

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

DR. REDDY'S LABORATORIES S.A. and
DR. REDDY'S LABORATORIES, INC.,
Petitioners,

v.

EYE THERAPIES, LLC
Patent Owner.

Case No. IPR2024-00467
U.S. Patent No. 11,833,245

DECLARATION OF ROBERT J. NOECKER, M.D., MBA

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I. Introduction

1. I, Robert J. Noecker, M.D., MBA, submit this declaration to state my opinion on the matters described below.

2. I have been retained by Eye Therapies, LLC, as an independent expert in this proceeding before the United States Patent and Trademark Office.

3. I understand that this proceeding involves U.S. Patent No. 11,833,245 (“the ’245 patent”), and that I have been asked to provide my opinions of whether the subject matter of the claims of the ’245 patent is patentable.

4. This declaration sets forth my opinions from the perspective of a person ordinarily skilled person in the art, which I have formed in this proceeding based on my education, training, clinical research, knowledge, personal and professional experience, my understanding as an expert in the field, and my study of the evidence.

5. I am being compensated for my time at the rate of \$750 per hour. This compensation is not contingent upon the nature of my findings, the presentation of my findings in testimony, or the outcome of this proceeding.

II. Qualifications and Professional Experience

6. My curriculum vitae is submitted with this declaration as Appendix A. I have summarized my educational and professional background below.

7. I received a Bachelor of Science in Biology from the Massachusetts Institute of Technology in 1985. I also received a Bachelor of Science in Materials

Science and Engineering, as well as a Bachelor of Science in Humanities and Engineering (Literature) from the Massachusetts Institute of Technology in 1986.

8. After completing my undergraduate studies, I went on to obtain an M.D. degree from the University of North Carolina School of Medicine in 1990. After completing medical school, I undertook an internship in internal medicine at the Moses H. Cone Memorial Hospital in Greensboro, North Carolina from July of 1990 until June of 1991. In July of 1991, I began my residency in ophthalmology at the University of Arizona. I completed that residency in June of 1994. I then went on to complete a clinical fellowship in ophthalmology at the New England Eye Center at Tufts University School of Medicine in Boston, Massachusetts from July of 1994 to June of 1995.

9. Since completing my residency and fellowship, I have held a number of academic positions at universities across the country. Starting in June of 1994, I held the position of Assistant Professor of Ophthalmology at Tufts University School of Medicine. In June of 1996, I returned to the Department of Ophthalmology at the University of Arizona, first as an Assistant Professor of Ophthalmology (1996-2002), and then as an Associate Professor of Ophthalmology (2002- 2003). During my time at the University of Arizona, I also served as Residency Director from July of 1998 until June of 2003, as a Faculty Member in the Biomedical Engineering Interdisciplinary Program in the Graduate College of the University of Arizona from

July of 1998 until December of 2003, and as the Associate Chair for Clinical Activities for the Department of Ophthalmology from July of 2002 until December of 2003.

10. In January of 2004, I became a member of the faculty of the Department of Ophthalmology at the University of Pittsburgh School of Medicine, first as a Visiting Associate Professor of Ophthalmology (2004-2007), then as an Associate Professor of Ophthalmology (2007-2009), and finally as a Professor of Ophthalmology (2009-2011). I also served as the Vice Chair of the UPMC Eye Center at the University of Pittsburgh School of Medicine from January 2004 through June 2011.

11. Since 2011, I have worked as an ophthalmologist and director of glaucoma at the Ophthalmic Consultants of Connecticut. I am on the staff of St. Vincent's Hospital, Hartford Hospital, and the West Haven Veteran's Hospital. I am a Clinical Professor at the Frank Netter School of Medicine at Quinnipiac University, and I am an Assistant Clinical Professor at Yale School of Medicine in the Department of Ophthalmology. I lecture, teach, and train ophthalmology residents, optometry residents, students, and medical students.

12. I have received a number of honors and awards throughout my career. Those awards include, among other things, being selected to the Best Doctors in America every year since 2004, as well as a Top Doctor by a number of other

services. Additionally, I have been selected as the Clinical Instructor of the Year by the ophthalmology residents three times during my tenure at the University of Pittsburgh and have received teaching awards at each institution where I have been a faculty member. I am currently the Acting President of Connecticut Glaucoma Society.

13. I have conducted research in the field of ophthalmology for nearly 30 years and have been an investigator on numerous clinical trials for ophthalmic products, a full list of which can be found in my curriculum vitae. *See Appendix A at 33-35*

14. Over the course of my career, I have authored or co-authored over 100 peer-reviewed publications and have had several hundred abstracts published. I also serve as a contributing editor for seven different publications and as a peer-reviewer for twelve additional publications. I frequently lecture on the subjects of diagnosis and treatment of ophthalmic disorders. My other qualifications are set forth in my curriculum vitae.

15. I have participated in multiple clinical trials for brimonidine and related ophthalmic medications and have published peer review papers on its use. I prescribe brimonidine on a daily basis (and have done so for over twenty years) for the treatment of multiple ocular conditions. I also treat patients on a daily basis with eye redness and the associated underlying conditions.

16. I have consulted for numerous pharmaceutical companies over the years. I also have served as an expert witness in the field of ophthalmology, and my testimony has been credited in court.

17. I have been a member of several professional associations for many years. I have been a member of the Association for Research in Vision and Ophthalmology since 1989, and a fellow of American Academy of Ophthalmology since 1991. I have also been a member of American Society for Cataract and Refractive Surgery since 1992, and an associate member of Association of University Professors in Ophthalmology since 1998. I have been and still am an active member of American Glaucoma Society since 2000. I have been a member of Connecticut Glaucoma Society and Connecticut Society for Eye Physicians since 2011. In 2020, I have been elected as a co-chair of Connecticut Glaucoma Society. And since 2021, I have been elected as the acting president of Connecticut Glaucoma Society.

III. Information Considered

18. In preparing my declaration accompanying Patent Owner's Response, I have considered U.S. Patent Nos. 11,833,245 ("the '245 patent"), including its claims and written description (i.e., the patent specification) as well as the public record of the '245 patent's examination before the U.S. Patent and Trademark Office ("USPTO"), also referred to as the prosecution history. I have also considered the

documents cited in this declaration and the documents listed in Appendix B. I have also relied on my professional and academic experience in the area of ophthalmology. I also considered all of the references discussed in this declaration.

19. To the extent I am provided additional documents or information, including any expert declarations produced by Dr. Reddy's Laboratories and Dr. Reddy's Laboratories, Inc. ("Petitioners") or additional documents produced by the Petitioners, I may offer further opinions.

IV. Testimony as Expert in Last Four Years

20. In the past four years, I have testified as an expert at deposition or trial in *In re Lumify*, Civil Action No. 21-16766 (RK) (RLS) (D.N.J.), *Bausch & Lomb Incorporated, et al. v. Dr. Reddy's Laboratories Ltd, et al*, C.A. No. 23-3463 (RK) (RLS) (D.N.J.), *ALLERGAN, INC. and ABBVIE CORPORATION Plaintiffs- and - JUNO PHARMACEUTICALS CORP.*, Canada Court File No. T-1994-21 (Federal Court), *Allergan Sales, LLC and Allergan, Inc. v. Sandoz, Inc. and Alcon Laboratories, Inc.*, Civ. A. No. 2:17-cv-10129-WHW-CLW (DNJ), and *Slayback Pharma LLC v. Eye Therapies LLC*, IPR2022-00142 (PTAB).

V. Level of Ordinary Skill in the Art

21. I have reviewed the '245 patent and the prosecution history of the '245 patent. I understand that the '245 patent claims priority to a provisional application filed on August 1, 2008. Based on my review of the '245 patent and its file history, I

have considered the qualifications of a person of ordinary skill in the art (“POSA”) at the time of the August 1, 2008, priority date of the ’245 patent.

22. I have been informed that the parties agree that the field to which the ’245 patent pertains is interdisciplinary. Under Patent Owner’s definition, a “POSA may be represented by a team of individuals with experience and various skills relating to eye care, including, *inter alia*, the medical and pharmaceutical formulation arts. The POSA would also have had access to team members with experience in chemistry, in designing and evaluating ophthalmic formulations, and/or in administering ophthalmic formulations to treat ocular conditions obtained by some combination of education and work experience.”

23. I understand that Petitioners have proposed a POSA “would have been a composite person (or team) that included a medical doctor and a pharmaceutical formulator. The medical doctor would be an ophthalmologist with at least three to four years of experience in clinical trials and FDA regulation of eye products and would have experience in the use of topical brimonidine and apraclonidine and topical vasoconstrictors such as naphazoline and tetrahydrozoline. The pharmaceutical formulator would have a doctorate in pharmaceuticals or a related degree and at least three to five years of experience developing eye drop formulations for clinical trial and regulatory approval.”

24. While I prefer Patent Owner's definition, regardless of which definition is applied, my opinions with respect to the '245 patent would not change. As of August 1, 2008, I would have been considered at least a person of ordinary skill in the art of the '245 patent, under both Patent Owner's and Petitioners' definitions.

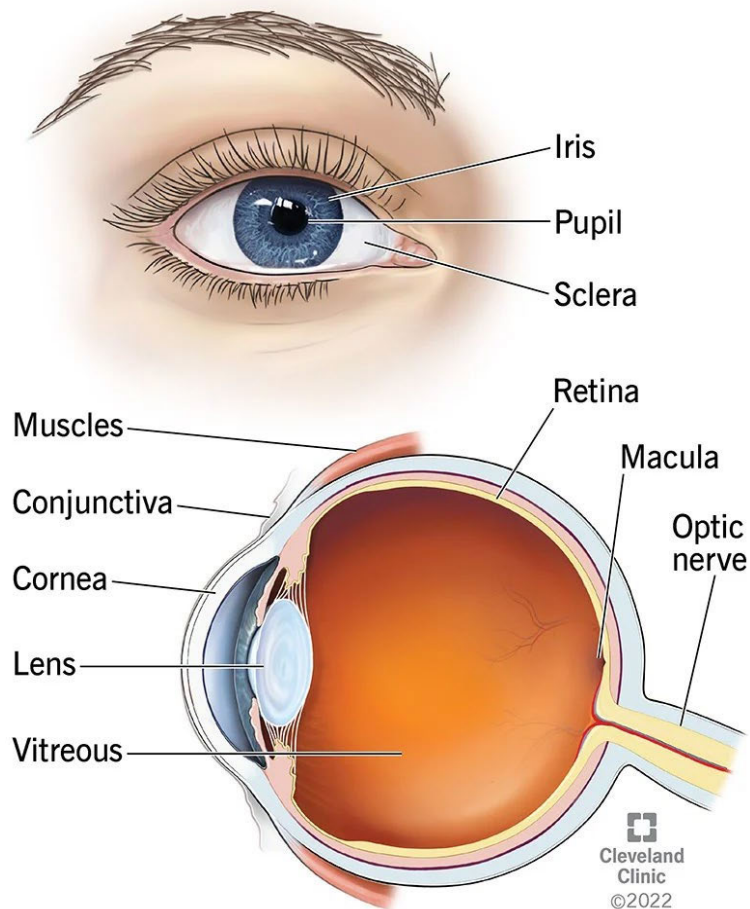
25. On the basis of my education and experience, I believe I am qualified to express the opinions provided below.

VI. Technical Background

A. Eye Redness

26. Red eye is broadly categorized into ocular hyperemia and hemorrhage. Ocular hyperemia refers to a common ophthalmic condition caused by vasodilation—an increase in the diameter of blood vessels on the eye—resulting in an influx of blood that “congests” the vessel and reddens the eye. It can occur in any of the visible layers of the eye that have vasculature, such as the conjunctiva or sclera (including the episclera), which are shown in the diagram below. Conversely, constricting dilated ocular blood vessels, known as vasoconstriction, can “decongest” them, which on the surface can reduce redness and make the eyes appear whiter. “Conjunctival blanching” is another way of referring to redness reduction or whitening of a reddened conjunctiva. EX-1009, Federal Register 1988 at 9; EX-2003 1; EX-1029, 2; EX-2040 (Laskar 10/29 Dep. Tr.), 51:17-52:8.

Eye anatomy



27. Ocular hyperemia can arise for various reasons, such as, for example, conjunctivitis caused by allergens (non-infectious), or virus or bacteria (infectious), irritants in the eye, or dry eye. A POSA could have reduced ocular hyperemia, if it arose from inflammation, by treating its root causes, e.g., anti-inflammatories, antihistamines or mast-cell stabilizers for ocular allergic reactions or lubrication drops for redness resulting from dry eyes. People with red eyes are often eager to efficiently manage the redness because there is a social stigma linked to red eyes, as

they are often associated with drinking, drug abuse, and lack of sleep. EX-2095, Bausch Press Release, at 1-2.

28. Hemorrhage occurs when ocular blood vessels rupture, break, or are cut, e.g., during surgery, leaking blood under the conjunctiva. Subconjunctival hemorrhage is a type of hemorrhage in which a significant amount of blood enters the ocular surface and forms blobs or patches of blood. Donnenfeld ¶52. Micro-vessel hemorrhage, another type of hemorrhage, occurs when small ocular blood vessels rupture and leak small amounts of blood onto the ocular surface, making the eyes appear pink and hyperemic. Donnenfeld ¶52.

29. This distinction between ocular hyperemia and hemorrhage matters from the clinical standpoint. Ocular hyperemia can be reduced by sufficiently vasoconstricting the blood vessels in the conjunctiva and the sclera using alpha-adrenergic agonists, which regulate constriction and dilation of blood vessels. On the other hand, hemorrhage—whether subconjunctival or micro-vessel hemorrhage—*cannot be reduced* through vasoconstriction once present and only dissipates with the passage of time.

B. Prior Art Redness Relievers

30. By August 1, 2008, it was well understood that reduction of ocular hyperemia and any associated eye redness can occur through vasoconstriction, which is primarily mediated by α_1 adrenergic receptor agonists. EX-1020, Griffith

2003 at 12-13 (“All selective α_1 -agonists are vasoconstrictors, which is the basis of their therapeutic activity.”); EX-2003, Derick 1995 at 4 (“In the eye, α_1 -adrenoceptors are located on vascular smooth muscle located in the conjunctiva, ciliary processes, retina, and choroid. Stimulation of these adrenoceptors leads to vasoconstriction.”), Table 2 (noting that the activation of α_1 receptors in the blood vessels of the conjunctiva triggers vasoconstriction); EX-1024, Lachkar 1998 at 3 (“Vasoconstriction is mediated mainly via α_1 -adrenergic receptors.... On the other hand, brimonidine tartrate may also produce vasodilation via the α_2 -adrenergic receptors on endothelial cells, which release endothelial-derived relaxing factor”); EX-2004, Raviola at 1 (“The vessels of the conjunctival and episcleral plexuses...have a simple wall, which consists of an endothelium....”); EX-1035, Burke 1996 at 2. (“compared to clonidine and apraclonidine, brimonidine would be the least likely to produce α_1 -adrenoceptor-mediated side effects, such as mydriasis and ocular vasoconstriction.”).

31. Dilation and constriction of blood vessels in the eye (also known as ocular vasodilation and vasoconstriction) are mediated by “adrenergic receptors,” for example α_1 and α_2 receptors, using chemical messengers, such as adrenaline or noradrenaline. Stamer ¶¶ 26-29. The mechanism of action of these adrenergic receptors is complex and not completely understood to this day, presenting different effects depending on which tissue is being considered. Stamer ¶ 32.

Although there are alpha- and beta-adrenergic receptors, I will focus the discussion on the alpha adrenergic receptors and the two major subtypes in the eye— α_1 and α_2 receptors—each of which has its own subtypes.

32. The activation of α_1 receptors mediates the fight-or-flight (excitatory) responses, also referred to as “ α_1 mediated effects,” including constricting blood vessels, increasing heart rate, reduction of bleeding, and dilating pupils. EX-2003, Derick 1995 at 2-3.

33. The activation of α_2 receptors mediates relaxation responses that decontracts smooth muscles, also referred to as “ α_2 mediated effects,” including dilating blood vessels and decreasing heart rate. *Id.* at 2, 5 (describing the sedative effect clonidine, an α_2 agonist). EX-1024, Lachkar 1998 at 3; EX-1019 at 3; EX-1067, Alphagan Label (2001) at 1, 4, 6, 9, 11, 14; EX-1068, Alphagan P Label (2005) at 1, 4. The activation of α_2 receptors is generally associated with more eye redness because dilation of ocular blood vessels can make the eyes appear redder as more blood flows through the enlarged blood vessels. It was known that brimonidine, a highly selective α_2 agonist, can “produce vasodilatation via the α_2 -adrenergic receptors on endothelial cells,” which are located in the front of the eye. Stamer ¶ 31; EX-1035, 5; EX-2004, 1 (“both conjunctival and episcleral blood vessels possess a continuous endothelium”).

34. Not coincidentally, the drugs available before August 2008 for reducing eye redness were either α_1 selective receptor agonists or mixed α_1/α_2 agonists having a predominant α_1 effect. EX-1009, Federal Register 1988 at 16 (listing approved ophthalmic vasoconstrictors, including ephedrine hydrochloride, naphazoline hydrochloride, phenylephrine hydrochloride, and tetrahydrozoline hydrochloride). Table 1 below lists exemplary redness relievers that became available on the market before August 1, 2008. Notably, these redness relievers contained α_1 or mixed α_1/α_2 adrenergic receptor agonists as the active ingredient. There was no redness reliever eye drop containing a selective α_2 agonist, let alone brimonidine.

Tradename	α -Agonist API	Agonist Type
Naphcon [®]	naphazoline 0.012%	Mixed α_1/α_2 agonist
Naphcon-A [®]	naphazoline 0.025%	Mixed α_1/α_2 agonist
All Clear [®]	naphazoline 0.012%	Mixed α_1/α_2 agonist
Ocu-Clear [®]	oxymetazoline 0.025%	Mixed α_1/α_2 agonist
Visine Original [®]	tetrahydrozoline 0.05%	Selective α_1 agonist
Visine Advances Redness Relief [®]	tetrahydrozoline 0.05%	Selective α_1 agonist
<i>Non-commercial; available to use without FDA approval as ocular redness reliver</i>	phenylephrine	Selective α_1 agonist
<i>Non-commercial; available to use without FDA approval as ocular redness reliver</i>	ephedrine	α - and β - agonist type

Table 1: FDA-approved Redness Relievers Available on the Market Before August 1, 2008

35. Unfortunately, despite being the standard of care and accepted by consumers, these over-the-counter (“OTC”) eye redness relievers caused various side effects, including rebound hyperemia, tachyphylaxis, and medicamentosa. EX-1001, ’245 patent at 2:37-44; EX-1009, Federal Register 1988 at 10; EX-1160, Abelson 2006 at 2; EX-1055, Spector at 1-2. Moreover, the redness reduction effects of these prior products were short-lived.

36. Rebound hyperemia is a side effect that occurs when a patient stops using a redness reliever. After initial redness reduction, the ocular blood vessels dilate even more to relieve an attendant ischemic condition and bring in needed oxygen, thereby causing more eye redness than before the administration of the redness reliever. EX-1001, ’245 patent at 4:55-61 (explaining that the art at the time “considered the complication of rebound hyperemia to be intrinsic to vasoconstriction, wherein blood flow is reduced, causing attendant ischemia with some inflammatory cascade, precipitating rebound hyperemia in many cases and often leading to medicamentosa”).

37. Tachyphylaxis—another common side effect associated with prior art redness relievers—refers to a rapidly decreasing response to a redness reliever following its initial administration. EX-1160, Abelson 2006 at 1. The rapid reduction in the efficacy of redness relievers can prompt the consumers to unwittingly instill more drops more frequently to obtain the same level of whitening, which misuse has

led to ocular toxicity as well as chronic swelling and redness (medicamentosa) even after discontinuation. *See id.*; EX-1001, 4:46-61. This could cause a chronic red eye that persists even after discontinuation of the offending eye drop. EX-1055, Spector 1994 at 1.

38. In 2008, eyecare professionals generally did not recommend OTC redness relievers to their patients due to these side effects, even though they were aware of patients using these products and accepted them as the standard of care for eye redness given the lack of alternative options available at the time. This changed when Lumify launched. Eyecare professionals, including myself, were surprised by the lack of side effects that were once thought to be inevitable results of using an eye redness reliever and started recommending Lumify to patients.

39. Because OTC products treat self-diagnosable conditions without health care provider's instructions, they are susceptible to misuse through overuse. Therefore, OTC products must not only be efficacious, but also be particularly safe. *See, e.g.* EX-2033, Drug Application Process for Nonprescription Drugs at 1-3; EX-2020, Sher. Dep. Tr. (8/10/2022) at 98:24-100:5.

VII. The '245 Patent

40. At a high level, '245 patent claims relate to methods for reducing ocular hyperemia (eye redness related to vasodilation) using 0.025% brimonidine as the only active ingredient for reducing ocular hyperemia.

A. Claims of the '245 Patent

41. The '245 patent has 28 claims. I understand that Petitioners have challenged the patentability of only claims 1, 2, 4-9, 11-17, 20-22, 25, and 27. Claims 1 and 8 are “independent” claims, which I understand are parent claims from which other claims depend. Claims 1 and 8 both recite “[a] method for reducing eye redness in a human subject having ocular hyperemia,” and require both administration of brimonidine at a concentration of 0.025% and actual reduction in ocular hyperemia. But I understand that claims 1 and 8 differ in their scope due to different “transitional phrases.”

42. Claim 1 reads as follows:

1. A method for reducing eye redness in a human subject having ocular hyperemia, *consisting of* topically administering to an eye of said human in need of said reduction of eye redness a composition in the form of an ocular drop consisting of 0.025% weight by volume brimonidine as the sole active ingredient, and one or more non-therapeutic components including benzalkonium chloride, wherein the ocular drop has a pH between 5.5 to 6.5, wherein the ocular hyperemia is reduced.

EX-1001, claim 1 (emphasis added).

43. I have been informed that “consisting of,” italicized above, as used in claim 1 is a closed transitional phrase, meaning that the claim does not include any components or steps that are not recited in the claim.

44. Claim 8, on the other hand, uses the transitional phrase “comprising” before describing the step of administering to the eye “brimonidine as the sole redness reducing active ingredient” to ocularly reduce redness. Claim 8 reads as follows:

8. A method for reducing eye redness in a human subject having ocular hyperemia, *comprising* topically administering to an eye of said human in need of said reduction of eye redness 0.025% weight by volume brimonidine as the sole redness reducing active ingredient, wherein the brimonidine is administered in the form of an ocular drop having a pH between 5.5 to 6.5, and wherein the ocular drop further comprises benzalkonium chloride, and wherein the ocular hyperemia is reduced.

EX-1001, claim 8 (emphasis added).

45. I have been informed that “comprising” is an open transitional term that not only includes the components and steps that are recited in the claim but is also open to those that are not recited in the claims.

46. The dependent claims include the following additional elements: “wherein the ocular drop induces a low incidence of rebound hyperemia in the eye of the human subject administered the ocular drop” (claims 2, 4-7, 9, and 11-14), “wherein the eye redness of said human is not associated with an ocular disease or the result of a surgical procedure on the eye” (claims 4, 7, 11, 14-15, 17, 20, and 22), “wherein the method retains normal intraocular pressure in the eye of the human subject administered the ocular drop” (claims 5, 7, 12, 14, 17, and 22), and “wherein

the ocular drop reduces redness in the eye to which the ocular drop was administered to improve the aesthetic appearance of said eye” (claims 6-7, 13-14, 16-17, 21-22, 25 and 27).

47. As discussed in the specification of the ’245 patent, the prior art redness relievers before the ’245 patent caused undesirable side effects, such as rebound hyperemia, which occurs when the level of eye redness is worse than what it was before the administration of an eye redness reliever. EX-1001, ’245 patent at 2:37-44, 4:46-54. Unlike prior art methods for reducing ocular hyperemia, the inventors surprisingly discovered that claimed methods are suitable for long-term, chronic use because they do not cause common side effects, such as rebound hyperemia (eye becoming redder after initial reduction in redness) and tachyphylaxis (tolerance to the drug). EX-1001, ’245 patent at 4:62-5:6.

B. Prosecution History of the ’245 Patent

48. I have reviewed the file history of the ’245 patent before the USPTO. I understand that while the application for the ’600 patent was still pending, the application for the ’245 patent was filed on January 30, 2023. *Compare* EX-1001, ’245 patent at Cover (filing date of January 30, 2023) *with* EX-2097, ’600 patent at Cover (issue date of March 7, 2023). I also understand that the ’245 patent was examined by the same U.S. patent examiner as the ’600 patent. *Compare* EX-1010,

'245 Patent File History, June 23, 2023 Office Action, at 212 *with* EX-2001, '600 Patent File History, December 1, 2022 Office Action, at 441.

49. I have been informed that within three months of allowing the claims of the '600 patent in view of ocular administration of the various medicated eye drops taught in Gil, Norden, and Dean (e.g., eye drops of brimonidine, steroids, anesthetics, NSAIDs, and a carbonic anhydrase inhibitor), the patent examiner started examining the application that would become the '245 patent with the knowledge and consideration of what these references disclosed. EX-2001, '600 Patent File History, January 25, 2023 Notice of Allowance), at 497; EX-1010, '245 Patent File History, April 13, 2023, Office Action), at 91.

50. During the prosecution of the '245 patent, I understand that the Patentee amended then pending claim 29 (issued claim 1), changing the transitional term “comprising” to “consisting of,” in response to a rejection received by the patent examiner in an Office Action. EX-1010, '245 Patent File History, May 31, 2023 Response to Office Action, at 185, 189. Specifically, the Patentee argued that “[b]y consisting of, it is meant that brimonidine is the sole active ingredient administered in the method for reducing redness of claim 29” EX-1010, '245 Patent File History, May 31, 2023 Response to Office Action, at 189. I understand that the Patentee also amended then pending claim 36 (issued claim 8), changing “brimonidine as the sole active ingredient” to “brimonidine as the sole redness

reducing active ingredient.” EX-1010, ’245 Patent File History, May 31, 2023 Response to Office Action, at 186. I understand that the Patentee noted that amended method claim 36, which, for context, operates in the ocular environment and contains the open-ended transition phrase “comprising,” “preclud[es] the use of additional active ingredients that may also cause vasoconstriction and reduction of hyperemia along with 0.025% brimonidine.” EX-1010, ’245 Patent File History, May 31, 2023 Response to Office Action, at 189. The Patentee further stated that the pending claims “relate to redness from ocular hyperemia rather than, for example, hemorrhage or other types of eye redness.” EX-1010, ’245 Patent File History, May 31, 2023 Response to Office Action, at 189.

51. I understand that the patent examiner subsequently issued a final rejection, stating that the amended claim 29 is ambiguous because the “transitional phrase ‘consisting of’ in the preamble” indicates that “the claim is closed to any further component within the ocular drop,” but the body of the claim recites “the ocular drop further comprises benzalkonium chloride.” EX-1010, ’245 Patent File History, June 23, 2023 Final Rejection, at 210. I understand that the patent examiner suggested amending claim 1 to recite “an ocular drop **consisting of** 0.025% weight by volume brimonidine as the sole active ingredient and benzalkonium chloride ...,” which the Patentee adopted. *Id.* I understand that the Patentee stated that “the transitional phrase ‘consisting of’ between the preamble and the body of claim 29

means that brimonidine is the sole active ingredient administered in the method for reducing redness of claim 29, and excludes other active ingredients (such as steroids, anesthetics, carbonic anhydrase inhibitors, or NSAIDs, for example) from the method.” EX-1010, ’245 Patent File History, June 30, 2023 Response to Office Action, at 288.

52. I understand that the patent examiner issued no further substantive office actions and allowed the claims over Gil, Norden, and Dean, which collectively taught only the ocular administration of eye drops containing brimonidine, steroids, anesthetics, carbonic anhydrase inhibitors, or NSAIDs. EX-1010, ’245 Patent File History, October 31, 2023, at 290 (Notice of Allowance). None of these references taught modes of administering these drugs other than ocularly, such as orally. Afterwards, I understand that the ’245 patent subsequently issued on December 5, 2023. EX-1010, ’245 Patent File History, at 413 (Issue Notification).

VIII. Claim Construction

A. Relevant Legal Principles

53. I have no formal legal training, but I have been informed by Patent Owner’s counsel about the appropriate legal standards as set forth below. In the event there are any modifications to the legal standards applicable to this declaration, I reserve the right to supplement my declaration to take into account any such modifications.

54. I have been informed and understand that a patent includes a specification containing the written description of one or more embodiments of the invention, drawings, examples, and figures, as well as one or more claims that point out and claim the subject matter of the invention.

55. The claims set forth the bounds of a patented invention's scope, and each claim defines a separate invention. I understand that a claim contains three parts: a preamble, a transitional phrase, and a body. I have been informed that the preamble bridges the preamble to the body of the claim and can be limiting as a statement of the intentional purpose for which the claimed method must be performed. I understand that terms such as "consisting of" and "comprises" are referred to as transitional terms/phrases, which inform whether additional steps or components are included within the scope of a claimed invention. From a non-lawyer's perspective, I understand that the term "consisting of" is a closed-ended term signifying restriction and exclusion of additional steps and components not recited in the claim, considering the context of the claim, whereas "comprises" is an open-ended term, requiring at least the recited steps and components but may be open to additional steps and components.

56. I have also been informed and understand that a dependent claim incorporates each and every element of the claim from which it depends.

57. I have been informed and understand that the patent claims, and their terms and phrases, are interpreted by the Board according to their ordinary and customary meaning to a person of ordinary skill in the art at the time the earliest application for patent was filed. I understand that interpreting a term or phrase contained in a patent claim involves reading the language of the full claim and considering other materials relevant to the claim, including 1) the context of other words and phrases that surround, for example, a disputed claim term, 2) the language of other claims, 3) the patent specification, and 4) the prosecution history. I have been informed that a term within a full claimed element should not be interpreted in isolation or divorced from the full claim element to which it belongs or from the claim as a whole. I understand the claims, specification and prosecution history form the intrinsic record for purposes of claim construction.

58. I have been informed that for claim construction purposes the specification can act as a dictionary, explaining the invention and how terms may be used in the claims. A construction of a term should be consistent with the specification and should most naturally align with the specification's description of the invention. In other words, I have been informed that proper claim construction requires reading a term or phrase in view the specification to understand how it is described and used in the context the invention discussed in the specification to accurately capture the inventor's intended meaning for that claim term or phrase.

But I understand that it is improper to read a limitation or preferred limitation, such as described in an example, from the specification into the claims.

59. I have also been informed that the prosecution history is also important in construing patent claims. It represents the result of a negotiation between the USPTO examiner and the patent applicant, and culminates in allowable subject matter covered by the claims of the issued patent. I understand it often happens that originally filed claims become narrowed during prosecution as part of that “negotiation” process, possibly informing the meaning of claim language by demonstrating how the inventor understood the invention as different, for example, from the prior art. As such, express representations made by the applicant to the examiner to convince the examiner of patentability and induce the patent grant can impact the claim scope. I also understand that, to the extent the same claim phrase is used in claims of a related patent originating from the same patent family, they should be construed the same absent a reason for interpreting them differently.

60. I understand that evidence extrinsic to the patent and its prosecution history may also be consulted, so long as it is not inconsistent with the claim language, the patent specification and the prosecution history. Such extrinsic evidence can include expert testimony. It can be useful to provide background on the technology to which the invention pertains, how the invention works, to ensure that the understanding of the technical aspects of the patent is consistent with that of

a person of ordinary skill in the art, or to establish that a term in a patent has a particular meaning in the pertinent field.

B. The Claims Are Limited to Methods for Reducing Eye Redness Requiring Actual Redness Reduction

61. I understand that the parties in this case do not dispute that the preamble “[a] method for reducing eye redness in a human subject having ocular hyperemia,” states that the method’s purpose is to reduce eye redness. However, in my opinion, when read in conjunction with the “wherein the ocular hyperemia is reduced” limitation, a POSA would understand that the claimed methods require actual reduction in ocular hyperemia.

C. The Transitional Phrase “Consisting of”

62. As discussed above, claim 1 recites “consisting of” as the transitional phrase between the preamble and the body of the claim. I have also been informed that when “consisting of” is used in conjunction with a claim term introduced with the indefinite article (“a” or “an”), that term is limited to its singular sense. Based on this understanding, in my opinion, the phrase “*consisting of* topically administering to an eye ... a composition in the form of *an ocular drop* consisting of 0.025% weight by volume brimonidine as the sole active ingredient” limits the claimed method to ocularly topically administering a single drop of 0.025% brimonidine as the only active ingredient in a single step, in which the single step is the only step taken to reduce eye redness.

63. I understand that the transitional phrase “consisting of” is closed-ended to additional steps or components, relative to the invention’s operative environment set forth in the preamble. I have been further informed that the body of the method then recites the steps and components used in the patented method’s environment, as defined by the preamble and often supplemented by language in the body of the claim. Here, the body of the method explicitly recites a single step: “topically administering to an eye ... an ocular drop consisting of 0.025% weight by volume brimonidine as the sole active ingredient....” EX-1001, ’245 Patent at 22:37-41. All other steps are excluded. The claim language refers later to “*the* ocular drop” in the singular form consistent with administering a single drop of 0.025% brimonidine.

64. The intrinsic record further supports this construction. For example, then pending claim 29 (issued claim 1) of the as-filed application originally included the open-ended transition term “comprising”—as in a method “comprising topically administering ... an ocular drop.” EX-1010, ’245 Patent File History, at 4. Because the transition was open ended, the claim included both the administration of one or more eye drops and one or more steps to reduce redness. The Patentee subsequently replaced “comprising” with the closed transitional phrase “consisting of” in response to an Examiner rejection, and made other minor clarifications, and stated that “the transitional phrase ‘consisting of’ ... means that brimonidine is the sole active ingredient administered in the method for reducing redness of claim 29, and excludes

other active ingredients ... from the method.” EX-1010, 288. The Examiner then allowed the claims over the art of record, including over Gil, Norden, and Dean. In my opinion, amending the claims to include the “consisting of” transition, rather than “comprising,” indicates that the Patentee narrowed the claim scope that would be beyond the single step, single drop method now claimed. EX-1010, 185, 189, 288.

