Zacks Small-Cap Research

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Eyegate Pharmaceuticals (EYEG-NASDAQ)

EYEG: Reinventing Ophthalmic Drug Delivery. Initiating At Buy

Current Recommendation	**Buy**
Prior Recommendation	N/A
Date of Last Change	02/18/2016
Current Price (02/19/16)	$2.80
Target Price	**$5.00**

OUTLOOK

EYEG is a pre-revenue stage company engaged in the development of drugs and drug delivery devices for diseases of the eyes. Their novel iontophoresis drug delivery platform offers a much less burdensome and non-invasive solution to current standard of care for diseases of the eye. Phase 3 pivotal study in anterior uveitis now enrolling – if positive will support NDA filing. Launch could happen by 2018. Out-licensing agreement recently consummated with Valeant/Bausch+Lomb. Clinicals in other indications also enrolling, which could eventually expand the label and respective target market size. Our DCF model, which incorporates indication-specific risk adjustments to account for potential clinical or regulatory failure for each of the three programs, currently values the shares at approximately $5. While representing attractive upside to the current share price, our calculated value should appreciate further on progression of EGP-437 through clinical trials in any of the indications as this would positively affect (i.e. decrease) our risk discounts.

SUMMARY DATA

52-Week High	**$20.00**
52-Week Low	**$1.59**
One-Year Return (%)	**N/A**
Beta	**N/A**
Average Daily Volume (sh)	**208,160**
Shares Outstanding (mil)	**8**
Market Capitalization ($mil)	**$21**
Short Interest Ratio (days)	**0.93**
Institutional Ownership (%)	**5**
Insider Ownership (%)	**N/A**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2016 Estimate	**N/A**
P/E using 2017 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**High,**
Type of Stock	**Small-Blend**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(in 000s of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	0 A	0 A	0 A	0 E	0 E
2016					0 E
2017					5.6
2018					7.6

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	-$3.23 A	-$0.24 A	-$0.19 A	-$0.20 E	-$2.51 E
2016					-$0.93 E
2017					-$0.33 E
2018					-$0.12 E

Zacks Projected EPS Growth Rate - Next 5 Years % **N/A**

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SNAPSHOT

Eyegate Pharmaceuticals, Inc. (EYEG) is a pre-revenue stage company engaged in the development of drugs and drug delivery devices for diseases of the eyes. Over $14M was raised through a February 2015 IPO and follow-on equity financing which is being used to advance their product pipeline through clinical validation. Currently under development is EGP-437, the company's lead therapeutic candidate which is in a late-stage, pivotal trial for uveitis and in earlier-stage studies for macular edema and cataract surgery. EGP-437, a reformulation of generic dexamethasone phosphate, and Eyegate II Delivery System, which uses iontophoresis to non-invasively and efficiently deliver drugs to the ocular tissues, are proprietary and patent-protected.

Current standard of care for delivery of drugs for eye diseases is liquid drops, for conditions affecting the surface and front (i.e. anterior) of the eye, and injections, for diseases in the back (i.e. posterior) of the eye. Standard of care suffers from certain significant drawbacks. The inefficiency of administration via drops (i.e. low bioavailability and rapid clearance) means limited effective penetration of the drug and an onerous dosing schedule which can result in non-compliance. The invasive nature of injections presents safety concerns, requires a trained professional for administration, involves a relatively high treatment burden and is an inherently unappealing procedure for the patient – all of which can also result in patient compliance problems. Non-compliance of recommended dosing for conditions such as uveitis and macular edema can result in serious complications including blindness.

Eyegate's platform offers a much less burdensome and non-invasive solution, has been used in over 1,700 treatments and takes less than five minutes to administer. And unlike injections which should be administered by an ophthalmologist, Eyegate's device potentially may be able to be used by less experienced clinical staff such as nurses. While other novel approaches to treat back-of-the-eye diseases are under development, Eyegate has the only non-invasive solution.

The ophthalmic therapy market is fairly concentrated with only three major companies; Alcon (a division of Novartis NYSE:NVS), Allergan plc (NYSE: AGN) and Bausch+Lomb (a division of Valeant Pharmaceuticals, NYSE: VRX) dominating the space. In July 2015 EYEG announced a licensing agreement, granting Valeant (Bausch+Lomb) worldwide rights to Eyegate II Delivery System and EGP-437 for uveitis indications as well as right of last refusal in other applications in return for upfront cash, development and regulatory approval milestones and sales royalties. This deal not only affords EYEG entry into the difficult-to-penetrate ophthalmic therapy market, but does so with some mitigated financial and product development risk.

EGP-437 completed a phase I/II dose-ranging study in non-infectious anterior uveitis. A phase III study followed, which while indicating EGP-437 treatment was as efficacious and safe as standard of care, barely missed the non-inferiority primary endpoint. Despite this, FDA communicated that if a planned new phase III study demonstrates non-inferiority, that that data, along with results of the earlier study, will be sufficient to support a New Drug Application (NDA) filing. The first of an expected 250 patients was enrolled in January. EYEG anticipates the trial will be fully enrolled at up to 60 sites in the U.S. by the end of 2016 and have top-line data in Q1 2017. Assuming positive results, the game plan will be to file the NDA for EGP-437 and 510(k) for Eyegate II Delivery System simultaneously.

Unlike anterior uveitis, which affects the front of the eye and is typically treated with drops, macular edema is a disease of the rear portion of the eye and which is conventionally treated with injections. Preclinical data as well as results from an ongoing phase Ia/IIb macular edema clinical trial have indicated that Eyegate II Delivery System can deliver drugs to the posterior of the eye. Additional data from this study is expected to be available by mid 2016. We think an eventual approved back-of-the-eye indication could have significant commercial appeal given the relatively substantial market sizes and issues with ocular injections.

A third indication, treatment following cataract surgery, represents the largest potential target market - up to 3M+ Americans. A phase Ib/IIa clinical trial in cataract surgery could have top-line data in 1H 2016.

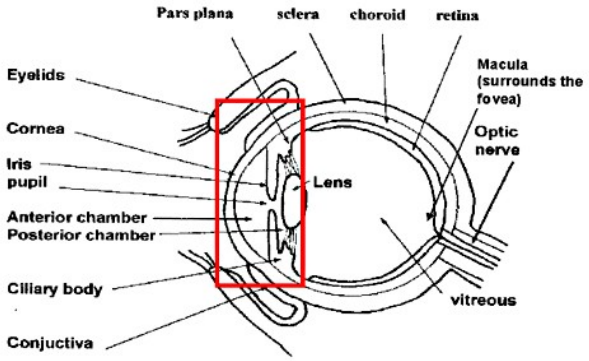
Our DCF model, which incorporates indication-specific risk adjustments to account for potential clinical or regulatory failure for each of the three programs, currently values the shares at approximately $5. While representing attractive upside to the current share price, our calculated value should appreciate further on progression of EGP-437 through clinical trials in any of the indications as this would positively affect (i.e. decrease) our risk discounts. We are initiating coverage of EYEG with a $5/share price target and Buy recommendation.

BACKGROUND

Non-Infectious Anterior Uveitis

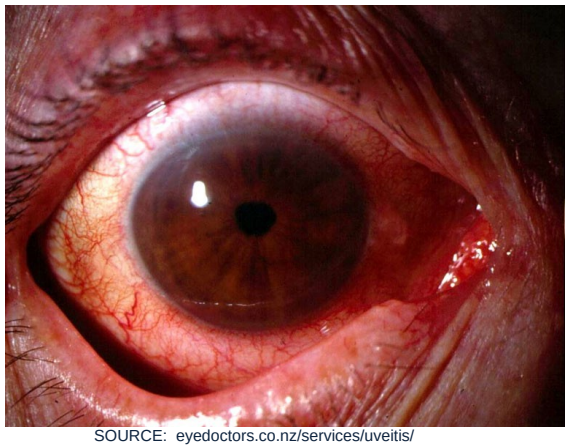
Uveitis is a generic term used to describe inflammation of the uvea. It can occur either in isolation or be the result of an underlying medical condition in other parts of the body. The uvea is the middle layer of the eye, below the white of the eye, and consists of the iris (colored portion), choroid layer (connective tissue) and ciliary body (secretes liquid). Infectious uveitis is caused by a virus or bacteria in the eye while non-infectious uveitis is endogenous, or the result of a disease elsewhere in the body.

Non-Infectious Anterior Uveitis



Eye Structures Involved in "Anterior Uveitis"

SOURCE: uveitis.net



SOURCE: eyedoctors.co.nz/services/uveitis/

Symptoms include redness, inflammation and pain in the eye, photophobia (extreme sensitivity to light), blurred vision and change in shape or size of the pupil. If left untreated, anterior uveitis can result in development of other complications including glaucoma, formation of synechiae, cataracts, macular edema, retinal detachment and, eventually, even blindness.

Prevalence of uveitis in the U.S. is roughly (estimates vary depending on source) 50 people per 100k population, or approximately 165k. U.S. incidence estimates also vary by study – the most cited study estimates range from a low of about 17 to a high of about 52 people per 100k population[1,2,3,4] - an average of ~35 per 100k, or approximately 115k incidents per year. Non-infectious uveitis, which is the initial indication that EYEG is pursuing, is the most common form of uveitis, accounting for about 75% of all cases and about 90% of these are located at the anterior of the eye (i.e. non-infectious anterior uveitis).

Estimated U.S. Incidence and Prevalence

	Uveitis	Non-Infectious	Non-Infectious Anterior
Incidence	115,000	86,250	77,625
Prevalance	165,000	123,750	111,375

[1] Acharya NR, Tham VM, Esterberg E, et al. Incidence and Prevalence of Uveitis: Results From the Pacific Ocular Inflammation Study. JAMA Ophthalmol. 2013;131(11):1405-1412. doi:10.1001/jamaophthalmol.2013.4237

[2] Darrell RW, Wagener HP, Kurland LT. Epidemiology of uveitis: incidence and prevalence in a small urban community. Arch Ophthalmol. 1962;68:502-514

[3] Gritz DC, Wong IG. Incidence and prevalence of uveitis in Northern California: the Northern California Epidemiology of Uveitis Study. Ophthalmology. 2004;111(3):491-500, discussion 500

[4] Suhler EB, Lloyd MJ, Choi D, Rosenbaum JT, Austin DF. Incidence and prevalence of uveitis in Veterans Affairs Medical Centers of the Pacific Northwest. Am J Ophthalmol.

Uveitis treatment involves arduous dosing regimen…

Dexamethasone phosphate is a corticosteroid, administered either orally in pill form or as an injection, which has anti-inflammatory and immune-response modifying effects. It is used for rheumatic diseases as well as other conditions such as allergies, intestinal disorders, eye diseases and other ailments. Topical corticosteroids are considered the first line of treatment for uveitis with dexamethasone and prednisolone acetate being the most widely used. Corticosteroids are used to reduce inflammation which is caused by the build-up of white blood cells in the anterior chamber (see diagram above) of the eye. The primary endpoints of EYEG's clinical trials evaluating EGP-437 and Eyegate Delivery System for the treatment of anterior uveitis are reduction of anterior chamber white blood cell count.

