of the components in this medication. Use of this product is contraindicated in viral infections of the external canal including herpes simplex infections.

According to the FDA Orange Book, Ciprodex patents expire between 2020 and 2025.

Exhibit 30: Ciprodex Otic FDA Orange Book Patents

Patent No.	Patent Expiration	Patent Name
6284804	8/10/2020	Topical suspension formulations containing ciprofloxacin and dexamethasone
6359016	8/10/2020	Topical suspension formulations containing ciprofloxacin and dexamethasone
8846650	6/4/2025	Method of treating middle ear infections

Source: FDA Orange Book, USPTO, SunTrust Robinson Humphrey

In the Phases II and III clinical trials, a total of 937 patients were treated with Ciprodex Otic. This included 400 patients with acute otitis media with tympanostomy tubes and 537 patients with acute otitis externa.

Exhibit 31: Ciprodex Otic Adverse Events For Acute Otitis Media In Pediatric Patients With Tympanostomy Tubes

Adverse Event	Incidence (N=400)
Ear discomfort	3.0%
Ear pain	2.3%
Ear precipitate (residue)	0.5%
Irritability	0.5%
Taste perversion	0.5%

Source: Ciprodex prescription information, Alcon, SunTrust Robinson Humphrey

Ciprodex Otic used different clinical endpoints (for AOMT) as compared to AuriPro (effusion during TTP surgeries) in evaluating its efficacy. According to Ciprodex Otic's prescription information, in a randomized, multicenter, controlled clinical trial, Ciprodex Otic dosed two times per day for seven days demonstrated clinical cures in the per protocol analysis in 86% of AOMT patients as compared to 79% for ofloxacin solution (0.3%, dosed two times per day for ten days). Among culture positive patients, clinical cures were 90% for Ciprodex Otic compared to 79% for ofloxacin solution, 0.3%. Microbiological eradication rates for these patients in the same clinical trial were 91% for Ciprodex Otic compared to 82% for ofloxacin solution, 0.3%.

Other ear drop products approved by the FDA include Alcon's Xtoro (finafloxacin otic suspension) for acute otitis externa; WraSer Pharmaceuticals' Cetraxal (0.2% ciprofloxacin otic solution) for acute otitis externa; and SALVAT's Cetraxal Otic (0.3% ciprofloxacin) for chronic suppurative otitis media and otitis externa.

In clinical stage development, SALVAT, a private biopharma company based in Barcelona, Spain, is developing ciprofloxacin 0.3% plus fluocinolone acetonide 0.025% otic solution for the treatment of acute otitis media with tympanostomy tubes (AOMT). SALVAT announced top-line reports from two Phase III studies on September 29, 2014.

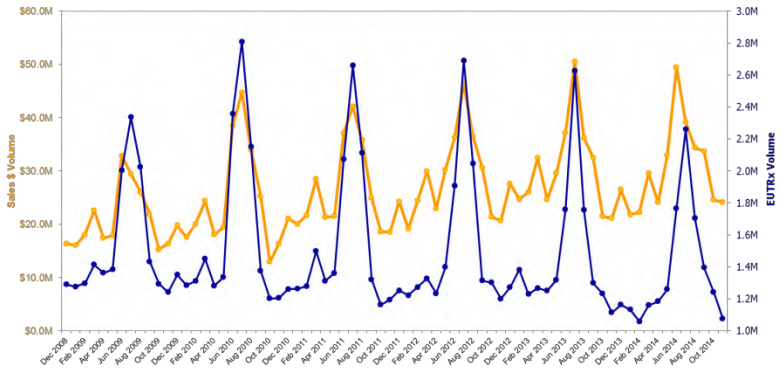
For the primary efficacy endpoint, time to cessation of otorrhea, a significant reduction was observed when comparing the combination to ciprofloxacin alone ($p<0.001$ and $p<0.05$) and to fluocinolone alone ($p<0.001$ in both studies). The results also showed that the principal secondary endpoint, sustained microbiological cure, was met with statistical significance ($p<0.001$) in each trial. The number of patients who experienced related adverse events during the two studies was low in all three treatment groups (ciprofloxacin plus fluocinolone otic solution 4.9%, ciprofloxacin alone 4.1% and fluocinolone alone 6.6%), with most being mild in severity and reversible. No serious related adverse event was reported in the studies.

It is difficult to compare AuriPro with SALVAT's product as the indications are different and primary endpoints from the studies were different (proportion of treatment failures versus time to cessation of otorrhea)

The Commercial Opportunity

There are approximately one million TTP procedures conducted each year in the U.S., and antibiotic ear drops are routinely used off-label, of which Alcon's Ciprodex is the market leader. Below we summarize Ciprodex's monthly EUTRx, sales, and pricing history. The seasonality of Ciprodex's EUTRx and sales is due to the higher incidence of swimmer's ear (otitis externa) during summer months.

Exhibit 32: Ciprodex Monthly And Annual Sales And EUTRx



Year	Annual Sales	Annual EUTRx
2014*	$336,068,011	15,243,142
2013	$362,943,180	17,403,714
2012	$346,015,950	18,189,138
2011	$314,393,901	18,490,709
2010	$292,419,820	19,029,040
2009	$253,588,763	18,417,528

**Excluding December 2014, Source: IMS, SunTrust Robinson Humphrey*

Exhibit 33: Ciprodex WAC Pricing History

Package Price	Effective	% Increase
$159.20	10/2/2014	5%
$151.60	1/2/2014	5%
$144.35	1/3/2013	8%
$133.65	1/3/2012	6%
$126.10	7/12/2011	4%
$121.25	1/4/2011	7%
$112.80	7/20/2010	7%
$105.40	1/5/2010	9%
$96.70	1/6/2009	8%
$89.95	1/7/2008	8%
$83.45	2/5/2007	/

Source: PriceRx, SunTrust Robinson Humphrey

Otonomy conducted a survey of ENT physicians in 2014. Based on the survey ENTs expressed a strong interest in using AuriPro in TTP procedures if it becomes commercially available.

The survey was based on an online interview of 55 ENTs who performed 25 or more TTP surgeries in the prior three months. When asked for the likelihood of using AuriPro during TTP procedures on a scale of 1 to 10 where 10 means “extremely likely” and 1 means “not at all likely,” 69% of the surveyed ENTs expressed a strong interest by ranking their interest with an 8, 9 or 10. Participants were asked to rate AuriPro on characteristics including safety, tolerability and frequency of complications, as compared to antibiotic ear drops. The AuriPro product profile was rated as better than antibiotic ear drops by more than 80% of respondents for compliance/adherence, approximately 50% for patient tolerability and achieving adequate drug exposure, and >33% for reducing the incidence of post-operative otorrhea, reducing the incidence of post-operative tube clogging and reducing the frequency of complications.

Otonomy intends to use approximately 40 specialized sales reps to target the fewer than 2,500 ENTs who perform 80% of TTP surgeries in the U.S.

What Is Next For AuriPro?

There are several future potential therapeutic indications for AuriPro, according to Otonomy some of the possible opportunities include:

Recurrent otic infections in patients with tympanostomy tubes
Acute otitis media with tympanostomy tubes (AOMT)
Acute otitis externa
Chronic suppurative otitis media (a perforated tympanic membrane with persistent drainage)
Prophylaxis following middle ear surgeries

The Company intends to initiate one or more clinical trials during 2015. Otonomy has global commercialization rights to AuriPro with patent protection in the U.S. out to 2030 without extensions.

OTO-104 For Ménière's Disease – The Second Asset Addressing A Larger Market

What Is Ménière's Disease?

Ménière's disease is a disorder of the inner ear that causes severe dizziness (vertigo), ringing in the ears (tinnitus), hearing loss, and a feeling of congestion in the ear. Ménière's disease usually is unilateral (affects only one ear). Among the symptoms, vertigo attacks are typically most troubling for patients since they disrupt daily activities and are difficult to anticipate and manage.

Ménière's disease can develop at any age, but it is more likely to occur in adults between 40 and 60 years of age. The National Institute on Deafness and Other Communication Disorders (NIDCD) estimates that approximately 615,000 individuals in the U.S. are currently diagnosed with Ménière's disease and that 45,500 cases are newly diagnosed each year.

The underlying cause of Ménière's disease is not well understood and there is no known cure. It is hypothesized that Ménière's disease is caused by the buildup of fluid in the compartments of the inner ear, labyrinth. The labyrinth contains the organs of balance (the semicircular canals and otolithic organs) and of hearing (the cochlea) (see Exhibit 11 for a depiction of the ear structure). The buildup of endolymph (fluid in labyrinth of the inner ear) interferes with normal balance and hearing signals between the inner ear and the brain, which causes vertigo and other symptoms.

What Are The Current Treatment Options?

The typical first-line treatment in the U.S. is low-salt diets and off-label use of diuretics to reduce the amount of body fluid (similar to the treatment of hypertension). Oral and IT steroids are used to treat patients with more persistent/severe symptoms. Multiple clinical and preclinical publications support the potential benefit of steroids to treat patients with Ménière's disease. For those who are unresponsive to steroid treatment, surgical or chemical ablation may be used with caution as irreversible hearing loss may happen. In the table below we summarize current treatments for Ménière's disease.

