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UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF CALIFORNIA
SACRAMENTO DIVISION

FRANK FERNANDEZ, a California consumer, individually and on behalf of all others similarly situated, Plaintiff, vs. TAKEDA PHARMACEUTICALS AMERICA, INC., an Illinois corporation; and ELI LILLY & COMPANY, an Indiana corporation; and DOES 1-100, inclusive, Defendants.	Case No.: CLASS ACTION COMPLAINT JURY TRIAL DEMANDED

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CLASS ACTION COMPLAINT

1. Plaintiff FRANK FERNANDEZ (referred to herein as "Plaintiff"), on behalf of himself and all others similarly situated, brings this action, brings this action for damages and equitable relief against Defendants Takeda Pharmaceuticals America, Inc., Eli Lilly & Company, and DOES 1 through 100, Inclusive (hereinafter, "Defendants") based on personal knowledge and upon the information and belief and the investigation and research of counsel.

2. This case is about two drug companies who fraudulently marketed the diabetes medication Actos (generically known as pioglitazone). Defendants knew that, if the medical community were aware that Actos could cause bladder cancer, it would not have been the blockbuster drug that they needed Actos to be. So, instead of being honest and forthright, the Defendants engaged in a decade-long scheme to mislead, manipulate, and stonewall the FDA, consumers, prescribers, and third-party payors into believing that Actos did not pose any significant risk for bladder cancer. The results were devastating—many thousands of patients ended up developing bladder cancer and the Defendants made billions. Defendants were able to sell millions of prescriptions for Actos that would never have been issued had the truth been known. This class action, brought on behalf of consumers in California seeks to recover damages for those consumers who were tricked into purchasing Actos prescriptions.

3. Actos was approved by the Food and Drug Administration ("FDA") on July 16, 1999 as an oral treatment for Type II diabetes, also known as non-insulin-dependent diabetes mellitus or adult-onset diabetes. Actos became one of the top selling drugs in the world. Millions of individuals in the United States have used Actos. The 2010 sales for Actos reached an excess of $2.63 billion.

4. When considering whether a drug is efficacious in assisting diabetic patients in meeting their glycemic targets, both glycemic control *and* the risk factor reductions (including reduction in serious side effects) should be considered.[1]

5. Ultimately, when considering glycemic control *and* risk factors associated with Actos,

[1] Transcript from *Joint Meeting of the Endocrinologic and Metabolic Drugs Advisory Committee and the Drug Safety Management Advisory Committee*, Dep't of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) (July 30, 2007) (testimony by Robert E. Ratner, M.D.) at 43.

Actos is not appropriate for diabetic patients such *as* Plaintiff as the drug's risk factors increases the diabetic patients' risk for, among other things, bladder cancer, congestive heart failure, and other cardiovascular adverse effects. Therefore, Actos has little to no health benefit to Plaintiff and the proposed Class.

6. Despite knowing the serious risk factors associated with Actos, and in efforts to increase the sales of Actos, Defendants embarked on a comprehensive and carefully-orchestrated scheme to promote Actos' safety, efficacy, and effectiveness through a fraudulent and deceptive marketing program to Plaintiff, physicians, and the public. Plaintiff and the proposed Class were among the principal victims of Defendants' wrongful scheme to promote and market Actos.

7. Defendants' conduct, as described herein, caused Plaintiff's injuries and damages because Plaintiff and the proposed Class paid for the high cost of this inefficacious and dangerous drug, including co-payments. Plaintiff and the proposed Class were required to pay more for Actos than other alternative treatments available on their respective health plans because of Defendants' deceptive schemes. Based on the misinformation disseminated by Defendants in making their decision to pay for Actos, Plaintiff and the Class have been directly harmed by their economic loss.

8. This is a proposed Class action on behalf of all consumers residing in the State of California, who have been prescribed and purchased or paid, in part or all, the purchase price for Actos. On information and belief, Plaintiff alleges the Class to be sufficiently numerous to make joinder of all members impossible. Common questions of law and fact exist, and Plaintiff's claims are typical of those of other Class members in that they are individuals who were prescribed and paid for, at least in part, Actos for the treatment of Type II diabetes.

9. Plaintiff seeks recovery for payments for Actos and the amounts by which Defendants were unjustly enriched on behalf of a California State class.

PARTIES

10. Plaintiff Frank Fernandez is a resident of the State of California whose principal place of residence is in Lathrop within the County of San Joaquin. Mr. Fernandez was prescribed and used Actos from approximately 2000 through 2010. Mr. Fernandez saw and relied upon false statements contained in Defendants' marketing materials related to safety and efficacy in deciding to use, and

continuing to use, Actos. Those statements included representations made on the label and/or medication guide.

11. Plaintiff never saw the September 15, 2010 FDA alert and was never told about the FDA's investigation by his prescriber.

12. During the period in which Plaintiff was purchasing and ingesting Actos, he did not know that Actos' drug label and advertising were deceptive or that they lacked material information about the drug's risk of causing bladder cancer.

13. During the period Plaintiff was purchasing and ingesting Actos, Plaintiff was never informed, nor did he read or see, any information about Actos' bladder cancer risks. Likewise, the Defendants did not convey any of Actos' bladder cancer risks to Plaintiff, his prescriber, the FDA (until 2010), or the public in general.

14. Between October 16, 2009 and August 8, 2011, Plaintiff did not see any media, journal articles, press releases, websites, letters, or statements concerning Actos and its association with bladder cancer.

15. Between October 16, 2009 and August 8, 2011, Plaintiff had no reason to believe he was the victim of consumer protection violation or that his purchase of Actos was made without required information.

16. Between October 16, 2009 and August 8, 2011, Plaintiff did not know that he had been deprived of material information or that the Actos label and advertising was misleading in any particular form.

17. Upon information and belief, Plaintiff's prescriber was never informed about Actos' association with bladder cancer while Plaintiff was purchasing and ingesting the drug between 2000 and 2010.

18. Information about Actos' risk of causing bladder cancer is information that a reasonable consumer and prescriber would consider important in making a purchasing and prescribing decision.

19. Had Plaintiff known that Actos increased the risk of causing bladder cancer, he would never have purchased and ingested the drug.

20. Defendant TAKEDA PHARMACEUTICALS U.S.A., INC., f/k/a TAKEDA PHARMACEUTICALS NORTH AMERICA, INC., ("TPNA") is a Delaware corporation, which has its principal place of business at One Takeda Parkway, Deerfield, Illinois, 60015. At all relevant times alleged herein, TAKEDA PHARMACEUTICALS U.S.A., INC., f/k/a TAKEDA PHARMACEUTICALS NORTH AMERICA, INC., was involved in the research, development, sales and marketing of pharmaceutical products including Actos and pioglitazone hydrochloride.

21. TPNA has transacted and conducted business within the State of California.

22. TPNA has derived substantial revenue from goods and products used in the State of California.

23. Eli Lilly & Company (Hereinafter "Lilly") is an Indiana corporation with its principal place of business located at Lilly Corporate Center, Indianapolis, Indiana 46285.

24. Lilly has transacted and conducted business within the State of California.

25. Lilly has derived substantial revenue from the goods and products used in the State of California.

26. Lilly expected or should have expected its acts to have consequences within the State of California, and derived substantial revenue from California state commerce.

JURISDICTION AND VENUE

27. This Court has subject-matter jurisdiction pursuant to 28 U.S.C. § 1332(d)(2). Members of the proposed classes are citizens of a different state than Takeda. Furthermore, the aggregate amount in controversy exceeds $5,000,000.

28. This Court has personal jurisdiction over Defendants because Takeda and Lilly have purposefully directed their marketing and sales of numerous pharmaceutical products to the State of California, as well as the other consumer bases represented by this lawsuit. Defendants have had substantial contacts with the State of California such that maintenance of the action is consistent with traditional notions of fair play and substantial justice.

29. This Court has personal jurisdiction over this action because the Plaintiff purchased and used Actos in the State of California, and he resides in the State of California, and Defendants marketed and promoted Actos in the State of California. This Court also has subject matter

jurisdiction by virtue of the fact that each Plaintiff suffered injury in the state of California.

30. This Court also has personal jurisdiction by consent of the Defendants to transfer this action to this judicial district. Moreover, the Defendants consented to personal jurisdiction by answering the original complaint.

31. Venue is proper before this Court pursuant to 28 U.S.C. § 1391(b). A substantial portion of the events giving rise to the claims alleged in this Complaint took place within the Eastern District of California.

FACTUAL BACKGROUND

32. Actos, like Avandia, is a medication intended to lower type II diabetics' blood sugar. Type II diabetics' blood sugar is elevated due to cellular insulin resistance, not the absence of insulin suffered by Type I diabetics. People with type II diabetes, for the most part, actually produce insulin but their cells resist absorbing it. According to the American Diabetes Association, Type 2 diabetes is the most common form of diabetes.

33. Insulin is a hormone, produced by cells in the pancreas, and is central to regulating carbohydrate and fat metabolism in the body. It causes cells in the skeletal muscles and fat tissue to absorb glucose from the blood. One of insulin's main jobs is to get cells to "open up" to take in glucose. While insulin normally operates like a key opening cells to admit and process blood sugar, in Type II diabetics, the cell surface resistance to insulin prevents its absorption, leading to extra-cellular, unabsorbed blood sugars, i.e. elevated blood glucose levels characteristic of Type II diabetes.

34. Actos and Avandia are members of a class of thiazolidinedione ("TZD") oral anti-diabetic medications ("OAD") that reduce insulin resistance, restore insulin admitting glucose into cells, and thereby lower blood glucose levels. Actos and other TZDs operate by activating a receptor in cells that initiates the process of reducing insulin resistance, a peroxisome proliferator-activated receptor ("PPAR").

35. There are several different kinds of PPARs: alpha, gamma, delta, and dual/mixed. Actos was originally considered to be primarily just a PPAR gamma activator, or "agonist." Each PPAR influences different DNA sections and gene expressions which then have different

downstream effects within the cell and the body in general. PPAR gamma, the primary target of TZDs, lowers insulin resistance and blood glucose levels. PPAR alpha activation, on the other hand is associated with lowering HDL ("good" cholesterol) and raising LDL ("bad" cholesterol). Dual agonists activate more than one PPAR, for example activating both alpha and gamma PPARs, thus initiating downstream effects related to both.

I. Early Actos History, Development and Approval

36. The development of Actos began in the 1980s. Takeda, which was originally a Japanese-based chemical company, sought to expand its pharmaceutical presence in the United States. To that end, Takeda partnered with the Upjohn Company, a pharmaceutical company with an established presence in the United States and familiarity with Food and Drug Administration ("FDA") regulations and protocols. Upjohn and Takeda partnered to begin research and development of an oral anti-diabetic treatment, which ultimately became Actos.

37. In 1986, Takeda conducted a 90–day beagle study, which yielded information suggesting the need for follow-up study and testing.

38. Early pre-clinical animal trials indicated that Actos was not as effective or as safe as Upjohn expected. So, in a letter dated September 21, 1993, Upjohn informed Takeda that it was not going to proceed with developing Actos. The letter explained (emphasis added):

> On September 20 our Pharmaceutical Executive Council, Upjohn's highest scientific decision-making body, carefully reviewed the results of the toxicology and clinical studies. The decision of the Council was that Upjohn will not go forward with pioglitazone in the clinic. The Council decided that ***further clinical development of pioglitazone could not be justified based on their concern regarding pioglitazone's margin of safety.***

39. Dr. Kiyoshi Kitazawa, the General Manager of Takeda in Japan and the lead Takeda contact on Actos development, acknowledged Upjohn's decision in a letter dated October 25, 1993. Takeda indicated that it understood Upjohn's position and that it would proceed with developing Actos independently. "In due consideration" of Takeda's plans to continue Actos development, Takeda asked Upjohn to frame their decision to withdraw participation in developing Actos as a "business decision" based on weak glucose reduction efficacy. The letter states:

> Regarding Upjohn's statement for the development status of pioglitazone, we would

> like to propose the following alternative or a similar instead of Upjohn's proposal in due consideration of our current development status.
>
> "In the very preliminary clinical evaluation in the U.S.A., pioglitazone did not show the reduction of blood glucose enough to satisfy Upjohn's in-house requirement. Any considerable work that would be needed is not in line with business needs for further development of Pioglitazone. Hence, all development on pioglitazone at Upjohn has ceased."

Takeda did not want Upjohn to state that it was pulling out of development because of the safety-toxicology issues raised by the animal trials. Takeda was afraid that such information would hinder its efforts to one day obtain FDA approval for Actos.

40. Takeda's request did not go unnoticed. Internally, Upjohn personnel circulated a memo on October 26, 1993, questioning the appropriateness of issuing such a statement. One Upjohn employee stated, "[s]ome of my colleagues are concerned about the lack of frankness (and honesty?) of the Takeda statement. We realise we are hemmed in by a confidentiality clause, but does this have the endorsement of our senior management."

41. Thereafter, Takeda proceeded with developing Actos on its own. On February 6, 1996, Takeda's Senior Research Head, T. Suzuki, sent the results of a recently completed rat study for Actos to K. Kitazawa. The study showed abnormal bladder cell and tumor formation in male and female rats, male mice, plus a kidney tumor in a female mouse. These were abnormal cell growths and precursors to bladder cancer. In addition, the study showed an increase in "transitional cell" carcinomas[2] in male rats.