Diagnosis and evaluation, which includes patient history and ocular examination, are done to rule out other possible causes and to determine severity of the disease. Anterior uveitis is classified as either mild, moderate or severe which determines the initial dosing regimen as well as frequency of follow up visits to an ophthalmologist. The follow-up schedule and prednisolone acetate dosing regimen in the table below are adapted from the reference guide, *Primary Care of the Anterior Segment*, by Louis Catania.[5]

Anterior Uveitis Dosing and Follow-Up Schedules

	Severity		
	Mild	Moderate	Severe
Frequency of follow-up visits	Every 4 to 7 days	Every 2 to 4 days	Every 1 to 2 days
Recommended dosing	Two to four times per day	Four times per day	Every 2 to 4 hours

The above table lists the recommended initial dosing. The total regimen can last four to six weeks and include 150 or more drops. Regular follow-up visits are necessary to ascertain response and determine if and when to begin tapering dosage as **regular use of corticosteroids is associated with certain adverse side effects including immune suppression, accelerating cataract formation and increased ocular pressure**. Eye drops are an inherently inefficient route of administration and, depending on how much of the drop gets in the eye (versus runs down the face) and penetrates protective tissue (eyes are adept at keeping out foreign substances), the amount of active ingredient that reaches its intended target can vary widely. This is another reason as to why drops must be dosed so frequently and regular check-ups are so important.

***Iontophoresis** is defined as the transfer of ions. It is the use of a weak electrical current to deliver drugs through or across tissue and other biologic substances. An ionic therapeutic substance is placed under an electrode of like-charge (i.e. ion and electrode are both of either positive or negative polarity). The like-charges create electropropulsion as two substances of similar charge repel, pushing the therapeutic substance into the tissue.*

The burdensome dosing schedule results in patient compliance issues. When patients fail to complete the recommended dosing regimen, the risk of treatment failure increases. In fact, lack of compliance is the most common cause of treatment failure. As noted above, significant complications can result if uveitis is not effectively treated.

EYEG's Treatment Solution: Eyegate II Delivery System and EGP-437

The Eyegate II Delivery System delivers a precise dose of EGP-437, a proprietary and reformulated version of (generic) dexamethasone phosphate, to the eye through the use of iontophoresis. The procedure is relatively fast, is non-invasive and is efficient in delivering drugs to their intended target within the ocular tissue. It has been used in over 1,700 treatments to-date.

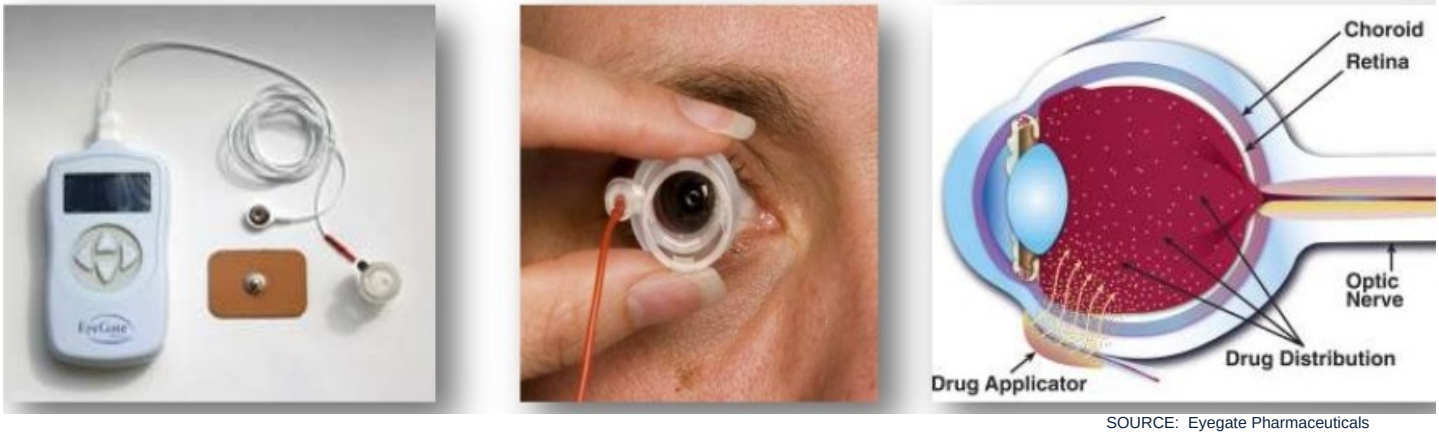
As opposed to the rigorous dosing schedule of eye drops for conditions such as anterior uveitis, treatment with EYEG's combination product can be completed in only one to four minutes over just two or three visits to an eye doctor. It has also been shown to effectively deliver drugs to the posterior of the eye, offering a non-invasive approach to traditional eyeball needle injections for treatment of conditions such as macular edema. As such, Eyegate believes their combination therapy provides a solution to the patient burden, non-compliance and invasiveness issues associated with conventional therapy.

[5] Catania, L. J. (1995). Primary care of the anterior segment. Norwalk, CT: Appleton & Lange

Eyegate II Delivery System consists of a small handheld generator, a return electrode and an ocular applicator. The generator produces and delivers the iontophoresis-inducing current. It is easily programmed through an LED screen for the correct dosage and current. The screen displays delivery of the current in real-time, the amount of the drug delivered and the treatment time remaining. The generator is the only portion of the delivery system and drug that is not a single-use disposable.

The return electrode, which is placed on the patient's forehead, is used to create a continuous current. The ocular applicator is filled with EGP-437, topical anesthesia is applied to the surface of the eye and the applicator is then placed over the sclera of the eye. A soft foam pad on the applicator makes contact with the eye – EYEG's instructional video (https://youtu.be/v7oSLe-bLWo) on their website notes that the applicator is as comfortable as a contact lens. Drug delivery commences when the generator is turned on, delivering a low electrical current to an electrode within the applicator and initiating iontophoresis.

The electrode electrolyzes water molecules within the applicator, converting them into either hydronium or hydroxide molecules, depending on whether positive (cathodic) or negative (anodic) polarity is used. Electropropulsion, created by the like-charged ions and molecules, pushes the drug molecules into the tissues of the eye until they reach their intended target. The drug delivery takes about one to four minutes, after which the applicator is removed and the procedure is completed. Dose can be changed by adjusting the current and application time.



SOURCE: Eyegate Pharmaceuticals

Issues of Traditional Ophthalmic Drug Delivery Address by Eyegate's System

Anterior Eye Conditions	Posterior Eye Conditions
• Rigorous dosing regimen	• Needle-in-the eye patient anxiety
• Biological barriers in eye inhibit drug penetration	• Several injections over multiple weeks required
• Patient non-compliance	• Risk of inflammation and infection
• Side effects; IOP, cataracts and others	• Requires experienced clinician & companion
	• Complications such as IOP, retinal detachment

Patents

Eyegate's technology is protected by eight patent families including 13 U.S. patents, 3 pending U.S. patent applications, 59 international patents and 15 pending international patents. The existing and pending (if issued) patents will expire between 2018 and 2029.

Below is the (16) results of our search (link: http://1.usa.gov/1NWFSnI) of the USPTO database using "Eyegate" as the Assignee Name. Patents 9,149,525 and 9,180,292 are held by Eyegate Pharmaceuticals while the others are held by their subsidiary EyeGate Pharma S.A.S.

Refine Search | AN/eyegate

	PAT. NO.	Title
1	9,238,131	Ocular iontophoresis device
2	9,192,512	Device for delivering medicines by transpalpebral electrophoresis
3	9,180,292	System and method for ocular iontophoresis with buffering
4	9,149,525	Delivery of corticosteroids through iontophoresis
5	8,771,256	Device delivering medicines by transpalpebral electrophoresis
6	8,611,994	Irritation-reducing ocular iontophoresis device
7	8,452,391	Ocular iontophoresis device
8	8,306,613	Irritation-reducing ocular iontophoresis device
9	8,099,162	Ocular iontophoresis device
10	7,937,142	Irritation-reducing ocular iontophoresis device
11	7,848,800	Device for delivering medicines by transpalpebral electrophoresis
12	7,771,403	Uniform feed connector for devices for the delivery of active principles
13	7,684,857	Device for medicine delivery by intraocular iontophoresis or electroporation
14	7,628,781	Medical usage connector assembly for the transfer of fluids
15	7,548,778	Irritation-reducing ocular iontophoresis device
16	7,164,943	Irritation-reducing ocular iontophoresis device

SOURCE: US Patent & Trademark Office, Patent Full Text and Image Database

Specific to EGP-437, U.S. patent # 9,149,525 "Delivery of corticosteroids through iontophoresis", which was granted in October 2015, covers a method of treating eye conditions using EGP-437 delivered by ocular iontophoresis and is not limited to a particular eye condition.

Specifically the patent claims are[6]:,

1. A method for iontophoretically delivering dexamethasone phosphate into the eye of a subject in need of such treatment, comprising: a) administering a formulation of dexamethasone phosphate to the eye of the subject; wherein the formulation comprises: i) 40 mg/mL of a dexamethasone phosphate solution; and ii) wherein the pH of the formulation has been adjusted to between 5.7 and 6.1 with a buffering agent; and b) performing ocular iontophoresis to the eye of the subject.
2. The method of claim 1, wherein the subject is being treated for an ophthalmic condition selected from uveitis, dry eye, post-operative inflammation, diabetic macula edema and corneal graft rejection.
3. The method of claim 1, wherein the subject is being treated for an inflammatory ophthalmic condition.
4. The method of claim 1, wherein the subject is being treated for uveitis.
5. The method of claim 1, wherein the subject is being treated for anterior segment uveitis or dry eye.
6. The method of claim 1, wherein the step of ocular iontophoresis is carried out prior to, during or after the step of administering the dexamethasone phosphate.
7. The method of claim 1, wherein the dexamethasone phosphate is delivered by an iontophoretic dose of about 0.5 mAmin to about 50 mAmin.

And another application related to the Eyegate II Delivery System has also been filed covering (per EYEG 10/15/15 P.R.) "claims for a delivery device containing a hydrogel applicator used to transport therapeutic substance across and / or through the eye." In October 2015 EYEG announced that they received a Notice of Allowance from the USPTO related to this application.

[6] USPTO. United States Patent 9,149,525. Jaffe, et al. October 6, 2015

Clinical Data in Non-Infectious Anterior Uveitis: EYEG has completed two non-infectious anterior uveitis clinical studies. The first, which completed in 2009, was a phase I/II dose-ranging study which demonstrated the combination product produced inflammation lowering effects with no corticosteroid mediated effects and found the most effective dose to be the lowest one tested. The second study, a phase III trial which used the dose found to be most effective in the prior dose-ranging study, just missed the primary efficacy endpoint of non-inferiority to standard of care. However, FDA recently communicated to EYEG that if a planned new phase III study demonstrates non-inferiority, that that data, along with results of the completed phase III study, will be sufficient to support a New Drug Application (NDA) filing.

- ***Phase I/II dose-ranging study: lowest dose deemed most effective…***

EYEG's first non-infectious anterior uveitis clinical trial was a phase I/II, single-arm dose-ranging study (clinicaltrials.gov ID:NCT00694135) to determine a safe and effective dose of EGP-437. Non-infectious anterior uveitis was defined as having anterior chamber cell (ACC) scores of ≥1.5 (on a scale of 0 – 4, lowest – highest), which corresponds to a cell count of ≥11. Enrollment of the multi-site, double-blind study consisted of 40 patients (40 eyes), all of which received treatment with EGP-437 delivered by iontophoresis via the Eyegate II Delivery System. Patients were randomized to receive one of four EGP-437 doses (dexamethasone phosphate ophthalmic solution 40mg/mL) with 10 patients in each arm; 1.6 mA-min @ 0.4 mA[7], 4.8 mA-min @ 1.2 mA, 10 mA @ 2.5 mA and 14 mA @ 3.5 mA. Each dose was administered only once and for approximately four minutes. Treatment was administered on Day 0, follow-up exams were conducted on Days 1, 7, 14 and 28.

