Ocular Therapeutix

Equity Research

Quick Take: Company Update

April 7, 2015

Price: $38.30 (04/6/2015)

Price Target: $60.00

OUTPERFORM (1)

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Key Data

Symbol	NASDAQ: OCUL
Market Cap (MM)	$820.2

A High Placebo Rate Doesn't Dissuade Us - Our Conviction Remains Unchanged

The Cowen Insight

While the Phase IIIb data for OTX-DP in post-op pain and inflammation failed to show statistical significance on a co-primary endpoint, we continue to believe that the platform technology is sound and differentiated. Our thesis continues to be predicated on the OTX-TP glaucoma program, which reports Phase IIb data in Q4 and we believe will be successful. We would add into this weakness.

Topline Data Is Disappointing, But Should Be An Isolated Event And Doesn't Lower Our Conviction In The Approach Or Other Clinical Programs

After reporting positive Phase IIIa data in early March for the ocular inflammation and pain program, Ocular reported disappointing topline data from the second OTX-DP Phase IIIb study, which missed one of the two co-primary endpoints (due to an abnormal placebo response), as we describe in detail below. Given the disappointing disclosure, we believe it is important to assess the trial results taking into consideration two key issues: (1) do the results have implications for the technology/company as a whole – meaning, is there a read-through from the results that would call into question the platform and approach as we analyze the other clinical programs; or (2), are the implications of the study results isolated to the specific indication – in this case the smaller, ocular inflammation and pain program. Importantly, our analysis following conversations with our consultants is that the disappointing outcome had more to do with trial design and an unexpectedly strong placebo performance rather than the effectiveness of the company's technology itself, as best demonstrated by the consistent efficacy results of the active arm in the two studies. This was further supported by the considerable difference in how the placebo arm performed across these two Phase III studies. Management noted that a disproportionate number of patients in the Phase IIIb placebo arm were: (1) using high doses of oral NSAIDs for other conditions (e.g., arthritis); and (2) receiving rescue anti-inflammatory topical eye drops, which potentially blunted the efficacy signal. In fact, using a post-hoc analysis of the absence and very minimal presence of inflammatory cells (between 0 and 0.5 on a scale of 0 to 4.0), the difference between the OTX-DP and placebo arms was highly statistically significant (66.3% in the treatment group and 42.5% in the placebo group, p=0.0004). However, the FDA uses the very stringent criteria of 0, or no inflammatory cells, but our consultants note that typically in practice having a score of 0.5 is considered a success and not clinically meaningful. Therefore, our consultants believe that including patients up to 0.5 on the 0-4.0 scale was relevant and shows that the drug is active, and that most clinicians would appear to be satisfied with this result. While we don't use this finding and consultant discussion as a means to argue that the study was successful – or that these data are sufficient for approval without another study – we do believe it reinforces the point that OTX-DP is active and the negative results were likely a trial-design/placebo-driven outcome. Furthermore, and as indicated above, these results appear to have no read-through to the other programs in development, namely OTX-

TP for glaucoma, which has Phase IIb data reading out in Q4 and has always been the largest component of our valuation.

We clearly dislike having to justify a failed study. However, the results need to be put into appropriate context as we attempt to ensure that they have no meaningful implications on the technology or other indications. Management will now meet with the FDA to discuss the pathway forward for the OTX-DP clinical program, which will likely need another confirmatory study in which we would assume Ocular will perform with more stringent criteria. This will likely cause a 6-12 month delay for this one indication, in this one program, and cost Ocular an additional $15MM. When factoring this one-year delay into our DCF valuation, a modest $3-4 share price reduction is observed relative to our $60 price target. Given the modesty of that potential valuation degradation, we are making no changes to our target. Clearly, the vast majority of our value expectations is being ascribed to OTX-TP for glaucoma, which we believe has a substantially larger market potential. Therefore, the OCUL share levels being indicated pre-market appears to be a severe overreaction, especially as our conviction in the platform technology remains firmly intact and unaffected by the study disclosure. For these reasons we would be adding aggressively on this break.