Exhibit 34: Ménière's Disease Current Treatment

Category	Treatment	Examples	Pros and cons
Medications for vertigo	Motion sickness medications	Meclizine (Antivert) or Diazepam (Valium)	may reduce the spinning sensation of vertigo and help control nausea and vomiting
	Anti-nausea medications	promethazine	may control nausea and vomiting during an episode of vertigo
Long-term medication use	Diuretic to reduce fluid retention	Dyazide, Maxzide	reducing the amount of fluid the body retains may help regulate the fluid volume and pressure in your inner ear.
Noninvasive therapies and procedures	Rehabilitation	Vestibular rehabilitation therapy	exercises and activities tmay help brain regain the ability to process balance information correctly
	Meniett device	Meniett pulse generator	application of positive pressure to the middle ear to improve fluid exchange
Middle ear injections	Antibiotics	Gentamicin	may reduce the frequency and severity of vertigo attacks; toxic to inner ear; may cause further hearing loss
	Steroids	Dexamethasone	may help control vertigo attacks in some people
Surgery	Endolymphatic sac procedures	/	may alleviate vertigo by decreasing fluid production or increasing fluid absorption
	Vestibular nerve section	/	usually correct problems with vertigo while attempting to preserve hearing in the affected ear
	Labyrinthectomy	/	remove both balance and hearing function from the affected ear

Source: SunTrust Robinson Humphrey, Mayo Clinic

What Is OTO-104?

OTO-104 is a suspension combining the steroid dexamethasone and P407 for the treatment of Ménière's disease and other inner ear conditions. Similar to AuriPro, OTO-104 exists as a liquid below room temperature and transitions to a gel following an intratympanic (IT) injection. A single IT injection of OTO-104 provides a full course of treatment.

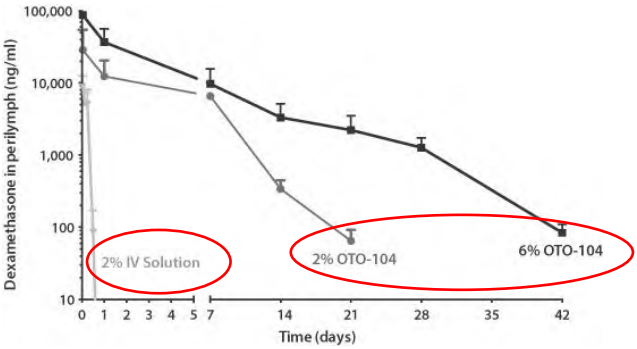
Otonomy is conducting a Phase IIb clinical trial with 140 patients to assess the reduction in vertigo frequency and improvements in tinnitus in patients with Ménière's disease. Otonomy suggests that this trial will potentially serve as one of the two pivotal, single-dose efficacy trials required to support U.S. regulatory approval. The Company expects to report results from this clinical trial in the 2Q15. If results are positive, Otonomy plans to initiate a second pivotal trial of OTO-104 in 2015. Otonomy has global commercialization rights to OTO-104 with patent protection in the U.S. until 2029 without extensions. The FDA has granted OTO-104 Fast Track Designation, which permits more frequent communications with the FDA.

Preclinical And Clinical Trial Data For OTO-104

Preclinical

In the preclinical studies, Otonomy shows that dexamethasone levels in the perilymph (inner ear fluid) can be measured more than one month after a single OTO-104 injection at both 2% and 6% dosages. In comparison, an IT injection of steroid solution provides less than 24 hours of drug exposure.

Exhibit 35: Dexamethasone Drug Concentration in Perilymph Following Single IT Injection of OTO-104 vs. IV Solution



Source: Otonomy

In addition to the PK profiling studies, the OTO-104 preclinical development program included pharmacological studies in established hearing loss models and extensive safety testing.

Since there are no preclinical models of Ménière's disease, Otonomy conducted studies to evaluate the pharmacological activity of a single IT injection of OTO-104 in standard models of acute onset hearing loss. Specifically, Otonomy demonstrated that OTO-104 provides a protective effect when given before exposure to loud noise or ototoxic chemotherapeutic agents. Administration of OTO-104 within two to three days of exposure to acoustic trauma promotes hearing recovery. These findings are consistent with published data for steroids, and supported dose selection for the Phase Ib clinical trial. Side effect profiles of systemic dexamethasone in humans is well characterized. Ototoxicity testing has included single- and multiple-dosing studies of OTO-104 in multiple species.

A Chronicle Of OTO-104 Clinical Development

Otonomy submitted an IND to the FDA in December 2009 to begin clinical development of OTO-104 for the treatment of vertigo associated with Ménière's disease. Based on discussions with the FDA from an End-of-Phase I meeting, Otonomy concluded that two pivotal, single-dose trials would be required to support the efficacy of OTO-104 in an NDA submission. The Company expected that the FDA would require multiple-dose clinical safety data for the approval. Otonomy plans to conduct one or more clinical trials lasting up to one year and totaling more than 300 patients in order to satisfy this requirement. It is possible that patients participating in the pivotal efficacy trials may also participate in the multiple-dose safety trials.

Otonomy has not yet conducted any multiple-dose clinical trials. Following completion of a Phase Ib clinical trial, the OTO-104 program was put on Full Clinical Hold due to adverse findings in a preclinical study evaluating the safety of repeated doses of OTO-104. OTO-104 was removed from Full Clinical Hold in July 2013 after Otonomy had generated additional preclinical data to submit to the FDA. The lifting of the clinical Hold permitted Otonomy to initiate the current Phase IIb single-dose clinical trial, and placed on Partial Clinical Hold the initiation of multiple-dose clinical trials in the U.S. pending the submission and review of additional preclinical data.

In June 2014, Partial Clinical Hold was removed by the FDA after Otonomy submitted additional preclinical data. Otonomy filed a Clinical Trial Authorization in the United Kingdom to initiate a multiple-dose safety study in Ménière's disease patients and received authorization to proceed in

June 2014. Otonomy intends to initiate one or more open-label, multiple-dose safety studies for OTO-104 in Ménière's patients.

Phase Ib

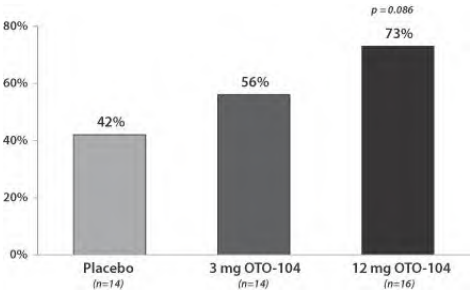
In February 2011, Otonomy completed a randomized, prospective, double-blind, placebo-controlled, Phase Ib clinical trial of a single IT injection of OTO-104 in patients with Ménière's disease. A total of 44 patients were enrolled and completed the trial. The trial design was virtually the same as the ongoing Phase IIb clinical trial, except that two different doses of OTO-104, 3mg and 12mg (only 12mg in Phase IIb), were assessed, and patients were observed for three months following treatment. The primary endpoint for efficacy was vertigo frequency during month three as compared to baseline, similar to the primary endpoint used in the Phase IIb clinical trial.

OTO-104 at both doses studied was well tolerated in the Phase Ib clinical trial. There were no serious adverse events and no instances of persistent conductive hearing loss associated with OTO-104 injection. Protocol pre-specified Adverse Events of Interest (AEIs) reported during the clinical trial included injection site perforation of the tympanic membrane, a single 12mg patient reporting vertigo during the procedure, and a single placebo patient with serous otitis media.

Of these AEIs, only injection site perforation of the tympanic membrane was reported in more than one patient. These perforations were predominantly described as pinhole perforations observed following IT injection of OTO-104. All but one of these perforations resolved spontaneously by the end of the clinical trial. In general, the safety events were consistent with those reported in published clinical trials with the use of IT injections of steroids.

The Phase Ib clinical trial was not designed to establish efficacy due to the small sample size. However, trends with respect to the clinical activity of OTO-104 were observed. The 12mg OTO-104 group experienced a mean reduction of vertigo frequency from baseline totaling 73% in month three compared to 56% at 3mg OTO-104 and 42% for placebo. In absolute terms, the 12mg OTO-104 group achieved a reduction in days with vertigo episodes from eight during baseline to two in month three.

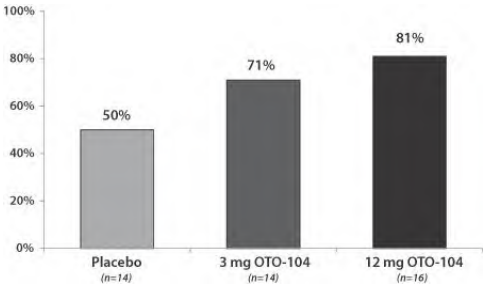
Exhibit 36: Phase Ib Clinical Trial Results for OTO-104 vs. Placebo: % Reduction in Vertigo Frequency from Baseline to Month Three



Source: Otonomy

Using a patient responder analysis, it is shown that 81% of patients in the 12mg OTO-104 group realized at least a **50% improvement in vertigo frequency** in month three versus baseline, compared to 71% at 3mg OTO-104 and 50% of patients receiving placebo.

Exhibit 37: Phase Ib Clinical Trial Results for OTO-104 vs. Placebo: % of Patients with ≥50% Improvement in Vertigo Frequency from Baseline to Month Three



Source: Otonomy

OTO-104 treatment also led to improvement in tinnitus, as measured by the Tinnitus Handicap Inventory (THI-25), which is a patient questionnaire that subjectively measure the impact of tinnitus on a patient's functional status. The average score at baseline was 52 to 58 for the three treatment groups corresponding to a Moderate Handicap grade. THI-25 is being assessed as an exploratory endpoint in the current Phase IIb trial.

