UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF FLORIDA

CASE NO. _____

JANE APPELBAUM, LINDA HALL, KENAOPE RUTANG, and DAWN DARROW, on behalf of themselves and all others similarly situated, Plaintiffs, v. TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., f/k/a Teva Global Respiratory Research, LLC, f/k/a Ivax Research LLC, f/k/a Ivax Research Inc., f/k/a Ivax Laboratories Inc., f/k/a Baker Norton Pharmaceuticals, Inc.; IVAX LLC, f/k/a Ivax Corporation; JANSSEN PHARMACEUTICALS, INC., f/k/a Ortho-McNeil-Janssen Pharmaceuticals, Inc., f/k/a Janssen Pharmaceutica Inc.; ORTHO-MCNEIL PHARMACEUTICALS, INC.; JANSSEN RESEARCH & DEVELOPMENT LLC f/k/a Johnson & Johnson Research & Development, L.L.C.; ALZA CORPORATION; JANSSEN ORTHO LLC; JOHNSON & JOHNSON; and, BAYER HEALTHCARE PHARMACEUTICALS, INC. f/k/a Bayer Pharmaceuticals Corporation, Defendants.	**CLASS ACTION** **JURY TRIAL DEMANDED**

CLASS ACTION COMPLAINT

JANE APPELBAUM, LINDA HALL, KENAOPE RUTANG, and DAWN DARROW ("Plaintiffs") hereby sue TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., f/k/a Teva Global Respiratory Research, LLC, f/k/a Ivax Research LLC, f/k/a Ivax Research Inc., f/k/a Ivax Laboratories Inc., f/k/a Baker Norton Pharmaceuticals, Inc.; IVAX LLC, f/k/a Ivax

Corporation; JANSSEN PHARMACEUTICALS, INC., f/k/a Ortho-McNeil-Janssen Pharmaceuticals, Inc., f/k/a Janssen Pharmaceutica Inc.; ORTHO-MCNEIL PHARMACEUTICALS, INC.; JANSSEN RESEARCH & DEVELOPMENT LLC f/k/a Johnson & Johnson Research & Development, L.L.C.; ALZA CORPORATION; JANSSEN ORTHO LLC; JOHNSON & JOHNSON; and BAYER HEALTHCARE PHARMACEUTICALS, INC. f/k/a Bayer Pharmaceuticals Corporation (collectively, "Defendants"), and allege as follows:

INTRODUCTION

1. This is a medical monitoring class action related to Defendants' wrongful conduct in connection with the development, design, testing, labeling, packaging, promoting, advertising, marketing, distribution, and selling of pentosan polysulfate sodium ("PPS") as Defendants' prescription drug Elmiron® ("Elmiron").

2. Defendants manufacture, promote, and sell Elmiron as a prescription drug that treats interstitial cystitis (also known as "IC" or "bladder pain syndrome"). Elmiron is manufactured as a capsule suitable for oral consumption.

3. Defendants knew or should have known that Elmiron, when taken as prescribed and intended, causes harmful retinal damage and pigmentary maculopathy.

4. Numerous patient reports, scientific studies, and even alerts by governmental agencies have established that Elmiron causes retinal damage, including Pentosan Polysulfate Sodium Maculopathy ("PPS Maculopathy" or "pigmentary maculopathy"), a signature condition caused by Elmiron toxicity.

5. Nevertheless, Defendants failed to warn, instruct, advise, educate, or otherwise inform Elmiron users, Elmiron prescribers, or United States governmental regulators about the risk

of pigmentary maculopathy or the need for medical, ophthalmological monitoring. At all relevant times, the U.S. label for Elmiron made no mention of risk to patients' eyes or vision.

6. Regular examinations, monitoring, and early detection are necessary to identify and possibly alleviate the devastating vision issues that Elmiron is causing and will continue to cause in the years to come. Recent scientific research has identified a specific test that is most suitable for identifying the Elmiron injury.

7. Plaintiffs accordingly bring this class action on behalf of themselves and a Class of Florida citizens (defined below) to implement a medical monitoring program for early detection, treatment, and study of these conditions for the remainder of Plaintiffs' and each Medical Monitoring Class Member's lives.

PARTY PLAINTIFFS

8. Plaintiff JANE APPELBAUM is a citizen of the state of Florida, residing in Broward County. Plaintiff APPELBAUM was diagnosed with interstitial cystitis and subsequently took Elmiron as prescribed by her physician from approximately 2004 to 2018. During the relevant time periods, Plaintiff APPELBAUM and her physicians were given no warning and had no knowledge of the serious risk of retinal damage and vision loss posed by Elmiron. As a result of her exposure to Elmiron, Plaintiff APPELBAUM is now at a significantly increased risk of contracting PPS maculopathy and requires ophthalmological monitoring for the early detection of this disease. Currently, Plaintiff APPELBAUM has not been diagnosed with Elmiron-associated maculopathy.

9. Plaintiff LINDA HALL is a citizen of the state of Florida, residing in Pasco County. Plaintiff HALL was diagnosed with interstitial cystitis and subsequently took Elmiron as prescribed by her physician from approximately 1996 until 2020. During the relevant time periods,

Plaintiff HALL and her physicians were given no warning and had no knowledge of the serious risk of retinal damage and vision loss posed by Elmiron. As a result of her exposure to Elmiron, Plaintiff HALL is now at a significantly increased risk of contracting PPS maculopathy and requires ophthalmological monitoring for the early detection of this disease. Currently, Plaintiff HALL has not been diagnosed with Elmiron-associated maculopathy.

10. Plaintiff KENAOPE RUTANG is a citizen of the state of Florida, residing in Orange County. Plaintiff RUTANG was diagnosed with interstitial cystitis and subsequently took Elmiron as prescribed by her physician from approximately 2005 until 2017. During the relevant time periods, Plaintiff RUTANG and her physicians were given no warning and had no knowledge of the serious risk of retinal damage and vision loss posed by Elmiron. As a result of her exposure to Elmiron, Plaintiff RUTANG is now at a significantly increased risk of contracting PPS maculopathy and requires ophthalmological monitoring for the early detection of this disease. Currently, Plaintiff RUTANG has not been diagnosed with Elmiron-associated maculopathy.

11. Plaintiff DAWN DARROW is a citizen of the state of Florida, residing in Seminole County. Plaintiff DARROW was diagnosed with interstitial cystitis and subsequently took Elmiron as prescribed by her physician from approximately 1998 to the present. During the relevant time periods, Plaintiff DARROW and her physicians were given no warning and had no knowledge of the serious risk of retinal damage and vision loss posed by Elmiron. As a result of her exposure to Elmiron, Plaintiff DARROW is now at a significantly increased risk of contracting PPS maculopathy and requires ophthalmological monitoring for the early detection of this disease. Currently, Plaintiff DARROW has not been diagnosed with Elmiron-associated maculopathy.

PARTY DEFENDANTS

Ivax Defendants

12. TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., f/k/a Teva Global Respiratory Research, LLC, f/k/a Ivax Research LLC, f/k/a Ivax Research Inc., f/k/a Ivax Laboratories Inc., f/k/a Baker Norton Pharmaceuticals, Inc., ("BAKER NORTON") is a former Florida limited liability company and corporation and a current Delaware corporation with a current principal place of business in Pennsylvania. At all relevant times, BAKER NORTON conducted business and developed Elmiron in Miami, Florida within the Southern District of Florida.

13. On approximately June 11, 1991, BAKER NORTON submitted the original New Drug Application ("NDA") for pentosan polysulfate sodium (NDA: 020193) ("original NDA").

14. Defendant IVAX LLC f/k/a Ivax Corporation ("IVAX" or "IVAX LLC") is a Florida limited liability company with, upon information and belief, no Florida citizen as a member.

15. Upon information and belief, at all relevant times, BAKER NORTON was a subsidiary of IVAX LLC. IVAX and BAKER NORTON conducted clinical trials on Elmiron that were used to support FDA approval of the drug.

16. Upon information and belief, at all relevant times, Defendant IVAX was actively involved in BAKER NORTON's business operations, including the early testing, developing, manufacturing, marketing, distributing, and selling of Elmiron.

17. In or about September of 1997, IVAX transferred the NDA and licensed the rights to Elmiron in the United States and Canada to Defendant ALZA CORPORATION ("ALZA"), for $75 Million in up-front payments and additional consideration.

18. IVAX LLC continued to report royalty revenues derived from the sale and distribution of Elmiron in S.E.C. filings through at least 2005.