42. In an effort to address this alarming bladder cancer data, Takeda enlisted the help Dr. Sam Cohen of the University of Nebraska Medical Center. Dr. Cohen attempted to devise an explanation of how rats exposed to Actos were getting bladder cancer that did not also implicate a similar risk to humans. This resulted in what has become known as the "Cohen hypothesis" which

[2] Transitional cell carcinoma (also known as urothelial cell carcinoma) is a type of cancer that typically occurs in the urinary system, i.e., the kidney, urinary bladder, and accessory organs. This type of cancer is distinct from squamous-cell carcinoma, which is a cancer that emerges in the epidermis of skin-type tissue and is one of the major forms of skin cancer. However, since squamous cells are also present in the lining of the bladder, digestive tract, lungs, and other areas of the body, squamous-cell carcinoma occurs as a form of cancer in diverse tissues such as the lips, mouth, esophagus, urinary bladder, prostate, lung, vagina, and cervix, among others. Although these two types of cancer are caused by different carcinogens, both can occur in the bladder, although squamous-cell carcinomas are rare and are usually associated with an obvious irritant like a catheter.

was presented in a white paper prepared by Dr. Cohen for Takeda to provide to the FDA.

43. The Cohen hypothesis posits that, when rats are exposed to Actos, it alters the pH level of male rats' urine which, in turn, leads to the formation of crystals. These crystals cause excess irritation in the bladder lining of the rat and this irritation leads to the formation of bladder cancer. Dr. Cohen explains that this condition would not affect humans because the formation of cancer-inducing crystals was particular to male rats. In addition, due to the way urine is retained by rats, it allows these crystals to irritate the cells lining the bladder. This urine retention did not occur in humans the same way.

44. The Cohen hypothesis, however, was a sham theory, designed to hide the observed bladder cancer risks. The cancer cells observed in the rat and mice studies were "transitional" cancer cells, generally caused by exposure to a carcinogen in the urine. The Cohen hypothesis, however, which was predicated on a crystal-irritation mechanism, could only explain the formation of squamous cancer cells, which are caused by direct irritation. The Cohen hypothesis, thus, failed to explain why rats and mice developed transitional cancer cells, hyperplasia and hypertrophy unrelated to crystal formations, i.e., transitional cell carcinoma and its precursors.

45. Additionally, Dr. Cohen's hypothesis rests, in part, on the fact that male rats are more susceptible to the development of calculi than female rats because males have a different urinary composition from females, which makes it easier for calcium-type stones or crystals to form. Dr. Cohen claimed that females can form these crystals, but the effect is usually less, which results in a lower incidence of, or even no, bladder cancer with Actos. However, in trying to replicate Dr. Cohen's work, Dr. Jennifer Southgate agreed that these calculi changes should only occur in male rats, but her findings included changes in female rat bladders, as well, and that these changes were due to proliferation of cell division occurring throughout the urinary tract. In other words, the hyperplasia was occurring in female rats as well, and this fact undermines another foundational prong of the Cohen Hypothesis. This is further supported by Dr. Southgate's research showing that the pH levels in rat urine were not sufficiently elevated to produce the calculi need to develop bladder tumors.

46. Notwithstanding, Takeda—and ultimately Lilly—embraced the Cohen hypothesis and

submitted Cohen's White Paper to the FDA as part of Actos' pre-approval materials. Takeda used the Cohen hypothesis to explain away the rat bladder cancer findings and streamline approval for humans.

47. As of July 31, 2002, the FDA informed Takeda it was no longer accepting the company's "Cohen Hypothesis" to explain bladder cancers found in test animals.

II. The FDA's Approval and Lilly's Involvement

48. Takeda submitted its New Drug Application ("NDA") for Actos on January 15, 1999, seeking an indication for the treatment of Type 2 diabetes. At the same time, Takeda began discussing a partnership with Eli Lilly and Company ("Lilly"), to aid in the marketing and selling of Actos once the FDA approved the drug. Lilly, however, was concerned about why Upjohn had cancelled its prior partnership with Takeda. In a facsimile transmission from Japan to the United States, on January 21, 1999, Kunio Iwatani of Takeda informed Larry Ellingson of Lilly that, although there were rumors about why Upjohn abandoned development of Actos, the FDA had never been told it was related to safety issues. The facsimile stated:

> Enclosed please find a copy of Upjohn's letter to US FDA dated January 7, 1994.
>
> In the letter Upjohn said that in preliminary clinical evaluation in the United States. pioglitazone did not satisfy Upjohn's internal requirement for reduction blood glucose; therefore, the considerable programs required for development of pioglitazone are not in line with Upjohn's business needs. --- They did not mention about safety of pioglitazone.
>
> . . .
>
> Although there may be rumors about the reasons of Upjohn's abandonment of pioglitazone development, specially from the viewpoints of safety issues, it might be advisable for us to keep saying that Upjohn's decision is based on the results of their internal business evaluation, and efficacy and safety of pioglitazone have been demonstrated clearly by Takeda.

Thus, Takeda and Lilly agreed to "stick to their story" (a frequent theme in this fraudulent enterprise) about Upjohn's abandonment of Actos development. Lilly knew that Takeda was not being truthful with the FDA about Upjohn's withdrawal and, in accord with their enterprise to sell Actos without properly warning about its risks, remained silent. It did not matter that the FDA was being misled about the actual reasons for Upjohn's decision or, for that matter, the existence of serious safety concerns regarding the use of Actos in humans.

49. Prior to entering into any agreement with Takeda, Lilly prepared a PowerPoint slide deck discussing the major contract terms between Takeda and Lilly. On that slide deck, "bladder cancer" is listed below the heading "most significant adverse event risks for pioglitazone[.]" This document demonstrates both Lilly's and Takeda's early knowledge of the potential risk of bladder cancer presented by Actos® to its consumers.

50. Thus, Takeda and Lilly entered in a "Co-Promotion Agreement" to act as distributors and "co-promoters" of Actos in the United States once Actos was approved by the FDA. The co-promotion agreement provided for an elaborate governance structure, designed to give each company an equal say in running the joint venture. Lilly and Takeda agreed to share in the profits and losses of marketing Actos. The agreement was to last for a period of seven years after the launch of Actos and, in addition, Lilly was to be paid a residual "co-promotion" fee on sales of Actos in the U.S. for a period of time following the expiration of the term of the agreement.

51. Under the Co–Promotion Agreement, Lilly agreed to a target of 800,000 primary details per year for Actos. And, over the course of seven years, this agreement amounts to more than five million presentations of Actos® by Lilly representatives made to U.S. doctors.

52. Also, under the terms of the co-promotion agreement, Lilly and Takeda agreed to undertake the promotion of Actos together, with each company's names and/or logos appearing with equal prominence on the product, sample packages, product label, and all promotional material. Thus, this joint venture to promote Actos was much broader than traditional marketing or advertising agreements. Lilly's role was not limited to detailing physicians. Rather, Lilly was charged with the broader overall marketing and promotion of Actos, including activities not traditionally associated with marketing, including: overseeing customer medical services; participation in clinical studies; participation in regulatory issues; exchange of information related to Adverse Events, Device Adverse Events; and post-marketing surveillance; and communications with the FDA about labeling issues.

53. Lilly was also charged with generating scientific materials about Actos, which despite the appearance of independence, were designed to persuade doctors to prescribe Actos. Lilly also explicitly agreed not to use data from clinical studies that would negatively affect sales of Actos,

which amounted to an agreement to hide from the public and the medical community results of clinical studies that showed problems with Actos.

54. The Co–Promotion Agreement also provided for a 3–year period following the end of the actual agreement during which Lilly was, nonetheless, to be paid a fee based upon the sales of Actos during that residual period—in acknowledgement of and due to the anticipated success of Lilly's marketing and promotion efforts: "In recognition that . . . Lilly's efforts . . . will be important in maximizing the commercial potential of Actos . . . and Actos will, in all probability, continue to be a commercial success even after Lilly is no longer participating in the promotion . . . Takeda shall pay Lilly a residual co-promotion fee on sales of Actos in the territory (all United States) . . . for an additional three years following the expiration of the term of the agreement."

55. Ronald Hoven, a former employee of Lilly, was responsible for certain marketing activities for Actos for Lilly in the United States from 2004 to 2006. He was the brand leader for diabetes care from 2003 to 2006, and led the strategy development and operational execution across all marketing channels, including Actos. Mr. Hoven was the marketing lead for the Takeda-Lilly Alliance, and knew that Lilly retained a financial interest in Actos even after the Co–Promotion Agreement ended in 2006, as the company continued to receive royalties on sales in the United States for the next three years. Mr. Hoven believed that resultant revenue, to Lilly, was over $200 million.

56. Lilly played not a passive, but an active role acting in tandem with Takeda, in developing the strategy for responding to the FDA's requests (discussed below), and that Lilly's communications about Actos were funneled to the highest executive levels in Takeda Japan. Specifically, communications from Lilly went directly to Mr. Saito, Senior Director, Pharmaceutical Development Division, Strategic Development Department (Takeda Pharmaceutical Company), for transmission to Takeda's CEO. Takeda, also, communicated important information to Lilly and kept Lilly apprised as new information became available throughout the course of the development and marketing process and suggested nuanced language for use in at least one study.

57. Takeda kept Lilly up to date on all issues relating to Actos and obtained Lilly's consent not to disclose information about the bladder cancer risk to Lilly distributors until Lilly had received Takeda's instructions.

58. Lilly, also, agreed with Takeda not to raise the bladder cancer issue during a telephone conference call with physicians in and around January, 2003.

59. In Comprehensive Meeting Materials dated August 5, 2002, a section entitled "Responses to FDA," refers to a four-way conference call among Lilly and several Takeda employees; the stated reason for the call was to "stress the importance of managing information" regarding an association between Actos and bladder cancer and confirm the future communication routes.

60. As an integral component of the co-promotion agreement, Takeda agreed to indemnify Lilly for any litigation or damages caused by Actos. Lilly was given significant royalties for helping Takeda promote Actos in the United States but did not have to worry about being liable for Actos-related safety issues, i.e., those issues that had caused Upjohn to pull out of development. Lilly knew that Actos was not a safe drug, but could still make money from its sale without incurring any of the risks.

III. Takeda and Lilly Use the Cohen Hypothesis to Obtain FDA Approval

61. Takeda's NDA was approved on July 15, 1999. In the FDA's June 30, 1999 Pharmacology Review for Actos, the medical reviewer who examined the NDA took note of the bladder cancer risks in rats and the proposed Cohen hypothesis. The reviewer observed "[i]n reference to the bladder cancer tumors, although the proposed mechanism of mechanical irritation by calculi is plausible, there are not sufficient data to conclusively determine that this mechanisms [sic] is wholly responsible for the bladder tumors observed in the male rats." Nonetheless, the reviewer grudgingly accepted Cohen's explanation because Actos had not shown a propensity to alter DNA information (genotoxicity). The reviewer concluded that the bladder cancer findings in the rat and mice studies were not sufficiently problematic to recommend rejecting approval.

62. Accordingly, Dr. Cohen, in collusion with Takeda and Lilly, was able to deceive the FDA about a material risk of Actos, by "explaining away" the bladder cancer risk observed in the rat studies with the Cohen hypothesis.

63. The conspiracy and collaboration to develop a sham explanation of the rat and mice bladder cancer data was done in furtherance of group effort to obtain FDA approval for Actos and to

market Actos as though it did not pose a risk of bladder cancer. Dr. Cohen was rewarded with payments from Takeda and the prestige of being an expert in the expanding OAD marketplace, and Takeda and Lilly were rewarded with a "plausible" explanation of the alarming bladder cancer data.

IV. Shortly After Approval, Takeda and Lilly Aggressively Promote Actos as Superior to Avandia

64. Once Actos was approved by the FDA, Takeda and Lilly began to aggressively market Actos in the United States.

65. The approval of Actos occurred shortly after a competing OAD TZD, Avandia, was approved. Avandia was researched and developed by GlaxoSmithKline, Inc. and is in the same class of OADs as Actos in that it increases insulin sensitivity through PPAR gamma activation. From the moment Actos entered the market, the two products battled head-to-head in the marketplace and this competition made the concealment of any bladder cancer risk all the more important.

66. Once Actos was on the market, Takeda and Lilly competed against Avandia by asserting that, unlike Avandia, Actos lowered bad cholesterol (LDLs) and raised good cholesterol (HDLs). Takeda and Lilly made this claim because Actos was shown, in addition to activating PPAR gamma, to also activate PPAR alpha. PPAR alpha is a sister protein to PPAR gamma, which regulates and affects how a cell engages in its metabolic process, i.e., how the cell uses energy. PPAR alpha typically presents or "activates" under conditions of energy deprivation. Takeda and Lilly had concluded that, in addition to being a PPAR gamma agonist (i.e., activator), Actos was also a PPAR alpha agonist, giving it similar qualities to fibrate (cholesterol lowering) medications. And, since PPAR alpha activation is associated with improving cholesterol profiles, Takeda and Lilly used this fact to claim that Actos provided, in addition to improving insulin sensitivity, improved cholesterol benefits. Avandia, however, did not have comparable PPAR alpha activation. Thus, since Type 2 diabetes is associated with obesity, the reduction of cholesterol risks in addition to controlling blood sugar operated as an "important hook" in convincing physicians of Actos' superiority over Avandia. Indeed, in sales representative training materials, Takeda and Lilly representatives were specifically instructed to promote Actos as superior to Avandia because Actos "has a small degree of PPAR [alpha] affinity and activity, while Avandia has been reported to have

none."

67. In line with this marketing approach, on October 27, 2000, several scientists for Takeda published Activation of Human Peroxisome Proliferator-Activated Receptor (PPAR) Subtypes by Pioglitazone in the Biochemical and Biophysical Research Communications medical journal. In this article, the Takeda scientists stated that Actos, in addition to being a PPAR gamma agonist, was also a weak PPAR alpha agonist, and that the scientists observed that Actos caused PPAR alpha activation.

