Equity Research

July 13, 2015

Biotechnology

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Ocular Therapeutix, Inc.

A Stellar Platform Technology For Eye Diseases

We are initiating coverage of Ocular Therapeutix with a $65/share price target and a Buy recommendation. Ocular's drug delivery technology is an innovative approach to delivering therapeutics to the front and back of the eye, an important consideration in various eye diseases where patients are either old or infirm. Ocular's approach of utilizing approved drugs with their delivery vehicle reduces clinical development risk, as the safety profile of the drug is already well-characterized. The recent failure of the second phase 3 OTX-DP trial to meet one of the two endpoints (a pooled analysis of the two pivotal phase 3 trials was significant for both endpoints) has created what we see as an opportunity for investors to climb aboard a compelling biotechnology story with an excellent management team.

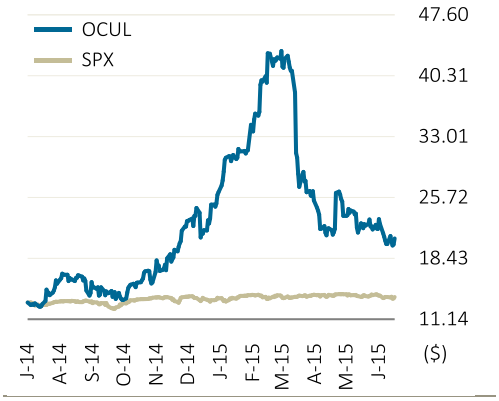
- **The company** is not limited by finding targets or having to worry about off-target effects with novel therapeutics; rather, management can focus on finding appropriate approved therapeutics to combine with its novel delivery technology to the front of the eye.
- **We would remind investors** that Gilead (GILD, Not Rated) was successful as a new entrant in HIV by discovering novel approaches to delivering combination therapies. While delivery is not 'sexy' like immuno-therapy, for example, it has a better risk/benefit profile.
- **While there is clinical development risk,** as was demonstrated by the second phase 3 for OTX-DP, this is typical of biotechnology drug development (where phase 3 trials work ~55% of the time). We believe that Ocular's management has learnt from the experience and is applying this to the third phase 3, to be initiated in 2H15.
- **Valuation:** Our $65 price target is based on a peak sales estimate of $1,400m (2024-28), probability adjusted and discounted back at SMID Biotechnology multiples (FY P/S 16X and discount rate of 20%) (Fig 1).

OCUL	$20.82
12 month target	$65.00
Upside	212.2%

BUY

52 week range	$12.64 - $43.27
Market Cap (m)	$445

Price Performance



Source: IDC

Estimates

	1Q14 A	2Q14 A	3Q14 A	4Q14 A	FY14 A	1Q15 A	2Q15 E	3Q15 E	4Q15 E	FY15 E	FY16 E
Sales	0	0	0	1	1	0	0	1	1	2	3
Net Income (Adj.)	(7)	(6)	(7)	(8)	(29)	(8)	(7)	(8)	(9)	(31)	(36)
Diluted EPS (Adj.)	(2.45)	(2.10)	(0.48)	(0.37)	(2.69)	(0.36)	(0.28)	(0.30)	(0.33)	(1.26)	(1.42)
Debt/EBITDA (x)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Source: BTIG Research Estimates and Company Documents ($ in millions, except per share amount)

$ in millions, except per share amount

Summary

Core Thesis

The recent failure of the second phase 3 trial for OTX-DP in post-cataract patients to meet one of the two primary endpoints (pain and inflammation) has created a compelling opportunity for investors, we believe. The pooled data for both the pivotal phase 3 trials was statistically significant (per the company 1Q15 earnings call), so the >50% sell-off in the share price since then is unwarranted, in our opinion.

The range and scale of the OTX-DP data in pain and inflammation are compelling and Ocular is moving ahead with a pain FDA filing, while running another phase 3 in pain and inflammation incorporating the learnings from the second phase 3 trial that did not meet the inflammation endpoint. If the third phase 3 trial is successful, Ocular will file a supplemental NDA with the FDA to add to the pain indication.

The platform nature of Ocular's technology and the excellent track record of management, combined with multiple quality shots on goals in mid/late stage development, make Ocular's current valuation undemanding, in our view. As we approach EY15, multiple phase 2 and phase 3 read-outs should catalyse a rerating of the shares.

Valuation

We value Ocular based on the estimated peak sales potential of its compounds in development, probability adjusted for stage of development and utilizing SMID biotechnology multiples (FY P/S of 16X and 20% discount rate).