As for the specific Phase IIIb results (n=240), the trial had two primary endpoints exactly like the first which was reported in early March: (1) the difference between OTX-DP and placebo for the absence of pain on day 8; and (2) the treatment difference between both groups for the absence of anterior chamber inflammatory cells on day 14. The trial hit on (1), but not (2). Regarding the pain endpoint, 77.5% of patients receiving OTX-DP reported an absence of pain on day 8 versus 58.8% with the vehicle control (p=0.0025). This pain relief was highly statistically significant as early as day 2. For the inflammatory endpoint, 39.4% of OTX-DP-treated patients showed an absence of inflammatory cells in the anterior chamber of the eye on day 14 versus 31.3% for vehicle control (p=0.2182). As we noted above, this placebo response was unusually high and likely caused the miss, especially when compared to the results from the first study below. There are a number of factors that could have affected the placebo arm in this case: (1) a significant number of patients were rescued during days 8-14 after the pain endpoint and before the inflammation endpoint. Hence, a signal for inflammation may not have emerged as patients were being rescued, which reduces the overall powering of the study; (2) Ocular did not exclude NSAID use and there was a higher rate of systemic anti-inflammatory use observed in the placebo arm, which could have affected the inflammation endpoint; and (3), there is a fair amount of subjectivity to the results as 3 placebo patients fell into the 0.5 category with respect to the presence of inflammatory cells (on a scale of 0-4.0) because the investigators observed a single cell, which could have been a pigment cell, or a false positive. Interestingly, the company did conduct a post-hoc analysis of the absence and very minimal presence of inflammatory cells (defined as 0 and 0.5 on the scale of 0-4.0) and the difference between the OTX-DP and vehicle placebo group was highly statistically significant (66.3% in the OTX-DP group and 42.5% in the placebo group, p=0.004). Importantly, our consultants believe this finding is clinically meaningful as a score of 0.5 is perfectly reasonable as opposed to the stringent 0 FDA criteria. Nonetheless, we acknowledge, that the stringent criteria is what will be necessary for FDA approval. However, we include this analysis to further support that the efficacy of the program appears intact, while the criteria/placebo response is likely the causative reason for the miss, which has implications for how we view the technology going forward.

Regarding the Phase IIIa OTX-DP study (n=247) reported about a month ago, it was a success as it met both primary efficacy endpoints by demonstrating a statistically significant reduction in pain and inflammatory cells in the anterior chamber of the

eye. Specifically, 33.7% of patients treated with OTX-DP showed an absence of inflammatory cells in the anterior chamber of the study eye at day 14 versus 14.6% of patients that received placebo (p=0.0015). Additionally, 76.1% of patients treated with OTX-DP reported absence of eye pain in the eye on day 8 versus 36.1% of patients that received placebo (p< 0.0001). Secondary efficacy endpoints for this first clinical trial have also now been evaluated and statistically significant differences were seen for the pain endpoint at days 2, 4, 14, and 30 and for the inflammatory endpoint at day 30. No statistically significant difference was observed for the absence of inflammatory cells at the other time points in this first trial. Lastly, statistically significant differences were seen for the absence of flare at days 8, 14, and 30, but not at days 2 or 4.

Importantly, topline safety results for both clinical trials demonstrate that there were no ocular or treatment-related serious adverse events and there were fewer adverse events in the treatment group than the placebo group. The overall results and secondary endpoints from the second trial – including a potential pooled analysis – are still be evaluated by Ocular and we may see full details presented at the American Society of Cataract and Refractive Surgery (ASCRS) meeting later this month. The company also announced that they will be meeting with the FDA later this month regarding the path forward. We assume a 6-12 month delay. But we do not believe there are any additional implications other than the delay in this single indication.

