UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF LOUISIANA

IN RE: ACTOS PRODUCTS LIABILITY LITIGATION **PAINTERS AND ALLIED TRADES DISTRICT COUNCIL 82 HEALTH CARE FUND, third-party healthcare payor fund, ANNIE M. SNYDER, a California consumer, RICKEY D. ROSE, a Missouri consumer, JOHN CARDARELLI, a New Jersey consumer, MARLYON K. BUCKNER, a Florida consumer, on behalf of themselves and all others similarly situated,** **Plaintiffs,** **v.** **TAKEDA PHARMACEUTICAL COMPANY LIMITED, a Japanese Corporation,** **TAKEDA PHARMACEUTICALS USA, INC., an Illinois corporation (fka TAKEDA PHARMACEUTICALS NORTH AMERICA, INC.),** **ELI LILLY AND COMPANY, an Indiana corporation,** **Defendants.**	**MDL No. 6:11-md-2299** **JUDGE DOHERTY** **MAGISTRATE JUDGE HANNA** **Civil Action No.: _____** **COMPLAINT** **CLASS ACTION** **JURY TRIAL DEMANDED**

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INTRODUCTION

1. This case is about Defendants Takeda Pharmaceutical Company Limited, Takeda Pharmaceuticals North America, Inc. (collectively "Takeda"), and Eli Lilly and Company ("Lilly") leading an illegal and fraudulent enterprise to sell the diabetes medication Actos (generically known as pioglitazone), while concealing the bladder cancer risks associated with Actos from consumers, prescribers, third-party payors, and the United States Food and Drug Administration ("FDA"). 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 prescription for Actos that would never have been issued had the truth been known. This class action, brought on behalf of consumers and third-party payors nationwide and in California, Missouri, New Jersey, and Florida, seeks to recover damages for the consumers and third-party payors who were tricked into purchasing and/or reimbursing Actos prescriptions.

PARTIES

2. Plaintiff PAINTERS AND ALLIED TRADES DISTRICT COUNCIL 82 HEALTH CARE FUND ("Painters Fund") is a health and welfare benefit fund with its domicile and principal place of business in the State of Minnesota. Plaintiffs Painter Fund is involved in the business of providing health benefits for covered members and their families. Plaintiff Painters Fund is a multiemployer employee welfare benefit plan within the meaning of the Employment Retirement Income Security Act, 29 U.S.C. § 1002(1) and § 1002(37).

3. Plaintiff ANNIE M. SNYDER is, and was at all material times herein, a citizen, resident, and domicile of the State of California, San Bernardino County.

4. Plaintiff RICKEY D. ROSE is, and was at all material times herein, a citizen,

resident, and domicile of the State of Missouri, Clay County.

5. Plaintiff JOHN CARDARELLI is, and was at all material times herein, a citizen, resident, and domicile of the State of New Jersey, Mercer County.

6. Plaintiff MARLYON K. BUCKNER is, and was at all material times herein, a citizen, resident, and domicile of the State of Florida, Duval County.

7. Defendant TAKEDA PHARMACEUTICAL COMPANY LIMITED ("TCP") is a Japanese corporation having a principal place of business at 1-1, Doshomachi 4-chome, Chuoku, Osaka, Japan. TPC is the largest pharmaceutical company in Japan.[1] According to its 2009 annual reports, TPC's annual sales exceeded $15 billion.

8. 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.

9. All Defendants related to TAKEDA PHARMACEUTICAL COMPANY LIMITED will be, collectively, referred to as "Takeda" for the purposes of this Complaint.

10. ELI LILLY AND COMPANY (hereinafter "Lilly") is an Indiana corporation with its principal place of business located at Lilly Corporate Center, Indianapolis, Indiana 46285.

11. Takeda and Lilly are referred to as "Defendants" for the purposes of this Complaint.

JURISDICTION AND VENUE

12. This Court has subject-matter jurisdiction pursuant to 28 U.S.C. § 1332(d)(2).

[1] Upon information and belief, Defendant TAKEDA PHARMACEUTICAL COMPANY LIMITED is the parent/holding company and exercising dominion and control over Defendants TAKEDA PHARMACEUTICALS U.S.A., INC., f/k/a TAKEDA PHARMACEUTICALS NORTH AMERICA, INC., TAKEDA PHAR MACEUTICALS INTERNATIONAL, INC., and TAKEDA DEVELOPMENT CENTER AMERICAS, INC., f/k/a TAKEDA GLOBAL RESEARCH & DEVELOPMENT CENTER INC., TAKEDA CALIFORNIA, INC., f/k/a TAKEDA SAN DIEGO, INC., and TAKEDA PHARMACEUTICALS, LLC.

Members of the proposed classes are citizens of a different state than Takeda. Furthermore, the aggregate amount in controversy exceeds $5,000,000.

13. 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.

14. 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 Central District for the District of California.

FACTUAL BACKGROUND

15. 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.

16. 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.

17. 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 resitance, a peroxisome proliferator-

activated receptor ("PPAR ").

18. 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 sectionsand 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

19. 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.

20. 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.*

21. 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.

22. 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."

23. 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.

[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.

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

25. 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.

26. 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.

27. 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.

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

28. 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.

29. 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.

30. 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.

31. 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.

32. 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.

33. 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.

34. 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. This was done using electronic wires and U.S. mail. In addition, Dr. Cohen's white paper was developed using communications that occurred over wires and through U.S. mail. Takeda and Dr. Cohen coordinated their conduct using electronic wires and U.S. Mail and relied on one another to effectuate their deception about the risks of bladder cancer associated with Actos.

35. The conspiracy and collaboration to develop a sham explanation of the rat and mice bladder cancer data was done in furtherance of an enterprise 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 was rewarded with a "plausible" explanation of the alarming bladder cancer data.

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

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

37. 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.

38. 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."

39. 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.

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

40. 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.

41. 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.

42. 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."

43. 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."

44. 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]

45. 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.

[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 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.

- 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.

46. 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.

47. 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 discussing the PPAR mechanism with the FDA. Takeda, 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.

48. Takeda communicated its strategy to Lilly via electronic wires. 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. On information and belief, 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 enterprise 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.

49. 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.

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

50. 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.

51. 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."

52. 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.

53. 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…"

54. 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."

55. 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.

56. 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 ongoing enterprise, 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.

57. 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.

58. 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.

VI. The PROactive and KPNC Data Raise Additional Alarm about Actos and Bladder Cancer

59. 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. 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*, Lancet, 266:1279-1286 (2005) (the "Dormandy paper").

60. 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.

61. 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[.]

62. 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[.]

63. 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."

64. 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 in furtherance of the enterprise. 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.

65. 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 using electronic wires and U.S. Mail and relied on one another to effectuate a misunderstanding about the PROactive trial within the medical community. This was done to facilitate the overall enterprise of concealing any association of Actos with bladder cancer.

66. 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).

67. 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.

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

68. 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.

69. 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.

70. 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.

71. 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.

72. In September 2006, Lilly ended its partnership with Takeda.

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

73. 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.

74. 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.

