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Pursuant to Local Rule 56.1, Class Plaintiffs submit the following statement of disputed and undisputed material facts in opposition to Defendants' Motion for Summary Judgment. Copies of all documentation referenced herein and in the accompanying Class Plaintiffs' Response to Defendants' Statement of Undisputed Material Facts Pursuant to Local Rule 56.1 are being filed as accompanying declarations and/or exhibits thereto.

**I. FACTS RELATED TO BIPOLAR AND OTHER MOOD DISORDERS**

**A. Neurontin's Inefficacy for Bipolar and Other Mood Disorders**

**1. FDA Clinical and Statistical Reviews**

1. On January 31, 1992, Parke-Davis submitted New Drug Application (NDA) 20-235: Neurontin (gabapentin) for the treatment of partial seizures.

Declaration of Ilyas Rona in Opposition to Defendants' Motion for Summary Judgment, Ex. 648, Pfizer\_LAlphs\_0084338. (Unless the context indicates otherwise, all references to "Ex." are to exhibits to the Rona Declaration.)

2. In January 1992, as part of Neurontin's NDA, the FDA began a Combined Medical-Statistical Review ("FDA Review") of Neurontin. Data from epilepsy, early migraine and spasticity trials were reviewed for safety. The FDA Clinical Reviewer was Cynthia McCormick.

Ex. 648, Pfizer\_LAlphs\_0084338 at 0084359

3. The Integrated Summary of Safety Information (ISS), a document created by Defendants that reviewed “the overall safety” of Neurontin in epilepsy trials, demonstrated a relative risk of depression with Neurontin use of 1.6 compared to placebo. The ISS identified depression as an “Adverse Event[] That Led to Withdrawal in a Substantial Number of Patients or That Were Potentially Serious Reasons for Withdrawal.”

Ex. 001, Garrity Deposition at 234; Ex. 002, Integrated Summary of Safety Information of Gabapentin Capsules (Item 8.6. of the gabapentin NDA) 720-02957\_(Official).pdf produced as part of Research Reports at 46; Ex. 002, 720-02957\_(Official).pdf at 118.

4. The FDA Review was completed in May 1993. It found that “[i]n the total exposed population of the NDA 78 (5.3%) patients reported depression as a serious adverse event...numerous examples were identified among the CRF’s [Case Report Forms] where a patient developed treatment emergent depression where pharmacological intervention was required and the report of a serious adverse event was not made...of the 78 patients who reported depression as an adverse event, 19 had no prior history of depression, and 22 patients required treatment for their symptoms.”

Ex. 648, Pfizer\_LAlphs\_0084338 at 0084474

5. The FDA Review further concluded that Neurontin caused serious events, including “clinically important depression,” that limited “the drug’s widespread usefulness.” Specifically, the FDA found Neurontin could exacerbate depression, which could “require intervention or lead to suicide, as it has resulted in some suicidal attempts.”

Ex. 648, Pfizer\_LAlphs\_0084338 at 0084477

6. The FDA Review recommended approval “for use in a specific [epileptic] population.” Five FDA reviewers, including Dr. Cynthia McCormick, signed this review between May and June 1993.

Ex. 648, Pfizer\_LAlphs\_0084338 at 084479.

7. The reports of depression included a case of challenge-dechallenge-rechallenge. Cases of challenge-dechallenge-rechallenge may be “considered evidence of causation.”

Ex. 648, Pfizer\_LAlphs\_0084338 at 0084467; Ex. 003, Exhibit 35, Pande Deposition; Ex. 004, Pande Deposition at 546-551; Ex. 005, Furberg Report at ¶28.

8. The 1992 FDA Review contained a “very strong safety signal that gabapentin increases the risk of depression with or without suicidal ideation.”

Ex. 005, Furberg Report at ¶28; Ex. 006, Supplemental Barkin Report at 2.

9. “The safety signal described by Dr. McCormick during the course of her review of gabapentin’s potential use in one specific patient population (patients with epilepsy) provides the first systematically-obtained data from clinical trials evidencing gabapentin’s effect on mood. This data indicates a lack of beneficial, and possible negative, effect on mood.” This evidence “would have been material to the physician making an informed decision to prescribe gabapentin for a mood disorder.” Ex. 006, Supplemental Barkin Report at 2 and 5.

10. The identification of a safety signal “places the burden on the Sponsor to conduct more research prior to promoting the drug.” During such research “the drug’s use should be specifically avoided in high-risk patients, that is those who already have the condition that the drug may cause or those who otherwise are at an increased risk of that event” and “it is misleading and unethical for a Sponsor to claim that the drug has a therapeutic benefit while denying the existence of evidence that the drug may lead to a worsening of outcomes in the same therapeutic area.” Ex. 005, Furberg Report at ¶30

11. A July 1994 memorandum sent from Janeth Turner to many company employees enclosed the FDA review asking recipients to “[p]lease review this not only for FDA’s opinion on this NDA approval, but also for what documents and information ultimately may become available under FOI [Freedom of Information Act] once an NDA is approved.”

Ex. 648, Pfizer\_LAlphs\_0084338 at 0084339

12. On May 23, 2008, the FDA issued a Statistical Review and Evaluation on Antiepileptic Drugs and Suicidality. The FDA concluded that “antiepileptic drugs,” including gabapentin, “are associated with increased risk of suicidality relative to placebo in randomized placebo-controlled trials. The effect appears consistent among the group of 11 drugs.”

Ex. 007, 2008-4372b1-01-FDA.pdf (“Statistical Review and Evaluation: Antiepileptic Drugs and Suicidality”).

2. Pande Bipolar Trial (945-209)

13. Despite the evidence that Neurontin increased the risk of depression with or without suicidal ideation, Defendants designed a trial to study Neurontin's efficacy in patients suffering from bipolar disorder. On January 2, 1996, Parke-Davis' protocol 945-209, entitled "Gabapentin: Adjunctive Treatment in Patients with Bipolar Disorder" was finalized. The study design was: double-blind, randomized, parallel group addition of gabapentin or placebo to previous treatment. The primary efficacy parameters included measures for both mania and depression. According to Dr. Atul Pande, Senior Director of Central Nervous System Worldwide Clinical Research, Protocol 945-209 was intended "to obtain the first evidence of efficacy, if it exists."

Ex. 008, 720-04174.pdf at 22; Ex. 004, Pande Deposition at 274.

14. The results of Parke-Davis's "early analysis" of study 945-209 were available on March 20, 1998. This analysis showed that study 945-209 was clearly negative for both the mania and depression measures, with Neurontin failing to outperform placebo.

Ex. 009, Exhibit 22, Pande Deposition; Ex. 004, Pande Deposition at 385-399; Ex. 008, 720-04174.pdf at 9.

### 3. Frye Bipolar Trial

15. In October 1998, Defendants learned of the results of a second placebo-controlled, double-blind trial that demonstrated that Neurontin was no more effective than placebo in treating bipolar disorder. The study's lead investigator was Dr. Mark Frye of the National Institute of Mental Health.

Ex. 010, Post RM, Denicoff KD, Frye MA et al. A History of the Use of Anticonvulsants as Mood Stabilizers in the Last Two Decades of the 20th Century. *Neuropsychobiology* 1998;38:152-166; Ex. 011, <http://content.karger.com/ProdukteDB/produkte.asp?Aktion=Ausgabe&Ausgabe=226272&ProduktNr=224082>; Ex. 012, WLC\_FRANKLIN\_0000052703.

4. Guille Bipolar Trial

16. In May 1999, Defendants learned of the results of a third placebo-controlled, double-blind trial that demonstrated that Neurontin was not more effective than placebo for mania. The study was conducted by investigators associated with Harvard Medical School.

Ex. 014, WLC\_CBU\_030410 at 030411.

5. Vieta Bipolar Trial (945-421-291)

17. On May 14, 1999, Pfizer-sponsored protocol 945-421-291 was initiated. The title of this protocol was: "A 1 Year Double-Blind, Randomized, Placebo-Controlled, Parallel Group, to Evaluate the Efficacy and Safety of Gabapentin (CI-945) as Add-On Treatment in Patients with Bipolar Disorder." This study involved 14 centers in Spain, and was completed on February 26, 2004.

Ex. 015, 945-291.pdf

18. Study 945-421-291 was negative in Ex. 015, 945-291.pdf  
its primary outcome, with Neurontin failing to outperform  
placebo in improving bipolar symptom severity.

6. Defendants Own Admissions Regarding Neurontin's Inefficacy to Treat Bipolar  
and Other Mood Disorders

19. Prior to marketing Neurontin to Ex. 016,  
psychiatrists, Parke-Davis admitted that there was a "lack  
PFIZER\_JMARINO\_0001274.  
of scientific rationale" to support Neurontin's use as a  
treatment for bipolar and other mood disorders.

20. Parke-Davis admitted that there was Ex. 017, Pfizer\_JMarino\_0001268.  
"no preclinical data [to] support the efficacy of gabapentin  
in acute mania."

21. After learning of the results of his Ex. 018, Exhibit 21, Pande  
own study, 945-209, as well as the results from the Frye  
Deposition; Ex. 004, Pande  
and Guille studies, Dr. Atul Pande admitted that  
Deposition at 350-367.  
Neurontin has a "weak, if any, anti-manic effect" and that  
there is "negligible evidence" supporting its use in bipolar  
disorder. Dr. Pande further admitted: "There is pretty  
good consensus among experts in the area that gabapentin  
is not a good anti-manic treatment."

22. Dr. Pande has admitted that Parke-Davis had “absolutely no evidence whatsoever that Gabapentin was likely to be antidepressant, and therefore felt it ethically unjustified to include depressed patients [in a mood trial].” Ex. 019, Pande Pittsburgh Transcript at 6.

23. Pfizer admits that psychiatrist opinion leaders refer to gabapentin as “the drug that does not work.” Ex. 20, Exhibit 41, Pande Deposition; Ex. 004, Pande Deposition at 616-617.

7. Plaintiffs’ Expert Opinion Establishes Neurontin’s Inefficacy to Treat Bipolar and Other Mood Disorders

24. When determining a drug’s effectiveness, the highest level of evidence, indeed the level of evidence upon which the FDA relies, comes from the double-blind randomized controlled trial. This “Gold Standard” is appropriately called “Level 1 Evidence.” Lesser levels of evidence, including case reports and consensus guidelines, are fraught with potential confounders and biases, and are therefore incapable of testing a hypothesis. Ex. 374, Kessler Report, ¶¶14-15; Ex. 023, Abramson Report, ¶¶22-23; Ex. 021, Barkin Report at 6; Ex. 365, Alldredge Report at 1; Ex. 163, Perry Report 5-6.

25. Dr. Jeffrey Barkin, a board-certified psychiatrist and Director of Maine's state Medicaid Drug Utilization Review Board, concludes: "[I]n reviewing all of the double-blind, placebo-controlled trials (Level 1 Evidence), no efficacy of gabapentin is demonstrated. I conclude that the clinical trial database of Level 1 Evidence consistently shows lack of efficacy of gabapentin for the treatment of bipolar disorder. Therefore, the use of gabapentin for the treatment of bipolar disorder, as monotherapy or adjuvant therapy, is unsupported by the scientific evidence."

Ex. 021, Barkin Report at 10; Ex. 022, Barkin- Exhibit 1.pdf.

26. Dr. Barkin further concludes: "[T]he scientific evidence clearly shows that gabapentin is ineffective as a treatment for bipolar disorder. Based on this scientific evidence, Neurontin should never have been recommended as a treatment for bipolar disorder." Dr. Barkin's opinion applies to all bipolar patients.

Ex. 021, Barkin Report at 10; Ex. 550, Barkin Depo at 481.

27. Dr. John Abramson, an expert and best-selling author on the impact of pharmaceutical company marketing on physician prescription writing, reaches the same conclusion: “In sum, four randomized controlled clinical trials testing the efficacy of Neurontin for bipolar disorders have been done. Of the two identified as sponsored by the manufacturer, one showed that Neurontin is significantly worse than placebo [Protocol 945-209, Pande et al.], and one showed no benefit [Protocol 945-421-291, Vieta et al.]. The study done by NIMH showed no benefit [Frye et al.]. Another presented in 1999 [Guille et al.] also showed no benefit.”

Ex. 023, Abramson Report ¶139.

**B. Intent to Fraudulently Market Neurontin for Bipolar and Other Mood Disorders**

28. Almost every month, Parke-Davis convened a meeting of the Neurontin Development Team. The Development Team consisted of high-level officials in Parke-Davis in charge of regulatory, clinical research, patents, marketing and manufacturing issues. Part of the Team’s responsibility was to develop uses and markets for Neurontin. Regular minutes were kept for all meetings.

Ex. 024, Knoop Deposition in US ex rel. Franklin v. Pfizer, 96-11651-PBS (D. Mass.) on Sep. 25, 2002 at 27-28, 225-255.

29. Despite having knowledge that Neurontin's usefulness was limited to the epilepsy population, and should not be used in patients with depression due to the risk that patient mood could worsen or even lead to suicide, Parke-Davis embarked on a course to market Neurontin to patients with mood disorders. On October 18, 1994, at a Neurontin Development Team meeting, Dr. Pande "reviewed anticonvulsants usage for psychiatric disorders." According to the minutes of this meeting, "[h]igh tolerance and safety" were presented as the number one characteristic "of gabapentin that suggests its utility in bipolar disorder." The FDA's findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use were not presented at this meeting. Instead, Dr. Pande suggested that Neurontin was associated with "improved affective, cognitive and social benefits" and reported that Defendants' patent counsel was examining the "patentability of a psychiatry indication for gabapentin."

Ex. 025, WLC\_CBU\_088767 at 088773-74.

30. One month later, on November 9, 1994, Dr. Pande once again “suggested that gabapentin has a utility in the treatment of psychiatric disorders based on its characteristics.” A marketing action plan was set, and Dr. Pande and Dr. Charlie Taylor [Research Fellow, Neuroscience Pharmacology for Parke-Davis and Pfizer] were instructed to provide documents to marketing for analysis of the “commercial potential of Neurontin in psychiatric indications.” Once again, the FDA’s finding of clinically significant depression, with or without suicidal ideation, associated with Neurontin use was not discussed.

Ex. 026, WLC\_CBU\_088732 at 088733. Ex. 004, Transcript of Deposition of Atul Pande, M.D. (“Pande Deposition”) at 41-52.

31. Two weeks later, on November 23, 1994, Mi Dong, a member of the Drug Development team, faxed an Exploratory Development Plan for Psychiatric Indications for Gabapentin to Dr. Olivier Brandicourt, a senior member of Marketing Planning at Parke-Davis. This plan admitted that “no preclinical data support the efficacy of gabapentin in acute mania.” Moreover, the plan did not recognize the FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use.

Ex. 017, Pfizer\_JMarino\_0001268.

32. On January 17, 1995, according to minutes of Neurontin Development Team meeting, John Boris, manager of product planning in the Marketing Department, “presented [an] overview of a potential new indication for gabapentin: bipolar disorder.” Boris noted that “[t]he bipolar disorder market is moderate in size representing \$250 to 300 million in annual sales growing at 6% per year” and that “[a] new agent with a premium price would potentially grow the market.” The FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use were not presented at this meeting.

Ex. 027, WLC\_CBU\_088726 at 088730.