65. Numerous examples in the specification further demonstrate administering a single drop of brimonidine in a single step as a means for reducing redness. Examples 1, 4, and 5, and Figures 5A-C all use a single drop of low-dose brimonidine to reduce redness better than prior art redness relievers. EX-1001, '245 Patent at 20:39-21:3, 21:61-22:22-34.

IX. The '245 Patented Methods Would Not Have Been Obvious

66. When considering the obviousness of the '245 patent, I have been asked to consider what a POSA seeking to develop a redness reliever eye drop would have done prior to August 1, 2008. In addition to forming my own opinions based on the state of the art at the time, I have also reviewed the declaration of Dr. Daniel Gil, a lead inventor on asserted prior art in this case. Gil Decl., ¶ 1. Although Dr. Gil's declaration stands on its own, I note that Dr. Gil's description of the thinking at the time at Allergan (the company responsible for Alphagan, a brimonidine medication used to treat glaucoma and high intraocular pressure inside the eye) regarding

repurposing brimonidine and brimonidine's pharmacology is consistent with my understanding of the art. Gil Decl., ¶¶ 23-24. The patent-in-suit went against conventional thinking regarding redness relievers in general and brimonidine specifically. Gil Decl., ¶ 25. In addition, I understand Patent Owner's other experts will also opine on issues of pharmacology and chemistry, and in my opinion a POSA would have consulted those team members as needed. *See* Section V above. For example, a medical doctor may have worked with a pharmacologist to determine the receptor and receptor activity needed for a redness reliever and may have worked with a chemist to modify existing compounds to obtain that activity as needed.

X. Legal Standards

67. I have no formal legal training, but I have been informed by Patent Owner's counsel about the appropriate legal standards as set forth below.

68. I have been informed and understand that obviousness considers whether the claimed invention, as a whole, considered against the prior art taken as a whole would have been obvious to a person having ordinary skill in the art at the time of the invention. I understand that in making an obviousness determination, it is improper to consider the prior art with a hindsight bias based on the teachings of the patent. One must not use the patent as a template to suggest how the elements of the prior art could have been combined.

69. I have also been informed and understand that the claimed invention and the prior art must each be looked at “as a whole.” One must also consider those portions of the prior art that “teach away” from the claimed invention. It is not sufficient to consider an isolated portion of one reference that is similar to what the patent discloses and claims, if either the reference as a whole or another reference or the prior art as a whole teaches or suggests something different from that isolated portion. I also understand that, in resolving whether an invention is obvious based on the teachings of multiple references, one must consider whether the combination yields no more than predictable results or achieves an unexpected result.

70. I have also been informed and understand that, in determining whether or not a patented invention would have been obvious, the following factors must be considered: the scope and content of the prior art, the differences between the prior art and the claims at issue, the level of ordinary skill in the art, and whatever objective indicia of non-obviousness may be present, such as unexpected results for the claimed invention compared to the prior art as well as industry praise or the commercial success for an embodiment of the invention.

71. I have also been informed and understand that the Petitioners have the burden of proving unpatentability of the challenged claims by a preponderance of the evidence (*i.e.*, more likely than not).

XI. Discussion of References

72. I understand that Petitioners contend that claims 1, 2, 4-9, 11-17, 20-22, 25, and 27 of the '245 patent are obvious. Petitioners rely on 5 references—Norden, Gil, Dean, Alphagan PDR, and Federal Register 1988—in their obviousness ground.

73. In my opinion, a POSA would have viewed these five references in the context of the landscape of the art at the time, including pertinent clinical references such as the Alphagan package inserts (EX-1067, EX-1068), the Alphagan NDA (EX-1030), and other references reflecting the clinical experience with commercial brimonidine products. The Technical Background section above (Section VI) describes some of the landscape of redness relievers, which a POSA would have considered highly relevant. Taken together, a POSA would not have focused on the references as Petitioners has here and would have been diverted away from the claimed invention for the reasons further explained below.

74. In my opinion, none of Petitioners' prior art references, individually or in combination, renders the claimed methods obvious. I understand that the Patent Examiner already considered Norden, Gil, Dean, Alphagan, and Federal Register 1988 and issued the '245 patent claims over them. EX-1010, '245 Patent File History at 146-165, 194. I also understand that the Patent Examiner reviewed the Board's decision in an *inter partes* review proceeding for the '742 patent, in which the Board found the claims of the '742 patent unpatentable based on obviousness and issued

the '245 patent, which include additional narrowing limitations, over the Board's decision in that proceeding. *Id.*, at 194.

75. Indeed, Petitioners' prior art references would have taught a POSA away from using brimonidine as the sole active ingredient at the claimed dose of a single drop of 0.025% reduce eye redness as claimed in the '245 patent. As explained below, as of August 1, 2008, it was well known that one of the most common side effects of administering brimonidine as an ocular drop was *causing* eye redness—the very symptom that the claimed methods are designed to treat, and that it was commonly associated with causing allergy, limiting its utility for example in glaucoma patients. *See generally*, EX-2028, Fudenberg 2008. Moreover, while it was also known that brimonidine can reduce eye redness, it was only at high concentrations, for example, 0.2% or above to trigger sufficient $\alpha 1$ activity. *See infra* § XII.E.1.c. And even then, 0.2% brimonidine only reduced eye redness in a small number of patients (~3.5%) making it, as a practical matter, unattractive and nonviable. EX-1030, Alphagan NDA at 109. Thus, a POSA would have expected that if the amount of brimonidine was lowered to a single drop of 0.025% (at least eight-fold lower), it would not exert sufficient vasoconstriction effects to reduce eye redness.

76. In my opinion, Petitioners advance an overly simplistic view of what they allege would have been obvious to a POSA before August 2008 seeking to

develop a better eye redness reliever based on the state of the art at that time. In my view, Petitioners' myopic focus on brimonidine just because at high concentrations it was known to have some whitening effect, particularly when it was known to cause hyperemia at lower concentrations and allergy generally (*see, e.g.*, EX-1068, Alphagan P Label at 4), is driven by hindsight knowledge of what the '245 patent discloses and then working backwards to assemble prior art references to give the impression that the '245 patented methods would have been obvious. I understand that such hindsight reasoning is impermissible in an obviousness challenge. Petitioners also turn a blind eye to the prior art that teaches brimonidine loses its redness reducing effect at concentrations below about 0.2%. Thus, they are not considering the art as a whole.

77. More realistically, I believe that the POSA looking to develop a redness reliever would have been discouraged from focusing on brimonidine, or compounds like it, that was known to cause eye redness as well as other ocular allergic reaction. *See* Section XII.A below. Instead, I believe the POSA would have sought to modify and improve the existing redness relievers, which had a high affinity for α_1 effects and were thus already effective redness reducers at low concentrations; alternatively, the POSA could have sought to address patients' root cause of eye redness (like dry eye or allergy) rather than focusing on the symptom, redness. Any of these modifications and improvements could have included structural and/or formulation

innovations to address the problems plaguing these well-known redness relievers. In each of these potential categories of options addressing root causes, there would have been multiple viable options for a POSA to explore, including repurposing old compounds or working with a chemist to develop (and then test) new compounds fit for the intended purpose—not amounting to a finite list, let alone one with predictable results. And even if the POSA would have considered brimonidine, it would have been counter-intuitive that lowering the amount brimonidine below about 0.2%, particularly to a single drop of 0.025%, would have yielded a product capable of meaningfully reducing redness—this finding was a true innovation over the body of art known about brimonidine in 2008.

78. Below, I provide a high-level summary of a few references that would have informed a POSA, along with Petitioners’. In general, a POSA at the time of the invention of the ’245 patent knew that brimonidine had been long approved as a prescription drug to lower high eye pressure and treat glaucoma, but that it has significant side effects—namely, ocular hyperemia (redness) and ocular allergic reactions that limited its utility.

Art	Date	Disclosure
U.S. Patent No. 3,890,319 (EX-2096)	June 1975	First disclosure of brimonidine.

Federal Register 1988 (EX-1009)	March 1988	The art at the time used α_1 or mixed α_1/α_2 agonists as ophthalmic vasoconstrictors to reduce redness. The active ingredient of redness reliever products known as of March 4, 1988 consisted of one of the following at the specified concentrations: (a) Ephedrine hydrochloride, 0.123%. (b) Naphazoline hydrochloride, 0.01 to 0.03%. (c) Phenylephrine hydrochloride, 0.08 to 0.2%. (d) Tetrahydrozoline hydrochloride, 0.01 to 0.05%. (Federal Register 1988 at 14.)
Derick 1995 (EX-2003)	1995	Activation of α_1 receptors was known to trigger vasoconstriction. Redness reduction (blanching) was known as an α_1 effect. “In the eye, α_1-adrenoceptors are located on vascular smooth muscle located in the conjunctiva, ciliary processes, retina, and choroid. Stimulation of these adrenoceptors leads to vasoconstriction. Significant vasoconstriction in the radial arteries of the major arterial circle of the iris occurs after the topical instillation of apraclonidine.” (p. 4.)
Burke 1996 (EX-1035)	November 1996	Among the known α_2 agonists, brimonidine was known to be least likely to trigger vasoconstriction.

		“These results suggest that compared to clonidine and apraclonidine, brimonidine would be the least likely to produce α_1-adrenoceptor-mediated side effects, such as mydriasis and ocular vasoconstriction.” (p. 2.)
Derick 1997 (EX-1029)	1997	Conjunctival blanching (whitening) was known to be observed only at higher concentrations of brimonidine. “Conjunctival blanching appeared to be dose related; it was observed bilaterally in eight patients in both the 0.2% and 0.5% treatment groups, five patients in the 0.08% group, and four in the vehicle control group.” (p. 4.)
Robin 1998 (EX-1023)	1998	It was not known whether brimonidine at “usual ophthalmic doses” cause α_1 effects. Brimonidine was known to be more likely than apraclonidine to cause systemic side effects. “The degree of selectivity is only important if tissue concentrations are within the range required for α_1 activity. If tissue or circulating levels of drug are insufficient to produce α_2 effects, then α_1 effects are highly improbable.”

		(p. 2.) “It is questionable whether $\alpha 1$ activation, either locally or systemically, occurs at usual ophthalmic doses.” (p. 3.) “Apraclonidine is far less likely to produce sedation, because it does not enter the central nervous system to the degree that brimonidine does, nor is it absorbed into the system circulation as effectively.” (p. 3.)
Alphagan 0.5% Label (EX-1067)	December 2001	Alphagan 0.5% showed a significantly higher rate of conjunctival blanching than Alphagan 0.2%. “The most common adverse events reported in association with the use of ALPHAGAN 0.5% ...was transient conjunctival blanching in 50% of patients... The following adverse reactions were reported in 1% to 4% of the patients...drowsiness/tiredness, and ocular irritation (encompassing discomfort, foreign body sensation, and ocular pain.” (p. 4.)

Alphagan 0.2% Label (EX-1067)	December 2001	Brimonidine 0.2% was known to cause ocular hyperemia and ocular allergic reactions in a significant number of patients while also causing conjunctival blanching (whitening) in some patients. “Adverse events occurring in approximately 10-30% of the subjects, in descending order of incidence, included oral dryness, ocular hyperemia...ocular allergic reactions... Events occurring in approximately 3-9% of the subjects, in descending order included...ocular irritation...conjunctival blanching....” (p. 9.)
Gil ('553 patent) (EX-1004)	September 2001	Brimonidine was known as an anesthetic for reducing ocular pain.
Norden (EX-1006)	July/August 2002	Brimonidine 0.2% administered twice within 10 min with other active agents (e.g., steroid, NSAID and antibiotic) in the same LASIK surgery dosing protocol purportedly reduced hemorrhage and micro-vessel hemorrhage.
Gil (AU '265) (EX-2118)	2002	Brimonidine was known to cause off target effects. “The prior art alpha2 adrenergic agonists, which activate all three alpha2 receptors, cause sedation,

		hypotension and bradycardia, preventing or severely limiting their use for treating diseases and disorders that are known to be ameliorated by them.” (p. 115.)
Griffith (EX-1020)	2003	Activation of α_2 receptors was known to mediate vasodilation and act in opposition to α_1 receptors. “All selective α_1-agonists are vasoconstrictors, which is the basis of their therapeutic activity.” (p. 12.) “Stimulation of central postsynaptic α_2- receptors leads to a reduction in sympathetic neuronal output and a hypotensive effect.” (p. 31.)
Alphagan P Label (EX-1068)	2005	Lower concentration Alphagan products (0.15%, 0.1%) did not report any conjunctival blanching (whitening). “Adverse events occurring in approximately 10-20% of the subjects receiving brimonidine ophthalmic solution (0.1- 0.2%) included: allergic conjunctivitis, conjunctival hyperemia, and eye pruritus. Adverse events occurring in

		approximately 5- 9% included...ocular allergic reaction....” (p. 4.)
Fudenberg (EX-2028)	2008	This article entitled “[e]fficacy, safety, and current applications of brimonidine” does not indicate that, as of 2008, a POSA thought to use brimonidine, much less a single drop of 0.025% brimonidine as the sole active ingredient to reduce eye redness.

A. Federal Register 1988 (EX-1009)

79. Federal Register 1988 is a publication of the final rule in the form of a final monograph under which OTC ophthalmic drug products, including redness reducers, can be generally recognized as safe, effective, and not misbranded. EX-2098 (FDA website regarding OTC Drug Review Process).

80. Federal Register 1988 does not mention brimonidine, nor does it suggest that brimonidine at 0.025% can be used to relieve eye redness. In fact, brimonidine is conspicuously missing from the list of monographed “vasoconstrictors.” EX-1009, Federal Register 1988, at 14. Moreover, no vasoconstrictor listed in Federal Register 1988 is a selective α_2 agonist, which would have further directed a POSA away from developing a redness reliever with an active ingredient that has not even been monographed for that purpose. This has not changed to date—brimonidine is still not included as an ophthalmic vasoconstrictor. Indeed, even in 2010, after the priority date of the ’245 patent, companies were

launching redness reliever drops using the monographed ingredient in the Federal Register 1988. This is because bringing a monographed product to the market is not only faster than a New Drug Application product, but also consistent with the traditional thinking at the time that α_1 agonists, are vasoconstrictors, as reflected in Federal Register 1988.

B. Derick 1995 (EX-2003)

81. Derick 1995 is a review article entitled “Adrenergic Agonist Medications: Basic Mechanisms.” In my opinion, a POSA reading Derick 1995 would have understood brimonidine, a highly selective α_2 agonist, to be the least promising candidate to relieve eye redness, particularly at a dose as low as a single drop of 0.025% brimonidine.

82. Derick 1995 explains that adrenergic agonists are “sympathomimetics,” which mimic catecholamine neurotransmitters naturally produced in the body, such as epinephrine and norepinephrine, which control responses in the sympathetic nervous system (SNS). EX-2003, Derick 1995 at 1. “The SNS mediates the flight-or-fight response to stress through the stimulation of adrenergic receptors on the heart and lungs and inhibition of the gastrointestinal system.” *Id.* at 4.

83. Derick 1995 explains that “[i]n contrast to β or α_1 adrenoceptor, stimulation of α_2 adrenoceptors appears to have an inhibitory effect on the SNS.” *Id.* at 2. Alpha-2 adrenoceptors may be located presynaptically and postsynaptically. *Id.*

Activation of presynaptic $\alpha 2$ adrenoceptors “starts a cascade of cellular activities leading to a decrease in norepinephrine release from the presynaptic terminus” *Id.* Activation of postsynaptic $\alpha 2$ adrenoceptors “also has an inhibitory effect on the SNS through inhibition of adenyl cyclase.” *Id.* at 3.

84. Both $\alpha 1$ and $\alpha 2$ adrenoceptors are found in the vascular smooth muscle in the eye, including the ocular blood vessels. *Id.* at 4. Stimulation of $\alpha 1$ receptors in “vascular smooth muscle located in the conjunctiva, ciliary processes, retina, and choroid...leads to vasoconstriction.” *Id.* On the other hand, stimulation of $\alpha 2$ receptors suppresses the release of norepinephrine, causing hypotension and sedation. *Id.* at 5.

85. Derick 1995 explains that $\alpha 1$ effects are needed for vasoconstriction of ocular blood vessels, which is why the commercial ophthalmic vasoconstrictors at the time contained $\alpha 1$ agonists. For example, Derick 1995 states that “[n]aphazoline, an imidazoline that is primarily an $\alpha 1$ agonist, is used topically as a nasal decongestant and ophthalmic vasoconstrictor.” *Id.* It suggests that if a POSA were to explore $\alpha 2$ agonists at all, the POSA would have explored other $\alpha 2$ agonists, such as apraclonidine, with less selectivity for $\alpha 2$ receptors and more selectivity for $\alpha 1$ receptors. *Id.* at 6 (“[a]praclonidine is a relatively selective $\alpha 2$ -agonist, but it exhibits some $\alpha 1$ activity.”). Derick 1995, however, conspicuously fails to mention any $\alpha 1$ -effects associated with brimonidine, stating instead that it is a “selective $\alpha 2$ -

adrenergic agonist” with “enhanced CNS absorption,” suggesting that it is more likely than apraclonidine to cause systemic side effects, such as sedation, hypotension, and vasodilation. *Id.*

C. Derick 1997 (EX-1029)

86. Derick 1997 is a publication entitled “Brimonidine Tartrate: A One-month Dose Response Study.” Derick 1997 states that both apraclonidine and brimonidine “produce similar alpha1 side effects, including dry mouth, fatigue, and conjunctival blanching.” EX-1029, Derick 1997 at 2. It explains, however, that “[c]onjunctival blanching appeared to be dose related; it was observed bilaterally in eight patients in both the 0.2% and 0.5% treatment groups, five patients in the 0.08% group, and four in the vehicle control group.” *Id.* at 4, 5. Derick 1997 concludes that “[c]onjunctival blanching was observed to occur more frequently in both the 0.2% and 0.5% treatment groups than in the 0.08% group or the vehicle control group.” *Id.* at 5. The incidence of conjunctival blanching at 0.08% was essentially the same as the vehicle control group, which is not unexpected given the later findings by Allergan showing a 0.2% minimum effective dose for blanching. *See infra* § XII.E.1.c. Derick 1997 thus would have led a POSA to expect that reducing the dose by more than threefold to a single drop of 0.025% would not likely produce any conjunctival blanching, and certainly not any of commercial value. *Id.*

D. U.S. Patent No. 6,242,442 (“Dean”) (EX-1007)

87. Dean is a U.S. patent entitled “Brimonidine and Brinzolamide for Treating Ocular Conditions” and generally discloses a combination treatment of brimonidine and brinzolamide for treating ocular diseases such as glaucoma, occlusion conditions, diabetic retinopathy, and ocular neovascularization. EX-1007, Dean at 2:21-27.

88. Dean is not directed to treating eye redness, nor does it suggest administering a single drop of 0.025% brimonidine as the sole active ingredient as a single step method to affirmatively reduce eye redness in a patient having ocular hyperemia. In fact, Dean states its [c]ombinations of brimonidine and brinzolamide represent a novel approach to producing potent and long lasting IOP lowering medications with fewer side-effects than observed when these are administered alone. EX-1007, Dean at 2:51-54. Dean teaches the combined administration of brimonidine and brinzolamide either in the same composition or as separate formulations administered sequentially. *Id.*, 2:55-57. Regarding side-effects, Dean notes that brimonidine as used in Alphagan “has been shown to cause the side effects of sedation and ocular hyperemia in an allergic like reaction in some patients.” *Id.*, 2:38-43. To reduce these side effects, Dean proposes using a relatively low concentration of brimonidine, but *only in combination with brinzolamide* to maintain the overall efficacy of the formulation in reducing intraocular pressure. *Id.*, 2:47-54.

89. Dean discloses a very broad concentration range of 0.01-0.2% brimonidine, and states that the preferred range is “0.1-0.2% by weight” when administered before but in sequence with brinzolamide. EX-1007, Dean at 5:23. As far as I know, no drug or drug regimen using brinzolamide with a low concentration ever received FDA approval. In fact, the only example in Dean using brimonidine as the sole active ingredient is Example 10. It contains 0.2% brimonidine—an amount approved for Alphagan—and noted by Dean to cause hyperemia. EX-1007, Dean at 6:60-7:8. To my knowledge, Simbrinza constitutes the only drug approved with these two active ingredients, and it is a fixed dose combination of 1% brinzolamide with 0.2% brimonidine.

90. Although Dean hypothesizes that when brimonidine is administered with brinzolamide, “brimonidine serves to constrict ocular vessels and thereby reducing the flux of blood through the anterior portion of the eye,” it does not mention at what dose this vasoconstriction is achieved. EX-1007, Dean at 2:57-60. Dean is silent as to any redness reducing effects of brimonidine.

E. U.S. Patent No. 6,294,553 (“Gil”) (EX-1004)

91. Gil is directed to a “method for treating ocular pain” using brimonidine. Gil includes five examples. Petitioners rely on Examples 1 and 4 for obviousness. But both examples are prophetic examples, and neither teaches nor suggests reducing eye redness in a human subject, particularly at the claimed dose of a single drop of

0.025% brimonidine as the sole active ingredient in a single-step method for reducing eye redness.

92. Example 1 is a description of a prophetic clinical study that seeks to only assess whether brimonidine repeatedly dosed at 0.03% (amounting to a dose significantly higher than a single drop of 0.03%) reduced pain following radial keratotomy surgery. EX-1004, Gil at 4:46-48, 4:53-61. The patients received one drop of 0.03% brimonidine “*every four hours* while awake one day prior to surgery and again *every 20 minutes* for the two hours just before surgery.” EX-1004, Gil at 4:54-58 (emphasis added). Additionally, after the surgery, the patients were given one drop of 0.03% “every four hours while awake for 14 consecutive days.” EX-1004, Gil at 4:58-61.

93. Regarding redness reduction, Example 1 neither mentions redness nor suggests an assessment of redness, let alone measuring redness reduction. Indeed, Gil does not explain how redness can be measured in this hypothetical study because it fails to provide even the most basic information a POSA needs to meaningfully evaluate redness reduction, such as inclusion or exclusion criteria or the timepoints at which redness should be measured to determine if any reduction occurred. Indeed, Example 1 does not provide actual study results of any type—not even of pain relief—which would have signaled to a POSA that Gil’s statements regarding brimonidine’s effects on neurogenic inflammation were speculative at best.

94. While Example 1 states that “[s]ymptoms of ocular inflammation (burning/stinging, tearing, etc.) are also recorded,” EX-1004, Gil at 4:63-65, that does not establish that redness is reduced. There are five cardinal symptoms of inflammation—swelling, pain, redness, heat, and loss of function—each of which may appear independent of one another. EX-2020, Sher. Dep. Tr. (8/10/2022) at 104:23-109:11 (admitting that an inflammatory event does not exhibit all symptoms of ocular inflammation). In other words, one may experience ocular pain without any eye redness; likewise, one can experience inflammation without redness. Thus, it is entirely possible that 10 drops of 0.03% brimonidine before the surgery and 56 drops of 0.03% brimonidine after the surgery relieved ocular pain without reducing eye redness—there may have been no redness to reduce at all, and other drugs may have confounded both *causing* redness and its potential relief. No conclusion can be drawn between brimonidine and redness based on this example.

95. Example 4 is a prophetic rabbit study for determining “the effects of brimonidine on ocular surface sensation” using the “Corneal Nerve Conduction Model,” which measures the “nerve traffic generated as the cornea is exposed to various stimuli.” EX-1004, Gil at 5:20-24, 5:34-35. The corneal nerve conduction model measures nerve signal transmission using electrodes and is incapable of measuring eye redness. Example 4 states that rabbit cornea is stimulated using various stimuli (e.g., capsaicin, potassium chloride, or fine hairs) and then brimonidine in

the dose range of 0.01% to 0.5% is applied to the cornea to evaluate what effect, if any, brimonidine has on its nerve signals, which is an indicator of ocular surface sensation. EX-1004, Gil at 5:31-37.

96. Example 5—the example in Gil that actually performed the Corneal Nerve Conduction Model—further confirms that Example 4 is designed only to assess brimonidine’s ability to reduce nerve pain from corneal irritation as an indicator of alleviating corneal pain in humans. EX-1004, Gil at 5:49-59. Example 5 states that the results of the corneal nerve conduction model in Example 4 “reflect what is occurring at the sensory receptor in the corneal epithelium.” *Id.* at 5:59-62.

97. Importantly, Example 5 uses *1 cc* of Alphagan (0.2% brimonidine), which is equivalent to 1 mL or 20-30 drops, suggesting that a POSA would have looked, if anywhere, to higher doses of brimonidine. EX-1004, Gil at 6:5-7, 6:9-13. In an overarching concluding paragraph of the specification summarizing the findings of the Examples, Gil states that “[w]hile further experiments would be desirable to validate these results, these results are indicative that brimonidine may be useful to decrease corneal sensory irritation and pain,” mentioning nothing about reducing neurogenic inflammation or reducing redness. *Id.* at 6:24-27.

98. I understand that Dr. Gil himself has submitted a declaration in this action and I have reviewed his declaration. His experience with brimonidine is consistent with my reading of his patent and the state of the art—POSAs would not

have considered brimonidine, let alone a single drop at 0.025%, if their aim was to develop an efficacious redness reliever prior to August 1, 2008. Gil Decl., ¶¶ 25-39.

F. The Alphagan Franchise of Brimonidine Products

99. Alphagan 0.2% was the first FDA approved drug containing brimonidine tartrate. It was approved in 1996 for lowering intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. EX-1030, Alphagan NDA; EX-1067, Alphagan 0.2% Label at 7. In 1997, the FDA approved Alphagan containing 0.5% brimonidine for preventing post-operative IOP elevations in patients undergoing argon laser trabeculoplasty. EX-2099, Drugs@FDA Alphagan 0.5%; EX-1067, Alphagan 0.5% Label at 2. The 0.5% product was never commercialized. Allergan then lowered the concentration of brimonidine to 0.15% (Alphagan P 0.15%), which was approved in 2001, and 0.1% (Alphagan P 0.1%), which was approved in 2005, both of which are indicated for lowering intraocular pressure in patients with open-angle glaucoma or ocular hypertension. EX-2035, Drugs@FDA Alphagan P 0.15%; EX-2036, Alphagan P 0.1% Approval Letter.

100. The data reflected in the Alphagan labels and the clinical studies in the Alphagan NDA indicate that brimonidine caused conjunctival blanching (whitening) at a high concentration of 0.5% in about 50% of the subjects. EX-1067, Alphagan 0.5% Label at 4; EX-1030, Alphagan NDA at 13. When the concentration of brimonidine was reduced to 0.2%, brimonidine exhibited lower incidences of

conjunctival blanching (3-9% of subjects) and triggered ocular hyperemia (eye redness) and ocular allergic reactions in 10-30% of the subjects. EX-1067, Alphagan 0.2% Label at 9. When the concentration was further reduced to 0.15%, brimonidine did not exhibit any incidence of conjunctival blanching, but the incidence of conjunctival hyperemia persisted in 10-20% of patients. EX-1068, Alphagan P 0.15% Label at 4.

101. I understand that Petitioners rely on Alphagan PDR (EX-1008) as a prior art reference in their obviousness combinations. Alphagan PDR is a chapter in 1998 Physicians' Desk Reference on Alphagan (Brimonidine tartrate ophthalmic solution) 0.2%. EX-1008, Alphagan PDR, 487. It explains that Alphagan contains 0.2% brimonidine and "is indicated for lowering intraocular pressure in patients with open-angle glaucoma or ocular hypertension." *Id.* Alphagan PDR notes that "ocular hyperemia, burning and stinging...conjunctival follicles, ocular allergic reactions, and ocular pruritus" are common adverse events occurring in approximately 10-30% of subjects administered with the product. *Id.* Given that Alphagan PDR discusses the use of brimonidine only at the high concentration of 0.2% for treating an entirely different purpose with a different mechanism of action, Alphagan PDR would not have led a POSA to the claimed methods.

G. Norden (EX-1006)

102. Norden is a paper discussing the effect of administering brimonidine on bleeding complications, including ocular hemorrhage and hyperemia, to patients undergoing LASIK surgery. EX-1006, Norden at 4. The formulation used in the study was brimonidine tartrate 0.2% (Alphagan). *Id.* Moreover, 0.2% brimonidine was administered *twice* before the LASIK surgery (15 and 5 minutes before the surgery), which would have delivered an amount of brimonidine that is close to a single drop of brimonidine formulated at 0.4%—about sixteen times greater than the claimed single drop of 0.025%.

103. The LASIK patients in Norden were administered various other active ingredients along with brimonidine before, during, and after the surgery. Norden explains that before LASIK surgery, patients' eyes were given ofloxacin (antibiotic) and diclofenac (non-steroidal anti-inflammatory (NSAID)). *Id.* at 4-5; EX-2020, Sher Dep. Tr. (1/27/2023) at 18:14-21:8. During the surgery, the eyes were irrigated with proparacaine, which is an anesthetic. *Id.* at 5. After the surgery, the eyes were given ofloxacin and prednisolone acetate (steroidal anti-inflammatory drug). *Id.* Prednisolone was known to be “the single strongest anti-inflammatory drop used in all of ophthalmology,” which would have unquestionably resolved any vasodilation in both the “test” and “control” groups thus normalizing vessel diameter between the

groups (and resolving any true vasodilative hyperemia) at the time of the examination. EX-2009, Donnenfeld Hr'g Tr. at 60:22-25, 61:25-61:8.

104. Norden concludes that “brimonidine minimizes subconjunctival hemorrhage without inducing flap slippage,” reducing LASIK-related bleeding and flap complications. EX-1006, Norden at 7. However, Norden points out that brimonidine may induce side effects, such as “brimonidine-induced desiccation, possible ischemia due to vasoconstriction of the anterior ocular vessels, and/or direct toxicity.” *Id.*

105. A POSA reading Norden would have questioned the validity of its conclusion regarding 0.2% brimonidine’s ability to prophylactically prevent bleeding complications due to several critical flaws in the clinical study design. First, Norden does not indicate that the redness of patients’ eyes was observed before administering 0.2% brimonidine prior to LASIK surgery. *See* EX-1006, Norden at 4-5. Instead, the bleeding complications in the patients’ eyes were observed only once—*after* LASIK surgery was performed on the patients’ eyes. *Id.* at 5. This is a critical flaw because patients likely had minimal eye redness before the LASIK surgery, which would have been exacerbated after the LASIK surgery. Although Norden concludes that the degree of bleeding complications induced by surgery was less in eyes that received brimonidine, these eyes would still have had significantly higher levels of redness than before undergoing the surgery. The study failed to

evaluate the level of *before* administering brimonidine prior to LASIK surgery, so one cannot draw any conclusion as to what effect, if any, brimonidine had on the patients' eye redness. It is entirely possible that brimonidine induced more bleeding complications in the eyes than before based on brimonidine's well known propensity to cause ocular hyperemia and ocular allergic reactions. EX-1067, Alphagan Label at 4, 9; EX-1068, Alphagan P Label at 4; EX-2101, Uretmen at 1 (reporting that brimonidine caused an allergic reaction and resulting severe hyperemia in LASIK patients such that the doctor had to postpone surgery).

106. Second, Norden's control, if there was any, was flawed. Norden appears to use one eye of each patient as control, administering brimonidine to one eye (the test eye) but not the other (the control eye), but Norden never compared the level of bleeding complications between the test eye and the control eye *in the same patient*. See EX-1006, Norden at 5-6. Instead, Norden simply counted the number of eyes having each grade of what Norden refers to as "hyperemia" (which a POSA would have understood is micro-vessel hemorrhage) in a scale of 1 to 4, without observing how the test eye and the control eye in the same patient compared with each other. See *id.* Moreover, even if Norden had compared bleeding complications in the eyes of the same patient, the control eye is not truly a control because the eyes in the same patient can have different baseline redness and react differently to brimonidine. Indeed, Norden acknowledges that the study was not randomized for the selection of

the eye to receive brimonidine, potentially introducing bias into the study. *Id.* at 5. But these issues were never addressed in Norden. It is also possible that the other active ingredients, such as the NSAID and the steroid, which can reduce eye redness, enhanced any effect of brimonidine. But because of multiple flaws in the design of Norden's study, including the alleged control (see the next paragraph), one cannot attribute any purported effect of reducing hyperemia to brimonidine alone.

107. Moreover, a POSA would have recognized that brimonidine may have been effective in preventing bleeding complications due to synergistic effects between brimonidine and other drugs administered in Norden (e.g., anesthetic, antibiotic, NSAID, or steroid). Thus, a POSA would not have interpreted Norden's study to inform a POSA about brimonidine's efficacy when it is used alone, much less as the only active ingredient in a single-step method for reducing eye redness. And Norden teaches nothing about the effects of brimonidine, alone or in combination with other active ingredients, when using a single drop of 0.025% brimonidine.

H. Desco 2005 (EX-1131)

108. Desco is entitled "Effect of prophylactic brimonidine on bleeding complications after cataract surgery." Desco describes that the patients were given a host of active agents along with brimonidine as part of the cataract surgery dosing regimen. Before the surgery, the patients received mydriatic drops (tropicamide

0.5%, atropine, and cyclopentolate hydrochloride 1%), diclofenac 0.1%, and phenylephrine 10%” EX-1131, Desco at 2. As explained in Federal Register 1988, phenylephrine was a known ocular vasoconstrictor at the time, which could have reduced eye redness on its own. Federal Register 1988 at 7089, 7091. Then, the patients were anesthetized using mepivacaine hydrochloride 2%, 5 cc (mL) of bupivacaine hydrochloride 0.75%, and 75 UI hyaluronidase. *Id.*

109. After the surgery, the patients received dexamethasone 0.05% (steroid), chloramphenicol ointment 1% (antibiotic). *Id.* Desco states that the “postoperative medication regime consisted of tobramycin 0.3% and dexamethasone 0.1% drops (Tobradex, Alcon Laboratories, UK) three times a day and diclofenac preservative free three times a day (Voltaren, CIBA Vision Ophthalmics, Atlanta, GA) for a month, and tropicamide drops noote [sic] (Alcon Laboratories, UK) for 3 days, to induce a soft mydriasis and avoid an inflammatory reaction after surgery.” *Id.* at 3. Chloramphenicol and tobramycin are antibiotics, which can treat eye redness associated with infection.