19. BAKER NORTON has owned the U.S. Trademark for "Elmiron" from 1992 through the present today, and continues to be listed on the package insert as the licensor of the trademark.

Johnson & Johnson Defendants

20. Defendant ALZA CORPORATION ("ALZA") is a corporation organized under Delaware law with its principal place of business in California. ALZA held the NDA for Elmiron from approximately April of 1998 until August of 2002.

21. As part of its business, ALZA is involved in the research, development, sales, and marketing of pharmaceutical products including Elmiron.

22. Upon information and belief, and at all relevant times, Defendant ALZA was in the business of and did advertise, promote, market, sell, and distribute the drug Elmiron.

23. Defendant JANSSEN PHARMACEUTICALS, INC., f/k/a Ortho-McNeil-Janssen Pharmaceuticals, Inc., f/k/a Janssen Pharmaceutica Inc., ("JANSSEN PHARMA") is a corporation organized under Pennsylvania law with its principal place of business in New Jersey.

24. JANSSEN PHARMA has held the U.S. Food and Drug Administration (FDA) New Drug Application (NDA) for Elmiron since approximately August of 2008.

25. As part of its business, JANSSEN PHARMA is involved in the research, development, sales, and marketing of pharmaceutical products including Elmiron.

26. Upon information and belief, and at all relevant times, Defendant JANSSEN PHARMA was in the business of and did advertise, promote, market, sell, and distribute the drug Elmiron.

27. Defendant ORTHO-MCNEIL PHARMACEUTICALS, INC. ("ORTHO PHARMA") is a corporation organized under Delaware law with its principal place of business in New Jersey.

28. ORTHO PHARMA held the NDA for Elmiron from approximately July of 2004 until August of 2008.

29. As part of its business, ORTHO PHARMA is involved in the research, development, sales, and marketing of pharmaceutical products including Elmiron.

30. Upon information and belief, and at all relevant times, Defendant ORTHO PHARMA was in the business of and did advertise, promote, market, sell, and distribute the drug Elmiron.

31. Defendant JANSSEN RESEARCH & DEVELOPMENT LLC, f/k/a Johnson & Johnson Research & Development, L.L.C. ("JANSSEN R&D") is a limited liability company organized under the laws of New Jersey with its principal place of business in New Jersey. JANSSEN R&D's sole member is Centocor Research & Development, Inc., a Pennsylvania corporation with its principal place of business in Pennsylvania.

32. JANSSEN R&D held the NDA for Elmiron from approximately August of 2002 until August of 2004.

33. As part of its business, JANSSEN R&D is involved in the research, development, sales, and marketing of pharmaceutical products including Elmiron.

34. Upon information and belief, and at all relevant times, Defendant JANSSEN R&D was in the business of and did advertise, promote, market, sell, and distribute the drug Elmiron.

35. Defendant JANSSEN ORTHO, LLC ("JANSSEN ORTHO") is a limited liability company organized under Delaware law with its principal place of business in Puerto Rico.

JANSSEN ORTHO's sole member is OMJ PR Holdings, a corporation incorporated in Ireland with a principal place of business in Puerto Rico. JANSSEN ORTHO manufacturers and packages Elmiron for Janssen Pharmaceuticals, Inc.

36. As part of its business, JANSSEN ORTHO is involved in the research, development, sales, and marketing of pharmaceutical products including Elmiron.

37. Upon information and belief, and at all relevant times, Defendant JANSSEN ORTHO was in the business of and did advertise, promote, market, sell, distribute, and report adverse events for, the drug Elmiron.

38. Defendant JOHNSON & JOHNSON is a corporation organized under New Jersey law with its principal place of business in New Jersey.

39. Upon information and belief, at all relevant times, JANSSEN PHARMA, ORTHO PHARMA, JANSSEN R&D, ALZA, and JANSSEN ORTHO have been wholly owned subsidiaries of JOHNSON & JOHNSON with their profits inuring to JOHNSON & JOHNSON'S benefit.

Bayer Defendant

40. Defendant BAYER HEALTHCARE PHARMACEUTICALS, INC., f/k/a Bayer Pharmaceuticals Corporation, ("BAYER"), a U.S. subsidiary of Bayer Healthcare AG ("Bayer AG"), is a corporation organized under Delaware law with its principal place of business in New Jersey.

41. Upon information and belief, in or around 2005, BAYER contracted on a co-exclusive basis with defendant JOHNSON & JOHNSON to advertise, promote, market, sell,

distribute, and report adverse events for, the drug Elmiron in the United States under a co-promotion agreement (the "Co-Promotion Agreement").[1]

42. Under the terms of the Co-Promotion Agreement, BAYER received the rights to co-promote Elmiron to the urology audience in the United States and receive full profit for prescription sales of Elmiron in the urology sector in the United States.[2]

43. Upon information and belief, BAYER continues to receive full profit for prescription sales of Elmiron in the urology sector in the United States.

44. Upon information and belief, BAYER promoted Elmiron through its network of pharmaceutical sales representatives, and would have been in direct contact with prescribing physicians and have access to adverse reaction information from those health care providers.

45. As part of its business, BAYER is involved in the research, development, sales, and marketing of pharmaceutical products including Elmiron.

46. Upon information and belief, and at all relevant times, Defendant BAYER was in the business of and did advertise, promote, market, sell, distribute, and report adverse events for, the drug Elmiron.

47. Defendants were jointly engaged in the business of designing, developing, manufacturing, testing, packaging, promoting, marketing, distributing, labeling, and/or selling Elmiron, and controlling the Elmiron NDA.

JURISDICTION & VENUE

48. This Court has original jurisdiction over this class action pursuant to the Class Action Fairness Act and 28 U.S.C. § 1332(d) because members of the proposed Class are citizens

[1] *See* Bayer Stockholders' Newsletter 2005, Interim Report as of Sept. 30, 2005 (2005), at 22.

[2] *Id.*

of Florida, a state different from Baker's Norton's home states of Delaware and Pennsylvania, Alza's home states of Delaware and California, Janssen Pharma's home states of Pennsylvania and New Jersey, Ortho Pharma's home states of Delaware and New Jersey, Janssen R&D's home state of New Jersey, Janssen Ortho's home state of Delaware, Johnson & Johnson's home state of New Jersey, and Bayer's home states of Delaware and New Jersey; and upon information and belief the value of the injunctive relief sought exceeds $5,000,000 exclusive of costs.

49. Defendants maintain a regular presence, conduct business, and otherwise specifically avail themselves of the Florida market. Individually and together, the Defendants have caused injury to Plaintiffs and others similarly situated within the State of Florida, arising from products manufactured and/or distributed by the Defendants which were sold, used, and consumed in the State of Florida.

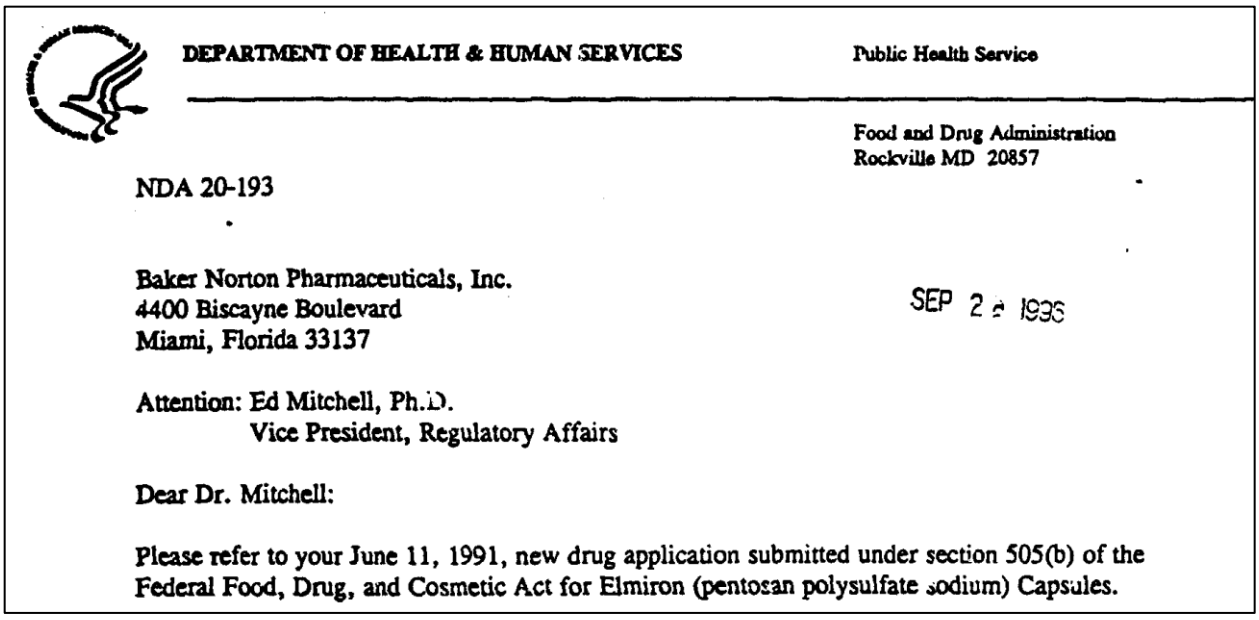
50. Venue is proper in this forum pursuant to 28 U.S.C. § 1391 because Defendants transact business in Florida and in Miami-Dade and Broward counties, and a substantial portion of the practices, events, and omissions complained of herein occurred in this judicial district.