33. On February 21, 1995, it was reported that the “NPC [New Products Committee] supports development of Neurontin for other indications and has asked for a formal proposal.” The NPC was a decision making body of senior management within Parke-Davis, and included Lodewijk J.R. de Vink, President of Warner-Lambert Company, Tony Wild, the President of Parke-Davis. The NPC directed John Boris to explore the marketing feasibility of an indication for bipolar with Dr. Pande and another senior scientist and to make a recommendation to the Neurontin Development Team prior to next NPC meeting.

Ex. 028, WLC\_CBU\_088721 at 088725; Ex. 024, Knoop Deposition in US ex rel. Franklin v. Pfizer, 96-11651-PBS (D. Mass.) on Sep. 25, 2002 at 228.

34. On February 23, 1995, John Montgomery sent a memorandum to John Boris regarding the Preliminary Marketing Assessment for Psychiatric Indications. This memorandum noted that “the prevalence and drug uses in these disorders [bipolar and anxiety disorders] represent attractive commercial potential for Neurontin.”

Ex. 029, Exhibit 6, Pande Deposition; Ex. 004, Pande Deposition at 52-61; Ex. 030, Pfizer\_JMarino\_0001834.

35. By March 14, 1995, the Marketing Planning group had been instructed to prepare a Marketing Assessment for bipolar disorder. Lene Ulrich, Director of the Epilepsy Disease Management Team, noted that “US prescription sales [of Neurontin] have not increased during the last three months.” Moreover, despite conceding that “[t]here was limited preclinical data to support work in mood disorders,” Dr. Pande recommended the adoption of a publication strategy, pointing out that a “publication study will be less expensive [than regulatory studies] and focus on what management organization and clinician want to know.”

Ex. 031, WLC\_CBU\_088713 at 088716-17; Ex. 032, Exhibit 8, Pande Deposition; Ex. 004, Pande Deposition at 122-135.

36. On March 23, 1995, Dr. Pande sent John Boris, Mark Pierce, vice president of Clinical Research, and Ron Martin, vice president of Drug Development, an interoffice memorandum attaching the projected costs of “doing one study each in the three psychiatric indications [bipolar disorder, social phobia, panic disorder].” Dr. Pande noted that were a full regulatory submission desired, he “would estimate the costs to [be] at least about 3 times the cost for a single study.”

Ex. 033, WLC\_FRANKLIN\_0000134637

37. On March 28, 1995, Dr. Atul Pande sent John Boris an interoffice memorandum in which he stated that “the object of a ‘publication strategy’ would be to disseminate the information as widely as possible through the world’s medical literature.”

Ex. 034,  
WLC\_FRANKLIN\_0000134638;  
Ex. 035, Exhibit 7, Pande  
Deposition; Ex. 004, Pande  
Deposition at 105-121.

38. In March and April 1995, Parke-Davis made a decision to market Neurontin for bipolar disorder without first conducting the multiple clinical trials that would have been required to obtain approval from the FDA. On March 30 and 31, 1995, the Neurontin Core Marketing Team Meeting agreed with Parke-Davis’s Marketing Council to do a “Publication Study” for bipolar disorder since the patent situation would limit a full indication development. Product Planning planned to make a “publication study” recommendation at the next NPC meeting in April.

Ex. 036,  
WLC\_FRANKLIN\_0000050304 at  
0000050315.

39. At the April 25, 1995 Neurontin Development Team Meeting, Ron Martin reported that the NPC had approved the conducting of a study in bipolar disorder, noting that the study “should be designed for publication rather than regulatory purposes.”

Ex. 037, WLC\_CBU\_088708.

40. Despite the lack of scientific rationale, Parke-Davis sought to protect its investment in marketing Neurontin for bipolar by seeking a patent for the use. On May 15, 1995, Dr. Pande filed a patent application claiming Neurontin as a “[m]ethod of treatment of mania and bipolar disorder.” The patent’s abstract states: “The present invention is a novel therapeutic use of gabapentin, its derivatives, and the pharmaceutical salts thereof. The compounds are useful in the treatment of mania in all its various forms whether acute or chronic, single or recurrent, and whether or not it is associated with depression. The invention further includes the treatment of bipolar disorder.” The summary of invention section further states: “This is a novel use for gabapentin which would not be obvious to a medical practitioner of ordinary skill.”

Ex. 038, Exhibit 3, Pande  
Deposition, U.S. Patent No.  
5,510,381

41. According to Dr. Atul Pande, “the basis for the invention was the behavioral effects that were seen in epilepsy patients.” Effects of gabapentin from 16 patients identified through a retrospective analysis of data from the controlled epilepsy trials were included in the patent application as “illustrative data.” Data from patients whose mood worsened or who became suicidal was not included.

Ex. 004, Pande Deposition at 254, 628.

42. On May 19, 1995 a final Marketing Assessment for Neurontin in psychiatric conditions including bipolar disorders was approved. The Marketing Assessment stated that the results of an exploratory study in bipolar disorder “if positive, will be publicized in medical congresses and published in peer-reviewed journals.”

Ex. 016, PFIZER\_JMARINO\_0001274; Ex. 039, Exhibit 10, Pande Deposition; Ex. 004, Pande Deposition at 149-192, 200-224.

43. Parke-Davis’s economic motivation to pursue bipolar disorder and other off-label psychiatric uses was clear: “the use generated by the 3 studies [in bipolar disorder, panic disorder and social phobia] in the US (\$40 to \$60 million a year in 1999 when patent extension ends) would largely justify the investment in the clinical program.” This represented an “attractive commercial opportunity.”

Ex. 016, PFIZER\_JMARINO\_0001274; Ex. 039, Exhibit 10, Pande Deposition; Ex. 004, Pande Deposition at 149-192, 200-224.

44. The Marketing Assessment  
conceded that there was a “lack of scientific rationale” to support Neurontin’s use as a treatment for bipolar disorder, but omitted any reference to the FDA’s finding of “clinically significant depression” occurring as a serious and frequent adverse event in patients receiving Neurontin. The omission was never corrected by Janeth Turner or other recipients of the Marketing Assessment who were aware of the FDA’s findings.

Ex. 016,  
PFIZER\_JMARINO\_0001274; Ex. 039, Exhibit 10, Pande Deposition; Ex. 004, Pande Deposition at 149-192, 200-224.

45. The Marketing Assessment  
explained that the publication strategy “would mirror Abbott’s (between 1988 and 1994) when only data from the first pivotal study [of valproic acid (Depakote)] was available. With these first results, Abbott was able to generate a tremendous interest in the psychiatric community and consequently the use indicated earlier [drug use surpassing the 400,000 level representing one-fifth of total drug uses and approximately one-quarter of total sales].”

Ex. 016,  
PFIZER\_JMARINO\_0001274; Ex. 039, Exhibit 10, Pande Deposition; Ex. 004, Pande Deposition at 149-192, 200-224.

46. According to the Marketing Assessment, the total cost of the study suggested as part of the “Publication Strategy” would be \$360,000. In contrast, the cost of full claim development was in excess of \$1,000,000.

Ex. 016, PFIZER\_JMARINO\_0001274; Ex. 039, Exhibit 10, Pande Deposition; Ex. 004, Pande Deposition at 149-192, 200-224.

47. At the time of the Marketing Assessment Neurontin captured 0% of bipolar disorder market. Parke-Davis expected no market share increase until 1997, when it expected that the results from a positive exploratory trial would be published. The Marketing Assessment predicted that pursuing a bipolar publication strategy would cause sales of Neurontin from bipolar prescriptions to grow beginning in 1997, and that such sales would reach \$20 to \$30 million by 1999.

Ex. 016, PFIZER\_JMARINO\_0001274; Ex. 039, Exhibit 10, Pande Deposition; Ex. 004, Pande Deposition at 149-192, 200-224.

48. Despite knowledge of the data linking Neurontin to depression, “Defendants chose to study their drug in a patient population considered at high-risk of depression with or without suicidal ideation.”

Although investigators in the prior epilepsy studies had been informed of such data, Parke-Davis deleted all references to such data in the version of the Investigator’s Brochure distributed to the investigators in the United States who studied Neurontin’s effect on patients with bipolar disorder. (The brochure distributed to investigators outside of the United States retained the references to depression data). The deletion of this data violated Parke-Davis internal standards for an investigators brochure, which “summarizes all of the safety information that is available at the time that any clinical study is being conducted.” A “responsible” drug company would have “included ...a warning that participants in research projects should be alert to the risk of depression with and without suicidal ideation.”

Ex. 006, Supplemental Barkin Report at 3; Ex. 004, Pande Deposition at 553; Ex. 040, 720-03362\_Investigators’\_Brochure.pdf ; Ex. 041, 720-03092\_Investigators’\_Brochure.pdf ; Ex. 005, Furberg Report ¶32.

49. On June 9, 1995, Parke-Davis held a Neurontin Psychiatric Advisory Board in Chicago. “The objective of this meeting was to identify the potential market and clinical trials protocols for gabapentin (Neurontin) therapy in the treatment of patients with psychiatric disorders [including bipolar disorder]. Dr. Pande and Dr. Taylor presented behavioral data collected from the epilepsy clinical trial database, in the form of “anecdotal reports suggest[ing] Neurontin’s efficacy for psychiatric uses.” The FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use were not disclosed to the advisors.

Ex. 042, Exhibit 11, Pande Deposition; Ex. 043, Exhibit 12, Pande Deposition; Ex. 044, Exhibit 13, Pande Deposition; Ex. 004, Pande Deposition at 254-272.

50. Several months later, on October 25, 1995, “[a] Decision Analysis meeting was held...to discuss indications for Neurontin related to the Life Cycle Plan. Initial analyses showed that bipolar disorders was the indication most favored for future study based on expected net present value (NPV) and the general location of the NPV distribution.” Based on the favorable NPV of promoting Neurontin for bipolar disorders, it was recommended that bipolar disorders be included in the Neurontin’s “Life Cycle Plan.”

Ex. 045, WLC\_CBU\_088676 at 088679.

C. **False and Misleading Marketing of Neurontin for Bipolar and Other Mood Disorders**

1. **False and Misleading Statements Made During Class Period**

a. *False and Misleading Statements—Teleconferences*

51. Between October 24, 1995 and June 25, 1996, Defendants held 13 teleconferences, with as many as 25 physician listeners each, during which they promoted Neurontin as effective for bipolar disorder based on favorable anecdotes.

Ex. 046,  
WLC\_FRANKLIN\_0000199943;  
Ex. 047,  
WLC\_FRANKLIN\_0000096571

52. The majority of these teleconferences were moderated by Dr. David Marcotte and Dr. Martin Stein, both psychiatrists.

Ex. 046,  
WLC\_FRANKLIN\_0000199943;  
Ex. 047,  
WLC\_FRANKLIN\_0000096571

53. Defendants knew Dr. Marcotte would present Neurontin as a mood-stabilizer and had prepared the outline for Dr. Marcotte's presentation, meeting with him "to go over the information." Parke-Davis did not provide Dr. Marcotte with a copy of the FDA's findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use.

Ex. 048,  
WLC\_FRANKLIN\_0000199668;  
Ex. 049,  
WLC\_FRANKLIN\_0000199997

54. Based on the pre-arranged outline, at each of these teleconferences, Dr. Marcotte presented anecdotes based on “1 to 2 patients” citing “success” and how “Neurontin evolved into a first line therapy option.”

Ex. 049,  
WLC\_FRANKLIN\_0000199997

55. Defendants also met with Dr. Stein and were aware that he would present favorable anecdotes related to Neurontin’s efficacy as a treatment for bipolar disorder. Parke-Davis did not provide Dr. Stein with a copy of the FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use.

Ex. 050,  
WLC\_FRANKLIN\_0000220839

56. Dr. Marcotte and Dr. Stein received \$500.00 per talk.

Ex. 051,  
WLC\_FRANKLIN\_0000065202

57. Dr. Stein would later lose his medical license in Virginia and District of Columbia for, among other things, inappropriate and excessive prescribing of drugs, including Neurontin.

Ex. 052,  
[http://www.washingtonpost.com/wp-dyn/content/article/2008/01/30/AR2008013004153\\_pf.html](http://www.washingtonpost.com/wp-dyn/content/article/2008/01/30/AR2008013004153_pf.html); Ex. 674,  
<http://archives.starbulletin.com/2003/10/26/news/index1.html>.

58. During the first trimester of 1996, Parke-Davis cancelled all off-label Neurontin teleconferences amid concerns over the FDA’s scrutiny of off-label marketing practices and the discovery of “a Neurontin off-label paper trail of teleconference calls that originated from the SE CBU [Customer Business Unit].”

Ex. 053,  
WLC\_FRANKLIN\_0000092698

b. *False and Misleading Statements—Dimond Article*

59. In February 1996, Defendants submitted an article entitled “Effect of Gabapentin (Neurontin®) on Mood and Well-Being in Patients with Epilepsy” to the journal *Progress in Neuro-Psychopharmacology & Biological Psychiatry* (“Dimond Article”). The authors were all employees of Parke-Davis and included Dr Pande.

Ex. 054,  
PFIZER\_LESLIETIVE\_0021163;  
Ex. 021, Barkin Report at 5.

60. The Dimond Article examined data from the five controlled trials in epilepsy, the same trials that the FDA reviewed when it found clinically significant depression associated with Neurontin. The authors purported to measure “global improvement data” in order to “assess the effects of gabapentin on mood.” However, the pooled scales used to measure mood were not scales that are capable of validly assessing mood.

Ex. 054,  
PFIZER\_LESLIETIVE\_0021163;  
Ex. 006, Supplemental Barkin  
Report at 4; Ex. 005, Furberg  
Report ¶¶34-35.

61. The authors reported that their

“[f]indings support anecdotal reports of improved affective status among patients taking gabapentin,” and that “present data suggest a beneficial effect of gabapentin on mood.” The article concluded that “the present analysis of general well-being with add-on gabapentin therapy suggests that not only did gabapentin-treated patients not fare any worse than placebo, they showed enhanced well-being. At the very least, these findings support gabapentin’s lack of adverse effects on mental functioning.” The FDA’s finding of clinically significant depression, with or without suicidal ideation, associated with Neurontin use, derived from the same data source, were not disclosed.

Ex. 054,  
PFIZER\_LESLIETIVE\_0021163  
(internal citations omitted); Ex.  
021, Barkin Report at 4.

62. Two of the authors of the Dimond Article were recipients of Janeth Turner's July 1994 memorandum disclosing the FDA's findings of clinically significant depression with or without suicidal ideation associated with Neurontin use, and thus they were aware of patients whose mood worsened while on Neurontin. Nevertheless, they chose to "ignore data indicating gabapentin's negative effect on mood." There was a "complete omission of any reference to the evidence that gabapentin increases the risk of depression with and without suicidal ideation."

Ex. 021, Barkin Report at 5; Ex. 005, Furberg Report ¶38.

63. The conclusion of the Dimond Article that "findings support gabapentin's lack of adverse effects on mental functioning" is "a false claim directly contradicted by the FDA's medical review."

Ex. 054, PFIZER\_LESLIETIVE\_0021163 at 414; Ex. 005, Furberg Report ¶36.

c. *False and Misleading Statements—Consultants Conferences*

64. On April 20, 1996, Defendants held Ex. 055, WLC\_CBU\_039398

a Consultants Conference on Affective Disorders in Marco Island, Florida attended by psychiatrists in the southeast. Drs. Marcotte and Stein gave presentations similar to those given during Defendants' teleconferences. Once again, the FDA's finding of clinically significant depression, with or without suicidal ideation, associated with Neurontin use were not disclosed to the consultants.