Results (table below): 19 of the 40 patients (48%) and 24 of the 40 patients (60%) achieved an ACC score of zero within 14 days and 28 days, respectively. Interestingly, the greatest proportion of patients achieving both ACC scores and ACC cell counts of zero at both the 14 day and 28 day follow-up were in the lowest dose (i.e. 1.6 mA) cohort. The lowest dose group also had the highest proportion of patients (80% vs. 60% of the other three groups) which experienced an ACC score reduction of 0.5 or more at Day 28. The mean change in ACC score from baseline to Day 28 ranged from a maximum of -2.25 in the 1.6 mA dose group to a minimum of -2.00 in the 14.0 mA dose group. The 1.6mA dose was chosen as the most effective dose. Achievement of an ACC score of zero by Day 14 was considered statistically significant (p=0.032) at a 95% CI. Treatment was well tolerated with no corticosteroid mediated effects.

		Treatment Group				
Characteristic	Statistic or Category	1.6 mA-min (N = 10)	4.8 mA-min (N = 10)	10.0 mA-min (N = 10)	14.0 mA-min (N = 10)	Total (N = 40)
ACC Score of Zero	Day 14	8 (80%)	6 (60%)	2 (20%)	3 (30%)	19 (48%)
	Day 28	8 (80%)	6 (60%)	5 (50%)	5 (50%)	24 (60%)
ACC Count of Zero	Day 14	4 (40%)	1 (10%)	1 (10%)	1 (10%)	7 (18%)
	Day 28	6 (60%)	2 (20%)	1 (10%)	5 (50%)	14 (35%)

SOURCE: Eyegate YE 2015 10-K

- ***Initial Phase III Study; Similar Clinical Response as PA Although Endpoint (Barely) Missed…***

The phase III randomized, double-blind, placebo-controlled study (clinicaltrials.gov ID:NCT01505088) that followed the dose-ranging trial was powered as non-inferiority to standard of care. The study was conducted at 45 U.S. sites and included 193 patients with non-infectious anterior uveitis (ACC count ≥ 11) which were randomized to treatment, consisting of Eyegate combination treatment of 4.0 mA-min @ 1.5mA on Day 0 and Day 7 (in addition to placebo drops for 28 days), or control, consisting of prednisolone acetate 1% eyedrops for 28 days (in addition to sham Eyegate treatment (sodium buffer solution) on Day 0 and Day 7).

While dexamethasone is one of the most potent of all corticosteroids and has anti-inflammatory effects that are as much as 10x greater than that of prednisolone, it does not penetrate the anterior chamber of the eye nearly as well as prednisolone. This is the reason that prednisolone is considered standard of care for anterior uveitis and why it was used as the control in these clinical studies. And while absorption of dexamethasone dosed as drops is inhibited by corneal and conjunctival barriers, these challenges are at least partially overcome with the use of iontophoresis which propels the drug into the tissue. And the drug's

[7] mA is abbreviation for milliampere (one thousandth of an ampere)

accommodating chemical profile make it highly water soluble which also adds to its attractiveness with iontophoresis delivery.

Per pre-study communications with FDA, prednisolone acetate (PA) administered at least 4x per day was the recommended standard of care (i.e. control). However, EYEG chose to use a more aggressive control regimen, administering PA 8x per day in week one, 6x per day in week two and 4x per day in weeks three and four (for a total of 154 drops over 28 days).

Primary endpoint was proportion of patients with ACC count of zero at Day 14 (i.e. complete response). Several **secondary** efficacy outcomes were also measured including proportion of patients with ACC counts at Days 7, 28 and 56, mean change from baseline in ACC count and score at Days 7, 14, 28 and 56 and proportion of patients with ACC count and score reduction from baseline of one or more units at Days 7, 14, 28 and 56, and time to anterior chamber cell count and score of zero.

Results were presented on two separate patient populations; intent to treat (ITT) and per protocol (PP). ITT is generally used in clinical trials to account for non-compliance of trial design, protocol deviations drop-outs or anything after randomization. ITT results are generally considered conservative to treatment effect. PP is typically considered the population that remained in the study through the measurement endpoints and did not violate any of the trial protocol

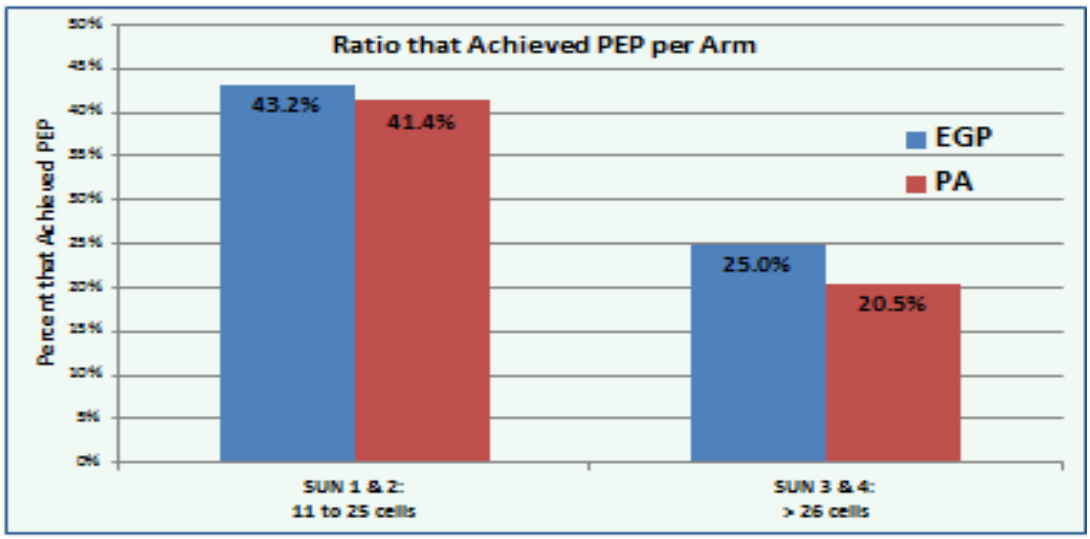
- **ITT**: defined as all randomized patients (193) who were treated with at least one dose of study medication, have a valid baseline efficacy and at least one valid post-randomization efficacy measurement and all data associated with these subjects, until the visit following initiation of any rescue therapy.
- **PP**: 169 patients met the PP population parameters which included those that had a Day 14 ACC count and without any significant protocol deviations. Of the ITT population, 24 patients had protocol violations prior to Day 14 including;
    - 14 in Eyegate treatment arm, 10 of which either needed to be rescued and/or did not receive the second (of two) iontophoresis treatments, 1 which needed non-ocular surgery, 2 which were unable to continue with follow-up visits and 1 which withdrew consent
    - 10 in the PA arm, 8 of which either needed to be rescued and/or did not receive the full amount of PA and 2 which had their Day 14 visit twelve and thirty days later than that visit timeframe

Results: (per information contained in company public filings) While response rates were similar in both the ITT and PP populations, non-inferiority (as pre-defined in the study protocol) was just missed.

- IIT: EGP-437 treatment arm had 32 (out of 96) patients with complete response (i.e. ACC count of zero at Day 14) while PA arm had 32 (of 97) with complete response. There was no difference in response rates between the two arms at a 95% C.I., however, the non-inferiority margin, at -12.94%, just missed statistical significance of the pre-determined non-inferiority margin of -10%
- PP: EGP-437 treatment arm had 31 (of 82) patients, or 37.8%, with complete response while PA arm had 31 (of 87), or 35.6%, with complete response. Again, while there was no difference in response rates, the non-inferiority margin (-12.37%) just missed the pre-determined non-inferiority margin (-10%) at a 95% C.I.

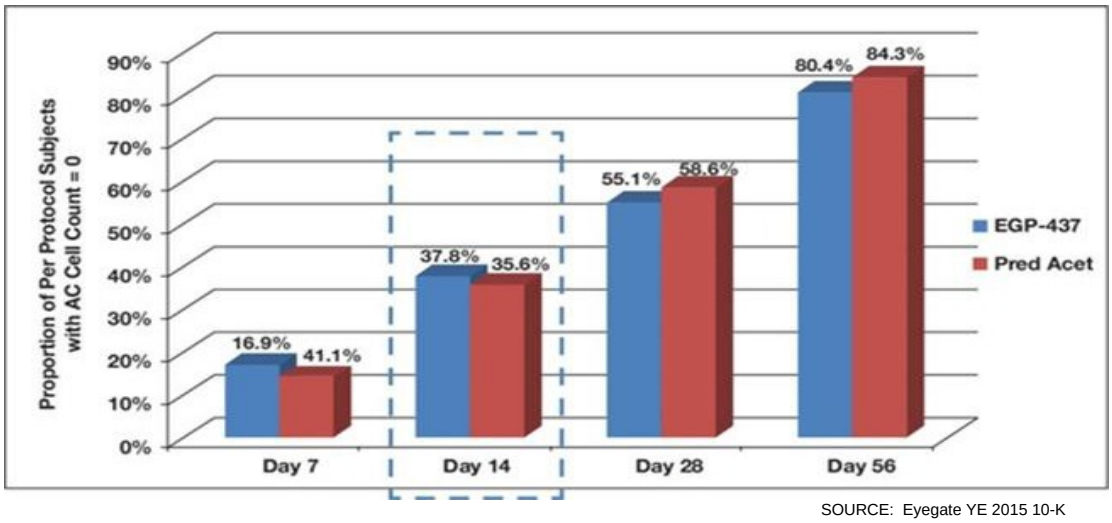
Additional Observations: Along with no difference in response rates between both arms on the primary endpoint, secondary measures and other observations also support the efficacy of EGP-437 combination therapy;

- Greater Proportion of High ACC Count Patients in EGP-437 Arm: a higher proportion of EGP-437 patients (52 of 96, or 54%) had baseline ACC counts greater than 25 as compared to those in the PA arm (40 of 97, or 41%). A post-hoc analysis was done on these high ACC count (i.e. potentially harder to treat) patients with better efficacy favoring the EGP-437 arm. Among the patients with baseline ACC of 11 to 25 cells, 43.2% of EGP-437 patients met the primary endpoint (i.e. ACC count of zero at Day 14) while only 41.4% of PA patients did. Among the patients with baseline ACC > 26 (i.e. – more severe cases), 25% of EGP-437 patients met the primary endpoint while only 20.5% of PA patients did (chart below).



SOURCE: Eyegate

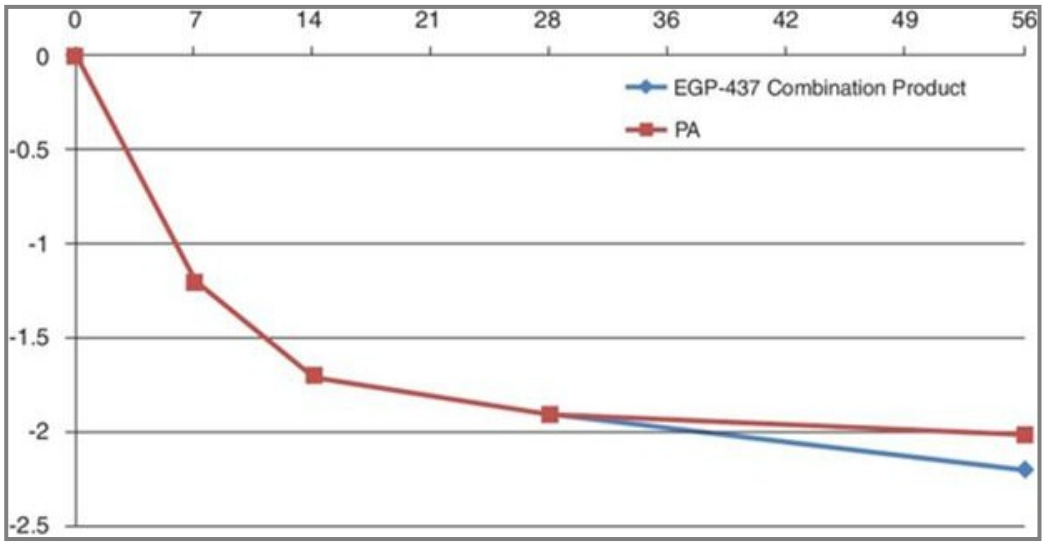
- Similar Complete Response Timeframes: "Time to anterior chamber cell count and score of zero" was a secondary endpoint. Despite the baseline difference in severity of disease (as measured by ACC count), the time to reach ACC count of zero was generally similar in both arms throughout the study (chart below). However, at Day 7, after just one iontophoresis treatment, the EGP-437 arm showed a statically significant superior response with 16.9% of patients achieving complete response, compared to just 14.1% of PA patients. This non-inferiority margin was -7.82%, within the pre-determined margin of -10% at 95% C.I.