75. 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.

76. 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, 34:1369-1371 (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.

77. 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).

78. 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.

79. 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.

80. 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.

81. 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.

82. 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.

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

IX. Spoliation: Takeda and the Enterprise Destroy Documents and Help Conceal Fraudulent Conduct

84. 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.

85. 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.

(emphasis in original). This litigation hold was distributed across the entire company.

86. 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.

87. 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.

88. 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.

89. 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.

90. 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.

91. 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.

92. 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 besubject 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.

93. 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.

THE ENTERPRISE

94. Defendants and the co-conspirators conducted or actively participated in conduct of an enterprise through a pattern of racketeering activity in violation of 18 U.S.C. § 1962(c). Additionally, and in the alternative, Defendants and the co-conspirators, through an agreement to commit two or more predicate acts, conspired to conduct or participate in the conduct of an enterprise through a pattern of racketeering activity in violation of 18 U.S.C. § 1962(d). The actions of Defendants and the co-conspirators (otherwise known as "Enterprise participants") were in furtherance of the enterprise and in violation of 18 U.S.C. § 1962(d).

95. The Enterprise participants include Takeda, Lilly, Dr. Samuel Cohen, Dr. Charles Burant, Dr. John Dormandy, and numerous other experts and scientists enlisted to further the enterprise's purpose. The enterprise is an association-in-fact between the Enterprise participants. The enterprise is distinct from, albeit primarily conducted by, Defendants, through the aforementioned co-conspirators/Enterprise participants, and had an ongoing existence.

96. The purpose of the enterprise was to conceal from patients, prescribers, third-party payors, and the FDA the risk that Actos posed in causing bladder cancer, so that the Enterprise participants could profit in some manner. Takeda and Lilly profited from the increased sales caused by consumers, prescribers, third-party payors, and the FDA being deceived about Actos' bladder cancer risks. Dr. Cohen, Dr. Burant, and Dr. Dormandy, among others, profited from various consulting fees and obtained prestige in the medical community as "experts" on the expanding and profitable OAD marketplace. Although Takeda was the leader of the enterprise, each Enterprise participant contributed to the purpose of concealing bladder cancer risks, whether it was through misleading the FDA, concocting sham medical explanations for them, or simply misrepresenting the data in the published literature. Each Enterprise participant actively contributed and advised the other Enterprise participants as part of the overall enterprise.

97. As alleged in detail above, Defendants and the enterprise used marketing plans and tactics, and Defendants and the co-conspirators executed these strategies to increase sales of

Actos throughout the United States, all while deceiving the FDA, patients, prescribers, and third-party payors about Actos and bladder cancer.

PLAINTIFF-SPECIFIC ALLEGATIONS

I. Plaintiff Painters Fund and Allied Trades District Council 82 Health Care Fund (Third Party Payor)

98. Plaintiff Painters and Allied Trades District Council 82 Health Care Fund ("Painters Fund") is a health and welfare benefit fund involved in the business of providing health benefits for covered members and their families. Plaintiff Painters Fund is governed by approximately eight (8) board members, who oversee the fund on behalf of the members.

99. As a third-party payor, Plaintiff Painters Fund reimburses claims for various drugs, including Actos, submitted by those pharmacies and healthcare providers covered by the plan.

100. Plaintiff Painters Fund relies on each member to submit claims for prescription medications that are medically reasonable and necessary for treatment. Since that decision is made by the prescribing physician and the patient, Plaintiff Painters Fund relies on those members and their prescribers to make informed decisions about which drugs will be prescribed and, in turn, submitted to Plaintiff Painters Fund for reimbursement.

101. The Enterprise participants, including Defendants, as described throughout this Complaint, misrepresented the risks of bladder cancer to consumers, prescribers, third-party payors, and the FDA. This deception caused members of the Plaintiff Painters Fund's plan to cause to be submitted claims for reimbursement that were neither medically necessary nor reasonable, and which would never have been prescribed absent the fraud. The enterprise's conduct, caused the Plaintiff to make payments for Actos that, absent the fraud, would never have occurred.

102. In addition, the Enterprise participants, as described throughout this Complaint, deprived each consumer and their prescriber of material information they needed to make an informed decision about whether to purchase Actos to treat Type 2 diabetes. This deception directly caused an overvaluation of the drugs, which resulted in monies being lost by the member

(through co-pays) and by Plaintiff Painters Fund (through reimbursement).

103. Plaintiff Painters Fund has the authority to determine which drugs are covered under its plan, although, Plaintiff Painters Fund entrusts the administration of claims and formulary determinations to Prime Therapeutics, LLC, based in Eagan, Minnesota.

104. In the year prior to the FDA's September 2010 alert indicating that the FDA would be investigating an Actos-bladder cancer association, Plaintiff Painters Fund was reimbursing approximately 460 Actos claims per month. Immediately after the FDA's 2010 alert, claims for Actos dropped 20%, to approximately 364 Actos claims per month. Then, after the FDA issued an official bladder cancer warning in June 2011, claims plummeted by *another* 50%, to approximately 188 claims per month. Thus, claims for Actos before there was any public awareness of a possible link between Actos and bladder cancer (pre-September 2010) and the number of claims after the bladder cancer warning was made (June 2011) dropped by over 60%, from 460 to 188 claims per month. Indeed, every month after the official bladder cancer warning issued, claims for Actos dropped. In the last month before Actos went generic, in August 2012, Plaintiff Painter Fund only received 91 claims for Actos. Thus, over 80% of all claims submitted to Plaintiff Painter Fund would never have been submitted if the truth about bladder cancer had been known. This drop in sales confirms the results of the physician survey conducted by Takeda in 2003 (*see* ¶ 55), which showed that 75% of physicians would not prescribe an OAD with bladder cancer risks.

105. As a result of Takeda's fraudulent concealment of the bladder cancer risk, Plaintiff Painters Fund reimbursed a significant number of claims for Actos that would never have been but for the fraud.

II. Plaintiff Annie M. Snyder

106. On or about October 16, 2009, Plaintiff Snyder was prescribed a 15 mg daily dose of Actos by her physician to treat Type 2 diabetes. Prior to starting the prescription, Plaintiff Snyder read and relied upon the Actos label.

107. Plaintiff Snyder continued to use Actos until, on or about August 8, 2011.

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

109. Plaintiff Snyder never saw the June 15, 2011 FDA bladder cancer warning and was never told about the FDA's warning by her prescriber.

110. In total, between October 16, 2009 and August 8, 2011, Plaintiff Snyder spent approximately $105 of her own money to purchase Actos. Plaintiff Snyder is unaware of how much was spent by her third-party payor insurance company.

111. During the period in which Plaintiff Snyder was purchasing and ingesting Actos, Plaintiff Snyder 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.

112. During the period Plaintiff Snyder was purchasing and ingesting Actos, Plaintiff Snyder was never informed, nor did Plaintiff Snyder read or see, any information about Actos' bladder cancer risks. Likewise, Takeda and the Enterprise participants did not convey any of Actos' bladder cancer risks to Plaintiff Snyder, her prescriber, the FDA (until 2010), or the public in general.