65. Three days later, on April 23, 1996, Ex. 038, Exhibit Number 3 to Deposition of Atul Pande, M.D.; U.S. Patent No. 5,510,381.  
Dr. Pande's application for a patent claiming Neurontin's "novel therapeutic use" for bipolar disorder was granted. The basis for claimed novelty was that Neurontin's use in treating bipolar "would not be obvious to a medical practitioner of ordinary skill."

66. In the second quarter of 1996, there Ex. 056, IMS Health - Detail Spreadsheet  
were only 566 detail contacts to psychiatrists by Parke-Davis sales persons concerning Neurontin. These contacts constituted only 2.12% of all Neurontin detail contacts to all physicians.

d. *May 1997 Psychiatric Advisory Board*

67. On May 17, 1997 Parke-Davis held a Neurontin Psychiatry Advisory Board Meeting. This meeting was attended by numerous physicians and Parke-Davis employees. Despite the presence of many prominent psychiatrists from around the country, Parke-Davis did not disclose the FDA's findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use.

Ex. 649,  
WLC\_FRANKLIN\_0000041723;  
Ex. 057, WLC\_CBU\_132086.

68. With the help of the paid advisors, Parke-Davis identified the tactics best suited to “[d]eliver the safety and efficacy message to [the] Psychiatric community” and to “[e]stablish a way for representatives to visit Psychiatrists’ offices.” These tactics included: “CME Programs,” to “[b]lanket Psychiatric convention market with satellite symposia, posters and papers,” to “[c]reate a slide kit which would entail new data from ongoing and future studies, Neurontin slides, and summary slides,” and to “[g]enerate mailings to the Psychiatric community on updated and relevant information on anticonvulsants and psychiatric disorders.” Rapid execution of “the studies and educational tactics mentioned above” was important “in order to bypass the other anticonvulsants within this market.” One of Parke-Davis’s advisors was Charles Nemeroff, who earned more than \$2.8 million in consulting fees from drug companies between 2000 to 2007, but failed to report at least \$1.2 million of that income to his university and violated federal research rules, according to documents provided to Congressional investigators.

Ex. 057, WLC\_CBU\_132086; Ex. 058,  
<http://www.nytimes.com/2008/10/04/health/policy/04drug.html?ref=health&pagewanted=print>

69. The Neurontin 1998 Situation Analysis distilled the findings of the advisors as follows: “The advisors suggested it would take only a minimal amount of information appropriately delivered to the psychiatric community to deliver a significant and rapid increase in Neurontin usage for psychiatric disorders. This area poses one of the most significant opportunities for Neurontin in 1998.” The tactics to achieve this growth in sales included:

CME Programs

Increased Parke-Davis involvement at psychiatric conventions

More advisory boards

Neurontin slide kit for psychiatrists

Increased sales rep visits and mailings to psychiatrists

According to John Knoop, a former product manager and Director of the Epilepsy Disease Team at Parke-Davis, the activities suggested were all examples of marketing tactics for Neurontin.

Ex. 059,  
WLC\_FRANKLIN\_0000056368 at  
0000056375; Ex. 024, Knoop  
Deposition at 18, 106-08, 122-26,  
213.

70. In the second quarter of 1997, there were only 660 detail contacts to psychiatrists representing only 3.81% of all detail contacts for Neurontin.

Ex. 056, IMS Health - Detail Spreadsheet

71. One month after the advisory board meeting, on July 1, 1997, Parke-Davis completed preparation of protocol 945-209 entitled Gabapentin: Adjunctive Treatment in Patients with Bipolar Disorder.

Ex. 008, 720-04174.pdf at 1.

72. The minutes of an October 16, 1997 meeting of the Neurontin Development Team note that when the studies for bipolar disorder (945-209) and social phobia (945-203) were “initiated, publishing the data was the main goal (the patent expires in the year 2000). At the recent R&D [Research and Development] meeting, the patent for these indications was discussed. The R&D committee asked the team to reevaluate our current development and publication strategy for these indications. The team needs to further the implication of generic competition in the year 2000 and the effect of the pregabalin.”

Ex. 650,  
WLC\_FRANKLIN\_0000052936

e. *Implementation of Tactics Recommended by Advisory Board*

i. *Congresses*

73. Following the recommendations of its psychiatric advisors, Parke-Davis developed standardized slide kits to be used in presentations to psychiatrists in Congresses and in journal supplements that summarized the proceedings. On November 15, 1997, Parke-Davis sponsored a CME lecture in conjunction with the 10th Annual U.S. Psychiatric & Mental Health Congress entitled: "New Frontiers in Social Phobia and Bipolar Disorders." In that presentation, which was prepared for Parke-Davis by CME, Inc., Neurontin's use as a "therapeutic option" for bipolar disorder was discussed, but the FDA's findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use were not disclosed.

Ex. 061, WLC\_CBU\_052403; Ex. 062, WLC\_FRANKLIN\_0000080341.

74. As a follow-on to this event, a supplement in the Psychiatric Times entitled “Treatment Advances in Social Phobia and New Options for Bipolar” was sent to 40,000 psychiatrists in February 1998. The supplement, which was prepared by CME, Inc., summarizes that same misleading presentation concerning Neurontin that was delivered at the Annual U.S. Psychiatric & Mental Health Congress,” without disclosing the FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use. In a separate Psychiatric Times supplement entitled “Bipolar Disorders Letter,” which was also prepared by CME, Inc., Neurontin’s “role in the treatment of bipolar depression,” its “antidepressant effect,” and its ability to be used for “antidepressant potentiation” were mentioned, but the FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use were not disclosed. Moreover, even though two of the editors of the supplement were also investigators of 945-209, there was no disclosure that in protocol 945-209, the depression scores of patients treated with Neurontin fared no better than those treated with placebo.

Ex. 063, WLC\_CBU\_131777; Ex. 064, WLC\_CBU\_074593; Ex. 061, WLC\_CBU\_052403

75. On November 21, 1998, Parke-

Ex. 065, CME0478-CME0512

Davis sponsored a CME lecture in conjunction with the 11th Annual U.S. Psychiatric & Mental Health Congress entitled: "New Frontiers in Social Phobia and Bipolar Disorders." In that presentation, which was essentially identical to the one used in the 1998 CME series with the same title, "Reports of Benefit" from using Neurontin as a treatment for bipolar disorder were discussed, but neither the 945-209 trial, the Frye trial, the Guille trial or the FDA's findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use were disclosed.

ii. *1998 CMEs*

76. Following the recommendations of its psychiatric advisors, Parke-Davis developed standardized slide kits to be used in presentations to psychiatrists in CMEs. In March and April 1998, Defendants sponsored 50 Continuing Medical Education (CME) dinners throughout numerous cities and telephonically during which a slide set entitled “Closing the Psychiatry-Neurology Divide: Emerging Uses of Anticonvulsants” were presented. Each meeting used the same slide kit, which made no mention of the negative results from protocol 945-209 or the FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use.

Ex. 066, WLC\_CBU\_012564; Ex. 067, Pfizer\_TMartin\_0001795

77. Dr. Barkin states that the slide kit falsely mentioned, “early evidence suggests antimanic, antidepressant and mood stabilizing effects,” but failed to mention either the FDA’s findings of clinically significant depression, with or without suicidal ideation, or the negative results of study 945-209.

78. Dr. Barkin further states that the slide kit “misleadingly concludes with a statement that ‘[c]ontrolled studies are needed to support open trials and case reports’ even though such a study was [already] conducted and it was negative for gabapentin.”

Ex. 021, Barkin Report at 11.

79. The meetings were organized by Medical Education Systems (MES). The misleading statements contained in the “Closing the Psychiatry-Neurology Divide: Emerging Uses of Anticonvulsants” slide kit was presented to almost 1000 physicians in 40 different cities.

Ex. 068,  
WLC\_FRANKLIN\_0000171583;  
Ex. 069,  
WLC\_FRANKLIN\_0000081633

80. The success of this program raised expectations at Parke-Davis. The April 1998 Neurontin Quarterly Review, in the section entitled “Psychiatry (BiPolar) Market,” reported that, were Neurontin to gain 10% of Depakote prescriptions, this would result in \$19.8 million dollars. Were Neurontin to gain 20% of Depakote prescriptions, this would result in \$39.6 million dollars.

Ex. 070, Pfizer\_JMarino\_0002486  
at 0002518.

81. Between July through October 1998, Defendants sponsored a CME activity entitled “New Frontiers in Social Phobia and Bipolar Disorder.” The meetings were organized by CME, Inc. Gabapentin was referred to as a “mood-stabilizer” without evidence to support that claim. Claims of benefit were made for multiple phases of bipolar disorder, including mania, bipolar depression, bipolar maintenance, rapid cycling, treatment resistance and mood instability, without citing supportive evidence.

Ex. 071, WLC\_CBU\_028064; Ex. 072, Exhibit 29, Pande Deposition; Ex. 004, Pande Deposition at 453-463.

82. Despite the fact that two members of the faculty for this CME were investigators from protocol 945-209, there is no mention of the study’s negative results that were by that point known by all investigators working on the study. Claims of efficacy “in the face of the results from 945-209, defy the known data from Defendants’ own Level 1 clinical trial.”

Ex. 071, WLC\_CBU\_028064; Ex. 072, Exhibit 29, Pande Deposition; Ex. 004, Pande Deposition at 453-463; Ex. 021, Barkin Report at 12.

83. Between July and October 1998, “New Frontiers in Social Phobia and Bipolar Disorder” was presented to 5,600 psychiatrists in 30 cities. By the end of 1998, 6,707 psychiatrists had attended the seminar, and an additional 3,000 were expected to attend in the first quarter of 1999.

Ex. 073, WLC\_FRANKLIN\_0000036437; Ex. 069, WLC\_FRANKLIN\_0000081633; Ex. 074, CME1478-CME1748; Ex. 075, CME0589 – CME0658; Ex. 076, Pfizer\_AFannon\_0008581 at 0008592.

iii. *1998 Monographs*

84. In May 1998, *CNS Spectrums* Ex. 077, WLC\_CBU\_012274

published a teaching monograph sponsored by Defendants entitled “Current Treatments in Bipolar Disorder.” This monograph stated: “Studies have shown that improved mood, lower anxiety and increased sociability were nearly twice as frequent among Neurontin patients, when compared to placebo patients.” No studies were cited to support this claim.

85. “Despite access to the results of a Ex. 021, Barkin Report at 12.  
non-anecdotal study (i.e. a Level 1 study), there is no mention of the results (nor even the occurrence) of 945-209” in this monograph.

86. The monograph concluded: “I Ex. 077, WLC\_CBU\_012274  
discuss these tolerability aspects of antiepileptic drugs [only the tolerability of gabapentin is discussed] in light of the evidence for their beneficial effects on bipolar disorder.”

87. In the conclusion, “there is clear elevation of anecdotal Level 3 Evidence...to create the illusion of solid evidence supporting an off-label use [for bipolar disorder]. In light of the results of 945-209, this statement is patently misrepresentative of the evidence-base.” Ex. 021, Barkin Report at 13.

88. This monograph stated: “Depakote and Tegretol have been joined by Neurontin and Lamictal as agents shown to be useful in the treatment of bipolar, and possibly unipolar depression.” Ex. 077, WLC\_CBU\_012274

89. “The existence of negative studies was not disclosed in this monograph...the best ‘evidence’ (Defendants’ own 945-209 study, completed July 1997) was neither presented nor available to prescribers.” Ex. 023, Abramson Report ¶259.

90. CNS Spectrums claims a circulation of 50,000. Ex. 078, <http://www.cnsspectrums.com/asp/AuthorGuidelines.aspx>.

91. Parke-Davis maintained its heightened focus on detailing psychiatrists. According to Dr. Rosenthal, “Spending on detailing to psychiatrists was particularly high during the period between June 1998 and November 2000.” Ex. 079, Rosenthal Report ¶28.

92. On July 24, 1998, Defendants sponsored a symposium entitled: “New Treatment Strategies in Psychiatry.” During this symposium an open-label trial, which Dr. Pande would refer to as an “anecdote,” was presented that suggested “that gabapentin may be an effective treatment for mania in bipolar patients.” Neither the negative results of 945-209 nor the FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use was disclosed during this symposium.

Ex. 080, Pfizer\_TMartin\_0001736; Ex. 019, Transcript of Dr. Pande’s June 18, 1999 presentation entitled “Combination Treatment in Bipolar Disorder” at the Third International Conference on Bipolar Disorder (“Pande Pittsburgh Transcript”) at 3; Ex. 081, Pfizer\_APande\_0000714.

93. The proceedings from this symposium were printed in a supplement to the *Cleveland Clinic Journal of Medicine* in 1998. The negative results of 945-209 were not disclosed in the publication, nor was there any attempt to alert psychiatrists to the association of Neurontin use with clinically significant depression with or without suicidal ideation.

Ex. 080, Pfizer\_TMartin\_0001736

94. “Parke-Davis had 43,000 copies of this supplement printed, 38,000 to be mailed to Cleveland Clinic Journal’s ‘psychiatry audience’ and an extra 5,000 copies that could be handed out to physicians through Parke-Davis’s door-to-door sales force.” According to John Knoop, a marketing director for Parke-Davis, Parke-Davis had an expectation that when they sponsored a supplement using funds from the Neurontin marketing budget that Neurontin would be mentioned.

Ex. 021, Barkin Report at 13; Ex. 082, SH\_0011442; Ex. 024, Deposition of John Knoop at 524.

iv. *Increasing Visits to Psychiatrists by Sales Representatives*

95. Following the recommendation of its advisors, Parke-Davis significantly increased its detailing of psychiatrists. In the second quarter of 1998, there were 2,231 detail contacts to psychiatrists representing 14.94% of all detail contacts, a 238% increase in the number of psychiatrist details from the same quarter in 1997. Details to psychiatrists surpassed details to neurologists. Between October 1999 and June 2000, except for one quarter, psychiatrists were the most detailed specialty.

Ex. 056, IMS Health - Detail Spreadsheet; Ex. 076, Pfizer\_AFannon\_0008581 at 0008588.

96. When Pfizer and Parke-Davis received inquiries on off-label uses of Neurontin, they sent a Standard Response Letters (SRL), or “Dear Doctor” letter, which purported to contain all relevant information needed to answer the inquiry. The Merlin and Pfoenix databases were used to track the inquiries and identify the SRLs sent.

Ex. 083, Vega Deposition at 41- 43, 316-317.

97. SRLs were supposed to be sent only in response to unsolicited requests for information from physicians. In reality, Defendants used the mailing of SRLs as a marketing tactic. Defendants’ sale representatives were trained to prompt physicians for requests for off-label information.

Ex. 084, PFIZER\_DPROBERT\_0014027

98. In December 1998, Defendants finalized a “Dear Doctor” letter entitled “treatment of bipolar depression and mood.” The letter was sent to 5,593 physicians. This letter did not mention the negative results of 945-209 or the Frye study, both of which were known to the company at the time.

Ex. 085, Merlin Database; Ex. 086, 0900000180003ebd.doc

99. This same SRL cited the Dimond Article as confirming that “gabapentin patients were more likely to show improvements in mood and general well being than placebo patients.” The letter contained no mention of the FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use.