V. Emerging Evidence about Dual PPAR Alpha/Gamma Agonists within FDA Prompts Bladder Cancer Concerns

68. Starting on July 28, 2002, Takeda began receiving calls from the FDA alerting them that there was a bladder cancer problem with glitazars (a new class of oral anti-diabetic drug that activated both alpha and gamma PPARs). The development of those glitazars was discontinued as a result. Lilly was informed of this problem immediately and was consulted about the appropriate strategy moving forward.

69. In an email dated July 31, 2002, sent from Claire Thom—one of the primary Takeda executives in charge of Actos—to various personnel at Takeda, Thom relayed the substance of the conversations she had been having with the FDA. The email bullet points the concerns being raised by the FDA, and explains:

> Underlying these issues is a fundamental belief by the agency that the 'Cohen hypothesis' for bladder tumors in the pioglitazone rat studies is not relevant. The agency is no longer satisfied that the tumor formation is a species specific finding nor that the origin is related to calculi formation. FDA disclosed that they have received data from a dual PPAR agonist (the Novo Nordisk compound) in which bladder tumors were found (not gender or species specific) in the absence of calculi. Based on these data, FDA has drawn the conclusion that tumor formation must be the result of class pharmacology instead of mechanical origin (calculi irritation). The agency is also not convinced that our findings are isolated to the the rat. They commented that our lack of findings in the mice, dog and monkey are unconvincing due to the limited duration of exposure and limited number of animals. In addition, FDA has further evidence from a bladder tumor promotion study in which pio was compared to another sponsor's compound and was shown to increase the formation of bladder tumors (have tumor promoting capabilities). Details on the design and results of this study could not be disclosed.
>
> We have been requested to respond to the FDA in writing within 3-4 weeks. We are currently pulling a detailed action plan together which we will share with you.

This information was also relayed to Lilly executives.

70. A summary of a conversation between Takeda personnel and the FDA's Dr. Jeri El-Hage, dated August 13, 2002, stated that "Dr. El-Hage noted that in light of the fact that several compounds that are dual PPAR agonist have discontinued development due to transitional cell tumors in the bladder and kidneys of male and female rats and in male mice, the Division [of the FDA] is becoming concerned." Dr. El-Hage expressed concern that PPAR gamma and PPAR alpha activation led to bladder cancer and believed this applied to Actos. Dr. El-Hage explained that these bladder tumors were not caused by the Cohen hypothesis because "in follow-up studies, there was no irritation or formation of calculi noted."

71. In the same conversation, Dr. El-Hage relayed the results of a recently completed "promoter" trial involving Actos. In that trial, rats were divided into three groups. The first group received Actos and a compound known to cause bladder tumors, i.e., a cancer initiator. The second group received a glitazar (the compound under investigation) and the initiator. The third group was just given the initiator. The results indicated that 85% of the animals in the group receiving Actos developed tumors, and only 15% of the animals in the third group developed tumors. Dr. El-Hage explained that "[b]ased on these findings, and the fact that other dual PPAR agonist have discontinued from development, the Division does not feel that the general population is being adequately informed about the possible risk of dual PPARs."

72. Dr. El-Hage, on behalf of the FDA, stated that she wanted the Actos label changed to "reflect the relatedness of tumor formation to mechanism (dual PPAR agonist) instead of the current language." Dr. El-Hage wanted Takeda to propose a method by which to monitor bladder toxicity in patients in long term Actos clinical trials. Dr. El-Hage also indicated the FDA's inclination to rescind testing Actos in children, which would have disallowed an additional six months of patent exclusivity.[3]

[3] Historically, drug companies were reluctant to engage in pediatric safety and efficacy studies for drugs already approved for adult populations. Drug manufacturers understood that, absent some information to the contrary, prescribing healthcare professionals would assume that drugs proven effective for adults could, at a reduced dosage, be effective in pediatric populations. Conducting a study that could potentially indicate otherwise was not in the manufacturer's interest. However, in

73. In response to the FDA's concern over Actos and bladder cancer, Takeda executives converged in an "Actos FDA Response Meeting" on August 12-13, 2002. Attending the meeting were approximately two dozen Takeda executives. During the meeting, Philip Collett, an executive with Takeda in Europe, outlined the strategy that Takeda successfully used to fend off a similar inquiry by the European equivalent of the FDA. In his PowerPoint presentation, Collett boiled their strategy down to:

- Persistence.
  - We stuck to Sam Cohen's hypothesis despite many challenges.
- Argued against clinical testing.
- Did not "turn over any stones"
  - eg. Did not undertake database searches.
- Supported by experts at every opportunity.

The minutes of the meeting stated:

Main Points from Takeda Europe Experience

- Takeda Europe successfully employed the following strategy:
  - Defended Cohen hypothesis, despite numerous challenges
  - Stressed the "one sex, one species" argument
  - Challenged authorities regarding implementing monitoring
  - plan
  - Offered to conduct a case control study post-approval

Highlights from PPAR Agonist Discussion

- The group extensively discussed many aspects of the PPAR mechanism and ultimately decided to not address mechanistic issues in the initial FDA response.

74. Ultimately, the outcome of these meetings was to resist any label changes (unless Avandia was required to do so as well), continue to assert the Cohen hypothesis, resist the monitoring of patients in clinical trials for bladder cancer, offer to conduct a case-control study, and to avoid

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the Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105–15, § 111, 111 Stat. 2296 (Nov. 21, 1997), Congress recognized the lack of pediatric safety and efficacy studies being conducted and created a powerful incentive to encourage pharmaceutical companies to engage in more robust pediatric research. Specifically, Congress amended the Food, Drug, and Cosmetic Act ("FDCA") to allow drug manufacturers to get an additional six months of patent exclusivity on drugs if they agreed to conduct and submit pediatric safety and efficacy studies to the FDA. See 21 U.S.C.A. § 355a. The value of allowing additional six-months of patent exclusivity, in the context of Actos, was worth over $2 billion in additional sales.

discussing the PPAR mechanism with the FDA. Takeda and Lilly, instead of taking steps to ensure its product was safe for humans, chose to engage in a deliberate strategy of obfuscation—the strategy successfully used in Europe.

75. Takeda communicated its strategy to Lilly and Lilly, in turn, instructed its sales force to stop promoting Actos as a dual PPAR agonist and to start telling prescribers that Actos was a selective PPAR gamma agonist—a fact that Lilly knew was false. Lilly thereafter engaged in the wholesale destruction of documents linking Actos to PPAR alpha activation, and made changes to its website in response to the FDA's 2002 inquiries. This was done in furtherance of the ongoing agreement to conceal bladder cancer risks. Lilly was fully aware that Takeda was changing its story and knew that representing Actos as a selective PPAR gamma agonist to the FDA was false. Nonetheless, Lilly contributed to the fraud by retooling its promotional efforts by instructing its sales force to pitch the new message.

76. Takeda and Lilly's strategy to avoid any bladder cancer warning worked. Takeda was able to convince the FDA that Actos was not a dual PPAR agonist, and that it was only an activator for PPAR gamma—not PPAR alpha. Takeda used numerous "experts" to support this claim and was able to avoid adding a bladder cancer warning to the label. One expert with whom Takeda and Lilly worked closely to accomplish this was Dr. Charles Burant at the University of Michigan. Dr. Burant conducted experiments to help Takeda and Lilly support the new regulatory message that Actos did not activate PPAR alpha. This strategy (of enlisting experts to spout false theories) was frequently used by Takeda and Lilly. Indeed, that was how the Cohen hypothesis was created. Coordination of these fraudulent theories was perpetrated using electronic wires and U.S. mail. Takeda and Lilly coordinated their conduct with Dr. Burant using electronic wires and U.S. Mail and relied on one another to effectuate a misunderstanding within the FDA about whether Actos causes PPAR alpha activation.

VI. Marketing of Actos as Superior to Avandia Because of PPAR Alpha Activation Poses Problems

77. Takeda, however, had a problem. Takeda and Lilly had continually marketed Actos as a PPAR alpha agonist so as to better compete against Avandia. Takeda and Lilly claimed that Actos'

PPAR alpha activation promoted better cholesterol profiles over Avandia, which only activated PPAR gamma. After the FDA's concern about dual PPAR agonists, however, Takeda and Lilly realized it needed to distance itself from Actos' PPAR alpha activation properties.

78. For example, in November 2002, when Lilly circulated a manuscript for a study linking Actos' lipid benefits to its PPAR alpha activation, Takeda executive Claire Thom reacted by emailing: "I think we should think 100 times before we make a deliberate reference to Actos PPAR alpha agonist activity as an explanation for lipid benefits." A couple of days later, on November 9, 2002, Thom emailed again, "I believe we need to do more than 'discuss' it. I think we are talking about making a very high level strategic decision…around whether we continue to deliberately point out the alpha activity of Actos."

79. Similarly, on December 4, 2002, Takeda marketing executive, Dan Orlando, wrote to Dr. Burant. In the email, Orlando expressed interest in continuing the promotion of Actos as a dual PPAR agonist so as to offer a superior safety profile over Avandia. Orlando stated that he had "[l]aid out my plans to get to work on a 'mixed PPAR' promotional message with Rich and he claimed that you might have some hesitancy there. Bottom line, all heads (Claire and Rich) are looking to you for direction[.]" Dr. Burant instructed Orlando that any message regarding Actos being a dual PPAR agonist posed significant risk. He stated:

> I really think you need to consider the whole franchise. Basically, the FDA is thumping you with the thought that mixed agonists cause bladder cancer and we just spent the last 4 months fighting this and will likely be doing it in the future…The first step is to dissociate pio from the other compounds, i.e. some sort of physical effect, but given the FDAs insistence that 'mixed agonists' are the bad guys, the first is to get away from them.
>
> [O]ne of the last items that was put to the FDA (please read the treatis[e] that was sent yesterday by Janet Haskins et al) is that IN THE RAT, there is no evidence of intrinsic ppar alpha activity…
>
> [T]he issue is pediatric indication, because if pediatric goes, I don't think that marketing the mixed agonist stuff will in any way make up for the loss in revenue from that hit, along with the potential losses from the 'cancer' stigmata that is surely to be used[.]

In essence, Dr. Burant was advising Takeda and Lilly that they needed to be careful in managing any dual PPAR agonist marketing because it could pose great financial risk.

80. Takeda and Lilly persisted in downplaying the relationship between Actos and bladder

cancer. In January 2003, as part of the "label negotiation strategy," Orlando advised that the decision had been made that "conducting market research on possible label language around bladder cancer would risk public awareness…" Linking the animal trial results to humans was seen as having a negative impact on sales: "In Marketing's assessment any of the proposed changes which imply a clinical connection would have an impact on sales. Any clinical language would likely be used by GSK to differentiate Avandia on safety…"

81. Then, on April 4, 2003, Claire Thom announced to Dr. Kitazawa that the strategy to fend off the FDA, in conjunction with numerous experts like Dr. Burant, had worked—"The FDA has agreed to our proposal to remove the language 'The relationship of these findings in male rats to humans is unclear' with no other language to be added to the label."

82. The bladder cancer problem, however, did not go away. In December of 2003, Takeda compiled and presented a PowerPoint entitled "Barriers to TZD Prescribing Qual Report." The report anticipated a future world in which Actos was associated with bladder cancer and how a warning about bladder cancer would affect sales. As part of the report, Takeda surveyed doctors regarding a new oral anti-diabetic drug that also contained a bladder cancer warning. Doctors responded very negatively. For instance, one prescriber stated "Bladder tumors? That would change my thinking altogether. I would not be likely to use the product." Another stated "[i]f there is a risk of bladder tumors, I would definitely not use it." In total, interest declined "greatly" in 75% of the surveyed physicians and interest declined "slightly" in the rest. This study and survey confirmed what Takeda already knew—any warning of bladder cancer for Actos would dramatically reduce prescriptions and sales. Accordingly, Takeda and the enterprise continued to make every effort to resist bladder cancer labeling.

83. The issue of telling the FDA one thing (Actos is a selective PPAR gamma agonist only) versus what marketing had been promoting (Actos' lipid benefits are related to its PPAR alpha activation) continued to be a problem for Takeda and Lilly. In August 2004, Takeda scientists, who were not aware of the PPAR alpha cover up, published a journal article indicating that Actos was a mixed PPAR gamma and PPAR alpha agonist. This article prompted an email to be sent to various Takeda executives by Miyazaki Masahiro on September 21, 2004, asking for people to express what

"regulatory impact" the article would have. In response, Takeda Europe Managing Director David Eckland circulated an email to Masahiro and other Takeda executives expressing serious concern with the publication of the article:

> Over the last 18 months or more…we have been vigorously defending Pioglitazone from consistent regulatory attack. Part of this has been based on the pharmacology of pioglitazone, which with your help we have defined as a pure gamma agonist at clinical concentrations. We have worked hard to produce a pharmacological hypothesis which allows the differentiation of Pioglitazone from [Avandia]…This recent paper…states repeatedly that pioglitazone has mixed gamma and alpha activity at clinical concentrations…I was very surprised to see this paper in print, without having had any preview, or advance notice of its submission or publication . . .
>
> The most severe impact could be that regulators will no longer believe us when we give explanations, which could lead to the suspension of pioglitazone from the market in Europe, and I am sure severe consequences in US market (especially as FDA have just included a s[t]atement in the US label to say that pio is a pure gamma agonist… Most likely, is that as a result of not believing us any more, regulators will now assert that pioglitazone is a mixed alpha gamma agonist, and that the likely toxicological implications are severe. This will lead to changes in the data sheet…describing the probability that Pioglitazone may cause cancer in man. There may be severe restrictions on using pioglitazone (eg limit duration of use to 6 months), and further long term clinical trials will become extremely difficult to do [(]from a regulatory prospective). I am sure our marketing colleagues could tell you of the potential impact on sales of our drug.

