

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549**

FORM 8-K

**CURRENT REPORT PURSUANT
TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934**

Date of report (Date of earliest event reported): **April 25, 2016**

EYEGATE PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of incorporation)

001-36672

(Commission File Number)

98-0443284

(IRS Employer Identification No.)

**271 Waverley Oaks Road
Suite 108
Waltham, MA**

(Address of principal executive offices)

02452

(Zip Code)

(781) 788-9043

(Registrant's telephone number, including area code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
 - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
 - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
 - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
-

Item 5.02.

Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.

On April 25, 2016 (the “Effective Date”), the Compensation Committee of the Board of Directors (the “Committee”) of EyeGate Pharmaceuticals, Inc. (the “Company”) appointed Ryan R. Brenneman as Chief Financial Officer of the Company. Following his appointment, Mr. Brenneman serves as the Company’s principal financial officer and principal accounting officer.

Prior to joining EyeGate, Mr. Brenneman, age 55, served as Senior Vice President and Chief Accounting Officer at CYS Investments, Inc., a NYSE-listed real estate investment trust (REIT) and mortgage-backed securities asset manager, from 2014 to 2015, where he was responsible for financial accounting, financial and SEC reporting, accounting policy and management reporting and financial analysis. Mr. Brenneman served as a chief financial officer consultant for several clients between 2012 and 2014. Previously, he served as Managing Director and Chief Accounting Officer at First Marblehead Corporation, a financial services company specializing in student loan origination and securitization services, from 2011 to 2012. Mr. Brenneman also spent four years at Freddie Mac, a real estate mortgage and securities asset manager, where he served as Controller – Multifamily Accounting from 2009 to 2011 and Controller – Investments and Capital Markets Accounting from 2007 to 2009. He has also held senior-level finance positions at organizations including Booz Allen Hamilton, Protiviti, Inc., InterSystems Corporation and NerveWire, Inc.

Mr. Brenneman holds a J.D. from Georgetown University, a Masters in Accountancy from George Washington University, an M.S. in Public Policy and Administration from the London School of Economics and an A.B. (cum laude) in Government from Bowdoin College. He is a licensed CPA in the District of Columbia and currently serves as an Adjunct Professor of Accounting at Brandeis University.

On the Effective Date, the Company entered into an offer letter with Mr. Brenneman. Pursuant to this letter, Mr. Brenneman will receive an annual base salary of \$250,000 and is entitled to receive a bonus of up to 30% of his annual base salary for the applicable fiscal year. Mr. Brenneman also received an option to purchase 41,732 shares of the Company’s common stock issued under the Company’s 2014 Equity Incentive Plan, which will become exercisable with respect to one-third (1/3) of the shares on the first anniversary of the Effective Date and with respect to the remaining shares in equal amounts during the 24 months following such anniversary, subject, in each case, to Mr. Brenneman’s continued employment with the Company. Additionally, Mr. Brenneman will be eligible to receive an option to purchase 20,866 shares of the Company’s common stock issued under the Company’s 2014 Equity Incentive Plan within two years of the Effective Date based on performance, in the discretion of the Committee.

The foregoing description of Mr. Brenneman’s offer letter is a summary and does not purport to be complete. Such description is qualified in its entirety by reference to the text of the offer letter, which is filed as Exhibit 10.1 to this Current Report on Form 8-K, and is incorporated herein by reference.

There are no related party transactions between the Company and Mr. Brenneman, and Mr. Brenneman is neither related to, nor does he have any relationship with, any existing member of the Board or any executive officer of the Company.

Item 7.01. Regulation FD Disclosure.

On April 26, 2016, the Company announced that it will present four poster presentations relating to the Company's ongoing development of its proprietary cross-linked hyaluronic acid polymer (CMHA-S) technology on May 1, 2016 at the 2016 Annual Meeting of the Association for Research in Vision and Ophthalmology (ARVO).

The Company hereby furnishes the four poster presentations as Exhibits 99.1, 99.2, 99.3 and 99.4 to this Current Report on Form 8-K.

The information furnished pursuant to Item 7.01, including Exhibits 99.1, 99.2, 99.3 and 99.4, shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") and will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent that the Company specifically incorporates it by reference.

The information furnished in this report, including Exhibits 99.1, 99.2, 99.3, 99.4, 99.5 and 99.6, shall not be deemed to constitute an admission that such information or exhibit is required to be furnished pursuant to Regulation FD or that such information or exhibit contains material information that is not otherwise publicly available. In addition, the Company does not assume any obligation to update such information or exhibit in the future.

Item 8.01. Other Events.

CFO Appointment Press Release

On April 27, 2016, the Company issued a press release announcing the appointment of Mr. Brenneman. A copy of the press release is furnished herewith as Exhibit 99.5.

ARVO Presentation Press Release

On April 26, 2016, the Company issued a press release announcing the poster presentations at the ARVO meeting. A copy of the press release is furnished herewith as Exhibit 99.6.

The information furnished pursuant to Item 8.01, including Exhibits 99.5 and 99.6, shall not be deemed "filed" for the purposes of Section 18 of the Exchange Act and will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent that the Company specifically incorporates it by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

The Company hereby files or furnishes, as applicable, the following exhibits:

- 10.1 Offer Letter between the Company and Ryan R. Brenneman, dated as of April 25, 2016.
- 99.1 Poster Presentation of the Company.
- 99.2 Poster Presentation of the Company.
- 99.3 Poster Presentation of the Company.
- 99.4 Poster Presentation of the Company.
- 99.5 Press Release of the Company regarding CFO Appointment.
- 99.6 Press Release of the Company regarding Poster Presentations.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

EYEGATE PHARMACEUTICALS, INC.

By: /s/ Stephen From
Stephen From
President and Chief Executive Officer

Date: April 29, 2016

Exhibit Index

10.1	Offer Letter between the Company and Ryan R. Brenneman, dated as of April 25, 2016.
99.1	Poster Presentation of the Company.
99.2	Poster Presentation of the Company.
99.3	Poster Presentation of the Company.
99.4	Poster Presentation of the Company.
99.5	Press Release of the Company regarding CFO Appointment.
99.6	Press Release of the Company regarding Poster Presentations.