51. All conditions precedent to this action have occurred, been performed, or have been waived.

FACTUAL ALLEGATIONS

A. Brief History of Elmiron

52. In September of 1996, the FDA approved Elmiron for treatment of interstitial cystitis ("IC"), also known as bladder pain syndrome. The approval letter was directed to BAKER NORTON, in Miami, Florida, which had spent years attempting to gain approval for the drug:



DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-193

Baker Norton Pharmaceuticals, Inc.
4400 Biscayne Boulevard
Miami, Florida 33137

SEP 2 6 1996

Attention: Ed Mitchell, Ph.D.
Vice President, Regulatory Affairs

Dear Dr. Mitchell:

Please refer to your June 11, 1991, new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Elmiron (pentosan polysulfate sodium) Capsules.

53. IC is a diagnosis that applies to patients with chronic bladder pain in the absence of other explanatory etiologies (or causes). The symptoms associated with IC range from discomfort to severe pain, and can include increased frequency and urgency of urination.

54. Under the IC treatment guidelines established by the American Urological Association ("AUA"), there are six lines of treatment for IC. According to the AUA, "first-line treatments" should be suggested to all patients and "sixth-line treatments" should be reserved for the most severe cases, with the remaining treatment options falling in between.

55. Elmiron is not a first-line treatment for IC. Rather, Elmiron is one of ten suggested second-line treatments, including three other oral medications: amitriptyline, cimetidine, and hydroxyzine.

56. The guidelines further include numerous third-, fourth-, fifth-, and sixth-line treatments. When first- and second-line treatments fail to provide relief, the third-, fourth-, fifth-, and sixth-line treatments involve more invasive procedures such as the use of a catheter to deliver medicated solutions directly to the bladder; Botox injections to the muscle wall of the bladder; implantation of neurostimulation devices to control muscle contractions in the bladder; or, in rare

cases, surgery to remove ulcers from the bladder or augment the bladder wall with an intestinal patch.

57. Defendants market Elmiron as "The Only Oral Medication FDA Approved to Treat the Bladder Pain or Discomfort of Interstitial Cystitis (IC)."[3] However, while Elmiron is the only oral medication approved by the FDA *specifically* for the purpose of treating IC, that statement is misleading in that ***it is not the only oral medication approved by the FDA that can be used to treat IC, and it is not the only IC treatment option***.

58. Rather, Elmiron is in fact one of *five* oral medications endorsed by the AUA Guidelines for use in treating IC, all of which are FDA-approved oral medications. Furthermore, the AUA Guidelines list *six lines* of treatment for IC, each of which contain multiple treatment options.

59. Indeed, in a March 2012 Citizen's Petition to the FDA, JANSSEN PHARMA did not make the same misrepresentation it made to the public, but rather qualified that "Although other medications may treat discrete symptoms [of IC], ELMIRON is the only ***orally-administered*** medication that is ***specifically*** approved for treatment of IC patients." (emphasis added)[4]

B. Poor Bioavailability and Efficacy of Elmiron

60. Though Defendants admit that the mechanism of action for Elmiron is unknown, Elmiron is thought to be a "chemical bandaid" that coats the epithelial cells of the bladder to

[3] ORTHOELMIRON, https://www.orthoelmiron.com/patient/about-elmiron (last visited Oct. 6, 2020).

[4] March 26, 2020 Janssen Citizen Petition requesting FDA adoption of appropriate bioequivalence requirements to govern approval of any abbreviated new drug application ("ANDA") relying on ELMIRON (pentosan polysulfate sodium) as its reference product (hereinafter "Janssen Citizen Petition") (emphasis added).

provide pain relief. The drug has poor oral bioavailability and absorption, requiring users to take long-term high doses of the drug, resulting in accumulation and ultimate toxicity over time.

61. Typical users take 100mg doses, 3 times per day, because only about 6% of the drug is absorbed to the epithelial cells of the bladder; the majority of the drug is excreted. However, the drug is also absorbed into retinal epithelial cells, which can result in retinal toxicity.

62. Users must ingest Elmiron for at least 3 to 6 months—and often longer—to achieve any benefit. One cohort reported that pain relief occurred in only 40% to 60% of patients.[5] Populations of patients receiving extended treatment (>2 years) showed no further improvement or worsening of symptoms, yet users often continue the drug for years.[6] In other trials, the improvement of certain IC symptoms with Elmiron was significant compared to Placebo (28% of treated subjects versus 13% of placebo controls), but the overall degree of improvement was not dramatic from a clinical standpoint.

63. In the March 2012 Citizen's Petition to the FDA requesting a bioequivalence study for any new generics coming to market—an effort to maintain its market position and block generics from coming to market— JANSSEN PHARMA admitted that "***the drug has low bioavailability, is poorly absorbed from the gastrointestinal tract, and cannot be reliably assayed by determining serum levels***."[7]

64. JANSSEN PHARMA further elaborated:

> ***ELMIRON has not yet been fully characterized***. ELMIRON contains a mix of many components, which vary in chain length (molecular weight), number and location of glucuronic acid sidechains, and number of location of sodium sulfate

[5] Philip M. Hanno, *Analysis of Long-Term Elmiron Therapy for Interstitial Cystitis*, Vol. 49, Issue 5, Supplement 1 UROLOGY 93–99 (1997).

[6] *Id.*

[7] *See* Janssen Citizen Petition (emphasis added).

> groups. ***Moreover, no definitive information exists to identify which of the components are active (i.e., responsible for the safety and efficacy of ELMIRON)*** . . . The information presented above demonstrates that due to the ***unknown etiology of IC, the inability to characterize ELMIRON and understand how it works in the body, the difficulty of measuring PPS in plasma, blood, or urine, and the lack of a reliable bioassay to measure the product's effects***, conventional methods of determining bioequivalence are inadequate."[8]

65. The low efficacy and bioavailability of Elmiron are particularly troubling in light of the significant risks of permanent vision loss and retinal issues caused by the drug. These design defects render Elmiron more dangerous than other drugs and treatment options designed to treat IC and cause an unreasonable increased risk of injury, including but not limited to permanent vision and retinal injuries.

C. Defendants' Failure to Test Elmiron

66. Defendants admit that "the mechanism of action of pentosan polysulfate sodium in interstitial cystitis is not known," and Defendants have failed to determine the mechanism of action of the drug.

67. In the Elmiron NDA file, the FDA noted that: "Elmiron works by binding to exposed epithelium," which may explain its apparent effect on the urinary bladder epithelium.

68. Defendants knew or should have known of the potential impact of the drug on other epithelial cells—particularly the retinal epithelial cells of the eye—but failed to adequately test for these adverse effects.

69. Defendants acknowledged that their Phase III testing of Elmiron was "subjective" and that "an objective measure" may be more appropriate. JANSSEN PHARMA stated:

> The Phase III studies on which the ELMIRON approval was initially based assessed the effect of the drug on subjects' pain and discomfort levels, as measured by the subjects' individual assessments. Pain and discomfort, while key symptoms of the IC diagnosis, are inherently subjective elements. Therefore, while patients'

[8] *Id.* (emphasis added).