Eckland was concerned that the publication would reveal that Takeda and Lilly had been deceiving regulatory agencies in the United States, and what impact that may have on their ability to market Actos.

84. Rather than concede that Actos was a dual PPAR alpha/gamma agonist and announce to physicians and patients that there was a bladder cancer connection, Takeda's executives worried about their credibility, the impact on sales, and how this study demonstrating Takeda and Lilly had been lying to the FDA got published without advance notice to Takeda executives.

85. This was not an isolated concern—a few days later, another Takeda executive, Mick Roebel, echoed Dr. Eckland's email, sending his own on September 30, 2004:

> 1) As you know, during recent labeling negotiations with FDA re: non-clinical findings, [Takeda] successfully pushed back on the Agency to reiterate that Actos is a selective PPAR gamma agonist. FDA accepted our label wording ("Urinary tract tumors have been reported in rodents taking experimental drugs with dual PPAR alpha/gamma activity; however, Actos is a selective agonist for PPAR gamma"). This new publication calls this statement into question, and (since it is our publication), it could appear that we intentionally mislead the Agency. Could the Agency decide to revisit the label wording in light of this new publication?

> 2) We have been devising a strategy to revisit the clinical hold for pediatric studies that we are currently under with Actos. It seems possible that companies with dual alpha/gamma compounds may find it more difficult to get FDA approval to do ped. studies. This new publication can only hurt us as we try to reinstitute ped. trials, and may adversely affect our ability to get 6 mo. additional exclusivity (pediatric exclusivity) for Actos if we're unable to pursue appropriate trials.
>
> re: suggestions - at other companies I've been at, a goal has been to tightly manage a product like Actos on a global basis, with research/development/commercial people all being on the "same page" and with a minimum of internal "surprises" arising. This can be difficult to do, but is key to protecting/opt[i]mizing the brand. I know we're trying to do this at Takeda also, and that over the past few years we're started to put global processes in place. However, as we all know, Actos is key to our short and (at least) medium term future, so we need to find a process to ensure that all pieces of the company that are dealing with Actos understand and support the product's profile/positioning, and that any new initiatives (preclinical or clinical studies, marketing approaches, etc) are consistent with this view.

Takeda and Lilly showed no concerns about the bladder cancer risks and even proposed to continue their efforts to test Actos in children so as to obtain an extra six months of patent exclusivity despite the risk. Capturing an extra six months of exclusive sales was worth billions of dollars to Takeda.

VII. The PROactive, Disproportionality Analysis, and KPNC Data Raise Additional Alarm about Actos and Bladder Cancer

86. As part of Takeda's and Lilly's marketing efforts for Actos, a clinical trial was conducted to see if Actos offered superior cardiovascular benefits over other drugs, i.e., Avandia. This clinical trial was called the PROactive (PROspective PioglitAzone Clinical Trial In MacroVascular Events) study.

87. One reason for conducting this trial was to ascertain whether an increased risk of bladder cancer existed, and Takeda agreed to inform the FDA in an expedited fashion of new cases of bladder cancer discovered during the study; to unblind those study subjects and, for any such subject taking pioglitazone, remove him or her from the clinical trial.

88. During the course of the clinical trial, 19 people developed bladder cancer: 14 were in the group taking Actos®, while 5 of them were in the control group. The PROactive study found that the group taking Actos had a statistically significant increase in bladder cancers than those in the placebo group.

89. Notwithstanding Takeda's earlier promise, however, it did not unblind the subjects who developed bladder cancer even after Takeda employees expressed concern about this failure to

unblind the cancers, in light of the earlier FDA agreement.

90. On March 10, 2004, Takeda justified this decision not to provide the information to the FDA by claiming that Takeda Europe Research & Development, Ltd. preferred not to break the study blind, given its obligation to European regulators. However, Takeda Europe Research & Development, Ltd. had not existed as a separate corporate entity for over two months.

91. It was published in 2005. *See* Dormandy J.A., et al., *Secondary Prevention of Macrovascular Events in Patients with Type 2 Diabetes in the PROactive Study (PROspective PioglitAzone Clinical Trial In MacroVascular Events): a Randomised Controlled Trial*, 266 Lancet, 1279-1286 (2005) (the "Dormandy paper").

92. Around this time, in 2005, Takeda also performed a statistical analysis of the FDA–Adverse Event Reporting System ("AERS") database, which tracks self-reported adverse events. That analysis showed a signal for bladder cancer when comparing Actos to all drugs in the FDA–AERS database; however, Takeda edited the table so as to omit this statistical analysis from the final reports provided by Takeda to the FDA, and thereby included only non-significant signals of Actos when compared to anti-diabetic drugs, insulin, metformin, sulfonylureas, and Avandia. Furthermore, Takeda failed to reveal to the FDA the result of the October 2005 Disproportionality Analysis showing a signal of excess bladder cancer among Actos patients, despite and in the face of the FDA's request, in May 2006, for "any recent data you may be aware of."

93. Also around this same time, Takeda had also finished its first preliminary analysis of data collected from the Kaiser Permanente Northern California ("KPNC") database, monitoring the incidence of bladder cancer in Actos users. Takeda had agreed to a request by the FDA to conduct an epidemiological study concerning the association between Actos and bladder cancer using the KPNC database. The protocol called for interim analyses and a nested case control to account for confounding factors.

94. In 2005, Takeda was required to submit the bladder cancer data from the PROactive Study and initial KMPC analysis to the FDA and European regulatory authorities. Both studies contained data showing an association between Actos and bladder cancer. Philip Collett sent an email to Takeda executives about the upcoming submission on August 5, 2005. This email prompted

a response from Wada Yasuhiko in Japan, which stated:

> As the reports on malignancy to the authorities are of critical importance for Actos, you are requested to pay very very careful attention to this matter by all means.
>
> To ensure that the interpretation is right to avoid unnecessary arguments against the safety of Actos, you better consult with the outside experts like epidemiologists in prior to your submission to EMEA/FDA.
>
> . .
>
> [W]e need to know the following scenario in terms of responses given by authorities you should predict when you submit the reports to EMEA and FDA from regulatory perspective.
>
> 1) Most likely scenario, 2) Best case scenario and 3) Worst case scenario[.]

95. In response, Mick Roebel, the Vice President of Regulatory Affairs in the United States, outlined the various best and worst-case scenarios:

> [T]he bladder cancer issue has died down in the US over the last several months. We continue to provide expedited Safety Reports for cases of bladder cancer to the Agency, as agreed in Feb. 2003. For PROactive specifically, we informed FDA in Mar. '04 of a number of cases of bladder cancer from the trial but told them we did not want to break the study blind at that time in order to maintain study integrity. We assured the Agency that the DSMB had approved the continuation of the study. FDA did not question us on this.
>
> Best Case Scenario
>
> As in the EU, it's not unlikely that the Metabolism and Endocrinology Div. at FDA will request some sort of labeling change. Best case is that this happens subsequent to our PROactive US submission and data review, and includes relatively benign wording around bladder cancer findings from the study along with "benefits" wording if trial is positive.
>
> Worst Case Scenario
>
> It seems pretty unlikely in the US that the FDA would try to remove the drug from the market given the equivocal safety data seen. However, the overall evaluation is, of course, a benefit/risk proposition and if the PROactive "benefit" turns out to be worse than neutral (decrease mortality, other?) this could change. A more likely "worst case scenario" could be for the Agency to ask for an immediate label change incorporating bladder cancer findings, possibly some sort of a "Dear Healthcare Provider" letter to be sent, and posting of pioglitazone on the new "Drug Watch" portion of the FDA Web page. This "Drug Watch" list, accessible to the public, is meant to identify drugs for which FDA is actively evaluating safety signals during a period of uncertainity while FDA and the Sponsor evaluate new, significant safety information. The situation would first be discussed by the new FDA Drug Safety Oversight Board prior to any posting; the company mayor may note be involved in! these discussions. If pioglitazone were to be posted, I would expect the media to pick this up. The Agency could also ask us to put together some sort of Risk

> Management plan for the product to minimize any possible bladder cancer risks associated with pioglitazone (ways to identify populations most at risk, only treat populations most benefiting from product, etc)
>
> Most Likely Scenario
>
> Depends on overall results of PROactive, but "most likely" is expected to be more like "best case" than like "worst case". Depending on how FDA views our pharmacovigilance plan[.]

96. Takeda executive Kiyoshi Kitazawa responded, stating that "As you understand very well, Actos is the most important product for Takeda and therefore we need to manage this issue very carefully and successfully not to cause any damage for this product globally."

97. Once again, Lilly was informed about this ongoing bladder cancer issue and how an FDA warning would impact its ongoing efforts to market and sell Actos in the United States and, by definition, in California. And, once again, Lilly's concerns were to protect Actos and hide the bladder cancer risk from, patients, prescribers, third-party payors, and the FDA.

98. When the PROactive study was published in the Lancet in 2005, it did not reveal the statistically significant increase in the risk of bladder cancer. Dr. John Dormandy, the lead author of the paper, conspired with Takeda and Lilly to misrepresent the data. Specifically, the PROactive paper published in 2005 reported that there were 14 (0.5%) cases of bladder neoplasms in the Actos group and 6 (0.2%) in the placebo group. In truth, one of the neoplasms in the placebo group had been deemed to be a benign tumor and, per the study's protocol, should not have been counted. This change in the data from 6 to 5, however, would have rendered a statistically significant difference between the Actos and placebo groups. Takeda and Lilly coordinated their conduct with Dr. Dormandy and relied on one another to effectuate a misunderstanding about the PROactive trial within the medical community. This was done to facilitate the overall goal of concealing any association of Actos with bladder cancer.

99. This deception was unveiled by independent scientists, Drs. Hillaire-Buys, Faillie, and Montastruc. These researchers recalculated the risk ratio after removing the benign tumor from the placebo group, and concluded that there was a statistically significant 2.83 times greater risk of bladder cancer amongst the PROactive participants randomized to Actos. In the October 29, 2011 Lancet, these researchers explained that "…this result shows a significant relation between

pioglitazone and bladder cancer, which has not been presented in the PROactive study reports… This finding, associated with the preclinical and clinical finding reported on the FDA website in 2004 (PPAR agonists were claimed to be multi-species, multistrain, multisex and multisite carcinogens), could have led to an alert 5 years sooner. With this in mind, pioglitazone prescription could have been restricted, and monitoring of patients strengthened." (emphasis added).

100. Dr. Dormandy's miscounting is reflected in the label change in 2006, stated:

> In two 3-year studies in which pioglitazone was compared to placebo or glyburide, there were 16/3656 (0.44%) reports of bladder cancer in patients taking pioglitazone compared to 5/3679 (0.14%) in patients not taking pioglitazone. After excluding patients in whom exposure to study drug was less than one year at the time of diagnosis of bladder cancer, there were six (0.16%) cases on pioglitazone and two (0.05%) on placebo.

This language, however, although properly reflecting the five reports of bladder cancer in the placebo group, it did not clarify the previous mistaken publication and correctly reflect the statistical significance of the bladder cancer risk for the patients exposed to Actos. Instead, it omitted the statistical comparison without reference to the previously published incorrect number and included language downplaying the connection, in addition to placing the information in the section of labeling related to animal findings, thereby suggesting it was not a human problem.

VIII. The FDA's Response to the PROactive and KPNC Data

101. In the latter part of 2005 and through July 2006, shortly after the submission of the PROacive and preliminary KPNC data to the FDA, Takeda sought approval for a drug combining Actos with another OAD, glimeprimide. The FDA's medical reviewer was Dr. Robert Misbin, who had been involved with the earlier evaluations of the link between Actos and bladder cancer in 2002. In this 2006 Medical Review, Dr. Misbin summarized the bladder cancer findings in the animal trials and two post-approval human trials:

> Bladder cancers were found in mice in preapproval studies of pioglitazone and in most, if not all, mixed PPAR agonists. In addition, Merck has found that both its PPAR agonist and pioglitazone promoted growth of bladder cancers in the presence of the tumor initiator BBN.
>
> . . .
>
> The following is a summary of new findings related to bladder cancer from phase 4 clinical trials lasting two years or longer.

> . . .
>
> Taking all cases, there were 17/3656 (0.47%) reports of bladder cancers in patients taking pioglitazone compared to 5/3679 (0.14%) in patients not taking pioglitazone. The one case of benign bladder tumor in a placebo patient in PROactive has been excluded. Of the three cases of bladder cancer in study 506, one was a recurrence. If we exclude this case, and restrict the analysis to new diagnoses, there are 16 cases on pioglitazone and 5 on placebo/glyburide. The odds ratio from the stratified analysis performed by FDA is 3.24 (95% CI limits: 1.2, 9.9), p=0.02. Excluding diagnoses within one year of starting the test drug, there were two cases bladder cancer on placebo and six on pioglitazone. All of these were from PROactive.

Dr. Misbin's analysis indicated that there was a statistically significant risk ratio of 3.24 for Actos in causing bladder cancer.

102. Elsewhere in his 2006 report, Dr. Misbin explained how Takeda, facilitated by Lilly and the enterprise, used the Cohen hypothesis to obfuscate a link to bladder cancer:

> Bladder tumors had been found in mice in preapproval studies of pioglitazone. Because there were no similar findings with troglitazeon or rosigiltazone (Avandia), FDA initially accepted the explanation offered by Takeda that the tumors were due to the presence of bladder calculi in the pioglitazone studies. It later became clear that most, if not all, mixed PPAT* agonists were associated with bladder tumors in animal toxicology studies. In addition, Merck found that both its PPAr agonist [redacted] and pioglitazone promoted growth of bladder tumors in the presence of a tumor initiator, BBN (butyl-nitrosbutyl nitrosamine). These issues were discussed with Takeda in a telecom of July 31, 2002.