Figure 1: Valuation

Valuation Variables		Comments
Peak Sales ($M)		
OTX-DP Post-cataract	500	BTIG estimates
OTX-DP Allergic Conjunctivits	150	BTIG estimates
OTX-TP Glaucoma	750	BTIG estimates
Peak Sales Year		
OTX-DP Post-cataract	2023	Approval 2017
OTX-DP Allergic Conjunctivits	2024	Approval 2018
OTX-TP Glaucoma	2025	
Probability		
OTX-DP Post-cataract	70%	Dexamethasone works in post-cataract surgery
OTX-DP Allergic Conjunctivits	55%	
OTX-TP Glaucoma	40%	Higher risk
Risk-adjusted Peak Sales ($M)		
OTX-DP Post-cataract	350	
OTX-DP Allergic Conjunctivits	83	
OTX-TP Glaucoma	300	
Median FY1 P/S Comps		
BTIG SMID Universe	15.7	June 2015, discounted back 7-9 years is 3-5X
Discount Rate		
Early Stage Biotech	19.7%	ROE of SMID Biotech Companies in June 2015
Risk-adjusted Valuation ($M)	**2,340.5**	
OTX-DP Post-cataract	1,303.8	
OTX-DP Allergic Conjunctivits	256.7	
OTX-TP Glaucoma	780.0	
Total	2,340.5	
Total/Share	75.5	
Cash on hand (m)	$137.50	Per 1Q15 PR + $70m raise 2Q15
FDSO (m)	25.36	
COH/Share	$5.42	

Source: Company reports, BTIG estimates

Risks

The key risks to our thesis would be the additional phase 3 inflammation trial not being successful and execution risk.

Company Profile

Ocular Therapeutics is a biopharmaceutical company that is focused on treatments for the eye. The company has an innovative hydrogel technology that serves as a platform to provide sustained delivery of therapeutic agents to the eye. The hydrogel technology is a bioresorbable proprietary formulation of polyethylene glycol, or PEG, which when constituted with water takes on a gelatinous consistency. Ocular develops and commercializes therapies that can be combined with its platform technology to overcome many of the significant limitations of existing eye drop-based therapies.

Poor patient compliance with eye drop regimens and the need for frequent administration of eye drops at high drug concentrations due to rapid washout by the tears can create challenges to the successful management of ocular diseases and conditions.

- For example, poor patient compliance can lead to diminished efficacy and disease progression, and high drug concentrations can create side effects.
- Ocular is developing therapies to replace standard of care eye drop regimens with its innovative drug eluting punctum plugs.
- The plugs are sustained release drug delivery depots that are inserted into a natural opening called the punctum located in the inner portion of the eyelid near the nose.
- The plugs are designed to release a therapeutic agent to the surface of the eye over an extended period.
- The goal for punctum plug product candidates is to change the management of many front of the eye diseases and conditions from frequent, pulsed eye drop therapy, characterized by significant variations in drug concentration over time, to longer term, sustained delivery of therapeutic agents to improve patient outcomes.

A key construct in the Ocular story is the company's focus on utilizing previously approved therapeutic agents and combining these agents with its hydrogel technology. Since the two key risk/reward variables in clinical development are the safety and efficacy profile of the drug being developed, Ocular's strategy reduces clinical development risk on the safety side. Drugs that are already approved have well-known safety profile, with millions of patient years of commercial usage. While Ocular's method of delivering these drugs to the eye might create some additional risk, it is minimal, in our opinion. In addition, Ocular can move its candidates through the development cycle efficiently, based on well-defined clinical and regulatory approval pathways.

The company's lead development product candidates are OTX-DP and OTX-TP. Ocular also sells ReSure Sealant, a hydrogel-based ophthalmic wound sealant approved by the FDA in January 2014 to close corneal incisions following cataract surgery.

1. OTX-DP incorporates dexamethasone, an FDA-approved corticosteroid known for its anti-inflammatory properties in the punctum plug.
    a. OTX-DP met statistical significance in its first phase 3 trial for post-surgical patients for both endpoints, achieving a statistically significant improvement in the reduction of inflammatory cells and in pain In March 2015. For the second phase 3 trial (FDA requires two successful phase 3 trials for an NDA, or new drug application, submission), OTX-DP was successful in meeting the pain endpoint, but not the inflammation endpoint. Currently Ocular has filed an NDA for the pain indication and will conduct another phase 3 trial for pain and inflammation, upon the successful completion of which it will file a label extension (assuming a successful approval of the drug by FDA).

   b. Ocular also initiated recruitment in a phase 3 trial for the treatment of allergic conjunctivitis. This followed the completion of a successful phase 2 in November 2014.
   c. Lastly, OTX-DP is in an exploratory phase 2 clinical trial for the treatment of inflammatory dry eye disease, which was started in January 2015.
2. OTX-TP incorporates **travoprost**, an FDA-approved prostaglandin analog that reduces elevated intraocular pressure. Ocular completed a phase 2a clinical trial of OTX-TP for the treatment of glaucoma and ocular hypertension in May 2014 and initiated a phase 2b clinical trial of OTX-TP for this indication in November 2014.
3. The company is also developing a **hydrogel depot** which can release therapeutic agents such as antibodies to the back of the eye, for diseases such as wet age related macular degeneration (wet AMD). This preclinical development would deliver the therapeutic agent over a sustained period following administration of a gel by an injection into the vitreous humor.
4. Ocular also has a pipeline of **earlier stage punctum plug product** candidates, including OTX-MP, which has completed a phase 1 clinical trial evaluating safety and pharmacokinetics in patients following cataract surgery.
5. Ocular launched **ReSure Sealant** in February 2014 in the U.S. through a network of ophthalmology-focused distributors. ReSure Sealant is approved to seal corneal incisions following cataract surgery and is the first and only surgical sealant to be approved by the FDA for ophthalmic use. In the pivotal clinical trials that formed the basis for FDA approval, ReSure Sealant provided superior wound closure and a better safety profile than sutured closure. The company plans to use the limited revenues expected from sale of ReSure Sealant to contribute to the funding of the product development pipeline and commercialization efforts.