Ex. 085, Merlin Database; Ex. 086, 0900000180003ebd.doc

v. *1999 CMEs*

100. In 1999, Parke-Davis sponsored another series of CMEs entitled: “New Frontiers in Anxiety, Substance Abuse and Bipolar Disorder.” These CMEs were nearly identical to the “New Frontiers in Social Phobia and Bipolar Disorder” series sponsored in 1998 and used nearly identical slides. In a standard slide set for this series of CMEs, Neurontin was referred to as one of the “newer mood stabilizers.” Seven case studies were presented. The presentation listed the “[n]eed for controlled studies (under way)” as a “disadvantage of gabapentin”. Two members of the faculty for this CME, however, were investigators for protocol 945-209, and were intimately aware that controlled studies existed.

Ex. 087, WLC\_CBU\_170490; Ex. 088, Exhibit 30, Pande Deposition; Ex. 004, Pande Deposition at 464-471; Ex. 089, CME0038-CME0057.

101. Dr. Barkin states: “In 1999, there were results from controlled studies *already available*...results from controlled studies already existed and therefore should have received a prominent place in any talk, including this one, that claimed to summarize the science behind gabapentin and bipolar disorder.”

Ex. 021, Barkin Report at 14 (emphasis in original).

102. “New Frontiers in Anxiety, Substance Abuse and Bipolar Disorder” was presented in the top 20 U.S. markets and 30 secondary markets. The total estimated attendance was 8,500.

Ex. 090, Pfizer\_NMancini\_0011631 at 0011657; Ex. 091, WLC\_CBU\_028356; Ex. 092, WLC\_CBU\_079924.

103. In the second quarter of 1999, there were 8,712 detail contacts to psychiatrists representing 37.81% of all detail contacts. According to Parke-Davis’s own internal data, there were approximately 7,300 details to psychiatrists in the month of February alone, “despite their (sic) being no FDA-approved indication for any psychiatric illness or symptoms.”

Ex. 056, IMS Health - Detail Spreadsheet; Ex. 076, Pfizer\_AFannon\_0008581 at 0008588; Ex. 023, Abramson Report ¶292.

vi. *Journal Articles*

104. On December 2, 1998, the Journal of the American Medical Association published Defendants' manuscript of the results of protocol 945-210. The abstract's conclusion was: "Gabapentin ... exhibits positive effects on mood and quality of life." This conclusion was not contained in the article itself, nor was there any disclosure of contradictory evidence, such as the FDA's findings of mood worsening, or the results of the companies own study in the area of mood, study 945-209.

105. The company distributed 175,000 copies of this misleading abstract to physicians through its sales force and medical affairs department.

Ex. 093, Backonja M, Beydoun A, Edwards KR, et al., Gabapentin for the symptomatic treatment of painful neuropathy in patients with Diabetes Mellitus. Journal of the American Medical Association, 1998;280:1831-6 ("Backonja Article").

Ex. 094, WLC\_CBU\_150515; Ex. 095, WLC\_CBU\_040534

106. In June 1999, *Epilepsia*, a journal with a circulation of 5,220, published a supplement, authored by Parke-Davis employee Leslie Magnus, entitled “Nonepileptic uses of Gabapentin.” The article suggests that there is data to support the use of gabapentin for bipolar disorder. The article discusses three publications: a series of case studies, an open label study and a case study of a single patient. No mention was made of either the 945-209 study or the Guille study. There is no rationale for discussing these reports [which Dr. Pande admits are only “anecdotes”] over, and to the exclusion of, the results of 945-209.”

Ex 096, Magnus L. Nonepileptic Uses of Gabapentin. *Epilepsia* 1999; 40(Suppl.6):S66-S72; Ex. 097, <http://www3.interscience.wiley.com/journal/119192632/issue>; Ex. 098, WLC\_CBU\_167738 at 167877; Ex. 021, Barkin Report at 13 (emphasis in original); Ex. 019, Pande Pittsburgh Transcript at 3; Ex. 081, Pfizer\_APande\_0000714.

107. On June 18, 1999, Dr. Pande presented results from protocol 945-209 at the Third International Conference on Bipolar Disorder in Pittsburgh, PA. in a lecture entitled “Combination Treatment in Bipolar Disorder.”

Ex. 099, <http://www.wpic.pitt.edu/Stanley/3rdbipconf/proceedings.htm>; Ex. 081, Pfizer\_APande\_000714; Ex. 100, Exhibit 40, Pande Deposition; Ex. 004, Pande Deposition at 599.

108. Neither the results of the Guille study, nor the results from the Frye study, nor the FDA’s finding of an increased risk of clinically significant depression, with or without suicidal ideation, associated with gabapentin use were disclosed in Dr. Pande’s presentation.

Ex. 081, Pfizer\_APande\_000714; Ex. 100, Exhibit 40, Pande Deposition; Ex. 004, Pande Deposition at 554-555, 599.

109. In his Pittsburgh presentation, Dr. Pande stated that “we when we began this study [protocol 945-209] had absolutely no evidence whatsoever that Gabapentin was likely to be antidepressant, and therefore felt it ethically unjustified to include depressed patients.”

Ex. 019, Pande Pittsburgh Transcript at 6.

110. In his Pittsburgh presentation, Dr. Pande referred to and displayed a slide of “anecdotes or a series of anecdotes from various authors describing good responses to Gabapentin treatment.”

Ex. 019, Pande Pittsburgh Transcript at 3; Ex. 081, Pfizer\_APande\_0000714.

111. On July 22, 1999, Dr. Atul Pande submitted the manuscript containing the results of 945-209 to the journal *Bipolar Disorders*, which has a circulation of 455. According to Dr. Abramson, the 945-209 study was subject to an extraordinary delay in the publication process. Even though the study was completed in July 1997, it took 20 months for a research report to issue, whereas “typically [research] reports are issued about 3 months after study completion.” Moreover, the research report that was issued in March 1999 contained no additional analysis beyond what was included in the Letter to Investigators in July 1998. In fact, the research report’s analysis section contains only a copy of the Letter to the Investigator.

Ex. 101, Pande AC, Crockett JG, Janney CA et al. Gabapentin in Bipolar Disorder: A Placebo-Controlled trial of adjunctive therapy. *Bipolar Disorders* 2000;2:249-255 (“Pande Article”) at 249; Ex. 102, Pfizer\_LKKnapp\_0026006; Ex. 023, Abramson Report ¶133.

112. In August 1999, the *Journal of Clinical Psychopharmacology* published a different article authored by Dr. Pande entitled “Treatment of Social Phobia With Gabapentin: A Placebo-Controlled Study.”

This article stated that “[i]n clinical studies of patients with epilepsy, gabapentin produced improvements in mood.” The Dimond Article is cited to support this statement, but no mention is made of the FDA’s contrary findings concerning mood.

113. Moreover, even though his article was accepted after revision on August 13, 1998, well after Dr. Pande as lead investigator had learned the results of 945-209, the results of 945-209 were not disclosed in the article.

114. “Parke-Davis distributed 25,000 copies of this publication to psychiatrists through the mail and another 125,000 to physicians through the door-to-door sales force. This is on top of a circulation of 8,000 for this journal.”

Ex. 103, Pande AC, Davidson JRT, Jefferson JW et al. Treatment of Social Phobia With Gabapentin: A Placebo-Controlled Study. *Journal of Clinical Psychopharmacology* 1999;19(4):341-48.

Ex. 021, Barkin Report at 13.

Ex. 021, Barkin Report at 13 (internal citations omitted); Ex. 104, WLC\_CBU\_134928; Ex. 102, PFIZER\_LKNAPP\_0026006.

115. Defendants finalized another Standard Response Letter on October 27, 1999 entitled “use in mood disorders,” which was sent to 1,992 physicians. This letter cited the Dimond Article in support of the statement that “[i]nitial reports of patients being treated with gabapentin for epilepsy showed that it had a positive effect on overall sense of well being in such areas as improved memory function, mood, perceptivity, social and occupational initiative, vivacity, energy, and cognition.” The FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use were not disclosed.

Ex. 085, Merlin Database; Ex. 105, 090000018002f0f9.doc

vii. *2000 CMEs & Monographs*

116. In 2000, Pfizer sponsored a presentation entitled “Anticonvulsants in Psychiatry: Historical Perspectives & New Therapeutic Directions.” In this presentation, gabapentin was listed as effective for both mania and depression. The citations were to open-label studies.

Ex. 106, VOX035086

117. Dr. Barkin summarized the state of the Level 1 evidence known to Pfizer: “[b]y 2000, the Defendants knew the results of both 945-209 and the Guille study. The Frye study would also be published in 2000. In other words, there were *three* double-blind placebo-controlled randomized trials that contained results unfavorable to gabapentin, yet this lecture, using Level 3 Evidence, claims gabapentin is effective for both mania and depression.”

Ex. 021, Barkin Report at 15 (emphasis in original).

118. After describing gabapentin as “effective,” this presentation disclosed the results of 945-209 including 3 slides focusing on the study’s “weaknesses.”

Ex. 106, VOX035086

119. According to Dr. Barkin: “This program is not merely littered with misrepresentations and inaccuracies, but is a frank distortion of the science. To conclude that gabapentin was effective, and thus recommend its use for the treatment of bipolar disorder, in the face of the mounting Level 1 Evidence to the contrary is not only illogical and ludicrous, but unethical.”

Ex. 021, Barkin Report at 15-16.

120. On February 10, 2000, a Neurontin Ex. 107, WLC\_CBU\_175353

T2 [Trimester 2] Tactics Meeting was held. On the agenda was a section entitled “Psych Strategy/Portfolio Initiatives,” under “Challenges,” “Weak efficacy data” and “‘Failed’ clinical study” are listed.

121. At an advisory board meeting convened by Parke-Davis in March 2000, Dr. Norman Sussman, one of the authors of the Cleveland Clinic Journal Supplement which favorably discussed Neurontin as a treatment for bipolar disorder, and a frequent speaker hired by Parke-Davis, admitted that the Neurontin marketing effort for bipolar lacked scientific support. Dr. Sussman stated as follows:

Ex. 108, RELATOR02281 at  
RELATOR02759 -  
RELATOR02798

Now, the point is, I'm talking about all these things that are happening -- almost everything I'm talking about appears in the form of letters to the editor or open case series. The amount of controlled trials, the evidence base for this, is not very good. And there is a sense of feeling awkward -- Elizabeth [von Hassell, the moderator of the advisory board meeting], this is something that we should address -- there's a sense of getting up there [as a paid Neurontin speaker] and talking about these things when, maybe, at best, there might be one or two controlled trials that support a given use. So, clinical use is running way ahead of what research is giving us. I mean, I can't remember, in psychiatry, anything like this, where there's such extensive use of drugs, without there necessarily being an indication or the data that we would consider gold standard. So, one of the questions that I have for you to think about is, can we say with any certainty that these drugs really work in the way that we're reporting? How confident are you, individually or as a group, that, even without the clinical trials, that we can get up in front of clinicians and say, look, trust us that these things do work.

122. At that point, Dr. Sussman had earned more than \$ 44,000 in speaking fees or honoraria promoting Neurontin, and had had never disclosed that the evidence supporting Neurontin's use in bipolar was "not very good." Dr. Sussman has also received \$750 to lend his name to a misleading, ghostwritten supplement published in 1998 by the Cleveland Clinic, where he failed to disclose that the evidence supporting Neurontin's use in bipolar was "not very good."

Ex. 109, VOX002819; Ex. 278, VOX003096; Ex. 372, VOX003321; Ex. 447, VOX003607; Ex. 482, VOX003708; Ex. 654, VOX003799; Ex. 655, VOX003846; Ex. 656, VOX011413; Ex. 657, VOX011862; Ex. 658, VOX012233; Ex. 659, VOX095290; Ex. 660, MDL\_VENDORS\_082339

123. In April 2000, Southern Clinical Neurological Society released a CME monograph, sponsored by Defendants, based on a symposium in the Netherland Antilles entitled "Spectrum of Uses of Antiepileptic Drugs: New Treatments, New Strategies." This monograph stated that "[g]abapentin...has been used alone or adjunctively to treat bipolar disorder, social phobia, migraine, neuropathic pain and substance abuse...the efficacy of...gabapentin in treating these diverse conditions may be due to overlapping mechanisms of action."

Ex. 110, MDL\_Vendors\_055236

124. This monograph further stated that Ex. 110, MDL\_Vendors\_055236  
“[s]everal small studies of bipolar disorder have shown  
promising results with gabapentin used as an adjunct to  
other psychotropic agents.”

125. This monograph incorrectly Ex. 110, MDL\_Vendors\_055236  
claimed that the “largest study of gabapentin for this  
indication [bipolar disorder] was a retrospective analysis  
of 73 patients...” even though Protocol 945-209 had  
enrolled 117 patients.

126. This monograph contained a CME Ex. 110, MDL\_Vendors\_055236  
post-test question that required physicians to choose  
gabapentin as one of the anticonvulsants which “have also  
shown mood-stabilizing properties” in order to answer the  
question correctly.

127. In this monograph, “no mention is Ex. 021, Barkin Report at 14.  
made of the negative Pande [945-209] and Guille studies.”

128. By omitting the results of 945-209, Ex. 021, Barkin Report at 14.  
“[t]he false and misleading implication is that gabapentin  
had been shown to be effective, rather than ineffective in  
the ‘largest study’ conducted to date.”

129. “Parke-Davis had 6,000 copies of this monograph printed, 5,000 to be mailed to physicians and an extra 1,000 copies that could be handed out to physicians through Parke-Davis’s door-to-door sales force.”

Ex. 021, Barkin Report at 14; Ex. D, SH\_0064555.0012057

130. In April and May 2000, Defendants sponsored a CME activity entitled “Anxiety & Bipolar Disorders: Challenges in Current Management.” In this presentation, gabapentin was listed as a “mood stabilizer.” Reports of benefit were presented, supported only by anecdotal evidence.

Ex. 112, WLC\_CBU\_028929; Ex. 113, WLC\_CBU\_108957.

131. “Anxiety & Bipolar Disorders: Challenges in Current Management” was presented in 43 locations with thousands of physicians attending in total. One particular presentation, in Dearborn, Michigan had close to 200 attendees.

Ex. 113, WLC\_CBU\_108957; Ex. 114, PFIZER\_CGROGAN\_0018672; Ex. 095, WLC\_CBU\_040534

132. Another Standard Response Letter, finalized by Defendants on May 18, 2000 and entitled “use in mood disorders,” was sent to 978 physicians. This letter cited the Dimond Article in support of the statement that “[i]nitial reports of patients being treated with gabapentin for epilepsy showed that it had a positive effect on overall sense of well being in such areas as improved memory function, mood, perceptivity, social and occupational initiative, vivacity, energy, and cognition.” The FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use were not disclosed.

Ex. 085, Merlin Database; Ex. 115, 090000018003bd75.doc

133. In October 2000, the Pande Article describing the results of 945-209 was published in *Bipolar Disorders*, a journal with a circulation of only 455. The results in the abstract state: “Both treatment groups had a decrease in total YMRS from baseline to endpoint, but this decrease was significantly greater in the placebo group (-9) than the gabapentin group (-6) ( $p < 0.05$ ). No difference between treatments was found for the total score on the HAM-D.”

Ex. 116, <http://www3.interscience.wiley.com/journal/120773981/issue>; Ex. 101, Pande Article at 249.

134. The conclusion in the abstract of the Pande Article states: “The findings of this study did not demonstrate that gabapentin is an effective adjunctive treatment when administered to outpatients with bipolar disorder.” Ex. 101, Pande Article at 249.