Exhibit 38: Tinnitus Handicap Inventory (THI-25) Scoring System

Questions
1.Because of your tinnitus is it difficult for you to concentrate?
2.Does the loudness of your tinnitus make it difficult for you to hear?
3.Does your tinnitus make you angry?
4.Does your tinnitus make you feel confused?
5.Because of your tinnitus do you feel desperate?
6.Do you complain a great deal about your tinnitus?
7.Because of your tinnitus do you have trouble falling asleep?
8.Do you feel as though you cannot escape your tinnitus?
9.Does your tinnitus interfere with your ability to enjoy social activities such as going out to dinner, cinema?
10.Because of your tinnitus do you feel frustrated?
11.Because of your tinnitus do you feel you have a terrible disease?
12.Does your tinnitus make it difficult for you to enjoy life?
13.Does your tinnitus interfere with your job or household responsibilities?
14.Because of your tinnitus do you find that you are often irritable?
15.Because of your tinnitus is it difficult for you to read?
16.Does your tinnitus make you upset?
17.Do you feel that your tinnitus has placed stress on your relationship with members of your family, friends?
18.Do you find it difficult to focus your attention away from your tinnitus and on to other things?
19.Do you feel that you have no control over your tinnitus?
20.Because of your tinnitus are you often tired?
21.Because of your tinnitus do you feel depressed?
22.Does your tinnitus make you feel anxious?
23.Do you feel that you can no longer cope with your tinnitus?
24.Does your tinnitus get worse when you are under stress?
25.Does your tinnitus make you feel insecure

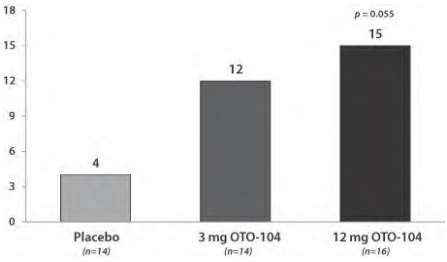
How to Score The Questionnair
YES = 4
SOMETIMES = 2
NO = 0

Total Score	Category	Explaination
0-16	Slight	Only heard in quiet environments
18-36	Mild	Easily masked by environmental sounds and easily forgotten with activities
38-56	Moderate	Noticed in presence of background noise, although daily activities can still be performed
58-76	Severe	Almost always heard, leads to disturbed sleep patterns and can interfere with daily activities
78-100	Catastrophic	Always heard, disturbed sleep patterns, difficulty with any activities

Source: SunTrust Robinson Humphrey, Arch Otolaryngol Head Neck Surg. 1996 Feb;122(2):143-8.

The mean reduction of THI-25 total score from baseline was 15 for the 12mg OTO-104 group, 12 for 3mg OTO-104, and 4 for placebo. Of note, the 15-point reduction for patients in the 12mg moved the category from Moderate grade at baseline to Mild at month three.

Exhibit 39: Phase Ib Clinical Trial Results for OTO-104 vs. Placebo: Mean Reduction in THI-25 Score from Baseline to Month Three



Source: Otonomy

Phase IIb

Otonomy is currently conducting a prospective, randomized, double-blind, placebo-controlled Phase IIb clinical trial to assess the efficacy/safety of OTO-104 in Ménière's disease with 140 patients in the U.S. and Canada. Otonomy expects the clinical can serve as one of the two pivotal, single-dose efficacy trials that the FDA will require to support an NDA filing. The trial is 90% powered to achieve statistical significance ($p<0.05$) for a 30% treatment effect, which was the level observed in the Phase Ib clinical trial.

The primary endpoint of the trial is identical to the one in the Phase Ib trial: reduction in vertigo frequency during month three following treatment compared to a one month baseline period. Otonomy noted that the endpoint was reviewed with the FDA at an End-of-Phase I meeting. Tinnitus is being assessed as an exploratory endpoint. The safety and tolerability of a single IT injection of OTO-104 will also be assessed.

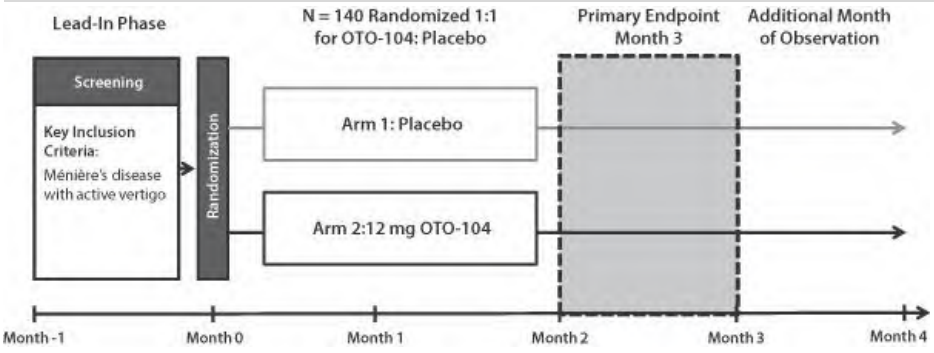
Exhibit 40: OTO-104 Phase IIb Study Design

Study	104-201102 OTO-104 for the Treatment of Meniere's Disease
Phase	II
Patient Number	140
Inclusion Criteria	Has a diagnosis of unilateral Meniere's disease and reports active vertigo for the 2 months prior to the study lead-in period Has experienced active vertigo during the lead-in period Has documented asymmetric sensorineural hearing loss Maintains current treatments for Meniere's disease while on-study
Exclusion Criteria	Is pregnant or lactating Has a history of immunodeficiency disease Previous did endolymphatic sac surgery Previous used IT gentamicin in the affected ear Has a history of tympanostomy tubes with evidence of perforation or lack of closure Has experienced an adverse reaction to IT injection of steroids Has used an investigational drug or device in the 3 months prior to screening Has previously been randomized to a trial of OTO-104
Treatment Cohorts	Single IT injection of 12 mg OTO-104 Single IT injection of placebo
Primary Endpoint	Efficacy: reduction in vertigo frequency
Secondary Endpoint	Safety: adverse events, otoscopic exams, audiometry, Word Recognition Score and tympanometry Efficacy: evaluation of tinnitus patient reported questionnaire and daily diary Efficacy: evaluation of patient reported questionnaires as a measure of impact on patient daily activities

Source: CliniTrials.gov, SunTrust Robinson Humphrey

In the trial patients enter into a one month observational period (month -1) for a baseline assessment to record their vertigo and tinnitus symptoms via a daily diary. Following the lead-in period, eligible patients are randomized 1:1 to a single IT injection of 12mg OTO-104 or P407 gel vehicle (placebo) at month 0. Patients are observed for up to four months following treatment with month three (weeks 9 through 12).

Exhibit 41: Design of OTO-104 Phase IIb Clinical Trial in Patients with Ménière's disease



Source: Otonomy

Otonomy expects to announce top-line results 2Q15.

Multi-Dose Safety Study

According to communications with the FDA, Otonomy is conducting a multi-dose safety study for OTO-104.

The clinical trial is a two-part prospective, randomized, placebo-controlled study to evaluate the safety of multiple doses of OTO-104 in subjects with unilateral Meniere's disease in the United Kingdom. A total of 125 patients are expected to be enrolled.

The first part is a randomized, placebo-controlled study comparing the safety profile of two IT injections of OTO-104 or placebo spaced three months apart (six months total).

The second part is an open-label extension where all subjects will receive an additional two IT injections of OTO-104 spaced three months apart. Each subject will participate on the study for a total of one year.

On Oct. 9, 2014, Otonomy enrolled the first patients in the safety study. As of Jan. 2015, the study is still recruiting patients according to ClinicalTrials.gov.

A Disease With No Treatments AND A Limited Competitive Landscape

There are no drugs currently approved by the FDA for the treatment of Ménière's disease. Treatments commonly used include a low-salt diet and off-label use of diuretics, oral steroids, and repeat IT injections of steroid solution. Patients who are unresponsive to treatment may resort to surgical or chemical ablation of vestibular function of the ear to relieve symptoms of vertigo.

A handful of companies are conducting clinical trials for Ménière's disease. Synphora AB, a Sweden biopharma company, is conducting a Phase II/III clinical trial with a formulation of latanoprost administered via single or repeat IT injections. Auris Medical Holding AG has indicated its intention to evaluate AM-111 in an open-label study of Ménière's patients.

On October 16, 2013 Synphora AB announced that dosing had initiated in a randomized, double-blind Phase II/III study of latanoprost as a treatment for Ménière's disease. A total of 120 patients will be included in the trial. As of December 31, 2014, the company is still recruiting patients according to

ClinicalTrials.gov. Latanoprost is a prostaglandin analogue that lowers otic pressure by increasing the outflow of aqueous fluid from the eyes through the uveoscleral tract. It has been approved (Xalatan manufactured by Pfizer) as a medication administered into the eyes to control the progression of glaucoma or ocular hypertension by reducing intraocular pressure. Synphora is hypothesizing that the same therapeutic rationale, the evacuation of fluid, could be applicable to Ménière's disease. Synphora has to date conducted two double-blind, randomized, cross-over, placebo-controlled clinical trials comprising in total 51 patients. No results have been announced officially on Synphora's website.