103. Dr. Misbin further explained that, in 2004, the FDA proposed amending the Actos label to include bladder cancer language, but that:

> Takeda declined to go along with this recommendation. In an attempt to come up with "physician-friendly" language that would be acceptable to Takeda, the following proposal for wording was faxed to Takeda on November 24, 2004:
>
> Urinary tract tumors have been reported in rodents taking experimental drugs with dual PP AR alpha/gamma activity.
>
> Initially, Takeda declined to go along with this wording. However, in a submission dated April 9, 2004, they proposed the following:
>
> Urinary tract tumors have been reported in rodents taking experimental drugs with dual PPAR alpha/gamma activity; however ACTOS is a selective agonist for PPAR gamma.
>
> The phrase "ACTOS is a selective agonist for PPAR gamma" was already in the label, so no new claims were being made.

Dr. Misbin noted Takeda's resistance to adding bladder cancer warnings as well as their insistence that Actos is a selective gamma agonist only, attempting to distinguish Actos from glitazars and their

link to bladder cancer. Misbin stated that Actos is more likely a dual agonist since Actos raised HDL and lowered LDL, a property of alpha agonism. He suggested that the selectivity language be removed from the Actos label.

104. Despite Dr. Misbin's recommendations, Takeda continued to not update the Actos warning label and continued to market Actos without warning patients and prescribers of the known bladder cancer risks. Indeed, Takeda and Lilly were receiving an average of more than 180 cancer reports each year (1,813 over ten years) from spontaneous sources, but Takeda and Lilly never included these cancer reports in the label, and never issued a Dear Doctor Letter to warn the medical community of the risk of developing cancer while taking Actos.

105. In September 2006, Lilly ended its partnership with Takeda. Although, Lilly continued to receive royalty payments through 2009.

IX. The 2009 KPNC Data and Actions by European Regulators Spur FDA to Conduct Independent Investigation and Issue Bladder Cancer Warning

106. In 2009, pursuant to the 2003 agreement Takeda made with the FDA to conduct periodic reviews of the KPNC data, a new report was submitted to the FDA. The results of the analysis were alarming. The data showed a statistically significant increase in the risk of bladder cancer for use of Actos longer than 24 months (risk ratio of 4.8) and for patients who took a cumulative dose over 28,000 mg (risk ratio of 4.6). These numbers were adjusted for possible confounding factors such as smoking history, high risk occupations, and urinary tract infections.

107. The FDA reacted to the interim KPNC report by announcing, on September 17, 2010, that it was conducting an on-going safety review of Actos for the potential increased risk of bladder cancer.

108. Approximately three months before the FDA announced its investigation, a false claims act case was filed by a whistleblower, Dr. Helen Ge. Dr. Ge was a Contract Physician with Takeda between September 2008 and January 2010 and was responsible for reviewing adverse events associated with various Takeda products, including Actos. During her time working for Takeda, Dr. Ge reviewed multiple adverse event reports involving Actos and bladder cancer. Dr. Ge concluded that Actos was causally related to a bladder cancer reported from a clinical trial. Takeda

management, however, pressured Dr. Ge to change her assessment and find, contrary to her medical opinion, that Actos was "unrelated" to the adverse bladder cancer event. Dr. Ge then initiated an investigation and discovered that Takeda had been systematically underreporting the incidence of bladder cancer in adverse event reports. Dr. Ge filed her complaint under seal on June 18, 2010 in the United District Court for the District of Massachusetts. In it, she reported that Takeda's Vice President over its Pharmacovigilance Department, Maria Paris, told her staff that adverse event reporting is one thing, but Takeda's profitability comes first.

109. While the FDA was reviewing the KPNC data, the American Diabetes Association published Piccinni, et al., *Assessing the Association of Pioglitazone Use and Bladder Cancer Through Drug Adverse Event Reporting*, *Diabetes Care*, 34 Am. Diabetes Assoc., 1369-1371 (June 2011), ahead of print on April 22, 2011. This study looked at adverse event reports made to the FDA between 2004 and 2009 and analyzed the association between anti-diabetic drugs and bladder cancer. The study concluded that "[i]n agreement with preclinical and clinical studies, AERS analysis is consistent with an association between pioglitazone and bladder cancer. This issue needs constant epidemiologic surveillance and urgent definition by more specific studies." The study found that one-fifth of the 138 bladder cancer reports for all drugs submitted between 2004 and 2009 were regarding patients taking Actos.

110. On June 9, 2011, the European Medicines Agency announced that it had been informed by the French Medicines Agency of its decision to suspend the use of pioglitazone-containing medicines (Actos, Competact) in France while awaiting the outcome of the ongoing European review. The decision by French regulators was based upon a retrospective cohort study in France using the French National Health Insurance Plan, which demonstrated a statistically significant increase in the risk for bladder cancer in males exposed to Actos for more than a year. The French cohort included 1.5 million patients with diabetes who were followed for four years (2006-2009).

111. On June 10, 2011, Reuters published a story stating that Germany had joined France in suspending the use of Actos after Germany's Federal Institute for Drugs and Medical Devices. ("BfArM") reviewed the results of the French study. BfArM recommended that doctors should not

put new patients on pioglitazone.

112. On June 15, 2011, the FDA issued this safety announcement, linking long term use of Actos to bladder cancer, based on the KNPC data, as well as the French study that led to Actos being suspended in France and Germany:

> The U.S. Food and Drug Administration (FDA) is informing the public that use of the diabetes medication Actos (pioglitazone) for more than one year may be associated with an increased risk of bladder cancer. Information about this risk will be added to the Warnings and Precautions section of the label for pioglitazone-containing medicines. The patient Medication Guide for these medicines will also be revised to include information on the risk of bladder cancer.
>
> This safety information is based on FDA's review of data from a planned five-year interim analysis of an ongoing, ten-year epidemiological study, described in FDA's September 2010 ongoing safety review and in the Data Summary below. The five-year results showed that although there was no overall increased risk of bladder cancer with pioglitazone use, an increased risk of bladder cancer was noted among patients with the longest exposure to pioglitazone, and in those exposed to the highest cumulative dose of pioglitazone.

After the FDA had conducted its own internal investigation, and after France and Germany had effectively removed Actos from the market, Takeda finally changed the Actos warning label to warn of a bladder cancer risk—a risk it knew or should have know about before the drug was ever approved by the FDA.

113. At the end of June 2011 was the American Diabetic Association's annual convention. In preparation for the marketing opportunities at that event, Takeda's marketing department prepared a PowerPoint presentation for their marketing personnel entitled "Strengthen Your Core." Takeda sales representatives were given a verbatim pitch that they were supposed to use to allay prescribers' concerns over bladder cancer. They were instructed, however, to "wait for [prescribers] to ask the question before using the verbatim. If no questions/concerns, do not discuss bladder cancer and sell, sell, sell!" Once again, the emphasis was on avoiding conveying bladder cancer information.

114. In September 2011, Takeda provided additional KPNC data pursuant to the FDA's request. It showed, again, a statistically significant increase in the risk of bladder cancer for use of Actos longer than 24 months (risk ratio of 4.4) and for patients who took a cumulative dose over 28,000 mg (risk ratio of 4.6). It also showed a statistically significant risk ratio of 9.4 for consumers of between 10,501 and 28,000 mg of Actos.

115. As Takeda's marketing department and executives predicted, once the bladder cancer warning was added to the Actos label in 2011, Actos sales collapsed. Expert analysis indicates that sales of Actos dropped shortly after the FDA issued its alert in 2010, and then again when the FDA issued the bladder cancer warning in 2011 (before Actos went generic). The precipitous drop, accounting for a decline of approximately 80% of sales, indicates that, because prescribers and patients did not know of the bladder cancer risk from 1999 through 2011, Takeda, Lilly, and the enterprise were able to sell many prescriptions for Actos that they otherwise would not have been able to absent the fraud. In other words, had Takeda issued bladder cancer warnings from the beginning, the enhanced warnings would have caused reduction of approximately 80% of sales.

116. In August 2012, Actos went generic, spawning the proliferation of less expensive generic competitors and ending the profitability of the enterprise.

X. The International Agency for Research on Cancer Deems Actos a Probable Human Carcinogen

117. In 2105, the International Agency for Research on Cancer ("IARC") conducted a comprehensive cancer evaluation of pioglitazone.

118. IARC was created in 1965 as the specialized cancer agency of the World Health Organization with support of the United States. IARC promotes international collaboration in cancer research, "bringing together skills in epidemiology, laboratory sciences, and biostatistics to identify the causes of cancer[.]" International Agency for Research on Cancer, *About IARC*, http://www.iarc.fr/en/about/ (last visited June 24, 2016).

119. IARC is transparent. The minutes and documents presented at its council meetings are publicly available and, thus, are subject to scientific scrutiny.

120. Starting in 1971, IARC began assessing whether chemicals were carcinogenic through the Monograph program. Monograph evaluations are performed by panels of international experts, selected on the basis of their expertise and the absence of actual or apparent conflicts of interest. The process involves a year-long evaluation of all publicly available information including: (a) human, experimental, and mechanistic data; (b) all pertinent epidemiological studies and cancer bioassays; and (c) representative mechanistic data. After reviewing the data, the monograph panel engages in a

rigorous (and public) public scientific debate and assigns the agent into one of four groups: Group 1 (Known Human Carcinogens); Group 2A (Probable Human Carcinogens); Group 2B (Possible Human Carcinogens); and Group 3 (Not Classified). Since the Monograph program's inception, IARC has reviewed 980 agents, with only 73 (about 7%) being assessed as probable carcinogens (Group 2A).

121. In 2015, IARC completed a year-long assessment of pioglitazone and issued an official monograph.

122. The IARC glyphosate panel consisted of 21 scientists members from 9 different countries. Among the members were Fredrick A. Beland and Lei Guo, of National Center for Toxicological Research at the United States Food and Drug Administration and June K. Dunnick and Ruth M. Lunn of the National Institute of Environmental Health Sciences. One of panel members, Chin-Hsiao Tseng was a paid advisory board member for Takeda and Lilly. And, in addition, Takeda had an observer, Paul Dolin, present at the meeting.

123. IARC systematically reviewed all the published literature, both from an epidemiological and toxicological perspective, and concluded that pioglitazone was a Group 2A carcinogen. The IARC working group concluded that "[a] positive association has been observed between pioglitazone and cancer of the bladder" and that "[t]here is sufficient evidence in experimental animals for the carcinogenicity of pioglitazone."

XI. The FDA Reaffirms the Bladder Cancer Risk in December 2016 and Continues to Mandate Bladder Cancer Warnings on the Actos Label

124. In 2016 the FDA conducted an updated review of the Actos bladder cancer risk and after reviewing all up-to-date data, concluded, once again, that the drug "may be linked to an increased risk of bladder cancer." FDA Drug Safety Communications, *Updated FDA Review Concludes that Use of Type 2 Diabetes Medicine Pioglitazone May be Linked to an Increased Risk of Bladder Cancer* (Dec. 12, 2016) at *1.[4]

125. The current label for Actos states, on the first page: "Bladder Cancer: May increase

[4] *Available at*: https://www.fda.gov/downloads/Drugs/DrugSafety/UCM532691.pdf.

the risk of bladder cancer." This statement is neither false nor misleading.

126. Plaintiff alleges that this statement should have been included on the Actos labeling and marketing material since the drug entered the market in 1999.

XII. Spoliation: Takeda and Lilly Destroy Documents and Worked to Conceal Their Fraudulent Conduct

127. Through July 2002, Takeda and Lilly openly promoted the lipid benefits of Actos over Avandia, pointing to the fact that Actos induced PPAR-alpha activation. On July 19, 2002, a product liability suit was filed against Takeda regarding Actos, and so Takeda's legal department circulated a litigation hold to preserve all documents concerning Actos. A litigation hold directs company personnel to not destroy documents related to some litigation despite the company's document retention policy authorizing destruction of documents when employees leave or after a certain amount of time has elapsed.

128. According to the 2002 Litigation Hold:

> A motion has been filed to add Takeda Pharmaceuticals North America, Inc. and Takeda Pharmaceuticals America, Inc. as defendants in a lawsuit. The plaintiff in this lawsuit seeks damage for personal injury and wrongful death allegedly resulting from the use of certain prescription drugs, including Actos.
>
> To be able to respond to discovery requests from the plaintiff, if that becomes necessary, we must take steps to preserve any documents that may be called for in this lawsuit.
>
> Until further notice, you are instructed to preserve any and all documents and electronic data which discusses, mentions, or relates to Actos. This means do not destroy, delete, throw away or otherwise discard any such documents or electronic data. This includes correspondence, records, and data, contained in your paper and electronic files, regardless of form and include email correspondence and attachments and electronic data.
>
> Action Steps:
>
> Please interpret this directive in its broadest sense to prevent the deletion or destruction of any recorded information and data relating in any way to Actos.
>
> Please take steps immediately to preserve such documents and data within your department.
>
> Please distribute his memo to members of your group and advise them of the importance of following these instructions.

129. This litigation hold was distributed across the entire company.

130. Takeda's 2002 hold was renewed on a number of occasions through 2011, including in 2003, 2006, 2007, 2008, and 2011. Specifically, an additional hold was imposed in December 2010 related to a document demand issued by the Texas Attorney General's office regarding Takeda's adverse event reporting. At first, during discovery in the federal Actos bladder cancer Multi-District Litigation ("MDL") proceedings coordinated in Lafayette, Louisiana, Takeda told the MDL Plaintiffs Steering Committee that the unavailability of certain employees' files was the result of the normal document retention policy—there was no litigation hold in place barring routine document destruction until February 2011.