> individual assessments based on these subjective impressions were useful in the Phase III ELMIRON trials to demonstrate a clinical benefit as compared to placebo, ***an objective measure is more appropriate*** for studies with clinical endpoints to assess bioequivalence.[9]

70. Furthermore, JANSSEN PHARMA not only failed to conduct pharmacokinetic ("PK") and pharmacodynamic ("PD") testing on the drug, but in fact advocated *against* such testing, stating:

> ***A PK study, while generally appropriate for drugs that are systemically absorbed, is inappropriate*** for determining bioequivalence of an oral dosage form of PPS. Although PPS is systemically absorbed and distributed to the bladder, it has extremely low bioavailability; even with the use of radioactive drug, PPS is difficult to detect in blood or plasma. Due to low serum concentration and the inherent complexity of the product, attempts by the manufacturer of the product, bene, to develop a sensitive and reliable bioassay have been futile. ***Indeed, Janssen is not aware of any analytical techniques presently available to predict or measure systemic concentration of PPS*** . . . Finally, because the mechanism of action of PPS and the pathophysiology of IC is unknown, ***there is no known pharmacodynamic marker other than clinical effect measured as reduction of pain***. (emphasis added)

71. PK and PD testing is not "inappropriate." An understanding of pharmacokinetics of a drug—including absorption, distribution, metabolism, and excretion—is a critical aspect of drug design and is crucial to understanding how the drug interacts with the human body and evaluate potential risks associated with the drug.

D. The Dangers of Elmiron

72. Despite study after study providing clear evidence of the dangers of PPS, Defendants failed to adequately investigate the threat that PPS poses to patients' eyes and vision or warn patients of the risk that they would suffer retinal injury and vision impairment.

73. A physician's usage study of PPS conducted in the late 1980s and early 1990s noted adverse events affecting vision, including optic neuritis and retinal hemorrhage. Defendants relied

[9] Janssen Citizen Petition (emphasis added).

upon this very study when seeking FDA approval for Elmiron and therefore had direct notice of the potential adverse effects.[10]

74. Reported adverse effects on vision included:[11]

> ***Blurred Vision. Left Central Optic Vein Occlusion***: A 32 year old white female without a prior history of eye trauma, hypertension, diabetes or previous significant ophthalmologic history complained of experiencing blurred vision.
>
> ***"Filmy Sensation Over Left Eye" Possible Left Optic Neuritis***: A 21 year old white female without any history of ophthalmological problems, head trauma, diabetes, or any previous neurological symptoms experienced a "filmy sensation over the left eye."

75. As early as 1991, available medical research also identified that PPS inhibits regrowth and proliferation of retinal pigment epithelial (RPE) cells,[12] and could thereby impair an important physiological pathway for retinal health.

76. Indeed, as set forth above, Defendants were on notice from the FDA of the possible effect on other epithelial cells, corroborating the risk Elmiron posed specifically to the RPE cells of the eye.

77. In fact, by 1992, PPS was also in Phase I trials for certain cancer treatments because of its "potent inhibition of cell motility," which further corroborates the role of PPS inhibiting cell regrowth and proliferation.

78. The FDA had serious concerns about Elmiron and rejected several applications for its approval, finding the conduct of some of the clinical trials "worrisome."

---

[10] A Statistical and Medical Review of an Amendment to the New Drug Application for Elmiron ® (Pentosan Polysulfate), NDA #20193, Appendix D (January 1996).

[11] *Id*.

[12] Katrinka H. Leschey, John Hines, Jeff H. Singer, Sean F. Hackett, and Peter A. Campochiaro, *Inhibition of Growth Factor Effects in Retinal Pigment Epithelial Cells*, 32 INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE 1770–1778 (1991).

79. Nevertheless, the FDA ultimately approved Elmiron in September of 1996. After that, new information continued to reveal the serious risk of eye and vision injuries related to Elmiron use.

80. Almost immediately after the FDA approved Elmiron, patients and doctors began reporting serious complications relating to eye and vision problems in patients taking Elmiron.[13]

81. From January of 1997 through March of 2020, 164 cases of eye disorders were reported to the FDA as adverse effects of Elmiron, ranging from blurred vision to maculopathy and blindness. Other reported symptoms include visual impairment, halo vision, and reduced visual acuity.[14]

82. In 2018, researchers from the Emory Eye Center published their concerns about the presentation of a unique eye disease they were seeing in patients taking Elmiron in the Journal of Ophthalmology.[15]

83. The researchers also summarized their findings in a letter to the editor of the Journal of Urology:

> We wish to alert readers to a concerning new observation of ***vision threatening retinal changes associated with long-term exposure to [Elmiron]***. We recently reported our findings of retinal pigmentary changes in six patients undergoing long-term therapy with [Elmiron]. These patients primarily described difficulty reading and/or trouble adjusting to dim lighting. Each patient had received a standard dosage of [Elmiron], ranging from 200 to 400 mg daily, for a median duration of 15.5 years. . . . ***Examination findings in patients with this condition are***

[13] According to the FDA Adverse Events Reporting System (FAERS) Public Dashboard, eight patients taking Elmiron reported serious adverse effects to their vision in the 1997 calendar year: https://fis.fda.gov/sense/app/d10be6bb-494e-4cd2-82e4-0135608ddc13/sheet/6b5a135f-f451-45be-893d-20aaee34e28e/state/analysis.

[14] To date, at least 123 patients have reported "serious" adverse effects to their vision. *Id*.

[15] William A. Pearce, Rui Chen, and Nieraj Jain, *Pigmentary Maculopathy Associated with Chronic Exposure to Pentosan Polysulfate Sodium*, 125 OPHTHALMOLOGY 1793–1802 (2018), https://www.ncbi.nlm.nih.gov/pubmed/29801663.

> ***suggestive of injury to the retina and the underlying retinal pigment epithelium***. . . . After extensive investigations, which included molecular testing for hereditary retinal disease, ***we found these cases to resemble no other retinal disease***.[16]

84. The study, "Pigmentary Maculopathy Associated with Chronic Exposure to [Elmiron]," focused on six women with IC who presented to the Emory clinic between May of 2015 and October of 2017, all with pigmentary maculopathy.[17] Maculopathy is a general term referring to any pathological condition that affects the macula, the central portion of the retina upon which visual acuity and sensitivity depend.

85. Most of these patients had difficulty reading and difficulty seeing in darkness. Two patients experienced a generalized dimming of their vision as the first symptom. Two others had difficulty with near vision: one had paracentral scotomas (vision loss) in part of her eye, while the other had metamorphopsia (distorted vision where straight lines become wavy).

86. All six patients underwent rigorous diagnostic imaging and DNA testing to determine if they had any genes associated with hereditary retinal loss. None had a family history of retinal disease or the discovery of any pathogenic process.

87. What they had in common was the use of Elmiron.

---

[16] William A. Pearce, Adam M. Hanif, and Nieraj Jain, Letter to the Editor Re: *FDA BRUDAC 2018 Criteria for Interstitial Cystitis/Bladder Pain Syndrome Clinical Trials*, 200 UROLOGY 1122 (2018) (emphasis added).

[17] William A. Pearce, Rui Chen, and Nieraj Jain, *Pigmentary Maculopathy Associated with Chronic Exposure to Pentosan Polysulfate Sodium*, 125 OPHTHALMOLOGY 1793–1802 (2018), https://www.ncbi.nlm.nih.gov/pubmed/29801663

88. Examinations of their eyes showed clear changes: "Nearly all eyes (10 eyes of 5 patients) showed subtle parafoveal pigmented deposits at the level of the retinal pigment epithelium (RPE)."[18]

89. All eyes "showed subtle vitelliform deposits that increased in number and extended beyond the major arcade of vessels in cases judged to be more severe. Four eyes of 2 patients showed RPE atrophy that was noted to increase in area and encroach on the central fovea over time."[19] Retinal imaging also found clear diseased regions, atrophy, or both.[20]

90. The youngest patient in the study was 37 years old. Diagnosed with IC at the age of 23 and on a steady dosage of Elmiron, she began showing visual symptoms (difficulty with near vision and difficulty reading) at the age of 30 — just six years after she was diagnosed with IC. She had the most severe damage in the study with deep scotomas of both eyes.[21]

91. The authors expressed concern that "the region of affected tissue may expand centrifugally over time."[22]

92. They concluded that "[c]linicians should be aware of this condition because it can be mistaken for other well-known macular disorders such as pattern dystrophy and age-related macular degeneration."[23]

---

[18] *Id*. at 1798.

[19] *Id.*

[20] *Id*.

[21] *Id*. at 1795, Table 2.

[22] *Id*. at 1800.

[23] *Id*. at 1801.

93. They also encouraged "drug cessation in affected patients," and "recommend[ed] that any patient with suggestive visual symptoms undergo a comprehensive ophthalmic examination."[24]

94. IC experts Robert Moldwin and Curtis Nickel responded to the Emory findings with concern: "***It is quite unlikely that urologists treating patients with [IC] ever would have made this association***."[25]

95. At the American Urology Association 2019 Annual Meeting in May of 2019, the Emory team submitted another study of ten IC patients who had taken Elmiron and experienced macular disease.[26]

96. The patients in this study had a median age of 59 years (range 38–68), and median time since IC diagnosis of 19 years (range 4–40). The most commonly reported symptoms were difficulty reading and difficulty adapting to dim lighting.