271 Waverly Oaks Road, Suite 108
Waltham, MA 02452

April 25, 2016

Ryan R. Brenneman, CPA, JD

Dear Ryan:

Eyegate Pharmaceuticals, Inc. (the "**Company**") is pleased to offer you employment with a start date as of April 25, 2015 (the "**Start Date**"). Your role shall be to serve as Chief Financial Officer (CFO) of the Company. This letter is intended to summarize some of the terms of your employment. We refer you to the policies, plans and practices of the Company for more details on the terms and conditions of your employment.

Your employment is considered "at will"; both you and the Company have the right to terminate your employment at any time for any reason. This letter does not constitute, and shall not be construed as, creating a contract or promise of employment for any set period of time.

You will report to Stephen From, the President and CEO of the Company, and will be responsible for all tasks attendant to the role of CFO of an R&D stage specialty pharmaceutical company, including but not limited to managing the financial statements, SEC reporting, audit of the financial statements, internal controls and Sarbanes-Oxley compliance, accounting function management including budgets and forecasts and financial strategy of the Company, and duties assigned to you by the CEO from time to time.

Your starting base salary is expected to be \$9,615.39 every two weeks (which annualizes to \$250,000), less applicable withholdings and deductions. In addition, you will be eligible to earn an incentive bonus/commission based on goals set by the Company shortly after your Start Date, with an annual target of up to thirty percent 30% of your base salary. You will also be eligible to receive Incentive Stock Options to purchase 20,866 shares of the Company's common stock within two years following the Start Date based on an evaluation of your performance, with such evaluation and the timing of such award to be determined in the sole discretion of the Compensation Committee of the Board of Directors.

In addition to the base salary and bonus opportunity, subject to approval by the Compensation Committee of the Board of Directors, you will be granted Incentive Stock Options to purchase 41,732 shares of the Company's common stock (the "**Options**"), effective upon the date of the next meeting of such committee after the date on which your employment with the Company commences (the "**Grant Date**"). The Options will vest based on your continued employment with the Company as follows: (a) one-third (1/3) of the shares subject the Options shall vest on the first anniversary of the Grant Date; provided however, that upon a Change of Control occurring prior to the first anniversary of the Grant Date, a pro rata amount of such shares calculated monthly based on the number of months passed since the Grant Date shall vest and become exercisable in full upon such Change of Control (no partial vesting shall occur for partial months); and (b) thereafter, one twenty-fourth (1/24) of the remaining shares on the last day of each of the twenty-four (24) consecutive months commencing with the month next following the first anniversary of the Grant Date. The Options shall, in all events, be subject to the terms of the Company's 2014 Equity Incentive Plan (the "**Plan**"). "**Change or Control**" means (a) the closing of any merger or consolidation of the Company with any other unrelated person or entity, or (b) the sale of all or substantially all of the assets of the Company to another unrelated person or entity, or (c) the sale of more than fifty percent (50%) of the total fair market value or total voting power of the stock of the Company to an unrelated party, such that, in each case, the transaction has been approved by the Company's stockholders, and in which the stockholders of the Company immediately prior to such merger, consolidation or sale shall, immediately after such merger, consolidation or sale, own less than fifty percent (50%) of the issued and outstanding capital stock of the person or entity that is the surviving company of any such merger or consolidation, or the acquirer in the case of any such sale of all or substantially all of the assets of the Company. In the event of a discrepancy between an option award and this offer letter, the terms of this offer letter shall prevail.

You will be eligible to participate in fringe benefit plans as may be generally available to other Company employees. Policies applicable to other employees of the Company shall also be applicable to you. Initially, this will include eligibility to participate in the Company's group health plan, reimbursement for Company approved travel (in accordance with the Company's expense reimbursement policies), and accrual of up to twenty (20) days per year of paid vacation time (accrued and useable in accordance with the Company's vacation policies). Vacation days stop accruing after reaching the maximum allowable accrual for the year, after which time no vacation time will be accrued until used.

Employment with the Company is contingent on verification of eligibility to work. Due to the Immigration Reform and Control Act of 1986, all employees hired after November 6, 1986, must provide verification of employment eligibility prior to commencement of employment. We will need you to provide proper identification on within the first three (3) days of work so that we can verify your employment eligibility. Your employment is also contingent on your execution of the Company's standard Employee Nondisclosure, Noncompetition, Nonsolicitation and Inventions Agreement, a copy of which is attached for your review and signature. Please sign and return the Employee Nondisclosure, Noncompetition, Nonsolicitation and Inventions Agreement on or before your first day of employment.

Additionally, you represent that you are not subject to and will not be subject to any agreements, restriction or obligations, including any noncompetition agreements or restrictions or any nondisclosure or confidentiality agreement or restrictions, which prevent you from performing (or in any other way adversely impact your ability to perform), your employment duties on behalf of the Company. Whether or not you are bound by the terms of any such agreements, you agree that during your employment with the Company, you will not disclose or use, or induce anyone at the Company to use, any confidential, proprietary or trade secret information or material belonging to any former employer or other person or entity.

The terms set forth herein shall not be modified except pursuant to a written agreement signed by both parties. This letter is governed by Massachusetts law.

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We look forward to your contributions towards the growth of the Company.
Sincerely,

Eyegate Pharmaceuticals, Inc.