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

114. Between October 16, 2009 and August 8, 2011, Plaintiff Snyder had no reason to believe she was the victim of consumer protection violations, RICO violations, or that her purchase of Actos was made without required information.

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

116. Upon information and belief, Plaintiff Snyder's prescriber was never informed about Actos' association with bladder cancer while she was purchasing and ingesting the drug between October 16, 2009 and August 8, 2011.

117. 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.

118. Had Plaintiff Snyder known that Actos increased the risk of causing bladder cancer, she would never have purchased and ingested the drug, and Plaintiff Snyder would never have submitted claims for reimbursement to her third-party payor insurance company.

III. Plaintiff Rickey D. Rose

119. On or about May 23, 2007, Plaintiff Rose was prescribed a 45 mg daily dose of Actos by his physician to treat Type 2 diabetes. Prior to purchasing and ingesting Actos, Plaintiff Rose was never informed about Actos' association with bladder cancer.

120. Plaintiff Rose continued to use Actos until on or about November 26, 2011.

121. Plaintiff Rose did not see the September 15, 2010 FDA alert and was never told about the FDA's investigation by his prescriber.

122. Plaintiff Rose did not see the June 15, 2011 FDA bladder cancer warning and was never told about the FDA's warning by his prescriber.

123. In November 2011, Plaintiff Rose learned that Actos posed bladder cancer risks on the television. Once he saw this warning, he ceased purchasing and ingesting Actos.

124. In total, between May 23, 2007 and November 26, 2011, Plaintiff Rose spent approximately $475 of his own money to purchase Actos. Plaintiff Rose's third-party payor insurance company paid approximately $7,876 in reimbursing Plaintiff Rose's Actos prescriptions.

125. During the period in which Plaintiff Rose was purchasing and ingesting Actos, Plaintiff Rose 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.

126. During the period Plaintiff Rose was purchasing and ingesting Actos, Plaintiff Rose was never informed, nor did Plaintiff Rose read or see, any information about Actos' bladder cancer risks. Likewise, Takeda and the Enterprise participants did not convey any of

Actos' bladder cancer risks to Plaintiff Rose, his prescriber, the FDA (until 2010), or the public in general.

127. Between May 23, 2007 and November 26, 2011, Plaintiff Rose did not see any media, journal articles, press releases, websites, letters, or statements concerning Actos and its association with bladder cancer.

128. Between May 23, 2007 and November 26, 2011, Plaintiff Rose had no reason to believe he was the victim of consumer protection violations, RICO violations, or that his purchase of Actos was made without required information.

129. Between May 23, 2007 and November 26, 2011, Plaintiff Rose did not know that he had been deprived of material information or that the Actos label and advertising was misleading in any particular.

130. Upon information and belief, Plaintiff Rose's prescriber was never informed about Actos' association with bladder cancer while he was purchasing and ingesting the drug between May 23, 2007 and November 26, 2011.

131. 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.

132. Had Plaintiff Rose known that Actos increased the risk of causing bladder cancer, he would never have purchased and ingested the drug, and Plaintiff Rose would never have submitted claims for reimbursement to his third-party payor insurance company.

IV. Plaintiff John Cardarelli

133. On or about August 8, 2006, Plaintiff Cardarelli was prescribed a 45 mg daily dose of Actos by his physician to treat Type 2 diabetes. Prior to purchasing and ingesting Actos, Plaintiff Cardarelli was never informed about Actos' association with bladder cancer.

134. Plaintiff Cardarelli continued to use Actos until on or about October 17, 2009.

135. Plaintiff Cardarelli did not see the September 15, 2010 FDA alert and was never told about the FDA's investigation by his prescriber.

136. Plaintiff Cardarelli did not see the June 15, 2011 FDA bladder cancer warning and was never told about the FDA's warning by his prescriber.

137. In late 2011, Plaintiff Cardarelli learned that Actos posed bladder cancer risks on the television. Once he saw this warning, he reached out to attorneys.

138. In total, between August 8, 2006 and October 17, 2009, Plaintiff Cardarelli spent approximately $350 of his own money to purchase Actos. Plaintiff Cardarelli's third-party payor insurance company paid approximately $10,238 in reimbursing Plaintiff Cardarelli's Actos prescriptions.

139. During the period in which Plaintiff Cardarelli was purchasing and ingesting Actos, Plaintiff Cardarelli 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.

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

141. Between August 8, 2006 and October 17, 2009, Plaintiff Cardarelli did not see any media, journal articles, press releases, websites, letters, or statements concerning Actos and its association with bladder cancer.

142. Between August 8, 2006 and October 17, 2009, Plaintiff Cardarelli had no reason to believe he was the victim of consumer protection violations, RICO violations, or that his purchase of Actos was made without required information.

143. Between August 8, 2006 and October 17, 2009, Plaintiff Cardarelli did not know that he had been deprived of material information or that the Actos label and advertising was misleading in any particular.

144. Upon information and belief, Plaintiff Cardarelli's prescriber was never informed about Actos' association with bladder cancer while he was purchasing and ingesting the drug

between August 8, 2006 and October 17, 2009.

145. 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.

146. Had Plaintiff Cardarelli known that Actos increased the risk of causing bladder cancer, he would never have purchased and ingested the drug, and Plaintiff Cardarelli would never have submitted claims for reimbursement to his third-party payor insurance company.

V. Plaintiff Marlyon K. Buckner

147. On or about May 6, 2005, Plaintiff Buckner was prescribed a 30 mg daily dose of Actos by her physician to treat Type 2 diabetes. Prior to purchasing and ingesting Actos, Plaintiff Buckner was never informed about Actos' association with bladder cancer.

148. Plaintiff Buckner continued to use Actos until on or about November 2012.

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

150. Plaintiff Buckner never saw the June 15, 2011 FDA bladder cancer warning and was never told about the FDA's warning by her prescriber.

151. In late 2012, Plaintiff Buckner learned that Actos posed bladder cancer risks on the television. Once she saw this warning, she reached out to attorneys and immediately ceased purchasing and ingesting Actos.

152. In total, between May 6, 2005 and November 2012, Plaintiff Buckner spent over $100 of her own money to purchase Actos. Plaintiff Buckner is unaware of how much was spent by her third-party payor insurance company.

153. During the period in which Plaintiff Buckner was purchasing and ingesting Actos, Plaintiff Buckner 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.

154. During the period Plaintiff Buckner was purchasing and ingesting Actos, Plaintiff Buckner was never informed, nor did Plaintiff Buckner read or see, any information about Actos'

bladder cancer risks. Likewise, Takeda and the Enterprise participants did not convey any of Actos' bladder cancer risks to Plaintiff Buckner, her prescriber, the FDA (until 2010), or the public in general.

155. Between May 6, 2005 and November 2012, Plaintiff Buckner did not see any media, journal articles, press releases, websites, letters, or statements concerning Actos and its association with bladder cancer.

156. Between May 6, 2005 and November 2012, Plaintiff Buckner had no reason to believe she was the victim of consumer protection violations, RICO violations, or that her purchase of Actos was made without required information.