97. Eye examinations showed symmetric pigmentary changes in the retina. Retinal imaging demonstrated that the abnormalities were primarily in the retinal pigment epithelium. They noted that their clinic has seen 156 patients with IC who did not have any Elmiron exposure — *and these patients showed no pigmentary maculopathy*.

---

[24] William A. Pearce, Adam M. Hanif, and Nieraj Jain, Letter to the Editor Re: *FDA BRUDAC 2018 Criteria for Interstitial Cystitis/Bladder Pain Syndrome Clinical Trials*, 200 UROLOGY 1122 (2018).

[25] J.C. Nickel and R. Moldwin, Reply to Letter to the Editor Re: *FDA BRUDAC 2018 Criteria for Interstitial Cystitis/Bladder Pain Syndrome Clinical Trials*, 200 UROLOGY 1122, 1123 (2018) (emphasis added).

[26] Jenelle Foote, Adam Hanif, and Nieraj Jain, *Chronic Exposure to Pentosan Polysulfate Sodium is Associated with Retinal Pigmentary Changes and Vision Loss*, 201 UROLOGY e688 (2019), https://www.auajournals.org/doi/10.1097/01.JU.0000556315.46806.ca

98. The Emory team concluded that structural changes of the retina are occurring in patients taking Elmiron, and they were unclear if stopping the medication would alter the course of the damage. They encouraged affected patients to discontinue the use of medications and to undergo comprehensive ophthalmic examinations.

99. Shortly thereafter, the Emory team published a study in the Review of Ophthalmology in July of 2019.[27]

100. "Our subsequent investigations," the team wrote, "demonstrated that this unique maculopathy is strongly associated with chronic [Elmiron] exposure, not IC itself or its other therapies. In fact, ***this characteristic maculopathy has, to date, been exclusively diagnosed in patients reporting prior [Elmiron] exposure***."[28]

101. The team further observed that claims data from a nationally present U.S. insurance company suggested that hundreds of thousands of individuals have likely been exposed to Elmiron in the U.S. The team also recognized a study finding that Elmiron-exposed patients had a significantly increased risk of being diagnosed with a new macular disease after seven years.

102. In September of 2019, the Emory team published additional research in the Journal of American Medical Association Ophthalmology ("JAMA Ophthalmology"), concluding that

[27] Adam M. Hanif and Nieraj Jain, *Clinical Pearls for a New Condition. Pentosan Polysulfate Therapy, a Common Treatment for Interstitial Cystitis, Has Been Associated with a Maculopathy*, REVIEW OF OPHTHALMOLOGY July 10, 2019, https://www.reviewofophthalmology.com/article/clinical-pearls-for-a-new-condition.

[28] *Id*. (emphasis added).

PPS maculopathy "is a vision-threatening condition that can manifest in the setting of long-term exposure to the drug."[29]

103. In November of 2019, a team from Emory and the University of Pennsylvania published an epidemiological study in the British Journal of Ophthalmology which concluded that "PPS users had significantly increased odds of having [maculopathy]."[30]

104. Also in 2019, a team from Kaiser Permanente Northern California treated a patient who was previously misdiagnosed with Stargardt disease, but was actually suffering from Elmiron-associated maculopathy.[31] In their case report, the ophthalmologists stressed that "***failure to diagnose a medication toxicity in a timely fashion may lead to preventable irreversible vision loss***."[32]

105. Another team of researchers found a 20% prevalence of a unique PPS-associated maculopathy among a cohort of patients being treated at the University of California, Los

[29] Adam Hanif et al., *Phenotypic Spectrum of Pentosan Polysulfate Sodium-Associated Maculopathy: A multicenter Study*, 137 JAMA OPHTHALMOLOGY 1275, 1282 (Sep. 5, 2019), https://jamanetwork.com/journals/jamaophthalmology/article-abstract/2749093.

[30] Nieraj Jain et al., *Association of Macular Disease with Long-Term Use of Pentosan Polysulfate Sodium: Findings from a U.S. Cohort*, BRITISH JOURNAL OF OPHTHALMOLOGY (published online first, November 6, 2019), https://bjo.bmj.com/content/early/2019/11/06/bjophthalmol-2019-314765.

[31] Robin A. Vora et al., *A Case of Pentosan Polysulfate Maculopathy Originally Diagnosed as Stargardt Disease*, 17 AMERICAN JOURNAL OF OPHTHALMOLOGY CASE REPORTS 100604 (published online first, January 2020), http://www.sciencedirect.com/science/article/pii/S2451993620300086?via%3Dihub.

[32] *Id*. (emphasis added).

Angeles.[33] Their study suggests "a significant risk of macular toxicity for PPS-treated patients," and that "more significant PPS exposure was associated with more severe atrophy."

106. Most recently, two physicians from Harvard Medical School published a case study indicating that the damage caused by Elmiron continues to progress long after cessation of the drug. [34] In their study, a patient continued to exhibit worsening symptoms of PPS-associated retinal maculopathy for at least 6 years after she stopped taking Elmiron.

107. The doctors noted "the present case adds a new layer of concern by demonstrating progressive maculopathy continuing for up to 6 years after cessation of PPS . . . this case emphasizes the need for a screening regimen that balances the demands on patients and physicians with the importance of prompt identification of early toxicity."[35]

108. The Interstitial Cystitis Network, a health publishing company dedicated to IC, launched its own patient survey on the heels of the Emory Eye Center findings. As of April of 2019, the IC Network had almost 1,000 survey participants, of which 53% reported eye disease.

109. Patient reports on the IC Network Support Forum include (all [*sic*]):[36]

a. June 23, 2019: "I have been diagnosed with macular degeneration and no one in my family has it. I have been on elmiron for 15 years. I decided even though the correlation is not extremely strong to go off it for the sake of my eyes . . . am hoping the degeneration will slow if not stop. Am not looking for it reverse course. Am also hoping that I do not go back to the pain . . .

[33] Derrick Wang et al., *Pentosan-Associated Maculopathy: Prevalence, Screening Guidelines, and Spectrum of Findings Based on Prospective Multimodal Analysis*, CANADIAN JOURNAL OF OPHTHALMOLOGY (in press, published online January 2020), http://www.canadianjournalofophthalmology.ca/article/S00008-4182(19)31272-4/fulltext.

[34] Rachel M. Huckfeldt and Demetrios G Vavvas, *Progressive Maculopathy After Discontinuation of Pentosan Polysulfate Sodium*, 50 OPHTHALMIC SURGERY, LASERS AND IMAGING RETINA 656–59 (2019), ncbi.nlm.nih.gov/pubmed/31671200.

[35] *Id*. at 658.

[36] Interstitial Cystitis Network Patient Support Forum, https://forum.ic-network.com/.

all I can do is try. I feel to be between a rock and a hard place. I am an artist so my eyes are truly needed to continue my work."

b. February 3, 2019: "I saw the article too and took it to my ophthalmologist. She was very excited to see the research. She said that my macular degeneration that had occurred after 18 years of taking Elmiron was an unusual shape that they had not seen before. She said that while it won't heal me, they hoped that they could stop this from happening to other patients."

c. March 25, 2019: "After 4 excruciating years, I was diagnosed with IC in 2003. I started on Elmiron and have taken it since then. I was diagnosed with macular degeneration in 2014. My severity is mild to moderate. The left eye is definitely worse. I can no longer drive at night. I'm pretty comfortable driving to places I am familiar with during the day. I am only 58. I dread the day I will not be able to drive."

110. All of this information was known by, and available to, Defendants at all relevant times.

111. The European Medicines Agency, a decentralized agency of the EU responsible for scientific evaluations, supervision, and safety monitoring of medicines in the EU, is specifically warning patients about Elmiron and advising that "[a]ll patients should have regular ophthalmic examinations for early detection of pigmentary maculopathy, particularly those with longterm use of PPS. In such situations, treatment cessation should be considered."[37]

112. Despite numerous signs of the potential for severe retinal side effects; multiple studies conducted at top research institutes; research being published in major peer-reviewed journals; and public warnings from a prominent EU health agency, ***Defendants failed to reasonably investigate the issue and warn patients and healthcare providers at all relevant times***.

[37] EUROPEAN MEDICINES AGENCY, PRODUCT INFORMATION. ELMIRON- PENTOSAN POLYSULFATE SODIUM 3, https://www.ema.europa.eu/en/documents/product-information/elmiron-epar-product-information_en.pdf.