Several Opportunities For Value Creation Exist

Our base case valuation model for Ocular assumes approval for OTX-TP in 2017, and U.S. peak sales eventually reaching approximately $450MM, which is a conservative penetration of roughly 5% of total U.S. glaucoma prescriptions by 2020. We also assume modest ex-U.S. sales for OTX-TP with a peak sales value of ~$150MM. For OTX-DP, we assume a successful approval in post-operative pain and inflammation, with steady growth and total peak sales of $300MM across all potential indications. Finally, we assume Ocular moves forward with OTX-MP and the product is launched in 2018/2019. Our peak sales estimate for the product is slightly above $100MM. We would note, our valuation does not attribute any value to the long-duration anti-VEGF hydrogel, which has the greatest potential upside of any of Ocular's products. If the company successfully enters the $3B+ and growing wet AMD market, with a transformational duration product, our valuation could inflect to 2-3x our base case $60 per share valuation.

Numerous Milestones Remain In 2015

As a reminder, Ocular has several upcoming milestones in 2015: (1) OTX-DP has also been evaluated in Phase II studies for allergic conjunctivitis, and after discussions with the FDA, have decided to move the program forward with two Phase III studies utilizing the Conjunctival Allergen Challenge (CAC) model; the studies are expected to begin in mid-2015; (2) OTX-DP is also being evaluated for the treatment of inflammatory dry eye disease, with Phase II data expected in Q4:2015; (3) feasibility studies with biopharmaceutical partners for the long-acting anti-VEGF hydrogel depot are ongoing and should be complete in H1:2015 with potential for a licensing agreement soon thereafter. Ocular's independent assessment of their hydrogel technology with Avastin has also been progressing and two papers on the data generated to date are expected at the ARVO meeting in May 2015; (4) Finally, and most importantly, patient enrollment for the OTX-TP Phase IIb study in glaucoma is on track and data is expected in Q4:2015.

The bottom-line is that all programs continue to progress as expected and the upcoming year contains a series of critical milestones. Our consultants continue to reiterate that Ocular's innovative drug delivery technology has the potential to serve a real unmet need of compliance in the markets that the company is targeting. As noted

above, we would add heading into a catalyst-rich 2015 with significant potential for value creation.

Specifics On Clinical Program Updates

OTX-TP: in November of last year Ocular announced the enrollment of its first patient in a randomized, blinded, active-controlled Phase IIb study comparing the product to timolol. The study will evaluate 80 patients across 10 clinical sites with topline results expected in Q4:2015. Recall, the Phase IIa data for OTX-TP looked promising as efficacy was comparable to twice-daily timolol with a duration of 2-3 months. The poor compliance for topical glaucoma eye drops is well understood by the physician community and the improvement in compliance seen with once-daily PGAs relative to treatments that require multiple daily drops suggests that a product that only requires administration every 2-3 months could have a profound impact on compliance. Despite our initial concerns about plug retention, our consultants noted that a treatment option that lasted anywhere between 60 and 90 days would be a "game changer" and that the 2-3 month duration of the product would fit well into the currently established glaucoma treatment protocol. The next generation NSR3 plug design will be used in the Phase IIb study and though early, management noted on the Q4:2014 earnings call that initial retention rate results look promising.

For perspective, at the 2015 Cowen Health Care Conference, nearly all of our surveyed clinicians suggested that if OTX-TP is successfully developed, the percentage of glaucoma patients who would be candidates for therapy is 50%+. Our glaucoma panelists noted that compliance is indeed a major issue and physicians want a sustained-release product. Importantly, it is well within the comfort zone of all ophthalmologists to place punctum plugs. Consolidating all of the feedback from our clinicians, we believe OTX-TP could be at least a $450MM product in the U.S. and approval in the E.U. and Japan, could provide additional upside.