157. Between May 6, 2005 and November 2012, Plaintiff Buckner did not know that she had been deprived of material information or that the Actos label and advertising was misleading in any particular.

158. Upon information and belief, Plaintiff Buckner's prescriber was never informed about Actos' association with bladder cancer while she was purchasing and ingesting the drug between May 6, 2005 and November 2012.

159. 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.

160. Had Plaintiff Buckner known that Actos' increased the risk of causing bladder cancer, she would never have purchased and ingested the drug, and Plaintiff Buckner would never have submitted claims for reimbursement to her third-party payor insurance company.

TAKEDA'S MOTIVES AND CAUSATION OF DAMAGE

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

162. The fraudulent scheme and enterprise was designed to, and did, cause Plaintiffs and members of the Classes to pay for Actos prescriptions that they otherwise would not have

absent the fraud. Moreover, as alleged above, the enterprise's 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' and the enterprise's improper conduct, Plaintiffs and members of the Classes would not have paid for as many or any Actos prescriptions.

USE OF THE MAILS AND WIRES

163. As alleged throughout this Complaint, Defendants and the Enterprise participants used thousands of mail and interstate wire communications in order to organize, create, develop, monitor and manage their fraudulent scheme. The scheme involved national marketing and sales plans and programs, and encompassed physicians and third-party payors across the country.

164. Defendants and the Enterprise participants' use of the mails and wires to perpetrate their fraudulent enterprise involved thousands of communications between 1999 and 2012.

165. The mails and wires were used to transmit fraudulent marketing materials about Actos being a selective PPAR gamma agonist, such materials being sent to doctors across the country via email and mail.

166. The mails and wires were used to transmit communications, including financial payments, between Takeda, Takeda executives and employees, Lilly, the enlisted scientists, and all those who helped conceal the bladder cancer risks. Many of those transmissions are identified above.

167. The mails and wires were used to transmit fraudulent communications to the FDA about Actos and bladder cancer, all in violation of federal law, with the express purpose of obtaining FDA approval and concealing bladder cancer risks. These communications occurred during telephone conferences with FDA personnel and in hundreds of NDA and sNDA submissions to the FDA. There were also hundreds of fraudulent communications sent to FDA through the wires as emails and facsimiles.

168. The mails and wires were used to transmit fraudulent adverse event reports to the

FDA concerning bladder cancer events and their association with Actos. Takeda personnel, in accord with the enterprise, deliberately altered adverse event reports in violation of federal law and transmitted these fraudulent adverse event reports over the wires.

169. The mails and wires were used to transmit and communications designed to transport misbranded drugs, i.e., contained misleading drug labels vis-à-vis bladder cancer risks, in violation of 21 U.S.C. § 352. These communications were designed to facilitate the transportation and selling of misbranded drugs in violation of federal law.

170. The mails and wires were used to transmit communications designed to coordinate the unlawful destruction of evidence and documents concerning the enterprise and Takeda and the Enterprise participants' fraudulent conduct. These communications were deliberately designed to conceal the alleged wrongdoing in this Compalint.

CLASS ALLEGATIONS

171. This matter is brought as a class action pursuant to Federal Rule of Civil Procedure 23, on behalf of consumers and third-party payors throughout the United States.

172. 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 Plaintiffs 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.

173. 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. Plaintiffs 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.

174. Plaintiffs and similarly-situated class members bear the ultimate responsibility for paying, co-paying, and/or reimbursing payments for Actos prescriptions.

175. Patients, prescribers, pharmacy benefit management systems ("PBMs"), pharmacy and therapeutic committee members, and third-party payors relied on Defendants' and the Enterprise's misrepresentations of Actos' safety profile. Prescribers relied on Defendants' and the Enterprise's misrepresentations of Actos' safety in prescribing the drug for their patients. Patients relied on Defendants' and the Enterprise's misrepresentations of Actos' safety in purchasing the drug. PBMs and pharmacy and therapeutic committees relied on Defendants' and the Enterprise's misrepresentations of Actos' safety when approving and/or placing Actos on formularies. Third-party payors relied on the Defendants' and the Enterprise's misrepresentations of Actos' safety in reimbursing and/or paying for prescriptions of Actos for their members.

176. The proposed National RICO Class is defined as:

> All consumers and entities in the United States of America and its territories, 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 RICO 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.

177. The proposed California Consumer 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.

178. The proposed Missouri Consumer Class is defined as:

All consumers and entities in the State of Missouri, 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 Missouri 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.

179. The proposed Massachusetts Consumer Class is defined as:

All consumers and entities in the Commonwealth of Massachusetts, 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 Massachusetts 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.

180. The proposed New Jersey Consumer Class is defined as:

All consumers and entities in the State of New Jersey, 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 New Jersey 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.

181. The proposed Florida Consumer Class is defined as:

All consumers and entities in the State of Florida, 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 Florida 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.

182. The National RICO Class and California, Missouri, Massachusetts, New Jersey, and Florida Consumer Classes will be referred to as the Classes collectively.

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

a. Numerosity: Millions of Actos prescriptions were written and/or purchased in the United States. Similarly, many hundreds of thousands of prescriptions were

written and/or purchased in California, Missouri, Massachusetts, New Jersey, and Florida.

b. Commonality: Questions of law and fact are common to all members of the Classes. Specifically, Defendants' misconduct was directed at all members of the Classes, their members, and their respective prescribing healthcare professionals. Thus, all members of the Classes 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: Plaintiffs' 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. All Plaintiffs paid for Actos, without knowledge that the drug significantly increases the risk of bladder cancer. Their claims are typical of the Classes.

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

184. The Classes are properly brought and should be maintained as class actions 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

d. The class action device presents far fewer management difficulties and provides the benefit of comprehensive supervision by a single court with economies of scale.

COUNT I: VIOLATIONS OF 18 U.S.C. § 1962(c)—RICO

185. Plaintiffs incorporate by reference all preceding paragraphs as if fully set forth herein.

186. Defendants are "persons" within the meaning of 18 U.S.C. § 1961(3) who conducted the affairs of the enterprise through the pattern of racketeering activity detailed throughout this Complaint in violation of 18 U.S.C. § 1962(c).

187. The enterprise is an association-in-fact within the meaning of 18 U.S.C. § 1961(4), consisting of Defendants and the Enterprise participants and other as yet unknown consultants, marketing firms and distribution agents employed by Takeda and Lilly to promote Actos. All entities are persons within the meaning of 18 U.S.C. § 1961(3) and acted to enable Defendants to fraudulently market and sell Actos.

188. The enterprise functioned as an ongoing organization and continuing unit. The enterprise was created and/or used as a tool to effectuate a pattern of racketeering activity. Each of these Enterprise participants, including Defendants, is a "person" distinct from the enterprise.