113. At all relevant times, Defendants also failed to alert patients to the need for ophthalmological monitoring while taking Elmiron or whether risks increase with higher doses or longer durations.

114. Other medications affecting vision have included instructions and warnings for users and prescribers. For example, the anti-malaria drug Plaquenil (hydroxychloroquine) is likewise associated with retinal toxicity. In the labeling for Plaquenil, manufacturer Concordia Pharmaceuticals, Inc., provides the following warning:

> Irreversible retinal damage has been observed in some patients who had received hydroxychloroquine sulfate. Significant risk factors for retinal damage include daily doses of hydroxychloroquine sulfate greater than 6.5 mg/kg (5 mg/kg base) of actual body weight, durations of use greater than five years, subnormal glomerular filtration, use of some concomitant drug products such as tamoxifen citrate and concurrent macular disease.
>
> A baseline ocular examination is recommended within the first year of starting PLAQUENIL. The baseline exam should include: best corrected distance visual acuity (BCVA), an automated threshold visual field (VF) of the central 10 degrees (with retesting if an abnormality is noted), and spectral domain ocular coherence tomography (SD-OCT).
>
> For individuals with significant risk factors (daily dose of hydroxychloroquine sulfate greater than 5.0 mg/kg base of actual body weight, subnormal glomerular filtration, use of tamoxifen citrate or concurrent macular disease) monitoring should include annual examinations which include BCVA, VF and SD-OCT. For individuals without significant risk factors, annual exams can usually be deferred until five years of treatment.
>
> In individuals of Asian descent, retinal toxicity may first be noticed outside the macula. In patients of Asian descent, it is recommended that visual field testing be performed in the central 24 degrees instead of the central 10 degrees. It is recommended that hydroxychloroquine be discontinued if ocular toxicity is suspected and the patient should be closely observed given that retinal changes (and visual disturbances) may progress even after cessation of therapy.[38]

[38] Plaquenil Patient Package Insert, revised June 2018, Concordia Pharmaceuticals, Inc., https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/009768Orig1s051lbl.pdf.

115. In stark contrast, until June of 2020, the Elmiron label read:[39]

WARNINGS

None.

116. At all relevant times, Defendants have failed to adequately warn or instruct patients, the medical community, or prescribers in the United States that Elmiron causes, is linked to, and is associated with vision threatening retinal changes, including vision loss.

117. At all relevant times, Defendants have failed to adequately warn or instruct patients, the medical community, or prescribers in the United States that patients taking Elmiron should undergo regular ophthalmological testing to detect pigmentary changes and discontinue use if such changes occur.

118. Defendants failed to mention vision-threatening retinal changes or the need for ophthalmological monitoring in any of the patient materials—including the Patient Education Flyer and Patient Brochure—the sources of information most likely viewed by physicians and patients.

119. At all relevant times, the labeling for Elmiron listed serious side effects that have been reported with Elmiron, but did not list vision threatening retinal changes.

120. At all relevant times, the labeling for Elmiron failed to provide adequate warnings and instructions, failed to caution that patients should be closely monitored, failed to adequately

[39] Elmiron Patient Package Insert, revised August 2004.

inform patients and physicians that vision threatening retinal changes have been associated with Elmiron use, and failed to contain any proper dosing considerations.

121. At all relevant times, JANSSEN PHARMA maintained a website promoting Elmiron, www.orthoelmiron.com, which included, among other topics, "About Elmiron," "How Elmiron Works," "Important Safety Information," and "Patient Information." Nowhere on the website did Defendants mention the potential for vision-threatening retinal changes associated with Elmiron use.

122. On June 24, 2019, Defendant JANSSEN PHARMA submitted its Supplemental New Drug application (sNDA) under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Elmiron (PPS) 100 mg capsules. This Prior Approval labeling supplement to its application provided revisions to the package insert Warnings section and Post-Marketing section, as well as an update to the Patient Labeling finally addressing the risk of vision threatening retinal changes associated with Elmiron use.

123. Defendants' sNDA, dated June 24, 2019, was not approved by the FDA until June 16, 2020. Defendants did not provide warnings anywhere on its product label or packaging referencing the risk of vision threatening retinal changes associated with Elmiron use until June 16, 2020.

124. As of no later than June 24, 2019, when Defendants submitted their sNDA to include warnings referencing the risk of vision threatening retinal changes associated with Elmiron use, Defendants knew of the risk of injury associated with their drug and failed to warn consumers and physicians, including Plaintiffs, Plaintiffs' physicians, and the public in general, of same.

125. The FDA has established reporting categories for post-approval changes to a drug's label. The Changes Being Effected supplement ("CBE") (21 CFR § 314.70(c)(3)) allows for

changes in the labeling of a drug product to reflect newly acquired information without prior approval from the FDA.

126. The CBE process allows for drug manufacturers to change a drug label more quickly than the sNDA process based on newly acquired information about the drug.

127. Defendants should have changed the Elmiron label to include warnings and instructions addressing the risk of injury associated with the drug as soon as they had notice of adverse reports relating to same.

128. By failing to use the FDA's CBE supplement to warn Plaintiffs, consumers, and physicians, of the risk of vision threatening retinal changes associated with using Elmiron, Defendants acted in a gross and flagrant character, evincing reckless disregard of human life, and of the safety of persons exposed to its dangerous drug.

129. Additionally, by failing to use the FDA's CBE supplement to warn Plaintiff, consumers, and physicians, of the risk of vision threatening retinal changes associated with using Elmiron, Defendants showed wantonness, recklessness, or a grossly careless disregard for the public's safety and welfare.

E. **Defendants Had a Duty to Protect U.S. Consumers, But Did Not**

130. At all relevant times, Defendants had a duty to craft an adequate label with respect to Elmiron.

131. At all relevant times, Defendants had a duty to ensure that the warnings in the Elmiron label were adequate, at all times, for as long as the drug remained available for sale in the United States.

132. At all relevant times, Defendants had a responsibility to conduct post- marketing surveillance and to continue to study the safety and efficacy of Elmiron, after the Elmiron NDA was approved, for as long as the drug remained available for sale in the United States.

133. At all relevant times, Defendants had a duty to revise the Elmiron label to include a warning regarding the risk of serious vision-related injuries as soon as there was reasonable evidence of a causal association between vision- related injuries and Elmiron use.

134. Upon information and belief, despite reasonable evidence of causal association, Defendants knowingly withheld and/or misrepresented information required to be submitted under FDA NDA regulations, concerning the safety and efficacy of Elmiron, including, but not limited to, raw data sets, documents, data analyses, and/or other information related to the risk of Elmiron users suffering vision-related injuries as a result of their Elmiron use. Such information was material and relevant to the risk of patients, like Plaintiffs, developing serious vision-related injuries as a result of taking Elmiron.

135. Upon information and belief, despite understanding Elmiron could cause vision-related injuries, Defendants knowingly withheld and/or misrepresented information required to be submitted under FDA NDA regulations, concerning the safety and efficacy of Elmiron, including, but not limited to, raw data sets, documents, data analyses, and/or other information related to the risk of Elmiron users suffering vision-related injuries as a result of their Elmiron use. Such information was material and relevant to the risk of patients, like Plaintiffs, developing serious vision-related injuries as a result of taking Elmiron.

F. How Defendants' Misconduct Endangered U.S. Consumers

136. Upon information and belief, had Defendants exercised reasonable care in testing and studying Elmiron, they would have discovered prior to seeking FDA approval, that long-

term Elmiron use can cause serious vision and retinal injuries, including, but not limited to, pigmentary maculopathy.

137. Upon information and belief, despite understanding that patients who would take Elmiron would likely remain on the medication for long periods of time, Defendants failed to test and study the long-term safety and efficacy of the drug, prior to seeking FDA approval.

138. Upon information and belief, despite post-approval adverse event reports and other clinical evidence, Defendants failed to continue to test and study the safety and efficacy of Elmiron, particularly in patients who used the drug for long periods of time.

139. Upon information and belief, from the date all Defendants received FDA-approval to market Elmiron in the United States, Defendants each made, distributed, marketed, and sold Elmiron without adequate warning to Plaintiffs or Plaintiffs' prescribing physicians that Elmiron was associated with and/or could cause serious vision and retina damage in patients who used it, and that all Defendants had not adequately conducted complete and proper testing and studies of Elmiron with regard to retina damage.