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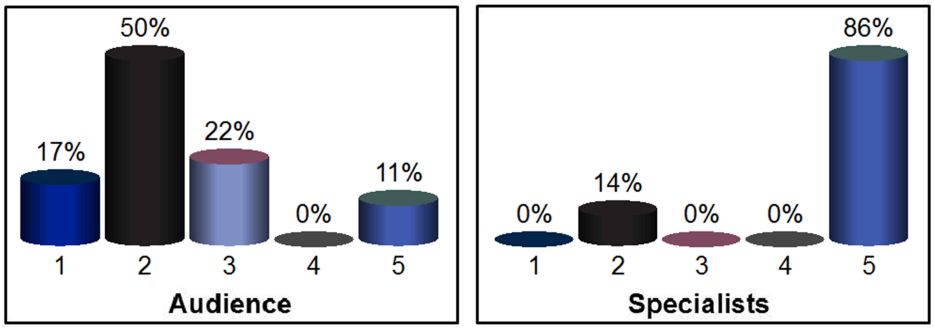
19. Ocular Therapeutix' OTX-TP is a travoprost punctum plug that lasts for 2-3 months and aims to fix compliance related issues and improve upon side effects with current glaucoma treatments. Assuming successful development of OTX-TP, the percentage of glaucoma patients who would be candidates for therapy are:

1. <10%
2. 20%
3. 30%
4. 40%
5. 50%+



Source: Cowen and Company 35th Annual Health Care Conference

OTX-DP: In January 2015, Ocular announced the enrollment of the first patient in a Phase II study evaluating OTX-DP for the treatment of dry eye. The randomized, double-blinded, vehicle-controlled study will evaluate 40 patients (up to 80 eyes) exhibiting signs and symptoms of dry eye disease. Clinical endpoints will include corneal and conjunctival staining, tear osmolarity, tear film break-up time, presence of the plug, ease of product use and visualization, and resorption of the plug following treatment. Patients will be enrolled at two U.S. sites, and in order to establish a baseline level of disease, they will initially be administered a placebo vehicle plug for 30 days. Patients who respond to the placebo plug in treatment of their dry eye will be excluded from the study, while those who continue to exhibit symptoms during the initial 30 days will continue into the treatment phase. Patients will then be randomized to receive either OTX-DP or a placebo vehicle plug. Topline data from the Phase II dry eye study are expected in Q4:2015.

Regarding the OTX-DP indication for allergic conjunctivitis, Ocular announced topline data from a Phase II study of OTX-DP in November of last year. The randomized, blinded, placebo-controlled study evaluated 68 patients across two clinical sites. The primary endpoints for the study were ocular itching and conjunctival redness at 14 days using a modified Conjunctival Allergen Challenge (CAC) model. OTX-DP demonstrated a statistically significant reduction in ocular itching and conjunctival redness at all measured days (14, 28, and 42). Using a 5-point scale, a mean difference greater than 0.5 units was seen at day 14, but a mean difference of 1.0 units was not seen at any of the measured days. Our consultants note that for currently approved topical treatments (emphasis on topical) for allergic conjunctivitis, a difference of 1.0 units is generally observed, but is not an absolute requirement as products have been approved by the FDA without meeting this criteria. Additionally, the previous FDA guidance of a treatment difference of 1.0 units is specifically tailored towards topical eye drop treatments. Ocular is using a new, sustained-release approach with OTX-DP that does not achieve the same peaks seen with topical agents. As a result, the findings from the Phase II study are not surprising and we believe it's important to remember that OTX-DP is providing a similar treatment effect over 42 days, compared to the meager 8-16 hours experienced with eye drops. Our consultants agree that the findings support continued development for the allergic conjunctivitis indication and the company has already met with the FDA to discuss adjustments for the Phase III trials. The CAC model will once again be utilized, and importantly, given the established safety data from the post-operative pain and inflammation trials, the Phase III allergic conjunctivitis should only require approximately 75 patients. Thus, the company's decision to pursue the additional indication provides a compelling risk/reward opportunity. The Phase III trials are expected to begin in mid-2015.