Auris Medical is developing AM-111 for the treatment of acute inner ear (sensorineural) hearing loss (ASNHL) and finished Phase II clinical trials. Auris indicated that it was preparing for Phase I/II clinical trials for Ménière's disease with the next milestone for this indication being mid-2015. According to results from the ASNHL trial, AM-111 was well tolerated and had no negative impact on hearing, balance or tinnitus. Adverse events were mostly local and procedure-related. Following IT injection, there were transient procedure-related effects such as ear discomfort or pain, incision site complications or middle ear infection in less than 5% of patients. AM-111 contains the synthetic peptide D-JNKI-1 (D-stereoisomer of c-Jun N-Terminal Kinase Inhibitor 1), an inhibitor of the JNK stress kinase coupled to an intracellular transporter, and is formulated in a biocompatible and biodegradable gel. It is administered in a single dose intratympanic injection into the middle ear. From there the drug diffuses through the round window membrane into the cochlea.

Exhibit 42: Ménière's Disease And Related Indication Clinical Trials

Sponsor	Interventions	Conditions	Phases	Enrollment	Last Updated	Title	Recruitment
Solvay Pharmaceutical	Drug: Betahistine 24 mg bid (Betaserc)	Meniere's Disease	Phase 4	20	12/21/2006	Effects of Betaserc on Vestibular Compensation in Patients Suffering From Disabling Meniere's Disease and Having Undergone Vestibular Neurotomy	Completed
Synphora AB	Drug: Latanoprost|Other: Placebo	Meniere's Disease	Phase 2/3	120	11/10/2013	Latanoprost for the Treatment of Meniere's Disease	Recruiting
Pfizer	Drug: Sildenafil	Meniere's Disease	Phase 2	180	1/30/2008	Sildenafil For Meniere's Disease	Completed
Abbott	Drug: Betaserc® (Betahistine Dihydrochloride)	Vertigo	Phase 4	309	6/13/2014	EffectiveneÃ® (Betahistine Dihydrochloride) in Patients With Vestibular Vertigo in Routine Practice	Completed
Phafag AG	Drug: Caroverin	Tinnitus	Phase 3	170	11/18/2011	Caroverin and Inner Ear Diseases	Suspended

Source: SunTrust Robinson Humphrey, ClinicalTrials.gov

What Is The Market Potential?

The initial target market for OTO-104 is the more than 600,000 patients diagnosed with Ménière's disease in the U.S.

Based on the survey Otonomy conducted in 2014 (the same survey for AuriPro), ENT physicians expressed strong interest in using OTO-104 to treat patients with Ménière's disease. According to Otonomy, 66 ENTs participated in the survey. When asked for the likelihood of using OTO-104 to treat Ménière's patients on a scale of 1 to 10, where 10 being "extremely likely" and 1 being "not at all likely," 57% of the respondents ranked their interest with an score of 8, 9 or 10.

For future label expansion, Otonomy plans to assess and prioritize additional opportunities for OTO-104 in conditions where ENTs currently use steroids off-label, including other balance disorders, sudden sensorineural hearing loss, other types of sensorineural hearing loss, and tinnitus. Otonomy have global commercialization rights to OTO-104 with patent protection in the U.S. until 2029 without extensions.

OTO-311 For Tinnitus – The Preclinical Asset That Fuels Long Term Growth

What Is Tinnitus?

Tinnitus is the perception of sound in the ears or head where no external source is present. It is also called "ringing in the ears" or "head noise."

The American Tinnitus Association reports that approximately 16 million patients in the U.S. have tinnitus symptoms severe enough to seek medical attention, and about two million patients cannot function on a normal day-to-day basis. According to American Academy of Otolaryngology Head and Neck Surgery, over 50 million people in the U.S. have experienced tinnitus and about one in five people in this population have bothersome tinnitus, which they claim is distressing and negatively affects their quality of life and/or functional health status.

The exact physiological causes of tinnitus are unknown. The most known common cause of tinnitus is exposure to loud noise, and a number of other factors are associated with the symptom, including heart or blood vessel problems, head and neck trauma, hormonal changes in women, ear and sinus infections, jaw misalignment, certain medications and thyroid problems. People with severe tinnitus may have trouble hearing, working, and sleeping.

What Are The Current Treatment Options?

Currently there is no cure and there are no FDA approved drugs for treating tinnitus. Several options are available that can help patients with tinnitus as described below.

- If the otolaryngologist finds a specific cause for the tinnitus, he or she can try to eliminate the noise, which may include removal of wax or hair from the ear canal, treatment of middle ear fluid, treatment of arthritis in the jaw joint, etc.
- Hearing aids with or without built-in ear-level maskers can be effective for some patients. Sound therapies that involve background music or noise may be used. The effects of tinnitus on quality of life may be improved by a course of counseling with cognitive behavioral therapy (CBT), which typically is a series of weekly sessions led by a trained professional.
- Routine prescription of medications including antidepressants, anticonvulsants, anxiolytics, or intratympanic injection of medications, can be used. But they are not recommended for treating tinnitus without an underlying or associated medical problem that may benefit from such treatment.
- Acupuncture may or may not be helpful in tinnitus as there are not enough quality studies of this treatment for tinnitus to make a recommendation. Transcranial magnetic stimulation is a new modality, however, similar to acupuncture, it cannot be recommended for tinnitus as long-term benefits are not proven.

Exhibit 43: Otitis Current Treatment

Category	Treatment	Explanation
Treating an underlying health condition	Earwax removal	Removing impacted earwax can decrease tinnitus symptoms
	Treating a blood vessel condition	Underlying vascular conditions may require medication, surgery or another treatment to address the problem
Noise suppression	White noise machines	These devices, which produce simulated environmental sounds such as falling rain or ocean waves, can be an effective treatment for tinnitus
	Masking devices	These devices produce a continuous, low-level white noise that suppresses tinnitus symptoms
	Tinnitus retraining	A wearable device delivers individually programmed tonal music to mask the specific frequencies of the tinnitus patients experience
Medications	Tricyclic antidepressants (e.g., amitriptyline and nortriptyline)	These medications are generally used for only severe tinnitus, as they can cause troublesome side effects, including dry mouth, blurred vision, constipation and heart problems
	Alprazolam (e.g., Niravam, Xanax)	May help reduce tinnitus symptoms, but side effects can include drowsiness and nausea

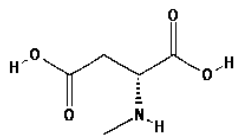
Source: SunTrust Robinson Humphrey, Mayo Clinic

What Is OTO-311?

OTO-311 is a sustained-exposure formulation of the N-Methyl-D-Aspartate (NMDA) receptor antagonist gacyclidine in development for the treatment of tinnitus. It will be administrated via an IT injection.

Exhibit 44: N-Methyl-D-Aspartate Structure; Gacyclidine Structure

N-Methyl-D-Aspartate



Gacyclidine

Source: National Library of Medicine

Unlike ciprofloxacin and dexamethasone, which are FDA approved drugs with known properties, gacyclidine is a new molecular entity. Gacyclidine is a non-competitive NMDA receptor antagonist and a phencyclidine derivative with neuroprotective properties. The molecule was originally developed for the treatment of traumatic brain and spinal cord injury in the late 1990's. It has been previously administered safely through IV to acute traumatic brain-injured patients. Experiments in guinea pigs have shown that local administration of gacyclidine to the cochlea suppressed salicylate induced tinnitus.

Historic clinical data provide some support for the use of NMDA receptor antagonists for the treatment of tinnitus. A report published in 2009 by Wenzel *et al*. in Germany administrated gacyclidine solution via a microcatheter (Durect RWµCath) into the round window niche in six patients with unilateral deafness associated with tinnitus as a compassionate treatment. After constant perfusion of gacyclidine for 40 to 63 hours, four out of six patients experienced a temporary relief from their tinnitus. No serious side effects were recorded in any of the cases.

Auris Medical and Merz Pharmaceuticals are conducting clinical trials to study the effect of other NMDA receptor antagonists (esketamine and neramexane respectively) in otitis patients.

Otonomy acquired from an affiliate of the NeuroSystec Corporation assets and patent rights related to gacyclidine, including data and intellectual property generated during the development program. In addition, Otonomy in-licensed from Durect Corporation the exclusive rights to a patent for using gacyclidine for the treatment of tinnitus.

Clinical Trial Data Review

Otonomy plans to file an IND application for OTO-311 with the FDA in order to initiate clinical development in 2015.

In November 2014 Otonomy obtained rights to gacyclidine clinical and non-clinical data from Ipsen. Under the terms of the agreement, Otonomy will have an exclusive license to use Ipsen's gacyclidine data to support the development and regulatory filings for OTO-311. These data include non-clinical studies which supported Ipsen's initiation of clinical studies for systemic administration of gacyclidine, and clinical data from several Phase I and Phase II clinical trials conducted by Ipsen. More than 300 patients were treated with systemic gacyclidine as a potential neuroprotectant in various neurologic trauma indications. Financial terms of the agreement were not disclosed.

According to PubMed, Ipsen was developing gacyclidine (GK-11) for the potential treatment of traumatic brain injury. Phase II clinical trials of the compound for this indication had been completed as of October 1999 and the company was looking for a partner. The Phase II trials for acute spinal cord injury generated disappointing results and development for this indication has been discontinued. However, the discontinuation was not due to a safety issue, as no unexpected serious drug-related AEs were reported during the study. Clinical laboratory abnormalities were reported with similar frequencies in all the groups (placebo, Gacyclidine 0.005mg/kg, 0.010mg/kg, and 0.020mg/kg injected intravenously twice at an interval of four hours).

What Is The Market Potential?