140. Upon information and belief, Defendants concealed and/or failed to completely disclose their knowledge that Elmiron was associated with and/or could cause retina damage as well as their knowledge that they had failed to fully test or study said risk.

141. Upon information and belief, all Defendants ignored the association between the use of Elmiron and the risk of developing permanent and disfiguring visual complications, including, but not limited to, pigmentary maculopathy and retina damage.

142. Upon information and belief, all Defendants failed to provide adequate instructions to U.S. healthcare professionals and patients regarding how to safely monitor and identify signs

of potentially serious visual complications associated with long-term Elmiron use.

143. Upon information and belief, all Defendants failed to warn U.S. healthcare professionals and patients, including Plaintiffs' prescribing physicians and Plaintiffs, regarding how to safely monitor and identify signs of potentially serious visual complications associated with long-term Elmiron use.

144. Upon information and belief, all Defendants failed to warn and/or to provide adequate instructions to U.S. healthcare professionals and patients, including Plaintiffs' prescribing physicians and Plaintiffs, regarding how to safely stop taking Elmiron in the event that potentially serious visual complications developed while using Elmiron.

145. Upon information and belief, all Defendants failed to warn U.S. healthcare professionals and patients, including Plaintiffs' prescribing physicians and Plaintiffs, of the true risk of retina damage to patients taking Elmiron as compared to other similarly efficacious pharmaceutical products.

146. All of Defendants' failures to provide adequate instructions and/or disclose information—which Defendants each possessed regarding the failure to adequately test and study Elmiron for the risk of serious visual complications—further rendered the Elmiron Package Insert, Medication Guide, and other educational and/or promotional materials inadequate.

147. Despite AERs from healthcare professionals and consumers around the world, beginning at least as early as 1997 until approximately September of 2019, Defendants never warned—in any country or market—of the risk of serious visual complications, including, but not limited to, pigmentary maculopathy.

TOLLING OF THE STATUTE OF LIMITATIONS

A. Discovery Rule Tolling

148. As a result of the acts and omissions of Defendants, Plaintiffs and Class members could not have discovered, through the exercise of reasonable due diligence, that exposure to Elmiron was associated with increased exposure to vision threatening retinal changes as set forth above. Thus, the applicable limitations periods did not begin to accrue until Plaintiffs and Class members discovered, or through the exercise of reasonable diligence should have discovered, Defendants' wrongful acts and omissions.

B. Fraudulent Concealment Tolling

149. All applicable statutes of limitation have also been tolled by Defendants' knowing and active fraudulent concealment and denial of the vision-threatening retinal changes associated with Elmiron throughout the time period relevant to this action.

150. Defendants are under a continuing duty to disclose the true character, quality, and nature of Elmiron to Plaintiffs and the Class members. At all relevant times, Defendants nevertheless failed to inform patients and doctors about the vision threatening retinal changes associated with Elmiron, as discussed above.

151. Plaintiffs and Class members reasonably relied upon Defendants' knowing, affirmative, or active concealment when they continued to use Elmiron as prescribed.

152. Because Defendants actively concealed the vision-threatening retinal changes associated with Elmiron, they are estopped from relying on any statutes of limitations defense.

C. Estoppel

153. Defendants were, and are, under a continuous duty to disclose to Plaintiffs and Class members the vision-threatening retinal changes associated with Elmiron. Instead, they

actively concealed the true character, quality, and nature of Elmiron and knowingly made misrepresentations and/or omissions about the safety of Elmiron and the vision-threatening retinal changes associated therewith.

154. Plaintiffs and Class members reasonably relied upon Defendants' knowing and affirmative misrepresentations and active concealment of material facts. Therefore, Defendants are estopped from relying on any defense based on statutes of limitations in this action.

IV. CLASS ALLEGATIONS

A. Class Definitions

155. Plaintiffs bring this action on their own behalf, and on behalf of all persons similarly situated, pursuant to Rules 23(a) and (b)(2) of the Federal Rules of Civil Procedure. This action satisfies the numerosity, commonality, typicality, adequacy, predominance, and superiority requirements of those provisions.

Medical Monitoring Class:

156. Plaintiffs bring this class action and seek to certify and maintain it as a class action under Rules 23(a) and (b)(2) of the Federal Rules of Civil Procedure on behalf of themselves and the following proposed Medical Monitoring Class:

> **All Florida citizens who have been prescribed and have taken Elmiron in Florida but have not been diagnosed with Elmiron-associated maculopathy.**

157. Excluded from the Medical Monitoring Class are Defendants, their employees, officers, directors, legal representatives, heirs, successors, and wholly or partly owned subsidiaries or affiliated companies; Class Counsel and their employees; and the judicial officers and their immediate family members and associated court staff assigned to this case.

158. Plaintiffs reserve the right to modify, expand, or amend the definitions of the proposed Class following the discovery period and before the Court determines whether class certification is appropriate.

159. Certification of Plaintiffs' claims for class-wide treatment is appropriate because Plaintiffs can prove the elements of their claims on a class-wide basis using the same evidence as would be used to prove those elements in an individual action alleging the same claims.

Numerosity

160. This action satisfies the requirements of Fed. R. Civ. P. 23(a)(1). There are thousands of patients taking Elmiron in Florida. Individual joinder of all Class Members is impracticable.

161. The identities of Class Members are ascertainable, as the names and addresses of all Class Members can be identified through prescription records. Plaintiffs anticipate providing appropriate notice to the certified class in compliance with Fed. R. Civ. P. 23(c)(2)(A) and/or (B), to be approved by the Court after class certification, or pursuant to court order under Fed. R. Civ. P. 23(d).

Commonality

162. This action satisfies the requirements of Fed. R. Civ. P. 23(a)(2) and 23(b)(3) because there are questions of law and fact that are common to all Members of the Class. These common questions predominate over any questions affecting only individual Class Members. The predominating common or Class-wide fact questions include, without limitation:

a. Whether Elmiron significantly increases the risk of vision threatening retinal changes;

b. Whether Defendants knew or should have known that Elmiron significantly increases the risk of vision threatening retinal changes;

c. Whether Defendants were negligent in selling Elmiron;

d. Whether Defendants were reckless in their testing protocols;

e. Whether Defendants failed to warn consumers regarding the risk of vision threatening retinal changes associated with Elmiron; and

f. Whether Plaintiffs and Class Members are entitled to equitable relief, including injunctive relief.

Typicality

163. This action satisfies the requirements of Fed. R. Civ. P. 23(a)(3) because Plaintiffs' claims are typical of the claims of each of the Class Members, as all Class Members were and are similarly affected and their claims arise from the same wrongful conduct of Defendants. Each Class Member was prescribed and exposed to Elmiron, and faces a significantly increased risk of vision-threatening retinal changes. The relief Plaintiffs seek in this action is typical of the relief sought for the absent Class Members.

Adequacy of Representation

164. Plaintiffs will fairly and adequately protect the interests of the Class Members. Plaintiffs are committed to the vigorous prosecution of this action and there is no hostility or conflict between or among Plaintiffs and the unnamed Class Members. Plaintiffs anticipate no difficulty in the management of this litigation as a class action.

165. To prosecute this case, Plaintiffs have chosen the undersigned law firms, who have substantial experience in the prosecution of large and complex class action litigation and have the financial resources to meet the costs associated with the vigorous prosecution of this type of litigation. Plaintiffs and their counsel will fairly and adequately protect the interest of all Class Members.

Superiority

166. This action satisfies the requirements of Fed. R. Civ. P. 23(b)(3). A class action is superior to other available methods for the fair and efficient adjudication of the rights of the Class Members. The joinder of individual Class Members is impracticable because of the vast number of Class Members who have been prescribed and taken Elmiron.

167. Because this is a claim for equitable relief, the expense and burden of individual litigation would make it difficult or impossible for individual Class Members to redress the wrongs done to each of them individually, such that most or all Class Members would have no rational economic interest in individually controlling the prosecution of specific actions. The burden imposed on the judicial system by individual litigation, and to the Defendants, by even a small fraction of the Class Members, would be enormous.

168. In comparison to piecemeal litigation, class action litigation presents far fewer management difficulties, far better conserves the resources of both the judiciary and the parties, and far more effectively protects the rights of each Class Member. The benefits to the legitimate interests of the parties, the court, and the public resulting from class action litigation substantially outweigh the expenses, burdens, inconsistencies, economic infeasibility, and inefficiencies of individualized litigation. Class adjudication is simply superior to other alternatives under Fed. R. Civ. P. 23(b)(3)(D).