189. Defendants, in concert with the other Enterprise participants, created and maintained systematic links for a common purpose, i.e., to aid in marketing Actos while concealing the drug's risk of causing bladder cancer. Each of the Enterprise participants received substantial revenue from the scheme. Such revenue was exponentially greater than it would have been if Actos was marketed appropriately and the true risks of Actos had been

disclosed. All Enterprise participants were aware of Takeda's involvement with the enterprise in promoting Actos, and aided that purposes through conducting illegal and fraudulent acts, i.e., wire fraud. Accordingly, each portion of the enterprise benefited from the existence of the other parts.

190. Defendants established the enterprise to accomplish goals that were instrumental to its scheme to market Actos as a having a superior safety profile than it actually possessed. Specifically, Takeda and Lilly conspired to promote Actos has having a superior safety profile any its competitors. It accomplished that end by concealing Actos' bladder cancer risks through misleading the FDA and the medical community.

191. The enterprise engaged in and affected interstate commerce, because, *inter alia*, it marketed, promoted, sold, purchased, or provided Actos to millions of individuals throughout the United States. The Actos transported in interstate commerce, however, was misbranded, in violation of 21 U.S.C. § 352 because the label contained misleading representations about Actos' association with bladder cancer.

192. Defendants exerted control over the enterprise and have participated in the operation or management of the affairs of the enterprise in coordination with the various Enterprise participants.

193. As detailed above, Defendants' pattern of racketeering activity includes acts indictable as mail fraud under 18 U.S.C. § 1341 and wire fraud under 18 U.S.C. § 1343. Defendants' fraudulent scheme consisted of, *inter alia*: (a) deliberately misrepresenting the bladder cancer risks of Actos to the FDA, consumers, prescribers, and third-party payoers; (b) providing or publishing or causing to have provided or published presentations and materials containing false and/or misleading information upon which physicians, Plaintiffs, and members of the Classes relied upon when choosing to prescribe, pay, or reimburse for Actos; (c) actively concealing, and causing others to conceal, information about the true safety risks of Actos; (d) intentionally misrepresenting and concealing Defendants and the Enterprise participants' role in the enterprise through the destruction of documents in violation of federal law and court orders;

and (e) misrepresenting and concealing the ties between the Defendants and other Enterprise participants.

194. In implementing their fraudulent scheme, Defendants were acutely aware that Plaintiffs and members of the Classes depend on the honesty and integrity of Defendants in representing the safety risks of Actos. It is impractical and unduly expensive for the members of the Classes to perform their own clinical trials or assemble all known medical evidence relating to Actos and bladder cancer. The members of the Classes also rely on federal law obligating Defendants and the Enterprise participants to provide fair and balanced information about their drug products and reasonably presume that when such marketing of Actos was conducted, it complied with federal law.

195. As detailed above, Defendants' pattern of racketeering activity also includes acts indictable under 18 U.S.C. § 1952 (use of interstate facilities to conduct unlawful activity).

196. At all times during the fraudulent scheme, Defendants and the Enterprise participants had a legal and ethical obligation of candor to, and honest dealing with, public and private payors, physicians, and the medical community.

197. The conduct of the enterprise described above constitutes "racketeering activity" within the meaning of 18 U.S.C. § 1961(1). Defendants chose to conduct is activities and transactions in such a manner that constitutes a "pattern of racketeering activity" within the meaning of 18 U.S.C. § 1961(5).

198. The above described racketeering activities amounted to a common course of conduct intended to deceive and harm Plaintiffs and the members of the Classes. Indeed, Plaintiffs were the primary victims of Defendants' fraudulent conduct. Defendants knew that, if they misrepresented Actos' risk of causing bladder cancer, physicians and patients would prescribe and purchase the drugs and Plaintiffs would foot the bill. Defendants knew that many if not most of all prescriptions for Actos would never have been made if the true risks of bladder cancer were known. Defendants' racketeering activities were part of ongoing business pursuits and constituted a continuing threat to the property of Plaintiffs and the Classes.

199. Defendants' motive in creating and operating the fraudulent scheme and the enterprise was to obtain additional revenues from the marketing and sale of Actos. The fraudulent scheme was designed to, and did, cause Plaintiffs and the Classes to pay for Actos prescriptions without being fully informed about the drug's true risks.

200. Plaintiffs and members of the Classes have been injured in their property by reason of these violations in that Plaintiffs and members of the Classes paid hundreds of millions of dollars for Actos that they would not have paid had Defendants not engaged in this pattern of racketeering activity.

201. The injuries to Plaintiffs and members of the Classes were directly and proximately caused by Takeda's racketeering activity. In the absence of Defendants' improper conduct, Plaintiffs and the Classes would not have been deprived of material information about Actos safety, thereby causing economic harm in the form of reimbursed payments and out-of-pocket expenditures.

202. Above all, the Enterprise participants, including Defendants, misled and deceived the FDA, physicians, the consumers who rely on their professional judgment, and third-party payors including Plaintiffs and the members of the Classes, about the risk of Actos causing bladder cancer. Defendants deprived prescribing healthcare providers of this material information which is needed to evaluate the risks and benefits of prescribing Actos and third-party payors of this same information which is utilized in determining whether the third-party payor will pay for such prescriptions. Consequently, Defendants with the help of the enterprise have led to Plaintiffs and the class members to pay for overvalued drugs and/or prescriptions that would never have been made absent the fraud.

203. Because of these violations of 18 U.S.C. § 1962(c), Defendants are liable to Plaintiffs and the Classes for three times the damages sustained, plus the costs of this suit, including reasonable attorneys' fees.

204. By reason of the foregoing, and as a direct and proximate result of Defendants' fraudulent misrepresentations, Plaintiffs and members of the proposed Classes have suffered

damages. Plaintiffs and the members of the Classes are entitled to compensatory damages, equitable and declaratory relief, punitive damages, costs and reasonable attorneys' fees.

COUNT II: VIOLATION OF 18 U.S.C. § 1962(d)—RICO CONSPIRACY

205. Plaintiffs incorporate by reference all preceding paragraphs as if fully set forth herein.

206. Section 1962(d) provides that it "shall be unlawful for any person to conspire to violate any of the provisions of subsection (a), (b) or (c) of this section."

207. Defendants and the other co-conspirators violated § 1962(d) by conspiring to violate 18 U.S.C. § 1962(c). The object of this conspiracy was to conduct or participate in, directly or indirectly, the conduct of the affairs of the enterprise described previously through a pattern of racketeering activity. Defendants conspired with the Enterprise participants to promote Actos while concleaing Actos' risk of causing bladder cancer.

208. Defendants and the Enterprise participants, as co-conspirators, engaged in numerous overt and predicate fraudulent racketeering acts in furtherance of the conspiracy, including material misrepresentations and omissions designed to defraud Plaintiffs and the Classes of money.

209. The nature of the co-conspirators' acts, material misrepresentations, and omissions in furtherance of the conspiracy gives rise to an inference that they not only agreed to the objective of an 18 U.S.C. § 1962(d) violation by conspiring to violate 18 U.S.C. § 1962(c), but they were aware that their ongoing fraudulent and extortionate acts have been and are part of an overall pattern of racketeering activity.