OTX-DP Phase 3 Clinical Trial Results: Biotech Development is Not Linear

Ocular's most advanced product, OTX-DP, is in phase 3 development for the treatment of ocular inflammation and pain following cataract surgery. The company ran two phase 3 trials (standard FDA requirement for filing new drug applications, or NDAs): one that was positive for both efficacy primary endpoints of inflammation and pain and the second, only for pain:

1. In the **first phase 3** clinical trial, OTX-DP met both primary efficacy endpoints, absence of pain at day 8 and absence of inflammatory cells at day 14, with statistical significance. In this first phase 3 clinical trial, 33.7% of OTX-DP treated patients showed an absence of inflammatory cells in the anterior chamber of the study eye on day 14 following drug product insertion, compared to 14.6% of those receiving placebo vehicle control punctum plug (p=0.0015). In addition, 76.1% of patients receiving OTX-DP reported absence of pain in the study eye on day 8 following insertion of the drug product, compared to 36.1% of those receiving placebo vehicle control punctum plug (p< 0.0001).
2. In this **second phase 3** clinical trial, 77.5% of patients receiving OTX-DP reported an absence of pain in the study eye on day 8 following insertion of the drug product, compared to 58.8% of those receiving placebo vehicle control punctum plug, a difference that was statistically significant (p=0.0025). However, 39.4% of OTX-DP-treated patients showed an absence of inflammatory cells in the anterior chamber of the study eye on day 14 following drug product insertion, compared to 31.3% of those receiving placebo vehicle control punctum plug , a difference that was not statistically significant (p=0.2182).

Ocular also evaluated the secondary efficacy endpoints of each of the phase 3 trials:

1. In the **first phase 3** clinical trial, statistically significant differences were seen for the absence of pain at days 2, 4, 14 and 30 in the OTX-DP treatment group compared to the placebo group. Statistically significant differences were seen for the absence of inflammatory cells at day 30 in the OTX-DP treatment group compared to the placebo group. There were no statistically significant differences seen in the secondary endpoint for absence of inflammatory cells at the other time points in the OTX-DP treatment group in the first phase 3 trial. Statistically significant differences were seen for the absence of flare at day 8, day 14 and day 30 but not at day 2 or day 4.
2. In the **second phase 3** clinical trial, a similar proportion of patients in the OTX-DP treatment group and the placebo group were observed to have an absence of inflammatory cells at days 2, 4, 8, 14 and 30. A statistically significant difference between treatment groups was not seen for the absence of inflammatory cells until day 60, at which time a greater proportion of patients in the OTX-DP group compared to the placebo group were observed to have an absence of inflammatory cells. Statistically significant differences were seen for the absence of pain at all post-operative visits (days 2, 4, 8, 14, 30 and 60) in the OTX-DP treatment group compared to the placebo group.

For safety, there were no ocular or treatment-related serious adverse events in the OTX-DP treatment group in either of the two phase 3 clinical trials. There were two serious adverse events in the OTX-DP treatment group in the first phase 3 clinical trial (1.2% incidence), compared with three serious adverse events in the placebo group (3.6% incidence). There were two serious adverse events in the OTX-DP treatment group in the second phase 3 clinical trial (1.3% incidence), compared with three serious adverse events in the placebo group (3.8% incidence). Overall, the rate of adverse events in the treated group was lower than in the placebo group.

It is interesting to us that for the inflammation efficacy endpoint, in both the first and second trials there did not seem to be a statistically significant effect versus placebo until the 30th day (first trial) and 60th day (second trial). Historical trial data has indicated that the effectiveness of steroids (vs. NSAIDs or another drug class and placebo)

in diminishing inflammation and flares is not linear, i.e., statistically significant differences can vary at specific time points, but the trend line of separation over time is consistent. Also, this separation versus placebo can be impacted by variables such as concomitant usage of NSAIDs, investigator measurement inconsistency, etc.

After meeting with the FDA in April 2015 Ocular came away with the following plan of action:

- File an NDA for an ocular pain indication based on the existing data from the phase 2 and phase 3 studies.
- Initiate another phase 3 trial for treatment of post-surgical ocular inflammation and pain in 2H15.
- This trial of approximately 340 patients will be randomized 1:1 (versus 2:1, OTX-DP:placebo, in the previous phase 3 trials) and will be modified based on learnings from the previous trials to exclude rescue medication at day 8 visit and the use of high dose NSAIDs like Naproxen.
- Assuming the third phase 3 trial is successful, Ocular will file for an NDA supplement to its pain NDA.

While the failure of the second phase 2 trial to hit the inflammation efficacy endpoint adds another layer of risk to the Ocular story, the robustness of the data for both trials and the fact that almost all other efficacy and safety parameters were consistent across the phase 2 and 3 trials add to our belief that OTX-DP is a safe and effective product and that the third phase 3 clinical trial has a better than average chance of success.