SOURCE: Eyegate YE 2015 10-K

- Similar Reduction in ACC Count of One or More Units: "Proportion of subjects with ACC count and score reduction from baseline of one or more units" was another secondary endpoint. On this measure the two arms were similar, although the non-inferiority margin (-13.97%) was just outside the non-inferiority margin at 95% C.I.

- Similar Change from Baseline ACC Score: "Mean change from baseline in ACC count and score" at Days 7, 14, 28 and 56 was another secondary endpoint. This was similar between both arms throughout the study (chart below) with an incremental benefit to the EGP-437 treatment group at Day 56



SOURCE: Eyegate YE 2015 10-K

- Safety: Lower Incidence of IOP in EGP-437 Arm: corticosteroid use is associate with an increase in intraocular pressure (IOC), which can eventually result in permanent damage to the eye. IOC measurements were taken at Days 7, 14, 28 and 56 and compared to baseline.
    - There were 2.4x more incidents of increase in IOP in the PA arm as compared to the EGP-437 arm. 17 incidents of an increase in IOP among 14 patients (of 96, or ~15%) were recorded in the EGP-437, compared to 41 incidents among 24 subjects (of 97, or ~25%) in the PA arm
    - No patients in the EGP-437 therapy arm experienced any significant increase (i.e. over 20mmHg) in IOP while one subject in the PA arm reported an IOP increase of 27mmHg. In terms of IOP-related adverse events, one patient in the EGP-437 arm reported an adverse event (~3 weeks following rescue) and six patients in the PA arm reported IOP-related adverse events. NOTE: EYEG's 10-K, where we sourced this trial data and information, did not provides specifics of the nature or severity of the adverse events, only that they were related to IOP

Key Takeaways:

- While the primary endpoint was (barely) missed, EGP-437 combination therapy appeared to be similarly effective as standard of care (i.e. PA)
- There was a trend in the data favoring EGP-437 combination therapy in patients with higher ACC counts (i.e. generally considered more difficult to treat)
- EGP-437 combination therapy consisted of two treatments at Days 0 and 7 with administration taking ~5 minutes each session. This compares to PA therapy which consisted of 4 – 8 eye drops every day over the course of four weeks, aggregating to a total of 154 drops. While the PA regimen was perhaps more aggressive than that recommended by FDA (of "at least four drops per day"), this highlights how much more burdensome conventional therapy is
- Safety was at least comparable, or perhaps favoring EGP-437 combination therapy particularly in lower IOP

❖ ***New, Pivotal Phase III Study Initiating..***

In May 2015 EYEG announced that FDA communicated that if a planned new phase III study demonstrates non-inferiority, that that data, along with results of the earlier phase III study (discussed above), will be sufficient to support a New Drug Application (NDA) filing.

This non-infectious anterior uveitis "confirmatory study" is randomized, double-blind, placebo-controlled and designed to demonstrate non-inferiority of EGP-437 combination therapy to PA 1%. Up to 250 patients (~125 each arm) with anterior segment uveitis (ACC count $\geq$ 11) are expected to enroll at approximately 60 U.S. sites. Primary efficacy endpoint is the same as the initial phase III study (i.e. ACC count of zero at Day 14).

Patients will be randomized to either three treatments of EGP-437 combination therapy (Days 0, 4 and 9) plus placebo eye drops or PA 1% plus sham EGP-437 combination therapy. The design of this confirmatory study, while similar to the initial phase III anterior uveitis trial, has some important differences which should improve the chances

of meeting the primary efficacy endpoint. This includes its larger size (greater chance of fleshing out statistical significance), three EGP-437 combination treatments (1.5 mA-min @ 2.7mA) instead of two (4.0 mA-min @ 1.5mA) and randomization based on severity of the disease (to eliminate the potential bias of more severe patients which was seen in the AGP-437 arm in the initial study).

	First Phase 3	Confirmatory Trial
Number of Subjects	193	250
Number of Treatments	2 (Day 0 and Day 7)	3 (Day 0, Day 4 and Day 9)
Randomization	1:1	1:1 and SUN scale severity
Primary Endpoint	ACC Count= 0 at Day 14	

SOURCE: Eyegate

Timelines: The first patient was enrolled in the confirmatory study in January 2016. Per EYEG's most recent public communications regarding timelines, they expect the study to be fully enrolled by current year-end and to have top-line data in Q1 2017. Those timelines may be do-able depending on the rate of enrollment. For comparison, per clinicaltrials.gov, the initial phase III study started in December 2011 and had a primary completion date (final data collection date for primary outcome measure) of February 2013 – or ~14 – 15 months. This ~14 months included 12 months of enrollment and 2-month follow-up period. While the confirmatory study will enroll ~23% more patients, the pace of enrollment should benefit from presumed use of some of the same clinical sites and investigators.

U.S. Regulatory Pathway: Assuming positive results (i.e. primary efficacy endpoint met and acceptable safety profile), EYEG expects to file for U.S. regulatory approval/clearance of both the Eyegate II Delivery system and EGP-437 simultaneously. Eyegate has already received confirmation from FDA that their delivery system is considered a Class II device but can pursue clearance through the (relatively simple) 510(k) clearance pathway. For EGP-437, which must be approved through a New Drug Application (NDA), Eyegate intends to file a 505(b)(2) NDA.

Relative to the device. EYEG's 510(k) will cite two existing iontophoresis devices which deliver drugs through the skin, one of which is DJO Global's (Empi's) Dupel II Buffered iontophoresis electrode for use of delivery of lidocaine and epinephrine. FDA has agreed that these are acceptable to use as predicates.

The 505(b)(2) NDA relates to, "an application that contains full reports of investigations of safety and effectiveness but where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference." It "permits FDA to rely, for approval of an NDA, on data not developed by the applicant."[8] FDA allows 505(b)(2) applications in circumstances where there are changes to an approved drug such as, formulation, dosage form, strength and route of administration, among others. EYEG has referenced Decadron, a topical dexamethasone formulation, which they believe they may be able to use the existing safety and efficacy literature of for filing of EGP-437 under the 505(b)(2) pathway.

Based on our communication with Eyegate, management is comfortable, based on their interaction and communication with FDA including the agency accepting a preclinical and clinical data protocol based on the 505(b)(2) NDA route, that this is an acceptable pathway. And importantly, EGP-437 has demonstrated what appears to be an acceptable safety profile in the five clinical studies in which it has been used. The initial phase I/II non-infectious anterior uveitis trial was conducted under the initial IND, submitted to FDA in April 2008. The IND was then subsequently amended for additional studies.

Follow-On Indications: Macular Edema and Cataract Surgery

While EYEG expects to enter the market with a non-infectious anterior uveitis indication, they have had their sights on a broader label and one that includes more prevalent ophthalmic diseases (i.e. larger market sizes) and harder to treat (i.e. potential for rapid market penetration) back-of-the-eye conditions. Macular edema, which is a swelling of the macula (center portion of the retina) due to a build-up of fluid leaking from blood vessels, is traditionally treated with drug injections, laser therapy or intravitreal implants. EYEG has initiated a phase Ib/IIa study in

[8] Guidance for Industry. Applications Covered by Section 505(b)(2). US Dept of HHS/FDA/CDER. Oct 1999

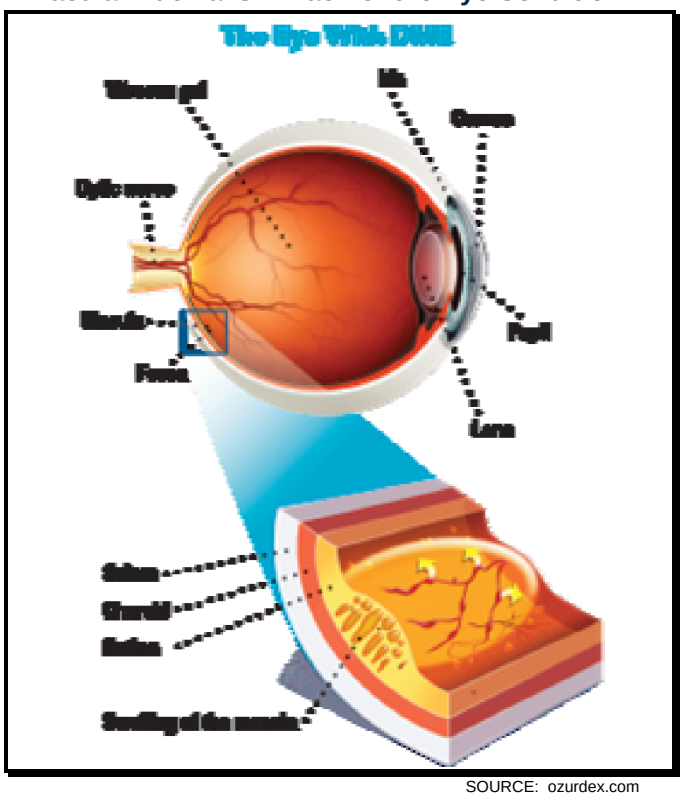
macular edema. Cataract, the leading cause of blindness, results in over 3 million cataract surgeries per year in the U.S. and may represent an attractive market for Eyegate's combination therapy.

- **Macular Edema:** ***EGP-437 can treat back of the eye, initial clinical data is positive…***

Formation of macular edema can be the result of a variety of conditions and circumstances. While it is most commonly associated with type 2 diabetes, age-related macular degeneration can be a direct cause. Chronic uveitis or blockage of a vein (retinal vein occlusion) can also be contributors as can complications following cataract surgery such as cystoid macular edema (cyst-like fluid build-up in macula).

Diabetic macular edema affects up to 7% of people with diabetes[9], or ~2M Americans. Estimated incidence of cystoid macular edema varies widely depending on the source, examination technique and definition of the condition but is believed to be ~1% - 14% of cataract surgery patients, or ~30k – 400K Americans. Standard of care of macular edema includes NSAID and cortisone drops, laser retinal photocoagulation, intravitreal injections (corticosteroids and anti-VEGF drugs) and intravitreal implants. These all have drawbacks; NSAID's can cause burning, stinging and even "corneal melting", laser retinal photocoagulation often damages nerve cells in the retina causing some vision loss, drops not only must be dosed continuously but they are highly inefficient in reaching the back of the eye and can have adverse side effect, injections are highly invasive, cause patient skittishness, risk infection and eye damage and require a trained ophthalmologist to administer, intravitreal implants can migrate within the eye which can cause permanent eye damage.