110. Desco states that vasoconstrictors *associated with anesthetics* are commonly used to reduce the occurrence of hemorrhage from capillaries and small arterioles. *Id.* at 4-5. Thus, if anything, Desco teaches that it is co-administration of two drops of 0.2% brimonidine (which effectively delivers the same amount of brimonidine as a single drop of 0.4% brimonidine) *with* other drugs (anesthetics,

NSAIDs, other vasoconstrictors (phenylephrine), antibiotics, and steroids) that will reduce blood vessel caliber.

I. Fudenberg 2008 (EX-2028)

111. Fudenberg 2008 is an expert opinion article entitled “Efficacy, safety, and current applications of brimonidine” published in 2008—around the same time as the ’245 patent priority date. Despite being published in 2008 on the “current applications of brimonidine,” Fudenberg 2008 conspicuously fails to mention that brimonidine can be used for reducing eye redness. Fudenberg 2008 thus demonstrates that a POSA did not view brimonidine, let alone at a dose as low as a single drop of 0.025%, as a viable option for a redness relieving drop prior to the discovery of the invention in the ’245 patent.

112. Fudenberg 2008, in my opinion, best reflects the contemporaneous state of the art regarding brimonidine at the time of the invention in an unbiased way—outside the context of patent litigation—and demonstrates, consistent with my opinions, that POSAs were not thinking about brimonidine for redness reduction at a dose as low as single drop of 0.025% as in the claims, in that timeframe. It further shows that there were many reasons why a POSA would *not* have selected brimonidine as a redness reliever considering multiple alternative viable options available to the POSA at the time. For example, Fudenberg 2008 states that “[c]hronic use of brimonidine is limited by the potential for allergy and intolerance,”

and the combination of “timolol/brimonidine was statistically significantly more comfortable” than brimonidine as the sole active ingredient. EX-2028, Fudenberg 2008 at 4. It also reports that “brimonidine is not licensed for use in children” due to “potentially fatal systemic side effects including: bradycardia, hypotension, hypotonia, apnea, dyspnea, hypoventilation, cyanosis and lethargy.” *Id.* Fudenberg 2008 cautions that brimonidine was known to cause “CNS depression mimicking opioid toxicity,” and thus, “extreme caution should be taken when treating children weighing <20 kg and those <6 years of age.” *Id.*

XII. Response to the Petitioner’s Purported Ground of Obviousness

A. “A Method for Reducing Eye Redness in a Human Subject Having Ocular Hyperemia”

113. Claim 1 recites “[a] method for reducing eye redness in a human subject having ocular hyperemia” as its preamble. As explained above in Section VIII.B, the preamble requires that the claimed single drop of 0.025% brimonidine be administered in a single step with the intention of reducing eye redness *to patients with ocular hyperemia*.

114. In my opinion, a POSA would not have viewed any of Norden, Gil, or Dean relevant to the claimed invention. Norden and Gil involve surgical trauma models, cutting and severely damaging blood vessels, and thus, neither is directed to the use of brimonidine in people with ocular hyperemia (i.e., eye redness caused

by vasodilation) that typical eye redness relievers would address. EX-2100, Dana Nov. 1, 2024 Dep. Tr. at 49:2-50:2.

115. Norden discloses preventing bleeding complications and flap adherence associated with LASIK surgery. EX-1006, Norden at 4, 7. Gil Example 1 is a prophetic example designed to prevent ocular pain associated with radial keratotomy surgery. Indeed, it does not even mention reducing eye redness, let alone ocular hyperemia. Gil Example 4 discloses performing stereotaxic surgery in a rabbit, which involves cutting the rabbit's conjunctiva and episclera to access the back of the rabbit's eyeball to hook an electrode to the ciliary nerve to assess brimonidine's ability to relieve ocular pain from corneal exposure to various stimuli. EX-1004, Gil at 5:18-46; *see also id.*, 5:48-6:28. I understand that Petitioners' expert, Dr. Galanis, agreed with me that Example 4 cannot be performed in humans nor can it be used for assessing reduction in ocular hyperemia. EX-2017, Galanis Jan. 14, 2024 Dep. Tr. at 136:16-137:1.

116. In my opinion, a POSA would also not have found Dean relevant to the claimed invention. Dean discloses the use of brinzolamide in combination with brimonidine to treat certain ocular diseases, including glaucoma, due to high intraocular pressure (IOP). EX-1007, Dean at 2:51-54. Brinzolamide and brimonidine were known as IOP lowering drugs (*id.*, 1:11-26), but they work via different mechanisms, so combining the two drugs reportedly "represent[ed] a novel

approach to producing potent and long lasting IOP lowering mediations.” EX-1007, Dean at 2:51-54. Dean hypothesizes that the bioavailability of brinzolamide could increase due to brimonidine’s ability to cause vasoconstriction. EX-1007, Dean at 2:57-65.

117. Dean, however, does not address redness reduction, let alone redness reduction in patients with ocular hyperemia. On the contrary, Dean states: “While brimonidine is a relatively safe compound it has been shown to *cause*...ocular hyperemia.” EX-1007, Dean at 2:38-41. Dean acknowledges that “[t]he mechanism by which brimonidine causes hyperemia is not well understood” and speculates that it may be dose related. *Id.*, 2:41-48. Dean never suggests brimonidine could have a beneficial effect on patients with ocular hyperemia.

118. I understand Petitioners and their expert argue that Dean teaches brimonidine can act as a vasoconstrictor and suggests brimonidine as a redness reducer. But there is no support for their inference that all vasoconstrictors, including brimonidine, would be redness relievers at all concentrations. The Federal Register 1988 is a publication of the final rule in the form of a final monograph under which OTC drug products can be generally recognized as safe, effective, and not misbranded. EX-1009 (Federal Register 1988) at 1; EX-2098 (FDA website regarding OTC Drug Review Process). The monograph states that “for ophthalmic vasoconstrictor drug products” (specifically listing four acceptable APIs—not

brimonidine), the labeling should identify the product as a “redness reliever or a vasoconstrictor (redness reliever).” EX-1009, Federal Register 1988 at 5. A POSA would not interpret the monograph to mean that *all* drugs that can vasoconstrict, much less at all concentrations, were known to be useful redness reducers. Indeed, drugs with the potential to vasoconstrict may fail at being a redness reliever due to, for example, efficacy, toxicity, and side effects.

119. Before Lumify, no OTC redness reliever contained a selective α_2 -receptor agonist. *See supra* § VI.B. There was no basis in the prior art to infer that brimonidine—let alone at a single drop of 0.025% brimonidine via a single step—would have been useful to reduce ocular hyperemia. Dean alone or in combination with the Federal Register 1988 does not provide such teaching.

120. In my opinion, a POSA, absent hindsight, would not have picked surgical trauma model references like Norden and Gil or glaucoma treatment references like Dean if their objective was to develop an improved method of reducing ocular hyperemia (due to vasodilation) as presently claimed. In fact, I understand that Petitioners’ definition of POSA requires “ophthalmologist with at least three to four years of experience in clinical trials and FDA regulation of eye products,” who would view the prior art to determine what would reasonably work for purposes of obtaining a commercially approved eye redness reliever. EX-1014, Galanis Decl., ¶ 60; EX-2017, Galanis Jan. 14, 2024 Dep. Tr. at 82:6-84:2.

121. That is consistent with how I would look at the prior art given the invention claimed in the '245 patent. I have been informed that it is also consistent with the law, which, for pharmaceutical inventions, considers the obviousness inquiry from the perspective of a skilled person confronted with the same problems as the inventor, including demands in the relevant market and design community, in developing a commercially viable pharmaceutical therapy—in this case, a commercially viable eye redness reliever.

122. This is confirmed by “state of the art” publications in 2008 describing brimonidine’s uses (not mentioning redness relief at all, and rather highlighting its limitations of use due to allergy), *see* EX-2028 (Fudenberg), and, importantly, by Dr. Gil himself—an industry expert who ran drug re-purposing efforts at the major pharmaceutical company Allergan for years. Indeed, Allergan attempted to repurpose brimonidine *repeatedly* and never considered using it as a redness reliever. *See* Gil ¶¶ 19-24. Notably, Allergan invented (and published) *other* formulations (excluding brimonidine) for use as ocular redness relief. *See* EX-2011, U.S. Patent No. 6,982,079.

123. When developing a new drug product, a POSA would first consider existing drugs approved by the FDA for the particular condition sought to be treated. These existing drugs are referred to as “monographed” drugs, and Federal Register 1988 shows that there were at least four monographed ocular

vasoconstrictors approved for relieving eye redness at the time of the invention—ephedrine hydrochloride (0.123%), naphazoline hydrochloride (0.01 to 0.03%), phenylephrine hydrochloride (0.089% to 0.2%), and tetrahydrozoline hydrochloride (0.01 to 0.05%). EX-1009, Federal Register 1988 at 14. These drugs were already known as potent eye redness relievers because of their high α_1 effects. A POSA would have more logically explored formulation and/or structural modifications to minimize their side-effects while maintaining their efficacy in developing a better eye redness reliever. *See* Gil Decl., ¶¶ 47-52.

124. Notably, even though it was known since the 1970s, brimonidine does not appear on Federal Register 1988 list of vasoconstrictors approved as a redness reliever. That was not a coincidence. Scientifically speaking, brimonidine was known as a highly selective α_2 agonist with minimal ability to trigger α_1 effects, including vasoconstriction of ocular blood vessels. EX-2005, Scruggs 2000 at 5 (“Brimonidine is 23-32-fold more α_2 selective than apraclonidine, and conjunctival blanching has been reported as an infrequent local effect of brimonidine, whereas it is seen in up to 85% of patients using apraclonidine.”); EX-1035, Burke 1996 at 2, Fig. 1; EX-1024, Lachkar 1998 at 3 (“[B]rimonidine tartrate may also produce vasodilation via the α_2 -adrenergic receptors on endothelial cells, which release endothelial-derived relaxing factor.”). Due to this high selectivity for α_2 , prior art taught that brimonidine is the least likely among other selective α_2 agonists,

including apraclonidine and clonidine, to produce an α_1 mediated effect, including vasoconstriction of ocular blood vessels. EX-1035, Burke 1996 at 2 (“These results suggest that compared to clonidine and apraclonidine, brimonidine would be least likely to produce α_1 -adrenoceptor-mediated side effects, such as mydriasis and ocular vasoconstriction”).

125. Brimonidine was approved in 1996 for treating glaucoma and ocular hypertension. But it was known to cause redness—the exact opposite of what the claimed methods were set out to achieve. In the Alphagan clinical studies, ocular hyperemia and ocular allergic reactions were among the most common adverse events for the Alphagan products, which persisted even when the concentration of brimonidine was reduced by half from 0.2% to 0.1%. *See* EX-1067, Alphagan Label at 9-10; EX-1068, Alphagan P Label at 4. As a result, those in the art considered brimonidine’s long-term use to be “limited by its propensity to cause ocular allergic reactions.” EX-2090, Rahman 2010 at 4. Indeed, one of the advantages touted by the ’245 patent for the claimed invention is that it can be used for long term cosmetic purposes or to address chronic eye redness. EX-1001, ’245 patent, 13:12-17.

126. Hyperemia associated with use of glaucoma drugs was, and still remains today, a significant problem. It is one of the most common reasons for noncompliance and discontinuation of glaucoma medication. *See* EX-2095, Bausch Press Release at 1-2. When dealing with a serious disease like glaucoma, many of

the adverse side-effects from brimonidine could be tolerated for the greater cause of preventing blindness. But with nonprescription, OTC redness-reducing products, these side-effects would have disincentivized a POSA from considering brimonidine when looking to develop a better redness reducer. EX-2020, Sher. Dep. Tr. (8/10/2022) at 98:24-100:5 (testifying that OTC redness relievers could be misused). Because OTC products treat a self-diagnosable condition without health care provider's instructions, increasing the potential for misuse and abuse, they must be particularly safe and efficacious. *Id.*

127. To the extent a POSA were considering brimonidine for use of reducing hyperemia to effectuate a whiter eye, which I disagree a POSA would have done, the POSA would not have thought brimonidine—particularly at a claimed dose as low as a single drop of 0.025%—would be effective in light of the fact that even where brimonidine triggered blanching (whitening), it had high rates of ocular hyperemia and ocular allergic reactions. EX-1067, Alphagan 0.2% Label at 9. Clinical data for Alphagan demonstrates that brimonidine generally causes redness (*see* EX-1067, Alphagan 0.2% Label at 9; EX-1068, Alphagan P Label at 4), but at higher doses (0.2% and 0.5%), some incidences of conjunctival blanching were observed as a side effect (*see* EX-1067, Alphagan 0.5% Label at 4 (reporting conjunctival blanching in 50% of patients); EX-1067, Alphagan 0.2% Label at 9 (reporting conjunctival blanching in 3-9%); EX-2005, Scruggs at 5 (“Brimonidine is

23-32-fold more α_2 selective than apraclonidine, and conjunctival blanching has been reported as an infrequent local effect of brimonidine, whereas it is seen in up to 85% of patients using apraclonidine.”); EX-1029, Derick 1997 at 3-5 (stating that “a dose response relation” was shown for brimonidine’s effects on conjunctival blanching, which occurred “more frequently in both the 0.2% and 0.5% treatment groups than in the 0.08% group or the vehicle control group.”)).

128. Thus, a POSA looking to develop a vaso-mediated eye redness reliever would have looked to α_1 agonists or mixed α_1 and α_2 agonists, such as naphazoline, tetrahydrozoline, and oxymetazoline, to maximize the α_1 -mediated vasoconstriction effects on the ocular blood vessels, or considered modifying those compounds in attempt to improve their efficacy and lower side effects. The POSA could have done so by consulting with a pharmacologist and/or chemist, and these would have been considered reasonable paths by the POSA.

129. If a POSA were to look to α_2 agonists at all, the POSA would have considered apraclonidine or clonidine, which are less specific for α_2 receptors than brimonidine, and therefore more likely than brimonidine to produce α_1 -mediated vasoconstriction effects at a concentration as low as 0.025% or could have further modified those compounds. *See also* Stamer ¶¶ 50-72; Gil Decl., ¶¶ 47-52. Moreover, the POSA would have had multiple options and could have consulted with a chemist regarding developing new compounds in line with this task, which

would have opened doors to a huge number of potential compounds. Gil Decl., ¶¶ 47-52.

B. “Consisting of Topically Administering ... an Ocular Drop Consisting of 0.025% [w/v] Brimonidine as the Sole Active Ingredient”

130. In my opinion, Norden, Gil, and Dean, individually or in combination, fail to teach or suggest using a single step administration of brimonidine as the sole active ingredient to reduce eye redness.

1. Norden

131. Norden discloses a multi-step method for assessing “the effect of prophylactic brimonidine on *bleeding complications* and flap adherence after [LASIK] surgery.” EX-1006, Norden at 4. I understand that Petitioners and their experts argue that a POSA would have been motivated to administer brimonidine alone to reduce redness because the “test” and “control” groups in Norden both received the same set of other active ingredients, and because the brimonidine test group showed less “hyperemia.” This is not how a POSA would have viewed the teachings of Norden.

132. The other active ingredients administered in Norden are not part of the set up for a “control” experiment, but rather are *necessary* active ingredients that must be administered for all LASIK surgeries to prevent excruciating pain and dangerous side effects. EX-2018, Sher Jan. 27, 2023 Dep. Tr. at 22:24-23:13

(Petitioners' expert admitting that removing the other ingredients would be malpractice).

133. Norden distinguished three types of bleeding complications common in LASIK surgery—subconjunctival hemorrhage, hyperemia, and superior micropannus. EX-1006, Norden at 6. I agree with Dr. Donnenfeld's opinion that a POSA would have understood that Norden's "hyperemia" is not vasodilative hyperemia as the '245 patent claims, but rather blood leakage or bleeding from the small number of red blood cells in the subconjunctival space (*i.e.*, micro-vessel hemorrhage). Donnenfeld, ¶¶ 50-55; EX-2009, Donnenfeld Hr'g Tr. at 59:20-61:8, 64:11-65:17, 67:13-68:17. I understand that in LASIK patients, micro-vessel hemorrhage can be caused by trauma to the eye by, for example, the blood-vessel-rupturing impact of LASIK surgery that makes the eye appear pink. Donnenfeld, ¶¶ 50-55. Unlike micro-vessel hemorrhages, subconjunctival hemorrhage appears as bright red patches or spots on the white of the eye. *See* § VI.A; *Id.* I agree with Dr. Donnenfeld that this is a clinically relevant distinction that Norden recognizes and records separately. *Id.*; Donnenfeld, ¶ 52.

134. Further, I agree with Dr. Donnenfeld that a POSA would have understood that the reduction in bleeding complications observed by Norden in the brimonidine group (EX-1006, Norden at 6) was due to brimonidine's narrowing of the blood vessels in the eye before surgery. Donnenfeld, ¶ 55. I also agree with Dr.

Donnenfeld's opinion that post-operatively, this resulted in less observable damage to the blood vessels, manifesting either as subconjunctival hemorrhage or micro-vessel hemorrhage (Norden's "hyperemia"). *Donnenfeld*, ¶ 55.

135. Importantly, in my opinion, a POSA would have understood that the observed differences between the "test" and "control" groups in Norden could not have been due to differences in vessel diameter at time of the second examination (at least 12 hours after surgery). Because brimonidine's half-life is 4-6 hours (EX-2009, Dana Hr'g Tr. at 33:21-34:22), by the second examination (2-3 half-lives later), the amount of brimonidine remaining on the ocular surface (and any vasoconstrictive effects) would be far less than the amount taught in the prior art necessary to result in redness reduction. *See infra* § XII.E.1.c (Alphagan Trials); EX-2009, *Donnenfeld Hr'g Tr.* at 60:5-19. In my opinion, this holds true even if the half-life is 6-8 hours as Petitioners and their experts allege. EX-2009, Dana Hr'g Tr. at 33:21-24.

136. Additionally, all patients received the corticosteroid prednisolone—"the single strongest anti-inflammatory drop used in all of ophthalmology"—four times per day for 4 days after surgery. EX-2009, *Donnenfeld Hr'g Tr.* at 60:22-25; *Donnenfeld*, ¶ 58. I agree with Dr. *Donnenfeld* that prednisolone would have unquestionably resolved any vasodilation in both the "test" and "control" groups thus normalizing vessel diameter between the groups (and resolving any true vasodilative hyperemia) at the time of examination. EX-2009, *Donnenfeld Hr'g Tr.*

at 61:25-61:8; Donnenfeld, ¶ 54. I also agree with Dr. Donnenfeld's conclusion that Norden's "hyperemia" must have been micro-vessel hemorrhage because "hyperemia" persisted in both groups, confirming that it is a bleeding complication that can only dissipate over time rather than through a vasoconstrictive agent. EX-2009, Donnenfeld Hr'g Tr. at 61:25-61:8; Donnenfeld, ¶ 54.

137. In my opinion, a POSA would have understood that any difference in redness reduction between the two groups could not be explained by brimonidine's vasoconstrictive effects at the time of the second examination. The fact that differences were observed is consistent with Norden's stated purpose of looking at differences involving bleeding, not hyperemia due to vasodilation.

138. Thus, Norden neither teaches nor suggests a single step of administering brimonidine as the sole active ingredient to reduce eye redness due to ocular hyperemia.

2. Gil

139. Gil is directed to a "method for treating ocular pain." EX-1004, Gil at 1:1, 1:11-13; EX-2016, Gil Hr'g Tr. at 154:12-18. I understand that Petitioners and their experts rely on Examples 1 and 4 of Gil to argue that a POSA would have used brimonidine as the only active ingredient to reduce redness. But they ignore other portions of Gil that undermine their position. Further, both Examples 1 and 4 are prophetic examples and lack data. EX-2014, Galanis Hr'g Tr at 802:16-22. When

viewed in its entirety, a POSA would have had no reason or motivation to modify Gil's teachings to arrive at the claimed invention.

140. Example 1 describes a clinical study that topically administers ***multiple drops of 0.03% brimonidine***—"one drop every four hours while awake one day prior to surgery and again every 20 minutes for the two hours just before surgery." EX-1004, Gil at 4:54-57. This represents about 10 separate administrations of brimonidine (*i.e.*, 10 steps) prior to surgery. Following surgery, each subject also receives one drop of brimonidine every four hours while awake for 14 days (an additional 56 administrations/steps). EX-1004, Gil at 4:58-60. Thus, the method of Example 1 is very different from the single step method of claim 1 of the '245 patent. Moreover, any efficacy assessed, including the evaluation of "pain intensity, pain relief, subjective global analgesic efficacy" using the method of Example 1 (if it had been performed) would fail to provide any motivation or reasonable expectation of success in arriving at the single step method of claim 1. EX-1004, Gil at 4:46-48, 4:53-61.

141. Example 1 is designed to evaluate the effects of administering a high dose of brimonidine on blocking perception of pain, not reducing eye redness. A POSA would have understood that blocking perception of pain by blocking neuronal transmission of pain from ocular *nerves* involves a completely different mechanism of action than constricting ocular *blood vessels* to relieve eye redness. Thus, based

on a prophetic example for which no data were provided and the requirement to administer multiple doses of 0.03% brimonidine to allegedly block perception of pain sensed by nerves, a POSA would not have leaped to the conclusion that a single drop of 0.025% brimonidine could be sufficient to vasoconstrict blood vessels and reduce eye redness.

142. Example 1 of Gil also fails to teach or suggest using brimonidine as the only active ingredient. The hypothetical study of Example 1 relates to the effect of brimonidine following radial keratotomy surgery. EX-1004, Gil at 4:46-48. Radial keratotomy is a predecessor surgical procedure to LASIK that involves cutting the cornea to reshape it and improve vision. Like LASIK, active ingredients besides brimonidine would have been necessarily administered as part of the dosing protocol for radial keratotomy in this study. EX-2013, Galanis PI Decl. at ¶126 (“The patients in Norden and Gil received other drugs as a necessity—the patients were undergoing surgical procedure on their eyes.”). EX-2018, Sher Dep. Tr. (1/27/2023), 15:8-16:18, 17:19-21:8, 23:5-13.

143. Additionally, Gil Example 1 is not a “controlled” experiment designed to evaluate brimonidine’s ability as the only active ingredient to prophylactically reduce pain but rather assesses brimonidine’s ability to relieve surgical pain when administered as part of the dosing regimen with other pain-relieving active ingredients. Given the traumatic surgical context of Example 1, a POSA would not

have expected from Gil Example 1 that administering brimonidine as the only active ingredient would have any meaningful pain reduction effect. Given the example's lack of data, a POSA could not have assessed any additive pain-relieving effect from brimonidine.

144. Nor would a POSA have gleaned from Example 1, or Gil as a whole, that a single administration of brimonidine alone would have reduced eye redness. Because Example 1 seeks to evaluate pain relief, not redness reduction, the only conclusion that the prophetic example draws is that multiple dosing 0.03% brimonidine before surgery, which results in a net administration of brimonidine greater than even a single dose of 0.2%, “appears to suggest that brimonidine administered preoperatively, blocks the perception of pain.” EX-1004, Gil at 5:1-2. Although it states that “[s]ymptoms of ocular inflammation (burning/stinging, tearing, etc.) are also recorded,” it is silent as to what effect, if any, brimonidine had on these symptoms. *Id.*, 4:62-65. A POSA would have understood that “burning and stinging” is not same as ocular hyperemia. *See* EX-2110, Shuman 1997, Table at 5 (listing burning/stinging as a separate ocular adverse event from ocular hyperemia).

145. Likewise, Gil Example 4 fails to teach or suggest using brimonidine as the only active ingredient in a single step method for reducing eye redness in a human subject. Example 4 uses a rabbit model to evaluate the “effect of brimonidine on ocular pain.” EX-1004, Gil at 5:20-21. It describes a surgical procedure involving

cutting ocular tissues, including the conjunctiva and episclera, surrounding the rabbit's eye to expose the ciliary nerve behind the rabbit's eyeball, and connecting a hook electrode to measure nerve signals to external corneal stimuli. *Id.*, 5:25-30; Example 4 postulates a broad dose-ranging study of 0.01% to 0.5% brimonidine—a 50-fold difference in endpoints that encompasses every known brimonidine concentration—to determine brimonidine's ability “to reduce *the* neurogenic response,” *i.e.*, ocular pain from external stimuli. *Id.*, 5:41-45.

146. It is undisputed that the “corneal nerve conduction model” in Example 4 study—which is designed to measure nerve signals, not blood vessels—cannot be performed on humans, evaluates only pain relief, and is incapable of assessing redness reduction, as admitted by Petitioner's own experts. EX-1004, Gil at 5:20-24; EX-2017, Galanis Jan. 14, 2024 Dep. Tr. at 136:21-137:1 (“Q. But you agree that the model itself is not capable of actually making an assessment of whether redness exists or whether it was reduced, correct? A. It measures pain, that's correct then.”); EX-2009, Donnenfeld Hr'g Tr. at 76:25-77:21; EX-2020, Sher. Dep. Tr. (8/10/2022) at 122:6-122:22 (admitting that Example 4 fails to disclose any data validating the corneal nerve conduction model for measuring eye redness.). As such, Gil's unsupported statement that brimonidine “is effective in reducing such neurogenic responses,” without any substantiating data, would not have led a POSA

to reasonably expect that brimonidine alone, particularly at the low concentrations, would have reduced pain or any downstream effects, including redness.

147. Moreover, *no* POSA would have believed that one could measure the level of ocular hyperemia, let alone reduction of ocular hyperemia, in the rabbits studied in Example 4. According to the experimental procedure outlined in Example 4, rabbit eyes are decimated by cutting ocular blood vessels and causing hemorrhage to the point that it is impossible to measure any impact of brimonidine on intact blood vessels. The rabbits are placed under deep anesthesia and a “stereotaxic apparatus” is surgically inserted by cutting the conjunctiva and the episclera, prying open a space in the eye—by physically moving the eyeball in one direction and the retroorbital bone in the other direction—to surgically expose the retroorbital space and place a hook electrode around the ciliary nerve. EX-1004, Gil at 5:25-28. At this point, the ocular blood vessels are severely cut and traumatized that there is no tissue from which hyperemia can be properly evaluated. Then, a chamber is placed on the rabbit’s cornea through which brimonidine is administered, the cornea is stimulated using capsaicin, salt, or fine hairs, and the “resultant nerve traffic from the cornea is recorded.” EX-1004, Gil at 5:31-34.

148. I understand that Dr. Gil agrees with me that Example 4 does not measure eye redness, nor does it teach or suggest that brimonidine can be used to reduce eye redness. EX-2009, Gil Hr’g Tr. at 113:6-113:19 (Dr. Gil testifying that

Example 4 “does not show any effect on redness”). Even if a POSA conducted a study related to brimonidine for pain as described in Example 4, the POSA would not have made the discovery of the ’245 patent. For example, patients included in the study may not have even had red eyes in the first place, so there would have been no redness to reduce; or they could have had ocular responses to brimonidine like hyperemia or allergy, as seen in the clinical data for Alphagan.

149. In my opinion, a POSA would have understood that administering low-concentration brimonidine would have necessitated multiple drops (*i.e.*, ***multiple steps***) to achieve an effective dose for relieving any pain and any pain associated redness. EX-2085, Galanis 10/19/2024 Dep. Tr. at 44:14-45:5. Thus, a POSA would have understood the speculative statement in Example 4 that “[b]rimonidine is effective in reducing such neurogenic responses” is, at most, brimonidine’s hypothesized ability to block nerve signals and relieve the perception of ocular pain, consistent with the purpose of the study. EX-1004, Gil at 5:44-45.

150. Thus, Example 4 neither teaches nor suggests a single step of administering brimonidine as the sole active ingredient to reduce eye redness.

3. Dean

151. Dean fails to teach or suggest topically administering brimonidine as the only active ingredient in a single step for reducing eye redness. Dean is a patent entitled “Brinzolamide and Brimonidine for Treating Ocular Conditions” and is

singularly focused on co-administering brimonidine and brinzolamide, whether in the same or separate eyedrops, for treating ocular diseases such as glaucoma. EX-1007, Dean at 2:21-27.

152. I understand that Petitioners and their experts rely on a statement in Dean that brimonidine “serves to constrict ocular vessels and thereby reducing the flux of blood through the anterior portion of the eye” (EX-1007, Dean at 2:57-60) and argue that a POSA would have understood this to mean that brimonidine reduces eye redness. I disagree. In my opinion, they improperly equate any amount of vasoconstriction with redness reduction without any supporting evidence. The prior art indicates only that high-concentration brimonidine exerts sufficient vasoconstriction to reduce eye redness. *See infra* § XII.E. Dean does not mention anything about using brimonidine to reduce eye redness, nor does it teach or suggest, absent hindsight, that the vasoconstriction effects discussed (EX-1007, Dean at 2:57-60) are sufficient to reduce eye redness, especially when the concentration of brimonidine is lowered below 0.2%, as discussed in § XII.E.1 below. Additionally, Dean teaches away from administering brimonidine alone because its entire inventive concept is the combined therapy of these two IOP lowering drugs to permit lower doses than when administered alone. EX-1007, Dean at 1:4-8, 2:51-54.

153. In fact, Dean would have taught a POSA away from administering brimonidine as the sole active ingredient at the claimed dose of a single drop of

0.025% brimonidine. Dean teaches that if brimonidine's concentration is lowered, then it must be administered with another active ingredient, brinzolamide, to maintain brimonidine's bioavailability to effectively lower the intraocular pressure for treating ocular diseases, such as glaucoma. *Id.* at 2:45-65. If brimonidine is administered alone, Dean teaches administering it at a high concentration of, for example, 0.2%. *Id.* at 5:20-27; 6:57-7:8 (Example 10).

154. To the extent Dean teaches that brimonidine vasoconstricts in the front of the eye but not the back of the eye, in my opinion, a POSA would have understood that reference to have been made with respect to the Alphagan product Dean identified in column 1, lines 20-25, which would have been at a concentration of either 0.2% or 0.5%. Moreover, that Dean states that brimonidine did not appear to vasoconstrict in the back of the eye aligns with brimonidine's ability to vasoconstrict, if anywhere, at high concentrations but not at low concentrations. By the time Alphagan would have reached the back of the eye, it would have had to pass through several layers of ocular tissue and its concentration would have been diminished. Gil Decl., ¶¶ 25-39; Stamer ¶¶ 61-72. At that reduced concentration, Alphagan would not have been expected to vasoconstrict.

155. Accordingly, Norden, Gil, and Dean, individually or in combination, fail to teach or suggest ocularly topically administering brimonidine as the only active ingredient in a single step for reducing eye redness.

4. None of Gil, Dean, or Federal Register 1988 teaches administering a single eyedrop of 0.025% brimonidine for reducing vasodilative hyperemia

156. I understand that Petitioners and their experts argue that the use of 0.025% brimonidine would have been obvious in view of Gil and Dean. I disagree. To begin, they conflate the claimed dose with concentration—overlooking that claim 1 is directed to a dose of a single drop of 0.025% brimonidine, not simply a concentration of 0.025%. Neither Gil nor Dean discloses using 0.025% brimonidine, much less a single drop of 0.025% brimonidine, for reducing ocular hyperemia.

a. Gil

157. Gil teaches the administration of brimonidine to reduce ocular pain, a symptom of neurogenic inflammation. EX-1004, Gil at 1:11-19. Gil notes that other neurogenic responses associated with ocular inflammation and pain may include, though not always, the possible downstream effects of edema, vasodilative-redness, vascular permeability, or pupillary constriction. EX-1004, Gil at 1:40-43, 5:40-41. Gil Example 1 hypothetically proposed evaluating the effects of repeat-dosing brimonidine at a concentration of 0.03% on ocular pain from surgery. EX-1004, Gil at 4:46-48, 4:54-61, 4:66-5:2. The patients received one drop of 0.03% brimonidine “every four hours while awake one day prior to surgery and again every 20 minutes for the two hours just before surgery.” EX-1004, Gil at 4:54-58. Additionally, after

the surgery, the patients were given one drop of 0.03% “every four hours while awake for 14 consecutive days.” EX-1004, Gil at 4:58-61.

158. In my opinion, even if one were to focus on the amount of brimonidine administered before surgery, which is fraction of the total amount of brimonidine administered, the patient would have received 10 drops of 0.03%, which is 12 times greater $[(10 \times 0.03)/0.025]$ than the single drop of 0.025% required by claim 1. Stamer, ¶ 42. Further, a POSA, in my opinion, would have understood that the repeat dosing in Gil is required, given the low concentration of brimonidine, so that the amount of brimonidine is high enough to relieve the pain from serious ocular surgery.

159. Prophetic Gil Example 4’s proposed dose-ranging study of 0.01% to 0.5% brimonidine in a rabbit model to evaluate brimonidine’s effect on ocular pain (EX-1004, Gil at 5:20-21) does not suggest that the entire range would be effective for reducing pain, or even any possible pain-associated redness. Nor would a POSA have expected that all concentrations, particularly the low-concentrations, within a 50-fold range, would have been expected to reduce pain, let alone reduce any sequelae thereof. EX-1004, Gil at 5:31-34. Example 4 hypothesizes, without any supporting data, that brimonidine is effective in reducing neurogenic responses, but it fails to identify what dose, if any, achieves that outcome, nor does it indicate which neurogenic responses are reduced. EX-1004, Gil at 5:31-45. Given the lack of

information in Example 4, a POSA would not have made the numerous unfounded assumptions to conclude that a single drop of 0.025% to be effective in reducing eye redness. In fact, it would have been contrary to a POSA's understanding of brimonidine's mechanism of action as a highly selective α_2 agonist.

160. In my opinion, if low concentrations within the range were selected, a POSA would have instilled multiple drops per application, consistent with Example 1, so that the total dose administered as part of the dosing regimen for a low concentration would at least approach an effective dose of approximately 0.2%. Stamer ¶42.