By: /s/ Stephen From
Name: Stephen From
Its: President and CEO

Receipt acknowledged:

/s/ Ryan R. Brenneman, CPA, JD
Ryan R. Brenneman, CPA, JD

April 25, 2016

Poster # 910-D0272

Safety and Efficacy of a Novel Crosslinked Hyaluronic Acid (CMHA-S), JDE-003, for Healing Corneal Ulcers



David Williams¹; Barbara Wirostko²; Brenda Mann^{2,3}
¹Department of Veterinary Medicine, University of Cambridge (Cambridge, UK);
²Jade Therapeutics, Inc. (Salt Lake City, UT); ³SentrX Animal Care (Salt Lake City, UT)



INTRODUCTION

Post-traumatic corneal stromal ulceration is painful and potentially sight-threatening; thus, a topical treatment that increases the rate of ulcer healing would be a valuable addition to the ophthalmic therapeutic armamentarium. Hyaluronic acid (HA) has a beneficial role in many physiologic processes, including wound healing¹, yet solutions of HA may be flushed from the eye too quickly when used topically. Alternatively, crosslinking HA may lead to better retention on eye. Crosslinked thiolated carboxymethyl HA (CMHA-S; Figure 1) has previously shown utility for reducing hyperaemia, irritation, and discharge in dogs with keratoconjunctivitis sicca (KCS)².

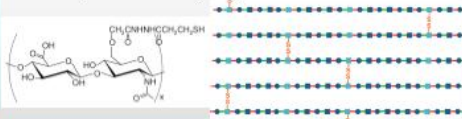


Figure 1. Left: Chemical structure of CMHA-S. Right: Schematic of disulfide crosslinked CMHA-S.

OBJECTIVES

- Assess safety and tolerability of crosslinked CMHA-S delivered topically on eye.
- Compare healing time of corneal stromal ulcers in cats and dogs in a clinical setting using crosslinked CMHA-S versus a non-crosslinked HA solution.

METHODS

Study 1: Safety and Tolerability in Rabbits

- NZW rabbits dosed topically 6x/day for 28 days (40 µl dose)
- Animals received crosslinked CMHA-S or vehicle (PBS)
- Clinical exams daily for tolerability
- Examined at 28 days for corneal thickness, systemic toxicity
- Study conducted in accordance with GLP for Nonclinical Laboratory Studies

Table 1. Treatment groups for safety and tolerability study

Group	N		Treatment	CMHA-S Concentration	Route (OU)
	Female	Male			
1	3	3	PBS	N/A	Bilateral
2	6	6	CMHA-S	0.4%	Bilateral
3	6	6	CMHA-S	0.75%	Bilateral

METHODS

Study 2: Efficacy in Cats and Dogs

- Animals diagnosed with naturally occurring acute corneal stromal ulceration; those with ocular surface infection or symptoms of KCS excluded from study
- Each species randomized into 2 groups (n=15 each)
 - Group 1: 0.75% crosslinked CMHA-S
 - Group 2: 0.3% non-crosslinked HA solution
- Study conducted double-masked
- Animals received 1-2 drops in affected eye, 3x/day, until healed
- Animals examined clinically by direct and indirect ophthalmoscopy and slit lamp biomicroscopy
- Ulcer presence evaluated by fluorescein staining; time to ulcer healing (no staining) documented
- Animals were entered into the study with full owner informed consent
- Study conducted in accordance with the welfare guidelines of ARVO and the Royal College of Veterinary Surgeons UK



RESULTS

Study 1: Safety and Tolerability in Rabbits

- Rabbits receiving 28 days of 6x/day therapy demonstrated:
 - No signs of inflammation
 - No change in corneal thickness
 - No system toxicity clinically or histopathologically

Study 2: Efficacy in Cats and Dogs

Feline stromal ulcers

- ♦Treated with CMHA-S healed in 21.0 ± 11.0 days
- ♦Treated with HA healed in 31.8 ± 10.3 days
- ♦No significant difference in age between groups (9.3 ± 3.7 yrs in CMHA-S group vs 8.6 ± 2.4 in HA group)
- ♦Healing time did not depend on breed or gender

Canine stromal ulcers

- ♦Treated with CMHA-S healed in 14.8 ± 4.1 days
- ♦Treated with HA healed in 18.3 ± 4.9 days
- ♦No significant difference in age between groups (7.3 ± 1.3 yrs in CMHA-S group vs 7.1 ± 1.9 in HA group)
- ♦Healing time did not depend on breed or gender

RESULTS

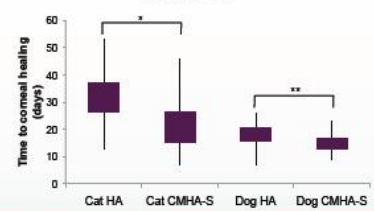


Figure 2. Corneal ulcer healing time in cats and dogs. Bars represent 95% confidence intervals of the means; lines represent range of values obtained. * p = 0.01; ** p = 0.04



Figure 3. Finnegan Bell, a 5yr old cat with a non-healing corneal defect. Left: At 35 days with no healing. Right: 10 days after beginning treatment with crosslinked CMHA-S.

CONCLUSIONS

- Crosslinked CMHA-S, delivered topically to the eye, is safe and well tolerated.
- Spontaneously occurring corneal ulcers in cats and dogs healed faster when treated with crosslinked CMHA-S than with a non-crosslinked HA solution.

REFERENCES

- 1.Chen WY, Abatangelo G. *Wound Repair Regen* 1999;7:79-89.
- 2.Williams DW, Mann BK. *PLoS ONE* 2014;9(8):e99786.

ACKNOWLEDGEMENTS

The authors would like to thank the staff at Absorption Systems where the rabbit study was performed, and Dr. Mamalis at Moran Eye Center (University of Utah), who performed the rabbit histopathology.

Questions? Email: dww33@cam.ac.uk

Websites: EyeGatePharmaceuticals.com; sentrxanimalcare.com

Crosslinked CMHA-S is currently sold globally for veterinary ocular use under the name Remend (Bayer Animal Health) and Aptus (Orion Pharmaceutical), and is being developed for human clinical use by Jade Therapeutics.