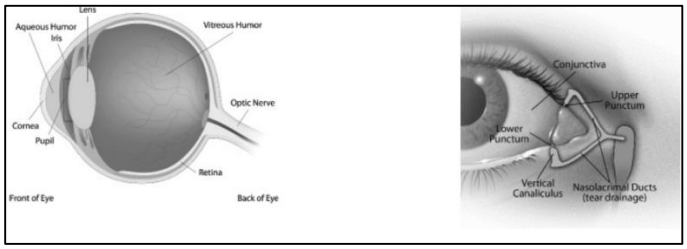
Phase 3 trials tend to progress to NDA approximately 60% of the time in drug development, with some indications, like ophthalmology having success rates as high as 70%. We believe that the third phase 3 trial has a 75-80% chance of success, based on the vast amount of previous successful phase 2 and phase 3 data that Ocular has and the learnings the company has acquired in running these large, predominantly successful clinical trials.

Eye Diseases Primer

The front of the human eye possesses focusing elements, consisting of the cornea on the surface of the eye, the lens and the aqueous humor, which is a transparent gelatinous fluid that fills the anterior and posterior chambers between the lens and the cornea. The tissue surrounding the eye also serves important functions. There is a natural opening, called a punctum, located in the inner portion of each eyelid near the nose.

The puncta open into nasolacrimal ducts, which collect and drain tears. The conjunctiva is the membrane covering the inside of the eyelids and the white part of the eye. It helps to protect the eye from microbes and to lubricate the eye. The back of the eye contains the retina, which is the light sensing layer of tissue; the vitreous humor, which is a transparent gel that fills the vitreous chamber between the lens and the retina; and the optic nerve, which transmits visual information from the retina to the brain.

Figure 2: Cross Section of the Eye and Tear Drainage System



Source: Company reports

Eye disease can be caused by many factors and can affect both the front and back of the eye. Diseases and conditions affecting the front of the eye are generally treated either with surgery or with medications delivered to the ocular surface by eye drops. Intravitreal injections are typically used to deliver medications to the back of the eye.

Types of eye diseases that Ocular is focused on are the following:

- Ocular i**nflammation** and pain are common side effects following ophthalmic surgery. Frequently performed ophthalmic surgeries include cataract, refractive vitreoretinal, cornea and glaucoma procedures. Physicians prescribe anti-inflammatory drugs, such as corticosteroids, which are typically administered through eye drops multiple times per day, following ocular surgery as the standard of care. These drugs improve patient comfort and also accelerate recovery through disruption of the inflammatory cascade resulting in decreased inflammation and reduced activity of the immune system. Third-party market data providers estimate that approximately 5 million ocular surgeries were performed in the U.S. in 2014.
- Allergic **conjunctivitis** is an inflammatory disease of the conjunctiva resulting primarily from a reaction to allergy-causing substances such as pollen or pet dander. The primary sign of this inflammation is redness and the primary symptom is acute itching. Allergic conjunctivitis ranges in clinical severity from relatively mild, common forms to more severe forms that can cause impaired vision. According to a study on the management of seasonal allergic conjunctivitis published in 2012 in the peer-reviewed journal *Acta Ophthalmologica*, allergic conjunctivitis affects 15% to 40% of the U.S. population. Ocular is targeting a subset of patients who have chronic or more severe forms of allergic conjunctivitis and are frequently treated with oral corticosteroids administered by eye drops.

- **Glaucoma i**s a progressive and highly individualized disease in which elevated levels of intraocular pressure are associated with damage to the optic nerve, which results in irreversible vision loss. Ocular hypertension is characterized by elevated levels of intraocular pressure without any optic nerve damage. Patients with ocular hypertension are at high risk of developing glaucoma. The increased intraocular pressure associated with uncontrolled glaucoma results in degeneration of the optic nerve in the back of the eye. Once glaucoma develops, it is a chronic condition that requires life-long treatment. According to the Glaucoma Research Foundation, approximately 2.2 million people in the United States suffer from glaucoma. In order to lower intraocular pressure, physicians typically initiate treatment by prescribing drugs administered as eye drops. These drugs either decrease fluid production or enhance fluid drainage. The classes of topical drugs used to treat glaucoma include prostaglandin analogs (PGAs), betablockers, alpha-adrenergic agonists and carbonic anhydrase inhibitors.
    - According to IMS Health data, approximately 31 million prescriptions were filled in the United States in 2013 for drugs administered by eye drops for the treatment of glaucoma, resulting in sales of approximately $2.1 billion.
    - A typical prescription provides approximately one month of treatment. According to IMS Health, PGAs account for approximately half of the prescription volume in the glaucoma market.
    - The market for drugs that are administered by eye drops for the treatment of glaucoma consists of both branded and generic products. Branded products have maintained premium pricing and significant market share. These products include Travatan Z (travoprost) marketed by Alcon (Novartis, NVS, Not Rated) and Lumigan (bimatoprost) marketed by Allergan (AGN, Not Rated). The relevant patents covering travoprost expired in December 2014. Commonly used generic drugs include latanoprost and timolol.
- **Dry eye** disease affects the ocular surface and is characterized by dryness, inflammation, pain, discomfort and irritation. The current standard of care for moderate to severe dry eye disease is the use of artificial tears and topical anti-inflammatory and immune modulating drugs administered by eye drops. The anti-inflammatory and immune modulating prescription drug market for the treatment of moderate to severe dry eye disease consists of Restasis, marketed by Allergan, and off-label use of corticosteroids and NSAIDs.