161. Example 5—which is an actual study conducted based on the protocols described in Example 4—confirms that both Examples 1 and 4 are solely concerned with brimonidine's ability to reduce nerve pain. EX-1004, Gil at 5:49-59. Example 5 states, “[i]n the rabbit neurophysiological model, one records from the primary sensory axons so the results reflect what is occurring at the *sensory receptor* in the corneal epithelium.” *Id.*, 5:59-62. It notably does not mention anything about measuring the changes in blood vessels using the model. Moreover, Example 5 of Gil used *1 cc* of 0.2% brimonidine (Alphagan) to test its efficacy on decreasing “sensory response” in the rabbit cornea to reduce ocular pain. EX-1004, Gil at 6:5-7, 6:9-13. In my opinion, a POSA would have understood that 1 cc, which is equivalent to 1 mL, contains about 20-30 drops of Alphagan, (0.2% brimonidine per

drop), which is a significantly higher dose than a single drop of 0.025% brimonidine. Thus, in my opinion, Example 5 confirms that a high dose of brimonidine, whether through administering a highly concentrated drop or administering multiple drops, is needed to reduce ocular pain, including any symptoms associated with pain, like redness.

162. Moreover, notwithstanding the broad range disclosed in Example 4, the use of copious amounts of high-concentration brimonidine (Alphagan 0.2%) in Example 5 (EX-1004, Gil at 6:5-13), would have conveyed to a POSA that, if a low concentration is selected from the range, multiple drops would have been needed. Gil, ¶¶ 45-46. This is all a POSA could have concluded from an animal model acknowledged by all experts to be incapable of assessing redness or its reduction and in a patent primarily focused on ocular pain relief. EX-2017, Galanis Jan. 14, 2024 Dep. Tr. at 125:9-14, 136:21-137:1; EX-1004, Gil at 2:53-55 (“The present invention is based on the unexpected finding that brimonidine efficiently relieves ocular pain....”)

b. Dean

163. It is my opinion that Dean likewise fails to teach or suggest using a single drop of 0.025% brimonidine for reducing eye redness.

164. In my opinion, Dean does not teach using brimonidine to reduce redness, much less in a person with ocular hyperemia. EX-2014, Galanis Hr’g Tr at

784:23-25. Dean does not provide any evidence that any of its brimonidine formulations, whether alone or combined with brinzolamide, cause sufficient vasoconstriction to reduce redness. *Id.* at 784:23-25. As discussed below in Section XII.E.1, from brimonidine's human clinical trial data available at the time, a POSA would have had no reasonable expectation that reducing the dose of brimonidine below 0.2%, let alone a single drop of 0.025% brimonidine, would have reduced eye redness. Thus, in my opinion, Dean neither teaches nor suggests dosing a single drop of low-concentration brimonidine.

165. Dean teaches co-administering two known IOP lowering drugs, brimonidine and brinzolamide, to treat glaucoma. EX-1007, Dean at 1:11-25. Dean states that this “represent[s] a novel approach to producing potent and long lasting IOP lowering medications,” which allows lower amounts of the drugs to be dosed “with fewer side-effects than observed when these [IOP-lowering drugs] are administered alone.” *Id.*, 2:51-54. Dean devotes a paragraph (EX-1007, Dean at 2:33-50) to solely discuss brimonidine, including its primary IOP efficacy and its side-effects. Dean notes that brimonidine causes hyperemia, though why it does is not well understood, and merely speculates that it may be dose related. EX-1007, Dean at 2:45-48. Notably, it concludes with respect to brimonidine that “lowering the overall dose of brimonidine *while maintaining IOP control* would be advantageous.” EX-1007, Dean at 2:48-50. A POSA would have understood that

Dean suggested lowering brimonidine's dose to lessen its side-effects, but not so low that it would eliminate brimonidine's primary purpose of exerting an IOP controlling effect.

166. I understand that Dr. Galanis has acknowledged that low-concentration brimonidine (*e.g.*, <0.05%) would not have been expected by POSAs to lower IOP. EX-2085, Galanis Oct. 19, 2024 Depo at 44:14-45:5. Relatedly, Dean teaches ocularly applying 1-3 drops of brimonidine 1-4 times/day. EX-1007, Dean at 5:20-27. Based on the natural constraint imposed by Dean to administer brimonidine at an amount that would maintain its important ability to control IOP, a POSA would have known that low-concentration brimonidine within the broad range of 0.01% to 0.2% would have required multiple drops of brimonidine. Dr. Galanis further testified that a single drop of less than 0.1% brimonidine might not have been expected to lower IOP. EX-2085, Galanis Oct. 19, 2024 Dep. Tr. at 44:14-45:5. That, of course, would have led the POSA when dosing brimonidine alone to formulate the drop in Dean's preferred range of 0.1% to 0.2%. Thus, a POSA would not have been motivated from Dean to administer a single drop of 0.025% brimonidine in a single ocular administration.

c. Federal Register 1988

167. Though brimonidine was known in 1988, the Federal Register 1988 does not mention using it as an ophthalmic vasoconstrictor or redness reliever. It

lists only ephedrine, naphazoline, phenylephrine, and tetrahydrozoline as vasoconstrictors for eye redness relief, none of which is an α -2 agonist like brimonidine. EX-1009, Federal Register 1988 at 14. I understand that Petitioners and their experts argue that the concentrations of *non-brimonidine* vasoconstrictors disclosed in Federal Register 1988—each with necessarily different pharmacologic profiles—would somehow have rendered the claimed dose of a single drop of 0.025% brimonidine for eye redness obvious. The vasoconstrictors in the Federal Register 1988 monograph were all α 1 and/or mixed α 1/ α 2 agonists, and their high α 1 effect made them effective redness relievers. *See* Table 1 above. But a POSA would not have interpreted the monograph to suggest that the highly selective α -2 agonist brimonidine, particularly at a single drop of 0.025% in a single step, would have been expected to exert sufficient vasoconstriction to reduce redness.

C. “Wherein the Ocular Hyperemia Is Reduced [by Administering a Single Drop of 0.025% Brimonidine]”

168. I understand that Petitioners and their experts argue that this efficacy limitation would have been obvious because it is an inherent property of the claimed method. I disagree.

169. I have been informed that a property is inherent if the property inherently and unavoidably flows from practicing the prior art. As explained above, none of Norden, Gil, or Dean, whether alone or in combination, inherently disclose

achieving actual redness reduction by administering a single drop of 0.025% brimonidine in a single step.

170. In fact, the prior art teaches the opposite. At 0.2% brimonidine, the Alphagan studies demonstrated that only 3.5% of patients experienced redness reduction, and at 0.15% and 0.1% brimonidine, none did. *See* § XII.E.1 below. And the Alphagan studies also confirmed that concentrations in these ranges actually cause redness. *Id.*

D. “One or More Non-Therapeutic Components Including Benzalkonium Chloride, Wherein the Ocular Drop Has a pH Between 5.5 to 6.5”

171. The art taught away from using BAK in an ophthalmic redness reliever, as it was known to be toxic and poorly-tolerated. A POSA would have been discouraged from using benzalkonium chloride (“BAK”) as a preservative in an ophthalmic formulation for reducing eye redness. Given the evolution of the art with preserved brimonidine products and the intended use of this invention, the art taught away from use of BAK in favor of gentler preservatives like Purite (among many other options). In general, BAK is considered a disfavored preservative—it is known to cause increased IOP, hyperemia, dry eye, and damage to corneal cells, and to exacerbate other eye disorders. EX-2042, Noecker 2001 at 1, 9 (stating that SOC, for example, is “a new generation of ophthalmic preservative that breaks down into natural tear components on instillation and thus has low potential to cause toxic

effects” compared to BAK, which “has demonstrated cytotoxic effects in cell culture, as well as in animal and human studies”). Where the prior commercial brimonidine formulations evolved from use of BAK to use of Purite (a gentle preservative), a POSA would have questioned reintroducing BAK into the equation, in particular, in a redness-relieving drop, where early, higher-dose brimonidine formulations containing BAK had high levels of hyperemia as a side effect—the state of the art in 2008 for a drop of this use would have discouraged the POSA from using BAK.

172. Regarding pH, a POSA would have known that physiological pH (i.e., ~7.4, around that of the newer brimonidine products) is “desirable” to avoid ocular side effects like irritation, burning, stinging, and—crucially—redness. Thus, particularly for a redness-relieving product, a POSA would have wanted to avoid both the claimed pH and claimed preservative (let alone the combination of the two), as both were known to *cause* eye redness, contravening the purpose of the invention.

173. As a general matter, a POSA would have recognized that it is preferable to formulate an ophthalmic product at or around the physiological pH (~7.4) to prevent burning and stinging that can initiate a blink reflex and wash brimonidine out of the eye. EX-1066, Agarwal at 2. When the pH of a formulation is further away from the physiological pH, the likelihood of eye irritation increases. For example,

an eye drop with an acidic pH (i.e., below pH 7) will often cause burning and stinging or redness.

174. The evolution of the Alphagan products further confirms this. Despite having a lower concentration of brimonidine, the Alphagan P products demonstrated comparable efficacy. A POSA would understand that this is attributable, at least in part, to the pH—the pH for the Alphagan P products was closer to the pKa (~7.78), so brimonidine was able to more readily permeate and reach its site of action. Thus, if a POSA were motivated to use brimonidine at 0.025% for reducing eye redness, which the Petitioners have not established, a POSA would have targeted, if anything, a pH above 7 (and close to physiological pH) to facilitate maximum penetration, for example, past the tear film and to the episclera and sclera.

E. No Reasonable Expectation of Success Administering a Single Drop of 0.025% Brimonidine to Reduce Ocular Hyperemia

175. As discussed above, a POSA, in my opinion, would not have been motivated by the asserted prior art, absent hindsight, to administer in a single step a single ocular drop of 0.025% brimonidine as the sole active agent to reduce eye redness caused by vasodilation with any reasonable expectation of success.

176. I understand that Petitioners and their experts argue that the “overlapping ranges” from Gil and Dean would have made it presumptively obvious to administer 0.025% brimonidine for reducing eye redness. I disagree. On the contrary, in my opinion, the prior art as whole taught away from a single

administration of a single drop of 0.025% brimonidine, and the invention enjoys significant objective indicia of non-obviousness, as discussed below.

1. Prior Art Taught Away from a Single Administration of a Single Eyedrop of 0.025% Brimonidine

177. From Gil, Norden, the Alphagan clinical studies, and Derick 1997, a POSA would have understood that the minimum effective dose needed to reduce ocular hyperemia would correspond to approximately 0.2% brimonidine, teaching away from administering a single drop of 0.025% brimonidine (*i.e.*, 1/8 of the minimum effective dose).

a. Gil and Norden

178. Even if Gil and Norden taught brimonidine could reduce ocular hyperemia (and in my opinion they do not), the amount of brimonidine reportedly used was an order of magnitude higher than the single drop of 0.025% of claim 1. For example, as explained in § XII.E.1.a, Gil repeatedly administers 0.03% brimonidine “every four hours while awake one day prior to surgery and again every 20 minutes for the two hours just before surgery.” EX-1004, Gil at 4:54-58. Thus, the amount of drug administered is equivalent to a single drop of about 0.2% brimonidine (6-7 drops x 0.03%), assuming that counts only the doses for the two-hour period prior to surgery. EX-2009, Dana Hr’g Tr. at 33:21-34:22. As discussed in § XII.E.1.a, Norden teaches a dose of approximately 0.4% (0.2%, administered twice within 10 min period) to prevent bleeding complications from LASIK surgery.

179. Thus, a POSA before August 1, 2008 would have had no reasonable expectation that lowering the dose administered in the multi-step studies of Norden and Gil to a single application of a single drop of 0.025% brimonidine would have reduced eye redness in view of its pharmacology. The prior art as a whole, including the human clinical studies reported for the Alphagan products and in Derick 1997, directed POSAs to significantly higher concentrations to obtain sufficient vasoconstriction to actually reduce redness.

**b. Pharmacology of Brimonidine Would Have
Counseled a POSA Against Lowering the Dose of
Brimonidine**

180. Even if a POSA were to pursue brimonidine as a redness reliever, which the POSA would not have done for at least the reasons discussed herein, the POSA would have, if anything, kept the concentration of brimonidine high enough to obtain α_1 -mediated vasoconstriction effects, but the POSA would have had no reasonable expectation of success of achieving a viable redness reliever using brimonidine.

181. While brimonidine is a highly selective α_2 agonist, it was known that brimonidine can elicit α_1 -mediated effects, such as vasoconstriction, when its concentration is sufficiently high, for example 0.5% or above. EX-2003, Derick 1995 at 1 (selective α_2 agonists at higher therapeutic concentrations will “produce[] conjunctival blanching, which is an α_1 effect.”). It was also known that brimonidine’s ability to mediate α_1 effects, including its ability to cause conjunctival blanching

(*i.e.*, whitening), is observed only at high concentrations, for example, 0.5% or above. *Id.* For example, the label for Alphagan 0.5% indicates that brimonidine at 0.5% triggered conjunctival blanching in 50% of subjects. EX-1067, Alphagan 0.5% Label at 4. When the concentration of brimonidine was reduced to 0.2%, brimonidine's ability to reduce eye redness was significantly compromised, exhibiting conjunctival blanching only in 3-9% of subjects while triggering ocular hyperemia (eye redness) in 10-30% of subjects. EX-1067, Alphagan 0.2% Label at 9.

182. Brimonidine is highly specific for α_2 receptors, so when brimonidine's dose is low (*e.g.*, a single drop of 0.025%), brimonidine will predominantly interact with α_2 receptors without any α_1 activation and thus a POSA would have understood that vasoconstriction, and certainly sufficient vasoconstriction to reduce redness, would be highly improbable. *See* EX-1023, Robin 1998 at 2 ("The degree of selectivity is only important if tissue concentrations are within the range required for α_1 activity. If tissue or circulating levels of drug are insufficient to produce α_2 effects, then α_1 effects are highly improbable."); *see also* Stamer, ¶¶ 50-72; Gil Decl., ¶¶ 25-39. Thus, if the concentration was lowered to reduce the α_2 effect associated with vasodilation and hyperemia, one would not expect any α_1 effect and redness reduction.

183. When brimonidine's concentration is at, for example, 0.2%, brimonidine begins to interact with α_1 receptors, triggering some α_1 -mediated vasoconstriction effects in subjects' eyes as suggested by conjunctival blanching, albeit still causing redness/allergy. *See id.*; EX-1067, Alphagan 0.2% Label at 9. When the concentration of brimonidine is even higher, for example, 0.5%, brimonidine triggers more consistent α_1 -mediated vasoconstriction effects, with blanching reported in 50% patients. EX-1067, Alphagan 0.5% Label at 4. As a result, brimonidine's ability to vasoconstrict was known to exist, if anywhere, only at high concentrations, with lower doses only causing redness without any reported vasoconstrictive effects. Thus, a POSA would have known that if brimonidine was ever going to work as an eye redness reliever, with which I disagree, the POSA would have used a *high* dose of brimonidine rather than *low*. This is consistent with the pharmacology of the molecule as explained by Drs. Stamer and Gil, and is consistent with the contemporaneously reported clinical studies, e.g., on Alphagan. *See* Stamer Decl. ¶¶73-83; Gil Decl., ¶¶ 25-39.

184. Dr. Galanis argues that Robin (EX-1023) would have motivated a POSA to use a selective α_2 agonist to reduce eye redness. EX-1014, Galanis Decl., ¶139. I disagree. As I explained earlier, Robin is entirely consistent with my opinion that a POSA would have targeted α_1 activation for vasoconstriction. EX-1023, Robin at 2 ("If tissue or circulating levels of drug are insufficient to produce α_2 effects, then

$\alpha 1$ effects are highly improbable.”). Moreover, as I explained above, Dr. Galanis’ reliance on Robin regarding the ability of brimonidine and apraclonidine to trigger vasoconstriction in the anterior segment is unsupported because the Zhan abstract, which Robin relies on for this statement, does not support it. In fact, Zhan did not even evaluate the conjunctiva, which Dr. Galanis calls “the most important targets for reducing eye redness because they are the most visible.” EX-1014, Galanis Decl., ¶140; EX-2102, Zhan at 3.

c. Alphagan Trials

185. In a clinical study of about 250 patients to evaluate the effectiveness of 0.5% brimonidine to reduce IOP, conjunctival blanching was observed at a rate of about 41% (in 183 patients). EX-1032, David 1993 at 2. In another clinical study in Alphagan’s NDA submission further confirms that 0.5% brimonidine exhibited “[s]ignificantly greater incidences of conjunctival blanching,” which its label confirms at 50%. EX-1030, Alphagan NDA at 13, Study S342-108-8042; EX-1067, Alphagan 0.5% Label at 4. When brimonidine’s concentration was lowered to 0.2%, the rate of conjunctival blanching sharply dropped to 6.8% while the incidence of ocular hyperemia increased to 10-30%. EX-1030, Alphagan NDA at 52. When the concentration was lowered further (0.15% and 0.1%) in Alphagan P, no conjunctival blanching was observed, although the incidence of hyperemia remained high. *See* EX-1068, Alphagan P Label at 1, 4 (conjunctival blanching not listed as an adverse

event). In my opinion, these data demonstrate brimonidine's dose-dependent effects on conjunctival blanching (redness reduction) and would have conveyed to a POSA that a minimum effective dose of brimonidine for reducing eye redness was approximately 0.2%.

186. A POSA would have been motivated to keep brimonidine's dose high ($> 0.2\%$), so that more of it can reach the deeper layers of the eye, such as the sclera and the episclera, to attempt to achieve vasoconstriction effects. Thus, even if a POSA were to combine Gil and Norden, which Petitioners have not established, a POSA would have known he needed to keep the concentration of brimonidine high, e.g., near or above 0.5%, to achieve redness reduction, but such high doses would be problematic for other reasons (like brimonidine-induced allergy and other side effects like sedation and cardiac issues), thus closing the door on brimonidine as a viable option. I understand that Dr. Gil will further opine on this issue, as a skilled person who actually worked on brimonidine in the relevant timeframe and sought to create other novel molecules when faced with certain negative side effects of brimonidine.

i. Conjunctival blanching means redness reduction

187. In my opinion, conjunctival blanching refers to any redness reduction. The Alphagan studies, as explained below, would not have led a POSA before

August 2008 to expect low-dose brimonidine to cause sufficient vasoconstriction to reduce redness.

188. I understand that Petitioners and Dr. Dana argue, without any supporting evidence, that conjunctival blanching is “not synonymous with vasoconstriction,” and it is a “dangerous adverse event” causing “significant whitening of the eye, which can lead to damage of vascular endothelial cells caused by lack of blood flow.” EX-1012, Dana Decl., ¶ 50. I disagree.

189. Petitioners’ own prior art reference, Federal Register 1988 (EX-1009), teaches that conjunctival blanching is any redness reduction in the eye. Specifically, Federal Register 1988, which is the FDA’s final monograph for OTC ophthalmic drug products, states that “redness is a symptom of irritation which can be relieved by a vasoconstrictor,” and the “action of a vasoconstrictor when applied to the surface of the eye is described in the literature as blanching, bleaching, and whitening of reddened conjunctiva.” EX-1009, Federal Register 1988 at 9. In my opinion, a POSA would have understood this statement to describe blanching as the method by which a redness reliever whitens the conjunctiva, assuming sufficient vasoconstriction to achieve blanching/whitening of the eye. The ’245 patent uses “whitening” as another way of describing redness reduction. EX-1001, 6:64 (“visibly effective whitening”), 14:23-39 (“more effective scleral whitening); Example 1 (“whitening brightening effects” with brimonidine).

190. Contrary to Petitioners' and Dr. Dana's argument, the FDA's monograph does not state anywhere that conjunctival blanching is such "significant" whitening to the point it causes ocular damage. Instead, conjunctival blanching is simply "an $\alpha 1$ -effect" (EX-2003, 1), which is the same effect exerted by $\alpha 1$ -agonist, tetrahydrozoline, discussed in the Federal Register 1988. EX-1009, Federal Register 1988 at 9.

191. In fact, the product monographs for both Alphagan and Alphagan P note that "[c]onjunctival blanching was observed primarily at the 0.35% and 0.5% concentrations and was generally mild or moderate in nature," further confirming that conjunctival blanching would not have been considered "a potentially dangerous adverse event." EX-2108, Alphagan Monograph 12; EX-2107, Alphagan Patient Leaflet at 2 ("whitening of the see-through layer which covers the surface of the eye"). Indeed, had it been so dangerous, the FDA would have pulled Alphagan from the market, based on my experience as a clinical investigator, including for the Alphagan trials. In fact, the Alphagan NDA indicates that no subjects were discontinued due to blanching, confirming that the blanching was not severe or worrisome. EX-1030, Alphagan NDA at 129.

192. Furthermore, in the '142 IPR, Slayback and its experts relied on Scruggs 2000 (EX-1023, 671) to equate blanching with whitening as motivation to use brimonidine to reduce redness. EX-2023, Laskar '142 IPR Decl., ¶93; EX-2022,

Sher '142 IPR Decl., ¶99; EX-2021, '142 IPR Pet., 20. Scruggs unequivocally teaches that “*conjunctival blanching* has been reported as an infrequent local effect of brimonidine.” EX-2005, Scruggs at 5. Dr. Laskar in fact unequivocally admitted that Scruggs is not limited to skin blanching but also teaches brimonidine “blanches, *i.e.*, whitens” the conjunctiva. EX-2040, Laskar Oct. 29, 2024 Dep. Tr at 53:20-54:13; EX-2023, Laskar '142 IPR Decl. ¶93.

**ii. Once Observed in the Alphagan Studies,
Conjunctival Blanching Would have been
Monitored and Reported if Observed in the
Alphagan P Studies**

193. Once an ocular surface event is observed for a drug in a clinical trial, it will be recorded and monitored going forward, even in future trials of the drug at different concentrations. EX-2008, Dana Jan. 12, 2024 Dep. Tr. at 116:13-117:15. I understand that Federal regulations require observing and reporting the frequency of potential adverse effects of FDA-approved drugs like Alphagan. *See* 21 C.F.R. §201.57(a)(11)(i); Karst Decl. ¶¶ 64-68, 88-94. This is particularly true for ophthalmic drugs for glaucoma patients for whom any change on the ocular surface must be monitored carefully to avoid dangerous effects.

194. Because conjunctival blanching was observed at concentrations of 0.5% and 0.35% (EX-2108, Alphagan Monograph at 12), the clinical investigators monitored and reported that Alphagan 0.2% caused conjunctival blanching in 3.8%

of patients. EX-2108, Alphagan Monograph at 8-9, Table 2. Table 2 indicates that it reports adverse events occurring in $\geq 1\%$ with Alphagan. *Id.*

195. The product monograph for the Alphagan P trials states that conjunctival blanching was observed at concentrations of 0.5% and 0.35%, indicating to a POSA that the investigators would have been monitoring patients for conjunctival blanching. EX-2108, Alphagan Monograph at 12. But none was reported, EX-2119, Alphagan P Monograph Table 2, 8-9, even though the table indicates that adverse events “[o]ccurring at $\geq 1\%$ with Alphagan P” would have been reported. *See also*, EX-1068, Alphagan P Label at 6. And, in fact, conjunctival blanching is not mentioned for adverse events reported in less than 1% of patients. *Id.* From the lack of reporting of conjunctival blanching for Alphagan P, POSAs would have understood that 0.15% brimonidine did not sufficiently vasoconstrict to reduce eye redness. These data would have also confirmed for POSAs that the minimum effective dose of brimonidine for reducing ocular hyperemia would have corresponded approximately to 0.2%. Thus, in my opinion, a POSA would have concluded that if it were observed in the Alphagan P studies, it would have been reported.

196. I understand that the Board dismissed the conjunctival blanching data in the Alphagan studies as “subjective.” As a clinical investigator who was involved in the Alphagan studies, I strongly disagree that a POSA would disregard the

conjunctival blanching data collected in clinical studies for FDA submission simply because it was subjectively evaluated by clinical investigators.

197. The conjunctival blanching data in the Alphagan labels and the NDA were collected from robust randomized, double-masked, and bilateral clinical studies designed for FDA approval—the “gold standard” for reliability in clinical trial studies. EX-1075, Alphagan Medical Review at 63 (the Alphagan Medical Review described the study as “a well-controlled, randomized, clinical trial”). These studies had a well-established protocol, which the FDA requires the clinical investigators to follow to minimize subjectivity and variability between the investigators. Before the study began, the clinical investigators would have met to develop protocols, including which adverse events to record and how to record them to ensure consistency and reliability in evaluating the measurements among investigators. EX-1075, Alphagan Medical Review at 63 (“[t]he methods and ophthalmologic tests used and their frequency were adequate to effectively monitor the subject population”).

198. As the Alphagan NDA indicates, the study protocol for monitoring and recording adverse events, including conjunctival blanching, began with an initial visit to determine a baseline for the adverse event, and subsequent evaluations for changes from baseline were measured using a scale. EX-1030, 53 (“Adverse Events: Number and Percentage of Subjects with *at Least One Severity Grade Increased*

from Baseline at One or More Follow-up Visits.”). The Alphagan NDA lists “Conjunctival Blanching” as one of the adverse events observed, which was “graded for severity (*trace, mild, moderate, or severe*).” EX-1030, Alphagan NDA at 119. Importantly, the baseline measurements and subsequent evaluations and grading of the adverse events were made and recorded by highly experienced ophthalmologists who would have been well-familiar with all the study’s protocols, thereby minimizing variability and ensure reliability of the collected data among the clinicians. EX-1075, Alphagan Medical Review at 63 (“The applicant’s evaluation of potential adverse effects for this pharmacological class of drug is adequate”).

199. An independent auditor would have monitored and checked the collected data from different investigators to ensure further accuracy and consistency, and then a statistician would have performed statistical analysis of the data before submitting it to the FDA. The FDA reviewed all the data, including the safety data, and approved the information to be included a package insert. EX-1075, Alphagan Medical Review at 38 (“Compliance with Good Clinical Practices” states “[a]ll trials were conducted under the review of approved Institutional Review Board committees”). Thus, the adverse events data identified on Allergan FDA-approved labels are highly reliable data, collected from well-controlled robust human clinical trials. EX-2008, Dana Jan. 12, 2024 Dep. Tr. at 108:20-122:11, 124:6-19.

d. Derick 1997

200. Derick 1997—a randomized, double-masked, bilateral, placebo-controlled dose-response clinical study published in the highly regarded peer-reviewed journal of *Ophthalmology*—further confirms brimonidine’s dose dependency for reducing eye redness. Derick found that “[c]onjunctival blanching was observed to occur more frequently in both the 0.2% and 0.5% treatment groups than in the 0.08% group or the vehicle control group,” leading the authors to observe a “dose response relation” for conjunctival blanching. EX-1029, Derick 1997 at 4-5 (“Not only was a *dose response relation shown for* the ocular hypotensive effects of brimonidine, but also for the effects on ... *conjunctival blanching*”). Indeed, the incidence of conjunctival blanching at 0.08%—still more than 3-times the dose of a single drop of 0.025% brimonidine—was effectively no better than the placebo-established-floor. *Id.* Hence, a POSA, in my opinion, would have understood that a dose higher than 0.08%, and likely at least 0.2% as reported in the Alphagan studies, would be required to observe redness reduction resulting from the administration of brimonidine, and, importantly here, a POSA would not have expected that if the dose was decreased, it would have induced sufficient vasoconstriction to reduce eye redness. EX-1029, Derick 1997 at 4-5.

201. This observation makes sense given brimonidine’s 1000:1 α_2 to α_1 selectivity. And even if the concentration of brimonidine was lowered to minimize

its α_2 effect to vasodilate blood vessels, the prior art taught that that would correspondingly make its α_1 effects (redness reduction) highly improbable. EX-1023, Robin 1998 at 2 (“If tissue or circulating levels of drug are insufficient to produce α_2 effects, then α_1 effects are highly improbable.”).

202. Given the collectively consistent observations in these clinical study reports, coupled with the other teachings in the prior art supporting brimonidine’s ability to ocularly vasoconstrict at high concentrations, a POSA would not have had any reasonable expectation that dropping the dose of brimonidine all the way to a single drop of 0.025% would trigger sufficient α_1 -mediated vasoconstriction effects to achieve redness reduction.

203. I understand the Petitioners and Dr. Galanis argue that a POSA would have been motivated to decrease the concentration of brimonidine to minimize its ability to lower the IOP in patients. EX-1014, Galanis Decl., ¶ 85. I disagree. Administering a brimonidine eyedrop would not lower the IOP below a normal IOP range due to the episcleral venous pressure, which would act as a biological safety net to prevent or buffer the IOP from dropping below the normal range. Their argument is hindsight driven because there is no point in reducing the concentration to avoid these unwanted effects when doing so would have eliminated brimonidine’s ability to achieve what they seek, that is, reduction of eye redness.

F. Petitioners Failed to Establish that Claim 8 of the '245 Patent Would Have Been Obvious

204. Like claim 1, claim 8 of the '245 patent requires “[a] method for reducing eye redness in a human subject having ocular hyperemia” (§ XII.A), a pinpoint concentration of “0.025% weight by volume of brimonidine” (§ XII.B), “wherein the ocular hyperemia is reduced” (§ XII.C), “a pH between 5.5 to 6.5” and “benzalkonium chloride” (§ XII.D) none of which is taught or suggested in Petitioners’ prior art.

G. Petitioners Failed to Establish That Challenged Dependent Claims Would Have Been Obvious

205. In my opinion, Petitioners’ obviousness arguments regarding the dependent claims of the '245 patent necessarily fail because it has failed to establish that their prior art references render the independent claims obvious.

1. “wherein the ocular drop induces a low incidence of rebound hyperemia in the eye of the human subject administered the ocular drop.”

206. Claims 2, 4-7 and 9, 11-14 of the '245 patent recite “wherein the ocular drop induces a low incidence of rebound hyperemia in the eye of the human subject administered the ocular drop.” Norden, like Gil, is entirely silent on whether the administration of 0.2% brimonidine induced low incidence of rebound redness. If anything, a POSA would have expected 0.2% to have induced a high incidence of rebound redness based on brimonidine’s propensity to cause hyperemia. *See* Section

XII.E.1.b; *see also* EX-2005, Scruggs at 671 (“Although brimonidine is almost 1000-fold more selective for the α_2 than the α_1 receptor subtype, its ability to cause vasoconstriction and reactive hyperaemia demonstrates that it has some α_1 mediated effects.”).

2. “wherein the eye redness of said human is not associated with an ocular disease or the result of a surgical procedure on the eye”

207. Claims 4, 7, 11, 14-15, 17, 20, and 22 of the '245 patent recite “wherein the eye redness of said human is not associated with an ocular disease or the result of a surgical procedure on the eye.” All parties agree that any eye redness disclosed in Norden is due to LASIK surgery and any eye redness disclosed in Gil is due to RK surgery (Example 1) or stereotaxic surgery (Example 4). Dean does not even mention eye redness, let alone using brimonidine for relieving ocular hyperemia. *See* § XII.B.3.

3. “wherein the method retains normal intraocular pressure in the eye of the human subject administered the ocular drop”

208. Petitioner’s prior art references, individually or in combination fail to teach or suggest this element. Norden and Alphagan fail to satisfy this element because they disclose administration of 0.2% brimonidine (two drops of 0.2% brimonidine in the case of Norden), which is a glaucoma medication that is indicated for lowering intraocular pressure. EX-1006, Norden at 4; EX-1067, Alphagan Label at 7. Gil also fails to satisfy this element because it discloses repeat-dosing 0.03%

brimonidine to reach a dose equivalent to a single drop of 0.2% brimonidine, which is indicated for lowering IOP. *See supra* § XII.E.1.a. Dean is directed to a combination of brimonidine and brinzolamide to treat “ocular diseases which have their etiology in compromised blood flow” such as glaucoma. EX-1007, Dean at 2:22-27. As such, Dean teaches against lowering the dose of brimonidine to the point that it would lose its ability to reduce intraocular pressure, which is the whole point of the invention. *Id.*, 2:47-50. Federal Register 1988 does not even mention brimonidine, let alone retaining normal intraocular pressure.

4. “wherein the ocular drop reduces redness in the eye to which the ocular drop was administered to improve the aesthetic appearance of said eye”

209. None of Norden, Gil, Alphagan, Dean, and Federal Register 1988 teaches or suggests the methods in claim 1 or 8.

XIII. Objective Indicia of Non-obviousness

210. I understand that the obviousness analysis must avoid hindsight reasoning. Objective indicia of nonobviousness must be considered as a part of the obviousness analysis to safeguard against hindsight reasoning. I understand that objective indicia may often provide the most probative and cogent evidence of non-obviousness in the record.

211. As explained below, it is my opinion that Lumify, which embodies the claimed methods in the '245 patent, demonstrate numerous objective indicia of non-

obviousness, including unexpected results, industry praise, and copying for the reasons explained below. I understand Mr. Jarosz will opine on how Lumify enjoyed commercial success.

212. Furthermore, in my opinion, as discussed above, the art as a whole taught away from using brimonidine as a redness reliever, particularly at the claimed dose of a single drop of 0.025%. *See* Section XII.B. As further discussed above, the Alphagan clinical studies showed that although brimonidine can cause conjunctival blanching at high doses, it also causes ocular hyperemia and ocular allergic reactions. *Id.* Moreover, as discussed above, BAK was known to irritate the eye and exacerbate redness, which would have further led a POSA away from the claimed invention. *See* Section XII.D; EX-2042, Noecker 2001.

1. Unexpected Results

213. In my opinion, Lumify has unexpectedly superior results compared to the closest prior art—prior art redness relievers on the market at the time of the invention.

a. Closest Prior Art

214. I understand that to determine whether a claimed invention exhibited unexpected results, those results must be compared against the closest prior art. In my opinion, the closest prior art for comparison purposes would have been against the closest commercial redness reliever in the prior art. These products were the standard

for redness reduction that all new redness relievers would have been compared against. I understand that showing superior redness reduction to these market leaders would have objectively indicated the inventiveness of a new redness reducer and significantly contributed to the art of ophthalmic decongestants as a whole.

215. In my opinion, the closest prior art would have been a specifically disclosed method of reducing redness administering a single drop of a redness reliever active ingredient as the sole active ingredient as the only step for reducing eye redness. That would necessarily disqualify Example 1 of Gil because it is not directed to a method of reducing eye redness but instead to a method of reducing pain by repeatedly dosing 0.03% brimonidine to the point that it reaches a dose close to 0.2%. It also does not administer brimonidine as the sole active, necessarily co-administering it with other actives like anesthetics and even NSAIDs and steroids. The same is true of Norden. It co-administers two drops of 0.2% brimonidine, which is equivalent to a drop of 0.4%, with other active ingredients.