135. The Pande Article contains the following biases: (a) Location Bias: Published in a journal with circulation of 455; (b) Time lag bias: Three years to publication from end of study; (c) Citation bias: Did not cite Guille, published during same time period; (d) Possible misrepresentation of data: The values differed for difference from baseline scores (YMRS and HAM-D outcomes) between the letter to investigators and the journal publication; and (e) Spin: Extensive rationale for negative findings in letter to investigators and the journal publication. Ex. 117, Dickersin Report at 26.

136. In October 2000, Albert Einstein College of Medicine released a CME monograph, sponsored by Defendants, entitled “Interface of Neurology and Psychiatry: Diagnostic and Treatment Issues.” This monograph contains a section entitled “New Options in the Management of Bipolar Disorders” in which the following statement is bolded: “The positive effects of gabapentin on quality of life, including improvements in affect and cognitive and social functioning, have been seen to increase with higher doses and are independent of its efficacy in seizure control. This suggests the possible efficacy of gabapentin in mood disorders.” The Dimond Article, which did not disclose the FDA’s findings of Neurontin’s association with depression, is cited as support for this statement.

Ex. 118, Pfizer\_MDana\_0001375 at 0001470.

137. The same section of the monograph further states that: “Reports of the use of gabapentin in bipolar illness are primarily from open-label or retrospective studies.” The same non-Level 1 case studies used in prior CME activities are cited as support.

Ex. 118, Pfizer\_MDana\_0001375 at 0001471.

138. In this monograph, “[t]here is no mention of Pande, Frye or Guille.” These Level-1 studies are not cited in the references listed in the section discussing bipolar disorder. The FDA’s findings of clinically significant depression, with or without suicidal ideation, are also not disclosed.

Ex. 021, Barkin Report at 16; Ex. 118, Pfizer\_MDana\_0001375 at 0001475-6.

139. Defendants distributed 7,000 copies of “Interface of Neurology and Psychiatry: Diagnostic and Treatment Issues” via direct mail to physicians.

Ex. 120, WLC\_CBU\_174105.

140. On November 10, 2000, Karen Ex. 121, Pfizer\_LCastro\_0000054

Katen, the executive vice-president of Pfizer's Pharmaceuticals Group, circulated a memorandum to other Pfizer vice-presidents informing them of certain "challenges" that the company faced because of Neurontin—the Franklin case, the federal grand jury, and the criminal investigation—and stating that "a number of decisions have been made relevant to the promotion and marketing of Neurontin which I believe appropriately respond to these challenges." These decisions included mandates that sales representatives "will call only on Neurologists and institution based epilepsy centers for Neurontin," that "all detailing will be for epilepsy only," and that sales representative participation in CMEs would be limited to programs "clearly related to epilepsy."

141. A new Standard Response Letter, finalized on October 28, 2000 and entitled "use in mood disorders," was sent to 306 physicians. Despite the fact that the Pande Article was published in the same month as the date of this letter, this letter referred only to "Data on file, Parke-Davis."

Ex. 085, Merlin Database; Ex. 122, 090000018006f819.doc

142. This SRL cited the Dimond Article in support of the statement that “[i]nitial reports of patients being treated with gabapentin for epilepsy showed that it had a positive effect on overall sense of well being in such areas as improved memory function, mood, perceptivity, social and occupational initiative, vivacity, energy, and cognition.” The FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use were not disclosed. During the time that this SRL was used, Pfizer’s medical director was Dr. Robert Glanzman. Dr. Glanzman was familiar with the devastating results of suicidal behavior, as his brother had committed suicide. Nevertheless, Dr. Glanzman found humor in Neurontin-related suicidality, joking that a 61-year old woman’s consumption of 54,000 mg of Neurontin, which resultd in a coma and respiratory depression requiring mechanical ventilation, was “History's most expensive suicide attempt.”

Ex. 085, Merlin Database; Ex. 122, 090000018006f819.doc; Ex. 662, PFIZER\_RGLANZMAN\_0071542.

143. A Standard Response Letter dated October 1, 2002 and entitled “effects on mood in patients with epilepsy,” was sent to 40 physicians. This letter contained a bullet point that “[g]abapentin had a beneficial effect on mood in patients with epilepsy in several studies.” There was no mention of the negative results from multiple double-blind randomized controlled trials (DBRCT) studying Neurontin’s effect on mood. There was no mention of the FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use.

Ex. 085, Merlin Database; Ex. 123,  
0900000180110c34.doc

144. A Standard Response Letter dated March 28, 2003, entitled “effects on mood in patients with epilepsy,” was sent to 6 physicians. This letter contained a bullet point that “[g]abapentin had a beneficial effect on mood in patients with epilepsy in several studies.” There was no mention of the negative results from multiple DBRCT studying gabapentin’s effect on mood. There was no mention of the FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use.

Ex. 085, Merlin Database; Ex. 124,  
0900000180141be7.doc

145. A Standard Response Letter dated May 22, 2003, entitled “effects on mood in patients with epilepsy,” was sent to 14 physicians. This letter contained a bullet point that “[g]abapentin had a beneficial effect on mood in patients with epilepsy in several studies.” There is no mention of the negative results from multiple DBRCT studying Neurontin’s effect on mood. There is no mention of the FDA’s findings of clinically significant depression, with or without suicidal ideation, associated with Neurontin use.

Ex. 085, Merlin Database; Ex. 125, 090000018014cbf6.doc

146. According to a 2004 Pfizer sales memo entitled “Neurontin Action Plan - POA2 – 2004,” Pfizer management instructed sales colleagues that there should be “No calls on Psychs!!!!”

Ex. 126, Pfizer\_JSchultz\_0000393

2. Continued Concealment After Class Period

a. *Failing to Provide Information Requested by the Cochrane Group*

147. The Cochrane Collaboration is an international, non-profit organization that provides systematic reviews of healthcare interventions, trusted for their lack of commercial influence and probing for data beyond the published medical literature. These reviews are published quarterly in the Cochrane Library along with updates of past reviews when relevant. Evidence incorporated into Cochrane reviews represents the totality of acceptable quality evidence reasonably available to prescribers and payers, and is presented independent of regulatory authorities' approval or lack of approval for the indications reviewed. Practicing physicians, who generally have neither the time nor the resources to exhaustively search the scientific evidence to determine what the weight of evidence suggests is the best treatment for a given condition, trust that the conclusions presented in Cochrane reviews present a fair distillation of all the scientific evidence.

Ex. 023, Abramson Report, ¶ 188;  
Ex. 117, Dickersin Report at 48.

148. Cochrane reviews must, however, rely upon manufacturers to provide results of studies that have not been published and details of studies that have been published to verify that the results presented are accurate and consistent with the pre-specified outcome measures identified in manufacturers' study protocols. If there is scientific evidence that is not available to Cochrane reviewers, it is very unlikely that practicing physicians—even if they made the effort to search the medical literature—would have access to this information. These data are requested as a scientific courtesy from the pharmaceutical industry and others, usually by mail or email. There is no way to “demand” or “subpoena” data from sponsors or investigators.”

149. In 2001, the Cochrane Collaboration published the protocol for their review entitled: “Gabapentin in the treatment of acute affective episodes in bipolar disorder: efficacy and acceptability.”

Ex. 023, Abramson Report, ¶ 189;  
Ex. 117, Dickersin Report at 48.

Ex. 127, Macritchie K, Geddes J, Young AH. Gabapentin in the treatment of acute affective episodes in bipolar disorder: efficacy and acceptability. Cochrane Database of Systematic Reviews 2007, Issue 2. Art. No.: CD003379. DOI: 10.1002/14651858.CD003379.pub2

150. On November 5, 2001, Dr. Pande sent an e-mail to Anne Stals of the Cochrane Collaboration responding to an October 22, 2001 letter from Dr. Karin Macritchie. In this e-mail, Dr. Pande provided “references concerning the use of gabapentin in patients with bipolar disorder.” There is no mention of the Frye or Guille studies, both DBRCT with negative results for gabapentin that Dr. Pande had known about for more than two years.

Ex. 128,  
PFIZER\_APANDE\_0005005; Ex.  
129, Exhibit 24, Pande Deposition;  
Ex. 004, Pande Deposition at 61-64.

151. On July 8, 2003, Dr. Karen Macritchie of the Cochrane Group again contacted Pfizer by e-mail asking whether they are “aware of any other trials, published or unpublished, complete or ongoing, which would meet our [Cochrane Group] inclusion criteria [double-blind, randomized controlled trial].”

Ex. 130, Pfizer\_APande\_0003413

152. On December 15, 2003, Dr. Karen Macritchie of the Cochrane group e-mailed Dawn Carroll at Pfizer and requested “original data and the overall results of any published or unpublished studies on gabapentin in bipolar disorder, which have been conducted by your company [Pfizer] for the purposes of our Cochrane Review.”

Ex. 131,  
PFIZER\_BPARSONS\_0030122

153. On December 23, 2003, Bruce Parsons responded to requests for “guidance” on Cochrane’s request: “I would not send unpublished Neurontin data to anyone outside Pfizer.”

Ex. 131,  
PFIZER\_BPARSONS\_0030122

154. On February 10, 2004, Dawn Carroll sent an e-mail to Lloyd Knapp re-stating Dr. Karen Macritchie’s “request for specific data that was not available in the publication [of the results of 945-209].” Carroll stated: “[t]he decision is ultimately yours as to what data we send to this group [Cochrane] - the risk is that in the cochrane review there is a statement saying - Pfizer declined to provide information requested! which does not look good for the company.”

Ex. 132, Pfizer\_LKnapp\_0112245

155. On February 23, 2004, Dr. Anitra Ex. 133, Pfizer\_BParsons\_0098666

Fielding, a Senior Pfizer Medical Advisor, sent an e-mail to numerous internal recipients stating: "I have been today forwarded numerous e mails of correspondance [sic] between various people following an initial request for information in October 2003 from the Cochrane bipolar disorder review team which are still apparently outstanding...They have requested specifically, unpublished information and data on gbp [gabapentin] in bipolar disorder and additional info on the Pande trial which was not incorporated into the publication...we need to respond in a timely fashion in order to build trust with our customers - a key Pfizer initiative. If we are not willing to provide this information then we need to get back to the Cochrane team asap as this has been going on for a considerable time now and does not reflect well on Pfizer...if we take 4 months to say sorry no....it would be much appreciated if this could be resolved promptly."

156. On March 12, 2004, Lloyd Knapp Ex. 134, Pfizer\_LKnapp\_0115557

sent an e-mail to Anne Maule of the Cochrane group stating: "I have set up a conference call for March 23rd...I would appreciate if you could pass this information to Professor Young and Dr. Macritchie."

157. On March 24, 2004, Anne Maule of Ex. 135, Pfizer\_LKnapp\_0116131  
the Cochrane group sent an e-mail to Pfizer employees  
alerting them that they had dialed into the conference call  
set up by Lloyd Knapp, “but there was no-one there.”

158. On November 7, 2004, Dr. Karen Ex. 136, Pfizer\_LKnapp\_0104674  
Macritchie of the Cochrane group contacted Pfizer yet  
again requesting “access to the original data from the  
Pande study on gabapentin in bipolar disorder for the  
purposes of our Cochrane review.”

159. In 2007, the Cochrane review of Ex. 127, Macritchie K, Geddes J,  
gabapentin in bipolar disorder was withdrawn “[d]ue to Young AH. Gabapentin in the  
the delay of converting this protocol to a review.” treatment of acute affective  
episodes in bipolar disorder:  
efficacy and acceptability.  
Cochrane Database of Systematic  
Reviews 2007, Issue 2. Art. No.:  
CD003379. DOI:  
10.1002/14651858.CD003379.pub2

160. “The inability of the Cochrane Ex. 023, Abramson Report ¶¶206,  
Collaboration to conduct a thorough review of gabapentin 208.  
treatment for bipolar disorder provides another example of  
the extent to which Defendants’ prevented independent  
analysis of their research data...Without Pfizer’s  
cooperation, the Cochrane reviewers were unable to  
complete their review of the efficacy of gabapentin for  
bipolar disorder.” Defendants’ inaction prevented  
independent analysis of their research data.

161. “The emails reviewed demonstrate Ex. 021, Barkin Report at 18.  
Pfizer’s obfuscation of the data on gabapentin as a  
treatment for bipolar disorder. The lack of cooperation of  
Pfizer with Cochrane is best seen by the withholding of  
data that shows a lack of efficacy. Their behavior in  
withholding the data from the Cochrane Group is fully  
consistent with all of Defendants’ other marketing  
schemes. If the data had demonstrated a beneficial effect  
of gabapentin on bipolar disorder, Pfizer would have  
shared the data with Cochrane.”

162. “Pfizer was...asked to provide data Ex. 117, Dickersin Report at 48.  
from unpublished trials and for published variables where  
additional information was needed to conduct the  
review...Pfizer was not willing to provide these data but  
did not want to appear noncompliant.”

b. *False and Misleading Publication of Vieta Study*

163. On June 7, 2005, the *Journal of Ex. 137, E Vieta, JM Goikolea, A  
Clinical Psychiatry* received the written manuscript of  
Pfizer-sponsored protocol 945-421-291. The lead author  
was Dr. Eduard Vieta. Martinez-Aran et al. A Double-  
Blind, Randomized, Placebo-  
Controlled, Prophylaxis Study of  
Adjunctive Gabapentin for Bipolar  
Disorder. *J Clin Psychiatry*, March  
2006;67:473-477 (“Vieta Article”).

164. On August 25, 2005, the *Journal of Ex. 137, Vieta Article  
Clinical Psychiatry* accepted the written manuscript of  
Pfizer-sponsored protocol 945-421-291.

165. In March 2006, the *Journal of*

Ex. 137, Vieta Article

*Clinical Psychiatry* published the written manuscript of Pfizer-sponsored protocol 945-421-291. The conclusion presented in this article's abstract was that "[t]his small, randomized clinical trial comparing the prophylactic efficacy of adjunctive gabapentin to placebo suggests that, despite lack of acute efficacy, treatment with gabapentin might provide some benefit on the long-term outcome of bipolar disorder."

166. The Vieta article falsely reported the results of 945-421-291 as positive when the results were in fact negative. The authors falsely stated that “all statistical analyses were done by intention to treat [ITT],” when in fact they were done on a highly selective sub-population (the per protocol or PP group). When the ITT population was analyzed—as required by the protocol—it was clear even to Pfizer that it was a failed trial with the conclusion that “[t]he primary efficacy parameter did not show statistically significant differences between gabapentin and placebo.” Culling out or “cherry picking” the PP subpopulation in lieu of the ITT population in order to make the trial appear positive is dishonest. Pfizer’s behavior was, according to Dr. Barkin, “unethical and a far cry from demonstrating efficacy through the randomized ITT population.” Given the compromise of randomization and introduction of biases, through the creation of a subgroup, Dr. Barkin doubts whether this study can even be considered Level 1 Evidence.

Ex. 021, Barkin Report at 9 quoting from Vieta et al. (Ex. 137) and 945-291.pdf (Ex. 015) (internal citations omitted.)