131. Despite the alleged February 2011 hold, Takeda destroyed Takeda executive Mr. Miyazaki's Actos-related computer records, emails and files in the spring and summer of 2011. Then Takeda asserted that its statement that there was no hold until February 2011 was a mistake—it was really August 2011, so destroying Mr. Miyazaki's files was okay. Eventually, Takeda's in-house counsel, Stacey Calahan, conceded that Takeda had destroyed a wealth of Actos-related documents between 2002 and 2011 inconsistent with the litigation holds that had been in place since 2002.

132. Indeed, despite actual knowledge of their duty to preserve evidence, files of at least forty-six witnesses across multiple continents were destroyed, deleted, or otherwise lost. Examples of the custodians whose files were destroyed in whole or in part, include a President of Takeda Global Research and Development (John Yates); Managing Director (Kiyoshi Kitizawa, David Eckland); Vice President, Pharmaceutical Research Division (Masaomi Miyamoto, Takashi Nonoyama); Director, Pharmaceutical Development Division (Mikihikio Obayashi); Senior Director, Pharmaceutical Development Division (Katsuhisa Saito); Representative Director, Chairman of the Board (Kunio Takeda), Senior Vice President – Sales (Harry (Dean) Hart); Senior Manager – Product Safety (Doug Joseph), Director Epidemiology, Pharmacovigilance (Annette Beiderbeck); and Vice President- Regulatory Affairs (Philip Collett), to name a few. At least 38 of the 46 custodians whose files were destroyed were deleted after 2002 when Takeda already had in place the 2002 Litigation Hold. Moreover, the files of these custodians were destroyed in a manner that contravened the retention policies that governed the destruction of documents during the relevant time.

133. In addition, Takeda and Lilly destroyed promotional materials indicating that Actos

was a PPAR alpha agonist, a part of their decision to abandon the PPAR alpha agonist promotional slant.

134. The manner and speed with which the files were destroyed, the characteristics of the custodians who were targeted (many senior executives involved in critical regulatory, safety, and science positions), and the widespread nature of the destruction indicate that the destruction was done in bad faith. It was done in furtherance of the enterprise.

135. In January 2014, United States District Judge Rebecca F. Doherty, the judge overseeing the MDL proceedings, issued a spoliation order finding that Takeda had destroyed or failed to preserve 46 custodial files of personnel who worked on Actos and in particular the Actos bladder cancer issue. The files of many senior executives who worked on Actos were destroyed, including Dr. Kitazawa's files. The importance of some of the documents that were destroyed was established by documents obtained from Upjohn which contained correspondence to, from and concerning Dr. Kitazawa.

136. During the first MDL bellwether trial, deposition testimony from Dr. Helen Ge was played regarding her work in Takeda's pharmacovigilance department. In October of 2009, Dr. Ge reviewed a report of a bladder cancer adverse event report from a study and deemed it related to Actos. When Takeda Japan queried the basis for her determination, she was directed by her United States superiors not to put her explanation in writing because it would be discoverable in litigation:

> Q. And in your response, you did not respond to even one of the questions asked by Japan; isn't that true?
>
> A. No. Because Michelle Peralta send me e-mail asking me to stop response. They don't want to establish any e-mail document traffic for future lawsuit. That's their purpose. That was Michelle Peralta came to my office and told me, hey, you got to stop responses to Japan. All these e-mail will be subject to subpoena.

This demonstrated that Takeda was fully aware of the litigation effect of writing emails and that Dr. Ge's research regarding the relationship between Actos and bladder cancer would be subject to litigation discovery.

137. At the conclusion of the MDL trial's testimony, Judge Doherty instructed the jury that Takeda had an obligation to retain Actos-related documents as of July 2002, but key Takeda executives' files related to Actos were destroyed and that spoliation had occurred. This conduct in

destroying documents in violation of the Federal Rules of Civil Procedure, federal law, and Court orders, was done in furtherance of Takeda and the enterprise's efforts to conceal any correlation between Actos and bladder cancer and the numerous ways in which Takeda and the enterprise misled the FDA, patients, prescribers, and third-party payors about the significant risk of Actos causing bladder cancer.

XIII. The MDL Bellwether Trial

138. A bellwether trial was conducted in the MDL proceeding where this case was originally filed.

139. That trial was conducted by consent of the parties, including the Defendants.

140. The trial was an intense and exhaustive process for all involved. During thirty-seven days of actual trial, the plaintiff trial team presented eighteen witnesses, the defendants presented eleven witnesses, and more than four hundred exhibits were admitted.

141. The jury ultimately returned a verdict against the Defendants, concluding that: (1) Actos increased the risk of bladder cancer, (2) Takeda and Lilly failed to disclose the bladder cancer risk, (3) Takeda and Lilly acted with "wanton and reckless disregard of the effects of its actions," and (4) Takeda and Lilly were respectively 75% and 25% at fault.

142. The federal district court overseeing the trial denied the Defendants' motion for judgment notwithstanding the verdict and explained:

> [T]his Court concludes that the Plaintiffs have pointed to substantial evidence, of such quality and weight, that was put into the record during the trial of this matter, to establish a legally-sufficient basis for the jury's finding reflecting that:
>
> [1] Actos® exposure creates an increased risk of bladder cancer;
>
> [2] that both Takeda and Lilly were aware that Actos® creates this increased risk;
>
> [3] that both Takeda and Lilly undertook a concerted, coordinated pattern of effort, of several years' duration, to prevent the FDA, the medical community, and the public from obtaining knowledge of this risk; and
>
> [4] that the primary reason for this effort was to preserve the tremendous profits generated by the sale of Actos® in the United States and worldwide.

In re Actos (Pioglitazone) Prod. Liab. Litig., No. 6:11-MD-2299, 2014 WL 4364832, at *1 (W.D. La. Sept. 2, 2014) (emphasis, numbering, and formatting added).

143. The district court also noted:

> At trial, the Plaintiffs presented evidence that the Defendants were aware of the risk of death by way of bladder cancer associated with Actos® use and that t***hey chose to conceal and obfuscate those risks in order to sell more product and to increase their profit***. . . . Defendants were aware of the potential danger of bladder cancer presented by Actos® use as early as 1999, 2002, and 2004, and have pointed to evidence that both of the Defendants engaged in ***concerted, sustained, deliberate, and coordinated efforts to conceal, withhold and obfuscate such information and knowledge from the public, the FDA, the medical community*** . . . . Beyond merely failing to warn, Plaintiffs presented evidence Takeda and Lilly ***obfuscated and worked to conceal relevant information from the scientific and medical communities, the FDA, the public*** . . . concerning an association between Actos® use and an increased risk of bladder cancer-again, ***all in the pursuit of profits***. Plaintiffs presented evidence this ***intentional concealment of known health risks reflects a deliberate and conscious decision to wholly disregard the well-being of Mr. Allen and those within the target population like Mr. Allen, i.e., diabetics*** for whom Actos® would likely be contraindicated. Plaintiffs presented evidence that this ***intentional conduct reflects the Defendants' deliberate choice, in effect, to sacrifice an identifiable group of individuals in pursuit of profit***, when a simple warning could have eliminated the risk of possible death for that identifiable group.

Id., at *39-41.

144. Plaintiff incorporates by reference the MDL Court order at *In re Actos (Pioglitazone) Prod. Liab. Litig.*, No. 6:11-MD-2299, 2014 WL 4364832 (W.D. La. Sept. 2, 2014).

145. In another order by the MDL Court, the court went into a detailed "reprehensibility" analysis to determine whether Takeda and Lilly's conduct was sufficiently reprehensible to warrant punitive damages. *See In re Actos (Pioglitazone) Prod. Liab. Litig. ("Actos II")*, No. 6:11-MD-2299, 2014 WL 5461859 (W.D. La. Oct. 27, 2014).

146. In that order the MDL Court noted:

> The evidence supports that from the beginning of their commercial alliance, Takeda and Lilly were aware of the possibility that Actos® posed an increased risk of bladder cancer. Despite having information that drove other competitors with Actos®, and potential competitors to Actos®, out of the relevant diabetes driven market, during the relevant time period Takeda and Lilly chose to move forward and acted to avoid full disclosure of that and other relevant information to the FDA; to refuse to include adequate warnings on the label, or to otherwise provide adequate warnings to physicians; to carefully avoid creating or acknowledging any evidence that might draw attention to the bladder cancer risk; and to claim, at all times, and in all relevant venues, that there was insufficient information to permit the conclusion that Actos® could cause or pose an increased risk of bladder cancer. In selling Actos® to millions of people throughout the world without providing adequate warnings of the increased risk of bladder cancer, Takeda and Lilly deprived physicians of the information necessary to perform their function in our medical care system and in so doing effectively wrote off an identifiable and significant, and perhaps, the most vulnerable segment of the population of diabetics—those whose blood glucose levels were out of the control and who for

> other medical reasons were vulnerable to an increased risk of bladder cancer—and consistently disregarded, denied, obfuscated and concealed that risk. ***The facts support that Takeda's and Lilly's willingness to callously allow their customers to ignorantly increase their risk of dying prematurely or significantly negatively impacting their health and well-being as a result of taking Actos®, by way of bladder cancer, is particularly reprehensible*** in light of the fact that (as Takeda repeatedly acknowledged in then documents), diabetics fighting for control over a very dangerous disease had viable alternatives available to them which did not carry the increased risk of bladder cancer in the form of Takeda's and Lilly's competitor, Avandia, or injectable insulin, and evidence presented supports Plaintiffs' arguments that Takeda and Lilly acted out of desire for and of profit.

Id., at *24.

147. Indeed, the MDL Court went on to explain that (1) "the harm caused by the Defendants' actions was physical, not 'merely economic,' and extraordinarily serious"; (2) "their conduct showed a total disregard of and for the general welfare and the health care system—more than 10 million, as of the time of the trial, had taken Actos® without full knowledge of its risks—. . . when Takeda and Lilly refused to warn their users and/or their physicians of the known risk of developing bladder cancer associated with the use of Actos®"; (3) "the target population of Takeda's and Lilly's conduct was a particularly fragile, and vulnerable one"; (4) "the Defendants engaged in a concerted, long-term effort to conceal and obfuscate information about the true risk of bladder cancer"; (5) "Defendants' campaign to conceal the complete truth . . . included both withholding information and, also, creating misleading evidence through the use of compensated experts, compensated physicians, and a careful, concerted, and orchestrated manipulation and attempt to control all the information to be provided to the public, medical community, and regulatory agencies in the United States and abroad"; (6) "the Defendants, time and again, placed a higher priority on protecting their brand, their sales, and their income, than on protecting the vulnerable population who were helping to create those very profits"; (7) "both Defendants engaged in activities designed to conceal that information and those risks known only to them, from regulators, the medical community, the public at large"; (8) "[t]he regulatory process involved in the area of pharmaceuticals during the relevant time period relied heavily, if not exclusively, upon the good faith compliance of regulated drug companies"; (9) "Takeda's and Lilly's conduct impacted not only Mr. Allen and Mrs. Allen, but, also, the general public and its health care system[.]" *Id.*, at *25-27.

148. Finally, the MDL Court summarized:

> As pharmaceutical companies, the Defendants were aware they were obligated to provide adequate warnings about their product . . . The jury verdict establishes that the jury found that this obligation was violated by both Takeda and Lilly. Implicit in the jury's finding is the conclusion that both Takeda and Lilly failed to provide an adequate warning of all potential dangers and, also, that in so doing both engaged in willful and wanton conduct. Inherent in that finding, and supported by the evidence presented at trial, is the finding ***Takeda and Lilly engaged in grievously reprehensible behavior, with their knowing and deliberate efforts to avoid providing adequate information and warnings to prescribing doctors and unsuspecting patients, and their willingness to allow those particularly vulnerable patients to, therefore, run a higher risk of bladder cancer and death, with no advance warning, all in the blind pursuit of profit***. The record is replete with evidence to support a finding of callous disregard of and for Mr. Allen, as well as general human life and well-being, and a deliberate effort to conceal, obfuscate, and manipulate known relevant information from the very agency charged with regulating drug companies for the benefit of and in order to protect the public safety and welfare, and from the physicians who relied upon such information in order to perform their role within the health care system and the public trust. The evidence supports a conclusion Takeda and Lilly, in the name of and in pursuit of profits reaching into the billions of dollars, chose to hide the information which would have allowed the FDA and the physicians to play their vital role to assess the risk and benefit of drugs, here Actos®, in order to regulate and selectively prescribe in the manner contemplated by the system of health care, and in so doing Defendants knowingly condemned an identifiable, and significant segment of the population to increased risk of death and/or grave bodily harm.

Id., at *27.

149. Plaintiff incorporates by reference the MDL Court order at *In re Actos (Pioglitazone) Prod. Liab. Litig. ("Actos II")*, No. 6:11-MD-2299, 2014 WL 5461859 (W.D. La. Oct. 27, 2014).

DEFENDANTS' MOTIVES AND CAUSATION OF DAMAGE

150. Defendants' motive in creating and operating the fraudulent scheme described herein was to obtain additional revenues from the marketing and sale of Actos.

151. The fraudulent scheme was designed to, and did, cause Plaintiff and members of the Classes to pay for Actos prescriptions that they otherwise would not have absent the fraud. Moreover, as alleged above, the Defendants' deceptive conduct caused an overvaluation of the drugs, which resulted in monies being lost by the member (through co-pays) and by the third-party payor (through reimbursement). In the absence of Defendants' improper conduct, Plaintiff and members of the Classes would not have paid for as many or any Actos prescriptions. Additionally, because of the Defendants' misconduct as alleged throughout this complaint, the Defendants were able to charge significantly higher prices for Actos prescriptions by concealing the bladder cancer risks. Those higher prices, based on fraudulent disclosure of the bladder cancer risks, were passed onto and paid

for by the Plaintiff and Class members. Had the Defendants not engaged in their misconduct, Plaintiff would have spent less money on Actos prescriptions.