Macular Edema Is A Back-of-the-Eye Condition



SOURCE: ozurdex.com

EYEG's phase Ib/IIa multi-site, open label proof-of-concept clinical study (clinicaltrials.gov ID: NCT02485249) **of EGP-437 therapy in patients with macular edema** associated with retinal vein occlusion (RVE), diabetic macular edema (DME) or post-surgical (cystoid) macular edema (CME) is ongoing. Subjects received three treatments of EGP-437 iontophoresis therapy at 14mA-min (3.5mA) on days 0, 4 and 9. Primary outcome was reduction in mean central subfield thickness on day 4, day, 9 and day 14. Ozurdex, a dexamethasone intravitreal implant marketed by Allergan (NYSE: AGN) and indicated for treatment of macular edema, retinal vein occlusion and non-infectious posterior uveitis, was administered as control to patients that did not respond to EGP-437 combination therapy at day 14 and were re-evaluated at day 28.

[9] Curr Diab Rep. 2012 Aug;12(4):346-54. doi: 10.1007/s11892-012-0283-6. *Current epidemiology of diabetic retinopathy and diabetic macular edema.* Ding J1, Wong TY.

In November 2015 EYEG announced results of the first-leg of the study, which included 19 patients (results on 18). Nine patients with pseudophakic eyes (i.e. those with implanted intraocular lens) were enrolled with the following conditions; six with DME, three with RVO. Nine patients with phakic eyes (i.e. those with natural lens) were enrolled with the following conditions; four with DME, three with RVO and two with CME. **Safety profile was considered excellent** with no increase in IOP – which is particularly noteworthy given that the dose in this study was three times that of the dose in the initial phase III anterior uveitis study.

There was a clear efficacy signal, demonstrating that EGP-437 combination therapy can deliver drugs to the back of the eye. The study also showed that pseudophakic eyes responded better than phakic eyes. Nine patients with pseudophakic eyes and nine phakic eyes were in the study.

- While **phakic eyes** responded relatively poorly, with just an 8% mean thickness reduction observed in only 2 of 9 patients and minimal or no response in the remaining seven, pseudophakic eyes showed a relatively strong response.
- Seven of nine **pseudophakic eye** patients had a positive response including three with greater than 25% reduction in edema at day 14, one of which showed a 67% reduction. Just three patients were given Ozurdex and only two of which showed minimal or no response to EGP-437 therapy.

Edema (μ)	V1 Day 0	V2 Day 4	V3 Day 9	V4 Day 14
Phakic	451	461 (-1.6%)	455 (-0.2%)	470 (-3.6%)
Pseudophakic	540	448 (17%)	416 (23%)	427 (21%)

7 of 9 Pseudophakic Showed Positive Response Incl. 3 >25% and 1 = 67%

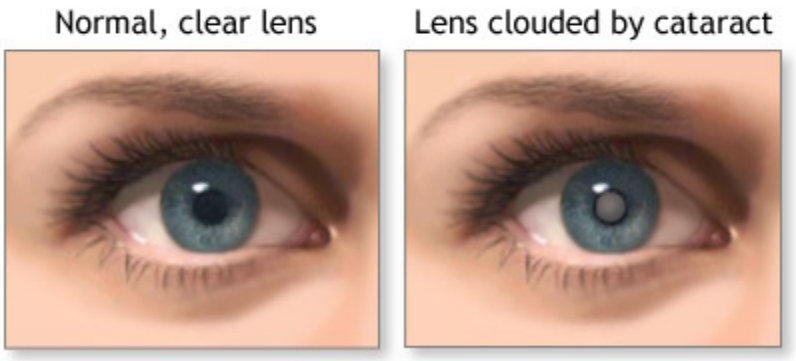
Patient Information				OCT Measurements				IOP			
	ME DX	Gender	DOB	Visit 1 Day 0	Visit 2 Day 4	Visit 3 Day 9	Visit 4 Day 14	Visit 1	Visit 2	Visit 3	Visit 4
PSEUDOPHAKIC SUBJECTS											
1	DME	Male	21-Dec-58	694	615	614	616	12	15	15	14
					11.4%	11.5%	11.2%				
2	CME	Female	23-May-54	623	569	512	566	14	15	12	10
					8.7%	17.8%	9.1%				
3	BRVO	Female	25-Dec-50	558	531	522	503	14	13	15	18
					4.8%	6.5%	9.9%				
4	pCME	Female	6-Dec-48	500	325	304	298	10	10	12	10
					35.0%	39.2%	40.4%				
5	DME	Male	21-Sep-52	758	392	249	273	16	14	13	17
					48.3%	67.2%	64.0%				
6	BRVO	Male	20-Sep-51	318	317	294	291	11	11	11	11
					0.3%	7.5%	8.5%				
7	DME	Female	2-Nov-53	521	496	515	523	18	18	20	20
					4.8%	1.2%	-0.4%				
8	BRVO	Female	24-Dec-26	502	413	358	368	12	14	13	16
					17.7%	28.7%	26.7%				
9	DME	Female	13-Feb-44	390	372	380	408	13	14	14	12
					4.6%	2.6%	-4.6%				
Mean				**540**	**448**	**416**	**427**	**15**	**14**	**14**	**14**
					17.1%	22.9%	20.9%				

The **second leg** will enroll an additional 15 patients; 5 with phakic eyes and 10 with pseudophakic eyes. Five (three with phakic, two with pseudophakic) of the patients in the first trial which had minimal or no response to EGP-437 therapy but did respond well to Ozurdex will continue in the second leg. As it was observed that edema comes back when the drug clears the tissues, this extension study will use a modified dosing regimen; three consecutive days of EGP-437 iontophoresis treatments at the same dose. And as data from the first leg demonstrated some patients with pseudophakic eyes responded better than those with phakic eyes, this second leg will also evaluate the efficacy of EGP-437 combination therapy in phakic versus pseudophakic eyes to collect additional data on the differences in the responses of both groups. Interim data is expected to be available in 1H 2016. Data from this study, assuming positive, will then be used to design a larger, later-stage clinical trial.

Our comments: Macular edema represents a potentially receptive and large market for EYEG given the seriousness and high incidence of the disease as well as the lack of conventional, effective non-invasive methods to treat it. EYEG's early stage studies have shown the ability to deliver EGP-437 to the back of the eye to treat conditions such as macular edema. As back-of-the eye conditions are more difficult to treat than, for example anterior uveitis, if effectiveness of EGP-437 combination treatment in macular edema is confirmed in larger studies, we think this indication could offer significant opportunity for EYEG.

- **Post Cataract Surgery:** ***EGP-437 can treat back of the eye, initial clinical data is positive…***

Cataract, or a clouding of lens, is most commonly the result of ageing and is the leading cause of blindness across the globe. Approximately 21 million people in the U.S. over the age of 40 have cataract in at least one eye, ~6 million of which have undergone surgery to have their lens removed. About 3.6 million cataract surgeries are performed in the U.S. each year and about 20 million worldwide.



SOURCE: A.D.A.M. / umm.edu

Standard of care to manage post-operative cataract surgery inflammation are NSAIDs and corticosteroids. EYEG conducted a phase II study (clinicaltrials.gov ID: NCT01602068) with EGP-437 combination treatment in cataract surgery which completed in 2013. They decided to apply EGP-437 treatment prior to (4.0 mA-min at 1.5 mA one day prior to surgery) surgery in order to avoid putting the delivery device directly on a post-surgery open wound. Primary endpoint was proportion of subjects with ACC count of zero on day 7. While we were unable to find the detailed results in the public domain, EYEG has noted that "the surgical procedure eliminates or washes out any remaining drug product from the ocular tissue that becomes inflamed post-surgery" - presumably indicating that the study failed to meet the efficacy endpoint.

EYEG has revised the trial design and expects to initiate another cataract surgery study. This open label, multi-site phase Ib/IIa clinical trial (clinicaltrials.gov ID: NCT02571556) will enroll up to 20 patients which have undergone unilateral cataract extraction and implantation of a monofocal intraocular lens. Patients will undergo EGP-437 combination treatment (4.0 mA-min at 1.5 mA) on days 0 (i.e. immediately after surgery) and 7. Follow-up will occur on days 1, 14 and 28. Primary endpoint is the same as the initial study (i.e. proportion of subjects with ACC count of zero on day 7). EYEG believes they will have top-line data in 1H 2016.

There are some therapeutic similarities between the uveitis and post cataract surgery indications in that both involve the same tissues, those being of the iris and ciliary body. As such, we think the positive outcomes of EYEG's anterior uveitis studies may bode well for the same result in post cataract surgery – although we acknowledge the differences of both indications including possible influences or difficulties related to surgery. That relationship along with the potential for positive outcomes from this cataract surgery pilot study means that later stage/pivotal studies in post cataract surgery could be fairly swift moving. We will be keeping a close on this 'eye' on this.

Similar to macular edema, we view cataract surgery as a considerably attractive market than that of anterior uveitis given its relatively large size (i.e. ~3 million U.S. surgeries each year). We expect the upcoming interim data to provide more insight into the potential utility of EGP-437 combination treatment in a potential cataract surgery indication.

Dry Eye: Shelved, at least for the time being

EYEG had, at one time, also been pursuing a dry eye indication, although has since shelved that program due to the difficulties associated with enrolling clinical trials for a condition that has different and varying etiologies. While EYEG has already completed a phase II and III clinical trial in the treatment of dry eye which showed EGP-437 combination therapy was associated with significant improvement in certain signs (such as corneal staining , tear film break-up and conjunctival redness) and symptoms (such as ocular discomfort) of dry eye, results were mixed with some efficacy endpoints met, while others were not. These studies used a "controlled adverse environmental system" (CAE) to reproduce the signs and symptoms of dry eye although EYEG has noted that if they were to conduct future dry eye clinical trials that they would use an alternative way to enroll the trial, without the use of CAE. While dry eye represents a large market (~5 million Americans over the age of 50 have it), given the difficulty in finding and enrolling a homogenous patient group for dry eye and the other indications (such as anterior uveitis, macular edema and cataract surgery) that may be more straightforward, EYEG has decided to put dry eye on the back burner.

Investment Considerations

Valeant (Bausch+Lomb)

The ophthalmic therapy market is fairly concentrated with only three major companies; Alcon, Allergan plc and Valeant Pharmaceuticals' Bausch+Lomb division dominating the space. In July 2015 EYEG announced a licensing agreement, granting Valeant worldwide rights to manufacture and commercialize the Eyegate II Delivery System and EGP-437 for the uveitis indication as well as right of last refusal in other applications. In return, EYEG received upfront cash ($1 million) and is eligible for up to $32.5 million in development, regulatory and sales milestones. EYEG will also receive ("high single digit") royalties on sales. We note that neither Eyegate or Valeant has disclosed how the milestones are structured. EYEG is responsible for product development and related costs for the anterior uveitis indication in the U.S. Valeant has the right to develop the product outside of the U.S. and will be responsible for associated development costs.

This deal not only affords EYEG entry into the difficult-to-penetrate ophthalmic therapy market, but does so with some mitigated financial and product development risk. We also view this partnership with one of the ophthalmology "majors" as a meaningful vote of confidence in the product. In a deal valued at $8.7 billion, Valeant acquired Bausch + Lomb in 2013 in order to bolt on capabilities in the growing ophthalmology market. Bausch & Lomb, which is the largest worldwide provider of contact lenses, has a broad product line that also includes ophthalmic pharmaceuticals and ophthalmic surgical products.

