Equity Research

Quick Take: Company Update

August 13, 2015

Price: $24.71 (08/12/2015)

Price Target: $55.00

OUTPERFORM (1)

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Key Data

Symbol	NASDAQ: OTIC
Market Cap (MM)	$598.0

Programs On Track; Heading Towards AuriPro Launch & OTO-104 Pivotal Trial Start

The Cowen Insight

Otonomy reported Q2 earnings and provided updates on its clinical programs. Importantly, the operational/commercial preparation will accelerate in H2 half as the AuriPro approval date nears, the OTO-104 Phase III program is initiated, and as OTO-311 enters the clinic. Given our consultants belief that the approach/technology is compelling, we believe OTIC shares remain undervalued.

AuriPro Approval Date By Year-End And Launch Expected In Early 2016; OTO-104 Pivotal To Start In Q4 Post EOPII FDA Meeting

Otonomy reported Q2 earnings and provided updates on its clinical programs. Importantly, AuriPro (sustained-release ciprofloxacin), for the treatment of middle ear effusion at the time of TTP surgery, has received NDA acceptance and we now await the December 25, 2015 PDUFA date as the Company continues to prepare for commercialization. And we – and our consultants – continue to believe it will receive a clean review. Worth noting, based upon previous FDA feedback, it appears that the Company will not be required to have an advisory committee meeting. Upon potential approval – which we believe will occur – Otonomy expects to launch the product in the first quarter of 2016 and commercial activities should continue to accelerate through the end of the year. On the commercial front, we would note that Otonomy has made some recent solid additions and that they appear to be taking a very deliberate, methodical approach to preparing for the product introduction. Recall, Otonomy also completed a one month Phase II trial for AuriPro in the first follow-on indication, acute otitis media in pediatric patients with tympanostomy tubes (AOMT), which demonstrated the feasibility of administering AuriPro. This is critical because it is the first demonstration of administering AuriPro in the physician's office while children are not under general anesthesia and this has significant implications for additional future follow-on indications. And in July, the Company initiated enrollment in a Phase II clinical trial for a second label expansion indication, otitis externa or swimmer's ear, which is a significant follow-on indication and the largest portion of branded CiproDex sales, which is the leading product in the space. This will be a on-month prospective, open-label trial enrolling 75 patients in order to assess the feasibility of administering AuriPro as a single-dose treatment for patients with otitis externa. The bottom line is that these expansion indications could more than double the market opportunity for AuriPro beyond the initial indication and we currently do not include them in our model. We continue to believe that Otonomy has a relatively impressive amount of development programs ongoing/planned and management continues to execute exceptionally well. Ultimately, we believe the company will be successful in developing these novel and innovative drugs for the treatment of various ear disorders – historically an area with a lack of treatment options – that serve real unmet needs and offer product profiles that our physician consultants find very attractive. Our consultants believe the Company's technology is novel, needed, and should provide significant value from these levels. Given several near-term events and

that our consultants believe that the approach/technology and these several programs are promising, we believe OTIC shares are undervalued here.

As for the OTO-104 clinical program, as we discuss in detail below, although the slight Phase IIb miss was disappointing, in actuality we believe that the learning from the study will now allow for the proper adjustments that should enhance the probability of success in Phase III. We expect further information from the Company's analysis of the trial to be shared during the upcoming October 7th investor day. Importantly, there will be no meaningfully delay as the Company plans to hold an End of Phase II meeting soon and initiate the first Phase III study during Q4, with the second to begin in Q1. We believe final results from these studies could come by mid-year 2017. Therefore, OTO-104 could be launched in the U.S. during 2018 assuming successful development. It is important to note that OTO-104 has been granted Fast Track Designation, so there is potential to receive an expedited 6-month regulatory review.

Otonomy is also developing a third drug candidate, OTO-311 (sustained-release gacyclidine), for the treatment of tinnitus, which is ringing in the ear in the absence of an external source. Approximately 16MM patients in the U.S. suffer from tinnitus severe enough to require medical attention. However, like Ménière's, there are no currently approved treatments for this debilitating condition and we expect this could be an additional meaningful future revenue stream for the Company if successfully developed. Otonomy expects to file an IND and initiate a Phase I clinical trial for OTO-311 in Q4.