Limitations of Eye Drops

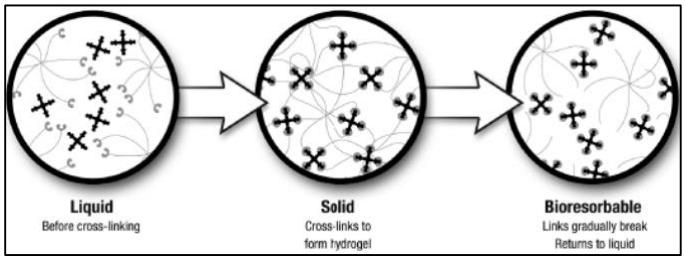
While eye drops are ubiquitous in treatment for front of eye diseases, they actually have severe limitations. The American Glaucoma Society (AGS) has characterized the problem with eye drops to be of the following nature:

- Compliance is poor, especially in older patients.
- Eye drops are actually difficult to use and not a very reliable drug-delivery system. The AGS notes that "…between 53–61% (of experienced glaucoma patients) regularly administer more than one drop at a time, many without even realizing it. These numbers are increased in those with poor vision from glaucoma, cataract, or retinal diseases. Eighty percent of these patients with visual comorbidities are unable to adequately instill a single eye drop at a time…"
- Physical disabilities can also interfere with the administration of eye drops. It is particularly difficult for older patients to master and perform this task proficiently. Eye drop administration requires both the technical ability to easily squeeze out a single drop and the hand-eye coordination to find the eye and squeeze the drop onto the eye. Older patients also suffer from related disease comorbidities that make it especially difficult to administer even a single drop.
- The AGS believes that increased cost is associated with lack of adherence. Glaucoma patients who go untreated, even for relatively short periods of time, run the risk of worsening vision loss and increased likelihood of requiring surgical intervention for their disease. Surgical intervention carries far greater risk than chronic medical therapy and increases health care costs, while vision loss from glaucoma has been associated with an increase in the rates of falls, depression, difficulty with facial recognition, inability to drive, reading difficulty, reduced physical activity, and nursing home admissions.
- Ocular has also noted that its research indicates that eye drops require frequent administrations at high concentrations, which leads to significant peak and valley dosing.

Hydrogel Platform

Ocular's bioresorbable hydrogel technology is based on the use of a proprietary form of PEG, or polyethylene glycol. The company creates hydrogels by cross-linking PEG molecules to form a network that resembles a three-dimensional mesh on a molecular level. The PEG molecules are branched, with four to eight branches or arms. Each arm bears a reactive site on its end that is capable of forming a network. When swollen with water, this molecular network forms a hydrogel.

Figure 3: Hydrogel Formation and Bioresorption



Source: Company reports

Ocular designs its hydrogels to slowly degrade in the presence of water, a process called hydrolysis, by inserting a biodegradable linkage between the PEG molecule and the cross-linked molecule. By appropriately selecting the number of arms of the PEG molecule and the biodegradable linkage, Ocular can design hydrogels with varying mechanical properties and bioresorption rates. Because the body has an abundance of water at a constant temperature and pH level, hydrolysis provides a predictable and reproducible degradation rate. The technology enables Ocular to make hydrogels that can bioresorb over days, weeks or several months.

Ocular's Punctum Plugs

A punctum is a natural opening located in the inner portion of the eyelid near the nose. There is a punctum in each of the lower eyelids and the upper eyelids. The puncta open into nasolacrimal ducts, which collect and drain tears produced by the eyes' lacrimal glands. Tears produced in the lacrimal glands sweep across the eye surface and drain through the puncta to the nasal cavity.

The section of the nasolacrimal duct immediately beyond the puncta is called the vertical canaliculus. Punctum plugs that do not contain an active drug are commonly used for treatment of dry eye disease by physically blocking tear drainage. Because punctum plugs stay in contact with the tear film, they are well suited for sustained delivery of drug to the eye.

Punctum plugs utilize Ocular's proprietary hydrogel technology and are embedded with an active drug. Following insertion through the punctum, the plugs swell in tear fluid to fill the vertical canaliculus, which secures the plugs in place. Ocular designs its plugs to release drug in a sustained fashion, tailored to each disease state, back through the punctum to the surface of the eye. Over time the plugs liquefy and are cleared through the nasolacrimal duct. If necessary due to excessive tearing, discomfort or improper placement, a healthcare professional can easily remove a punctum plug by a simple process of pushing the soft plug back through the punctum.

For acute conditions, such as post-surgical ocular inflammation and pain and allergic conjunctivitis, Ocular has designed the punctum plugs to provide a sustained release of therapeutic levels of drug for the duration of treatment. For chronic diseases, such as glaucoma, Ocular has designed its punctum plugs for repeat

administration with extended dosing periods. The plugs come as thin, dry rods to facilitate insertion through the narrow punctal opening.

ReSure Sealant for Ocular Wound Closure

ReSure Sealant as a liquid painted onto the corneal incision. Within about 15 seconds, the sealant cross-links and transforms into a smooth, lubricious hydrogel that seals the wound. ReSure Sealant dissipates as healing progresses and does not require removal.