216. Petitioners and Dr. Galanis argue that the closest prior art would have been Gil because it discloses administering low concentration brimonidine. EX-1014, Galanis Decl., ¶ 148. I disagree. It is inaccurate and improper to reduce the '245 patent claims to "administering low concentration brimonidine" ignoring other elements recited in the claims. As explained earlier in Sections XII.B.2 and XII.B.4.a, Gil fails to teach several elements of the '245 patent claims, including the

preamble, which sets forth the essence of the invention—a method for reducing eye redness. In my opinion, a POSA would not have compared the '245 patent claims, which are entirely drawn to a method for reducing eye redness, against a reference that was entirely concerned with administering brimonidine to relieve pain in ocular nerves. Gil's Example 1 says nothing about redness reduction and merely “appears to suggest” that brimonidine “blocks the perception of pain.” EX-1004, Gil at 5:1-2.

217. Dr. Galanis stated that “[a] more probative unexpected results analysis would compare the claimed methods (as embodied by Lumify) to the Gil's administration of 0.03% brimonidine [alone] to reduce neurogenic inflammation (including redness). EX-1014, Galanis Decl. ¶ 151; EX-2017, Galanis Jan. 14, 2024 Dep. Tr. 155:9-19. Dr. Galanis conceded that his proposed comparator from the prior art is what he believes would have been obvious from the prior art. *Id.* But that embodiment is not disclosed or exemplified in Gil. Indeed, Dr. Galanis admitted that to make his proposed comparison it would require disassembling Gil Example 1 by taking it outside of RK surgery and stripping away all of the other drugs necessarily co-administered with brimonidine in that example in order to test 0.03% brimonidine alone against Lumify in humans with eye redness. EX-2017, Galanis Jan. 14, 2024 Dep. Tr. 156:23 to 157:18. That is a study Gil never did and, as I have been informed, a patent owner is not required to do that for purposes of an unexpected results comparison.

218. In my opinion, Visine L.R., which is a redness reliever, is the closest prior art. Like the invention, Visine L.R. is administered as a single drop in a single step. Like the invention, Visine L.R. is topically administered at the same concentration (0.025%) of a vasoconstrictor in a single drop application. Also, like the invention, Visine achieves redness reduction.

219. Dr. Galanis argues that if objective indicia (what he calls secondary considerations) “actually derive from something other than what is *novel* in the claim, then there is no nexus to the merits of the claimed invention.” EX-1014, Galanis Decl. ¶ 147. To that end, he states that allegedly because “the prior art taught low concentration of brimonidine, including ranges of concentration that encompass 0.025%” and Gil Example 1 disclosed 0.03% brimonidine to treat RK patients, that is tantamount to a disclosure of 0.025% brimonidine and destroys nexus. *Id.* I disagree.

220. I have been informed that the separate disclosure of individual limitations, where the invention is a unique combination of three interdependent properties, does not negate nexus. Concluding otherwise, I understand, would mean that nexus could never exist where the claimed invention is a unique combination of known elements from the prior art. I further understand that a patent owner can show that it is the claimed combination as a whole that serves as a nexus for the objective

evidence, and proof of nexus is not limited to only when objective evidence is tied to the supposedly “new” feature(s).

221. Even if Petitioners are correct (they are not) that 0.03% brimonidine is known in the prior art, that does not negate nexus where, as here, the invention’s novelty is not “low-dose brimonidine” per se or its use to reduce pain. Instead, the ’245 patented methods’ novelty resides in the claimed invention as whole—being at least a novel method of reducing eye redness by administering 0.025% brimonidine as the sole active ingredient to a person with ocular hyperemia. EX-1001, ’245 patent, claim 1. I understand that the Board already held that the Gil patent does not destroy the novelty of a method of using low-dose brimonidine to reduce eye redness. EX-1003, ’142 IPR FWD at 35-36.

222. Even if Petitioners are correct (they are not) that Gil is the closest prior art, which is not correct for the reasons discussed above, a POSA’s expectation would have been that brimonidine at 0.01% to 0.5% would relieve ocular pain. Surprisingly and unexpectedly, however, the inventor of the ’245 patent discovered that 0.025% brimonidine reduced eye redness via a mechanism of action entirely different from relieving nerve pain.

b. Brimonidine exhibited superior redness reduction effects compared to the closest prior art

223. Brimonidine at 0.025% would not have been expected to effectively reduce eye redness, where its where its minimal α_1 effect would be overpowered by

brimonidine's tendency to cause eye redness. EX-1023, Robin 1998 at 2 (“The degree of selectivity is only important if tissue concentrations are within the range required for α_1 activity. If tissue or circulating levels of drug are insufficient to produce α_2 effects, then α_1 effects are highly improbable.”). This expectation was consistent with the clinical studies for brimonidine, showing that as its concentration decreased, so too did its potential ability to vasoconstrict, with blanching noted only at 0.2% and 0.5%, but at 0.1% and 0.15%, only *causing* hyperemia. EX-1067, Alphagan 0.5% Label at 4; EX-1030, Alphagan NDA at 109; EX-1068, Alphagan P Label at 4. If anything, given brimonidine's high α_2 selectivity, a POSA would have expected it to vasodilate and cause eye redness, not reduce it, consistent with “hyperemia” being consistently listed as a main side effect of brimonidine. EX-1030, Alphagan NDA at 52, 86, 109.

224. Contrary to the expectation, Lumify exhibited unexpected, effective, long-lasting redness reduction compared to the closest prior art—far superior to Visine and other products that have been leading redness relievers in the industry, as substantiated by its quick rise to the #1 eye doctor recommended redness relieving drop. *See, e.g.*, EX-1001, '245 patent at 3:25-46, 20:1-3, 20:36-21:3, Figs. 4A-4E; EX-2066, The Science of Lumify at 1.

i. Visine L.R. (oxymetazoline 0.025%)

225. A head-to-head randomized Phase II clinical efficacy study comparing brimonidine (0.025% and 0.01%) and oxymetazoline (active ingredient in Visine L.R.) further demonstrated 0.025% brimonidine's superior ability to reduce eye redness. A POSA would have expected oxymetazoline, a mixed α_1/α_2 agonist with 200 times higher affinity for α_1 receptors (EX-2026, Ruffolo 1984 at Fig. 2a), to outperform brimonidine, but 0.025% brimonidine unexpectedly demonstrated superior redness reduction than oxymetazoline at all timepoints evaluated in the study. EX-2103, IND clinical study No. 10-100-0008 at 50. The study demonstrated that 0.025% brimonidine unexpectedly reduced redness more than about 3 to 6.5 times better than oxymetazoline. *See id.*

226. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

227. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

228. As shown in Table 2 above, at all timepoints of redness assessment [REDACTED]

[REDACTED], 0.025% brimonidine consistently produced about 3 to 6.5 times more reduction in redness in the conjunctiva and episclera than 0.025% oxymetazoline, which was surprising given oxymetazoline's 200 times greater potency to exert its α_1 vasoconstriction effect and produce greater redness reduction than brimonidine.

ii. Visine Original (tetrahydrozoline 0.05%)

229. Brimonidine at 0.01% and 0.018% was compared against Visine Original containing tetrahydrozoline 0.05%. A POSA would have expected tetrahydrozoline 0.05%, which is a selective α_1 receptor agonist, to significantly outperform brimonidine 0.01% and 0.018% due to its higher selectivity for α_1 and a higher concentration of the active ingredient, but brimonidine surprisingly outperformed tetrahydrozoline.

230. Example 1 of the '245 patent is a study comparing the efficacy 0.01% brimonidine against tetrahydrozoline 0.05% (Visine Original). Figure 4A copied below illustrates the baseline redness in a patient, to whom 0.05% tetrahydrozoline was administered in the right eye (shown as “OD”) and 0.01% brimonidine in the left eye (shown as “OS”).

Fig 4a: pretreatment baseline – contact lens irritation and allergic reaction



FIG. 4A

(EX-1001, '245 patent at Fig. 4A: Baseline redness before administration of any eye drops.)

231. Brimonidine, a highly selective α_2 agonist with a lower α_1 affinity, would have been expected to underperform tetrahydrozoline, a selective α_1 agonist, but the results unexpectedly showed brimonidine's superior efficacy in reducing eye redness, as shown below:

Fig 4b: Tetrahydrozoline 0.05% OD

Brimonidine 0.01% OS



(EX-1001, '245 patent at Fig. 4B: Comparison of tetrahydrozoline 0.05% v. brimonidine 0.01%.)

232. Brimonidine (0.018%) showed similar unexpected superior results when compared to 0.05% tetrahydrozoline in a clinical study, surprisingly producing more than twice the amount of reduction of redness than tetrahydrozoline (68.71% v 31.06%). EX-1001, '245 patent at Example 4.

233. Although the concentrations of brimonidine studied in Example 1 (0.01%) and Example 4 (0.018%) were lower than 0.025% recited in claims 1, 2, and 15 of the '245 patent, brimonidine still showed significantly better reduction of eye redness than tetrahydrozoline, indicating that 0.025% would have shown even better redness reduction.

iii. Naphcon (naphazoline 0.25%)

234. Brimonidine (0.02%) showed unexpectedly superior results to Naphcon-A (containing naphazoline 0.25%) as well. A POSA would have expected brimonidine to underperform naphazoline because brimonidine's affinity for α_1 receptors is ~500 times lower than naphazoline, which is a mixed α_1/α_2 agonist. But, surprisingly, brimonidine-treated patients exhibited more reduction in eye redness than naphazoline-treated patients. EX-1001, '245 patent at Example 2.

iv. Real-world benefits attributable to the claimed invention

235. The unexpected superiority of 0.025% brimonidine in reducing eye redness also led to a cascade of real-world benefits for users of Lumify. In several

clinical studies, brimonidine unexpectedly demonstrated multiple advantageous properties, which prior art ocular commercial vasoconstrictors did not possess.

236. Lumify is clinically proven to work in one minute and lasts up to 8 hours, 30% longer than prior OTC redness relievers. *See, e.g.*, EX-1083, Visine Original Label; EX-1079, Naphcon A Label; EX-1143, Visine L.R. Label at 3. The FDA independently confirmed Lumify's rapidity and duration of action as being advantageous to OTC consumers. EX-2027, NDA Summary at 5. Additionally, and surprisingly, Lumify is clinically proven to avoid rebound hyperemia or significant tachyphylaxis. EX-2104, 11-100-0015 Clinical Study Report at 2; EX-2105, 13-100-0005 Clinical Study Report at 3, 6. Indeed, the FDA agreed that Lumify lacked these side-effects and considered that to be a significant advantage to OTC consumers. EX-2027, NDA Summary at 2.

237. In sum, Lumify has multiple advantageous properties compared to the prior art ocular commercial vasoconstrictors, including its surprisingly superior redness reducing capability, its rapidity of onset and duration of action, and the lack of rebound hyperemia or tachyphylaxis. In my view, these unexpected superior properties and advantages constitute meaningful differences in kind and independent objective indicia of nonobviousness. Indeed, as discussed below, these unexpected results were quickly recognized and praised by the industry, leading to Lumify becoming the #1 eye doctor recommended redness relieving drop and capable of

repeated use without the adverse events reported with other OTC redness relievers and the Alphagan products.

2. Lumify—the commercial embodiment of the patented invention—enjoyed significant industry praise

238. Lumify is the first and only OTC eye drop developed with low-concentration brimonidine tartrate for the treatment of ocular redness due to minor eye irritation. EX-2095, Bausch Press Release at 1. Its unique and patented formulation, which contains low-concentration brimonidine (0.025%), has yielded an efficacy and safety profile for Lumify that far exceeds that of other redness relievers on the market (e.g., Clear Eyes, Visine, and Rohto). Lumify not only reduces redness unexpectedly better than these other commercial products, but it has a rapid onset of action (one minute) that lasts up to eight hours, exceeding the other redness relievers (six hours) by over 30%. That is not all. Lumify's use of low-concentration brimonidine surprisingly and advantageously lacks rebound hyperemia and has no significant tachyphylaxis. This is especially important for OTC products subject to potential misuse through overuse, for it could avoid ocular toxicity that could lead to medicamentosa.

239. But I am not alone in my views of Lumify—the #1 eye-doctor recommended redness reliever on the market. Other medical practitioners have praised Lumify's performance, similarly recognizing its efficacy in reducing eye redness without side effects that were commonly seen in prior art redness relievers.

Dr. Paul Karpecki noted that “[h]aving a drop that reduces redness without the side effects of rebound hyperemia or tachyphylaxis . . . is a very exciting option that I look forward to recommending to my patients.” EX-2066, *The Science of Lumify* at 2; EX-2095, Bausch Press Release at 1. As another example, Dr. Melissa Toyos explained that “[f]or all my patients who have occasional eye redness, I always recommend LUMIFY. They’re amazed at how well it works My patients are happy, so I’m happy.” EX-2066, *The Science of Lumify* at 3. Dr. Toyos further stated that “Lumify redness reliever drops specifically reduce redness due to minor eye irritations while reducing concerns of rebound hyperemia, dependency or tachyphylaxis—conditions that can lead to serious or permanent damages to the eye. I am excited to recommend Lumify to my patients to effectively relieve redness” *Id.* at 4. Even after Lumify® obtained FDA approval, people remained skeptical that it could deliver the promised results, but after using Lumify®, they were shocked to find that it delivered the promised results. *See, e.g.*, EX-2109, *Lumify Lovers* at 1.

240. In my opinion, these praises coming directly from eye care professionals is unusual for a redness reliever. I understand that Mr. Ferris will explain how eye care professionals were hesitant to recommend any eye redness relievers because they were known to cause undesirable side effects, such as rebound hyperemia and tachyphylaxis. Lumify® changed that. As the testimonials from the

eye doctors confirm, eye care professionals recommend Lumify® to patients without worrying about the undesirable side effects of the prior art redness relievers. *See* EX-2106, Enhancing the Management of Red Eye. Indeed, I have recommended Lumify to my patients before I began consulting for this case.

241. Even the FDA, the gatekeeper of safe and efficacious drugs for U.S. consumers, recognized that Lumify's brimonidine tartrate ophthalmic solution 0.025% "did not show tachyphylaxis or rebound congestion," and the "absence of tachyphylaxis or rebound congestion with an OTC ophthalmic vasoconstrictor to relieve redness of the eye is a potential advantage for the OTC consumer." EX-2027, Lumify NDA Summary Overview at 3.

242. In addition, Lumify's ability to efficaciously reduce eye redness with little or no rebound hyperemia has further unforeseen advantages for glaucoma patients. Various glaucoma medications can cause eye redness. For glaucoma patients, that could become a potential serious problem if it causes them to not regularly take their medication. Noncompliance puts them on a slippery slope toward blindness. By so effectively reducing redness without rebound hyperemia, Lumify can advantageously foster compliance and reduce the risk of patients experiencing permanent vision loss.

3. Nexus between the claimed invention and the objective indicia of nonobviousness

243. I understand that the objective indicia of nonobviousness must have nexus to the claimed invention. I have been informed that if a marketed product embodies the claimed features, and is coextensive with them, then nexus is presumed, and the burden shifts to the party asserting obviousness to present evidence to rebut the presumed nexus. Here, nexus should be presumed because Lumify embodies the challenged claims of the '245 patent and is coextensive with them, as explained below. I understand that the Petitioners have not provided any contrary evidence sufficient to rebut nexus.

244. The '245 patent claims cover the use of a commercially successful OTC redness reducer, Lumify, which quickly became the #1 eye doctor recommended redness relieving drop within three months of its launch in 2018. Ferris ¶¶7, 24.

245. Lumify has been acclaimed by eye doctors for its safety and efficacy, and these attributes have made Lumify an instant marketplace success. As explained above in Section XIII.1, Lumify is unexpectedly superior in reducing redness compared to prior art OTC redness relievers. But it also surprisingly and beneficially works within one minute and reduces redness for up to eight hours, 30% longer than the closest Visine products. EX-2050, Lumify label at 2 (“Lasts up to 8 hours”); EX-1065, Visine Label at 1 (“put 1 to 2 drops in the affected eye(s) up to 4 times daily”). Doctors have particularly praised Lumify because, unlike the other commercial

redness reducers, it has little or no rebound hyperemia (i.e., eyes becoming redder than before after the drug wears off) or tachyphylaxis (rapid decrease in drug effectiveness after repeated uses over time). Lumify's marketplace success has spurred generic companies, including Petitioners, to seek FDA approval for generic copies of Lumify, and led to this patent challenge.

246. Based on my review of the draft carton and container labels for Lumify ("Lumify label"), the challenged claims of the '245 patent cover the administration of Lumify based on the instructions provided in the Lumify label, as further explained below.

a. Claim 1

247. 1[a] "*A method for reducing eye redness in a human subject having ocular hyperemia,*": The Lumify label indicates that Lumify is "brimonidine tartrate ophthalmic solution 0.025% redness reliever eye drops" for use to "relieve[] redness of the eye due to minor irritations." *See, e.g.,* EX-2050, Lumify label at 2. A POSA would have understood that "redness of the eye due to minor irritations" refers to ocular hyperemia. *See, e.g.,* EX-1001, '245 patent at 1:25.

248. 1[b] "*consisting of topically administering to an eye of said human in need of said reduction of eye redness a composition in the form of an ocular drop consisting of 0.025% weight by volume brimonidine as the sole active ingredient, and one or more non-therapeutic components including benzalkonium chloride*": The

Lumify label indicates that Lumify is “brimonidine tartrate ophthalmic solution 0.025% redness reliever eye drops.” *See, e.g.*, EX-2050, Lumify label at 2. Lumify is formulated as “eye drops” that are instilled in the affected eyes. *Id.* The Lumify label instructs users to “instill 1 drop in the affected eye(s) every 6-8 hours.” *Id.* Use of a single ocular drop of Lumify “[w]orks in 1 minute” and “[l]asts up to 8 hours.” EX-2050, Lumify label at 2. The sole active ingredient listed in the Lumify label is “brimonidine tartrate,” which is present at a concentration of 0.025% weight by volume brimonidine. *Id.*; EX-2046, NDA 208144, Section 2.3.P.1.1 Finished Product Composition (excerpt). As non-therapeutic components, Lumify contains, for example, benzalkonium chloride, boric acid, and sodium borate decalhydrate. EX-2050, Lumify label at 2.

249. *I[c]* “*wherein the ocular drop has a pH between 5.5 to 6.5*”: The pH of Lumify is ■■■. *See, e.g.*, EX-2046, NDA 208144, Section 2.3.P.1.1 Finished Product Composition (excerpt).

250. *I[d]* “*wherein ocular hyperemia is reduced*”: The Lumify label indicates that Lumify “relieves redness of the eye due to minor eye irritations.” *See, e.g.*, EX-2050, Lumify label at 2. Lumify’s clinical studies established that “brimonidine tartrate 0.025% provides rapid and effective relief for ocular redness.” EX-2027, NDA Summary Review at 5. For example, a clinical study evaluating the efficacy and safety of brimonidine tartrate ophthalmic solution 0.025% used four

times daily in a population of adult and geriatric subjects with ocular redness concluded that “[REDACTED]

[REDACTED]” EX-2105, Clinical Study Report 13-100-0015 at 6; *see also* EX-2104, Clinical Study Report 11-100-0015 at 2. Other clinical studies for Lumify further established that Lumify significantly reduced ocular redness. EX-1139, Ackerman at 1, 4; 6-8; EX-1140, McLaurin at 1, 3-7; EX-1141, Torkildsen at 2, 4-6, 8-9. Based on the clinical study data for Lumify, the FDA concluded that “brimonidine tartrate 0.025% provides rapid and effective relief for ocular redness.” EX-2027, NDA Summary Review at 5.

b. Claim 8

251. 8[a]: *“A method for reducing eye redness in a human subject having ocular hyperemia,” See 1[a] above.*

252. 8[b]: *“comprising topically administering to an eye of said human in need of said reduction of eye redness 0.025% weight by volume brimonidine as the sole redness reducing active ingredient,” See 1[b] above.* The sole redness reducing active ingredient listed in the Lumify label is “brimonidine tartrate,” which is present at a concentration of 0.025% weight by volume brimonidine.

253. 8[c]: *“wherein the brimonidine is administered in the form of an ocular drop having a pH between 5.5 to 6.5,” See 1[c] above.*

254. 8[d]: *“and wherein the ocular drop further comprises benzalkonium chloride, and wherein the ocular hyperemia is reduced.”* See 1[b] and 1[d] above.

c. Dependent Claims

255. In my opinion, Lumify satisfies every element of each independent claim (as shown above) and at least dependent claims 2, 4-5, 7, 9, 11-12, 15, and 20 of the '245 patent (as shown below), each of which depends from claim 1 or claim 8, and incorporates all elements of the independent claim from which it depends.

i. “wherein the ocular drop induces a low incidence of rebound hyperemia in the eye of the human subject administered the ocular drop.”

256. Claims 2 and 9 of the '245 patent recite “wherein the ocular drop induces a low incidence of rebound hyperemia in the eye of the human subject administered the ocular drop.” Claims 4-5 and 11-12 depend, directly or indirectly, from claim 2 or claim 9 and, therefore, also incorporate this claim element.

257. The administration of Lumify to the eye of a human subject satisfies “wherein the ocular drop induces a low incidence of rebound hyperemia in the eye of the human subject administered the ocular drop,” as shown by the results of clinical studies conducted with Lumify. For example, an integrated analysis of four clinical trials for safety and efficacy data for brimonidine tartrate ophthalmic solution 0.025% reported that “rebound redness was rare.” EX-1139, Ackerman at 1, 5-8. Another clinical study report stated that Lumify showed “negligible rebound

redness.” EX-1140, McLaurin at 1, 6-7. Another clinical study report for Lumify concluded that “no rebound redness was observed.” EX-1141, Torkildsen at 43, 49-50.

ii. “wherein the eye redness of said human is not associated with an ocular disease or the result of a surgical procedure on the eye”

258. Claims 4, 11, 15, and 20 of the ’245 patent recite “wherein the eye redness of said human is not associated with an ocular disease or the result of a surgical procedure on the eye.” Claim 7 depends from claim 4 and, therefore, also incorporates this claim element.

259. The administration of Lumify to the eye of a human subject satisfies “wherein the eye redness of said human is not associated with an ocular disease or the result of a surgical procedure on the eye.” The Lumify label indicates that Lumify is used to “relieve[] redness of the eye due to minor eye irritations.” *See, e.g.*, EX-2050, Lumify label at 2. Redness due to minor eye irritations is not associated with an ocular disease or the result of a surgical procedure on the eye. In fact, the Lumify label indicates “[s]top use and ask a doctor if you experience eye pain, changes in vision, continued redness or irritation of the eye, condition worsens or persists for more than 3 days.” *Id.*

iii. “wherein the method retains normal intraocular pressure in the eye of the human subject administered the ocular drop”

260. Claims 5 and 12 of the '245 patent recite “wherein the method retains normal intraocular pressure in the eye of the human subject administered the ocular drop.”

261. The administration of Lumify to the eye of a human subject satisfies “wherein the method retains normal intraocular pressure in the eye of the human subject administered the ocular drop” based on the clinical study reports for Lumify. For example, an integrated analysis of four clinical trials for safety and efficacy data for brimonidine tartrate ophthalmic solution 0.025% reported that “there was no substantial effects on intraocular pressure.” EX-1139, Ackerman at 7; *see also* EX-1140, McLaurin at 6.

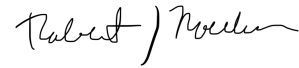
4. Petitioners failed to rebut the presumption of nexus

262. I understand that Petitioners argue that the presumption of nexus is rebutted because the “low concentration brimonidine” was known in the prior art. Pet., 64. I disagree. To begin, the claims are not drawn to “low concentration of brimonidine” per se, nor to its use to reduce pain. Instead, the claims are drawn to a method for affirmatively reducing eye redness in a human subject by topically administering a pinpoint concentration of 0.025% brimonidine as the sole active ingredient (claim 1) or sole redness reducing active ingredient (claim 8) and one or more non-therapeutic components including benzalkonium chloride, wherein the

ocular drop has a pH between 5.5 to 6.5. No prior art discloses this claimed invention. (*See* Section XII).

I declare under penalty of perjury that the foregoing is true and correct.

DATED: November 19, 2024

A handwritten signature in cursive script, appearing to read "Robert J. Noecker".

Robert J. Noecker, M.D., MBA

APPENDIX A

CURRICULUM VITAE

ROBERT J. NOECKER, MD, MBA

Business Address: Ophthalmic Consultants of Connecticut
1375 Kings Highway
Fairfield, CT 06824
203-366-8000
203-330-4598(fax)

Home Address: 50 Church Road
Easton, CT. 06612
412-526-1757 (cell)

Email: noeckerrj@gmail.com

Date & Place of Birth: June 30, 1964, Nyack, New York

EDUCATION

9/82-6/85 **B.S.** Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts
9/82-6/86 **B.S.** Materials Science and Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts
9/82-6/86 **B.S.** Humanities and Engineering (Literature), Massachusetts Institute of Technology, Cambridge, Massachusetts
8/86-5/90 **M.D.** University of North Carolina School of Medicine, Chapel Hill, North Carolina
8/98-8/2000 **M.B.A.** University of Arizona, Eller School of Management, Tucson, Arizona

POSTDOCTORAL

Internship and Residency

7/90-6/91 **Intern in Medicine**, Moses H. Cone Memorial Hospital, Greensboro, North Carolina
7/91-6/94 **Resident in Ophthalmology**, University of Arizona, Tucson, Arizona

Fellowship

7/94-6/95 **Clinical Fellow in Ophthalmology (Glaucoma)**, New England Eye Center, Tufts University School of Medicine, Boston, Massachusetts

April 28, 2022

LICENSURE & BOARD CERTIFICARON

1992 - 2015	Arizona No. 21029
1993 - 2007	Massachusetts No. 78727
1996 - present	American Board of Ophthalmology
2003 - 2014	Pennsylvania No. MD422990
2011 - present	Connecticut No. 049731
2011 – present	New York No. 261542-1

ACADEMIC APPOINTMENTS

7/94-6/96	Assistant Professor of Ophthalmology , Tufts University School of Medicine, Boston, MA
7/96-6/02	Assistant Professor of Ophthalmology , University of Arizona School of Medicine, Tucson, Arizona
7/98-6/03	Residency Director , University of Arizona School of Medicine, Tucson, Arizona
7/98-12/03	Faculty Member , Biomedical Engineering Interdisciplinary Program, University of Arizona Graduate College, Tucson, Arizona
7/02-12/03	Associate Professor of Ophthalmology , University of Arizona School of Medicine, Tucson, Arizona
7/02-12/03	Associate Chair for Clinical Activities , Department of Ophthalmology, University of Arizona School of Medicine, Tucson, Arizona
7/02-12/03	Associate Residency Director , University of Arizona School of Medicine, Tucson, Arizona
7/02-12/03	Associate Clinical Professor of Ophthalmology , University of Arizona School of Medicine, Tucson, Arizona
1/04-7/07	Visiting Associate Professor of Ophthalmology , University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania
1/04-06/11	Vice Chair , UPMC Eye Center, Department of Ophthalmology, University of Pittsburgh School of Medicine
8/07-06/11	Associate Professor of Ophthalmology , University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania
2/08-06/11	Vice Chair of Information Technology , UPMC Eye Center, Department of Ophthalmology, University of Pittsburgh School of Medicine
2/08-06/11	Vice Chair of International Affairs , UPMC Eye Center, Department of Ophthalmology, University of Pittsburgh School of Medicine
8/09-06/11	Professor of Ophthalmology , University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania
1/12- present	Assistant Clinical Professor , Yale University School of Medicine, New Haven, Connecticut
8/13- present	Clinical Professor , Quinnipiac School of Medicine, New Haven, Connecticut

April 28, 2022

HOSPITAL APPOINTMENTS

7/94-6/96 **Ophthalmologist**, New England Eye Center, New England Medical Center, Boston, MA
7/94-6/96 **Director**, New England Eye Center at St. Elizabeth's Medical Center, Boston, MA
7/94-6/96 **Staff Physician**, Department of Ophthalmology, Veterans Administration Medical Center, Boston, MA
7/94-6/96 **Staff Physician**, St. Elizabeth's Medical Center, Boston, MA
7/96-12/03 **Ophthalmologist**, University Medical Center, Tucson, Arizona
7/96-12/03 **Staff Physician**, Kino Community Hospital, Tucson, Arizona
7/96-12/03 **Staff Physician**, Veterans Administration Medical Center, Tucson, Arizona
7/96-12/03 **Director**, Clinical Studies Unit, Department of Ophthalmology, University of Arizona
7/99-12/03 **Director**, Glaucoma Service, Department of Ophthalmology, University of Arizona
1/04- 06/11 **Director**, Glaucoma Service, UPMC Eye Center, Department of Ophthalmology, University of Pittsburgh School of Medicine
4/05-6/11 **Staff Physician**, Department of Surgery, Division of Ophthalmology, VA Pittsburgh Healthcare System
7/07-06/11 **Assistant Medical Director**, eRecord Physician Advisory Council, University of Pittsburgh Medical Center
7/11-present **Staff Physician**, St. Vincent's Medical Center, Bridgeport, Connecticut
3/12-present **Staff Physician**, Veterans Administration Medical Center, West Haven, Connecticut
4/14-present **Staff Physician**, Hartford Hospital, Hartford, Connecticut

HOSPITAL/DEPARTMENT COMMITTEES

1997-2004 University Medical Center; OR Committee
1997-2004 University Medical Center; Laser Safety Committee
1999-2004 University Medical Center; Hours of Operation Team of the Perioperative Process Improvement Project
1999-2004 Ophthalmology Department; Facilities Steering Committee
1999-2004 University Physicians Ambulatory Surgery Center Management Committee
2004-2011 UPMC Ophthalmology Surgical Purchasing Committee
2004-2011 UPMC Technology Committee
2004-2011 UPMC Operating Room Committee
2004-2011 UPMC Eye Center Residency Committee
2004-2011 UPMC Ophthalmology Surgical Purchasing Committee
2004-2011 UPMC Eye Center Operations Committee
2005-2011 UPMC Eye Center eRecord Committee
2006-2011 UPMC eRecord Physician Advisory Council
2007-2011 UPMC Ophthalmology Commodity Management and VAT Chair
2012-2017 Quality Committee, St Vincent's PHO

April 28, 2022

ACADEMIC ACTIVITIES

1997-2004 Preceptor, College of Medicine, Longitudinal Clinical Curriculum
1997-2004 Preceptor, College of Medicine, Preparation for Clinical Medicine
1997-2004 Evaluator, College of Medicine, Preparation for Clinical Medicine
1997-2004 Interviewer, College of Medicine, Admissions
1997-2004 Clinical Advisor, College of Medicine, Third-Year Medical Students
1998-2004 Sponsor, Honors College, Undergraduate Research Grant Program
1999-2004 Grader, University Composition Board, Upper-Division Writing Proficiency Exam
2004-2011 Research Preceptor, University of Pittsburgh School of Medicine
2012-present Research Preceptor, Yale University School of Medicine
2012-present Clinical Preceptor, Yale University School of Medicine
2011-present Clinical Preceptor, St. Vincent's Hospital
2014-present Clinical Preceptor, Frank Netter School of Medicine, Quinnipiac University

AWARDS & RECOGNITION

1994 Resident of the Year, Department of Ophthalmology, University of Arizona
1997 American Medical Association; Physician's Recognition Award in Continuing Medical Education
2000 Best Surgical Instructor, Department of Ophthalmology, University of Arizona
2001 The Joint Commission on Allied Health Personnel in Ophthalmology, Faculty Award for Five Years of Distinguished Service
2002 The American Academy of Ophthalmology, Achievement Award for Distinguished Service
2004 Selection to Best Doctors of Tucson
2004 Best Doctors in America
2005 Who's Who in America 2005
2005 Best Doctors in America
2006 America's Top Ophthalmologists, Consumers' Research Council of America
2006 James R. Carl, MD Clinical Instructor of the Year Award
2006 Best Doctors in America
2006 Nursing and Allied Health Program of the Hawaiian Eye 2006 Meeting Award of Excellence
2007 Best Doctors in America
2007 UPMC's Award for Commitment and Excellence in Service (ACES)
2007 James R. Carl, MD Clinical Instructor of the Year Award
2008 Best Doctors in America
2008 James R. Carl, MD Clinical Instructor of the Year
2009 America's Top Ophthalmologists
2009 Best Doctors in America
2010 Best Doctors in America
2011 Best Doctors in America
2011 Best Doctors in Pittsburgh
2011 Best Glaucoma Lecture, Royal Hawaii Eye Meeting
2012 Best Doctors in America
2012 INFORMS 2012 Case Competition Second Place Winner

April 28, 2022

2013 Best Doctors in America
 2013 American Academy of Ophthalmology Senior Achievement Award
 2014 Best Doctors in America
 2014 Clinical Instructor of the Year, Yale University Department of Ophthalmology
 2015 Best Doctors in America
 2015 Connecticut Best Doctors
 2016 Top 100 Professionals
 2016 Best Doctors in America
 2017 Leading Physicians of the World
 2017 Best Doctors in America
 2017 Castle and Connolly Top Doctors
 2018 Best Doctors in America
 2018 Red Book of Ophthalmologists
 2018 Castle and Connolly Top Doctors
 2018 3rd place SLAG poster presentation
 2019 Best Doctors in America
 2019 Castle and Connolly Top Doctors
 2020 Best Doctors in America
 2020 Castle and Connolly Top Doctors in New York
 2021 Best Doctors in America
 2021 Castle and Connolly Top Doctors
 2022 Best Doctors in America
 2022 Castle and Connolly Top Doctors in Connecticut
 2022 America's Most Honored Doctors

MEMBERSHIPS IN PROFESSIONAL SOLICITES

1986 Member, American Medical Association
 1989 Member, Association for Research in Vision and Ophthalmology
 1991 Fellow, American Academy of Ophthalmology
 1991 Member, Arizona Ophthalmological Society
 1991 Member, Tucson Ophthalmological Society
 1992 Member, American Society for Cataract and Refractive Surgery
 1993 Member, SPIE- International Society for Optical Engineering
 1994 Member, Massachusetts Medical Society
 1996 Member, Pima County Medical Society
 1996 Member, Chandler Grant Glaucoma Society
 1998 Member, Research to Prevent Blindness
 1998 Associate Member, Association of University Professors in Ophthalmology
 2000 Active Member, American Glaucoma Society
 2005 Member, Pittsburgh Ophthalmology Society
 2005 Member, PAO Pennsylvania Academy of Ophthalmology
 2006 Member, Allegheny County Medical Society
 2011 Member, New York Glaucoma Society

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2011 Member, Connecticut Glaucoma Society
 2011 Member, Connecticut Society for Eye Physicians
 2020 Co-Chair, Connecticut Glaucoma Society
 2021 Acting President, Connecticut Glaucoma Society

PROFESSIONAL ORGANIZATION COMMITTEES

2005-2006 American Glaucoma Society Finance Committee
 2012-2016 American Glaucoma Society Practice Management Subcommittee
 2013-2017 American Glaucoma Society Finance Committee
 2014-2019 New England Ophthalmology Society Program Committee
 2014-present New England Ophthalmology Society Foundation Committee
 2017- present ASCRS Glaucoma Program Committee
 2021-present American Academy of Ophthalmology, Glaucoma Program Committee

JOURNALS - CONTRIBUTING EDITOR

1998- present *Review of Ophthalmology*
 2000- present *Ophthalmology Management*
 2003- present *Glaucoma Todas*
 2009- present *eyetube Ophthalmic Video Resource* (<http://eyetube.net/channels/glaucoma/>)
 2009- present *Case Reports in Medicine*
 2009-present *Refractive Eyecare*
 2009- present *Advanced Ocular Cari*
 2006-2012 *Young Ophthalmologist*
 2017-present *Eye World Editorial Board*
 2017-present *Glaucoma Physician*

JOURNALS - PEER-REVIEWER

American Journal of Ophthalmology
Archives of Ophthalmology
Ophthalmic Surgery and Losers
Ophthalmology
Investigative Ophthalmology and Visual Science
British Journal of Ophthalmology
Journal of Glaucoma
Journal of Cataract and Refractive Surgery
Journal of Anesthesia
Journal of Ocular Pharmacology & Therapeutics
European Journal of Ophthalmology
Clinical Ophthalmology
Graefe's Ophthalmology

COMMUNITY SERVICE

1996-2004 Volunteer, Arizona Mobile Eye Unit

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1996-2004 Volunteer, Lions Surgery Mission, Nogales, Arizona
 2005-2011 Volunteer, Friends of the Congressional Glaucoma Caucus Foundation Screenings
 2008-2011 EyeCare America (ECA) Glaucoma EyeCare Program

TELEVISION/NEWSPAPER/RADIO

Ocular Sports Injuries, KOLD-TV, Tucson, AZ, November 11, 1996.
Glaucoma, KOLD-TV, Tucson, AZ, January 20, 1997.
Glaucoma Therapy, Discovery Health, May, 2003
SLT, Feature Segment on Healthcast, WTAE-TV, Pittsburgh, PA, December 10, 2004
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New Glaucoma Surgical Therapy, WTNH, September 28, 2012
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Intense pulsed light for treatment of ocular surface disease, Connecticut 12 on Health, Norwalk,
 CT, January 31, 2013.