Low-Hanging Fruit is Anterior Uveitis

While the market size of non-infectious anterior uveitis is much smaller than that of potential follow-on indications, it is the one that is furthest along in development, is already licensed to Valeant and has the clearest regulatory path. As such, we view this as the low-hanging fruit opportunity. If all goes to plan, we think reasonable expectations relative to anterior uveitis are;

- Top-line data from phase III confirmatory study in Q1 2017
- Full data analysis completed, regulatory packages (505(b)(2) NDA for EGP-437, 510(k) for device) prepared and submitted 2H 2017
- FDA approval / clearance of EGP-437 and delivery device 1H 2018
- Launch in U.S. by Valeant in 2H 2018. At which point EYEG would have received development and regulatory approval milestones
- EYEG has not disclosed the specific royalty rate on sales for the uveitis indication only noting that it is in the 'high single digits'. Our model uses 8% as the assumed rate
- U.S. prevalence of anterior uveitis is ~110k, much smaller than either macular edema or cataract surgery. Penetration / adoption of EYEG's therapy in anterior uveitis may be somewhat measured, even over the long-term, given the headwinds of corticosteroid market saturation. Despite their burdensome dosing regimen and adverse risk profile, steroids are well entrenched, are effective and patients/clinicians may be more forgiving of their drawbacks than they might be of injections

- As such, while we view anterior uveitis as the most near-term opportunity and one which EYEG may be able to clip sizeable development and regulatory milestones, we think macular edema and cataract surgery may hold much more sales royalty potential, particularly over a longer duration

Macular Edema, Cataract Surgery Are Bigger, and Maybe More Receptive, Markets
While macular edema and cataract surgery are at earlier stages of development than is the anterior uveitis indication, these other indications represent much larger market opportunities. Points of interest relative to these indications;

❖ **Macular Edema**
- Eyegate therapy response observed, particularly in pseudophakic eyes. Second leg of study will look closer at difference in phakic vs. pseudophakic response. Top-line data could be available 1H 2016
- Full-data set and analysis could be late 2016/1H 2017
- Assuming second leg data is positive, ME will move to larger clinicals – potentially directly to pivotal phase III
- Anticipate pivotal study timelines could be as long as two years from start (late 2017?) to completion (late 2019?)
- Expect interest from Valeant to license for ME indication potentially as early as entry into late-stage clinical trials or possibly earlier depending on strength of data sets
- Analysis, regulatory package, filing and FDA response/approval happen by late 2020 and launch late 2020/early 2021?
- We ballpark the U.S. ME market at approximately 2.2 million people but think EYEG's target market may be restricted to pseudophakic eyes, which comprise account for about 30%[10] (or ~660k) of the total ME market. This still represents a sizeable market and one that is about 6x the size of that of anterior uveitis (~110k)

❖ **Post Cataract Surgery**
- Cataract surgery is at somewhat of a similar (i.e. early) stage as macular edema. And while we think the evidence to-date of ME is more supportive of efficacy in that indication, given that targeted tissues with post cataract surgery are similar to those with anterior uveitis (which has the most supporting evidence of efficacy to-date), cataract surgery may be able to move through later stage/pivotal studies fairly swiftly. However, the differences of anterior uveitis and post cataract surgery patients (most noteworthy of which is surgical intervention) could result in differences in efficacy. So, given the early clinical stage of post cataract surgery as well as the potential that surgical intervention may confound an efficacy signal that may otherwise be expected to be similar to that of anterior uveitis, our model (as explained in more detail below) incorporates a relatively low probability of success for cardiac surgery. This could be updated if the pilot study shows positive results
- Phase II study which completed in 2013, used Eyegate therapy prior to cataract surgery. Failed to meet endpoint as was found that the surgical procedure washed the drug out of the eye
- New phase II clinical study will use Eyegate therapy post-surgery
- If the pilot study results are positive, EYEG may be able to move directly to phase 3 – which could initiate as early as later this year or early next. Assuming that happens, pivotal studies could wrap up in late 2017/early 2018 and, if all goes well, FDA approval and entry into the U.S. commercial market possibly happening in 2018 – 2019
- ~3.6 million cataract surgeries are performed in the U.S. every year. Target market for Eyegate's therapy may more likely be a sub-segment of this. Inclusion criteria of the upcoming phase II study requires implantation of monofocal intraocular lens. This represents ~30% of the aggregate cataract surgery market or ~1.1 million people, making it the largest market (by far) of EYEG's current focused programs and approximately 10x as large as anterior uveitis

Home Use
Eyegate has indicated that they may also pursue regulatory approval for home use for certain chronic conditions such as macular degeneration and note in their January 2016 investor presentation that they have initiated a collaboration for that purpose. Home use, in our opinion, would significantly broaden the size of the overall target markets and likely accelerate adoption for eye-drop related conditions as patients would be able to perform the treatment in the comfort of their home. However, as FDA approval specific to home use would be required and will likely necessitate additional clinical studies demonstrating that individuals (i.e. non-

[10] Congdon N1, Vingerling JR, Klein BE, West S, Friedman DS, Kempen J, O'Colmain B, Wu SY, Taylor HR; Prevalence of cataract and pseudophakia/aphakia among adults in the United States. Arch Ophthalmol. 2004 Apr;122(4):487-94.

clinicians) can correctly and safely perform the procedure (and these studies could be lengthy and require substantially more resources), given the lack of foresight relative to timing or feasibility, we do not currently incorporate any assumptions in our outlook or model related to an at-home indication.

VALUATION / RECOMMENDATION

Given the pre-revenue stage of Eyegate, typical valuation methodologies such as P/E, P/EG, P/S and others which require financial metrics as components are unsuitable. As such, we believe the most appropriate valuation methodology is discounted cash flow.

Regarding milestones that EYEG is eligible to receive from Valeant. As milestones could be a significant portion of any revenue that EYEG recognizes, we think it is relevant to provide a comment. It is unclear how the milestones are structured as neither EYEG or Valeant has disclosed this information. EYEG's prospectus dated November 11, 2015 notes that, "The Company is eligible to receive milestone payments totaling up to $32.5 million, upon and subject to the achievement of certain specified developmental and commercial milestones. In addition, the Company is eligible to receive royalties based on a specified percent of net sales of the Product throughout the world, subject to adjustment in certain circumstances."

The language in the July 10, 2015 press release announcing the licensing agreement is somewhat different and reads, "Under the agreement, EyeGate will receive an upfront cash payment, development-based milestone payments related to the completion of development for the indication of anterior uveitis and an approval-based milestone payment upon receipt of FDA approval of the Product. Additionally, the Company would receive royalties based on net sales, as well as additional milestone payments based on the achievement of certain cumulative sales milestones."

So there is no information that relates to timing/triggers/deliverables of potential payments and it is also unclear whether the $32.5M is related only to development and FDA approval or if it also relates to commercialization and sales. We are taking a conservative approach and assuming that not only is the $32.5M also related to commercialization/sales, but that the majority of it is back-weighted (i.e. – not related to development and FDA approval). This, like all of our assumptions, is subject to updating if and when new information becomes available that is at odds with our inputs.

Our model incorporates the following assumptions:

General assumptions:

- we have discounted all modeled milestones and royalties related to each indication to account for risk of regulatory and/or commercialization failure. These respective risk discounts are subject to change based on change in risk profile (i.e. decreasing with clinical trial and regulatory progression)
- while Valeant has currently only licensed rights for the anterior uveitis indication, we assume that if and when macular edema and cataract surgery demonstrate positive results in later stage clinical trials, that Valeant will also license rights to these indications. For consistency purposes, we assume the aggregate milestones and royalty rates are the same as for anterior uveitis
- assume all sales royalties are at 8% (EYEG has disclosed the anterior uveitis indication will pay "high single digits")
- operating expenses trend higher with progression of each indication through later-stage clinical trials and related regulatory activities. Following launch, operating expenses fall as Valeant is responsible for sales and marketing and EYEG's R&D activities temper

Anterior Uveitis Indication:

- 80% probability of successful FDA approval/clearance and launch for anterior uveitis indication. All modeled milestones and royalties related to anterior uveitis are initially discounted by 20% (i.e. 1 – 0.80) to account for risk of regulatory or commercialization failure
- Receipt of development milestones begins in 2017
- Receipt of FDA approval/clearance and launch in 2018 and receipt of regulatory milestones as well as additional development milestones in that same year
- $300 cost per application x 3 applications (per clinical trial protocol) = $900/patient. Cost increases at rate of inflation
- U.S. market size of ~110k, increasing at the rate of population growth. Less than 1% penetration through 2019, mid-single digit penetration by 2023 and 10% in 2026 (the out-year in our 10-yr DCF model)

Macular Edema Indication:

- 50% probability of successful FDA approval/clearance and launch for macular edema indication. All modeled milestones and royalties related to macular edema are initially discounted by 50% to account for risk of regulatory or commercialization failure
- Receipt of development milestones begins in 2017
- Receipt of FDA approval/clearance and launch in 2020 and receipt of regulatory milestones as well as additional development milestones in that same year
- $300 cost per application x 3 applications (per clinical trial protocol) = $900/patient. Cost increases at rate of inflation
- U.S. market size of ~660k, increasing at the rate of population growth. Less than 1% penetration in 2020, mid-single digit penetration by 2023 and 12% in 2026

Cataract Surgery Indication:

- 15% probability of successful FDA approval/clearance and launch for cataract surgery indication. All modeled milestones and royalties related to cataract surgery are initially discounted by 85% to account for risk of regulatory or commercialization failure
- Cataract surgery may be the indication which the risk discount could be reduced the most significantly in the near term. Positive results from the pilot study (top-line expected ~mid-2016) could prompt this haircut reduction, which could positively influence our valuation of the company
- Receipt of development milestones begins in 2017
- Receipt of FDA approval/clearance and launch in 2018 and receipt of regulatory milestones as well as additional development milestones in that same year
- $300 cost per application x 2 applications (per clinical trial protocol) = $600/patient. Cost increases at rate of inflation
- U.S. market size of ~1.1M, increasing at the rate of population growth. Less than 1% penetration in 2018, mid-single digit penetration by 2021/2022 and 15% in 2026

Key Initial Assumptions

	Probability of success	Year of launch	Treatment cost	Market size ('000s)	Penetration		
					< 1%	Mid-Single	Yr 2026
Anterior Uveitis	80%	2018	$900	110	2019	2023	10%
Macular Edema	50%	2020	$900	660	2020	2023	12%
Cataract Surgery	15%	2018	$600	1,100	2018	2021/2022	15%

DCF Currently Values EYEG at $5/Share, Progression Through Clinicals Should Push Value Higher…

The above assumptions along with other inputs in our DCF including a 10% discount rate and 2% terminal growth rate, results in a current DCF-generated valuation of approximately $5/share. While representing attractive upside to the current share price, our calculated value should appreciate further on progression of EGP-437 through clinical trials in any of the indications as this would positively affect (i.e. decrease) our risk discounts. We are initiating coverage of EYEG with a $5/share price target and Buy recommendation.

Risks:

- **Regulatory:** EYEG anticipates following the 505(b)(2) NDA pathway for FDA approval of EGP-437 and 510(k) clearance pathway for the Eyegate II Delivery device. FDA has already communicated that the delivery system will be considered a Class II (i.e. low-moderate risk) device but can follow the 510(k) (i.e. – relatively simple) clearance pathway and has agreed that the predicate devices that EYEG intends to cite in their 510(k) filing are acceptable. And while we think it is reasonable to assume (given EYEG's communications with FDA) the 505(b)(2) pathway will be deemed acceptable for EGP-437 there is risk that FDA requires a traditional NDA. If that were the case, EYEG would need to conduct clinical trials to demonstrate EGP-437 is safe and effective. These clinical studies could be lengthy and require significant financial resources. And as our financial model, valuation and price target are based on the assumption that the shorter and less expensive 505(b)(2) NDA will be deemed acceptable, if a traditional NDA is required, this would negatively affect our estimates.