In the pivotal clinical trials that formed the basis for FDA approval, ReSure Sealant provided superior wound closure and a better safety profile than sutured closure. Ocular believes that the market opportunity for a surgical sealant following cataract surgery may be modest because sutures are used in only approximately 14% of cataract surgeries.

Intellectual Property

OCUL has in-licensed all of its patent rights from Incept, LLC, an intellectual property holding company. Amarpreet Sawhney, Ocular's President and Chief Executive Officer, is a general partner of Incept and has a 50% ownership stake in Incept. The license from Incept is limited to the field of human ophthalmic diseases and conditions.

As of June 30, 2014, OCUL has licensed from Incept a total of 18 U.S. patents, five U.S. patent applications and foreign counterparts of some of these patents and patent applications. Ten of the 18 licensed U.S. patents and four of the five licensed U.S. patent applications cover the technology that underlies OCUL's punctum plug product candidates, ReSure Sealant or its intravitreal hydrogel depot.

Competition

OTX-DP

Icon Biosciences, Inc. (private) reported a positive phase 3 in April 2015 for IBI-10090, a biodegradable for injection of dexamethasone into the eye to treat inflammation associated with cataract surgery. Shortly thereafter the abstract was presented at American Society of Cataract and Refractive Surgery (ASCRS) & American Society of Ophthalmic Administrators (ASOA). The data is fairly impressive for inflammation, in our opinion.
However we would point out that IBI-10090's phase 3 demonstrates good efficacy in reducing inflammation post-surgery, without addressing the endpoint of pain (which OTX-DP does). We would posit that this therapy would be utilized for patients with particularly severe inflammation post-surgery.

OTX-TP

Allergan is conducting phase 2 clinical development of Bimatoprost Sustained Release, a biodegradable intraocular implant consisting of a PGA and a biodegradable polymer matrix to treat glaucoma. ForSight VISION5 (private) is conducting phase 2 clinical development of the Helios insert, a sustained release ocular insert placed below the eyelid, for the treatment of glaucoma. In addition, several other companies have announced their intention to develop products for treatment of glaucoma using sustained release therapy, although each of these is at an early stage of development.

It is clear that this space is competitive. However we would note that OTX-TP is already in phase 2b development (since November 2014) and we believe that Ocular's delivery mechanism (via punctum plus) is still superior from a risk/reward perspective to other approaches.

ReSure Sealant

ReSure Sealant is the first and only surgical sealant approved for ophthalmic use in the United States. Outside the United States, Beaver Visitec (private) is commercializing its product OcuSeal, which is designed to provide a protective hydrogel film barrier to stabilize ocular wounds. This product is not currently available in the United States. Sutures are the primary alternative for closing ophthalmic wounds. In addition, a technique called stromal hydration, which involves the localized injection of a balanced salt solution at the wound edges, is often used to facilitate the self-sealing of a wound.

We view ReSure Sealant as a product that introduces Ocular to the ophthalmology physician community, as it develops OTX-DP, OTX-TP and other follow-on products.

Pipeline

Currently Ocular has multiple mid/late stage clinical trials ongoing. The following are its lead products:

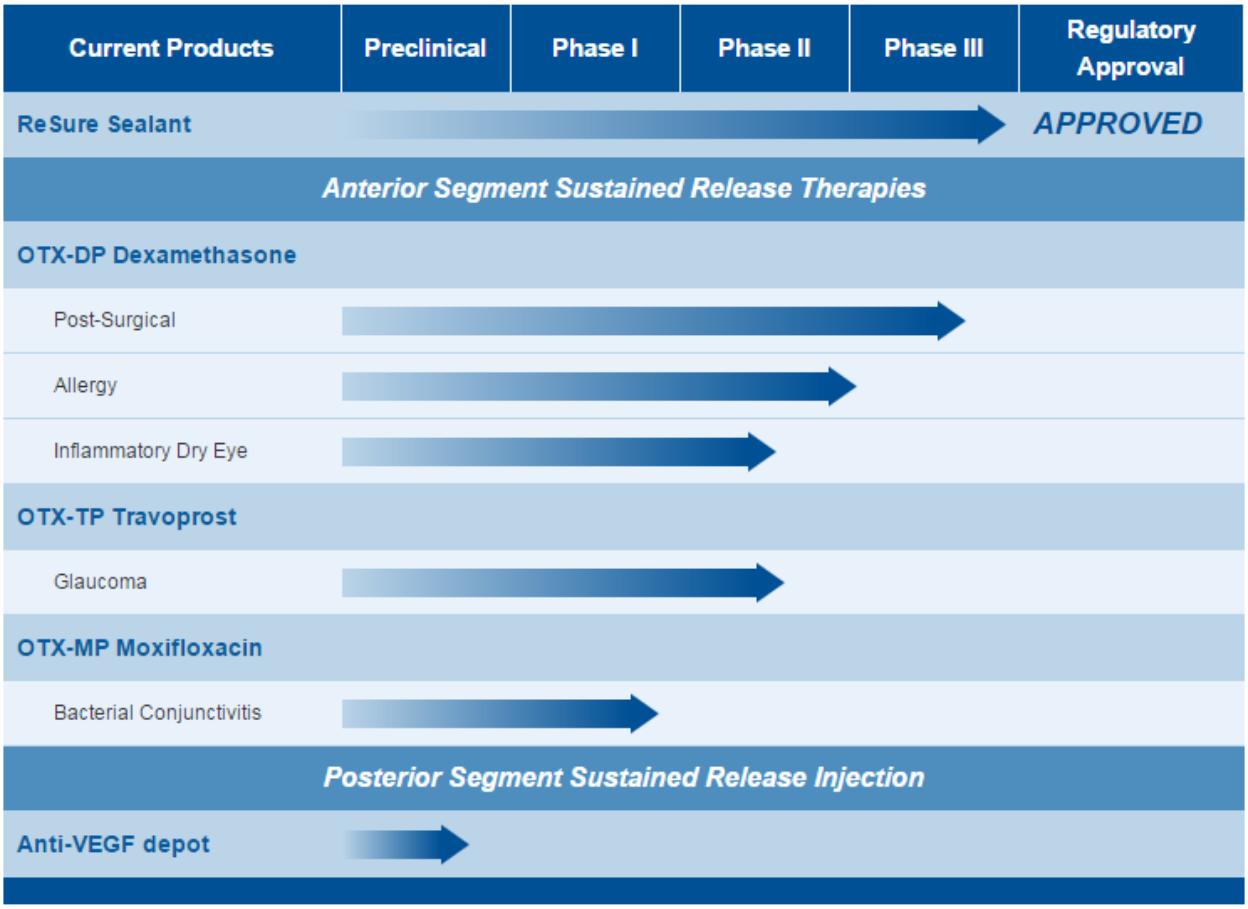
1. OTX-DP just completed two pivotal phase 3 trials for pain and inflammation related to **post-cataract** surgery. The company plans on filing an NDA for a pain indication in 2H15 and will initiate another pivotal phase 3 for inflammation in 2H15, which is expected to run for 12-18 months. If this trial is successful, the company will file a supplemental NDA in EY/16 or early 2017.