167. The Vieta Article contains the

Ex. 117, Dickersin Report at 26.

following biases: (a) Selective outcome reporting:

Outcome reported was not primary or secondary outcome;

(b) Selective analysis: Analysis excluded approximately half of patients randomized, including for reasons such as

“lack of efficacy” (though article claimed ITT [Intention

To Treat]); (c) Misrepresentation of data: Research report

findings do not agree with publication; (d) Spin:

Discussed the lack of statistical significance of secondary

outcomes (patient-rated) to support significance found

with primary outcome (physician-rated) as indication of

longer-term benefits reflected by the primary outcome; (e)

Design bias: Primary outcome variable based on physician

report: change at 12 months in Clinical Global Impression

Scale, a physician-rating instrument; (f) Design bias:

Opportunity for manipulation of randomization: the

randomization was generated by sponsor prior to use of

SAS software. No attempt to conceal allocation was

mentioned.

168. “The results of the intent-to-treat analysis were not published. However, the results of the per protocol analysis were published in 2006 as if they were the results from the intent-to-treat analysis. This article claims (falsely) that ‘all analyses were done by intention to treat.’”

Ex. 023, Abramson Report ¶138 quoting from Vieta et al. (Ex. 137)

169. “[A]nalyzes on ‘per protocol’ populations, created after randomization, are fraught with potential biases. Moreover, the reader of this article [the Vieta article] could not have known that these results were from a ‘per protocol’ population. Since readers only could have known this if they had access to the research report that was controlled by Defendants, Defendants thus subverted physicians’ ability to function as learned intermediaries.”

Ex. 023, Abramson Report ¶138.

170. “The creation of a subgroup is troubling however as the PP [per protocol] group is a small subselection of the original ITT group. Moreover, the exclusion of patients after randomization can defeat the very purpose of randomization, thus introducing biases.”

Ex. 021, Barkin Report at 9.

#### **D. Results of Fraudulent Marketing Campaign**

##### **1. Class-wide Prescriptions**

171. According to IMS NDTI data, psychiatrists were not “actively prescribing Neurontin for any on- or off-label indication until the fourth quarter of 1995. Subsequent to 1995, off-label uses of Neurontin by psychiatrists increase[ed] dramatically.” Neurontin was “predominantly prescribed by this specialty for the off-label treatment of bipolar and other psychiatric illness.”

Ex. 138, Revised Conti Declaration ¶43.

172. According to IMS NDTI data, between 1994 and 2007, psychiatrists’ quarterly use of Neurontin for on-label indications did not surpass 16,000 uses per quarter. In contrast, psychiatrists’ quarterly use of Neurontin for bipolar and other mood disorders peaked at 246,714 uses in the second quarter of 2002.

Ex. 138, Revised Conti Declaration, Figure 19 (revised).

173. The number of psychiatrists prescribing Neurontin grew from “approximately 100-200 in 1994-1995 to approximately 16,000 per month in 2002.”

Ex. 138, Revised Conti Declaration ¶38.

174. According to IMS NDTI data, between 1994 and 2007, there was virtually no growth in the number of Neurontin on-label uses.

Ex. 138, Revised Conti Declaration, Figure 19 (revised).

175. Only 141 psychiatrists prescribed Neurontin in March 1995, accounting for only 2.7% of all physicians who prescribed Neurontin in March 1995.

Ex. 139, WLC\_CBU\_132108.

176. Bipolar disorder accounted for only 2.1% of Neurontin uses in March and April 1995. Ex. 139, WLC\_CBU\_132108.

177. According to the Neurontin 1997 Situation Analysis, dated May 29, 1996, “Neurontin drug use for bipolar disorder is not significant. It represented less than 1% (3/96 MAT) of the uses within the AED class...the use of Neurontin in this area is not expected to increase in the short term. This was confirmed by market research conducted at the APA annual meeting in New York in April 1996, where over a hundred psychiatrists were surveyed. They indicated that at the present time their use of Neurontin is not significant and that they do not expect it to increase in the near future.” Ex. 140, WLC\_CBU\_090238

178. The number of new prescriptions by psychiatrists “grew from about 4,000 per month in 1996 to a peak of roughly 120,000 per month in 2001.” Ex. 138, Revised Conti Declaration ¶33.

179. On July 19, 1996, John Rizzo sent a memorandum to numerous Parke-Davis employees with the subject “Neurontin Background For Monotherapy Positioning Study.” In this memorandum, John Rizzo wrote: “Currently, [psychiatrists] write very little anticonvulsants except Depakote.” Ex. 141, WLC\_FRANKLIN\_0000032164 at 0000032167.

180. In May 1997, data from Scott-Levin's PDDA, presented as part of a Neurontin Quarterly Brand Review, showed that there were only 12,000 uses of Neurontin for bipolar disorder representing only 1.0% of Neurontin's overall drug use.

Ex. 076, Pfizer\_AFannon\_0008581 at 0008586 and 0008606.

181. In February 1999, according to data presented as part of Neurontin's Quarterly Brand Review, there were approximately 7,300 details to psychiatrists "despite their being no FDA-approved indication for any psychiatric illness or symptoms."

Ex. 076, Pfizer\_AFannon\_0008581 at 0008588; Ex. 023, Abramson Report ¶292.

182. In February 1999, data from Scott-Levin's PDDA, presented as part of a Neurontin Quarterly Brand Review, showed that there were 275,000 uses of Neurontin for bipolar disorder representing a 23-fold increase from May 1997. By February 1999, use of Neurontin for bipolar disorder represented 13.3% of Neurontin's overall drug use.

Ex. 076, Pfizer\_AFannon\_0008581 at 0008586 and 0008606.

183. According to the Neurontin 2001 Situation Analysis, dated June 28, 2000, "Neurontin's use in bipolar disorder has increased by 1700% from Sept 97 to Sept 99."

Ex. 142, Pfizer\_JMarino\_0002350 at 0002368.

184. Between the third quarter of 1997 and the third quarter of 1999, detail contacts to psychiatrists went from 541 (representing 3.12% of all detail contacts) to 8,393 (representing 38.27% of all detail contacts).

Ex. 056, IMS Health

185. By September 2001, bipolar disorder and depression accounted for 57% of Neurontin's use for psychiatric indications. Psychiatric Disorders and Pain States combined for 82% of Neurontin's use in September 2001.

Ex. 143, Pfizer\_AFannon\_0011044

186. On June 6, 2002, Dr. Larry Alphas (Director Clinical Development, CNS) gave a presentation to Steve Ryder, a senior scientist at Pfizer and member of the clinical development team. In this presentation, Dr. Alphas noted that, despite the lack of any psychiatric indication, Neurontin use for all psychiatric disorders represented over 35% of all Neurontin use.

Ex. 144, Pfizer\_AFannon\_0011317;  
Ex. 145, Pfizer\_AFannon\_0011315

187. In this same presentation, Dr. Alphas noted that the "[m]arket growth for Neurontin is slowing" and that "[p]ayers are moving towards 'evidence based medicine.' Some psychiatrist opinion leaders refer to gabapentin as 'the drug that does not work.'"

Ex. 144, Pfizer\_AFannon\_0011317;  
Ex. 145, Pfizer\_AFannon\_0011315

188. In March 2008, the *Journal of Psychiatric Practice* published an article authored by Dr. Timothy Carey entitled: “Gabapentin in the Treatment of Mental Illness: The Echo Chamber of the Case Series.”

Ex. 146, TS Carey, JW Williams, JM Oldham et al. Gabapentin in the Treatment of Mental Illness: The Echo Chamber of the Case Series. *Journal of Psychiatric Practice*, 2007;14(suppl 1):15-27 (“Carey Article”).

189. This article reports on 29 studies related to gabapentin and bipolar disorder “published between 1997 and 2007, with the greatest number of articles published in 1998 and 1999.” These 29 publications included 15 uncontrolled case series and 6 single case reports.

Ex. 146, Carey Article; Ex. 023, Abramson Report ¶131; Ex. 021, Barkin Report at 9-10.

190. Carey et al. noted that “[d]espite the generally weak study design in the identified populations, the authors of the articles often commented on the promising nature of gabapentin therapy for bipolar disorder” and that “randomized trials in heterogeneous populations demonstrated little if any evidence of such efficacy.”

Ex. 146, Carey Article; Ex. 023, Abramson Report ¶131; Ex. 021, Barkin Report at 9-10.

191. Carey et al. concluded that “[t]he number of reports and their distribution in many different journals created a type of ‘echo chamber’ effect, through which the sheer number of publications and citations may give legitimacy to the practice of using gabapentin for bipolar disorder.”

Ex. 146, Carey Article; Ex. 023, Abramson Report ¶131; Ex. 021, Barkin Report at 9-10.

192. Carey et al. further concluded that a “cursory examination of the literature identified in this review reveals repeated references to a promising new treatment. Our more detailed examination demonstrates multiple poor quality observational studies which collectively represent an echo chamber encouraging utilization of the medication based on minimal evidence. The literature on gabapentin represents a cautionary tale for industry, researchers, and journal editors.”

2. Individual Class Representatives

a. *Gary L. Varnam*

193. Gary Varnam suffers from bipolar disorder and received numerous prescriptions for Neurontin over a period of more than three years. Mr. Varnam has testified that Neurontin was “completely ineffective in treating my bipolar disorder” and “gave me no benefit.” He also testified that he had asked to be “switched” off of Neurontin.

194. Mr. Varnam was first prescribed Neurontin by Dr. John Arness in February 2001.

Ex. 146, Carey Article; Ex. 023, Abramson Report ¶131; Ex. 021, Barkin Report at 9-10.

Ex. 147, Transcript of Deposition of Gary Varnam on February 7, 2008 at 28 (lines 2-22), 52.

Memorandum of Law in Support of Defendants' Motion for Summary Judgment

195. In September 1999, Dr. Arness discussed Neurontin's use in psychiatric uses with Laurie Winslow, a Parke-Davis sales representative and area business manager located in Maine.

Ex. 376, Arness Merlin; Ex. E, SH\_0064555.0017771.

196. Dr. Arness received a Medical Information Request letter from Parke-Davis concerning "treatment of bipolar depression and mood disorder."

Ex. 376, Arness Merlin

197. The letter Dr. Arness received was a letter which contained a false, misleading, inaccurate and omissive summary of the available evidence of Neurontin for bipolar and other mood disorders. The letter omits any reference to the FDA's finding of depression, with or without suicidal ideation, associated with Neurontin use, Parke-Davis's own internally completed Pande study, which showed the placebo was *superior* to gabapentin as a treatment for bipolar disorder, or the negative results of the Frye and Guille studies. In place of the Level-1 evidence that was known to the company, the letter discusses favorable unscientific and anecdotal evidence, including the misleading and deceptive Dimond article, which made several unsubstantiated claims that have no scientific or clinical value, and which omitted any reference to the evidence that Neurontin increases the risk of depression with or without suicidal ideation.

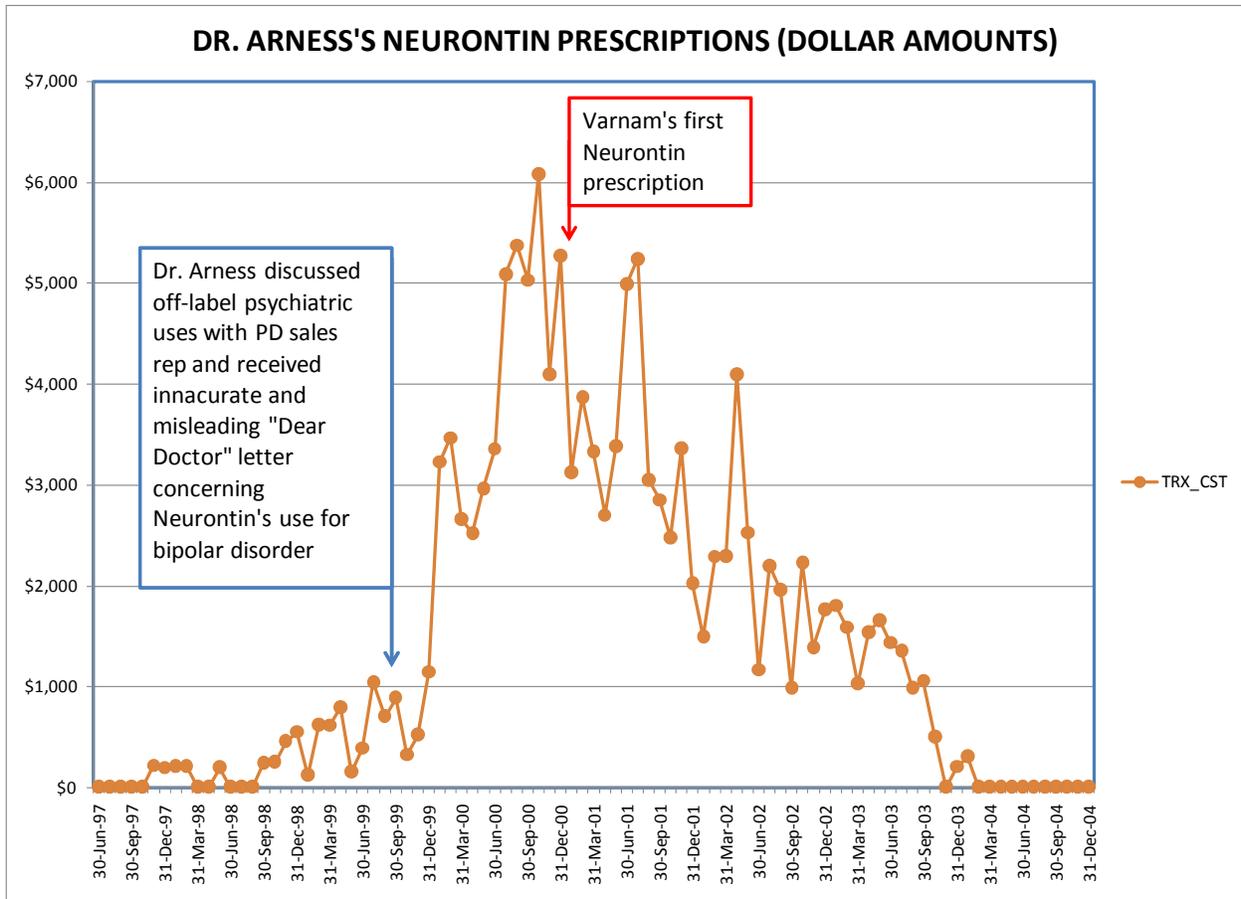
Ex. 086, 0900000180003ebd.doc;  
Ex. 005, Furberg Report, at 17-18.

198. This letter was the most widely distributed letter on bipolar and other mood disorders, distributed to more than 5,500 physicians, mostly psychiatrists, in the United States.

Ex. 085, Merlin database.

199. Following his receipt of this letter, Ex. 149, Arness Wolters Kluwer.

Dr. Arness's prescriptions of Neurontin skyrocketed.



200. In the two years prior to the letter, the cost of Dr. Arness's Neurontin prescriptions averaged only \$289 per month. In the two years after he received the "Dear Doctor" letter, the average cost of Dr. Arness's Neurontin prescriptions soared to \$3486 per month, a 1100% increase. Varnam's initial Neurontin prescription occurred precisely at the peak of this massive surge in prescriptions that occurred after Dr. Arness received the inaccurate and misleading "Dear Doctor" letter. In total, Dr. Arness wrote more than \$83,600 in Neurontin prescriptions after having been detailed on Neurontin.

Ex. 149, Arness Wolters Kluwer.

201. Gary Varnam was subsequently treated by Dr. Beverly Grimm, who took him off the drug. Dr. Grimm began prescribing in late 1999, shortly after Dr. Arness received the false and misleading "Dear Doctor" letter.