The Valuation Looks Attractive Here

Our base case valuation model assumes a U.S. approval and subsequent launch of AuriPro by the second quarter of 2016 and we believe U.S. peak sales could reach approximately ~$500MM for middle ear indications, assuming a penetration of roughly 30% of U.S. antibiotic ear drop prescriptions by 2025. We also assume modest EU sales beginning in 2018 for AuriPro with a peak sales value of $300MM +. For OTO-104, we assume U.S. approval and launch in 2018. Assuming a peak 15% penetration of Ménière's patients results in a $750MM+ U.S. peak sales potential. We also expect approval in the EU in 2020 with peak sales eventually reaching $400MM +. Worth noting, our estimates for both products could ultimately be conservative as our consultants suggest each has very logical and viable follow-on indications that the Company is exploring. European approval could also potentially come sooner than we model. Approvals/partnerships in the rest of the world could also provide further upside. We would also note that our valuation does not attribute any potential sales of OTO-311, which like OTO-104, is competing in a market with no currently approved treatments and could potentially have significant pricing flexibility and provide further upside beyond our base case valuation. Using the sales estimates provided above, we arrive at a DCF valuation of $55 per share. Label expansion of AuriPro and OTO-104 is likely and should provide further upside. An eventual approval and launch of OTO-311, the Company's earlier stage candidate for tinnitus to enter the clinic this year, could provide even further upside.

Our Clinician Consultants Believe AuriPro Phase III Clinical Data Support Approval

For AuriPro, Otonomy has completed two identical Phase III trials (Study 302 and Study 303) in 532 total pediatric patients across ~60 sites in the U.S. and Canada and the results of these trials form the basis for the NDA submission. Importantly, AuriPro achieved its primary efficacy endpoint along with several secondary endpoints. AuriPro reduced the risk of treatment failure by an average of 49% ($p<0.001$) and also reduced the proportion of patients that were treatment failures due to otorrhea or use of antibiotics by an average of 62% ($p\leq0.004$) across both trials. AuriPro was well-

tolerated, and there were no notable differences in safety between patients treated with AuriPro or sham. Of note, the AuriPro gel did not cause any increase in the incidence of tube clogging relative to sham in either the Phase II or Phase III studies. Overall, our consultants found the Phase III data to be impressive and highlighted that in terms of safety, efficacy, and convenience, AuriPro's product profile would provide a superior option relative to current antibiotic ear drops.

Our View On The Ménière's Program's Probability Of Success Remains Unchanged And We Believe The Phase III Program Will Now Be Enriched

In May, Otonomy reported topline Phase IIb results for OTO-104 (sustained-release dexamethasone) in Ménière's disease. Unfortunately, the primary endpoint of the reduction of vertigo frequency at month 3 versus baseline – as discussed further below – narrowly missed statistical significance (p=0.067). However, statistical significance was reached on 5 out of 6 prospectively-defined, vertigo-based secondary endpoints at various time points, and importantly, the data from these various endpoints all seemed to trend in the same positive direction. Although disappointing, in actuality we believe that the learning from the Phase IIb study will now allow for the proper adjustments that should enhance the probability of success in Phase III and we believe there will be no meaningful delay. And given the results from this dataset, we believe the drug is indeed active and that the learnings from this exploratory Phase IIb study will now allow management to prospectively design the Phase III program with a more specific and appropriate baseline patient criteria, and with the proper powering. Specifically – although the analysis is not yet complete – it appears that the more severe patients (higher baseline vertigo frequency) had an increased response to OTO-104 treatment. Moreover, patients at the very top of the range (16-20 vertigo days) don't have consistent clinical responses and provide added variability, so these patients may be excluded. Given the very near miss, we believe a fully enriched study with that patient population and with greater powering would likely more easily meet the hurdle for statistical significance. Additionally, during the upcoming End Of Phase II meeting with the Agency, the Company will aim to pursue the count of definitive vertigo days endpoint as a primary endpoint in Phase III while using the Poisson statistical test, which is commonly used and appears most appropriate for this population. Recall, in the prior Phase IIb results this prospectively defined endpoint was positive (p=0.03). The bottom line is that there does not appear to be a change in the timeline of this program and that the lessons learned from this more robust study only increases our conviction that the Phase III design will be enhanced, providing an even greater chance of success. And not to be naive, one could take the view that if this Phase IIb study had barely reached statistical significance, it could have made management complacent, which might have resulted in a single Phase III study designed the same way, which could have led to a higher risk of failure – and ultimately more time lost. However, with this near miss, we believe it will force management to be incrementally more comprehensive – and ironically – may lead to a more robust/enriched Phase III program that in actuality will have a lower risk profile.

As for the specifics of the Phase IIb Ménière's study, there was a narrow miss on the primary endpoint of the reduction in vertigo frequency during month 3 following treatment with OTO-104 when compared to a one month baseline period (43% for placebo and 61% for OTO-104; p=0.067). Importantly, there was an average reduction in days with vertigo from 8 to 3. Additionally, statistical significance was reached on multiple prospectively defined secondary endpoints at various time points (5 out of 6 hit statistical significance), and the data from these various endpoints all seem to trend in the same positive direction. Further, a prospectively defined subgroup analysis – not post-hoc – suggests an increased OTO-104 treatment effect in patients with higher baseline vertigo frequency, all while the placebo response remained at similar levels. No drug-related serious adverse events were observed and there were no

safety concerns with audiometry, tympanometry, and otoscopy. There were persistent perforations in only 2.6% of patients treated with OTO-104, which was consistent with the prior Phase Ib results and previously published literature.