- **Clinical Trial Failure:** while our model and assumptions incorporate risk discounts (i.e. risk of failure) for each of the currently pursued indications, we may be underestimating the risk that EGP-437 fails to meet clinical trial efficacy or safety endpoints.

- **Valeant May Not License Other Indications:** Valeant has licensed rights to the anterior uveitis indications and has the right of last refusal for any others. As we believe macular edema and cataract surgery represent more attractive markets than that of anterior uveitis, we think it is a reasonable assumption that, if clinical data supports efficacy, Valeant will license rights to these indications as well. However, if they do not and EYEG is not able to find another licensing partner with similar terms, commercialization and related financial contribution to EYEG for these indications could be negatively impacted.

- **Additional Capital May Be Required:** As of the most recent reporting period (9/30/15) EYEG had $9.9M in cash on the balance sheet. Balance sheet is clean with no debt or preferred. Cash burn, which has recently averaged ~$1M/quarter will likely increase with the recent initiation of additional clinical studies. While milestones from Valeant may offset some or all of cash burn, as the milestones structure and triggers have not been disclosed, the majority may be back-ended (i.e. – related to commercialization as opposed to development or regulatory) or clinical studies/regulatory-related milestones may not be met. As such, EYEG may need to raise additional capital which could be dilutive to existing shareholders. While we have incorporated an assumption that EYEG will raise additional capital through the public markets, they may require more than our estimates or transactions may be consummated at less favorable pricing/terms

- **Reimbursement:** If third-party reimbursement is not available or deemed insufficient to incentivize use of Eyegate's system, adoption, uptake and related sales and royalty stream could be negatively affected. While already established products and procedures are billed and reimbursed under dedicated CPT and J-codes (such as Ozurdex for intravitreal injection), Eyegate/Valeant will need to apply for dedicated codes after commercialization. Granting of codes lies with the American Medical Association's CPT Editorial Panel - which bases its decision on a review of clinical data, peer-reviewed literature and interest in the technology from clinicians. In the meantime, EYEG's therapy may be reimbursable through temporary CPT codes, although there may be some ambiguity to payment rates and collectability.

- **Novel Product vs. Established Therapies:** Eyegate's therapy is novel and will compete with already well established products and procedures. Adoption of novel products, even those with superior benefits and efficacy, can be slow. While we have taken this into account in our financial projections (i.e. low single digit market penetration over the initial several years for each indication), our assumptions could still prove more aggressive than how reality plays out.

FINANCIAL MODEL

Eyegate Pharmaceuticals Inc. (figures in 000s of $)

	2014 A	Q1A	Q2A	Q3A	Q4E	2015 E	2016 E	2017 E	2018 E
Anterior Uveitis									
Probability reaches market	-	-	-	-	-	-	80%	80%	80%
U.S. Market Size	-	-	-	-	-	-	110,000	112,200	114,444
Penetration %	-	-	-	-	-	-	0.0%	0.0%	0.3%
Number of patients	-	-	-	-	-	-	**0**	**0**	**343**
EYEG Royalty rate	-	-	-	-	-	-	8%	8%	8%
Cost per procedure	-	-	-	-	-	-	$900	$923	$946
Revenue (millions) w/haircut	-	-	-	-	-	-	**$0.00**	**$0.00**	**$20.78**
Milestones w/ haircut	-	-	-	-	-	-	**$0.00**	**$4,000.00**	**$5,600.00**
AU Total Revenue	-	-	-	-	-	-	**$0.0**	**$4,000.0**	**$5,620.8**
Macular Edema									
Probability reaches market	-	-	-	-	-	-	50%	50%	50%
U.S. Market Size	-	-	-	-	-	-	660,000	673,200	686,664
Penetration %	-	-	-	-	-	-	0.0%	0.0%	0.0%
Number of patients	-	-	-	-	-	-	**0**	**0**	**0**
EYEG Royalty rate	-	-	-	-	-	-	8%	8%	8%
Cost per procedure	-	-	-	-	-	-	$900	$923	$946
Revenue (millions) w/haircut	-	-	-	-	-	-	**$0.00**	**$0.00**	**$0.00**
Milestones w/ haircut	-	-	-	-	-	-	**$0.00**	**$1,250.00**	**$1,250.00**
ME Total Revenue	-	-	-	-	-	-	**$0.0**	**$1,250.0**	**$1,250.0**
Cataract Surgery									
Probability reaches market	-	-	-	-	-	-	15%	15%	15%
U.S. Market Size	-	-	-	-	-	-	1,100,000	1,122,000	1,144,440
Penetration %	-	-	-	-	-	-	0.0%	0.0%	0.2%
Number of patients	-	-	-	-	-	-	**0**	**0**	**2,289**
EYEG Royalty rate	-	-	-	-	-	-	8%	8%	8%
Cost per procedure	-	-	-	-	-	-	$600	$615	$630
Revenue (millions) w/haircut	-	-	-	-	-	-	**$0.00**	**$0.00**	**$17.31**
Milestones w/ haircut	-	-	-	-	-	-	**$0.00**	**$375.00**	**$750.00**
CS Total Revenue	-	-	-	-	-	-	**$0.0**	**$375.0**	**$767.3**
Product Sales/Royalites	-	-	-	-	-	-	$0.0	$0.0	$38.1
Dvlpmnt / Reg Milestones	-	-	-	-	-	-	$0.0	$5,625.0	$7,600.0
Total Revenues	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$5,625.0	$7,638.1
YOY Growth	-	-	-	-	-	-	-	-	*35.8%*
Cost of Revenues	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.00	$0.0
Gross Income	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$5,625.0	$7,638.1
Gross Margin	-	-	-	-	-	-	-	-	-
R&D	$531.1	$321.4	$604.1	$407.6	$548.0	$1,881.1	$3,466.0	$4,081.0	$4,221.0
%R&D	-	-	-	-	-	-	-	*72.6%*	*55.3%*
SG&A	$1,931.0	$782.8	$939.5	$946.2	$949.0	$3,617.5	$3,891.0	$4,254.0	$4,450.0
%SG&A	-	-	-	-	-	-	-	*75.6%*	*58.3%*
Operating Income	($2,462.1)	($1,104.3)	($1,543.6)	($1,353.8)	($1,497.0)	($5,498.6)	($7,357.0)	($2,710.0)	($1,032.9)
Operating Margin	-	-	-	-	-	-	-	-	-
Total, other income (exp)	$910.6	($1,696.8)	$2.2	($1.8)	$0.0	($1,696.3)	$0.0	$0.0	$0.0
Pre-Tax Income	($1,551.5)	($2,801.1)	($1,541.4)	($1,355.5)	($1,497.0)	($7,195.0)	($7,357.0)	($2,710.0)	($1,032.9)
Taxes	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Net Income	($1,774.0)	($11,028.3)	($1,541.4)	($1,355.5)	($1,497.0)	($15,417.0)	($7,357.0)	($2,710.0)	($1,032.9)
YOY Growth	-	-	-	-	-	-	-	-	-
Net Margin	-	-	-	-	-	-	-	-	-
EPS	($9.20)	($3.23)	($0.24)	($0.19)	($0.20)	($2.51)	($0.93)	($0.33)	($0.12)
YOY Growth	*-56.3%*	*579.6%*	*-93.7%*	*-111.9%*	*-90.6%*	*-72.7%*	*-62.9%*	*-64.5%*	*-63.2%*
Diluted Shares O/S	193	3,418	6,363	7,162	7,650	6,148	7,900	8,200	8,500

Brian Marckx, CFA

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LEADERSHIP

Management

Stephen From
President and Chief Executive Officer
Stephen has served as Eyegate's President, Chief Executive Officer, and director since October 2005. Prior to joining EyeGate, he was the Chief Financial Officer at Centelion SAS, an independent biotechnology subsidiary of Sanofi-Aventis. Previously, Mr. From spent several years as an investment banker specializing in the biotechnology and medical device sectors as Director in the Global Healthcare Corporate and Investment Banking Group and Head of European Life Sciences for Bank of America Securities. Mr. From holds a BSc from the University of Western Ontario, an accounting diploma from Wilfred Laurier University and has qualified as a Chartered Accountant in Ontario, Canada.

Michael Raizman, MD
Consulting Chief Medical Officer
Michael is a specialist in laser vision correction and treatment of the cornea with Ophthalmic Consultants of Boston. He is also an Associate Professor of Ophthalmology at Tufts University School of Medicine where he has directed the Corneal Fellowship Training Program. Dr. Raizman has also served on the full-time faculty of Harvard Medical School. He is on the editorial board of the Archives of Ophthalmology and Therapeutic Updates in Ophthalmology, and is author of over 60 medical articles. Dr. Raizman holds a MD from the University of Michigan Medical School.

Michael A. Patane, PhD
Consulting Chief Scientific Officer
Michael was most recently an Executive Director in Global Discovery Chemistry at Novartis, where he was responsible for the infectious disease and ophthalmology drug discovery units. Previously, he was Director of Medicinal Chemistry at Millennium Pharmaceuticals where he led oncology and metabolic diseases drug discovery. Michael holds a BS in chemistry from Fordham University, a PhD in synthetic organic chemistry from USC, and completed a Post-Doctoral appointment at The Scripps Research Institute.

Michael Manzo
Vice President of Engineering
Michael joined EyeGate in October 2006 and has served in his current role since 2008. Mr. Manzo has over 30 years of experience in product development and manufacturing in the medical device industry. Prior to joining Eyegate, Mr. Manzo was President and Chief Operating Officer (2002 – 2006) at Jenline Industries, Ltd., which is now part of Helix Medical, LLC. He has also worked with a number of start-up companies in areas such as cardiology, radiology, urology and laproscopic surgery. Mr. Manzo holds an MBA from Suffolk University and a Bachelor of Science Degree in engineering from University of Massachusetts, Lowell.

Lisa Brandano
Director of Clinical Operations
Lisa joined the Company from Cato Research (CATO) where she served as Assistant Managing Director of their Boston Office and Director of Clinical Trial Operations. She was involved in the oversight and facilitation of global clinical operations. Her Clinical Research experience includes monitoring and project management of various neurology, hematology, and cardiovascular gene therapy studies spanning Phases 1, 2, and 3. Prior to this she held clinical research coordinator and laboratory science roles at Beth Israel Deaconess Medical Center in Boston. She holds a BS in biology from Emmanuel College, and since 2003, she has been a certified clinical research associate (CRA) with the Association of Clinical Research Professionals (ACRP).

Board of Directors

Paul Chaney
Chairman
Paul has served as a director since September 2007. He is co-founder, President & CEO of PanOptica, Inc, a private venture-backed biopharmaceutical company that licenses and develops drugs for the treatment of important ophthalmic conditions, and has held such positions since March 2009. Prior to founding PanOptica, Paul was Executive Vice President and President of Eyetech Pharmaceuticals Inc. Previously, he was Chief Operating Officer of Eyetech, where he was responsible for the launch of Macugen, the first anti-VEGF treatment for neovascular age-related macular degeneration (wet-AMD), and was part of the executive team which led Eyetech's initial public offering in 2004 through the Company's acquisition by OSI Pharmaceuticals. Paul has over 30 years of experience in the biopharmaceutical and ophthalmic medical device industry, including a variety of senior management positions at Pharmacia Corporation. He began his career as a sales representative for The Upjohn Company in 1980. Paul earned a double BA in English and Biological Sciences from the University of Delaware.