ELECTRONIC MEDIA

Noecker RJ, Patterson E. Primary open angle glaucoma. In: *E-medicine online textbook*, 1999.
 Noecker RJ, Patterson E. Angle closure glaucoma. In: *E-medicine online textbook*, 1999.
 Noecker RJ Medtronic AAO ECP Course Video Email, 2004.
 Noecker RJ Glaucoma Medication, Effect of Glaucoma Therapy on the Ocular Surcace
 In: *Audio-Digest Ophthalmology* Vol 44 Issue 01 iSSN 0271-1281 January 2006
 Noecker RJ Glaucoma Topics, When Is It Time to Refer Your Patient?
 In: *Audio-Digest Ophthalmology* Vol 45 Issue 23 ISSN 0271-1281 October 2007
 Update on Glaucoma: Roundtable Discussion Series. Updateonglaucoma.com 2007
 Do computer glasses really work? [http://lifehacker.com/5980509/do-computer-glasses-really-work?](http://lifehacker.com/5980509/do-computer-glasses-really-work?popular=true)
[popular=true](http://lifehacker.com/5980509/do-computer-glasses-really-work?popular=true) January 31, 2013.

TEACHING EXPERIENCE

COURSES AND LECTORES

1997 Course Director, “*Glaucoma I: Review of Glaucoma and Tonometry for Ophthalmic Technicians*,” Accredited by the Joint Commission on Allied Health Personnel in

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Ophthalmology (JCAHPO). Tucson, AZ, January 18, 1997.

Instructor, Glaucoma course for primary care physicians, Davis Monthan Air Force Base, Tucson, AZ, February 18, 1997.

Instructor, *"Glaucoma Medications,"* University of Arizona College of Pharmacy, Tucson, AZ, March 3 & 5, 1997.

Course Director, *"Introduction to First Assisting in Cataract Surgery,"* Accredited by the Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO). Tucson, AZ, March 21-23, 1997.

Course Faculty, Glaucoma Course, Southern California College of Optometry Continuing Education Course, Flagstaff, AZ, April 16, 1997.

Course Director, *"Retina I: Review of Macular Degeneration, Diabetic Retinopathy and Fundus Photography for Ophthalmic Technicians,"* Accredited by the Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO), Tucson, AZ, April 19, 1997.

Course Director, *"Refractometry and Retinoscopy I for Ophthalmic Technicians,"* Accredited by the Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO), Tucson, AZ, July 19, 1997.

Course Faculty, *"Selective Laser Trabeculoplasty,"* Nantucket Glaucoma '97, Nantucket, MA, August 15, 1997.

Instructor, *"General Examination/Tonometry,"* University of Arizona College of Medicine, Ophthalmology Practicum, August 20 & 27, 1997.

Instructor, *"Surgical Pharmacology,"* Annual Meeting of the Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO), San Francisco, CA, October 28, 1997.

Course Faculty, *"Ocular Infectious Disease,"* Arizona Optometric Association, Flagstaff, AZ, November 9, 1997.

Course Director, *"Ocular Infectious Disease for Ophthalmic Technicians and Opticians,"* Accredited by the Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO) and the American Board of Optometry, Tucson, AZ, November 22, 1997.

1998 Guest Speaker, *"Recent Trends in Glaucoma Therapy,"* Reno Ophthalmological Society, Reno, NV, February 19, 1998.

Course Faculty, *"Recent Advances in the Treatment of Glaucoma,"* 31st Annual Southwestern Clinical Pharmacy Seminar, Tucson, AZ, February 21, 1998.

Instructor, *"Treatment of Glaucoma,"* University of Arizona College of Pharmacy, Tucson, AZ, March 12, 1998.

Instructor, *"Glaucoma Case Review,"* University Medical Center Ambulatory Care Conference, Tucson, AZ, March 16, 1998.

Invited Speaker, *"Ocular Effects of Drugs,"* Tucson Police Department Drug Recognition Program, Tucson, AZ, March 24, 1998.

Course Director, *"Cataract Surgery, Keratometry and Biometry for Ophthalmic Technicians,"* Accredited by the Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO), Tucson, AZ, March 28, 1998.

Course Faculty, *"Use of Anti-Glaucoma Agents in the Perioperative Period."*

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Pharmacology of Cataract and Refractive Surgery,” American Society of Cataract and Refractive Surgery 1998 Symposium on Cataract, IOL and Refractive Surgery, San Diego, CA, April 18, 1998.

Co-Instructor, “*Teaching Residents Phacoemulsification Course,*” American Society of Cataract and Refractive Surgery 1998 Symposium on Cataract, IOL and Refractive Surgery, San Diego, CA, April 19, 1998.

Course Director, “*Introduction to Retinoscopy for Ophthalmic Technicians,*” Accredited by the Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO). Tucson, AZ, July 25, 1998.

Course Faculty, “*Ocular Pharmacology I & II, Anterior Segment Trauma and Mock Orals,*” The Osler Institute 29th Ophthalmology Board Review Course, San Francisco, CA, October 15, 1998.

Co-Instructor, “*Transscleral Diode Laser Cyclophotocoagulation,*” 1998 Annual Meeting of the American Academy of Ophthalmology, New Orleans, LA, November 8-9, 1998.

Instructor, “*Surgical Pharmacology,*” The Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO) Annual Continuing Education Program for Ophthalmic Medical Personnel, New Orleans, LA, November 9, 1998.

Instructor, “*Pharmacology of Glaucoma Medications,*” The Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO) Annual Continuing Education Program for Ophthalmic Medical Personnel, New Orleans, LA, November 9, 1998.

Instructor, “*Laser Treatment of Glaucoma,*” The Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO) Annual Continuing Education Program for Ophthalmic Medical Personnel, New Orleans, LA, November 9, 1998.

Invited Lecturer, “*Medical Therapy of Glaucoma,*” The California Hispanic-American Ophthalmology Society, San Diego, CA, November 17, 1998.

1999 Co-Instructor, “*Anterior Segment Case Presentations and Discussions,*” University of Wisconsin 1999 Winter Symposium, Tucson, AZ, January 16, 1999.

Invited Speaker, “*Selective Laser Trabeculoplasty,*” The Ophthalmological Society of South Africa, Capetown, South Africa, February 16, 1999.

Instructor, “*Pharmacology of Cataract Surgery,*” University of Arizona College of Pharmacy, Tucson, AZ, March 11, 1999.

Instructor, “*Glaucoma Medications,*” University of Arizona College of Pharmacy, Tucson, AZ, March 11, 1999.

Invited Speaker, “*Diabetic Induced Glaucoma,*” The California Hispanic-American Medical Association, San Diego, CA, April 7, 1999.

Invited Speaker, “*New Trends in Glaucoma Therapy,*” San Antonio Ophthalmologic Society, San Antonio, TX, April 17, 1999.

Invited Speaker, “*Glaucoma Topics and Recent Trends,*” Annual Clinical Assembly of the American Osteopathic Colleges of Ophthalmology and Otolaryngology—Head and Neck Surgery, Orlando, FL, April 24, 1999.

Invited Speaker, “*Glaucoma Challenges,*” New England Eye Center, Tufts University School of Medicine, Boston, MA, May 18, 1999.

Invited Lecturer, “*Case Studies in the Management of Glaucoma Patients,*” Perspectives in Glaucoma CME Course, Phoenix, AZ, June 5, 1999.

Invited Lecturer, “*Glaucoma Management and Case Studies,*” Arizona Optometric Association Spring Congress, Tucson, AZ, July 11, 1999.

Course Director, “*Introduction to Contact Lenses for Ophthalmic Technicians,*” Accredited by the Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO). Tucson, AZ, July 14, 1999.

Invited Speaker, “*Cases in Glaucoma Management,*” Barnett & Dulaney Eye Center, Phoenix, AZ, July 27, 1999.

Visiting Professor, “*Trends in the Medical Management of Glaucoma,*” Grand Rounds Conference, Oxford Ophthalmology Department, Oxford University, Oxford, England, September 6, 1999.

Co-Instructor, “*Cyclodestruction: The State of the Art,*” 1999 Annual Meeting of the American Academy of Ophthalmology, Orlando, FL, October 24, 1999.

Instructor, “*Laser Treatment of Glaucoma,*” Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO) Annual Continuing Education Program for Ophthalmic Medical Personnel, Orlando, FL, October 24, 1999.

Instructor, “*The Stressless Transition to Topical Clear Cornea Phacoemulsification for Residents and Accomplished Surgeons,*” 1999 Annual Meeting of the American Academy of Ophthalmology, Orlando, FL, October 26, 1999.

2000 Co-Instructor, “*Glaucoma Cases,*” University of Wisconsin Mid-Winter CME Symposium, Tucson, AZ, January 15, 2000.

Course Faculty, “*Treatment Goals and Adjunctive Therapy; Current Glaucoma Practice,*” Ocular Drug and Surgical Therapy Update CME Meeting, Laguna Niguel, CA, March 4, 2000.

Visiting Professor, “*Difficult Glaucomas,*” Stanford University Ophthalmology Grand Rounds, Palo Alto, CA, March 6 & 7, 2000.

Instructor, “*Pharmacology of Glaucoma,*” University of Arizona College of Pharmacy, Tucson, AZ, March 9, 2000.

Invited Speaker, “*Re-Thinking Our 1st Line Medical Therapy*” and “*Difficult Glaucomas,*” Capital Eye Symposium, Washington, DC, April 1, 2000.

Course Faculty, “*A Neuroprotective Therapeutic Paradigm for Vision Sparing in Glaucoma,*” Glaucoma 2000: Evolving Medical Therapy for a Multifactorial Disease, Annenberg Center CME Program, April 11, 2000 and June 7, 2000.

Invited Speaker, “*Current Glaucoma Practice: Treatment Goals and Patterns,*” American Optometric Association 103rd Annual Congress, June 21, 2000.

Invited Speaker, “*Ocular Manifestations in Parkinson’s Disease,*” American Parkinson Disease Association, Green Valley Parkinson’s support group, Green Valley, AZ, September 1, 2000.

Instructor, “*Laser Treatment of Glaucoma,*” Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO) Annual Continuing Education Program for Ophthalmic Medical Personnel, Dallas, TX, October 24, 2000.

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- Co-Instructor,** *“Cyclodestruction: The State of the Art,”* American Academy of Ophthalmology Annual Meeting, Dallas, TX, October 24, 2000.
- Instructor,** *“The Stressless Transition to Topical Clear Cornea Phacoemulsification for Residents and Accomplished Surgeons,”* American Academy of Ophthalmology Annual Meeting, Dallas, TX, October 25, 2000.
- Course Faculty,** *“A Neuroprotective Therapeutic Paradigm for Vision Sparing in Glaucoma,”* Glaucoma 2000: Evolving Medical Therapy for a Multifactorial Disease, Annenberg Center CME Program, Charlotte, NC, November 2, 2000.
- 2001 Instructor,** *“Glaucoma Cases,”* University Medical Center Ambulatory Care Conference, Tucson, AZ, January 9, 2001.
- Invited Speaker,** *“New trends in the Treatment of Glaucoma,”* Southern Arizona Optometric Society Meeting, Tucson, AZ, January 9, 2001.
- Invited Lecturer,** *“Treatment of Glaucoma,”* National Clinical Consulting Meeting, Scottsdale, AZ, February 21, 2001.
- Course Faculty,** *“Neuroprotection: Connecting Research to Real Practice,”* Ocular Surgery News CME Symposium, Houston, TX, February 22, 2001.
- Course Faculty,** *“Neuroprotection: Connecting Research to Real Practice,”* Ocular Surgery News CME Symposium, Orlando, FL, March 8, 2001.
- Invited Lecturer,** *“Evaluation of brimonidine use in elderly patients previously on chronic, non-selective beta blocker therapy for glaucoma,”* The 3rd International Glaucoma Symposium I.G.S., Prague, Czech Republic, March 25, 2001.
- Course Faculty,** *“Neuroprotection: Connecting Research to Real Practice,”* Ocular Surgery News CME Symposium, San Francisco, CA, April 5, 2001.
- Instructor,** *“Don’t Worry...Go Topical: Transition to Topical Clear Cornea Phacoemulsification,”* American Society of Cataract and Refractive Surgery 2001 Symposium on Cataract, IOL and Refractive Surgery, San Diego, CA, April 29, 2001.
- Invited Lecturer,** *“Treatment of Glaucoma,”* National Clinical Consulting Meeting, Scottsdale, AZ, August 23, 2001.
- Course Faculty,** *“Neuroprotection: Connecting Research to Real Practice,”* Ocular Surgery News CME Symposium, Seattle, WA, November 1, 2001.
- Instructor,** *“Lasers in Glaucoma,”* 105th Annual Meeting of the American Academy of Ophthalmology, New Orleans, LA, November 11, 2001.
- Instructor,** *“Alternative/Adjunctive Therapies for Glaucoma,”* 105th Annual Meeting of the American Academy of Ophthalmology, New Orleans, LA, November 14, 2001.
- Instructor,** *“Laser Treatment of Glaucoma,”* Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO) Annual Continuing Education Program for Ophthalmic Medical Personnel, New Orleans, LA, November 14, 2001.
- 2002 Guest Speaker,** Current Concepts in Glaucoma Therapy Meeting, El Paso, TX, January 10, 2002.
- Course Faculty,** *“Effect of Preservatives in Chronic Therapy,”* Slack Incorporated Hawaii 2002 Physicians Program, Waikoloa, HI, January 23, 2002.

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Course Faculty, *"Effect of Preservatives in Chronic Therapy,"* 5th Annual Ocular Drug and Surgical Therapy Update Meeting, Dana Point, CA, February 16, 2002.

Invited Lecturer, *"Treatment of Glaucoma,"* National Clinical Consulting Meeting, Scottsdale, AZ, February 28, 2002.

Course Faculty, *"Neuroprotection,"* 3 Targets for Glaucoma Management Symposium, Los Angeles, CA, March 16, 2002.

Invited Lecturer, *"Advances in the Treatment of Glaucoma,"* Delhi Ophthalmic Society Meeting, Delhi, India, April 6, 2002.

Course Faculty, *"Neuroprotection,"* 3 Targets for Glaucoma Management Symposium, Dallas, TX, April 13, 2002.

Course Faculty, *"Neuroprotection,"* 3 Targets for Glaucoma Management Symposium, San Francisco, CA, May 18, 2002.

Instructor, *"Take the Stress Out: State-of-the-Art Cataract Surgery,"* American Society of Cataract and Refractive Surgery 2002 Symposium on Cataract, IOL and Refractive Surgery, Philadelphia, PA, June 4, 2002.

Course Faculty, *"Neuroprotection,"* 3 Targets for Glaucoma Management Symposium, Raleigh, NC, June 8, 2002.

Course Faculty, *"Neuroprotection,"* 3 Targets for Glaucoma Management Symposium, Pittsburgh, PA, June 29, 2002.

Course Faculty, *"Neuroprotection,"* 3 Targets for Glaucoma Management Symposium, Baltimore, MD, September 14, 2002.

Visiting Professor, *"Where Lumigan fits into Common Clinical Practice,"* University of Alberta Department of Ophthalmology Grand Rounds, October 3, 2002.

Course Faculty, *"Neuroprotection,"* 3 Targets for Glaucoma Management Symposium, Detroit, MI, October 12, 2002.

Instructor, *"Laser Treatment of Glaucoma,"* Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO) Annual Continuing Education Program for Ophthalmic Medical Personnel, Orlando, FL, October 19, 2002.

Co-Instructor, *"Lasers in Glaucoma,"* The Joint Meeting of the American Academy of Ophthalmology and the Pan-American Association of Ophthalmology, Orlando, FL, October 20, 2002.

Instructor, *"Alternative/Adjunctive Therapies for Glaucoma,"* The Joint Meeting of the American Academy of Ophthalmology and the Pan-American Association of Ophthalmology, Orlando, FL, October 21, 2002.

2003 Course Faculty, *"Ocular Surface Issues in Chronic Glaucoma Therapy,"* 2003 Royal Hawaiian Eye Meeting, Maui, HI, January 22, 2003.

Course Faculty, *"Effects of Preservatives on the Ocular Surface in Chronic Therapy,"* 6th Annual Ocular Drug and Surgical Therapy Update, Dana Point, CA, February 15, 2003.

Course Faculty, *"What is all the Controversy About?"* Simplifying Glaucoma Management CME Conference, Killington, VT, March 1, 2003.

Invited Lecturer, *"A comparison of the IOP-lowering efficacy of bimatoprost and latanoprost in patients stratified by baseline diagnosis: ocular hypertension vs. glaucoma,"*

4th International Glaucoma Symposium-I.G.S., Barcelona, Spain, March 22, 2002.

Instructor, “*Cannabinoids and Other IOP-Lowering Agents*,” 4th International Glaucoma Symposium-I.G.S., Barcelona, Spain, March 22, 2002.

Instructor, “Remove the Stress and Enjoy the Challenge: Taking the Stress Out of State-of-the-Art Cataract Surgery,” American Society of Cataract and Refractive Surgery 2003 Symposium on Cataract, IOL and Refractive Surgery, San Francisco, CA, April 14, 2003.

Course Faculty, “*Current Issues in Glaucoma Therapy*,” Mountain West Council of Optometrists 2003 Congress, Las Vegas, NV, May 18, 2003.

Course Faculty, “*Alpha Adrenergic Agonists*” and “*Anti-Fibrosis Agents*,” First Annual Ocular Surgery News Symposium on Glaucoma, Las Vegas, NV, June 6-7, 2003.

Course Faculty, “*Major Clinical Trials for Glaucoma*,” Arizona Ophthalmological Society Annual Scientific Meeting, Las Vegas, NV, June 7, 2003.

Course Faculty, “*Current Concepts in the Medical Management of Glaucoma*,” Arizona Ophthalmological Society Annual Scientific Meeting, Las Vegas, NV, June 7, 2003.

Instructor, “*Laser Treatment of Glaucoma*,” Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO) Annual Continuing Education Program for Ophthalmic Medical Personnel (Subspecialty Day), Anaheim, CA, November 15, 2003.

Co-Instructor, “*Lasers in Glaucoma*,” The Annual Meeting of the American Academy of Ophthalmology, Anaheim, CA, November 16, 2003.

Co-Instructor, “*Alternative/Adjunctive Therapies for Glaucoma*,” The Annual Meeting of the American Academy of Ophthalmology, Anaheim, CA, November 18, 2003.

Invited Lecturer, “*Cataract Surgery in the Glaucoma Patient: Anticipation and Preparation*,” New England Ophthalmological Society Meeting, Boston, MA, December 12, 2003.

2004 Course Faculty, “*Alternative Therapy for Glaucoma*,” 2004 Royal Hawaiian Eye Meeting, Kauai, HI, January 28, 2003.

Course Faculty, “*Bleb Leaks, Blebitis and Endophthalmitis*,” 2004 Royal Hawaiian Eye Meeting, Kauai, HI, January 28, 2003.

Course Faculty, “*Assessing Ocular Blood Flow*,” 2004 Royal Hawaiian Eye Meeting, Kauai, HI, January 28, 2003.

Scientific Poster Presentation “*Pharmacoeconomic Analysis of a Literature Review of the Lipid Class of Anti-Glaucoma Medications*,” 2004 AGS Meeting, Sarasota, FL March 06, 2004

Scientific Poster Presentation, “*Pigment dispersion and glaucoma related to in-the-bag placement of the AcrySof® SA60 IOL*,” 2004 AGS Meeting, Sarasota, FL, March 05, 2004

Scientific Poster Presentation, “*A Multicenter, Randomized, Investigator-Masked Comparison of the Efficacy of Bimatoprost 0.03% versus Travoprost 0.004% in African Americans with Glaucoma or Ocular Hypertension*,” 2004 AGS Meeting, Sarasota, FL, March 05, 2004

Scientific Poster Presentation, “*Evaluation of the Effect of Various Artificial Tears on Latanoprost-Induced Corneal Toxicity in Rabbits*,” 2004 ARVO Meeting, Fort Lauderdale, FL, April 25, 2004

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Scientific Poster Presentation, “*Bimatoprost Affects Hydraulic Conductivity of Outflow Cell Monolayers,*” 2004 ARVO Meeting, Fort Lauderdale, FL, April 28, 2004

Scientific Poster Presentation, “*A Multicenter, Investigator-Masked, Randomized Comparison of the IOP-Lowering Efficacy of Bimatoprost 0.03% versus Travoprost 0.004% in African Americans with Glaucoma or Ocular Hypertension,*” 2004 ARVO Meeting, Fort Lauderdale, FL, April 28, 2004

Scientific Poster Presentation, “*Pressure-Lowering Efficacy of Bimatoprost and Latanoprost: Effect of Baseline Mean Diurnal IOP,*” 2004 ARVO Meeting, Fort Lauderdale, FL, April 28, 2004

Scientific Poster Presentation, “*The effect of topical cyclosporine on latanoprost-induced conjunctival inflammation,*” 2004 ARVO Meeting, Fort Lauderdale, FL, April 29, 2004

Scientific Poster Presentation, “*Penetration of 4th Generation Fluoroquinolones into the Rabbit Aqueous Humor Using a Lidocaine Gel Mixture,*” 2004 ARVO Meeting, Fort Lauderdale, FL, April 29, 2004

Scientific Poster Presentation, “*Aqueous Levels of Moxifloxacin and Gatifloxacin Following Different Pre and Post-Operative Topical Dosing Protocols,*” 2004 ARVO Meeting, Fort Lauderdale, FL, April 29, 2004

Scientific Poster Presentation, “*Comparison of the Effectiveness of Vigamox™ and Zyar™ against Aspergillus fumigatus and Candida albicans,*” 2004 ARVO Meeting, Fort Lauderdale, FL, April 29, 2004

Course Instructor, “*Controversies in Lens Implant Selection for the Aging Eye,*” ASCRS Symposium on Cataract, IOL and Refractive Surgery, San Diego, CA, May 01, 2004

Moderator/Speaker, “*Mechanisms of Selective Laser Trabeculoplasty,*” ASCRS Symposium on Cataract, IOL and Refractive Surgery, San Diego, CA, May 01, 2004

Scientific Poster Presentation, “*Comparison of the Effect of Brimonidine Purite on Rabbit Corneal Epithelium,*” ASCRS Symposium on Cataract, IOL and Refractive Surgery, San Diego, CA, May 01, 2004

Scientific Poster Presentation, “*Incidence of Iris Pigmentation Changes with Latanoprost and Bimatoprost,*” ASCRS Symposium on Cataract, IOL and Refractive Surgery, San Diego, CA, May 01, 2004

Guest Speaker, “*The Effect of Glaucoma Therapy on the Ocular Surface,*” COS Chicago Ophthalmological Society, Navy Pier, Chicago, IL, May 15, 2004

Course Faculty, “*Glaucoma Medications, Alpha Adrenergic Agonists,*” OSN Ocular Surgery News Symposium, The Venetian, Las Vegas, NV, June 06, 2004.

Course Faculty, “*Glaucoma Surgery, Anti-Fibrosis Agents,*” OSN Ocular Surgery News Symposium, The Venetian, Las Vegas, NV, June 07, 2004.

Course Faculty, “*Angle Closure and Other Complicated Glaucomas, Neovascular Glaucoma*” OSN Ocular Surgery News Symposium, The Venetian, Las Vegas, NV, June 11, 2004.

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Course Faculty, “*Managing Late Complications of Trabeculectomy, Leaking Bleb*,” OSN Ocular Surgery News Symposium, The Venetian, Las Vegas, NV, June 12, 2004.

Invited Speaker, “*Pressure Lowering Efficacy of Bimatoprost and Latanoprost: Effect on Baseline Mean Diurnal Intraocular Pressure (IOP)*.” SEAGIG 2004, Kuala Lumpur Malaysia, August 26, 2004.

Invited Speaker, “*Comparison of The Effect of Brimonidine .02% Vs. Brimonidine Purite® on Rabbit Corneal Epithelium*.” SEAGIG 2004, Kuala Lumpur, Malaysia, August 26, 2004.

Course Director, Anterior Segment Update, University of Pittsburgh, Pittsburgh, PA , September 18, 2004

Invited Lecturer, “*New Diagnostic Methods for Glaucoma: OCT and Other Technologies*” Anterior Segment Update, University of Pittsburgh, Pittsburgh, PA September 18, 2004

Invited Lecturer, “*Update on Glaucoma Laser Therapy*” Anterior Segment Update, University of Pittsburgh, Pittsburgh, PA September 18, 2004

Course Instructor, “*Clinical Applications of ECP*.” ECP Course, Boston, MA, September 25, 2004.

Invited Speaker, “*Effects of Glaucoma Therapy on the Ocular Surface*.” Grand Rounds, University Hospitals of Cleveland, Case Western Reserve University, September 29, 2004.

Course Instructor, “*Strategies to Prevent Disease Progression*.” FORGE CME Program, Orlando, FL, October 02, 2004.

Invited Lecturer, “*Neovascular glaucoma: Potential Novel Approaches*.” Angiogenesis and its Inhibition, Herberman Conference Center, Hillman Cancer Center, Pittsburgh, PA, October 09, 2004

Invited Lecturer, “*Patient Perspectives in Glaucoma Management*” CME Symposium “Winds of Change: An Evidence Based Approach” AAO & SOE Joint Meeting, New Orleans, October 22, 2004

Invited Speaker, “*Second-Line Glaucoma Management: Considerations in Selecting Safer, More Effective Adjunctive Agents*” AAO & SOE Joint Meeting, New Orleans, October 22, 2004

Invited Speaker, “*Tips and Techniques for Successful SLT Treatment*” AAO & SOE Joint Meeting, New Orleans, October 22, 2004

Invited Speaker, “*The Truth About Silicone IOLs (biocompatibility, ease of use, use with silicone oils)*” AAO & SOE Joint Meeting, New Orleans, October 22, 2004

Invited Speaker, “*Weight of Evidence: Choosing Medical Therapy in Glaucoma*” Allergan Consultant Meeting, San Diego, CA, November 13, 2004

Invited Speaker, “*FORGE Program*” Allergan Consultant Meeting, Baltimore, MD, November 16, 2004

Invited Speaker, “*SLT Tips for Clinical Success*” Lumenis CORE Meeting, Pittsburgh, PA, November 17, 2004

Invited Speaker, “*SLT Tips for Clinical Success*” Lumenis CORE Meeting, Grand Rapids, MI, November 18, 2004

Invited Speaker, “*SLT Tips for Clinical Success*” Lumenis CORE Meeting,

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Alexandria, VA, November 23, 2004

- 2005 Invited Speaker**, “*Update on Optic Nerve and Nerve Fiber Layer Imaging*,” Kansas City Society of Ophthalmology and Otolaryngology Annual Clinical Conference, Kansas City, Missouri January 7, 2005.
- Invited Speaker**, “*Effect of Glaucoma Therapy on the Ocular Surface*,” Kansas City Society of Ophthalmology and Otolaryngology Annual Clinical Conference, Kansas City, Missouri January 7, 2005.
- Invited Speaker**, “*Role of Endocyclophotocoagulation in Glaucoma Management*,” Kansas City Society of Ophthalmology and Otolaryngology Annual Clinical Conference, Kansas City, Missouri January 7, 2005.
- Guest Lecturer**, “*FORGE Structural Evaluations*,” CME Symposium, The Royal Hawaiian Eye J Meeting, Hawaii, January 17, 2005.
- Guest Lecturer**, “*Glaucoma Overview*,” Nursing Program, The Royal Hawaiian Eye Meeting, Hawaii, January 19, 2005.
- Guest Lecturer**, “*Glaucoma Medications*,” Nursing Program, The Royal Hawaiian Eye Meeting, Hawaii, January 19, 2005.
- Guest Lecturer**, “*Glaucoma Therapy and the Ocular Surface*,” Nursing Program, The Royal Hawaiian Eye Meeting, Hawaii, January 19, 2005.
- Course Director**, “*Ophthalmic Technician Education Series: Tonometry and Lensometry*,” Accredited by the Joint Commission on Allied Health Personnel in Ophthalmology (JCAHPO). Pittsburgh, PA February 05, 2005.
- Course Director**, “*Ophthalmologic Endo-Cyclophotocoagulation*,” Accredited by the Accreditation Council for Continuing Medical Education. Pittsburgh, PA February 19, 2005.
- Guest Lecturer**, “*A Comparison of ALT and SLT*,” Eye on the Bayou, The 54th Annual Symposium of the New Orleans Academy of Ophthalmology, New Orleans, LA, February 20, 2005
- Guest Lecturer**, “*What’s New in Glaucoma: Cutting Edge Advances*” Seco International, 2005, Atlanta, GA, February 24, 2005
- Scientific Poster Presentation** “*Evaluation of Bimatoprost 3.33% versus Latanoprost 0.005%: A Bilateral Monocular Trial*”, American Glaucoma Society (AGS) 2005 Annual Meeting, Snowbird, UT, March 03, 2005
- Moderator**, “*FORGE Focusing Ophthalmology on Reframing Glaucoma Evaluation*”, March 10, 2005
- Scientific Poster Presentation** “*Evaluation of Bimatoprost 0.03% versus Latanoprost 0.005%: A Paired Comparison Study*”, ARVO 2005 Annual Meeting, Fort Lauderdale, FL., May 1-5, 2005

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Course Director, Anterior Segment Update, University of Pittsburgh, Pittsburgh, PA , May 07, 2005

Scientific Poster Presentation “*Evaluation of Bimatoprost 0.03% versus Latanoprost 0.005%: A Paired Comparison Study*,” ARVO, Fort Lauderdale, FL May 01-06, 2005

Invited Speaker, “Real Efficacy, Breakfast Symposium “SURGE Sound Understanding of REAL Glaucoma Efficacy” Annual OSN Glaucoma Symposium, Las Vegas, NV June 17, 2005

Invited Speaker, “Surgical Complication – Grand Rounds, High IOP” Third Annual Ocular Surgery News Symposium, OSN Glaucoma Symposium, Las Vegas, NV June 18, 2005

Invited Speaker, “Other Consideration in Glaucoma Surgery, Cyclodestructive Procedures” Third Annual Ocular Surgery News Symposium, OSN Glaucoma Symposium, Las Vegas, NV June 18, 2005

Scientific Poster Presentation, “NTG and Bilateral Monocular Trial Study Posters” AIGS World Glaucoma Congress, Vienna, Austria July 06-09, 2005

Guest Speaker, “Corneal Pachymetry – How does it help me manage my glaucoma patients?” Innovations in Glaucoma and Anterior Segment Therapies, Cape Cod, MA September 17, 2005

Guest Speaker, “Imaging: An Everyday Perspective on OCT, HRT, and GDX” Innovations in Glaucoma and Anterior Segment Therapies, Cape Cod, MA September 17, 2005

Guest Speaker, “Cataract Surgery in the Glaucoma Patient” Innovations in Glaucoma and Anterior Segment Therapies, Cape Cod, MA September 17, 2005

Course Faculty, “SURGE: Sound Understanding of REAL Glaucoma Efficacy” AAO Annual Meeting, Chicago, IL October 15, 2005

Scientific Poster Presentation, “Comparison of the IOP-Lowering Efficacy of Bimatoprost and Travoprost in Black Patients With Glaucoma or Ocular Hypertension” AAO Annual Meeting, Chicago, IL October 16, 2005

Course Instructor, “Lasers in Glaucoma” AAO Annual Meeting, Chicago, IL October 16, 2005

Scientific Poster Presentation, “Improved Nerve Fiber Layer Assessment Using Eye OCT Raster Scanning” AAO Annual Meeting, Chicago, IL October 17, 2005

2006 Guest Lecturer, “*Reframing Disease Severity*” SURGE CME Lunch Symposium, The Royal Hawaiian Eye Meeting, Hawaii, January 16, 2006

Guest Lecturer, “*Optimization of Patient Therapy*” SURGE CME Lunch Symposium, The Royal Hawaiian Eye Meeting, Hawaii, January 16, 2006

Guest Presenter, “*Endoscopic and Transscleral Cyclophotocoagulation*,” The Royal Hawaiian Eye Meeting, Hawaii, January 18, 2006.