Treatment of tinnitus can represent a significant market opportunity for several reasons:

- Large patient population – an estimated seven to 12 million patients in the U.S. have tinnitus symptoms severe enough to seek medical attention (this is in comparison to approximately 1M TTP procedures performed per year targeted by AuriPro, and approximately 0.6M Ménière's disease patients targeted by OTO-104)
- Severe and debilitating symptom that affect quality of life
- Lack of FDA-approved drugs to treat the disease

If OTO-311 is approved by the FDA in the future, Otonomy could use a channel strategy for sales and marketing. It can market this product to ENT physicians with the same focused, specialized sales force that will be promoting other product candidates, such as AuriPro and OTO-104, which could be approved before OTO-311. The Company has global commercialization rights to OTO-311 with patent protection in the U.S. until at least 2031.

Who Are The Competitors?

There are no drugs currently approved by the FDA to treat tinnitus. As discussed above, treatments for tinnitus include the use of audio masking devices, cognitive behavioral therapy, and the off-label administration of antidepressants, and anti-anxiety medications, etc.

A handful of companies are conducting clinical trials for tinnitus.

- Auris Medical Holding AG - conducting Phase III clinical trials evaluating repeat IT injections of AM-101 in patients with acute and post-acute inner ear tinnitus.
- Autifony Therapeutics - intends to initiate Phase II testing for their oral product candidate for tinnitus.
- Merz Pharmaceuticals GmbH - suspended development of oral neramexane for chronic tinnitus while its partner in Japan, Kyorin Pharmaceuticals Co., continues with a Phase II clinical trial for tinnitus.
- Novartis AG - completed a Phase II clinical trial for chronic tinnitus.

Below, we summarize current trials listed in ClinicalTrials.gov related to therapeutics in development to treat tinnitus.

Exhibit 45: Tinnitus Clinical Trials

Sponsor/Collaborators	Phases	Interventions	Last Updated	Title	Recruitment	Conditions	Enrollment	NCT Number
Auris Medical, Inc.	Phase 3	Drug: AM-101	3-Jun-14	AM-101 in the Treatment of Acute Tinnitus 3	Recruiting	Tinnitus	600	NCT02040194
	Phase 3	Drug: AM-101	3-Jun-14	AM-101 in the Treatment of Post-Acute Tinnitus 2	Recruiting	Tinnitus	300	NCT02040207
	Phase 3	Drug: AM-101	3-Jun-14	AM-101 in the Treatment of Acute Tinnitus 2	Recruiting	Tinnitus	330	NCT01803646
	Phase 3	Drug: AM-101	3-Jun-14	AM-101 in the Treatment of Post-Acute Tinnitus 1	Recruiting	Tinnitus	330	NCT01934010
	Phase 2	Drug: AM-101	12-Feb-13	Efficacy of AM 101 in Patients With Acute Inner Ear Tinnitus	Completed	Tinnitus	248	NCT00860808
	Phase 2	Drug: AM-101	22-Jul-13	Comparison of Single Versus Repeat Doses of AM-101 in the Treatment of Acute Inner Ear Tinnitus	Completed	Tinnitus	82	NCT01270282
Autifony Therapeutics Limited	Phase 2	Drug: AUT00063	11-Dec-14	Evaluating Possible Improvement in Tinnitus Severity After 28 Days Dosing of the Study Drug AUT00063 Compared to Placebo	Recruiting	Tinnitus, Subjective	150	NCT02315508
Bayer	Phase 2	Drug: Levitra (Vardenafil, BAY38-9456)	8-Dec-14	Vardenafil in Tinnitus	Completed	Tinnitus	43	NCT00666809
Korea Otsuka Pharmaceutical	Phase 2	Drug: Cilostazol	21-May-14	A Study on the Effect of Cilostazol in Patients With Chronic Tinnitus	Completed	Tinnitus	50	NCT01378650
Merz Pharmaceuticals GmbH	Phase 3	Drug: Neramexane mesylate	27-Nov-12	Efficacy, Safety, Tolerability of Neramexane in Patients With Subjective Tinnitus	Completed	Subjective Tinnitus	455	NCT00955799
	Phase 3	Drug: Neramexane mesylate	25-Mar-10	Efficacy, Safety and Tolerability of Neramexane in Patients With Subjective Tinnitus	Completed	Subjective Tinnitus	400	NCT00739635
	Phase 3	Drug: Neramexane mesylate	30-Jun-10	Efficacy, Safety and Tolerability of Neramexane in Comparison to Placebo in Patients With Subjective Tinnitus	Completed	Subjective Tinnitus	400	NCT00772980
	Phase 3	Drug: Neramexane mesylate	27-Nov-12	Open-Label, Long-Term Treatment Study, to Assess the Long-Term Safety and Tolerability and Efficacy of Neramexane in Patients	Terminated	Subjective Tinnitus	821	NCT00827008
	Phase 2	Drug: Neramexane|	10-Mar-11	Neramexane for Tinnitus	Completed	Tinnitus	431	NCT00405886
NeuroSystec Corporation	Phase 1	Drug: NST-001	18-Apr-13	Safety Study for NST-001 and the Neuroject Injection Set to Treat Tinnitus	Terminated	Tinnitus	8	NCT00957788
Novartis	Phase 2	Drug: BGG492A	24-Apr-12	Study of BGG492 in Patients With Chronic Subjective Tinnitus	Completed	Chronic Subjective	96	NCT01302873
Phafag AG	Phase 3	Drug: Caroverin	18-Nov-11	Caroverin and Inner Ear Diseases	Suspended	Tinnitus	170	NCT01174979

Note: only include industry sponsored trials; only include interventional trials with therapeutics; Source: ClinicalTrials.gov, SunTrust Robinson Humphrey

What Is The IP Estate?

Otonomy's patent estate includes approved patents and applications for AuriPro, OTO-104, OTO-311, and other active agents as potential future product candidates using the proprietary technology. Overall it includes 55 issued patents and allowed patent applications, and >85 pending patent applications for products and technologies.

Exhibit 46: Otonomy IP Estate

Source: Company presentation

AuriPro IP Estate

Otonomy co-owns a patent family with The Regents of the University of California (or UC) for the composition and therapeutic use of AuriPro. Through an exclusive license agreement, Otonomy has acquired UC's rights in this patent family including one issued U.S. patent and two pending U.S. applications, and the expiry date is April 2030. Otonomy noted that this patent and any future U.S. patents issuing from the related applications are expected to be Orange Book (OB) listed. This family also includes issued patents or allowed applications in Australia, Canada, Korea, Philippines, Russia, South Africa and Taiwan; and pending applications in Argentina, Brazil, China, Europe, India, Israel, Japan, Jordan, Mexico, Pakistan, Singapore, Thailand, Uruguay and Venezuela.

Otonomy has filed two solely owned U.S. patent applications directed to certain therapeutic uses of AuriPro and a solely owned U.S. provisional application directed to manufacturing methods of AuriPro.

OTO-104 IP Estate

Otonomy co-owns a patent family with UC for the composition and therapeutic use of OTO-104. Through an exclusive license agreement, Otonomy has acquired UC's rights in this patent family, including four issued U.S. patents, one allowed U.S. application and one pending U.S. application. The expiry dates of the U.S. patents range from May to September 2029. According to Otonomy, these patents are expected to be Orange Book listed. Otonomy owns a patent family for additional therapeutic uses of OTO-104, and an issued U.S. patent for manufacturing methods of OTO-104, the expiry date of this which is April 2030.

OTO-311 IP Estate

Otonomy co-owns two patent families with UC for the composition and therapeutic use of OTO-311, including one issued U.S. patent and one pending U.S. application. The expiry date of the U.S. patent is April 2031, and Otonomy expects it to be Orange Book listed. These families also include issued patents or allowed applications in Europe and other countries. Otonomy has licensed from

Durect a patent family for the therapeutic use of OTO-311, which includes one issued U.S. patent and one allowed Japanese application. The expiry date of the U.S. patent is June 2024, and the patent is expected to be Orange Book listed.

Other Patents And IP

For future product candidates, Otonomy co-owns eight patent families with UC for other active agents, including anti-TNF agents, auris pressure modulators, CNS modulators, cytotoxic agents, anti-apoptotic agents, bone-remodeling modulators, free radical modulators, and ion channel modulators. Otonomy solely owns a patent family for alternative formulations. Otonomy has acquired from IncuMed LLC, an affiliate of the NeuroSystec Corporation, patent families for formulations and devices that deliver active agents, e.g., OTO-311, into the ear for treatment.

In addition to patents, Otonomy has filed for trademark registration at the USPTO for “AuriPro” and “ProAuric.” The Company seeks to protect proprietary information such as trade secrets using confidentiality agreements with commercial partners, collaborators, employees and consultants and invention assignment agreements with employees, and other means.

License And Other Agreement

The Regents of the University of California

In November 2008, Otonomy entered into an exclusive license agreement with UC which was subsequently amended in January 2010, June 2010, and November 2012. Under the license agreement, UC granted Otonomy an exclusive license under UC’s rights to patents and applications that are co-developed and co-owned for the treatment of human otic diseases.

Otonomy’s financial obligations under the license agreement include annual license maintenance payments until Otonomy commercialize the first product covered under the license agreement, development milestone payments of up to $2.7 million per licensed product, of which $0.9 million has been paid for AuriPro and $0.3 million has been paid for OTO-104 (but such milestone payments are reduced by 75% for any Orphan indication product), and a low single-digit royalty on net sales of licensed products. For each sublicense Otonomy is obligated to pay UC a fixed percentage of all royalties as well as a sliding scale percentage of non-royalty sublicense.