Morton F. Goldberg, MD
Morton has served as a director since June 2008. Since 2003 he has served as the Joseph E. Green Professor of Ophthalmology at the Wilmer Eye Institute, Johns Hopkins University School of Medicine. From 1989 to 2003 he served as the

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Director and William Holland Wilmer Professor of Ophthalmology at the Wilmer Eye Institute. Prior to this, he was a Professor and Chairman of the Department of Ophthalmology at the University of Illinois College of medicine in Chicago for nearly 20 years. Dr. Goldberg trained at Johns Hopkins as a resident and chief resident, and holds a joint appointment at the Johns Hopkins Applied Physics Laboratory. He is also a past President of the Association for Research in Vision and Ophthalmology, the Macula Society, and the Association of University Professors of Ophthalmology. Dr. Goldberg received his undergraduate degree with honors from Harvard College and his MD with honors from Harvard Medical School.

Praveen Tyle, PhD
Praveen has served as a director since June 2008. He is currently President, Chief Executive Officer and Member of the Board of Directors of Osmotica Pharmaceutical Corp., and a member of the board of Orient EuroPharma Co., Ltd. of Taiwan. Dr. Tyle has nearly 30 years of experience in the pharmaceutical industry with the majority of his tenure in senior executive leadership positions in areas of research and development, manufacturing, quality, business development and operations. He previously served as global Executive Vice President, Chief Scientific Officer and Managing Director of Osmotica Pharmaceutical Corp.'s Marietta, Georgia site. Prior to joining Osmotica, Dr. Tyle served as Executive Vice and Chief Scientific Officer for the United States Pharmacopeia ("USP"). Prior to joining USP, Dr. Tyle served as Senior Vice President and Global Head of Business Development and Licensing at Novartis Consumer Health, as well as Senior Vice President & Global Head of Research and Development. Dr. Tyle holds a doctorate in pharmaceutics and pharmaceutical chemistry from the Ohio State University and a BS in Pharmacy (honors) from the Institute of Technology, Banaras Hindu University in India.

Thomas Balland
Thomas has served as a director since September 2012. He a Managing Director at IPSA, a venture capital firm that he joined in 2002. In addition to EyeGate, Mr. Balland has invested in and serves on the boards of several biotech and medtech companies including CMC Biologics, Immutep S.A., SpineVision SA and SpineGuard S.A. He was also on the boards of several companies that were acquired by larger entities in the life sciences industry, including Technolas Perfect Vision GmbH. Prior to joining IPSA in 2002 Mr. Balland held various positions with Mars, Inc. and Up&Up. He has degrees in engineering and finance from INSA Lyon and ESCP-EAP respectively.

Thomas E. Hancock
Thomas has served as a director since January 2007. He has over fourteen years of experience in the biopharmaceutical industry and equity capital markets. Since September, 2004, he has been the a Principal of Nexus Medical Partners where he has been responsible for several investments, including A&G Pharmaceuticals Inc., Magellan Biosciences, Inc., and Panacos Pharmaceuticals, Inc. Prior to joining Nexus Medical Partners, Thomas was a Senior Equity Analyst and Managing Director at US Bancorp Piper Jaffray, covering both the biopharmaceutical and drug discovery tools markets. He has also held numerous positions at Genentech, Inc. and COR Therapeutics, Inc. Mr. Hancock has a BS in Molecular Biology and a MBA from UC Berkeley.

Bernard Malfroy-Camine, PhD
Bernard has served as a director since July 2012. He is a scientist-turned-entrepreneur with nearly 30 years of experience in biotechnology and drug discovery. Since May 2013, he has been President and CEO of ViThera Pharmaceuticals, Inc. He has also served as Director, Business Development US Operations at Voisin Consulting, Inc. since September 2012. In October 2008, Dr. Malfroy-Camine established MindSet Rx, Inc., a virtual company which is a continuation of Eukarion, Inc., a Biotech company he had founded in 1991, and of which he was President and CEO. Dr. Malfroy-Camine has over 80 scientific publications and holds approximately 20 patents. He has a Master's degree in Mathematics and Physics from Ecole Polytechnique (Paris) and a Ph.D. in Neurobiology from University Paris VI.

Mounia Chaoui, PhD
Mounia has served as a director since October 2013. Since May 2013, she has been a general partner at Turenne Capital, a healthcare growth and venture capital company. She has also served, since January 2013, as CEO of Finbiomed sarl, a financial consulting company. Prior to 2013, Ms. Chaoui served as Chief Executive Officer and Managing Partner at Inserm Transfert Initiative, a seed capital fund, from January 2012 to December 2012, and as principal, then general partner, of Ventech Venture Capital, from July 2001 to January 2012. She brings investor experience in life sciences and expertise in building international syndications. Ms. Chaoui has sat or is still sitting on the boards of BioVex Group, Inc., Cellerix, S.A., Covagen AG, Funxional Therapeutics Ltd., Inserm Transfert Initiative, Groupe Sebbin SAS, Scynexis, Inc., TiGenix NV and Xytis Pharmaceuticals Ltd. Ms. Chaoui graduated as an engineer from École Centrale de Paris and holds a Ph.D. in Molecular Biophysics.

Scientific Advisory Board

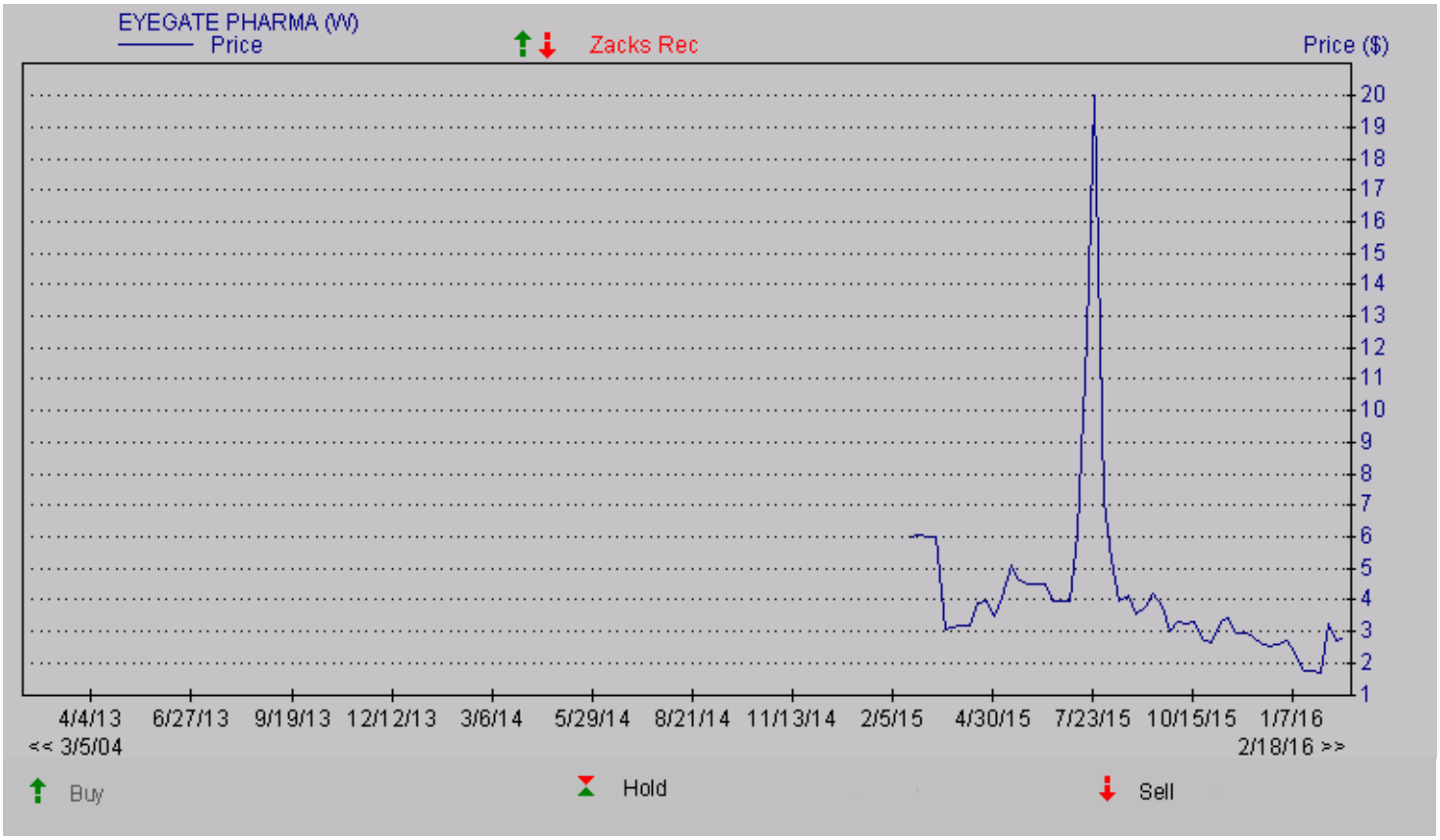
C. Stephen Foster, MD
C. Stephen Foster, MD, is Founder and Director of the Massachusetts Eye Research and Surgery Institute (MERSI), and Clinical Professor of Ophthalmology at Harvard Medical School. Dr. Foster is Founder and President of the Ocular Immunology and Uveitis Foundation. In 1980 he created the Ocular Immunology and Uveitis Service at the Massachusetts Eye and Ear Infirmary and in 1984 founded the Uveitis and Ocular Immunology Fellowship Training Program. He is the author of over 500 publications, has won numerous awards and has been repeatedly listed in America's Top Doctors and Best Doctors in America. Dr. Foster holds a BS degree in Chemistry from Duke University and a MD from the Duke University School of Medicine.

Jean-Marie Parel, PhD

Jean-Marie Parel, PhD, is Professor of Ophthalmology and Director of the Ophthalmic Biophysics Center at the Bascom Palmer Eye Institute. He also holds an appointment to the Henri and Flore Lesieur Chair in Ophthalmology at the University of Miami Miller School of Medicine and a secondary appointment in the Department of Biomedical Engineering. Dr. Parel's research interests include developing novel polymers, laser systems, devices for advanced ophthalmic diagnostics and therapy, and the study of optical and mechanical properties of ocular tissues. He is a Board member of Adventus Technology, an Honorary Faculty of Université de Liège School of Medicine (Belgium), and an Honorary Faculty of Université de Paris. Dr. Parel holds a PhD from the Université de Paris.

Michael Raizman, MD
Michael Raizman, MD, is a specialist in laser vision correction and treatment of the cornea with Ophthalmic Consultants of Boston. He is also an Associate Professor of Ophthalmology at Tufts University School of Medicine where he has directed the Corneal Fellowship Training Program. Dr. Raizman has also served on the full-time faculty of Harvard Medical School. He is on the editorial board of the Archives of Ophthalmology and Therapeutic Updat es in Ophthalmology, and is author of over 60 medical articles. Dr. Raizman holds a MD from the University of Michigan Medical School.

HISTORICAL ZACKS RECOMMENDATIONS



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Buy/Outperform: The analyst expects that the subject company will outperform the broader U.S. equity market over the next one to two quarters.
Hold/Neutral: The analyst expects that the company will perform in line with the broader U.S. equity market over the next one to two quarters.
Sell/Underperform: The analyst expects the company will underperform the broader U.S. Equity market over the next one to two quarters.

The current distribution is as follows: Buy/Outperform- 23.5%, Hold/Neutral- 53.9%, Sell/Underperform – 16.8%. Data is as of midnight on the business day immediately prior to this publication.