Ex. 147, Transcript of Deposition of Gary Varnam on February 7, 2008 at 21 (lines 4-8), Ex. 551, Grimm Wolters Kluwer.

b. *Jan Frank Wityk*

202. Jan Wityk suffers from bipolar disorder, and her psychiatric symptoms included bouts of suicidal thoughts. Ms. Wityk took Neurontin for several years, but she "never got better." The only reason she took Neurontin was to be a compliant patient.

Ex. 150, JanFrankWityk-8.pdf; Ex. 151, Transcript of Deposition of Jan Frank Wityk on February 5, 2008, at 147 (lines 4), 178-79.

203. In December 1997, Jan Wityk was examined by Dr. Nagaveni Ragothaman, who suggested various drugs as potential treatment, including Zoloft and Ativan. Neurontin was not one the drugs discussed, and as of that point in time, Dr. Ragothaman had never prescribed Neurontin.

Ex. 150, JanFrankWityk-8.pdf; Ex. 653, Ragothaman Wolters Kluwer.

204. Dr. Ragothaman was detailed at least three times by Parke-Davis in 1999. On February 4, 1999, Dr. Ragothaman discussed Neurontin's use in "Bi-Polar" with Parke-Davis sales representative Steve Alberti. On February 11, 1999, as a result of this conversation, a copy of the very same fraudulent "Dear Doctor" letter that Dr. Arness received was mailed to Dr. Ragothaman.

Ex. 679, Ragothaman Merlin; Ex. 086, 0900000180003ebd.doc; Ex. 005, Furberg Report, at 17-18.

205. Less than one week later, Dr. Ragothaman decided to recommend Neurontin to Ms. Wityk, despite never having prescribed the drug before. One month later, on March 17, 1999, Dr. Ragothaman wrote her very first Neurontin prescription ever—to none other than Ms. Wityk.

Ex. 152, JanFrankWityk-9.pdf; Ex. 653, Ragothaman Wolters Kluwer.

206. Dr. Ragothaman discussed the use of Neurontin for “Mood Disorder” with Steve Alberti again in June 1999. In September 1999, Dr. Ragothaman had yet another discussion about Neurontin’s use for bipolar with a Parke-Davis sales representative, this time with Roger Williams, who noted in an internal record of the sales call that she “desires data on the clinical efficacy of Neurontin for Bi-Polar Disorder.” Once again, Dr. Ragothaman received the “Dear Doctor” letter that she had received earlier, which made no mention of the Frye and Guille studies that were known to Parke-Davis by that time.

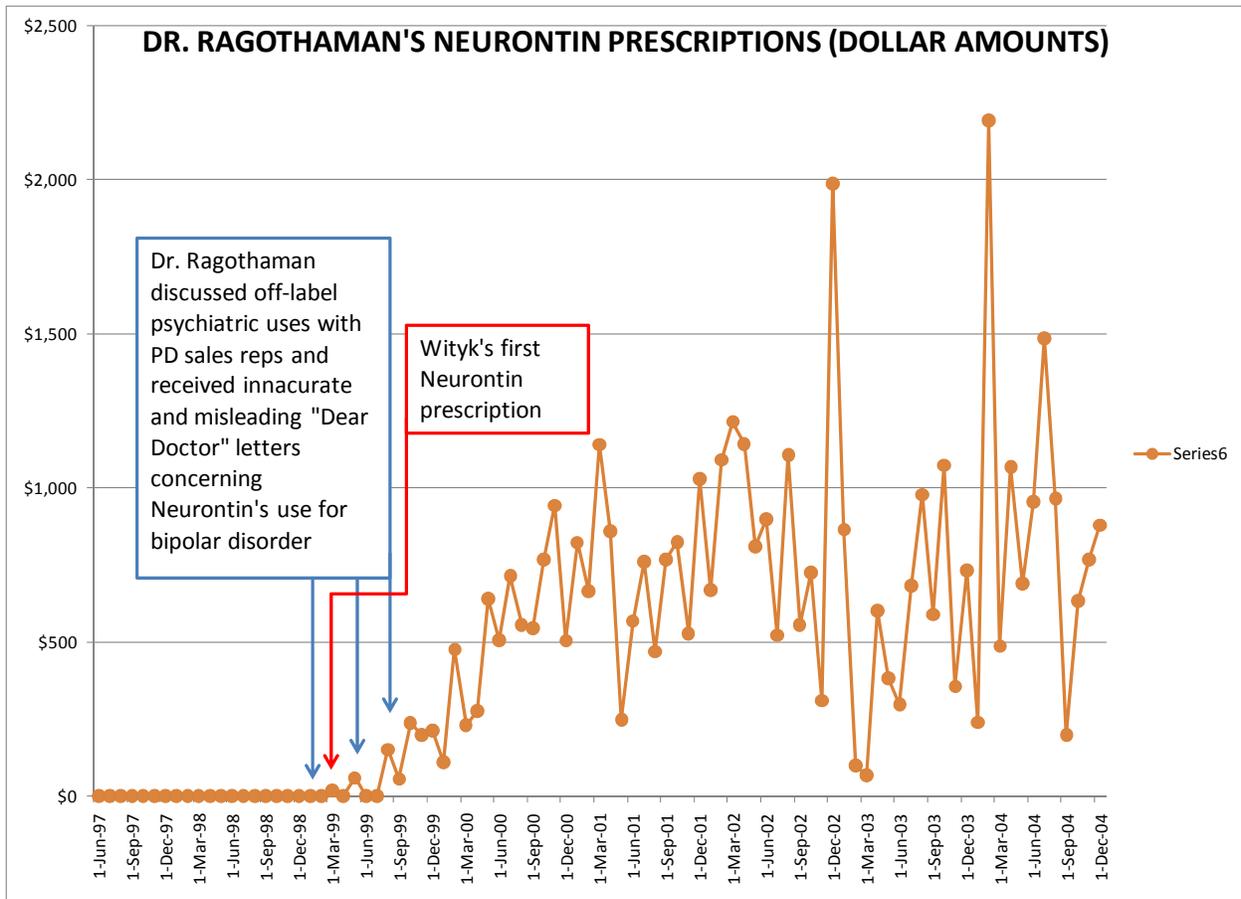
Ex. 679, Ragothaman Merlin; Ex. 086, 0900000180003ebd.doc.

207. This letter was the most widely distributed letter on bipolar, distributed to more than 5,500 physicians, mostly psychiatrists, in the United States.

Ex. 085, Merlin database.

208. Following her receipt of this letter, Dr. Ragothaman went from a non-prescriber of Neurontin to a steady prescriber, and her prescriptions of Neurontin skyrocketed.

Ex. 653, Ragothaman Wolters Kluwer.



209. Although she had never written a single Neurontin prescription prior to being detailed by Parke-Davis, after being detailing and receiving misleading “Dear Doctor” letters, Dr. Ragothaman went on to write a total of \$41,302 of Neurontin prescriptions. This included Jan Wityk’s prescriptions to treat bipolar disorder; Jan Wityk received the very first Neurontin prescription written by Dr. Ragothaman.

Ex. 653, Ragothaman Wolters Kluwer; compare JanFrankWityk-9.pdf. (Ex. 152) with Wolters Kluwer.

210. Ms. Wityk was subsequently treated by Dr. Jerrold Gray, who continued to prescribe Neurontin to her and increased her daily dosage. Ms. Wityk testified that Dr. Gray had admitted that he routinely discussed Neurontin's use for bipolar with Pfizer sales reps:

At the time I began starting to see Dr. Gray, he was gung-hoe [sic] on Neurontin, telling me that one of the drugs that I was currently on was old school, that the drug reps were pleased with the off-label success of Neurontin for people with bipolar disorder like myself. And that I should give it some consideration and thought to changing medications as the drug representatives had seen amazing results.

211. Ms. Wityk testified that she informed Dr. Gray that Neurontin was not providing a meaningful benefit, and that Dr. Gray's response, based on conversations with Parke-Davis sales representatives, was to increase the daily dose of Neurontin. Ms. Wityk testified:

I know that during one of my very first visits with Dr. Gray, he did relay to me that he had discussed the fact that I was not getting better on the Neurontin with the drug, specifically with the drug representative who told him that they just needed to continue to titrate me to a higher dose until I was receiving benefit. That I just wasn't on a high enough dose yet.

In September 2001, Dr. Gray agreed to discontinue prescribing Neurontin for Ms. Wityk. It is Ms. Wityk's testimony that "Neurontin was ineffective for the entire time that [she] was on it."

Ex. 151, Transcript of Deposition of Jan Frank Wityk on February 5, 2008, at 57 (lines 3-13) (emphasis added).

Ex. 661, JanFrankWityk-13.pdf; Ex. 151, See Transcript of Deposition of Jan Frank Wityk on February 5, 2008, at 145 (lines 12-20) and at 192.

## II. FACTS RELATED TO PAIN

**A. Neurontin's Inefficacy For Pain**

1. Gorson—Painful Diabetic Neuropathy Trial

212. In January 1996, Parke-Davis finalized the protocol for a double-blind placebo controlled trial studying Neurontin in patients with painful diabetic neuropathy, the first clinical trial studying Neurontin's use in neuropathic pain. The study was conducted by Dr. Gorson of St. Elizabeth's Hospital in Boston.

Ex. 013,  
WLC\_FRANKLIN\_0000100239

213. By September 1996, Parke-Davis was aware that the results of Dr. Gorson's study were negative as two of the pain measures, results were "similar for gabapentin and placebo." This led Dr. Gorson to conclude and report to Parke-Davis that "Gabapentin, at a dose of 900 mg/day, is probably no more effective than placebo in the treatment of painful diabetic neuropathy."

Ex. 111,  
WLC\_FRANKLIN\_0000100273;  
Ex. 148,  
WLC\_FRANKLIN\_0000100266;  
Ex. 153,  
WLC\_FRANKLIN\_0000100264;  
Ex. 154,  
WLC\_FRANKLIN\_0000100271;  
Ex. 155,  
WLC\_FRANKLIN\_0000100272.

2. Backonja—Painful Diabetic Neuropathy Trial (945-210)

214. On April 24, 1996 Defendants' protocol 945-210 entitled "A Double-Blind Placebo-Controlled Trial of Gabapentin For Treatment of Painful Diabetic Neuropathy" was finalized. 945-210 was the second trial studying Neurontin's use in neuropathic pain

Ex. 156, Research Report No. 720-03908, protocol 945-210; 720-03908.pdf produced by Defendants as part of Research Reports.

outside of postherpetic neuralgia (PHN). The periods covered were: July 2, 1996 through March 20, 1997.

215. Plaintiff's expert biostatistician, Nicholas P. Jewell, Ph.D., reviewed unpublished data relating to the study and found that Study 945-210 "provides no basis of any clinical efficacy of gabapentin over placebo in reducing pain."

Ex. 157, Jewell Report at 1.

216. Although superficially favorable, the trial had a biased design that resulted in unblinding of results. Plaintiff's expert John Abramson, M.D. found, "[T]he forced titration design of study 945-210 created potential bias in favor of Neurontin as a result of the increased prevalence of CNS-related adverse events... side effects which results in the blind being broken for many of the patients associated with pain relief. Dr. Abramson found: "for the remaining patients, still blinded to treatment allocation, Neurontin failed to provide significant relief from the pain of diabetic neuropathy."

Ex. 023, Abramson Report ¶¶ 152, 162.

217. Defendants had known about Neurontin's potential for unblinding patients since April 10, 1996, three months before study 945-210 was commenced. By June 18, 1998, Parke-Davis was aware of the possibility that the results of 945-210 were corrupted

Ex. 158, Miller RG, Moore D, Young LA, et al., Placebo-controlled trial of gabapentin in patients with amyotrophic lateral sclerosis. *Neurology*, 1996;47:1383-88; Ex. 159, <http://www.neurology.org/content/vol47/issue6/>; Ex. 023, Abramson Report ¶157 (internal citation omitted); Ex. 160,

because of unblinding. By July 1, 1998, Parke-Davis's own pain experts conceded "that patients with more severe AEs [adverse events] tend to believe that they are on a study drug (which would probably be a good guess) and therefore tend to have better efficacy data, thus unblinding and corrupting the study."

PFIZER\_LLAMOREAUX\_000905  
8; Ex. 161,  
Pfizer\_TMF\_CRF\_061889

3. Reckless—Painful Diabetic Neuropathy Trial (945-224)

218. Defendants' protocol 945-224 entitled "A Double-Blind Placebo-Controlled Trial With 3 Doses of Gabapentin for Treatment of Painful Diabetic Peripheral Neuropathy" was finalized. This was the third clinical trial studying Neurontin's use in neuropathic pain outside of postherpetic neuralgia (PHN). The periods covered were May 29, 1998 through September 7, 1999.

Ex. 162, Research Report No. 720-04130; 720-04130.pdf produced by Defendants.

219. Protocol 945-224 showed "no beneficial effect on primary or secondary outcomes of any dose of gabapentin from 600-2400 mg/day for painful DPN."

Ex. 163, Perry Report: Appendix - Gabapentin Project Study detail summaries, Study No. 6 at 1.

220. Protocol 945-224 "showed no dose-dependent efficacy for gabapentin (indeed no efficacy whatsoever for the primary outcome) but at least a strong suggestion of dose-dependent toxicity. It was a much larger trial than that of Backonja

Ex. 163, Perry Report at 70.

[protocol 945-210] and therefore more definitive.”

221. The Defendants were aware of the negative results of 945-224, potentially as early as October 26, 1999, when the randomization code was broken, but certainly no later than February 7, 2000, when the research report for protocol 945-224 was issued. The research report states: “Compared to placebo, none of the gabapentin groups was shown to be effective for the treatment of painful diabetic neuropathy.

Ex. 162, Research Report No. 720-04130; Ex. 164, Pfizer\_LeslieTive\_00020949; Ex. 117, Dickersin Report at 33.

4. Morello—Painful Diabetic Neuropathy Trial

222. By September 1999, Parke-Davis was aware of the negative results of the Morello study which indicated “no significant difference between gabapentin and amitriptyline.” This was the fourth study of Neurontin for neuropathic pain outside of PHN. The Defendants recognized that the Morello study was “negative.”

Ex. 165, Morello, CM, Leckband SG, Stoner CP, et al. Randomized Double-blind Study Comparing the Efficacy of Gabapentin With Amitriptyline on Diabetic Peripheral Neuropathy Pain, Arch Intern Med. 1999;159:1931-1937 (“Morello Article”); Ex. 166, PFIZER\_RGLANZMAN\_0040034

5. Serpell—Neuropathic Pain Trial (945-306)

223. On February 3, 1999, Defendants’ finalized protocol 945-306 entitled: “A Double Blind Placebo Controlled Trial of Gabapentin for the Treatment of Patients Exhibiting Symptoms of Neuropathic Pain.” This clinical trial was the 5th trial studying Neurontin’s

Ex. 167, Protocol 945-430-306, Research Report No. 430-00125; 430-00125.pdf produced by Defendants as part of Neurontin Research Reports (“Protocol 945-306”).

use in neuropathic pain outside of postherpetic neuralgia (PHN). Protocol 945-306 covered the periods June 17, 1999 through February 8, 2000.

224. By May 5, 2000, Defendants were aware of the negative results for protocol 945-306.

Ex. 167, Protocol 945-306 at 22 (emphasis added).

According to the internal research report for protocol 945-306, the study failed to show a statistically significant p-value, indicating that, for the primary endpoint, Neurontin *was no more effective* than placebo. This was the 5th negative study of Neurontin for neuropathic pain outside of strictly PHN.