Jade Therapeutics is a wholly owned subsidiary of Eyegate Pharmaceuticals, Inc. Financial Disclosure: Mann, SentrX (E.S), Jade (E.S), Wirostko, Jade (E.S)



Crosslinked Carboxymethylated Hyaluronic Acid (CMHA-S)-based Ocular Sustained Delivery of Antibiotics

Hee-Kyoung Lee¹; Benjamin Ham¹; Shirley Luo¹; Brittany Coats²; Nathaniel Cady³; Brenda Mann¹; MaryJane Rafii¹; Barbara Wirotko¹

¹Jade Therapeutics Inc. (a subsidiary of Eyegate Pharmaceuticals Inc.), 675 Arapeen Drive, Salt Lake City, UT

²Department of Mechanical Engineering, University of Utah, Salt Lake City, UT

³Colleges of Nanoscale Science & Engineering, SUNY Polytechnic Institute, Albany, NY



Poster #: 1124 - B0296

INTRODUCTION

Corneal ulcers, an ocular emergency and a leading cause of blindness globally, require compounded off-label topical antibiotics and/or approved fluoroquinolones at a very inconvenient hourly round-the-clock multiple day administration to prevent corneal vision loss. Jade Therapeutics is developing a topical hydrogel/hyaluronic acid (CMHA-S) biodegradable film to deliver small molecules in sustained-release (SR) formulation to overcome hourly dosing challenges. Jade developed the molding procedure for manufacturing precise/reproducible films, and assessed the in vitro feasibility of this novel ocular film product.

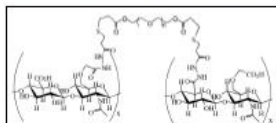


Figure 1. The structure of cross-linked CMHA-S with PEGDA

METHODS-Continued



Figure 3. Films have been fabricated in Cady B (Left) and Cady Bv2 (Right). The yellow dye was added to visualize the films clearly. After drying for two days, the films were ready for release study.

RESULTS-Continued

Table 1. Released Besi-HCl amount (µg) at each day. The accumulated amount was shown in Figure 4.

Day	0.00	0.04	0.08	1	2	3	4	5	6	7	8	9
75µg	9	17	14	15	14	12	9	6	1	0		
150µg	10	18	22	22	20	18	18	14	12	11	9	2

Zone of inhibition (ZOI) was compared between pre-sterilized film and Ethylene oxide (EtO)-sterilized film. The efficacy of Besifloxacin was evaluated against *S. Aureus*. ZOI dimensions for pre-sterilized film and post-sterilized film were 3.4 x 3.6 cm, and 3.1 x 3.8 cm, respectively. ZOI experiment suggests the efficacy of Besifloxacin remained unchanged after EtO sterilization.

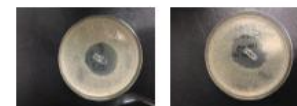


Figure 5. Zone of inhibition (ZOI) was compared between pre-sterilized film (Left) and EtO-sterilized film (Right). The efficacy of Besifloxacin was evaluated against *S. Aureus*.

RESULTS

Mold preparation was optimized to enable better molding and the release of the films from the molds. The functional molding procedure was established to produce a variety of film shapes and sizes. The films were successfully fabricated with all 4 drugs. The drug release resulted in burst within 1-2 days with Moxifloxacin-HCl, Moxifloxacin-free base, and Vancomycin (data not shown). Besifloxacin, however, was continuously released through day 6 (for 75 µg Besifloxacin, 1 µg release at day 6) and day 11 (150 µg Besifloxacin, 1 µg release at day 11). The accumulated released drug was close to 100%.

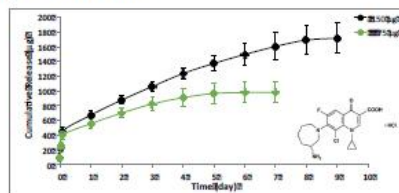


Figure 4. Release profiles from Besi-HCl films fabricated in Cady Bv2 mold. Two different amounts of Besi-HCl (75 µg and 150 µg) were loaded in the films. Y-axis is the cumulative release of Besi-HCl.

METHODS

The film shape was designed in three different geometries to yield films with different cross-sectional shapes. CMHA-S (16 mg/ml) films were fabricated in poly-dimethylsiloxane (PDMS)-based molds using proprietary thiolated carboxymethylated HA and poly(ethylene glycol) diacrylate (PEGDA), as a cross-linker. Moxifloxacin-HCl, Moxifloxacin-free base, Vancomycin, and Besifloxacin-HCl were formulated into the liquid polymer solution prior to cross-linking. Polymerized CMHA-S gel was dried at room temperature overnight to create thin clear and pliable films. Drug release in phosphate buffered saline (PBS) was monitored by UV absorption. Released drug amount was calculated from the standard solution.

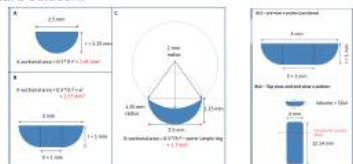


Figure 2. Three different geometries (A, B, & C) were designed (Left). Bv2 is a revised shape with the bigger dimension (Right).

CONCLUSION & FUTURE WORK

- Besifloxacin-containing CMHA-S films yielded reproducible sustained in vitro release for up to 6-11 days.
- This film may ultimately lead to a commercially viable product to meet the medical needs of a single-application antibiotic to the eye to avoid hourly dosing.
- This system could be potentially expanded to deliver other antimicrobials to treat other indications such as ophthalmic fungal or viral infections.
- Optimizing the film fabrication methodology is in progress.
- In-life animal studies on film retention in the inferior fornix is in progress.
- Measuring the drugs in tear and tissue levels is in progress.

ACKNOWLEDGEMENTS

We thank the financial support from NSF SBIR Phase 2 (Award # 1430921). Jade Therapeutics Inc. is a wholly owned subsidiary of Eyegate Pharmaceuticals Inc. Questions? Email: hlee@eyegatepharma.com

Poster# 1127 - B0299

DESIGN OPTIMIZATION TO IMPROVE RETENTION OF A CARBOXYMETHYLATED HYALURONIC ACID (CMHA-S) DRUG-DELIVERY DEVICE

Jourdan Colter¹, Nathaniel Cady PhD², Hee-Kyoung Lee PhD³, Brenda Mann PhD³, Barbara Wirostko MD³, Brittany Coats PhD¹

¹ Department of Mechanical Engineering, University of Utah, Salt Lake City, UT USA

² Colleges of Nanoscale Science and Engineering, SUNY Polytechnic Institute, Albany, NY USA

³ Jade Therapeutics Inc. (A wholly owned Subsidiary of EyeGate Pharmaceuticals Inc.), Salt Lake City, UT USA



INTRODUCTION

Novel polymer, carboxymethylated hyaluronic acid (CMHA-S, Jade Therapeutics, SLC), is emerging as a controlled and localized means for drug-delivery in the treatment of ophthalmic conditions including corneal ulcers, injuries, and infections [1]. These CMHA-S films offer improved drug bioavailability, safety, and therapeutic effectiveness from existing therapies due to their biocompatibility and drug delivery capabilities [2]. However, retention of the films in the ocular environment is poor due to the high lubricating properties of hyaluronic acid [3].