210. As a direct and proximate result of Defendants' and the Enterprise's overt acts and predicate acts in furtherance of violating 18 U.S.C. § 1962(d) by conspiring to violate 18 U.S.C. § 1962(c), as described throughout this Complaint, Plaintiffs and the members of the Classes have been injured in their business or property as set forth more fully above.

211. Defendants sought to and have engaged in the commission of and continue to commit overt acts, including the following unlawful racketeering predicate acts discussed

extensively herein, including but not limited to:

a. Multiple instances of mail and wire fraud violations of 18 U.S.C. §§ 1341 and 1342;

b. Multiple instances of mail fraud violations of 18 U.S.C. §§ 1341 and 1346;

c. Multiple instances of wire fraud violations of 18 U.S.C. §§ 1341 and 1346; and

d. Multiple instances of unlawful activity in violation of 18 U.S.C. § 1952.

212. Because of these violations of 18 U.S.C. § 1962(d), Defendants are liable to Plaintiffs and the members of the Classes for three times the damages Plaintiffs and the Class members have sustained, plus the cost of this suit, including reasonable attorney's fees.

213. By reason of the foregoing, and as a direct and proximate result of Defendants' fraudulent misrepresentations, Plaintiffs and the Classes have suffered damages. Plaintiffs and the Classes are entitled to compensatory damages, equitable and declaratory relief, punitive damages, costs and reasonable attorneys' fees.

COUNT III: VIOLATIONS OF CAL. CIV. CODE §§ 1750, *et seq.*

214. Plaintiffs incorporate by reference all preceding paragraphs as if fully set forth herein.

215. 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.

216. Plaintiff Snyder and the California Consumer 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 Snyder and California Consumer Class purchased and/or paid for Actos for personal and/or family and/or household use during the relevant time period.

217. 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 Snyder and California Consumer 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.

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

a. § 1770(a)(2): Defendants represented to Plaintiff and the California Consumer 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 Snyder and the California Consumer 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.

219. 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.

220. Plaintiff Snyder and the California Consumer 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).

221. Pursuant to Cal. Civ. Code § 1782, Defendants have been put on notice of its fraudulent conduct by previously filed cases. Thus, no pre-suit notice is required at this time.

COUNT IV: VIOLATIONS OF CAL. BUS. & PROF. CODE §§ 17200, *et seq*.

222. Plaintiffs incorporate by reference all preceding paragraphs as if fully set forth herein.

223. 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.

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

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

I. Unlawful Business Practices

226. As set forth in the preceding paragraphs, Defendants has engaged in the unlawful business practice of misleading Plaintiff Snyder and the California Consumer 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).

227. As a result of Defendants' unlawful business practices, Plaintiff Snyder and the California Consumer Class purchased Actos without sufficient information regarding a material aspect of the drug. Specifically, Plaintiff Snyder and the California Consumer Class were misled into believing that Actos was safer than it actually is. Plaintiff Snyder and the California

Consumer Class reasonably relied upon Defendants' misrepresentations regarding Actos in deciding whether to purchase and use the drug.

228. In addition to engaging in unlawful marketing practices, Defendants also engaged in an unlawful method of competition. Defendants deliberately misled Plaintiff Snyder and the California Consumer 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 Snyder and the California Consumer 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 Snyder and the California Consumer Class paying a substantially higher price and/or making addition prescriptions for Actos.

II. Fraudulent Business Practices

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

230. 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.

231. 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 Snyder and the California Consumer Class were misled about Actos's safety and, accordingly, purchased Actos without knowing a material aspect of the drug.

III. Unfair Business Practices

232. As set forth in the preceding paragraphs, Defendants engaged in an unfair business practice of misleading Plaintiff Snyder and the California Consumer Class regarding

Actos' risk of causing bladder cancer.

233. 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.

234. 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.

235. The harm to Plaintiff Snyder and the California Consumer 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 Snyder and the California Consumer Class.

COUNT V: VIOLATIONS OF CAL. BUS. & PROF. CODE §§ 17500, *et seq.*

236. Plaintiffs incorporate by reference all preceding paragraphs as if fully set forth herein.

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

238. 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.

239. Defendants has 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.

240. 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.

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

242. Accordingly, pursuant to California's False Advertising Law, specifically Cal. Bus. & Prof. Code § 17535, Plaintiff and the California Consumer 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 VI: VIOLATIONS OF MO. REV. STAT. §§ 407.010, *et seq.*

243. Plaintiffs incorporate by reference all preceding paragraphs as if fully set forth herein.

244. This Count is brought pursuant to the Missouri Merchandising Practices Act, § 407.010, *et seq.*

245. At all times relevant hereto, Plaintiff Rose and the Missouri Consumer Class were persons within the meaning of Mo. Rev. Stat. § 407.010(5).

246. At all times relevant hereto, Plaintiff Rose and Missouri Consumer Class were purchasers within the meaning of Mo. Rev. Stat. § 407.025.1.

247. At all times material hereto, Defendants conducted trade or commerce within the meaning of Mo. Rev. Stat. § 407.010(7).

248. The Missouri Merchandising Practices Act, § 407.020.1, provides in pertinent part:

> The act, use or employment by any person of any deception, fraud, false pretense, false promise, misrepresentation, unfair practice or the concealment, suppression, or omission of any material fact in connection with the sale or advertisement of any merchandise in trade or commerce … in or from the state of Missouri, is declared to be an unlawful practice. … Any act, use or employment declared

unlawful by this subsection violates this subsection whether committed before, during or after the sale, advertisement or solicitation.

249. Defendants engaged in misrepresentations, unlawful schemes, and courses of conduct that induced Plaintiff Rose and members of the various classes to purchase Actos through one or more unfair and/or deceptive acts and/or practices alleged in this Complaint.

250. Defendants' failure to disclose and deliberate conduct in concealing Actos' bladder cancer risks were material to Plaintiff Rose and the Missouri Consumer Class, in that they concerned facts that would have been important to a reasonable consumer in making a decision whether to purchase Actos.

251. Defendants' misrepresentations and deceptive acts and omissions were likely to mislead reasonable consumers acting reasonably under the circumstances such as Plaintiff Rose.

252. Defendants' conduct as alleged herein was unfair in that: (1) it offended public policy; (2) it was immoral, unethical, oppressive, or unscrupulous; and/or (3) it caused substantial economic injury to consumers, namely Plaintiff Rose and members of Missouri Consumer Class.

253. Defendants' unfair and/or deceptive acts and/or practices alleged in the preceding paragraphs occurred in connection with Takeda's conduct of trade and commerce in Missouri for promoting and selling Actos.

254. Defendants' unfair and/or deceptive acts and/or practices violate the Missouri Merchandising Practices Act., Mo. Rev. Stat. § 407.020.1.

255. As a direct and proximate result of Defendants' violations of the Missouri Merchandising Practices Act, Mo. Rev. Stat. § 407.020.1, Plaintiff Rose and members of the Missouri Consumer Class sustained a loss, i.e., damages in an amount to be proven at trial.