Background On The Initial OTO-104 Phase Ib Ménière's Data

Generally, we view the OTO-104 development risk as relatively low given that IT steroid injections are already used quite frequently in practice and appear to be moderately effective. The goal of OTO-104, is simply to provide higher and sustained concentration of dexamethasone relative to existing injections. In a Phase Ib clinical trial, OTO-104 demonstrated a significant mean reduction in vertigo frequency (pivotal primary endpoint) during month 3 relative to baseline. There was a clear dose response as a 56% and 73% (p-value=0.086; n=16) reductions in vertigo frequency in month 3 was observed with the 3mg and 12mg OTO-104 dosing cohorts. The 73% reduction in the 12mg group was equivalent to a reduction in days with vertigo from 8 at baseline to 2 in month 3. A day with vertigo is defined as an episode lasting at least 20 minutes and being completely debilitating. Interestingly, 50% of patients in this study had no vertigo in the third month. Furthermore, 81% of patients in the 1mg OTO-104 arm had at least a 50% improvement in vertigo frequency in month 3 versus baseline. Clearly, the 12mg OTO-104 group was not statistically significant, but we would note that it is due to the study arm only having 16 patients and the fact that it was even close (0.036 off) is impressive. In general, a single injection of OTO-104 was well tolerated and there were no serious adverse events observed during the trial. Moreover, there were no instances of persistent conductive hearing loss associated with OTO-104 injection. In the EU, a multiple-dose U.K safety study has completed enrollment in April and we generally expect a potential European launch at least 1-2 years later as the priority post launching in the U.S. market will be to expand in additional indications.

Valuation Methodology And Risks

Valuation Methodology

Pharmaceuticals/Specialty

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

Investment Risks

Pharmaceuticals/Specialty

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

Risks To The Price Target

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

Addendum

Stocks Mentioned In Important Disclosures

Ticker	Company Name
OTIC	Otonomy

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Assumption: The expected total return calculation includes anticipated dividend yield

Cowen and Company Rating System until May 25, 2013

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

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Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	476	59.20%	110	23.11%
Hold (b)	314	39.05%	7	2.23%
Sell (c)	14	1.74%	0	0.00%

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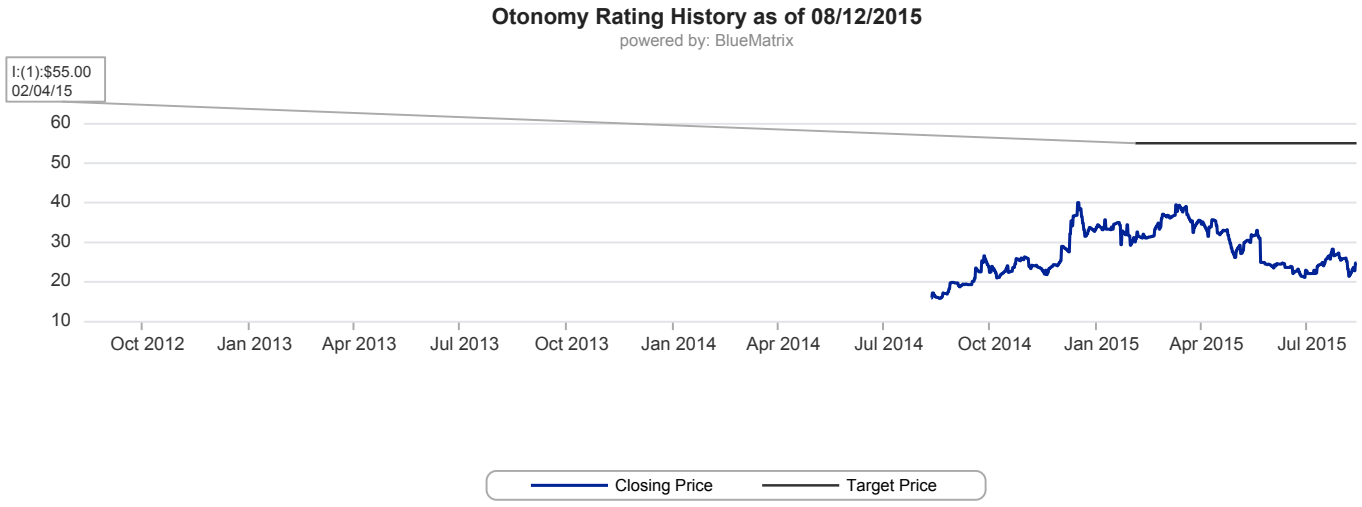

Legend for Price Chart:

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

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