Unless earlier terminated, the agreement will continue in effect until expiration of the longest lived patent licensed to Otonomy.

Durect Corporation

In April 2013, Otonomy entered into an exclusive license agreement with Durect as a part of an asset transfer agreement with IncuMed LLC, an affiliate of the NeuroSystec Corporation. Durect granted Otonomy an exclusive, worldwide, royalty-bearing license for certain patents and applications that cover OTO-311 product candidate, and related know-how. Otonomy made a one-time payment of $0.2 million and is obligated to make certain one-time milestone payments up to a $5.3 million in connection with the development/commercialization of products containing

gacyclidine. Certain rights licensed from Durect are a sublicense from the Institut National de la Sante et de la Recherche Medicale (INSERM) which was owned jointly by INSERM and Durect.

Otonomy is obligated to make one-time milestone payments of up to $2.3 million for the first licensed product. Upon commercializing a licensed product, Otonomy is obligated to pay Durect tiered low single-digit royalties on annual net sales by Otonomy or sublicensees of the licensed products. Each sublicense Otonomy grants to a third party is subject to payment to Durect of a low double-digit percentage of all non-royalty payments Otonomy receives. Otonomy is also obligated to pay INSERM, on behalf of Durect, for a low single-digit royalty payment on net sales by Otonomy or sublicensees.

Commercialization

Sales And Marketing

Otonomy currently has no marketing or sales force capabilities in place to commercialize a potential therapeutic. Otonomy plans to commercialize AuriPro, OTO-104 and other products in the U.S. with its own sales force targeting approximately 5,000 ENTs who perform the majority of TTP surgeries as well as treat Ménière's disease and tinnitus. The Company's initial targets for AuriPro are fewer than 2,500 ENTs who may perform approximately 80% of the TTP surgeries in the U.S. with approximately 40 sales reps.

For OTO-104, Otonomy expects its initial target audience will be approximately 4,000 ENTs contributing to approximately 80% of the prescription volume for the pharmaceutical class most frequently prescribed by ENTs.

For Ex-U.S. commercial opportunities, Otonomy noted that it planned to evaluate whether to commercialize by itself or to seek partners.

Pricing & Reimbursement

It is expected that AuriPro will be reimbursed as a physician-administered drug in the U.S. The Company will need to assess where the majority of pediatric TTP procedures are performed, for formulary and reimbursement preparation. The reimbursement process for AuriPro would be the same as for other acute setting drugs, such as antibiotics. In our model we assume an AWP of $250 per treatment course, which we derived by assessing the cost of currently administered antibiotics off-label for the treatment of TTP. In this case Ciprodex Otic is administered twice daily for seven days or 14 total administrations with a cost per total course of treatment of $159.2. The pricing is in line with the Company guidance of $200 to $250.

Reimbursement for OTO-104 is different from AuriPro, and it is separate from the IT injection procedure itself and based on the product's average selling price. Otonomy expects that OTO-104 would be distinct from any other J-Code drug (a billing code for drugs administered other than oral method, chemotherapy drugs; examples of J-Code drugs include Humira and Barazyme), and that it would be assigned a unique J-Code. The company noted that this could simplify billing and enable electronic adjudication by payers according to the average selling price. For the purposes of our model, we assume an AWP of $6000 per patient per year. We have taken the aggregate cost of dexamethasone and the cost of administration and applied that to OTO-104. The total cost of

corticosteroid administration is $3,000 per injection, and patients may need as many as four injections per year.

Manufacturing

Otonomy currently contracts with third parties for the manufacturing of its product candidates. The Company noted that it did not own and had no plans to build its own clinical or commercial manufacturing capabilities. The use of contracted manufacturing is more cost-efficient and has eliminated the need for direct investment in manufacturing facilities.

The basis for the formulation of Otonomy current product candidates is P407, a thermos-reversible polymer. The Company currently purchases P407 from a single supplier on a purchase-order basis and Otonomy does not have a long-term supply agreement.

AuriPro is a suspension containing the antibiotic ciprofloxacin and P407. Otonomy currently uses a single third-party contract manufacturer to produce AuriPro pursuant to a development and clinical supply agreement and is in the process of formalizing a commercial supply agreement.

OTO-104 is a suspension containing the steroid dexamethasone and P407. Otonomy currently uses two third-party contract manufacturers to produce OTO-104. Otonomy is currently evaluating its supply chain for the commercial manufacture of OTO-104.

OTO-311 is a suspension containing gacyclidine and P407. Otonomy has not yet selected a manufacturer for the raw material or finished goods supply as OTO-311 is in preclinical development.

Management And Compensation

Management Team

David A. Weber, Ph.D. Chief Executive Officer and President

Dr. Weber has served as Otonomy's president and CEO and on board of directors since November 2010. Prior to joining the company, he served from February 2004 to April 2010 as the CEO of MacuSight, Inc., a developer of a sustained-delivery formulation of sirolimus for the treatment of severe ophthalmic diseases. Prior to MacuSight, Dr. Weber served as acting CEO of Oculex Pharmaceuticals, Inc., a specialty pharmaceutical company focused on the development and commercialization of intraocular pharmaceuticals and drug delivery systems, until its acquisition by Allergan in 2003. Dr. Weber has also held management positions with Oral-B Laboratories Procter & Gamble. Dr. Weber received his doctorate in medical microbiology from Creighton University and his master's degree and bachelor's degree in biological sciences from Wichita State University.

Paul E. Cayer, Chief Financial and Business Officer

Mr. Cayer has served as Otonomy's CBO since October 2008, and CFO since October 2010, and secretary since February 2011. Prior to joining Otonomy, Mr. Cayer served from 2005 to 2008 as SVP, corporate development for Verus Pharmaceuticals, Inc., a specialty pharmaceutical company focused on the treatment of allergic and respiratory disorders in children. From 2001 to 2005, Mr.

Cayer served as the CFO and SVP, business development of Targeted Molecules Corporation, a biopharmaceutical company. Mr. Cayer has also held various management positions with Gensia Pharmaceuticals, Inc., a biopharmaceutical company, Acuson, a provider of medical ultrasound systems, Castle & Cooke, a consumer products company and served as consultant with Booz-Allen & Hamilton, a management and technology consulting firm. Mr. Cayer received his master's degree in business and bachelor's degree in biomechanical engineering from Harvard University.

Carl LeBel, Ph.D., Chief Scientific Officer

Dr. LeBel has served as Otonomy's CSO since April 2009. Dr. LeBel has more than 25 years of pharmaceutical research and development experience. From 2003 to 2007, Dr. LeBel served as executive director and from 1993 to 2003 in a variety of other positions, at Amgen. From 1991 to 1993, Dr. LeBel served as research scientist at Alkermes. From 1990 to 1991, Dr. LeBel served as a consultant at Arthur D. Little, Inc., a management and technology consulting firm. He is a scientific fellow of the American Academy of Otolaryngology—Head & Neck Surgery. Dr. LeBel received a doctorate in biomedical sciences/toxicology from Northeastern University and a bachelor's degree in chemistry from the University of Detroit.

Robert Michael Savel, II, Chief Technical Officer

Mr. Savel has served as Otonomy's CTO since January 2014. From 2011 to December 2013, Mr. Savel served as GM and SVP of operations for Optimer Pharmaceuticals, Inc. From 2010 to 2011, Mr. Savel served as SVP and CTO for Inspire Pharmaceuticals, Inc., an ophthalmic pharmaceutical company. From 2008 to 2010, Mr. Savel served as president of Savel Enterprises LLC, a management consulting firm. From 2007 to 2008, Mr. Savel served as the SVP of Technical Operations for PDL BioPharma, an antibody manufacturer. Earlier in his career, he held leadership operating positions with Johnson & Johnson, including the position of vice president, Quality and Compliance. Mr. Savel received his bachelor's degree in mechanical engineering from Virginia Polytechnic Institute and State University.

Compensation

Otonomy's executive compensation is determined by a Compensation Committee, which, except for Dr. Jay Lichter, is independent. The Compensation Committee makes compensation decisions regarding the executive officers, and oversees compensation policies, plans and benefit programs.

We believe that the compensation rules established for Otonomy are fair and are aligned with shareholder interest. A significant part of the total compensation package includes bonus and option awards, which are an incentive for the management team to meet the short- and long-term goals of the corporation. Executive compensation is summarized in the exhibit below.