STUDY AIMS: (1) Utilize a three-dimensional computational model of the eye to evaluate retention of multiple geometrical designs. (2) Utilize the same model to determine surface friction ratios that immobilize CMHA-S film in the inferior fornix. (3) Evaluate the retention of several geometric designs using *in vivo* rabbit studies.



Figure 1. Preliminary bio-erodible CMHA-S film used as a drug-delivery vehicle (left). Clear hydrated CMHA-S film placement beneath the lower eyelid (middle). CMHA-S film dislodged (right).

METHODS

A 3D finite element model of the adult human eye, inferior fornix, and CMHA-S film was created based on anatomical dimensions and material properties in the literature (Fig. 2). A sursumduction eye movement was simulated, and displacement of the film relative to the globe was measured. Eight different CMHA-S film geometries varying in size and cross-section were evaluated in the model to determine which resulted in the best retention. For one of the geometries, the optimal friction ratio for retention of the CMHA-S film within the inferior fornix was found by iteratively sweeping through coefficients of friction on each side of the hydrogel (μ_{globe} , μ_{lid}). Retention of several geometries was evaluated in New Zealand White Rabbits (N=6) for 8 days.

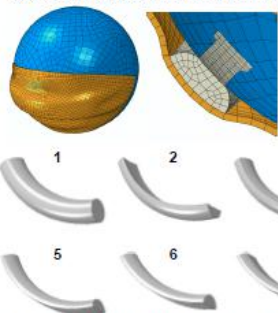


Figure 2. Simplified globe, lower eyelid and CMHA-S film representing film placement in the inferior fornix (left), and cross-section of the film placed between the globe and lower eyelid (right).

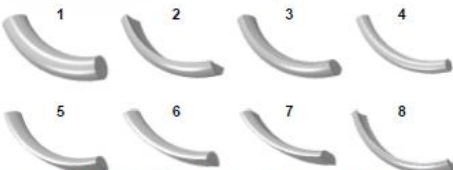


Figure 3. Eight CMHA-S film geometries tested in the inferior fornix FE model.

RESULTS – GEOMETRY OPTIMIZATION

Increasing μ_{lid} reduced displacement in all geometries, with Geometries 5 and 6 most strongly affected. Geometries 2 and 7 had least displacement, and were least influenced by changing μ_{lid} . Cylindrical geometries (1 and 4) completely dislodged and were excluded from further analysis.

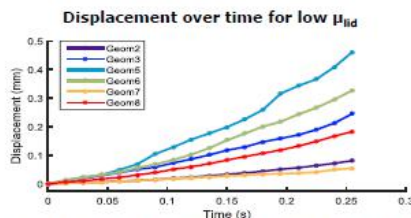


Figure 4. Mean nodal displacement of the CMHA-S films during the simulation, where μ_{lid} is low (0.1), and less strongly resists film displacement. Globe-side friction is low ($\mu_{\text{globe}} = 0.05$).

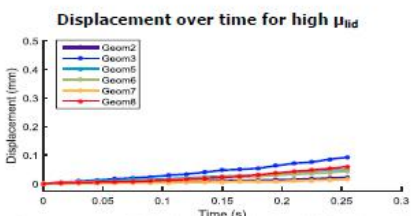


Figure 5. Mean nodal displacement of the CMHA-S films during the simulation, where μ_{lid} is high (0.15), and more strongly resists film displacement. Globe-side friction is low ($\mu_{\text{globe}} = 0.05$).

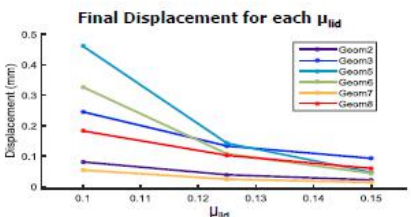


Figure 6. Mean nodal displacement the end of the simulation shown for increasing values of μ_{lid} . Globe-side friction is constant ($\mu_{\text{globe}} = 0.05$).

RESULTS – FRICTION OPTIMIZATION

Equal friction on each side of the film ($\mu_{\text{globe}} = \mu_{\text{lid}}$) resulted in complete dislodging from the inferior fornix. There was a linear relationship between μ_{globe} and μ_{lid} ($y = 1.4x + 0.07$) that resulted in immobilization of the film (Geometry 5) during globe rotation.

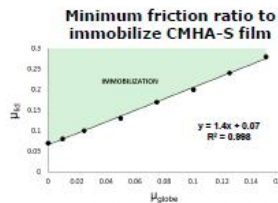


Figure 7. Relationship between friction of the CMHA-S film with the lid (μ_{lid}) and globe (μ_{globe}) that is required to immobilize Geometry 5 in the lower fornix of the eye during regular eye movement.

RESULTS – IN VIVO STUDIES

Retention of films in the inferior fornix of healthy rabbits (nictitating membranes removed) yields highly variable data ranging from 24 hours to 7 days. Dislodgement was influenced by the size and thickness of the films. The inferior fornix appears to be better for retention than the superior fornix. Further information on the frictional interaction between the film and sclera/eyelid is needed to improve retention *in vivo*.