2. OTX-DP in allergic **conjunctivitis** has phase 2 data already presented. A phase 3 (N=72) was initiated in June 2015 with an EY15 read-out. A second phase 3 will start in 3Q15 with a 1H16 readout.

3. OTX-DP in **inflammatory eye disease** has an exploratory (N=40) phase 2 ongoing with an expected readout in 4Q15.

4. OTX-TP in **glaucoma** is in phase 2 development (N=80), with enrolment almost complete. A readout is expected in 4Q15. While this study is on the larger side for a phase 2 glaucoma study, it is not powered to demonstrate a statistically significant benefit.

Figure 4: Ocular's Pipeline



Source: Company reports, BTIG estimates

Company Management

Amar Sawhney, Ph.D. - President, Chief Executive Officer and Chairman of the Board of Directors

Dr. Sawhney has served as President, Chief Executive Officer and a member of our Board since co-founding the company in 2006, and he was elected as Chairman of the Board in June 2014. Dr. Sawhney served as CEO of Augmenix, an affiliate of Ocular Therapeutix, from 2008 until April 2014. In addition, he is a general partner of Incept, LLC, an intellectual property holding company. Previously, Dr. Sawhney founded Confluent Surgical and served as its President and CEO prior to its acquisition by Covidien plc. He also was a technology founder of Focal, Inc., a biopharmaceutical company acquired by Genzyme Corporation, and a founder of AccessClosure, Inc., acquired by Cardinal Health in 2014.

Brad Smith - Chief Financial Officer

Mr. Smith brings over 20 years of experience in the life sciences, serving as Chief Financial Officer for several public and private emerging growth biotechnology, medical device and healthcare information technology companies. Prior to joining Ocular Therapeutix in March 2014, Mr. Smith served as CFO at OmniGuide Surgical, and previously as CFO at NeuroMetrix. He also held CFO and senior financial roles at various other healthcare companies, including Synarc, Inc., Focal, Inc., PatientKeeper, and CytoTherapeutics.

Peter Jarrett, Ph.D. - Chief Scientific Officer

Dr. Jarrett has more than 30 years of R&D experience, ranging from discovery to commercialization. Dr. Jarrett joined Ocular Therapeutix in 2007. Previously, he was Vice President of R&D at Focal, subsequently being named VP of Biomaterials R&D at Genzyme upon the latter company's acquisition of Focal. Dr. Jarrett began his career in Corporate R&D of American Cyanamid, later moving to the Davis and Geck division. At Cyanamid, Focal, Genzyme and Ocular, Dr. Jarrett developed bioresorbable polymers for medical devices and drug delivery systems, resulting in numerous patents and publications.