CLASS ACTION ALLEGATIONS

152. Plaintiff brings this suit on his own behalf and on behalf of all persons similarly situated. Such a representative action is necessary to prevent and remedy the deceptive, unlawful and unfair practices alleged herein.

153. As discussed at length in this Complaint, Defendants and the Enterprise participants have engaged in a comprehensive program to mislead consumers, prescribing healthcare professionals, and third-party payors about Actos' risk of causing bladder cancer. Defendants' conduct has been directed at consumers, third-party payors, and prescribers in all states in a uniform manner—using the same misleading and deceptive drug labels and same misleading and deceptive promotional practices. Class action law has long recognized that, when a company engages in misconduct that has uniformly harmed a large number of claimants such as Plaintiff and the putative class members they seek to represent, class resolution can be an effective tool to redress the harm. This Complaint is, thus, well suited for class-wide resolution.

154. Defendants' deceptive and misleading marketing scheme increased the number of prescriptions of Actos written and filled since the drug was approved in 1999. Defendants knew that revealing the truth about the risks of Actos causing bladder cancer would significantly reduce the number of prescriptions written for the drug. Because Defendants withheld material information and made deliberately misleading statements about the risk of Actos and baldder cancer, consumers, prescribers, and third-party payors did not have the knowledge necessary to make informed decisions regarding Actos prescriptions. Plaintiff and members of the classes were unaware of Defendants' scheme, paid and/or reimbursed for payments for these prescriptions without knowing the true risk. Although more effective, safer, and less expensive alternatives are available, Defendants' promotion and marketing of Actos' safety and effectiveness has been highly successful, resulting in Defendants receiving billions of dollars in profits, representing ill-gotten gains to which Defendants are not entitled.

155. Plaintiff and similarly-situated class members bear the ultimate responsibility for

paying, co-paying, and/or reimbursing payments for Actos prescriptions.

156. The proposed class is defined as:

All consumers and entities in the State of California, who paid or incurred costs for the drug Actos, for purposes other than resale, between 1999, i.e., when the drug was approved, and the present. Excluded from the California Consumer Class are employees of Takeda, including its officers or directors, the Court to which this case is assigned, and those consumers who are presently seeking a personal injury claim arising out of their use of Actos.

157. The Class is properly brought and should be maintained as a class action under Rule 23(a), satisfying the class action prerequisites of numerosity, commonality, typicality, adequacy because:

a. Numerosity: Hundreds of thousands of Actos prescriptions were written and/or purchased in California.

b. Commonality: Questions of law and fact are common to all members of the Class. Specifically, Defendants' misconduct was directed at all members of the Class and their respective prescribing healthcare professionals. Thus, all members of the Class have common questions of fact and law, i.e., whether Defendants engaged in a comprehensive program and conspiracy of deceptive marketing in promoting the use of Actos without warning of its serious risk of causing bladder cancer.

c. Typicality: Plaintiff's claims are typical of the claims of the members of the putative Classes because their claims arise from the same course of conduct by Defendants, i.e., false, misleading, and deceptive marketing and a racketeering conspiracy. Plaintiff paid for Actos, without knowledge that the drug significantly increases the risk of bladder cancer. His claims are typical of the Classes.

d. Adequacy: Plaintiff will fairly and adequately represent and protect the interests of the Classes since his interests in vindicating his own claims are shared with all members. In addition, Plaintiff is represented by attorneys who are competent and experienced in both consumer protection and class action litigation.

158. The Class is properly brought and should be maintained as a class action under Rule

23(b) because a class action in this context is superior. Pursuant to Rule 23(b)(3), common issues of law and fact predominate over any questions affecting only individual members of the putative Classes. Defendants deliberately engaged in a widespread program to mislead consumers and prescribing healthcare professionals about Actos' risks of bladder cancer. Proceeding with these class actions is superior to other methods for fair and efficient adjudication of this controversy because, inter alia,:

a. Individual joinder of the individual members is wholly impracticable;

b. The economic damages suffered by the individual members may be relatively modest compared to the expense and burden of individual litigation;

c. The court system would benefit from a class action because individual litigation would overload court dockets and magnify the expense to all parties; and

COUNT I: VIOLATIONS OF CAL. CIV. CODE §§ 1750, *et seq.*
Violation of California Consumer Legal Remedies Act

159. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

160. California's Consumer Legal Remedies Act, Cal. Civ. Code §§ 1750, *et seq.* makes it unlawful to engage in unfair methods of competition and unfair or deceptive acts or practices intended to result, or which result, in the sale or lease of goods or services to any consumer.

161. Plaintiff and the Class were, and continue to be, at all times material to the Complaint, "consumers" and "persons" as defined by the Cal. Civ. Code § 1761. Plaintiff purchased and/or paid for Actos for personal and/or family and/or household use during the relevant time period. Each payment for Actos by Plaintiff and the proposed Class members constitutes a "transaction" within the meaning of Civil Code sections 1761(e) and 1770.

162. Defendants had a duty to disclose the risks and efficacy of their prescription drug.

163. As alleged throughout this Complaint, Defendants deliberately engaged in deceptive and unlawful marketing in violation of Civ. Code § 1770(a) by failing to disclose material information to the Plaintiff and the Class about Actos' risk of causing bladder cancer. Defendants failed to adequately disclose material information about Actos' safety and, in so doing, deprived consumers of an ability to make an informed decision.

164. Defendants' concealment and deceptive practices, in violation of the CLRA, were designed to induce Plaintiff and the proposed Class members to purchase Actos.

165. Specifically, Defendants violated the following proscribed practices pursuant to Cal. Civ. Code § 1770(a) with the purpose of inducing Plaintiff and the Class to purchase and ingest Actos:

a. § 1770(a)(2): Defendants represented to Plaintiff and the Class, by not making a mention of the risk, that Actos did not cause bladder cancer in humans. This gave a false certification of Actos' safety. Moreover, omitting material information concerning to the actual results of those clinical trials and adverse events that showed Actos increased the risk of bladder cancer was a false certification of the drug's safety profile.

b. § 1770(a)(7): Defendants misrepresented to Plaintiff and the Class that Actos was of a particular standard, quality, or grade., i.e., not a significant risk to causing bladder cancer. In truth, Actos did pose a significant risk of causing bladder cancer in contravention of the representations on the drug label. Takeda's failure to properly disclose the bladder cancer risk constituted a misrepresentation of a material standard, quality, or grade.

166. Defendants' concealment of the bladder cancer risk, as describer throughout this Complaint, was a material omission that consumers and prescribing healthcare professionals should have known about prior to purchasing or prescribing Actos for the treatment of Type 2 diabetes.

167. Each of the representations Defendants made regarding Actos were material, consistent, uniform, and widespread. Defendants specifically targeted Plaintiff and the proposed Class members and their doctors, and third-party payors. In fact, Defendants intended for their representations to induce Plaintiff and the proposed Class members.

168. Defendants' deceptive marketing scheme concerning Actos violates the CLRA because, *inter alia*, Defendants:

a. knowingly concealed, suppressed, or omitted material information regarding Actos' safety and effectiveness from Plaintiff and the proposed Class members, and to their financial detriment;

b. knowingly misrepresented the safety and efficacy of Actos from Plaintiff and the

proposed Class' members to their financial detriment; and

c. marketed, promoted, and advertised Actos as a safe and effective drug when the purported safety and effectiveness is deceptive and unfounded.

169. Plaintiff and the Class lost money as a result of Defendants' deceptive and unlawful marketing practices pursuant to Cal. Civ. Code § 1770(a), through the purchase of Actos that was illegally advertised and marketed in violation of Cal. Civ. Code § 1770(a). Defendants' concealment, suppression, omissions, misrepresentations, deceptions, and/or unconscionable practices caused Plaintiff and the proposed Class' members to suffer ascertainable losses in the amount of the monies they overpaid for Actos, and/or paid for more Actos prescriptions, without knowing the drug's efficacy or lack thereof for which it is marketed, promoted, or advertised.

170. Plaintiff and the proposed Class' members would not have overpaid and/or paid for more Actos prescriptions had they known of Defendants' deceptive and misleading marketing scheme, or the extent of said scheme.

171. Pursuant to Cal. Civ. Code § 1782, Defendants have been put on notice of its fraudulent conduct by the originally filed complaint and, pursuant to the statute, have not taken any action to correct the harm caused by their CLRA violations. Thus, pursuant to Cal. Civ. Code § 1782(d), this amended complaint seeks all equitable and legal remedies available under the CLRA.

172. Plaintiff and the class are entitled to an award of attorneys' fees and costs against defendants pursuant to the provisions of Civil Code section 1780(d).

173. Wherefore, Plaintiff, on behalf of himself and all others similarly situated, demand judgment as set forth hereinafter.

COUNT II: VIOLATIONS OF CAL. BUS. & PROF. CODE §§ 17200, *et seq.*
Violations of the California Unfair Competition Law

174. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

175. California's Unfair Competition Law ("UCL"), Cal. Bus. & Prof. Code §§ 17200, et seq., protects both consumers and competitors by promoting fair competition in commercial markets for goods and services. California's Unfair Competition Law is interpreted broadly and provides a cause of action for any unlawful, unfair, or fraudulent business act or practice. Any unlawful, unfair,

or fraudulent business practice that causes injury to consumers falls within the ambit of California's Unfair Competition Law.

176. Defendants engaged in substantial advertising and marketing of Actos within the State of California.

177. Because of Defendants' unlawful, fraudulent, and unfair business practices, Plaintiff and the Class were misled into purchasing and using Actos.

I. Unlawful Business Practices

178. As set forth in the preceding paragraphs, Defendants have engaged in the unlawful business practice of misleading Plaintiff and the Class regarding Actos' true safety. Defendants' deceptive and unlawful marketing practices have violated numerous California laws, including, inter alia: Cal. Civ. Code §§ 1709, et seq. (fraudulent deceit); Cal. Civ. Code §§ 1571, et seq. (fraud); Cal. U. Com. Code §§ 2313-15 (breach of express and implied warranty); Cal. Bus. & Prof. Code §§ 17500, et seq. (false advertising and marketing); and Cal. Civ. Code §§ 1750, et seq. (violations of California's Consumer Legal Remedies Act).

179. As a result of Defendants' unlawful business practices, Plaintiff and the Class purchased Actos without sufficient information regarding a material aspect of the drug. Specifically, Plaintiff and the Class were misled into believing that Actos was safer than it actually is. Plaintiff and the Class reasonably relied upon Defendants' misrepresentations regarding Actos in deciding whether to purchase and use the drug.

180. In addition to engaging in unlawful marketing practices, Defendants also engaged in an unlawful method of competition. Defendants deliberately misled Plaintiff and the Class about Actos' safety profile and thereby artificially inflated Actos' competitive advantage over other less expensive alternatives, i.e., metformin, sulfonylureas, and Avandia. Because Plaintiff and the Class (as well as the FDA and the medical community) were unaware of Actos' bladder cancer risk, they were more likely to purchase Actos as opposed to a competing OAD. The market was unable to correctly valuate Actos and, therefore, Defendants gained an unlawful competitive advantage over competing drugs. This unlawful method of competition resulted in Plaintiff and the Class paying a substantially higher price and/or pay for additional prescriptions for Actos.

II. Fraudulent Business Practices

181. As set forth in the preceding paragraphs, Defendants engaged in the fraudulent business practice of misleading Plaintiff and the Class regarding Actos' safety.

182. A business act or practice is "fraudulent" under California's Unfair Competition Law if it actually deceives or is likely to deceive members of the consuming public.

183. As set forth in the preceding paragraphs, Defendants engaged in a comprehensive scheme to mislead the FDA, consumers, prescribers, and third-party payors regarding Actos' risk of causing bladder cancer. Because of Defendants' fraudulent business practices, Plaintiff and the Class were misled about Actos's safety and, accordingly, purchased Actos without knowing a material aspect of the drug.

III. Unfair Business Practices

184. As set forth in the preceding paragraphs, Defendants engaged in an unfair business practice of misleading Plaintiff and the Class regarding Actos' risk of causing bladder cancer.

185. A business practice is unfair when it offends an established public policy or when the practice is immoral, unethical, oppressive, unscrupulous, or substantially injurious to consumers.

186. Defendants' deceptive and unlawful marketing practices offend public policy and are fundamentally immoral, unethical, oppressive, unscrupulous, or substantially injurious to consumers. Defendants misled consumers about Actos' safety, which subjected hundreds of thousands of consumers to an unknown risk of bladder cancer. This conduct offends any notion of public policy and is truly unethical.

187. The harm to Plaintiff and the Class caused by Defendants' unfair business practices outweighs any countervailing benefits to consumers or competition, and could not reasonably have been known and avoided by consumers. Furthermore, Defendants' unfair business practices cannot be excused for any business justification, motive, or rationale in light of the severity of Defendants' misconduct and the harm caused to Plaintiff and the Class.

188. Additionally, Defendants' business practices are unlawful in that Defendants' conduct constitutes breaches of common law including unjust enrichment and violations of FDA Regulations which prohibit marketing of materials that are not fair and balanced. *See* 21 C.F.R. 99.103; 21 C.F.R.

§201.5; 21 C.F.R §99.205; 21 C.F.R. §201.6(a); 21 U.S.C. §360aaa; 360aaa-1; 502(a) and 201(n) of the FDCA (21 U.S.C. 352(a) and 321(n)).