Exhibit 47: Compensation For Otonomy Named Executive Officers in 2013

Name and Principal Position	Year	Salary ($)	Bonus ($)[1]	Option Awards ($)[2]	Total ($)
David A. Weber, Ph.D. President and Chief Executive	2013	428,500	107,125	559,052	1,094,677
Carl LeBel, Ph.D. Chief Scientific Officer	2013	337,500	67,500	180,467	585,467
Paul E. Cayer Chief Financial and Business	2013	305,000	61,000	180,467	546,467

(1) Bonus payments earned in 2013; (2) The aggregate grant date fair value of stock options granted during 2013. These amounts do not reflect the actual economic value that will be realized by the named executive officer upon the vesting of the stock options, the exercise of the stock options, or the sale of the common stock underlying such stock options. Source: Otonomy filings

Exhibit 48: Outstanding Equity Awards at Year-End 2013

Name	Vesting Commencement	Number of Securities Underlying Unexercised Options Exercisable	Unexercisable	Option Exercis	Option Expiration
David A. Weber, Ph.D.[1]	11/21/2010	3,355,000	—	0.09	11/21/2020
	5/18/2011	2,018,704	—	0.09	6/15/2021
	9/1/2013	7,416,588	8,000,000	0.05	12/20/2023
Carl LeBel, Ph.D.[2]	6/16/2010	218,750	31,250	0.08	6/16/2020
	11/19/2010	809,375	240,625	0.09	11/19/2020
	9/18/2012	218,750	481,250	0.03	9/18/2022
	9/1/2013	0	4,976,602	0.05	12/20/2023
Paul E. Cayer[3]	6/16/2010	262,500	37,500	0.08	6/16/2020
	11/19/2010	809,375	240,625	0.09	11/19/2020
	9/18/2012	218,750	481,250	0.03	9/18/2022
	9/1/2013	0	4,976,602	0.05	12/20/2023

(1) Dr. Weber was granted an option to purchase 8,535,000 shares of common stock on June 3, 2014 at an exercise price of $0.18 per share. The option vests with respect to 25% of the shares subject to the option on April 23, 2015, and 1/36th of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date. All of the shares underlying this option are subject to an early exercise provision. (2) Dr. LeBel was granted an option to purchase 2,990,000 shares of common stock on June 3, 2014 at an exercise price of $0.18 per share. The option vests with respect to 25% of the shares subject to the option on April 23, 2015, and 1/36th of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date. (3) Mr. Cayer was granted an option to purchase 2,990,000 shares of common stock on June 3, 2014 at an exercise price of $0.18 per share. The option vests with respect to 25% of the shares subject to the option on April 23, 2015, and 1/36th of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date. Source: Otonomy filings

Financials

In 3Q14 Otonomy reported cash and cash equivalents of $165.2M, or $7.8 per share based on basic shares outstanding. Total operating expenses for the quarter were $9.4M.

In January 2015, Otonomy closed a follow-on public offering of 2.9M shares of its common stock for total gross proceeds of approximately $86 million before deducting underwriting discounts and commissions and other offering expenses.

We believe Otonomy is sitting on a cash balance of more than $220M, which we anticipate is sufficient to fund operations through 2016/2017. We forecast AuriPro receiving approval by the FDA between YE15 and 1H16, and being launched in 2016. We forecast OTO-104 for Ménière's disease approval and launch in 2H17. Finally we believe the Company will raise funds through an equity raise of 3M shares before the launch of OTO-104 in 2017.

Exhibit 49: Otonomy, Inc. Quarterly P&L Model

(in millions)	2012A	2013A	Q1+Q2:14A	Q3:14A	Q4:14E	2014E	Q1:15E	Q2:15E	Q3:15E	Q4:15E	2015E
Product Revenues											
U.S. Total AuriPro Revenue from TTP Surgery (MM)											
Royalty of EU Sales of AuriPro Booked by Otonomy (20%) (MM)											
U.S. Total OTO-104 Revenue For Ménière's disease											
Royalty of EU Sales of OTO-104 Booked by Otonomy (20%) (MM)											
WW Total Product Revenues Booked by Otonomy	-	-	-	-	-	-	-	-	-	-	-
Collaboration revenue (cost)											
Licensing payment to University of California	-	-	-	-	-	-	-	-	-	-	-
Licensing payment to DURECT Corporation	(0.0)										
Licensing payment to INSERM	-										
Total Collaboration Revenue (Cost)	**(0.0)**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
Total Revenues	**(0.0)**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
Operating Expenses											
COGS	-	-	-	-	-	-	-	-	-	-	-
Research and Development	8.5	16.3	24.6	7.4	10.7	42.6	18.0	18.0	18.0	18.0	72.0
General and Administrative	2.4	3.5	5.2	2.0	2.4	9.6	3.0	3.1	3.3	3.4	12.8
Sales Force	-	-	-	-	-	-	-	-	-	-	-
Total Operating Expenses	**10.9**	**19.9**	**29.8**	**9.4**	**13.1**	**52.2**	**21.0**	**21.1**	**21.3**	**21.4**	**84.8**
Income (Loss) from Operations	**(11.0)**	**(19.9)**	**(29.8)**	**(0.0)**	**(13.1)**	**(42.8)**	**(21.0)**	**(21.1)**	**(21.3)**	**(21.4)**	**(84.8)**
Other income (loss)											
Interest expense	-	-	(0.0)	(0.0)	(0.0)	(0.1)	-	-	-	-	-
Change in fair value of convertible preferred stock warrant liability	-	-	(3.3)	(2.6)	(2.0)	(7.9)	-	-	-	-	-
Other income (loss), net	-	-	0.0	0.0	0.0	0.1	-	-	-	-	-
Total other income (loss)	**3.4**	**0.3**	**(3.3)**	**(2.6)**	**(2.0)**	**(7.9)**	**-**	**-**	**-**	**-**	**-**
Net Income (Loss)	**(7.6)**	**(19.6)**	**(33.1)**	**(12.0)**	**(15.0)**	**(60.1)**	**(21.0)**	**(21.1)**	**(21.3)**	**(21.4)**	**(84.8)**
Accretion to redemption value of convertible preferred stock	(0.8)	(0.5)	(0.0)	(0.0)	(0.0)	(0.1)	-	-	-	-	-
Net income attributable to common stockholders	**(8.4)**	**(20.1)**	**(33.1)**	**(12.0)**	**(15.0)**	**(60.2)**	**(21.0)**	**(21.1)**	**(21.3)**	**(21.4)**	**(84.8)**
Tax rate	-	-	-	-	-	-	-	-	-	-	-
Income Tax	-	-	-	-	-	-	-	-	-	-	-
Net Income (Loss) per Share - Basic	**(3.38)**	**(7.64)**	**-**	**(1.23)**	**(0.71)**	**(3.88)**	**(0.87)**	**(0.87)**	**(0.87)**	**(0.86)**	**(3.46)**
Net Income (Loss) per Share - Diluted	**(3.38)**	**(7.64)**	**-**	**(1.23)**	**(0.64)**	**(3.63)**	**(0.80)**	**(0.79)**	**(0.79)**	**(0.79)**	**(3.17)**
Weighted average common shares outstanding - basic	2.5	2.6	-	9.8	21.2	15.5	24.1	24.4	24.6	24.9	24.5
Weighted average common shares outstanding - diluted	2.5	2.6	-	9.8	23.4	16.6	26.3	26.6	26.9	27.1	26.7

Source: SunTrust Robinson Humphrey and company reports

Exhibit 50: Otonomy, Inc. Annual P&L Model

(in millions)	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Product Revenues														
U.S. Total AuriPro Revenue from TTP Surgery (MM)					12.0	32.3	49.9	68.6	79.5	86.5	93.8	101.4	109.5	112.8
Royalty of EU Sales of AuriPro Booked by Otonomy (20%) (MM)					0.4	3.0	6.2	9.6	13.3	15.4	16.7	18.1	19.6	21.1
U.S. Total OTO-104 Revenue For Ménière's disease					-	40.9	216.3	326.0	399.6	454.3	513.3	546.5	580.6	615.7
Royalty of EU Sales of OTO-104 Booked by Otonomy (20%) (MM)					-	3.4	20.9	35.8	44.3	53.2	62.7	68.6	74.8	77.1
WW Total Product Revenues Booked by Otonomy	-	-	-	-	12.4	79.7	293.4	440.0	536.7	609.3	686.4	734.6	784.5	826.7
Collaboration revenue (cost)														
Licensing payment to University of California	-	-	-	-	(0.4)	(2.4)	(8.8)	(13.2)	(16.1)	(18.3)	(20.6)	(22.0)	(23.5)	(24.8)
Licensing payment to DURECT Corporation	(0.0)													
Licensing payment to INSERM	-													
Total Collaboration Revenue (Cost)	**(0.0)**	**-**	**-**	**-**	**(0.4)**	**(2.4)**	**(8.8)**	**(13.2)**	**(16.1)**	**(18.3)**	**(20.6)**	**(22.0)**	**(23.5)**	**(24.8)**
Total Revenues	**(0.0)**	**-**	**-**	**-**	**12.0**	**77.3**	**284.6**	**426.8**	**520.6**	**591.0**	**665.8**	**712.6**	**761.0**	**801.9**
Operating Expenses														
COGS	-	-	-	-	1.8	11.0	39.9	59.2	71.9	81.1	91.1	97.2	103.5	109.3
Research and Development	8.5	16.3	42.6	72.0	60.0	65.0	75.0	75.0	78.1	88.7	99.9	106.9	114.1	120.3
General and Administrative	2.4	3.5	9.6	12.8	14.0	14.5	15.0	16.0	17.0	18.0	18.5	19.0	20.0	20.5
Sales Force	-	-	-	-	10.0	20.0	20.4	20.8	21.2	21.6	22.1	22.5	23.0	23.4
Total Operating Expenses	**10.9**	**19.9**	**52.2**	**84.8**	**85.8**	**110.5**	**150.3**	**171.0**	**188.2**	**209.4**	**231.5**	**245.6**	**260.6**	**273.5**
Income (Loss) from Operations	**(11.0)**	**(19.9)**	**(42.8)**	**(84.8)**	**(73.8)**	**(33.2)**	**134.2**	**255.8**	**332.4**	**381.6**	**434.3**	**467.0**	**500.3**	**528.4**
Other income (loss)														
Interest expense	-	-	(0.1)	-	-	-	-	-	-	-	-	-	-	-
Change in fair value of convertible preferred stock warrant liability	-	-	(7.9)	-	-	-	-	-	-	-	-	-	-	-
Other income (loss), net	-	-	0.1	-	-	-	-	-	-	-	-	-	-	-
Total other income (loss)	**3.4**	**0.3**	**(7.9)**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
Net Income (Loss)	**(7.6)**	**(19.6)**	**(60.1)**	**(84.8)**	**(73.8)**	**(33.2)**	**134.2**	**255.8**	**332.4**	**381.6**	**434.3**	**467.0**	**500.3**	**528.4**
Accretion to redemption value of convertible preferred stock	(0.8)	(0.5)	(0.1)	-	-	-	-	-	-	-	-	-	-	-
Net income attributable to common stockholders	**(8.4)**	**(20.1)**	**(60.2)**	**(84.8)**	**(73.8)**	**(33.2)**	**134.2**	**255.8**	**332.4**	**381.6**	**434.3**	**467.0**	**500.3**	**528.4**
Tax rate	-	-	-	-	-	*0.0*	*0.1*	*0.1*	*0.2*	*0.3*	*0.4*	*0.4*	*0.4*	*0.4*
Income Tax	-	-	-	-	-	(1.0)	10.7	30.7	59.8	103.0	152.0	163.4	175.1	184.9
Net Income (Loss) per Share - Basic	**(3.38)**	**(7.64)**	**(3.88)**	**(3.46)**	**(2.98)**	**(1.20)**	**4.70**	**8.69**	**10.97**	**12.22**	**13.51**	**14.10**	**14.67**	**15.04**
Net Income (Loss) per Share - Diluted	**(3.38)**	**(7.64)**	**(3.63)**	**(3.17)**	**(2.76)**	**(1.12)**	**4.41**	**8.17**	**10.32**	**11.52**	**12.75**	**13.34**	**13.89**	**14.27**
Weighted average common shares outstanding - basic	2.5	2.6	15.5	24.5	24.7	27.7	28.6	29.4	30.3	31.2	32.2	33.1	34.1	35.1
Weighted average common shares outstanding - diluted	2.5	2.6	16.6	26.7	26.7	29.6	30.5	31.3	32.2	33.1	34.1	35.0	36.0	37.0