Income Statement

Ocular Therapeutix Statement of Operations	Dec-12	Dec-13	Mar-14	Jun-14	Sep-14	Dec-14	Dec-14	Mar-15	Jun-15	Sep-15	Dec-15	Dec-15	Dec-16	Dec-17	Dec-18	Dec-19
$ Millions	2012A	2013A	1Q14A	2Q14A	3Q14A	4Q14A	2014A	1Q15A	2Q15E	3Q15E	4Q15E	2015E	2016E	2017E	2018E	2019E
Collaboration revenue	-	-	-	-	-	0.312	0.312	0.188	0.188	0.188	0.036	0.600	1.000	1.500	1.500	1.500
Product revenues	0.010	-	0.027	0.097	0.143	0.193	0.460	0.238	0.300	0.350	0.512	1.400	1.800	16.349	55.928	163.892
Total revenues	**0.010**	**-**	**0.027**	**0.097**	**0.143**	**0.505**	**0.772**	**0.426**	**0.488**	**0.538**	**0.548**	**2.000**	**2.800**	**17.849**	**57.428**	**165.392**
Cost of product revenue	0.007	-	0.009	0.020	0.032	0.030	0.091	0.056	0.050	0.055	0.050	0.211	0.250	1.500	10.000	23.000
Research and development	11.540	10.517	4.958	4.292	4.482	5.148	18.880	4.719	4.800	5.000	5.600	20.119	23.000	28.000	32.000	40.000
Selling and marketing	0.657	0.625	0.310	0.535	0.479	0.658	1.982	0.870	0.900	1.000	1.000	3.770	6.000	15.000	22.000	30.000
General and administrative	1.477	1.761	1.575	1.196	1.926	2.216	6.913	1.894	1.900	2.000	2.400	8.194	9.000	11.000	13.000	15.000
Total expenses	**13.681**	**12.903**	**6.852**	**6.043**	**6.919**	**8.052**	**27.866**	**7.539**	**7.650**	**8.055**	**9.050**	**32.294**	**38.250**	**55.500**	**77.000**	**108.000**
(Loss) Income from Operations	**(13.671)**	**(12.903)**	**(6.825)**	**(5.946)**	**(6.776)**	**(7.547)**	**(27.094)**	**(7.113)**	**(7.162)**	**(7.517)**	**(8.502)**	**(30.294)**	**(35.450)**	**(37.651)**	**(19.572)**	**57.392**
EBITDA	**(13.267)**	**(12.499)**	**(6.732)**	**(5.795)**	**(6.637)**	**(7.383)**	**(26.547)**	**(6.940)**	**(7.162)**	**(7.517)**	**(8.502)**	**(30.294)**	**(35.450)**	**(37.651)**	**(19.572)**	**57.392**
Interest income	0.004	0.013	0.001	0.001	0.005	-	0.007	0.040	0.005	0.005	0.001	0.051	0.050	0.050	0.050	0.050
Interest expense	(0.377)	(0.441)	(0.043)	(0.257)	(0.412)	(0.407)	(1.119)	(0.505)	(0.050)	(0.050)	(0.050)	(0.655)	(0.050)	(0.050)	(0.050)	(0.050)
Other income (expense), net	(0.049)	0.014	(0.141)	(0.190)	(0.111)	-	(0.442)	(0.010)	(0.010)	(0.010)	(0.010)	(0.040)	(0.050)	(0.050)	(0.050)	(0.050)
Total other (expense) income	**(0.422)**	**(0.414)**	**(0.183)**	**(0.446)**	**(0.518)**	**(0.407)**	**(1.554)**	**(0.475)**	**(0.055)**	**(0.055)**	**(0.059)**	**(0.644)**	**(0.050)**	**(0.050)**	**(0.050)**	**(0.050)**
Net (loss) income before provision for income taxes	**(14.093)**	**(13.317)**	**(7.008)**	**(6.392)**	**(7.294)**	**(7.954)**	**(28.648)**	**(7.588)**	**(7.217)**	**(7.572)**	**(8.561)**	**(30.938)**	**(35.500)**	**(37.701)**	**(19.622)**	**57.342**
Income tax benefit																
Net (loss) income	**(14.093)**	**(13.317)**	**(7.008)**	**(6.392)**	**(7.294)**	**(7.954)**	**(28.648)**	**(7.588)**	**(7.217)**	**(7.572)**	**(8.561)**	**(30.938)**	**(35.500)**	**(37.701)**	**(19.622)**	**57.342**
Accretion of redeemable convertible preferred stock to redemption value	(0.035)	(0.027)	-	(0.005)	-	(0.006)	(0.011)	-								
Diluted EPS	**(5.60)**	**(5.11)**	**(2.45)**	**(2.10)**	**(0.48)**	**(0.37)**	**(2.69)**	**(0.36)**	**(0.28)**	**(0.30)**	**(0.33)**	**(1.26)**	**(1.42)**	**(1.48)**	**(0.75)**	**2.16**
Weighted-average shares - diluted	2.523	2.609	2.860	3.045	15.166	21.289	10.653	21.363	25.363	25.616	25.873	24.554	25.045	25.546	26.056	26.578

Source: Company reports, BTIG estimates

Appendix: Analyst Certification and Other Important Disclosures

Analyst Certification

I, Hartaj Singh, hereby certify that the views about the companies and securities discussed in this report are accurately expressed and that I have not received and will not receive direct or indirect compensation in exchange for expressing specific recommendations or views in this report.

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Company-Specific Regulatory Disclosures

Ocular Therapeutix, Inc. (OCUL)

Valuation

Ocular Therapeutix Valuation

Our Ocular price target of $65 is based on a Peak Sales estimate of $1,400m (2024-28), probability adjusted and discounted back at SMID Biotechnology multiples (FY P/S 16X and discount rate of 20%).

Risks

The key risk to our thesis would be the additional phase 3 inflammation trial not being successful and execution risk.

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Ocular Therapeutix, Inc. (OCUL)

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