CONCLUSIONS & FUTURE WORK

- Film geometry and the pocket that forms around the film were important in mitigating film displacement.
- All geometries were affected by change in friction on the lid side, however some were more strongly affected than others.
- The ratio of coefficient of friction between the CMHA-S film and globe/lid was critical to retention in the inferior fornix. Specifically, a ratio of 1.4:1 was required for immobilization of Geometry 5.
- Complete design optimization will require experimental quantification of the frictional interface between the CMHA-S film and eye.
- Differences in friction on each side of the film will be introduced by surface micropatterning or by chemical modification.
- In vivo* studies will be repeated in a larger animal model for better representation of human inferior fornix pocket depth.

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The opinions or assertions contained herein are the private view of the author and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

Abstract

Introduction: Hyaluronic acid, a ubiquitous expressed polysaccharide, is of great interest in the bioengineering and regenerative medicine communities for use as an off-the-shelf biomaterial. In this study, cross-linked carbonylmethylated hyaluronic acid (CMHA-S)-based film strips were utilized to provide a sustained release of recombinant human growth hormone (rHGH) and facilitate the repair and regeneration of damaged ocular tissues. Our purpose was to test the hypothesis that CMHA-S strips, with and without loaded rHGH, are biocompatible in vivo and can be securely and safely retained in the eye for the treatment of corneal epithelial chemical burns.

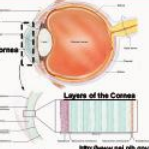
Methods: The nictitating membranes of 30 New Zealand white rabbits (~3.0 kg) were removed 3 wks prior to wound creation and strip placement. Burns 5.5 mm in diameter were created by placing a circular filter paper soaked in 1N NaOH centrally onto the cornea for 30 seconds. Wounds were immediately rinsed with sterile buffered saline, and the eye evaluated using the McDonald-Shadduck ophthalmic exam and fluorescein staining. Animals were randomly grouped (n=5 per group) for treatment with control CMHA-S strips or with CMHA-S strips containing 50 or 150 µg/strip of rHGH. At one and two weeks post strip placement, eyes were evaluated by slit lamp and in vivo confocal microscopy. Corneal histology was performed using H&E and Masson's Trichrome stain.

Results: Upon re-hydration, CMHA-S strips exhibited swelling to yield a clear soft oblong strip of ~4 mm wide by ~15 mm long, able to be manipulated with forceps and placed into the lower eye cul-de-sac. All strips were retained in the eye for a minimum of 96 hrs, with a maximum retention time of 14 days post placement. Wounds treated with rHGH loaded films exhibited a trend in faster wound closure compared to those treated with unloaded strips. Loaded and unloaded strips were biocompatible and did not reveal any pathological effects to the eye or surrounding tissues clinically or on histopathology.

Conclusions: CMHA-S film strips are biocompatible and easily retained in the ocular cul-de-sac. Furthermore, when compared to unloaded strips, the rHGH-loaded strips are capable of modulating the re-epithelialization of acute corneal burns. These results advance the overall efforts to develop the first FDA-approved ocular pharmaceutical indicated for corneal wound healing.

Introduction and Objectives

- The Cornea
 - Outermost Eye Layer
 - Avascular and Translucent
 - Physical/OV Protection
 - Oxygen Exchange
 - 75% total focusing power
 - Susceptible to injury
- Five Corneal Layers
 - Epithelium
 - Bowman's Layer
 - Dilemma
 - Descemet's Membrane
 - Endothelium
- There are no marketed products available for the highly unmet medical need of treating the reported series of 432 eyes with ocular trauma^{1,2} that occurred during Operation Iraqi Freedom and Operation Enduring Freedom.
- Given that ~7% of all battlefield injuries occur to the extremities,³ the self-administration of topical drops to eyes is often difficult leading to the need for the developed CMHA-S sustained delivery system.⁴
- In this study, we examine the feasibility, safety and efficacy of using the CMHA-S strip system of cross-linked hyaluronic acid in a rabbit model of wound healing.⁵
- We also examined the use of the system when incorporated with recombinant human growth hormone (rHGH).
- rHGH has been shown to facilitate corneal wound healing in vivo.⁶
- We aim to determine the effectiveness of this treatment on the ocular surface in an alkali burn model of ocular a wound healing.
- Goal
 - > Establish and test the CMHA-S strip system containing rHGH in an alkali burn model of ocular wound healing.
- Future Deliverable
 - > An approved pharmaceutical for ocular wound treatment.



Methods

- Nictitating Membrane Removal**
 1. Lidocaine injected into the membrane.
 2. Membrane excised (Westcott scissors).
- Chemical Burn Creation**
 - 5.5 mm NaOH (1N) chemical burn 3 weeks post NM removal
- CMHA-S Strip Placed**
 - Fluorescein stained burn with cul-de-sac strip placement.
- Post Injury Analysis**
 - White light images
 - Fluorescein images
 - In vivo confocal microscopy
 - Optical coherence tomography (OCT)
 - H&E staining (Day 14)
 - Masson's trichrome staining (Day 14)

Results

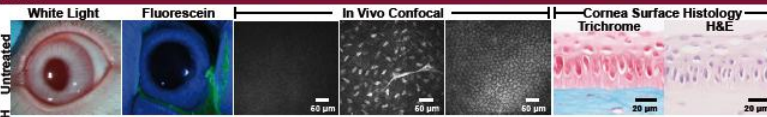
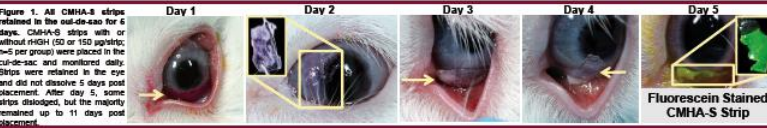


Figure 2. No pathology observed as a result of CMHA-S strip placement. One week after the placement of CMHA-S HA strips, slit lamp, fluorescein, and confocal images were taken. Two weeks after strip placement, tissues were harvested and processed. Trichrome and H&E staining of the cornea epithelium revealed no pathology two weeks post strip placement.

Figure 3. Characterization of the alkali burn model. Two weeks after corneal burn creation and strip placement, tissues were harvested, processed, and stained with Trichrome (A), H&E (B) and picrosirius red stain (C). Histology revealed a thin corneal epithelial layer and abnormal collagen structure in the burned cornea confirming corneal damage observed by fluorescein.