Scientific Poster Presentation, “*Evaluation of Bimatoprost 0.03% versus Latanoprost 0.005%: A Paired-Comparison Study*” The World Congress of Ophthalmology, Sao Paulo, Brazil February 19 – 24, 2006.

Scientific Poster Presentation, “*Efficacy of Brimonidine 0.15% as Adjunctive Therapy with Latanoprost 0.005% in Patients with Open Angle ASCRS ASOA Symposium & Congress*,”

San Francisco, CA, March 17-19, 2006.

Scientific Poster Presentation, “*The Effect of Probe Placement on Endoscopic Cyclophotocoagulation Laser Energy Transmission*” ARVO, Fort Lauderdale, FL April 30, 2006

Scientific Poster Presentation, “*Ocular Hypotensive Efficacy of Brimonidine 0.15% as Adjunctive Therapy With Latanoprost 0.005% in Patients With Open-Angle Glaucoma or Ocular Hypertension*” ARVO, Fort Lauderdale, FL April 30, 2006

Scientific Poster Presentation, “*UGH Syndrome Associated With the Acrysof SA60 at Intraocular Lens Following Placement Within the Capsular*” ARVO, Fort Lauderdale, FL April 30, 2006

Scientific Poster Presentation, “*Morphologic Evaluation Of Bevacizumab (Avastin®) Treated Corneal Stromal Fibroblasts*” ARVO, Fort Lauderdale, FL, May 01, 2006

Scientific Poster Presentation, “*Reproducibility of Retinal Layer Thickness Measurements Using a Novel Macular Segmentation Software*” ARVO, Fort Lauderdale, FL, May 02, 2006

Scientific Poster Presentation, “*Macular Retinal Segmentation and Composite Retinal Image for Glaucoma Detection*” ARVO, Fort Lauderdale, FL May 02, 2006

Scientific Poster Presentation, “*Optical Coherence Tomography (OCT) Quality Evaluation Revisited With Common Classification Criteria*” ARVO, Fort Lauderdale, FL May 02, 2006

Scientific Poster Presentation, “*Pilot Study of the Relationship Among Depression and Visual Impairment in Older Adults*” ARVO, Fort Lauderdale, FL May 02, 2006

Scientific Poster Presentation, “*Evaluation of Heidelberg Retina Tomography (HRT 3) in Healthy Eyes*” ARVO, Fort Lauderdale, FL May 02, 2006

Scientific Poster Presentation, “*Heidelberg Retina Tomograph (HRT) II vs. HRT 3: What Is the Difference?*” ARVO, Fort Lauderdale, FL, May 03, 2006

Scientific Poster Presentation, “*Frequency of Diagnostic Procedures Amongst Patients Diagnosed as Ocular Hypertension, Primary Open Angle Glaucoma, and Glaucoma Suspects in Western Pennsylvania*” ARVO, Fort Lauderdale, FL, May 03, 2006

Scientific Poster Presentation, “*The Utility of Venting Slits and Punctures in Modifying Glaucoma Drainage Device Outflow Facility*” ARVO, Fort Lauderdale, FL, May 04, 2006

Guest Lecturer, “*Phaco-ECP Technique*” Ocular Surgery News Las Vegas: Improving your Odds 2006 Symposium, Las Vegas, NV June 08, 2006

Course Faculty, “*Glaucoma Therapy: Scratching the Surface*” The 29th Annual Midwest Glaucoma Symposium, Pittsburgh, PA September 15, 2006

Course Faculty, “*Cyclophotocoagulation Then and Now*” The 29th Annual Midwest Glaucoma Symposium, Pittsburgh, PA September 16, 2006

Invited Speaker, “*Current Glaucoma Therapy*” Sino US Joint Symposium on Ophthalmology, Shanghai, China September 21, 2006

Guest Chair, “*Predicting the Future—The Role of Optic Nerve Imaging in OHTS*”

“ Managing

Glaucoma: A Full Spectrum Approach AAO Annual Meeting, Las Vegas, NV, November 11, 2006

Guest Lecturer, “*Cataract Surgery with Co-Existing Conditions*”. 2006 ASORN Annual

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Meeting, Las Vegas, NV, November 11, 2006.

Course Instructor, “*Basic Imaging in Ophthalmology*” AAO Annual Meeting, Las Vegas, NV, November 11, 2006

Course Instructor, “*Laser Treatment of Glaucoma*” AAO Annual Meeting, Las Vegas, NV, November 11, 2006

Course Instructor, “*Lasers in Glaucoma*” AAO Annual Meeting, Las Vegas, NV, November 12, 2006

2007 Guest Lecturer, “*Glaucoma Testing Options*” Nursing and Allied Health General Session, The Royal Hawaiian Eye Meeting, Hawaii, January 16, 2007

Course Faculty, “*Adherence I n Medical Therapy-Experience with an Electronic Adherence*

Monitor” The Royal Hawaiian Eye Meeting, Hawaii, January 17, 2007

Course Faculty, “*Endoscopic Cyclophotocoagulation - Clinical Experience and Recent Findings*” The Royal Hawaiian Eye Meeting, Hawaii, January 17, 2007

Scientific Poster Presentation, “*Effect of Audible and Visual Reminders on Adherence in Glaucoma Patients Using a Commercially Available Dosing Aid*” AGS, San Francisco, CA, March 2007

Scientific Poster Presentation, “*Brimonidine Purite 0.15% Versus Dorzolamide 2% Used as Adjunctive Therapy to Latanoprost*” AGS, San Francisco, CA, March 2007

Scientific Poster Presentation, “*Clinical Evaluation of a Novel Gold Micro-Shunt for Reduction of IOP in Refractory Glaucomas*” AGS, San Francisco, CA, March 2007

Scientific Poster Presentation, “*Evaluation of Diurnal Control of Intraocular Pressure After a Single Drop of Bimatoprost 0.03% or Travoprost 0.004%*” IGS, Athens, Greece, March, 2007

Scientific Poster Presentation, A Bleb-Free Approach to Reduction of IOP in Treatment of ARVO, Ft Lauderdale, FL, May 2007

Scientific Poster Presentation, *A Multicenter Evaluation of Methods to Promote Patient Acceptance of Hyperemia Associated with Bimatoprost Therapy for Glaucoma or Ocular Hypertension*, World Glaucoma Congress, Singapore, July 2007

Scientific Poster Presentation, *Brimonidine Purite 0.15% versus Dorzolamide 2% Used as Adjunctive Therapy to Latanoprost*, World Glaucoma Congress, Singapore, July 2007

Invited Speaker, Basic Science of Care Course, University of Pittsburgh School of Medicine, September 19, 2007

Course Director, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” AAO Annual Meeting, Las Vegas, NV, November 11, 2007

Lead Instructor, “*Laser Treatment of Glaucoma*” AAO Annual Meeting, Las Vegas, NV, November 11, 2007

Course Director, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” Skills Transfer Lab, AAO Annual Meeting, Las Vegas, NV, November 12, 2007

Scientific Poster Presentation, *Evaluation of Microbial Growth in Topical Glaucoma Medications with and without Benzalkonium Chloride*, AAO Annual Meeting, Las Vegas, NV, November 2007

2008 Guest Lecturer, “How to Manage the Progressing Glaucoma Patient” Hawaiian Eye, CME, Lunch Symposium, The Royal Hawaiian Eye Meeting, Hawaii, January 21, 2008

Invited Speaker *The Glaucoma Patient with Cataract: What's a Surgeon to Do?*, The Royal Hawaiian Eye Meeting, Hawaii, January 23, 2008

Invited Speaker, *Use of Anti-Vegf Agents in Glaucoma*, Nursing and Allied Health Program, The Royal Hawaiian Eye Meeting, Hawaii, January 24, 2008

Scientific Poster Presentation, *Comparison of Post-Operative IOP Control Using Different Polyglactin Sutures for Cinching of Baerveldt Tubes*, American Glaucoma Society, Washington, DC, March 2008

Scientific Poster Presentation, *Intra-Operative Intracameral Dexamethasone Reduces Inflammation in Glaucomatous Eyes*, American Glaucoma Society, Washington, DC, March 2008

Invited Speaker, *Laser Treatment of Glaucoma*, Pittsburgh Ophthalmologic Society, Pittsburgh, PA, March 07, 2008

Invited Speaker, *Novel Strategies in the Therapeutic Management of Glaucoma*, ASCRS-ASOA Chicago, IL, April 06, 2008

Scientific Poster Presentation, *A Descriptive Cross-Sectional Survey Assessing the Demographic Variations in the Prevalence of Complementary and Alternative Medicine Use in Patients visiting UPMC Eye Center* ARVO 2008 Annual Meeting, April 2008

Scientific Poster Presentation, *Reproducibility of Measurements of Aqueous Velocity Within Schlemm's Canal With Spectral Domain Optical Coherence Tomograph*, ARVO 2008 Annual Meeting, April 2008

Scientific Poster Presentation, *Glaucomatous Progression Detection by Perimetry Using Visual Field Index (VFI) and Global Parameters*, ARVO 2008 Annual Meeting, April 2008

Scientific Poster Presentation, *DSAEK Combined With Phacoemulsification: Compensating for the Hyperopic Shift*, ARVO 2008 Annual Meeting, April 2008

Scientific Poster Presentation, *Evaluating Glaucoma Progression Using a Latent Class Model for MD, PSD, AGIS, and VFI With RNFL as Covariate*, ARVO 2008 Annual Meeting, April 2008

Scientific Poster Presentation, *Automated Extraction of Optic Nerve Head Parameters From Spectral Domain Optical Coherence Tomography*, ARVO 2008 Annual Meeting, April 2008

Invited Speaker, *Novel Strategies in the Therapeutic Management of Glaucoma*, ASCRS 2008 Annual Meeting, Chicago, IL April 06, 2008.

Invited Speaker, *Treatment Algorithms for SLT*, 2nd Biannual European Glaucoma Laser Surgery Symposium, Sardinia, Italy, June 12, 2008

Course Director, *Anterior Segment Update*, Nemacolin Woodlands, Farmington, PA, September 06, 2008

Glaucoma Laser Therapy: Innovations and Advice From the Experts

Course Director, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” AAO Annual Meeting, Atlanta, GA, November 8-11, 2008

Course Director, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” Skills Transfer Lab, AAO Annual Meeting, Atlanta, GA, November 8-11, 2008

- 2009** **Invited Speaker**, “*Imagining in Glaucoma*” Research Study Club of Los Angeles’ 77th Mid-Winter Clinical Conference, Los Angeles, CA January 17, 2009
Invited Speaker, “*Medical & Surgical Treatments of Glaucoma*” Research Study Club of Los Angeles’ 77th Mid-Winter Clinical Conference, Los Angeles, CA January 17, 2009
Invited Speaker, “*Imagining in Glaucoma*” University of Rochester School of Medicine & Dentistry 54th Annual Ophthalmology Conference, Rochester, NY, March 20-21, 2009
Invited Speaker, “*Medical & Surgical Treatments of Glaucoma*” University of Rochester School of Medicine & Dentistry 54th Annual Ophthalmology Conference, Rochester, NY, March 20-21, 2009
Scientific Poster Presentation, “*Long-Term Follow-Up of Suture Versus Fibrin Glue-Assisted Glaucoma Drainage Device Surgery*” American Glaucoma Society, San Diego, CA, March 2009
Scientific Poster Presentation, “*Long-Term Clinical Outcomes of Baerveldt Glaucoma Implant Tube Placement in the Sulcus Versus the Anterior Chamber*” American Glaucoma Society, San Diego, CA, March 2009
Invited Speaker, “*Combined Endoscopic Cyclophotocoagulation*” ASCRS Glaucoma Day Program, ASCRS 2009, San Francisco, April 4-6, 2009
Course Co-Instructor, Innovative Uses of Adhesives in Anterior Segment Surgery ASCRS 2009, San Francisco, April 4-6, 2009
Invited Lecturer, “*How EMR and IT have helped to make quality, safety, and operations better....or worse*” The Basic Science of Care course, Pittsburgh, PA, September 09, 2009
Course Director, *Anterior Segment Update*, Nemacon Woodlands, Farmington, PA, September 12, 2009
Course Director, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” AAO Annual Meeting, San Francisco, CA, October 25, 2009
Course Director, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” Skills Transfer Lab, AAO Annual Meeting, San Francisco, CA, October 25, 2009
Course Director, “*International Teleophthalmology Symposium*”, Pittsburgh, PA October 31, 2009
- 2010** **Guest Lecturer**, “*Grand Rounds CME Lectures*”, USF Eye Institute, Tampa, FL March 18, 2010
Course Faculty, “*Innovative Uses of Adhesives in Anterior Segment Surgery*” AAO Annual Meeting 2010, Chicago, Illinois, 2010.
Scientific Poster Presentation, “*Long-Term Clinical Outcomes of Baerveldt Glaucoma Implant Tube Placement in the Sulcus Versus the Anterior Chamber*” American Glaucoma Society, San Diego, CA, March 2010
Invited Speaker, “*Combined Endoscopic Cyclophotocoagulation*” ASCRS Glaucoma Day Program, ASCRS 2010, San Diego April 4-6, 2010

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Course Co-Instructor, Innovative Uses of Adhesives in Anterior Segment Surgery ASCRS 2009, San Francisco, April 4-6, 2010

Course Director, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” AAO Annual Meeting, Chicago, Ill, October 25, 2010

Course Director, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” Skills Transfer Lab, AAO Annual Meeting, Chicago, Ill, October 25, 2010

- 2011** **Course Director**, “Evaluation of an Outpatient Electronic Health Record System” HIMSS, Orlando, Florida February 2, 2011
- Course Faculty**, “Use of teleretina program to identify patients with glaucoma and macular degeneration. VA National Teleretina Symposium, February 24, 2011
- Course Faculty**, “*Endoscopic Cyclophotocoagulation*” AGS Surgery Day Program, AGS 2011, Dana Point, California March 4-6, 2011
- Invited Speaker**, “*Surgical Disasters*” ASCRS Glaucoma Day Program, ASCRS 2011, San Diego April 4-6, 2011
- Course Director**, “*Effect of preservatives on the ocular surface.*” World Glaucoma Congress, Paris, France, July 2, 2011
- Course Faculty**, “Complications of gold shunt and canaloplasty surgery.” World Glaucoma Congress, Paris, France, July 2, 2011
- Course Faculty**, “*Selective Laser Trabeculoplasty as primary therapy for glaucoma.*” World Glaucoma Congress, Paris, France, July 2, 2011
- Invited Speaker**, “*Innovations in Glaucoma Surgical Therapy*” Cape Cod National Glaucoma Symposium, Brewster, MA July 26, 2011
- Invited Speaker**, “*Imaging in Glaucoma Diagnosis and Therapy*” Cape Cod National Glaucoma Symposium, Brewster, MA July 26, 2011
- Invited Speaker**, “*Innovations in Glaucoma Surgical Therapy*” Connecticut Optometry Society Annual Meeting, Mystic Connecticut, September 15, 2011
- Invited Speaker**, “*Evaluation of the Optic Nerve*” Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, October 22, 2011
- Invited Speaker**, “*Acute Eye Conditions*” St Vincent’s Medical Center Grand Rounds, Bridgeport, Connecticut, October 15, 2011
- Course Instructor**, “Innovative Uses of Adhesives in Anterior Segment Surgery” American Academy of Ophthalmology 2011, Orlando, October 24, 2011
- Course Director**, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” AAO Annual Meeting, Orlando Florida, October 25, 2011
- Course Director**, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” Skills Transfer Lab, AAO Annual Meeting, Orlando, FL, October 25, 2011
- Course Instructor**, “*Endoscopic Cyclophotocoagulation*” American Academy of Ophthalmology 2011, Orlando, October 24, 2011
- Session Moderator**, “*Innovations in Glaucoma Treatment*” Yale University Annual Glaucoma Symposium, New Haven, Connecticut, November 4, 2011
- Invited Speaker**, “*Combined Cataract and Glaucoma Surgery*” OSN New York Annual Ophthalmology Meeting, New York, New York November 16, 2011.

Invited Speaker, “*Innovations in Glaucoma Surgery*”. Nassau County Ophthalmology Surgical Meeting, Garden City, NY December 4, 2011.

- 2012 Guest Lecturer,** “*Secondary Glaucomas*” Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, January 19, 2012
- Guest Lecturer.** *Glaucoma Reveiw*” Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, March14, 2012
- Course Instructor,** “*Special Interest Group: Endoscopic Cyclophotocoagulation*” American Glaucoma Society Annual Meeting 2012, New York, NY March 5, 2012
- Invited Speaker,** “*OKAP review*” Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, March 14, 2012
- Invited Speaker,** “*Imaging in Glaucoma Diagnosis and Therapy*” Dallas Ophthalmology Society 34th Annual Meeting, Dallas, TX March 30, 2012
- Invited Speaker,** “*Formulations of glaucoma medications and generics*” Dallas Ophthalmology Society 34th Annual Meeting, Dallas, TX March 30, 2012
- Invited Speaker,** “*Combined Cataract and Glaucoma Surgery*” Dallas Ophthalmology Society 34th Annual Meeting, Dallas, TX March 30, 2012
- Course Co-Director,** “*New devices for glaucoma surgery*” Advances in Anterior Segment Surgery Meeting, Fairfield, CT April 10, 2012.
- Course Co-Director,** “*New adhesive for use in cataract surgery*” Advances in Anterior Segment Surgery Meeting, Fairfield, CT April 10, 2012.
- Course Co-Director,** “*The Use of Intense Pulsed Light (IPL) for treatment of ocular surface disease*” Advances in Anterior Segment Therapy and Surgery Meeting, Fairfield, CT April 10, 2012.
- Invited Speaker,** “*Imaging in Glaucoma*” ASCRS Glaucoma Day Program, ASCRS Annual Meeting 2012, Chicago April 20, 2012
- Course Instructor,** “*Adhesives in Glaucoma Surgery*” ASCRS Annual Meeting 2012, Chicago April 22, 2012
- Invited Speaker,** “*Optimizing Glaucoma Therapy*” Thailand Ophthalmology Society Semi-Annual Meeting, Bangkok, Thailand May 25, 2012
- Invited Speaker,** “*Update on Neuroprotection in Glaucoma Therapy*” Thailand Ophthalmology Society Semi-Annual Meeting, Bangkok, Thailand May 25, 2012
- Invited Speaker,** “*Evolving Role of Brimonidine in Glaucoma Therapy*” Philippines Glaucoma Society, Manila, Philippines May 26, 2012
- Invited Speaker,** “*Express Minishunt Surgery*” Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, August 14, 2012
- Course Instructor,** “*Innovative Uses of Adhesives in Anterior Segment Surgery*” American Academy of Ophthalmology 2011, 2012, Chicago, IL, November 10-13 , 2012
- Course Director,** “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” AAO Annual Meeting, Orlando Florida, 2012, Chicago, IL, November 10-13 , 2012
- Course Director,** “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” Skills Transfer Lab, AAO Annual Meeting, 2012, Chicago, IL, November 10-13 , 2012
- Course Instructor,** “*Endoscopic Cyclophotocoagulation*” American Academy of

Ophthalmology 2012, Chicago, IL, November 10-13 , 2012

Invited Speaker, *"Minimally Invasive Glaucoma Surgery - Ready or not, here it comes!"*

OSN New York Annual Ophthalmology Meeting, New York, New York November 16, 2012.

Invited Speaker, *"Perspectives in Femtosecond Cataract Surgery"* OSN New York Annual Ophthalmology Meeting, New York, New York November 16, 2012.

Invited Speaker, *"Controversies in Ocular Surface Disease Management"* OSN New York Annual Ophthalmology Meeting, New York, New York November 18, 2012.

Featured Speaker, "Management of Complex Refractive IOL Cases", NASSAU SURGICAL SOCIETY CLINIC DAY, December 5, 2012.

Featured Speaker, "Update on Microinvasive Glaucoma Devices", NASSAU SURGICAL SOCIETY CLINIC DAY, December 5, 2012.

Featured Speaker, "Glaucoma Case Studies", NASSAU SURGICAL SOCIETY CLINIC DAY, December 5, 2012.

Featured Speaker, "Glaucoma Update: Detection and Monitoring of Glaucoma Progression", Wills Eye Hospital Glaucoma Symposium, December 15, 2012.

2013 Guest Lecturer, *"Laser Treatment of Glaucoma"* Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, January 17, 2013

Guest Lecturer, *"OKAP Review Course"* Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, March 19, 2013

Invited Speaker, "Insights on the Risk of Glaucoma Progression" Phoenix Ophthalmology Society Meeting, Phoenix, Arizona, April 4, 2013.

Invited Speaker, *"ECP and Cataract Surgery – PRO"* ASCRS Glaucoma Day Program, ASCRS 2013, San Francisco, CA April 19, 2013

Invited Speaker, *"Controversies in Medical and Laser Treatment"* ASCRS Glaucoma Day Program, ASCRS 2013, San Francisco, CA April 19, 2013

Invited Speaker, *"Minimally Invasive Glaucoma Surgery"* Cape Cod Innovations in Ophthalmology Meeting, Brewster, MA May 31-June 2, 2013.

Invited Speaker, *"Use of Adhesives in Glaucoma Surgery"* Cape Cod Innovations in Ophthalmology Meeting, Brewster, MA May 31-June 2, 2013.

Invited Speaker, *"Shunts, Tubes and Trabs"* Cape Cod Innovations in Ophthalmology Meeting, Brewster, MA May 31-June 2, 2013.

Featured Speaker, *"Current Role of Lasers in Glaucoma Therapy"* Yale University Ophthalmology Annual Research Day, New Haven, Connecticut, June 21, 2013

Featured Speaker, *"Evolving advances in Glaucoma Surgery"* Yale University Ophthalmology Annual Research Day, New Haven, Connecticut, June 21, 2013

Featured Speaker, *"Update on Eyelid Lesions and Procedures"* Connecticut Optometry Society Meeting, Rocky Hill, Connecticut, May 23, 2013.

Featured Speaker, *"Update New Office Technologies"* Connecticut Optometry Society Meeting, Fairfield, Connecticut, June 9, 2013.

Featured Speaker, *"Update New Office Technologies"* Connecticut Optometry Society Meeting, Fairfield, Connecticut, June 23, 2013.

Featured Speaker, "Update on Microinvasive Glaucoma Devices", St. Luke's Annual

Ophthalmology Meeting, Manila, Phillipines August 24-25, 2013.

Featured Speaker, “Update on Imaging in Glaucoma”, St. Luke’s Annual Ophthalmology Meeting, Manila, Phillipines August 24-25, 2013.

Featured Speaker, “ECP for Glaucoma Therapy”, St. Luke’s Annual Ophthalmology Meeting, Manila, Phillipines August 24-25, 2013.

Featured Speaker, “Adhesives for Glaucoma Surgery”, St. Luke’s Annual Ophthalmology Meeting, Manila, Phillipines August 24-25, 2013.

Featured Speaker, “Update on Microinvasive Glaucoma Devices”, St. Luke’s Annual Ophthalmology Meeting, Manila, Phillipines August 24-25, 2013.

Featured Speaker, “Update on Lasers for Glaucoma”, St. Luke’s Annual Ophthalmology Meeting, Manila, Phillipines August 24-25, 2013.

Featured Speaker, “New Glaucoma Drainage Device Technique. St. Luke’s Annual Ophthalmology Meeting, Manila, Phillipines August 24-25, 2013.

Invited Speaker, “*Treatment of Glaucoma and Cataract*” OSN New York Annual Ophthalmology Meeting, New York, New York September 6-8, 2013.

Invited Speaker, “*Challenging Cases in Glaucoma*” OSN New York Annual Ophthalmology Meeting, New York, New York September 6-8, 2013.

Invited Speaker, “*Hot Topics in Glaucoma*” OSN New York Annual Ophthalmology Meeting, New York, New York September 6-8, 2013.

Invited Speaker, “*Controversies in Ocular Surface Disease Management*” OSN New York Annual Ophthalmology Meeting, New York, New York September 6-8, 2013.

Guest Faculty, “*Comprehensive ECP*” 36th Annual Midwest Glaucoma Symposium, Pittsburgh, PA , September 27-28, 2013

Course Instructor, “Innovative Uses of Adhesives in Anterior Segment Surgery” American Academy of Ophthalmology 2013, New Orleans, LA, October 18-21 , 2013

Course Director, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” New Orleans, LA, October 18-21 , 2013

Course Director, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” Skills Transfer Lab, AAO Annual Meeting, New Orleans, LA, October 18-21 , 2013

Course Instructor, “*Endoscopic Cyclophotocoagulation*” American Academy of Ophthalmology New Orleans, LA, October 18-21 , 2013

Invited Speaker, “*Selective Laser Trabeculoplasty in Clinical Practice*” Russian Ophthalmology Society Meeting, Moscow, Russia December 5-8, 2013.

2014 Guest Lecturer, “*Laser Treatment of Glaucoma*” Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, January 18, 2014

Guest Lecturer, “*OKAP Review Course*” Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, March 20, 2014

Invited Speaker, “*ECP Pearls*” American Glaucoma Society Program, Washington DC, February 28, 2014

Invited Speaker, “*What Technology is Currently Available and What will be approved shortly*” ASCRS, REACT program New York, New York, March 1, 2014

Invited Speaker, “*How to implant a trabecular microbypass*” ASCRS, REACT program

New York, New York, March 1, 2014

Instructor, "*MIGS and Cataract Surgery wet lab*" ASCRS, REACT program New York, New York, March 1, 2014

Invited Speaker, "*Minimally Invasive Glaucoma Surgery*" Pittsburgh Ophthalmology Society Meeting March 21, 2014.

Invited Speaker, "*Formulation Issues in Ophthalmic Medications*" Pittsburgh Ophthalmology Society Meeting March 21, 2014.

Invited Speaker, "*Laser Assisted Cataract Surgery in the Glaucoma Patient*" Pittsburgh Ophthalmology Society Meeting March 21, 2014.

Featured Speaker, "*Neuroprotection in Glaucoma Therapy*" Review of Ophthalmology Meeting Chicago, Illinois March 24, 2014.

Invited Speaker, "*Filtering Surgery in Glaucoma*" New England Ophthalmology Society Meeting, Boston, MA April 11, 2014.

Invited Speaker, "*Iridoplasty- Forgotten Friend*" Glaucoma Subspecialty Day, ASCRS Annual Meeting, Boston, MA April 25, 2014.

Course Director, " ASCRS Course: Ultimate MIGS Triple Procedure 26-305" ASCRS Annual Meeting, ASCRS 2014, Boston, MA April 26, 2014

Course Faculty ASCRS Course: Innovative Uses of Adhesives in Anterior Segment Surgery 28-401 ASCRS Annual Meeting 2014, Boston, MA April 26, 2014

Featured Speaker, "*Steroids and Glaucoma*" Review of Ophthalmology CME Symposium, New York, New York, May 14, 2014

Invited Speaker, "*Selective Laser Trabeculoplasty in Clinical Practice*" New England Ophthalmology Society Meeting, Boston, MA May 30, 2014.

Featured Speaker, "*Update on Laser Treatment of Glaucoma*" SUNY Downstate Ophthalmology Annual Research Day, Brooklyn, New York June 12, 2014

Featured Speaker, "*Update on MIGS Procedures*" SUNY Downstate Ophthalmology Annual Research Day, Brooklyn, New York June 12, 2014

Featured Speaker, "*Update on Imaging*" SUNY Downstate Ophthalmology Annual Research Day, Brooklyn, New York June 12, 2014

Course Faculty, "*Micropulse Laser Treatment of Glaucoma*" European Society of Cataract and Refractive Surgery Meeting, London, England September 13, 2014.

Featured Speaker, "*Current anterior segment and glaucoma surgery*" Association of Veterinary Ophthalmologists Annual Meeting, Fort Worth, Texas October 12, 2014

Course Instructor, "Innovative Uses of Adhesives in Anterior Segment Surgery" American Academy of Ophthalmology Chicago, Illinois, October 18-21, 2014

Course Director, "*Glaucoma Laser Therapy: Innovations and Advice From the Experts*" American Academy of Ophthalmology Chicago, Illinois, October 18-21, 2014

Course Director, "*Glaucoma Laser Therapy: Innovations and Advice From the Experts*" Skills Transfer Lab, American Academy of Ophthalmology Chicago, Illinois, October 18-21, 2014

Course Instructor, "*Endoscopic Cyclophotocoagulation*" American Academy of Ophthalmology Chicago, Illinois, October 18-21, 2014.

Invited Speaker, "*Top 3 Pearls for Cataract Surgery in Glaucoma Patients*" OSN New

York Annual Ophthalmology Meeting, New York, New York November 15, 2014

Invited Speaker, “*Top 3 Pearls for Adopting MIGS*” OSN New York Annual Ophthalmology Meeting, New York, New York November 15, 2014

Invited Speaker, “*Glaucoma Case Conference*” OSN New York Annual Ophthalmology Meeting, New York, New York November 15, 2014

Invited Speaker, “*Top 3 Pearls for Successful Filtering Surgery*” OSN New York Annual Ophthalmology Meeting, New York, New York November 15, 2014

Invited Speaker, “*Controversies in Ocular Surface Disease Management*” OSN New York Annual Ophthalmology Meeting, New York, New York November 16, 2014

2015 Guest Lecturer, “Course Faculty, “Micropulse Laser Treatment of Glaucoma”

Hawaiian Eye Symposium, The Royal Hawaiian Eye Meeting, Hawaii, January 16, 2015

Guest Lecturer, “*OKAP Review Course*” Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, February 9, 2015.

Invited Speaker, “*Istent and cataract surgery*” New England Ophthalmology Society Meeting, Boston, MA April 11, 2015.

Invited Speaker, “*ECP Symposium*” ASCRS Annual Meeting 2015 San Diego, CA April 21, 2015.

Course Faculty ASCRS Course: Innovative Uses of Adhesives in Anterior Segment Surgery ASCRS Annual Meeting 2015 San Diego, CA April 21, 2015.

Invited Speaker, “*SLT in Clinical Practice*” New England Ophthalmology Society Meeting, Boston, MA April 11, 2015.

Guest Lecturer, “*Glaucoma Surgery Wet Lab*” Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, July 20, 2015.

Moderator, “*Pharmacology*” New England Ophthalmology Society Meeting, Boston, MA September 11, 2015.

Invited Speaker, “*Femto Laser Applications*” OSN New York Annual Ophthalmology Meeting, New York, New York October 25, 2015.

Invited Speaker, “*Adopting MIGS Refining Tubes and Trabs*” OSN New York Annual Ophthalmology Meeting, New York, New York October 25, 2015.

Invited Speaker, “*Video Case Conference*” OSN New York Annual Ophthalmology Meeting, New York, New York October 25, 2015.

Invited Speaker, “*Challenges in Ocular Surface Disease*” OSN New York Annual Ophthalmology Meeting, New York, New York October 25, 2015.