COUNT VII: VIOLATIONS OF N.J.S.A. §§ 56:8-1, *et seq.*

256. Plaintiffs incorporate by reference all preceding paragraphs as if fully set forth herein.

257. At all times relevant to this action, there was in full force and effect the New Jersey Consumer Fraud Act ("NJCFA"), N.J.S.A. 56:8-1 *et seq.*, which was enacted and

designed to protect consumers against unfair, deceptive, or fraudulent business practices.

258. N.J.S.A. 56:8-2 provides:

> The act, use or employment by any person of any unconscionable commercial practice, deception, fraud, false pretense, false promise, misrepresentation, or the knowing, concealment, suppression, or omission of any material fact . . . Whether or not any person has in fact been misled, deceived or damaged thereby, is declared to be an unlawful practice.

259. At all relevant times, Plaintiff Cardarelli and the New Jersey Consumer Class, and Defendants were "persons" within the meaning of N.J.S.A. § 56:8-1.

260. Actos, which was manufactured, marketed, and sold by Defendants, are merchandise within the meaning of the NJCFA, and Plaintiff Cardarelli and the New Jersey Consumer Class are consumers within the meaning of the NJCFA and entitled to the statutory remedies made available therein.

261. Defendants violated the NJCFA by representing that Actos had characteristics, uses, and benefits which it did not have and advertising the drug as having characteristics, uses, and benefits which Defendants knows Actos does not have, i.e., that Actos does not cause bladder cancer.

262. Defendants violated the NJCFA by advertising and promoting Actos in the manner described above, when they knew, or should have known, that those representations and advertisements were false and/or misleading.

263. Defendants intended that Plaintiff Cardarelli and the New Jersey Consumer Class would rely on its deception by purchasing the Actos, unaware of the material facts described above, i.e., that the drug posed a significant risk of bladder cancer. This conduct constitutes consumer fraud within the meaning of the NJCFA.

264. Defendants' conduct, as alleged herein, constitutes unlawful, unfair, and/or deceptive business practices within the meaning of the NJCFA.

265. Defendants' conduct was malicious, fraudulent, and wanton, and provides misleading information Actos is safer than it actually is, when in fact scientific evidence clearly indicates that Actos significantly increases the risk of bladder cancer.

266. Defendants' conduct has proximately caused damage to Plaintiff Cardarelli and the New Jersey Consumer Class, in the form of, *inter alia*, monies spent to purchase Actos they otherwise would not have, in an amount to be proven at trial.

267. Had Defendants disclosed all material information regarding Actos in its advertising, marketing, and/or labeling, Plaintiffs Cardarelli and the New Jersey Consumer Class would not have purchased the Actos, would have paid less, or would have placed a significantly different value on the product than what they received.

268. As a result of Defendants' violations of the foregoing state consumer protection statute, Plaintiff Cardarelli and the New Jersey Consumer Class are entitled to compensatory damages, double damages, treble damages, statutory damages, punitive or exemplary damages, and/or restitution.

COUNT VIII: VIOLATIONS OF FLA. STAT. §§ 501.201, *et seq.*

269. Plaintiffs incorporate by reference all preceding paragraphs as if fully set forth herein.

270. This cause of action is brought pursuant to the Florida Deceptive and Unfair Trade Practices Act, Fla. Stat. §§ 501.201, *et seq*. ("FDUTPA"). The purpose of the FDUTPA is to "protect the consuming public . . . from those who engage in unfair methods of competition, or unconscionable, deceptive, or unfair acts or practices in the conduct of any trade or commerce." Fla. Stat. § 501.202(2).

271. Plaintiff Buckner is a consumer as defined by Fla. Stat. § 501.203 and Actos is a good within the meaning of the FDUTPA. Defendants is engaged in trade or commerce within the meaning of the FDUTPA.

272. Fla. Stat. § 501.204(1) declares unlawful "[u]nfair methods of competition, unconscionable acts or practices, and unfair or deceptive acts or practices in the conduct of any trade or commerce." The FDUTPA also prohibits false and misleading advertising.

273. Fla. Stat. § 501.204(2) states that "due consideration and great weight shall be given to the interpretations of the Federal Trade Commission and the federal courts relating to

[section] 5(a)(1) of the Federal Trade Commission Act."

274. Defendants violated the FDUTPA by representing that Actos had characteristics, uses, and benefits which it did not have and advertising the drug as having characteristics, uses, and benefits which Defendants knows Actos does not have, i.e., that Actos does not cause bladder cancer.

275. Defendants violated the FDUTPA by advertising and promoting Actos in the manner described above, when they knew, or should have known, that those representations and advertisements were false and/or misleading.

276. Defendants intended that Plaintiff Buckner and the Florida Consumer Class would rely on its deception by purchasing the Actos, unaware of the material facts described above, i.e., that the drug posed a significant risk of bladder cancer. This conduct constitutes consumer fraud within the meaning of the FDUTPA.

277. Defendants' conduct, as alleged herein, constitutes unlawful, unfair, and/or deceptive business practices within the meaning of the FDUTPA. Defendants violated the FDUTPA by engaging in the unfair and deceptive practices as described herein which offend public policies and are immoral, unethical, unscrupulous and substantially injurious to consumers.

278. Defendants' conduct was malicious, fraudulent, and wanton, and provides misleading information Actos is safer than it actually is, when in fact scientific evidence clearly indicates that Actos significantly increases the risk of bladder cancer.

279. Defendants' conduct has proximately caused damage to Plaintiff Buckner and the Florida Consumer Class, in the form of, *inter alia*, monies spent to purchase Actos they otherwise would not have, in an amount to be proven at trial.

280. Had Defendants disclosed all material information regarding Actos in its advertising, marketing, and/or labeling, Plaintiffs Buckner and the Florida Consumer Class would not have purchased the Actos, would have paid less, or would have placed a significantly different value on the product than what they received.

281. Defendants' unfair and deceptive practices are likely to mislead—and have misled—consumers acting reasonably in the circumstances, and in violation of Fla. Stat. § 500.04, and 21 U.S.C. § 343.

282. As a result of Defendants' violations of the foregoing state consumer protection statute, Buckner and the Florida Consumer Class are entitled to compensatory damages, double damages, treble damages, statutory damages, punitive or exemplary damages, and/or restitution.

COUNT IX: VIOLATIONS OF MINN. STAT. § 325F.69

283. Plaintiffs incorporate by reference all preceding paragraphs as if fully set forth herein.

284. Minnesota Statutes § 325F.69, subd. 1 makes it unlawful for any person by use of "any fraud, false pretense, false promise, misrepresentation, misleading statement or deceptive practice, with the intent that others rely thereon in connection with the sale of any merchandise, whether or not any person has in fact been misled, deceived, or damaged thereby…."

285. Takeda is a "person" pursuant to Minn. Stat. § 325F.68.

286. By engaging in the conduct described in this Complaint, Takeda violated Minn. Stat. § 325F.69.

287. By making the misrepresentations set out in this Complaint, which are hereby incorporated, Takeda used false pretenses, false promises, misrepresentations, and misleading statements, all with the intent that others, including Plaintiffs and members of the proposed Classes rely on those statements, in the course of the sale and promotion of Actos for the treatment of Type 2 .