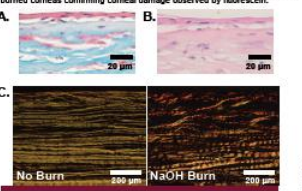
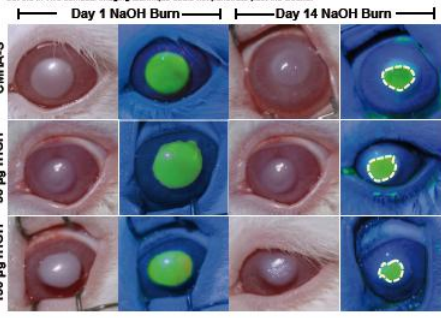


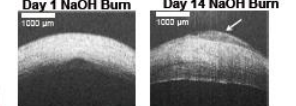
Figure 4. rHGH is consistently released over time from CMHA-S strips in vitro. Strips loaded with rHGH (75 or 150 µg/strip) were placed in human corneal epithelial cell (HCEC) defined media (Gibco). Samples (n=3) of media (0-120 h) were flash frozen at the indicated time points and analyzed for rHGH via ELISA. Results revealed a significant (2-way ANOVA with Bonferroni-Holms correction for pairwise comparisons, ***p<0.001) and sustained release of rHGH (µg) from the CMHA-S films over time compared to unloaded strips at both doses.

Figure 5. rHGH modulates wound healing. On Day 1 and Day 14 after the creation of a corneal alkali burn and the placement of CMHA-S HA strips either loaded or unloaded with rHGH (50 or 150 µg), white light, fluorescein, and confocal images were taken. Results revealed a decrease in the overall size of the corneal epithelial defect when observing the wounds by fluorescein staining. Confocal images (not shown) taken on Day 14 post corneal alkali burn creation reveal epithelial and stromal damage as a result of the corneal alkali burn, but the in vivo confocal imaging technique could not penetrate past the wound.



Results

Figure 8. Optical coherence tomography (OCT) analysis of alkali ocular burns. Further analysis of the burns by OCT revealed that the cornea thickened between Day 1 and Day 14 post burn. By Day 14, edema and inflammation can be seen in the cornea (arrow).



Conclusions

- Nictitating membrane removal was successful without complications and completely healed 3 weeks post surgery.
- CMHA-S strips are a biocompatible corneal wound treatment option capable of remaining in the cul-de-sac.
- No corneal or ocular pathology was associated with the use of CMHA-S strips on ocular alkali burns.
- CMHA-S strips utilized in conjunction with other treatments such as rHGH may be a suitable treatment for ocular wounds resulting in an increase in wound healing.
- Future Directions
 - > Further determine how CMHA-S strips containing therapeutics affect ocular alkali burns in our animal model.
 - > Incorporate other growth factors like rHGH into the CMHA-S strips as a therapeutic for ocular surface wounds.
 - > Establish a dose ranging assay for determining the safety and efficacy of therapeutics being released from CMHA-S strips.
 - > Assist in the FDA approval process for the use of pharmaceuticals in the treatment of ocular wounds.

Acknowledgements

The authors would like to gratefully acknowledge Mr. Andre Albers for assistance in obtaining professional photographic images and Scott Thomas-Sanson for her technical assistance in conducting these studies. OPT Gina L. Griffin, Dr. David O. Zamora, and Dr. Anthony J. Johnson are employees of the U.S. government and this work was prepared as part of their official duties. This work was funded in part by Jade's SBIR (W81WH14-2-0025). Jade Therapeutics is developing CMHA-S for clinical use. Jade is a wholly owned subsidiary of Epique Pharmaceuticals, Inc. This work was also supported by the U.S. Army Medical Research and Materiel Command (MR&C) Clinical and Rehabilitative Medicine Research Program.

Disclaimer

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or reflecting the views of the Department of Defense or the Department of the United States Army. This research was funded by the U.S. Army Medical Research and Materiel Command. This study was conducted under a protocol reviewed and approved by the US Army Medical Research and Materiel Command Institutional Animal Care and Use Committee (IACUC) and in accordance with the approved protocol. This study has been conducted in compliance with the Animal Welfare Act, the implementing Animal Welfare Regulations and in accordance with the principles of the Guide for the Care and Use of Laboratory Animals.

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EyeGate Pharma Appoints Ryan R. Brenneman as Chief Financial Officer

WALTHAM, Mass., April 27, 2016 — EyeGate Pharmaceuticals, Inc. (NASDAQ:EYEG) (“EyeGate” or the “Company”), a specialty pharmaceutical company that focuses on developing and commercializing therapeutics and drug delivery systems for treating diseases of the eye, today announced the appointment of Ryan R. Brenneman, CPA, JD, as its Chief Financial Officer, effective April 25, 2016. Mr. Brenneman will lead the Company’s financial and administrative operations.

“Ryan has a unique skill set and a wealth of public company experience, qualities we believe will be instrumental to EyeGate as we continue to advance both EGP-437 and our recently acquired cross linked hyaluronic acid (CMHA-S) platform technology for the treatment of ophthalmic disorders,” said Stephen From, President and Chief Executive Officer of EyeGate Pharmaceuticals. “He has significant expertise in financial reporting and controls, governance and regulatory matters which will be valuable to us as we grow and advance the Company. I am confident that his experience and contributions will have a significant impact on EyeGate’s success.”

Mr. Brenneman has 18 years of proven experience in finance, corporate affairs, accounting and management at public and private companies in a range of industries including financial services, real estate, management consulting and technology. Prior to joining EyeGate, Mr. Brenneman served as Senior Vice President and Chief Accounting Officer at CYS Investments, Inc., a NYSE-listed real estate (REIT) and mortgage-backed securities asset manager, where he was responsible for financial accounting, financial and SEC reporting, accounting policy and management reporting and financial analysis. Previously, he was Managing Director and Chief Accounting Officer at First Marblehead Corporation, a financial services company specializing in student loan origination and securitization services. He spent over four years at Freddie Mac, a real estate mortgage and securities asset manager, where he served as Controller – Multifamily Accounting and Controller – Investments and Capital Markets Accounting. He has also held senior-level finance positions at organizations including Booz Allen Hamilton, Protiviti, Inc., InterSystems Corporation and NerveWire, Inc. and has served as an Independent CFO Consultant to several companies in the Boston area.