Anti-VEGF Hydrogel: Finally, Ocular continues to make progress with its long-acting anti-VEGF hydrogel depot. The company is working with four confidential biopharmaceutical partners on feasibility studies, which are expected to be completed in H1:2015. Initial findings suggest a duration toward the high-end of the 4-6 month range. The product is well-tolerated in animal models and importantly, the hydrogel appears to be delivering a meaningful amount of drug in the eye. Given the nature of the development timeline for a duration-based product, if the data is positive in H1, the company would expect to begin clinical trials in 12-18 months. Interestingly, Ocular is also independently evaluating their hydrogel technology in combination with compounded Avastin. The studies are progressing well and the company expects to present two papers on the initial findings at the Association for Research in Vision and Ophthalmology (ARVO) meeting in May 2015. It is worth noting that drug duration with the hydrogel technology is highly customizable and that the initial data for the Avastin hydrogel is likely not indicative of the maximum duration of the potential

treatment. Ocular has already had pre-IND discussions with the FDA on the necessary requirements to initiate a Phase I clinical study of the Avastin hydrogel and it does appear that the program could move forward. Management noted that the FDA discussions have also been helpful in understanding the regulatory requirements if one of the partnered programs does move forward.

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

Ocular Therapeutix' valuation is primarily based upon its clinical development programs and failure of its late-stage development programs could have a significant negative impact on its valuation.

Addendum

Stocks Mentioned In Important Disclosures

Ticker	Company Name
OCUL	Ocular Therapeutix

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

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Assumption: The expected total return calculation includes anticipated dividend yield

Cowen and Company Rating System until May 25, 2013

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

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

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

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

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Cowen And Company Rating Definitions

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Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	450	58.67%	103	22.89%
Hold (b)	302	39.37%	8	2.65%
Sell (c)	15	1.96%	0	0.00%

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

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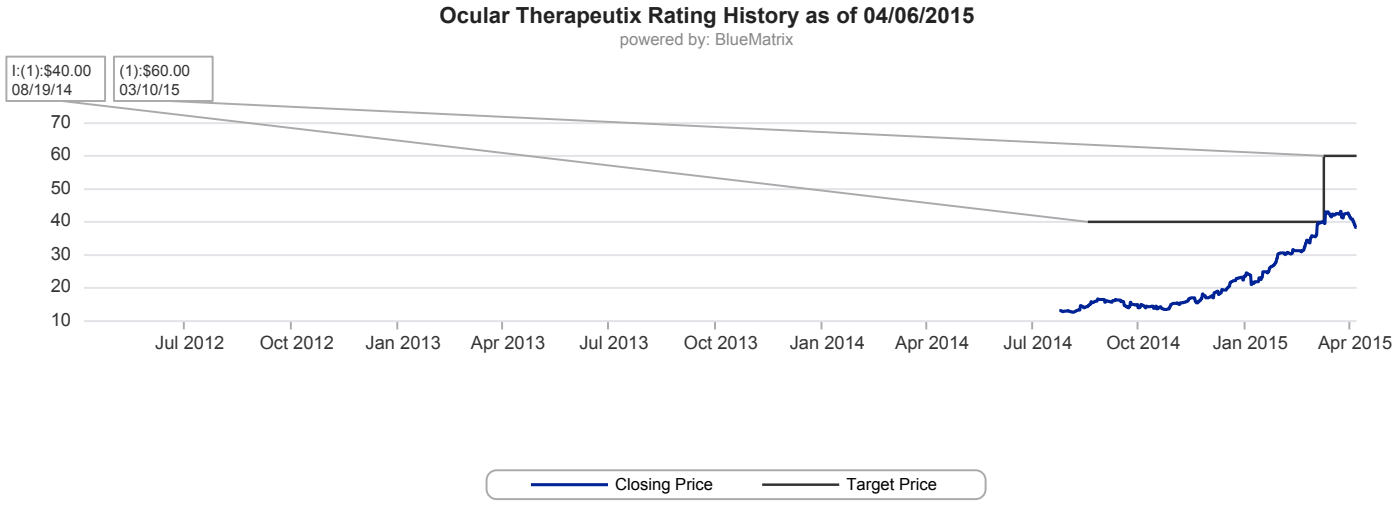

Legend for Price Chart:

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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