169. Plaintiffs are unaware of any obstacles likely to be encountered in the management of this action that would preclude its maintenance as a class action. Rule 23 provides the Court with the authority and flexibility to maximize the efficiencies and benefits of the class mechanism and reduce management challenges. The Court may, on motion of Plaintiffs or on its own determination, certify classes for claims sharing common legal questions; utilize the provisions of

Fed. R. Civ. P. 23(c)(4) to certify particular claims, issues, or common questions of law or of fact for class-wide adjudication; certify and adjudicate bellwether class claims; and utilize Fed. R. Civ. P. 23(c)(5) to divide any Class into subclasses.

Requirements of Fed. R. Civ. P. 23(b)(2)

170. Defendants have acted or failed to act in a manner generally applicable to the Class Members in the Medical Monitoring Class, thereby making appropriate final injunctive relief or corresponding declaratory relief with respect to the Class.

CLAIMS FOR RELIEF

Count I — Medical Monitoring

171. Plaintiffs and the Medical Monitoring Class incorporate the factual allegations set forth in paragraphs 1 to 147 as if fully set forth herein and further allege as follows:

172. Plaintiffs and the Medical Monitoring Class assert equitable claims under Florida law for medical monitoring against Defendants arising from the wrongful acts and negligence detailed above and below.

173. At all material times, Defendants had a duty to exercise reasonable care and had the duty of an expert in all aspects of the design, formulation, manufacture, compounding, testing, inspection, packaging, labeling, distribution, marketing, promotion, advertising, sale, warning, post-sale warning, testing, and research to assure the safety of the product when used as intended or in a way that Defendants could reasonably have anticipated, and to assure that the consuming public—including Plaintiffs, the Class, and their respective physicians—obtained accurate information and adequate instructions and warnings for the safe use or non-use of Elmiron.

174. At all material times, Defendants had a duty to warn Plaintiffs, the Class, their respective physicians, and the general public of Elmiron's dangers and serious side effects,

including severe and potentially irreversible vision loss and retinal damage, since it was reasonably foreseeable that an injury would occur due to proper use of Elmiron.

175. At all material times, Defendants failed to exercise reasonable care and the duty of an expert. Defendants knew, or in the exercise of reasonable care should have known, that Elmiron was not, in fact, properly manufactured, designed, compounded, tested, inspected, packaged, labeled, warned about, distributed, marketed, advertised, formulated, promoted, examined, maintained, sold, or prepared.

176. Defendants' myriad failures to act with reasonable care and the duty of an expert include, but are not limited to:

a. Negligent and careless research and testing of Elmiron;

b. Negligent and careless design or formulation of Elmiron;

c. Negligent and careless failure to give adequate warnings that would attract the attention of Plaintiffs, Class Members, their respective physicians, and the general public, of the dangerous, unsafe, and deleterious nature of Elmiron and the risks associated with its use;

d. Negligent and careless failure to provide instructions and warnings for the safe use of Elmiron to avoid injury;

e. Negligent and careless failure to explain the mechanism, mode, and types of adverse events associated with Elmiron, including but not limited to the dangers of vision loss and retinal damage posed by Elmiron;

f. Negligent representations that Elmiron was safe;

g. Negligent and careless failure to issue adequate post-sale warnings that Elmiron is likely to cause serious and potentially irreversible vision loss and retinal damage.

177. As a direct and proximate result of Defendants' wrongful acts and negligence detailed above, Plaintiffs and the Class were exposed to Elmiron without knowing of Elmiron's dangerous nature.

178. As a direct and proximate result of Defendants' wrongful acts and negligence detailed above, and Plaintiffs' and the Class's exposure to Elmiron, Plaintiffs and the Class have a significantly increased risk of suffering serious and potentially irreversible vision loss and retinal damage.

179. The significantly increased risk of serious and potentially irreversible vision loss and retinal damage makes periodic diagnostic medical examinations—beyond the monitoring normally recommended in the absence of a significantly elevated risk—reasonable and necessary.

180. A medical monitoring program is necessary for early detection and treatment of the aforementioned latent conditions. Research has revealed that the presenting visual symptoms for Elmiron patients are vague, and retinal changes on conventional examination are subtle. Without referral to a specialist with modern imaging instrumentation, Elmiron-associated maculopathy is likely to remain undetected. Many existing cases may masquerade as similar-appearing conditions.

181. The Emory research team has identified a series of nonstandard tests most suitable for identification of the Elmiron injury: "The fundus findings in [Elmiron]-associated maculopathy… exhibit a distinctive clinical phenotype on multimodal imaging that's best appreciated by using [fundus autofluorescence]."[40] Fundus autofluorescence is necessary to distinguish Elmiron-associated maculopathy from other maladies.

182. An easily administered, cost effective monitoring program exists. Indeed, an unrelated prescription medication, Hydroxychloroquine, was found to result in similar vision related issues as those associated with Elmiron, and an easily administrated and cost effective screening program has been created to screen and monitor patients for those effects.

[40] Hanif and Jain, *supra*.

183. Plaintiffs seek for the Court to exercise its equitable powers to create, supervise, and implement (or cause to be created, supervised, and implemented), and for the Court to order Defendants to fund, an appropriate medical monitoring plan that provides routine medical testing, monitoring, and study of Plaintiffs and the Medical Monitoring Class, for the remainder of Plaintiffs' and each Medical Monitoring Class Member's lives.

184. Plaintiffs and the Medical Monitoring Class seek for such medical monitoring program to institute comprehensive and appropriate diagnostic tests for the early detection and diagnosis of pigmentary maculopathy and other serious vision threatening retinal changes associated with Elmiron.

185. The medical monitoring program is reasonable and necessary as a result of Plaintiffs' and the Medical Monitoring Class's increased risk of serious vision threatening retinal changes associated with Elmiron.

186. Plaintiffs' and the Medical Monitoring Class's increased risk of serious vision threatening retinal changes associated with Elmiron necessitates a more comprehensive medical monitoring program than the ordinary medical screening generally practiced, recommended, or required for the unexposed population, thus the required regimen is different from that recommended in the absence of Plaintiffs' and the Medical Monitoring Class's exposure.

187. The medical monitoring program is reasonably necessary according to contemporary scientific principles, medical literature, and expert opinion, as early detection of the vision changes associated with Elmiron improves prognoses and overall treatment. Without the program, the serious vision threatening retinal changes associated with Elmiron may go undiagnosed and, as a result, untreated, while those suffering from them can benefit from medical treatment.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs, on behalf of themselves and all other similarly situated Class Members, request that the Court enter judgment against Defendants as follows:

(1) Declare this action to be a proper class action maintainable under Rule 23(b)(2) of the Federal Rules of Civil Procedure and designate and appoint Plaintiffs as Class representatives and Plaintiffs' chosen counsel as Class Counsel;

(2) Enter an injunction against Defendants to require them to implement a medical monitoring program for Plaintiffs and Class Members;

(3) Retain jurisdiction over this action to ensure Defendants comply with such a decree;

(4) Declare, in accordance with Florida law, that Plaintiffs and Class Members will not be precluded by the rule against splitting claims from bringing claims for whatever physical injuries that are later attributed to Elmiron.

(5) Award Plaintiffs and Class Members their reasonable attorneys' fees and costs, as allowed by law; and

(6) Award Plaintiffs and Class Members any further and different relief as this case may require or as determined by this Court to be just, equitable, and proper under the circumstances.

DEMAND FOR JURY TRIAL

Pursuant to Fed. R. Civ. P. 38(b), Plaintiffs demand a jury trial for any and all issues triable by a jury.

Respectfully submitted: October 9, 2020.

/s/*Benjamin Widlanski* Benjamin Widlanski, Esq. bwidlanski@kttlaw.com Florida Bar No. 1010644 Tal J. Lifshitz, Esq. tjl@kttlaw.com Florida Bar No. 99519 **KOZYAK TROPIN & THROCKMORTON LLP** 2525 Ponce de Leon Blvd., 9th Floor Coral Gables, FL 33134 Telephone: (305) 372-1800 Facsimile: (305) 372-3508 *Counsel for Plaintiffs*	*/s/ Francisco R. Maderal* Francisco R. Maderal, Esq. frank@colson.com Florida Bar No. 0041481 Susan S. Carlson, Esq. susan@colson.com Florida Bar No. 957453 Alexandra Mullenax, Esq. Alexandra@colson.com Florida Bar No. 1018657 **COLSON HICKS EIDSON** 255 Alhambra Circle, Penthouse Coral Gables, Florida 33134 Telephone: (305) 476-7400 Facsimile: (305) 476-7444 *Counsel for Plaintiffs*