Mr. Brenneman holds a J.D. from Georgetown University, a Masters in Accountancy from George Washington University, an M.S. in Public Policy and Administration from the London School of Economics and an A.B. (cum laude) in Government from Bowdoin College. He is a licensed CPA in the District of Columbia, and currently serves as an Adjunct Professor of Accounting at Brandeis University.

“I am proud to become a part of the dynamic team at EyeGate and help lead the Company to a new level of development. With the second Phase 3 trial of EGP-437 in uveitis ongoing, and having recently completed the acquisition of Jade Therapeutics, this is truly an exciting time for the Company,” added Mr. Brenneman. “I look forward to contributing to the Company’s future success as we work toward our goal of bringing to market novel therapies for patients suffering from diseases of the eye.”

About EyeGate:

EyeGate is a clinical-stage specialty pharmaceutical company that is focused on developing and commercializing therapeutics and drug delivery systems for treating diseases of the eye. EGP-437, the Company’s lead product candidate, incorporates a reformulated topically active corticosteroid, Dexamethasone Phosphate that is delivered into the ocular tissues through EyeGate’s proprietary innovative drug delivery system, the EyeGate® II Delivery System. In addition to EGP-437 and the EyeGate® II Delivery System, the Company is developing several preclinical candidates based on a proprietary Cross-Linked Hyaluronic Acid (CMHA-S) platform. The lead product based on this platform, JDE-003, is expected to enter clinical trials for the repair of corneal epithelial defects in late 2016. For more information, please visit www.EyeGatePharma.com.

Safe Harbor Statement:

Some of the statements in this press release are “forward-looking” and are made pursuant to the safe harbor provision of the Private Securities Litigation Reform Act of 1995. These “forward-looking” statements include statements relating to, among other things, the commercialization efforts and other regulatory or marketing approval efforts pertaining to EyeGate’s products, including EyeGate’s EGP-437 combination product, and those of Jade Therapeutics, Inc., a wholly owned subsidiary of EyeGate, as well as the success thereof, with such approvals or success may not be obtained or achieved on a timely basis or at all. These statements involve risks and uncertainties that may cause results to differ materially from the statements set forth in this press release, including, among other things, certain risk factors described under the heading “Risk Factors” contained in EyeGate’s Annual Report on Form 10-K filed with the SEC on March 30, 2016, or described in EyeGate’s other public filings. EyeGate’s results may also be affected by factors of which EyeGate is not currently aware. The forward-looking statements in this press release speak only as of the date of this press release. EyeGate expressly disclaims any obligation or undertaking to release publicly any updates or revisions to such statements to reflect any change in its expectations with regard thereto or any changes in the events, conditions or circumstances on which any such statement is based.

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EyeGate Pharma to Present Four Posters at ARVO 2016 Annual Meeting Supporting Development of CMHA-S

WALTHAM, Mass., April 26, 2016 — Eyegate Pharmaceuticals, Inc. (NASDAQ:EYEG) (“EyeGate” or the “Company”), a specialty pharmaceutical company that focuses on developing and commercializing therapeutics and drug delivery systems for treating diseases of the eye, today announced that four abstracts supporting the ongoing development of its proprietary technology cross-linked hyaluronic acid polymer (CMHA-S) have been accepted for poster presentation at the upcoming 2016 Annual Meeting of the Association for Research in Vision and Ophthalmology (ARVO) being held May 1-5, 2016 in Seattle, WA.

Barbara Wirostko M.D., Chief Medical Officer of EyeGate, commented, “We are excited to present these data at ARVO, one of the preeminent events in the ophthalmic space. We believe the CMHA-S platform has significant potential across a range of ophthalmic indications. The results of these preclinical studies reinforce this belief and support the further evaluation of this technology. Our development programs are on-track, and we look forward to initiating a clinical trial of our lead CMHA-S asset, JDE-003, later this year.”

Logistical details for the four posters are as follows:

Poster 910 – D0272: Safety and efficacy of a novel cross-linked hyaluronic acid polymer (CMHA-S), JDE-003, for increasing the healing rate in corneal ulcers

Presenting Author: David Williams DVM & Brenda Mann PhD
 Poster Session: Corneal Regenerative Medicine. Session # 144
 Date, Time: Sunday, May 1; 1:30 PM – 3:15 PM PT
 Location: Exhibit / Poster Hall, Posterboard D0272

Poster 1124 – B0296: Crosslinked carboxymethylated hyaluronic acid (CMHA-S)-based ocular sustained delivery of antibiotics

Presenting Author: Hee-Kyoung Lee PhD
 Poster Session: New drugs
 Date, Time: Sunday, May 1; 3:15 PM- 5:00 PM PT
 Location: Exhibit / Poster Hall, Posterboard B0296

This abstract has also been selected for a poster competition, being held Tuesday, May 3 from 1:00-2:30 PM in Room 2AB

Poster 1127 – B0299: Design optimization to improve retention of a carboxymethylated hyaluronic acid (CMHA-S) drug delivery device

Presenting Author: Jourdan Colter and Brittany Coats PhD
 Poster Session: New drugs
 Date, Time: Sunday, May 1; 3:15 PM – 5:00 PM PT
 Location: Exhibit / Poster Hall, Posterboard B0299

Poster 1265 – D0213: Human growth hormone released from a biocompatible hyaluronic acid biomaterial modulates wound healing in an in vivo corneal chemical burn model

Presenting Author: CPT Gina Griffith PhD
 Poster Session: Corneal Wound Repair and Healing
 Date, Time: Sunday, May 1; 3:15 PM – 5:00 PM PT
 Location: Exhibit / Poster Hall, Posterboard D0213

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