Source: SunTrust Robinson Humphrey and company reports

Company Description

Otonomy is a clinical-stage biopharmaceutical company focused on the development and commercialization of therapeutics for otic diseases. Otonomy has developed a proprietary technology to deliver drugs which are retained in the ear for an extended period of time. Based on this technology, Otonomy has three product candidates in clinical and preclinical development. Its lead product candidate, AuriPro, is a sustained-exposure formulation of the antibiotic ciprofloxacin which has recently completed two Phase III clinical trials for middle ear effusion during tympanostomy tube placement (TTP) surgery and is preparing for an NDA filing in 1Q15. The second product candidate, OTO-104, is a sustained-exposure steroid that is in a Phase IIb clinical development for patients with Ménière's disease. Otonomy expects to report results from this trial in 2Q15. Its third product candidate, OTO-311, is in preclinical development for the treatment for tinnitus.

Investment Thesis

We view Otonomy as an attractive clinical stage biotechnology play. Otonomy is building an otology powerhouse in a large and under-addressed space with limited competition. The Company differentiates via a proprietary Sustained Exposure technology, which solves the issues of delivering drugs successfully to the mid/inner ear. We view the technology as largely de-risked with successful Phase III trial results from AuriPro, and Phase Ib trial results from OTO-104 in delivering different drugs in distinct otic indications. An NDA submission for lead asset AuriPro is expected in 1Q15 with an FDA decision as early as YE15; top-line results for OTO-103 Phase IIb addressing the larger market of Ménière's disease is expected in 2Q15.

Valuation and Risks

Our price target of $47 is determined by taking an average of three different model methodologies. We reach a 12-month price target of $51.0 with a discounted earnings model, a price target of $45.7 with a discounted cash flow model, and a price target of $43.1 with a clinical NPV model. Details of these models are contained within this report.

Regulatory risk of AuriPro: while AuriPro's Phase III clinical trials met their clinical endpoints and we believe the drug is approvable, there is no guarantee that the FDA will approve the product. One data point that is more concerning is the trials' secondary endpoint that evaluated the cumulative proportion of patients considered treatment failures due to an observation of otorrhea. A significant difference of failure rate is seen between the two sham groups (16% vs 28%). Although the reduction in the rate of otorrhea by AuriPro was statistically significant in both trials ($p=0.038$ and $p<0.001$), the FDA may have questions regarding the data.

Commercial risk of AuriPro: Otonomy has not previously launched or marketed products. In order to successfully commercialize AuriPro, Otonomy needs to secure payer coverage and AuriPro needs to be included in the formulary list of hospital outpatient facilities and ambulatory surgery centers. The decision will be based on not only the clinical data, but also pricing of AuriPro, which is still unknown. Should AuriPro fail to be covered by formularies, we expect it will significantly dim AuriPro's commercial prospects.

Otonomy also needs to build sales/marketing infrastructure, including sales force, medical science liaisons (MSL), etc., to commercialize AuriPro. According to Otonomy, the Company expects to launch AuriPro with 30 to 40 reps (with a maximum of 80 reps including those for OTO-104).

Clinical risk of OTO-104 and OTO-311: OTO-104's Phase Ib demonstrated some therapeutic signals in reducing vertigo frequency. However, the study was not designed and powered to do so, and the results may not translate into the current Phase IIb trial.

Technology risk of sustained exposure formulation technology: In theory, the sustained exposure formulation technology should be applicable to other otic indications. Preclinical studies

have demonstrated the possibility of co-formulating Poloxamer 407 (P407) with different therapeutic agents. However, different drugs will change the properties of co-polymers, including transition temperature, bioadhesive force, etc., which could make the co-formulation of drugs with P407 more difficult or even impossible.

Competition risk: A handful of other companies are developing therapeutics in the otic field, and some examples are listed below. We believe Otonomy's clinical assets with sustained exposure formulation technology offer an appealing treatment option to physicians and patients. However competitors may have a first-to-launch advantage if they launch products earlier or have better pricing/reimbursement coverage.

Companies Mentioned in This Note

Auris Medical Holding AG (EARS, $4.35, NR)
Novartis (NVS, $97.41, NR)
Sanofi (SNY, $46.93, NR)
Salvat (Private)
WraSer Pharmaceuticals (Private)
Synphora AB (Private)
Pfizer (PFE, $32.02, Reduce)

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I, Edward Nash , hereby certify that the views expressed in this research report accurately reflect my personal views about the subject company(ies) and its (their) securities. I also certify that I have not been, am not, and will not be receiving direct or indirect compensation in exchange for expressing the specific recommendation(s) in this report.

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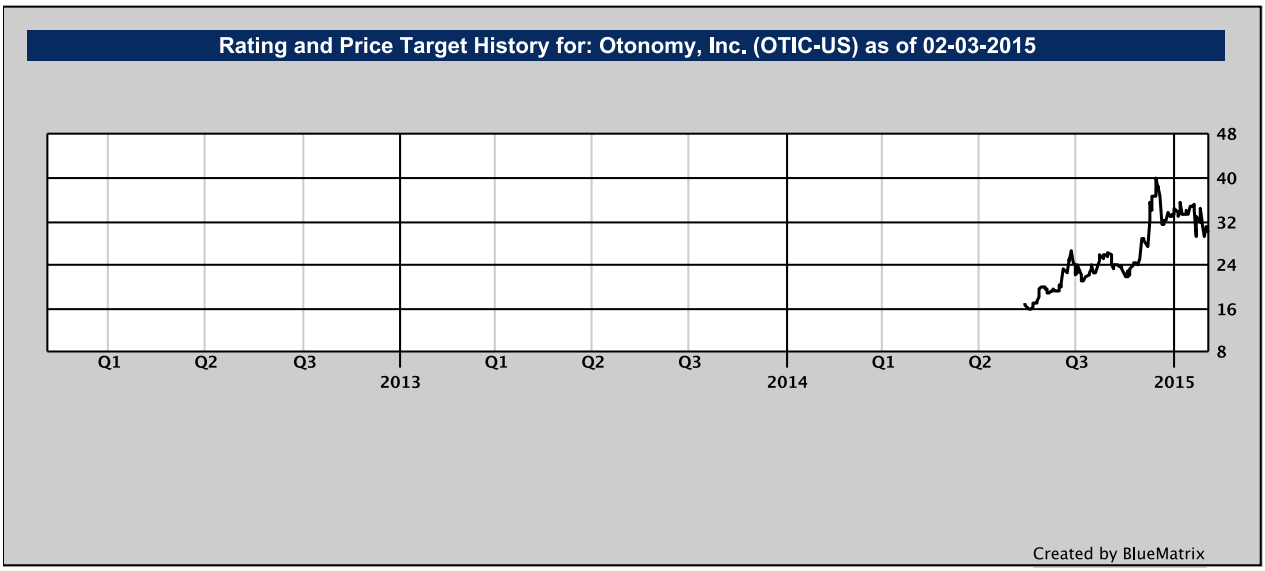

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- **Reduce** – total return ≤ negative 10% (5% for low Beta securities)
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**Price targets are within a 12-month period, unless otherwise noted
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Legend for Rating and Price Target History Charts:
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I = initiate coverage
T = transfer coverage

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