288. The facts Forest misrepresented as alleged in this Complaint were material to Plaintiffs, Plaintiff Painters Fund's members, physicians, prescribers and their representatives' decisions about whether to purchase Actos, in that they concerned facts, i.e., whether the drug causes bladder cancer, that would have been important to a reasonable consumer in making a decision whether to purchase Actos.

289. Takeda's misrepresentations and deceptive acts and omissions were likely to

mislead reasonable consumers acting reasonably under the circumstances such as Plaintiffs and physicians under Plaintiff Painters Fund's plan.

290. Takeda's wrongful conduct and use of false pretenses, false promises, misrepresentations, and misleading statements regarding Actos and its association with PPAR alpha agonism and an association with bladder cancer were done with the intent that others rely on those statements in making a decision to purchase and/or prescribe Actos.

291. Plaintiffs and members of the proposed classes and their representatives, received the misrepresentations and omissions described herein when deciding to purchase Actos.

292. As a result of Takeda's fraud, false pretense, false promises, misrepresentations, misleading statements and deceptive practice practices relating to the sale of Actos, Plaintiffs and putative class members have suffered actual damages in that they purchased and paid for Actos while being deprived of material information.

293. As a direct, proximate, and foreseeable result of Takeda's violations of Minn. Stat. § 325F.69, subd. 1, Plaintiffs and the putative class members sustained damages in an amount to be determined at trial.

COUNT X: VIOLATIONS OF MINN. STAT. § 325D.13

294. Plaintiffs incorporate by reference all preceding paragraphs as if fully set forth herein.

295. Minnesota Statutes § 325D.13 provides that, "[n]o person shall, in connection with the sale of merchandise, knowingly misrepresent, directly or indirectly, the true quality, ingredients or origin of such merchandise."

296. By engaging in the conduct described herein, Takeda violated Minn. Stat. § 325D.13.

297. By making the misrepresentations set out in this Complaint, which are hereby incorporated, Takeda misrepresented the true quality of Actos by failing to disclose a material aspect of the drug, i.e., that Actos is associated with increased risks of bladder cancer.

298. The facts Takeda misrepresented as alleged in this Complaint were material to

Plaintiffs, Plaintiff Painter Fund's members, and their representatives' decisions about whether to purchase Actos, in that they concerned facts that would have been important to a reasonable consumer and prescriber in making a decision whether to purchase and/or prescribe Actos.

299. Takeda's misrepresentations and deceptive acts and omissions were likely to mislead reasonable consumers acting reasonably under the circumstances such as Plaintiffs and Plaintiff Painters Fund's members.

300. Plaintiffs and the class members and their representatives, received the misrepresentations and omissions described herein when deciding to purchase Actos.

301. As a result of Takeda's fraud, false pretense, false promises, misrepresentations, misleading statements and deceptive practice practices relating to the sale of Actos, Plaintiffs, Plaintiff Painters Fund, and Plaintiff Painter Funds' members suffered actual damages in that they purchased and paid for Actos that they would not have had the truth about bladder cancer been known.

EXEMPLARY DAMAGES ALLEGATIONS

302. Plaintiffs incorporate by reference each and every prior and subsequent allegation of this Complaint as if fully restated here.

303. Defendants' conduct as alleged herein was done with oppression, fraud, and malice. Defendants were fully aware that Actos posed a risk of causing bladder cancer to patients, as documented in their own clinical trials and internal company documents. Nonetheless, Defendants deliberately crafted their drug label to mislead consumers, prescribers, third-party payors and the FDA about the bladder cancer risks—willfully ignoring the mortal danger Actos posed to consumers. Moreover, Defendants' comprehensive program of deceptive marketing was done in willful violation of federal and state law and with complete disregard for the safety and wellbeing of the Plaintiffs and the members of the Classes. Defendants' conduct was not done by accident or through some justifiable negligence. Rather, Defendants knew that they could turn a profit by misleading the, consumers, prescribers, third-party payors, and the FDA about risks of Actos causing bladder cancer. Indeed, by stonewalling the FDA for over a

decade, Defendants were able to obtain substantial profit at the expense of people's health, while it maintained exclusivity over the product. Such conduct was done with a conscious disregard of consumer rights and safety. This fact is demonstrated by Takeda, even after the bladder cancer warning was issued in 2011, instructing sales representatives to "not discuss bladder cancer and sell, sell, sell!" (*See* ¶ 80.) It is also confirmed by instructions by Takeda's Vice President over its Pharmacovigilance Department, Maria Paris, that "adverse event reporting is one thing, but Takeda's profitability comes first." (*See* ¶ 75.) This overt and conscious disregard for patient safety and consumer rights warrants exemplary damages.

DEMAND FOR JURY TRIAL

304. Plaintiffs respectfully request a trial by jury on all claims triable as a matter of right.

PRAYER FOR RELIEF

305. 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 respective Classes;

b. Designate each Plaintiff as a representative for the respective Classes and Plaintiffs' undersigned counsel as Class Counsel;

c. Issue a judgment against Takeda that:

   i. Grants Plaintiffs and the various Classes alleged herein a refund of all moneys acquired by Takeda by means of its deceptive and unlawful marketing of Actos;

   ii. Grants Plaintiffs and the Classes alleged herein an award of restitution and/or disgorgement of Takeda's profits from its deceptive and unlawful marketing of Actos in violation of the consumer protection and RICO claims;

iii. Grants Plaintiffs and the various Classes alleged herein any actual or compensatory damages for the payments or reimbursements made by plan members for Actos in such amount to be determined at trial and as provided by applicable law;

iv. Grants Plaintiffs and the various Classes alleged herein exemplary, treble, and punitive damages sufficient to punish and deter Takeda and others from future deceptive and unlawful marketing practices;

v. Grants Plaintiffs and the various Classes alleged herein pre-judgment and post-judgment interest;

vi. Grants Plaintiffs and the various classes alleged herein reasonable attorneys' fees and costs of suit; and

vii. Grants Plaintiffs and the various Classes alleged herein such other and further relief as the Court deems just and proper under the circumstances.

DATED: July 22, 2014

Respectfully submitted,

BAUM, HEDLUND, ARISTI & GOLDMAN, P.C.

/s/ Michael L. Baum

Michael L. Baum (CA Bar No. 119511)
R. Brent Wisner (CA Bar No. 276023)
12100 Wilshire Blvd., Suite 950
Los Angeles, CA 90025
Tel: (310) 207-3233

PENDLEY, BAUDIN & COFFIN, LLP
Christopher L. Coffin (LA Bar No. 27902)
Nicholas R. Rockforte (LA Bar No. 31305)
1515 Poydras Street, Suite 1400
New Orleans, LA 70112
Tel: (504) 355-0086

LARSON KING, LLP
T. Joseph Snodgrass (MN Bar No. 231071)
Shawn M. Raiter (MN Bar No 240424)
30 East 7th Street
St. Paul, MN 55101
Tel: (651) 312-6500

Counsel for Plaintiffs and Putative Classes