189. Plaintiff has standing to pursue this claim because the Plaintiff has suffered injury in fact and loss of money and/or property as a result of the wrongful conduct alleged herein.

190. As a direct and proximate result of Defendants' unfair and deceptive business practices, Plaintiff and the members of the class have suffered injury in fact.

191. Plaintiff and the proposed Class would not have paid for Actos but for Defendants' scheme described herein.

192. As a direct and proximate result of Defendants' unfair and deceptive business practices, Defendants have been unjustly enriched and should be ordered to make restitution to Plaintiff and members of the class pursuant to Business and Professions Code Sections 17203 and 17204, including restitution of all monies paid to Defendants for Actos, disgorgement of all profits accruing to Defendants because of Defendants' unlawful, unfair and fraudulent business practices and appropriate declaratory relief as described herein.

193. Wherefore, Plaintiff on behalf of himself and all others similarly situated, demand judgment as set forth hereinafter.

COUNT III: VIOLATIONS OF CAL. BUS. & PROF. CODE §§ 17500, *ET SEQ.*
Violation of the California False Advertising Law

194. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

195. Plaintiff and the Class bring a cause of action against Defendants pursuant to Cal. Bus. & Prof. Code §§ 17500, et seq. ("California's False Advertising Law").

196. The purpose of California's False Advertising Law is to protect consumers from false or misleading advertising and promotions. California's False Advertising Law prohibits the false or deceptive advertising of products to consumers in any form of media, when the company placing the advertisement knows, or should have known, that the advertisement would be likely to mislead consumers about a material aspect of a product.

197. Defendants have used advertising on its packaging and through various media outlets to sell and market Actos directly to consumers, prescribers, and third-party payors. The

advertisements and labeling are deceptive, untrue, or misleading during the class period, pursuant to California's False Advertising Law because they misstate Actos' bladder cancer risk.

198. In making and disseminating the statements alleged herein, Defendants knew that the statements were untrue or misleading, and that it acted in violation of California's False Advertising Law.

199. As a result of Takeda's deceptive and unlawful marketing of Actos, Defendants improperly and illegally obtained money from Plaintiff and the Class.

200. Accordingly, pursuant to California's False Advertising Law, specifically Cal. Bus. & Prof. Code § 17535, Plaintiff and the Class seek the disgorging of Defendants' ill-gotten gains and/or award full restitution of all monies wrongfully acquired by means of its false advertising in California, and for such other relief as set forth below.

COUNT IV: UNJUST ENRICHMENT

201. Plaintiff incorporates by reference all preceding paragraphs as if fully set forth herein.

202. Defendants have been and continue to be enriched by their deceptive acts and omissions alleged herein.

203. These deceptive acts and omissions allow Defendants to gain millions of dollars in profits in the State of California that would not have been gained but for Defendants' deceptive acts and omissions.

204. Plaintiff and the proposed Class members and those similarly situated paid Defendants an amount that exceeds the value of the product identified herein as a result of Defendants' acts and omissions.

205. Plaintiff and the Class members suffered damages due to the Defendants' acts and omissions as alleged herein.

206. Defendants have and continue to be unjustly enriched as a result of their deceptive acts and omissions.

207. Defendants lack any legal justification for engaging in a course of deceptive acts and omissions as alleged herein at Plaintiff and the Class expense.

208. No other remedy at law can adequately compensate Plaintiff and the Class members

for the damages occasioned by Defendants' conscious choice to engage in a course of deceptive acts and omissions.

PRAYER FOR RELIEF

209. WHEREFORE, Plaintiff, individually and on behalf of the various classes described herein, pray for the following relief:

a. Find that this action satisfies the prerequisites for maintenance of a class action pursuant to Federal Rules of Evidence 23(a) and (b)(3), and certify the Class;

b. Designate Plaintiff as a representative for the Class and Plaintiff's undersigned counsel as Class Counsel;

c. Issue a judgment against the Defendants that:

i. Grants Plaintiff and the Class a refund of all moneys acquired by the Defendants by means of its deceptive and unlawful marketing of Actos;

ii. Grants Plaintiff and the Class an award of restitution and/or disgorgement of Takeda's profits from its deceptive and unlawful marketing of Actos;

iii. Grants Plaintiff and the Class any actual or compensatory damages for the payments or reimbursements made for Actos in such amount to be determined at trial and as provided by applicable law;

iv. Grants Plaintiff and the Class exemplary, treble, and punitive damages sufficient to punish and deter Defendants and others from future deceptive and unlawful marketing practices;

v. Grants Plaintiff and the Class pre-judgment and post-judgment interest;

vi. Grants Plaintiff and the Class reasonable attorneys' fees and costs of suit; and

vii. Grants Plaintiff and the Class such other and further relief as the Court deems just and proper under the circumstances.

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DEMAND FOR JURY TRIAL

210. Plaintiff and the Class hereby demands a trial by jury on all issues for which a right to jury trial exists.

DATED: May 8, 2018

Respectfully submitted,

BAUM, HEDLUND, ARISTEI & GOLDMAN, PC

/s/ R. Brent Wisner

Pedram Esfandiary (SBN 312569)
R. Brent Wisner (SBN 276023)
Michael L. Baum (SBN 119511)
12100 Wilshire Blvd., Suite 950
Los Angeles, CA 90025
Phone: (310) 207-3233

JS 44 (Rev. 08/16)

CIVIL COVER SHEET

The JS 44 civil cover sheet and the information contained herein neither replace nor supplement the filing and service of pleadings or other papers as required by law, except as provided by local rules of court. This form, approved by the Judicial Conference of the United States in September 1974, is required for the use of the Clerk of Court for the purpose of initiating the civil docket sheet. *(SEE INSTRUCTIONS ON NEXT PAGE OF THIS FORM.)*

I. (a) PLAINTIFFS

Frank Fernandez, a California consumer, individually and on behalf of all others similarly situated,

(b) County of Residence of First Listed Plaintiff San Joaquin County
(EXCEPT IN U.S. PLAINTIFF CASES)

(c) Attorneys *(Firm Name, Address, and Telephone Number)*
Michael L. Baum, Esq. , R. Brent Wisner, Esq.
BAUM, HEDLUND, ARISTEI, & GOLDMAN, P.C., 12100 Wilshire Blvd., Suite 950, Los Angeles, CA 90025, (310) 207-3233

DEFENDANTS

TAKEDA PHARMACEUTICALS AMERICA, Inc., an Illinois corporation; and ELI LILLY & COMPANY, an Indiana corporation; and DOES 1-100, inclusive

County of Residence of First Listed Defendant Lake County, Illinois
(IN U.S. PLAINTIFF CASES ONLY)

NOTE: IN LAND CONDEMNATION CASES, USE THE LOCATION OF THE TRACT OF LAND INVOLVED.

Attorneys *(If Known)*

II. BASIS OF JURISDICTION *(Place an "X" in One Box Only)*

- ☐ 1 U.S. Government Plaintiff
- ☐ 3 Federal Question *(U.S. Government Not a Party)*
- ☐ 2 U.S. Government Defendant
- ☒ 4 Diversity *(Indicate Citizenship of Parties in Item III)*

III. CITIZENSHIP OF PRINCIPAL PARTIES *(Place an "X" in One Box for Plaintiff and One Box for Defendant)*

(For Diversity Cases Only)

	PTF	DEF		PTF	DEF
Citizen of This State	☒ 1	☐ 1	Incorporated *or* Principal Place of Business In This State	☐ 4	☐ 4
Citizen of Another State	☐ 2	☐ 2	Incorporated *and* Principal Place of Business In Another State	☐ 5	☒ 5
Citizen or Subject of a Foreign Country	☐ 3	☐ 3	Foreign Nation	☐ 6	☐ 6

IV. NATURE OF SUIT *(Place an "X" in One Box Only)*

Click here for: Nature of Suit Code Descriptions.

CONTRACT
- ☐ 110 Insurance
- ☐ 120 Marine
- ☐ 130 Miller Act
- ☐ 140 Negotiable Instrument
- ☐ 150 Recovery of Overpayment & Enforcement of Judgment
- ☐ 151 Medicare Act
- ☐ 152 Recovery of Defaulted Student Loans (Excludes Veterans)
- ☐ 153 Recovery of Overpayment of Veteran's Benefits
- ☐ 160 Stockholders' Suits
- ☐ 190 Other Contract
- ☐ 195 Contract Product Liability
- ☐ 196 Franchise

REAL PROPERTY
- ☐ 210 Land Condemnation
- ☐ 220 Foreclosure
- ☐ 230 Rent Lease & Ejectment
- ☐ 240 Torts to Land
- ☐ 245 Tort Product Liability
- ☐ 290 All Other Real Property

TORTS

PERSONAL INJURY
- ☐ 310 Airplane
- ☐ 315 Airplane Product Liability
- ☐ 320 Assault, Libel & Slander
- ☐ 330 Federal Employers' Liability
- ☐ 340 Marine
- ☐ 345 Marine Product Liability
- ☐ 350 Motor Vehicle
- ☐ 355 Motor Vehicle Product Liability
- ☐ 360 Other Personal Injury
- ☐ 362 Personal Injury - Medical Malpractice

PERSONAL INJURY
- ☐ 365 Personal Injury - Product Liability
- ☐ 367 Health Care/ Pharmaceutical Personal Injury Product Liability
- ☐ 368 Asbestos Personal Injury Product Liability

PERSONAL PROPERTY
- ☒ 370 Other Fraud
- ☐ 371 Truth in Lending
- ☐ 380 Other Personal Property Damage
- ☐ 385 Property Damage Product Liability

CIVIL RIGHTS
- ☐ 440 Other Civil Rights
- ☐ 441 Voting
- ☐ 442 Employment
- ☐ 443 Housing/ Accommodations
- ☐ 445 Amer. w/Disabilities - Employment
- ☐ 446 Amer. w/Disabilities - Other
- ☐ 448 Education

PRISONER PETITIONS

Habeas Corpus:
- ☐ 463 Alien Detainee
- ☐ 510 Motions to Vacate Sentence
- ☐ 530 General
- ☐ 535 Death Penalty

Other:
- ☐ 540 Mandamus & Other
- ☐ 550 Civil Rights
- ☐ 555 Prison Condition
- ☐ 560 Civil Detainee - Conditions of Confinement

FORFEITURE/PENALTY
- ☐ 625 Drug Related Seizure of Property 21 USC 881
- ☐ 690 Other

LABOR
- ☐ 710 Fair Labor Standards Act
- ☐ 720 Labor/Management Relations
- ☐ 740 Railway Labor Act
- ☐ 751 Family and Medical Leave Act
- ☐ 790 Other Labor Litigation
- ☐ 791 Employee Retirement Income Security Act

IMMIGRATION
- ☐ 462 Naturalization Application
- ☐ 465 Other Immigration Actions

BANKRUPTCY
- ☐ 422 Appeal 28 USC 158
- ☐ 423 Withdrawal 28 USC 157

PROPERTY RIGHTS
- ☐ 820 Copyrights
- ☐ 830 Patent
- ☐ 840 Trademark

SOCIAL SECURITY
- ☐ 861 HIA (1395ff)
- ☐ 862 Black Lung (923)
- ☐ 863 DIWC/DIWW (405(g))
- ☐ 864 SSID Title XVI
- ☐ 865 RSI (405(g))

FEDERAL TAX SUITS
- ☐ 870 Taxes (U.S. Plaintiff or Defendant)
- ☐ 871 IRS—Third Party 26 USC 7609

OTHER STATUTES
- ☐ 375 False Claims Act
- ☐ 376 Qui Tam (31 USC 3729(a))
- ☐ 400 State Reapportionment
- ☐ 410 Antitrust
- ☐ 430 Banks and Banking
- ☐ 450 Commerce
- ☐ 460 Deportation
- ☐ 470 Racketeer Influenced and Corrupt Organizations
- ☐ 480 Consumer Credit
- ☐ 490 Cable/Sat TV
- ☐ 850 Securities/Commodities/ Exchange
- ☐ 890 Other Statutory Actions
- ☐ 891 Agricultural Acts
- ☐ 893 Environmental Matters
- ☐ 895 Freedom of Information Act
- ☐ 896 Arbitration
- ☐ 899 Administrative Procedure Act/Review or Appeal of Agency Decision
- ☐ 950 Constitutionality of State Statutes

V. ORIGIN *(Place an "X" in One Box Only)*

☒ 1 Original Proceeding ☐ 2 Removed from State Court ☐ 3 Remanded from Appellate Court ☐ 4 Reinstated or Reopened ☐ 5 Transferred from Another District *(specify)* ☐ 6 Multidistrict Litigation - Transfer ☐ 8 Multidistrict Litigation - Direct File

VI. CAUSE OF ACTION

Cite the U.S. Civil Statute under which you are filing ***(Do not cite jurisdictional statutes unless diversity)***:
Cal. Civ. Code §§ 1750, et seq; Cal. Bus. & Prof. Code §§ 17200, et seq; Cal. Bus. & Prof. Code §§ 17500, et seq

Brief description of cause:
Violations of CA Consumer Protection Laws

VII. REQUESTED IN COMPLAINT:

☒ CHECK IF THIS IS A **CLASS ACTION** UNDER RULE 23, F.R.Cv.P.

DEMAND $

CHECK YES only if demanded in complaint:
JURY DEMAND: ☒ Yes ☐ No

VIII. RELATED CASE(S) IF ANY

(See instructions):

JUDGE _____ DOCKET NUMBER _____

DATE
05/08/2018

SIGNATURE OF ATTORNEY OF RECORD
/s/ R. Brent Wisner

FOR OFFICE USE ONLY

RECEIPT # _____ AMOUNT _____ APPLYING IFP _____ JUDGE _____ MAG. JUDGE _____