2016 Guest Lecturer, “Laser Treatment of Glaucoma” Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, January 18, 2016

Guest Lecturer, “*OKAP Review Course*” Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, March 20, 2016

Invited Speaker, “*ECP Pearls*” American Glaucoma Society Meeting, Fort Lauderdale Florida March 3-6, 2016

Invited Speaker, “*MIGS and Cataract Surgery*” ASCRS, YES program New York, New York, March 1, 2016

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Instructor, "*MIGS and Cataract Surgery wet lab*" ASCRS, YES program New York, New York, March 1, 2016

Invited Speaker, "*Transforming Ophthalmic Care with Sustained Therapies*" Ocular Therapeutics Investor Program program New York, New York, April 6, 2016

Invited Speaker, "*Filtering Surgery in Glaucoma*" New England Ophthalmology Society Meeting, April 11, 2016

Invited Speaker "*Electrophysiology PERG*" ASCRS Glaucoma Subspecialty Day, Boston, MA May 6, 2016

Panel Member "*OCT vs UBM: Which Technology, When?*" ASCRS Glaucoma Subspecialty Day, Boston, MA May 6, 2016

Invited Speaker "*The lighter side of Cyclodestruction: MP3CPC and ECP*" ASCRS Glaucoma Subspecialty Day, Boston, MA May 6, 2016

Course Faculty ASCRS Course: Innovative Uses of Adhesives in Anterior Segment Surgery 28-401 ASCRS Annual Meeting, Boston, MA May 7, 2016

Invited Speaker, "*Selective Laser Trabeculoplasty in Clinical Practice*" New England Ophthalmology Society Meeting, Boston, MA May 30, 2016

Invited Speaker "*Micropulse Technology in Glaucoma*" The Manhattan Glaucoma Symposium 2016, New York, New York, June 1, 2016

Course Instructor, "Innovative Uses of Adhesives in Anterior Segment Surgery" American Academy of Ophthalmology October 18-21, 2016

Course Director, "*Glaucoma Laser Therapy: Innovations and Advice From the Experts*" American Academy of Ophthalmology October, 2016

Course Director, "*Glaucoma Laser Therapy: Innovations and Advice From the Experts*" Skills Transfer Lab, American Academy of Ophthalmology October 18-21, 2016

Course Instructor, "*Endoscopic Cyclophotocoagulation*" American Academy of Ophthalmology October 18-21, 2016

Invited Speaker, "*Treatment of Glaucoma*" OSN New York Annual Ophthalmology Meeting, New York, New York November 15, 2016

Invited Speaker, "*Challenging Cases in Glaucoma*" OSN New York Annual Ophthalmology Meeting, New York, New York November 15, 2016

Invited Speaker, "*Controversies in Ocular Surface Disease Management*" OSN New York Annual Ophthalmology Meeting, New York, New York November 16, 2016

- 2017 Guest Lecturer,** "*Treatment Options for Glaucoma*", Connecticut Society for Eye Physicians Annual Scientific Meeting, Plainville, Connecticut, January 13, 2017
- Guest Lecturer,** "*Laser Treatment of Glaucoma*" Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, January 18, 2017
- Guest Lecturer,** "*OKAP Review Course*" Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, March 20, 2017
- Invited Speaker,** "*ECP Pearls*" American Glaucoma Society Program,, February 28, 2017
- Invited Speaker,** "*MIGS and Cataract Surgery*" ASCRS, YES program New York, New York, March 1, 2017
- Invited Speaker,** "*MIGS and Cataract Surgery wet lab*" ASCRS, YES program New York,

New York, March 1, 2017

Invited Speaker, “*Filtering Surgery*” Glaucoma Subspecialty Day, ASCRS Annual Meeting, April 25, 2017

Course Director, “ ASCRS Course: Ultimate MIGS Triple Procedure 26-305” ASCRS Annual Meeting, ASCRS 2014, April 26, 2017

Course Faculty ASCRS Course: Innovative Uses of Adhesives in Anterior Segment Surgery 28-401 ASCRS Annual Meeting 2014, April 26, 2017

Invited Speaker, “*Surgical Advances in Glaucoma Therapy*” 14th Annual National Glaucoma Symposium, Cap Cod, MA July 29, 2017

Invited Speaker, “*Glaucoma Surgery Grand Rounds*” 14th Annual National Glaucoma Symposium, Cap Cod, MA July 30, 2017

Invited Speaker, “*Controversies in Glaucoma*” 14th Annual National Glaucoma Symposium, Cap Cod, MA July 30, 2017

Invited Speaker, “*Selective Laser Trabeculoplasty in Clinical Practice*” New England Ophthalmology Society Meeting, Boston, MA September 10, 2017

Course Instructor, “Innovative Uses of Adhesives in Anterior Segment Surgery” American Academy of Ophthalmology October 18-21, 2017

Course Director, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” American Academy of Ophthalmology October 18-21, 2017

Course Director, “*Glaucoma Laser Therapy: Innovations and Advice From the Experts*” Skills Transfer Lab, American Academy of Ophthalmology October 18-21, 2017

Course Instructor, “*Endoscopic Cyclophotocoagulation*” American Academy of Ophthalmology October 18-21, 2017

Invited Speaker, “*Treatment of Glaucoma*” OSN New York Annual Ophthalmology Meeting, New York, New York November 15, 2017

Invited Speaker, “*Challenging Cases in Glaucoma*” OSN New York Annual Ophthalmology Meeting, New York, New York November 15, 2017

Invited Speaker, “*Controversies in Ocular Surface Disease Management*” OSN New York Annual Ophthalmology Meeting, New York, New York November 16, 2017

2018 Course Faculty, “*Sub-cyclo concept: technology and mechanism of action*” The Royal Society, London, England January 11, 2018.

Guest Lecturer, “*Laser Treatment of Glaucoma*” Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, January 18, 2018

Guest Lecturer, “*OKAP Review Course*” Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, March 20, 2018

Invited Speaker, Innovative Uses of Adhesives in Anterior Segment Surgery ASCRS Annual Meeting April 26, 2018

Course Faculty, “*Micropulse Laser Treatment of Glaucoma*” Yale Glaucoma Symposium New Haven, CT, September 10, 2018.

Course Faculty, “*Cypass Glaucoma Drainage Device Update*” Yale Glaucoma Symposium New Haven, CT, September 10, 2018.

Invited Speaker, “*Treatment of Glaucoma*” OSN New York Annual Ophthalmology Meeting, New York, New York November 15, 2018

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- Invited Speaker**, "*Challenging Cases in Glaucoma*" OSN New York Annual Ophthalmology Meeting, New York, New York November 15, 2018
- Invited Speaker**, "*Controversies in Ocular Surface Disease Management*" OSN New York Annual Ophthalmology Meeting, New York, New York November 16, 2018
- 2019 Guest Lecturer**, "*Laser Treatment of Glaucoma*" Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, January 18, 2019
- Invited Faculty**, "*Current techniques and devices for angle surgery in glaucoma*" Congreso Anual de Oftalmología, Bogota, Colombia, February 8, 2019.
- Invited Faculty**, "*Ocular surface disease and preservatives*" Congreso Anual de Oftalmología, Bogota, Colombia, February 8, 2019.
- Invited Faculty**, "*Micropulse laser treatment in glaucoma*" Congreso Anual de Oftalmología, Bogota, Colombia, February 8, 2019.
- Invited Faculty**, "*Femtolasar assisted cataract surgery in the glaucoma patient*" Congreso Anual de Oftalmología, Bogota, Colombia, February 8, 2019.
- Invited Faculty**, "*MIGS: Pros y Contras*" Congreso Anual de Oftalmología, Bogota, Colombia, February 8, 2019.
- Invited Faculty**, "*Current techniques and devices for angle surgery in glaucoma*" Congreso Anual de Oftalmología, Bogota, Colombia, February 8, 2019.
- Invited Faculty**, "*Progression of glaucoma on OCT or not?*" Congreso Anual de Oftalmología, Bogota, Colombia, February 8, 2019.
- Invited Faculty**, "*Current concepts in combined cataract and glaucoma surgery*" Congreso Anual de Oftalmología, Bogota, Colombia, February 9, 2019.
- Guest Lecturer**, "*OKAP Review Course*" Yale University Ophthalmology Resident Lecture Series, New Haven, Connecticut, March 20, 2019
- Invited Speaker**, "*Laser Cyclophotocoagulation*" Manhattan Eye and Ear Glaucoma Symposium New York, April 25, 2019.
- Featured Speaker**, "*Pro- Laser Cyclophotocoagulation in Mild to Moderate Glaucoma*" ASCRS Subspecialty Day. San Diego California May 10, 2019
- Moderator**, "*Medications and Lasers*" ASCRS Subspecialty Day. San Diego California May 10, 2019
- Featured Lecturer**, "*Glaucoma Update*" National Glaucoma Society Annual Meeting, Newport Beach, CA October 20, 2019
- Featured Lecturer**, "*Glaucoma Surgery Grand Rounds*" National Glaucoma Society Annual Meeting, Newport Beach, CA October 20, 2019
- Invited Speaker**, "*Update on medications in Glaucoma*" OSN New York Annual Ophthalmology Meeting, New York, New York November 15, 2019
- Invited Speaker**, "*Controversies in Ocular Surface Disease Management*" OSN New York Annual Ophthalmology Meeting, New York, New York November 16, 2019
- 2020 Invited Speaker**, "*Learning Surgery from YouTube- Pearls and Pitfalls*" MIGS- travaganza 2020: A New Hope. A Glaucoma Symposium Bascom Palmer Eye Institute, Miami, Florida, January 25, 2020.
- Invited Speaker**, "*Mistakes I have made and how not to repeat them*" MIGS- travaganza

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2020: *A New Hope. A Glaucoma Symposium* Bascom Palmer Eye Institute, Miami ,Florida, January 25, 2020.

Panel Member, “*Use the Force of an Expert Panel Case Presentations“ MIGS- travaganza 2020: A New Hope. A Glaucoma Symposium* Bascom Palmer Eye Institute, Miami, Florida, January 25, 2020.

Instructor, “*Power up your Lightsabers Wet Lab“ MIGS- travaganza 2020: A New Hope. A Glaucoma Symposium* Bascom Palmer Eye Institute, Miami Florida, January 25, 2020.

Invited Speaker, “*Experience and Pearls using the Hydrus Trabecular microbypass”* Hartford Hospital Eye Surgery Center, Newington Connecticut, February 11, 2020.

Expert Panelist, “*The coming era for advancements in glaucoma therapies”* Ophthalmology Innovation Summit at SECO, March 4, 2020.

Featured Lecturer, “*Update on diagnosis and management of Glaucoma ”* National Glaucoma Society Lecture Series, Fairfield, CT June 14, 2020

Course Instructor, “*An Overview of Ab-Interno iTrack™ Canal-Based Glaucoma Surgery”*, World Glaucoma Congress, Capetown, South Africa, June 20, 2020.

2021

2022 Invited Faculty, “*Paracentesis for IOP redcution”*, Connecticut Optometry Society, Fairfield, CT. March 31, 2022.

Invited Speaker, “*Endoscopic and Transscleral Laser Therapy”*, Association of Cataract and Refractive Surgery Annual Meeting, Glaucoma Sub-Specialty Day, Washington, DC. April 22-26, 2022.

Course Faculty, “*Posterior Segment OCT”*, Basic Skills Section, Association of Cataract and Refractive Surgery Annual Meeting, Washington, DC. April 22-26, 2022.

Course Instructor, “*Endoscopic Cyclophotocoagulation”*, Association of Cataract and Refractive Surgery Annual Meeting, Washington, DC. April 22-26, 2022.

Course Instructor, “*MIGS Skills Transfer Laboraratory Session”*, Association of Cataract and Refractive Surgery Annual Meeting, Washington, DC. April 22-26, 2022.

SYMPOSIA

Selective Laser Trabeculotherapy: An Innovative Treatment for Glaucoma. Ocular Surgery News symposium at the 1999 Annual Meeting of the American Academy of Ophthalmology. October 24, 1999.

Chemical Injury. Traumatic Glaucoma: Mechanisms and Management. The Joint Meeting of the American Academy of Ophthalmology and the Pan-American Association of Ophthalmology. October 21, 2002.

Glaucoma Trials: What are the Key Findings? Simplifying Glaucoma Management: Medical Approaches for Busy Practices. EyeWorld Educational Symposium at the American Society of Cataract and Refractive Surgeons Symposium on Cataract, IOL and Refractive Surgery. April 12, 2003.

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Making Sense of the Signs in Glaucoma: Management Strategies That Work. Health Answers Symposium sponsored by the FCG Institute for Continuing Education. New York City, NY. June 20, 2003.

In which patients can UBM be helpful?; The hypotensive lipids maze: Is there a difference in how they work?; Trabeculectomy: One procedure, so many variations...Why?. 7th Annual Yale Glaucoma Symposium, Westbrook, CT. September 26, 2003.

Making Sense of the Signs in Glaucoma: Management Strategies That Work. Health Answers Symposium sponsored by the FCG Institute for Continuing Education. Newport, RI. October 18, 2003

FORGE: Focusing Ophthalmology on Reframing Glaucoma Evaluation, Las Vegas, NV, June 12, 2004

“Focusing on Reframing Glaucoma Evaluation” SEAGIG Young Ophthalmologist Symposia, SEAGIG 2004, Kuala Lumpur Malaysia, August 25, 2004.

“Glaucoma: The Importance of Low Intraocular Pressure (IOP). How To Get There and Maintain The Health of the Eye.” SEAGIG 2004, Kuala Lumpur Malaysia, August 26, 2004.

“ECP and Cataract Surgery Symposium”, ASCRS 2013, San Francisco, CA April 19, 2013

MIGS symposia with FDA, American Glaucoma Society Pre-meeting. Washington, DC February 28, 2014.

Surviving the Learning Curve : Introducing New Procedures into Your Clinical Practice. American Glaucoma Society Annual Meeting, Washington, DC, February 27, 2014.

ASCRS Panel Glaucoma Surgical 2-L, ASCRS Annual Meeting, Boston, MA April 27, 2014

Pharmacology of Ophthalmology. Session Moderator. New England Ophthalmology Meeting, Boston, MA, September 11, 2015.

Innovation in Access to Branded Therapy. Expert Panelist. American Glaucoma Society Meeting, Washington, DC, February 28, 2020.

The Coming Era for Advancements in Glaucoma Therapies. Expert Perspectives. OIS Ophthalmic Summit at SECO, Atlanta, Georgia. March 4, 2020.

“Best Papers of ASCRS Annual Meeting 2022”, Expert Panelist. Association of Cataract and Refractive Surgery Annual Meeting, Washington, DC. April 26, 2022.

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CURRENT GRANT SUPPORT

Glaukos Evaluation of Aqueous Shunt to Decrease IOP (Principal Investigator)

Santen, Evaluaton of Aqueous Shunt to Decrease IOP (Principal Investigator)

Iridex, Evaluation of Micropulse Technology for Glaucoma

PRIOR GRANT SUPPORT

Advanced Medical Optics Surgical Technique Videos. (Principal Investigator)

Merck Imaging of retina and optic nerve in Alzheimers patients (Principal Investigator)

Iridex Histopathology of Laser Trabeculoplasty (Principal Investigator)

Advanced Medical Optics Teaching Novel Techniques for Seton Implantation (Principal Investigator)

eRecord Enterprise Services/CLIQS - Evaluation of Powerchart for Operative Report Dictation in Ophthalmology (Principal Investigator)

Glaukos Evaluation of Shunt to Decrease IOP (Principal Investigator)

Alcon Evaluation of Glaucoma Medications on Ocular Surface (Co-Investigator)

Merck/Alzheimer Effects of Glaucoma Medications on the Ocular Surface (Co-Investigator)

Allergan A Multicenter, Masked, Randomized, Sham-controlled, Parallel-group, 6-Month (Plus 6-Month Extension) Study to Evaluate the Safety and Effects on Visual Function of Brimonidine Tartrate Posterior Segment Drug Delivery System (Brimonidine Tartrate PS DDS) Applicator System in Patients with Primary Open-Angle Glaucoma (Principal Investigator)

Coherent Laser Use of Double Frequency Nd:YAG for Selective Laser Trabeculoplasty (Principal Investigator)

Merck Sharp & Dohme Addition of Trusopt versus Pilocarpine to Timoptic XE for Treatment of Glaucoma (Co-Investigator)

Allergan Corp. Assessment of Increased Iris Pigmentation through Video Monitoring (Principal Investigator)

Pharmacia & Upjohn A 1-year, double-masked, randomized, 3-arm parallel group study comparing the effect of 0.005% latanoprost (Xalatan) and fixed combination 0.005% latanoprost 0.5% timolol eye drops to 0.5% timolol on corneal endothelial cell counts and corneal thickness in patients with open angle glaucoma or ocular hypertension. (Principal Investigator)

Allergan Corp. Evaluation of Refresh Tears on Tear Film Break-Up Time and Effect of Artificial Teardrops on Corneal Epithelial Healing following Excimer Laser Ablation. (Principal Investigator)

Allergan Corp. Evaluation of Artificial Tear Solutions on the Corneal Epithelium (Principal Investigator)

Allergan Corp. Evaluation of Alphagan versus Trusopt in the Treatment of Glaucoma or Ocular Hypertension in Mexican-Americans (Principal Investigator)

American Health Assistance Foundation, National Glaucoma Research. A Tissue Engineered Aqueous Drainage Device (Co-Investigator)

Pharmacia & Upjohn A Randomized, 5-year Postmarketing Safety Study of Xalatan Compared to "Usual Care" in Patients with Open Angle Glaucoma or Ocular Hypertension (Principal Investigator)

Allergan Corp. Evaluation of Alphagan in Elderly Glaucoma Patients Stabilized on Chronic

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(6 mos) Beta Blocker Therapy (Principal Investigator)

Allergan Corp. A Multi-Center, Double-Masked, Randomized, Parallel, Three-Month Study (with treatment extended to one year) of the Safety and Efficacy of AGN 192024 0.03% Ophthalmic Solution, Administered Once-Daily or Twice-Daily Compared with Timolol 0.5% Ophthalmic Solution Administered Twice-Daily, in Subjects with Glaucoma or Ocular Hypertension (Principal Investigator)

Allergan Corp. A Multi-Center, Double-Masked, Randomized, Split-Parallel Group Comparison of an Artificial Tear to Cyclosporine 0.1% Ophthalmic Emulsion used Twice Daily for up to Six Months in Patients with Mild to Moderate Keratoconjunctivitis Sicca. (Principal Investigator)

Atrium Medical Corp. Ocular Shunt for Glaucoma Treatment. (Co-Investigator)

Allergan Corp. A Multi-Center, Double-Masked, Randomized, Parallel Study of the Safety and Efficacy of 0.2% Brimonidine Tartrate/0.5% Timolol Combination Ophthalmic Solution Twice-Daily or Alphagan Three-Times-Daily for Three Months (Plus 9-Month, Masked Extension) in Patients with Glaucoma or Ocular Hypertension. (Principal Investigator)

Merck A Parallel, Randomized, Observer-Masked, Multi-Center Study Comparing the Ocular Hypotensive Effect of 2% Dorzolamide Hydrochloride/0.5% Timolol Maleate Ophthalmic Solution to the Concomitant Administration of 0.2% Brimonidine Tartrate Ophthalmic Solution and 0.5% Timolol Maleate Ophthalmic Solution in Patients with Ocular Hypertension or Primary Open Angle Glaucoma. (Principal Investigator)

Valley Forge A One-Year, Multi-Center, Double-Masked, Placebo-Controlled, Parallel, Safety and Efficacy Study of 2% Pirenzepine Ophthalmic Gel in Children with Myopia. (Principal Investigator)

Akorn Evaluation of PIROXICAM (0.3%) Ophthalmic Solution Versus Placebo in Inhibition of Intraoperative Miosis During Cataract Extraction. (Principal Investigator)

Whitaker Foundation Imaging the Healing Response of Glaucoma Implants. (Co-Investigator)

Allergan A Multicenter, Investigator-Masked, Randomized, Parallel Study of the Efficacy and Safety of AGN 192024 0.03% Ophthalmic Solution (QD) Compared with Latanoprost 0.005% Ophthalmic Solution (QD) in Patients with Glaucoma or Ocular Hypertension for 3 Months of Treatment (with Treatment Extended to Month 6). (Principal Investigator)

Allergan A Multicenter, Double-Masked, Randomized, Parallel, Extension Study Evaluating the Safety and Efficacy of AGN 192024 0.03% Ophthalmic Solution Compared with Timolol 0.5% Ophthalmic Solution, in Patients with Glaucoma or Ocular Hypertension.

Allergan Corp. Evaluation Refresh – Endura Tears in patients with dry eyes.. (Principal Investigator)

Valley Forge Use of pirenzepine for retardation of Myopic Progression in Children – Extension. (Principal Investigator)

Valley Forge Use of pirenzepine for retardation of Myopic Progression in Children – Open Label. (Principal Investigator)

Biogen ABI-007, Bone Marrow, Irofulven, IROF-007, Leukemia, Lung, OSI, Pancreatic. (Sub-Investigator)

Allergan Corp. Comparison of Bimatoprost and Latanoprost in the Treatment of Normal Tension Glaucoma. (Principal Investigator)

Allergan Corp. Efficacy of Brimonidine Purite 0.15% in Patients Presently on Latanoprost

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Monotherapy. (Principal Investigator)

Allergan Corp. Hypotensive Lipids – EXT2. (Principal Investigator)

Allergan Corp. 48 Month trial for Memantine. (Principal Investigator)

Allergan Corp. Travatan versus Lumigan in African-Americans. (Principal Investigator)

Genentech Macular degeneration study (Marina) rhu Fab V2 vs Sham injection (Sub-investigator)

Genentech Macular degeneration study (Anchor) rhu Fab V2 vs Visudyne. (Sub-Investigator)

University of Arizona/RPB Genetic linkage study of primary open angle glaucoma in Mexican Americans (Principal Investigator)

University of Arizona/RPB Selenium levels in Glaucoma Patients. (Principal Investigator)

Lumenis SLT/Med Trial. (Principal Investigator)

University of Arizona/RPB Tear lactoferrin levels on glaucoma patients. (Principal Investigator)

Pharmacia (Pfizer) Xalatan –5 year safety study. (Principal Investigator)

Allergan IOP lowering efficacy of Bimatoprost and Latanoprost as adjunctive agents in subjects presently using Brimonidine. (Principal Investigator)

Valley Forge/Novartis Pirenzepine for Myopia – Open Label study 2nd year (Principal Investigator)

Merck Safety of Experimental Cardiovascular M132-03 Heart Study (Sub-Investigator)

Lumenis Evaluation of IPL for treatment of meibomian gland disease (Principal Investigator)

Ocular Therapeutics Evaluation of an Ocular Sealant in Cataract Surgery (Principal Investigator)

Aquesys/Allergan, Evaluation of Aqueous Shunt to Decrease IOP (Principal Investigator)

Innfocus/Santen, Evaluation of IMS Aqueous Shunt to Decrease IOP (Principal Investigator)

Glaukos, Evaluation of microbypass shunt combined with cataract surgery to lower IOP in patients with glaucoma (Principal Investigator)

MEDICAL MONITOR

Lumenis November 2006- December 2008.

Ocular Therapeutics September 2011- 2017

SOLX, June 2012- 2017

SCIENTIFIC ADVISORY BOARDS

Inotek, November, 2104- 2018

EndoOptiks 2001-present

MEDICAL DIRECTOR

ISP Surgical Inc., 2016- present

Tula Medical, Inc 2017- present

PEER-REVIEWED JOURNAL ARTICLES

1. Kost J, Noecker R, Kunica E, Langer R. Magnetically controlled release systems: Effect of polymer composition. *J Biomedical Materials Research* 19:935-940; 1985.
2. Cowden K, Giammara B, Georgiade N, Noecker R, Hanker J. "Effects of Compression

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- During Formation on the Mechanical Strengths and Physical Properties of Composite Hydroxyapatite/Plaster Implants for Bone Reconstruction. *Materials Research Society Symposium Proceedings* 110:263-268; 1987.
3. Noecker R, Branner W, Cohen K. Intraocular Lens Explantation with and without Penetrating Keratoplasty. *Ophthalmic Surgery* 20:849-854; 1989.
 4. Cohen K, Tripoli N, Noecker R. Prospective Analysis of Photokeratoscopy for Arcuate Keratotomy to Reduce Postkeratoplasty Astigmatism. *Refractive and Corneal Surgery* 5:388-393; 1989.
 5. Noecker RJ, Cohen KL. Contact lens related corneal ulcers. *NCMJ* 51:269-271; 1990.
 6. Schuman JS, Jacobson JJ, Puliafito CA, Noecker RJ, Reidy WT. Experimental use of semiconductor diode laser in contact transscleral cyclophotocoagulation in rabbits. *Arch Ophthalmol* 108(8):1152-1157; 1990.
 7. Schuman JS, Noecker RJ, Puliafito CA, Jacobson JJ, Shepps GJ, Wang N. Energy levels and probe placement in contact transscleral semiconductor diode laser cyclophotocoagulation in autopsy human eyes. *Arch Ophthalmol* 109(11):1534-1538; 1991.
 8. Cook RL, Noecker RJ, Suits GW. Time allocation of students in a traditional curriculum. *Acad Med* 67(4):279-281; 1992.
 9. Allinson RW, Metrikin DC, Fante R, Noecker R. Phacoemulsification by residents. *Ophthalmology* 99:1481-2; 1992.
 10. Hodes BL, Noecker RJ, Prendiville, K. Autosomal dominant inheritance of iridogoniodysgenesis and cataract. *Ophthalmology* 100(2):168-172; 1993.
 11. Noecker RJ, Allinson RW, Snyder RW. Resident phacoemulsification experience using the in situ nuclear fracture technique. *Ophthalmic Surg* 25(4):216-21; 1994.
 12. Noecker RJ, Kramer TR, Ellsworth LG, Snyder RW. Endolenticular Phacovaporization of the lens in human autopsy eyes using the erbium:YAG laser: A histopathologic study. *SPIE Ophthalmic Technologies IV* 2126:315-322; 1994.
 13. Kramer TR, Noecker RJ, Ellsworth LG, Yarborough JM, Snyder RW. Laser trabecular ablation on human autopsy eyes using the erbium:YAG laser. *SPIE Ophthalmic Technologies IV* 2126:242-250; 1994.
 14. Ellsworth LG, Kramer TR, Noecker RJ, Yarborough JM, Snyder RW. Retinotomy using erbium:YAG laser equipped with a contact probe on human autopsy eyes. *SPIE Ophthalmic Technologies IV* 2126:101--108; 1994.
 15. Kramer TR, Noecker RJ, Miller JM, Clark MC. Langerhans cell histiocytosis with orbital involvement. *Am J Ophthalmol* 124(6):814-824; 1997.
 16. Roh SY, Noecker RJ, Schuman JS. Evaluation of coexisting optic nerve head drusen and glaucoma with optical coherence tomography. *Ophthalmology* 104(7):1138-1144; 1997.
 17. Latina MA, Sibayan SA, Shin DH, Noecker RJ, Marcellino G. Q-Switched 532 nm Nd:YAG laser trabeculoplasty (selective laser trabeculoplasty): a multicenter pilot, clinical study. *Ophthalmology* 105(11):2082-2088; 1998.
 18. Roh SY, Noecker RJ, Schuman JS. Effect of optic nerve head drusen on nerve fiber layer thickness. *Ophthalmology* 105(5):878-885; 1998.
 19. Boswell CA, Noecker RJ, Mac M, Snyder RW, Williams SK. Evaluation of an aqueous drainage glaucoma device constructed of ePTFE. *J Biomed Mater Res (Appl Biomater)*

- 48(5):591-595; 1999.
20. Noecker RJ, Golightly SF. Pharmacology of ocular surgery. *J Ophthalmic Nurs Technol*, 18(3):101-108; May/June 1999.
 21. Noecker RJ. Changing the paradigm for first-line treatment may result in healthier, happier patients. *J Ophthalmic Nurs Technol* 19(2):96-98; March/April 2000.
 22. Noecker RJ, Kramer TR. Comparison of the acute morphologic changes after selective laser trabeculoplasty and argon laser trabeculoplasty in human eye bank eyes. *Ophthalmology* 108:773-779; 2001.
 23. Morgan P, Proniuk S, Blanchard J, Noecker RJ. Effect of temperature and light on the stability of latanoprost and its clinical relevance. *Journal of Glaucoma* 10:401-405; 2001.
 24. Noecker R. Effects of common ophthalmic preservatives on ocular health. *Advances in Therapy* 18(5):205-215; 2001.
 25. Stamer WD, Golightly SF, Hosohata Y, Ryan EP, Porter AC, Varga E, Noecker RJ, Felder CC, Yamamura HI. Cannabinoid CB₁ receptor expression, activation and detection of endogenous ligand in trabecular meshwork and ciliary process tissues. *European Journal of Pharmacology* 431:277-286; 2001.
 26. Noecker RJ, et al. Brimonidine 0.2% as a replacement for beta blockers in geriatric patients with glaucoma. *Advances in Therapy* 19(2):91-97; 2002.
 27. Noecker RJ, Dirks MS, Choplin NT, Bernstein P, Batoosingh AL, Whitcup SM. A six-month randomized clinical trial comparing the intraocular pressure-lowering efficacy of bimatoprost and latanoprost in patients with ocular hypertension or glaucoma. *Amer J Ophthalmol* 135(1):55-63; 2003.
 28. Noecker RJ, Earl ML, Mundorf T, Peace J, Williams RD. Bimatoprost 0.03% versus travoprost 0.004% in black Americans with glaucoma or ocular hypertension. *Advances in Therapy* 20(2):121-128; March/April 2003.
 29. Herrygers LA, Noecker RJ. Effect of preservatives in chronic ocular therapy. *Clinical and Surgical Ophthalmology* 1/21(3):88-94; 2003.
 30. Noecker RJ, Herrygers LA. Effect of preservatives in chronic ocular therapy. (Submitted)
 31. Lee PP, Walt JG, Doyle JJ, Kotak SV, Evans SJ, Budenz DL, Chen PP, Coleman AL, Feldman RM, Jampel HD, Katz LJ, Mills RP, Myers JS, Noecker RJ, Piltz-Seymour JR, Ritch RR, Schacknow PN, Serle JB, Trick GL. A multicenter, retrospective pilot study of resource utilization and costs associated with severity of disease in glaucoma.
 32. Noecker RJ, Herrygers LA, Anwaruddin R. Corneal and conjunctival changes caused by commonly used glaucoma medications. *Cornea* 2004 Jul;23(5):490-6
 33. Herrygers LA, Noecker RJ. Comparison of the effects of Fluress and Fluoracaine on the corneal surface.
 34. Gossage KW, Noecker RJ, Barton JK. Using optical coherence tomography to evaluate glaucoma seton healing response in rabbit eyes.
 35. Lane LC, Levine J, Herrygers L, Noecker RJ. Comparison of corneal surface effects of gatifloxacin and moxifloxacin using intensive and prolonged dosing protocols. *Cornea* 2005 Jan; 24(1):66-71.
 36. Levine JM, Noecker RJ, Lane LC, Herrygers L, Nix D, Snyder RW. Comparative penetration of moxifloxacin and gatifloxacin into the rabbit aqueous humor after topical

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- dosing.
37. Robert J Noecker, MD and Melissa L. Earl, MPH. An update on bimatoprost (Lumigan) in glaucoma therapy. *Therapy September 2004 Vol 1. No 1*
 38. Robert J Noecker, MD Therapeutic Update: Lifestyle Changes and Glaucoma *Glaucoma Today 2004*
 39. Walt JG, Noecker RJ, Romani R. Cost-Effectiveness of Monotherapy Treatment with the Lipid Class of Medications for Glaucoma. *Value in Health*. 2003;6.
 40. Dirks MS, MD, Noecker RJ MD, Earl M, MPH, Roh S MD, Silverstein S MD, Williams Robert MD A Three-Month Clinical Trial Comparing the IOP-Lowering Efficacy of Bimatoprost and Latanoprost in Patients with Normal-Tension Glaucoma. *Ophthalmology* 2005.
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 42. Mills RP, Budenz DL, Lee PP, Noecker RJ, Walt JG, Siegertel LR, Evans SJ, Doyle JJ. Categorizing the stage of glaucoma from pre-diagnosis to end-stage disease. *Am J Ophthalmol*. 2006 Jan;141(1):24-30.
 43. Noecker RJ, Walt Jg Cost-effectiveness of monotherapy treatment of glaucoma and ocular hypertension with the lipid class of medications. *Am J Ophthalmol*. 2006 Jan;141(1 Suppl):15-21.
 44. Kahook MY, Schuman JS, Noecker RJ Needle Bleb Revision of Encapsulated Filtering Bleb With Bevacizumab Ophthalmic Surgery, *Lasers & Imaging*. 2006 March/April Vol 37, No 2.
 45. Kahook MY, Schuman JS, Noecker RJ Intravitreal Bevacizumab in a Patient with Neovascular Glaucoma Ophthalmic Surgery, *Lasers & Imaging*. 2006 March/April Vol 37, No 2.
 46. Kahook MY, Raju, L, Schuman JS, Noecker RJ Iris Retraction Syndrome After Clear Cornea Phacoemulsification The Internet Journal of Ophthalmology & Visual Science. 2006. Volume 3 Number 2
 47. Noecker RJ. The Management of Glaucoma and Intraocular Hypertension: Current Approaches and Recent Advances. *Therapeutics and Clinical Risk Management* 2006;2(2) 193-206
 48. Noecker RJ., Kahook M Glaucoma Drainage Devices. *Techniques in Ophthalmology* 4(2):69-73, 2006
 49. Robert J. Noecker, Melissa L. Earl, Thomas K. Mundorf, Steven M. Silverstein and Michael P Phillips Comparing bimatoprost and travoprost in black Americans. *Current Medical Research and Opinions*, Vol 22, No. 11, 2006, 2175-2180
 49. Noecker RJ. Travoprost/Timolol A Viewpoint by Robert J. Noecker. *Drugs Aging* 2006; 23 (7):598-599
 50. Noecker R. Intraocular pressure-lowering efficacy of bimatoprost 0.03% and travoprost 0.004% in patients with glaucoma or ocular hypertension. *Br J Ophthalmol*. 2006 Nov;90(11):1336-7.
 51. Noecker RJ, Earl ML, Mundorf TK, Silverstein SM, Phillips MP. Comparing bimatoprost and Travoprost in black Americans. *Curr Med Res Opin*. 2006 Nov;22(11):2175-80.

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52. Dirks MS, Noecker RJ, Earl M, Roh S, Silverstein SM, Williams RD. A 3-month clinical trial comparing the IOP-lowering efficacy of bimatoprost and latanoprost in patients with normal-tension glaucoma. *Adv Ther.* 2006 May-Jun;23(3):385-94.
53. Noecker RJ. Comparison of initial treatment response to two enhanced-viscosity artificial tears. *Eye Contact Lens.* 2006 May;32(3):148-52.
54. Stein DM, Wollstein G, Ishikawa H, Hertzmark E, Noecker RJ, Schuman JS. Effect of corneal drying on optical coherence tomography. *Ophthalmology.* 2006 Jun;113(6):985-91.
55. Kahook MY, Schuman JS, Noecker RJ. Trypan blue-assisted neodymium:YAG laser treatment for bleb. *J Cataract Refract Surg.* 2006 Jul;32(7):1089-90.
56. Kahook MY, Noecker RJ, Pantcheva MB, Schuman JS. Location of glaucoma drainage devices relative to the optic nerve. *Br J Ophthalmol.* 2006 Aug;90(8):1010-3. Epub 2006 Apr 13.
57. Cronin TH, Kahook MY, Lathrop KL, Noecker RJ. Accuracy and Performance of a Commercially Available Dosing Aid. *Br J Ophthalmol.* 2006 Aug 17; [Epub ahead of print] PMID: 16916873
58. Kahook MY, Noecker RJ. Fibrin Glue Assisted Glaucoma Drainage Device Surgery. *Br J Ophthalmol.* 2006 Aug 17; PMID: 16916877
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APPENDIX B

Appendix B
Declaration of Robert J. Noecker, M.D., MBA
In Support of Patent Owner's Response (IPR2024-00467)

List of Materials Considered

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- CONFIDENTIAL 10-100-0008 Clinical Study Report (Excerpted) (EX-2103)
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