6. POPP—Neuropathic Pain Trial (945-271)

225. By no later than September 6, 2001, Defendants were aware of the negative results of research protocol 945-271 (“POPP”) entitled: “Gabapentin vs.

Ex. 168, Pfizer\_LCastro\_0043325;  
Ex. 169, Pfizer\_LCastro\_0027113;  
Ex. 170,  
PFIZER\_LKNAPP\_0021650

Placebo in Patients with Neuropathic Pain. A Randomized, Double-Blind, Cross-Over, Multi-Center Study in the Nordic Area.” The efficacy results were that “gabapentin did not statistically significantly reduce Mean Pain Intensity Score compared with placebo.” POPP included a substudy to examine the effects of gabapentin on hyperalgesia an allodynia. The results of the substudy were that there was “no difference between placebo and

gabapentin.” This was the 6th negative clinical trial studying Neurontin’s use for neuropathic pain outside of PHN.

226. On September 13, 2001, Pfizer began referring to 945-271 as “the negative POPP study,” and admitted that there was “an underlying negative halo about Neurontin’s efficacy.”

Ex. 119,  
PFIZER\_RGLANZMAN\_0134417

7. FDA’s Rejection of Neuropathic Pain Indication

227. On June 6, 2001, Pfizer filed a supplemental new drug application (sNDA) seeking approval to market Neurontin as a treatment for neuropathic pain. At the time it filed the sNDA, Pfizer knew that the FDA would not approve the sNDA either for a broad neuropathic pain indication, especially in areas where there were no studies, or where the company purportedly had one positive study. The FDA informed Pfizer that the application would be “refused to file,” meaning that it was obvious the application would not be approved. The FDA did, however, offer to have the application reviewed by an Advisory Committee of outside pain experts.

Ex. 171, Pfizer\_Lknapp\_0047459;  
Ex. 172,  
PFIZER\_LCASTRO\_0008052; Ex.  
173, PFIZER\_MPIERCE\_0000049;  
Ex. 174,  
PFIZER\_AGARRITY\_0002516;  
Ex. 175,  
PFIZER\_LKNAPP\_0050487.

228. Based on the Defendants’ expert consultants meeting at Crowne Plaza, Pfizer’s marketing

Ex. 176,  
PFIZER\_LKNAPP\_0023057; Ex.  
177, PFIZER\_LCASTRO\_0008362

team leader concluded that it would be in Pfizer's "best interest" to "avoid an Advisory Committee [] review" of the neuropathic pain data. Accordingly, on January 14, 2002, Pfizer narrowed its neuropathic pain sNDA to seek only the narrow indication of postherpetic neuralgia.

8. Multiple Negative Nociceptive Trials

229. Defendants conducted multiple DBRCTs studying Neurontin for the treatment of nociceptive pain. All of these trials were negative. The results were never published. In 1999, Defendants completed protocol number 1032-001 entitled: "A Single-Dose, Double-Blind, Placebo-Controlled, Comparative Efficacy Study of Gabapentin Combination With Naproxen Sodium in Patients With Postoperative Dental Pain." The results of 1032-001 were negative, as Neurontin failed to outperform placebo, indicating that it was ineffective for the treatment for nociceptive pain. In 2000, Defendants completed protocol 1035-001 and an addendum study entitled "A Single-Dose, Double-Blind, Placebo-Controlled, Comparative Efficacy Study of Gabapentin and Hydrocodone, Alone or in Combination, in Patients with Postoperative Dental Pain." The results of both 1035-001 and the addendum were negative, as

Ex. 117, Dickersin Report at 27-29; Ex. 663, 720-04378.pdf at 1-65; Ex. 664, 720-04483\_(Official).pdf at 1-41; Ex. 665, 720-04479.pdf at 1-78; Ex. 666, 720-04455.pdf at 1-54; Ex. 667, 720-04471.pdf at 1-58.

Neurontin failed to outperform placebo, again indicating that Neurontin was an ineffective treatment for nociceptive pain. In 2000, Defendants also completed protocol 1032-002 entitled "A 4-Week, Randomized, Double-Blind, Placebo- and Positive-Controlled, Parallel-Group, Multicenter Study of Gabapentin in Combination With Naproxen Sodium in Patients With Acute Osteoarthritis of the Knee." The results of 1032-002 were similarly negative, as Neurontin failed to outperform placebo in relieving pain, further indicating that Neurontin was an ineffective treatment for nociceptive pain. In August 2000, Defendants completed yet another protocol, 1035-002, entitled "A Single-Dose, Double-Blind, Placebo-Controlled, Comparative Efficacy Study of Gabapentin and Hydrocodone Combinations in Patients With Postoperative Pain Following Major Orthopedic Surgery." As with the other trials, the results of 1035-002 were negative, as Neurontin did not outperform placebo, nor did the addition of Neurontin to hydrocodone outperform hydrocodone alone, further indicating that Neurontin was not an effective treatment for nociceptive pain.

9. Defendants' Pain Experts Concluded that Neurontin is Ineffective for Pain

230. On September 6, 2001 Pfizer held a consultants meeting at the Crowne Plaza hotel in Ann Arbor, Michigan. In attendance were numerous Pfizer employees, Pfizer's paid "pain experts" Mitchell Max, Robert Dworkin and Gary Bennett and Paul Leber, the former head of the Division of Neuropharmacologic Drug Products at the FDA. Pfizer held the meeting to discuss the evidence that supported Neurontin's efficacy for Neuropathic pain and whether or not to seek FDA approval for a neuropathic pain indication Ex. 178, Pfizer\_LKnapp\_0050385.

231. After all the evidence was presented, Defendants' experts concluded that "the evidence is not convincing to support a broad neuropathic pain claim." Ex. 178, Pfizer\_LKnapp\_0050385.

232. The presentation and discussion at the Crowne Plaza meeting included data from several clinical trials that had been concealed from physicians and would remain so for years. This data included the negative results of 945-224, the fact that the claimed statistical significance of 945-306 was "predominantly the result of the PHN patients," and the "negative" results of 945-271 ( the POPP study). Once these results were presented at the meeting, Dr. Max [Defendants' retained Ex. 178, Pfizer\_LKnapp\_0050385.

pain expert] commented “you’re done.”

233. Defendants’ summary of the Crowne Plaza consultants meeting admitted: “Importantly, gabapentin is not effective in non-neuropathic models of pain.”

Ex. 178, Pfizer\_LKKnapp\_0050385.

234. A similar negative opinion of Neurontin was shared by the investigators for the POPP study, who informed Pfizer that “Neurontin may be a drug for overall ‘well-being’ and not NeP [neuropathic pain],” and that even under best case circumstances, Neurontin’s efficacy was only “slight.”

Ex. 119,  
PFIZER\_RGLANZMAN\_0134417

235. On July 2, 2002, Defendants consulted with two pain experts concerning the differentiation of new compounds for treating pain. Once again, Pfizer was informed that the “success of gabapentin is not due to its efficacy, it is less efficacious than Tricyclic antidepressants (TCA)...”

Ex. 651,  
PFIZER\_LKNAPP\_0070537

10. Recent Clinical Trials Have Further Established Neurontin’s Inefficacy for Neuropathic Pain

236. On March 13, 2005, the *New England Journal of Medicine* (NEJM) published an article authored by Dr. Ian Gilron et al. entitled: “Morphine, Gabapentin, or Their Combination for Neuropathic Pain”

Ex. 179, Gilron I, Bailey JM, Dongsheng T, et al., Morphine, Gabapentin, or Their Combination for Neuropathic Pain, *N Engl J Med*, 2005;352:1324-34.

and reported that in contrast to morphine, “gabapentin did not produce significantly better results than placebo with regard to the primary outcome of this trial.”

237. Moreover, the current issue (April 2009) of the journal *Pain* contains an article entitled “A randomized, placebo-controlled trial of oxycodone and of gabapentin for acute pain in herpes zoster.” The authors report that in contrast to oxycodone, “gabapentin did not provide significantly greater pain relief than placebo” in this group of neuropathic pain patients.

Ex. 180, Dworkin RH, Barbano RL, Tying SK et al. A randomized, placebo-controlled trial of oxycodone and of gabapentin for acute pain in herpes zoster. *Pain*, 2009;142(3):209-217.

11. Plaintiffs’ Experts Establish that Neurontin is Ineffective for Pain

238. Dr. Thomas L. Perry undertook a “thorough and scientifically valid analysis of all relevant double blind randomized clinical trials (DBRCT).” Dr. Perry’s analysis included the results of suppressed clinical trials that were not available to other reviewers. As a result of his analysis, Dr. Perry concluded “Neurontin is not an effective drug for the treatment of Neuropathic pain.” Neurontin has “at best a clinically insignificant average effect on pain scores” that is “essentially clinically meaningless.”

Ex. 163, Perry Report at 1, 34.

239. “There is no reason to think that the other large DBRCT [involving Neurontin] were exempt

Ex. 163, Perry Report at 37-38 (emphasis in original).

from the effect observed by Dr. Jewell in the Backonja trial.” Therefore, even Dr. Perry’s analysis “**significantly exaggerates the apparent analgesic effects of the drug.**”

240. According to Defendants, the best evidence of Neurontin’s efficacy is the Backonja study, a forced titration trial in diabetic peripheral neuropathy. While the results appeared favorable, Dr. Jewell demonstrated that the apparent effects all occurred after potential unblinding, suggesting that patient bias rather than true pain relief explained the results. Ex. 157, Jewell Report at 14.

241. Dr. Perry also found that Neurontin is "completely ineffective for the treatment of non-neuropathic pain." According to Dr. Perry, Defendants' trials show "**uniformly and conclusively that gabapentin is not useful for acute pain.**" Ex. 163, Perry Report at 2, 50 (emphasis in original).

**B. Intent to Fraudulently Market Neurontin for Pain**

1. Defendants Plan to publish favorable anecdotal stories presented as scientific data to create “a drumbeat in the literature”

242. On November 9, 1994, Parke-Davis held a Neurontin Development Strategy Meeting to discuss a “strategy to defend Neurontin,” which included the development of “new indications.” Neurontin’s “commercial potential” for the new indications was Ex. 181, WLC\_CBU\_085826; Ex. 025, WLC\_CBU\_088767

discussed. Larry Perlow, M.D., Defendants' Vice-president of Portfolio Management-Marketing Operations received a copy of this memorandum.

243. On November 28, 1994, Larry Perlow met with Gary Mellick, an osteopathic doctor in Ohio, to discuss use of Neurontin in pain. After the meeting, Larry Perlow reviewed clinical trial data from the epilepsy trials and informed Dr. Mellick that there was no evidence that Neurontin improved pain. In fact, pain reports in the epilepsy trials were comparable between Neurontin and placebo and that there were reported cases of pain worsening with Neurontin treatment. According to an internal November 1994 Parke-Davis memo, “[w]hether Dr. Mellick is on to valid uses of Neurontin - remains to be seen - I think we are covering our tail in all cases - I keep making the case for our only area of promotion can be -Adjunctive Therapy” for current AED’s.”

Ex. 182,  
WLC\_FRANKLIN\_0000098352;  
Ex. 183,  
WLC\_FRANKLIN\_0000216306

244. At the Development Team Meeting held on January 17, 1995, the team discussed a “New Indication for Neurontin (pain).” Leslie Magnus-Miller stated that “[i]n order to pursue any formal program on this indication, we need to develop the rationale and

Ex. 027, WLC\_CBU\_088726

assemble preclinical/clinical data for a marketing assessment.”

245. On February 21, 1995, it was reported that the NPC [New Products Committee] supported the development of Neurontin for new indications and has asked for a formal proposal. John Boris was ordered to “discuss the marketing feasibility of new indications with [Elizabeth] Garofalo [Director of Clinical Research]/[Atul] Pande [Senior Director of Central Nervous System Worldwide Clinical Research] and make recommendations to [Ron] Martin [Vice President of Drug Development] by March 9 for the NPC meeting.”

Ex. 028, WLC\_CBU\_088721

246. On March 14, 1995, Lena Ulrich, a member of the Marketing Department, noted that Neurontin prescriptions had not increased during the last three months.

Ex. 031, WLC\_CBU\_088713

247. In March 1995, at a Core Marketing Team Meeting, it was noted that some preliminary qualitative research (focus groups) with Neurologists during the American Academy of Neurologists to explore additional off-label uses for neuropathic pain and migraine.

Ex. 184, WLC\_CBU\_100422

248. On March 31, 1995, Parke-Davis sent Dr. Mellick a check for \$750.

Ex. 185,  
WLC\_FRANKLIN\_0000090053;  
Ex. 186,  
WLC\_FRANKLIN\_0000090054  
Ex. 187,  
WLC\_FRANKLIN\_0000090221

249. On May 5, 1995, Larry Perlow congratulated Dr. Mellick on the acceptance of his manuscript concerning Reflex Sympathetic Dystrophy (RSD) and Neurontin.

250. In May 1995, a letter to the editor by Dr. Mellick, reporting on 9 anecdotal case reports of patients with RSD being treated with Neurontin, was published in the *Journal of Pain and Symptom Management*. According to Dr. Mellick, all patients received “good” or “excellent” pain relief from Neurontin. Dr. Mellick made no reference to the data from epilepsy trials showing comparable reports of pain between the Neurontin and placebo patients or cases where patient pain worsened under Neurontin, which he learned from Larry Perlow.

Ex. 188,  
WLC\_FRANKLIN\_0000035726

251. On July 24, 1995, the Marketing Planning Department issued a Marketing Assessment for Neurontin in neuropathic pain that included the recommendations of the NPC to conduct an exploratory study in neuropathic pain and to publish the results of the study only “if positive.”

Ex. 189,  
WLC\_FRANKLIN\_0000166608

252. The Marketing Assessment noted that neuropathic pain represented “an attractive commercial opportunity” for Neurontin, despite the lack of clinical data supporting the use the drug as a treatment for pain. The Marketing Assessment called for anecdotal data to be pooled and presented at pain conferences as scientific data by various pain specialists, including Drs. Gorson and Roper in Boston, Drs. Mann and Finkel in North Carolina, Dr. Rosner in New York, and Dr. Weismann in Georgia. The Marketing Assessment then called for “exploratory” clinical trials to be conducted at these same pain centers, with the results presented at pain conferences. The Marketing Assessment estimated that the revenue generated from the implementation of this publication strategy in pain could generate \$20 million to \$25 million a year by 1999. The Marketing Assessment made no reference to data from the epilepsy trials that showed cases of worsened pain while on Neurontin.

Ex. 189,  
WLC\_FRANKLIN\_0000166608

253. Parke-Davis signed an agreement with Dr. Gorson to conduct a clinical trial studying Neurontin for DPN (diabetic peripheral neuropathy). According to the contract, Dr. Gorson would received \$30,000 for the study in three installments, with the first

Ex. 190,  
WLC\_FRANKLIN\_0000100268

\$10,000 payment at study initiation, the second \$10,000 payment at patient completion, and the third \$10,000 payment at manuscript completion.

254. On August 11, 1995, Parke-Davis entered into a 4-month consulting agreement with Dr. Mellick, paying him \$5,000 in order to continue the “relationship” between Parke-Davis and Dr. Mellick.

Ex. 191,  
WLC\_FRANKLIN\_0000090214;  
Ex. 192,  
WLC\_FRANKLIN\_0000090215

255. In August 1995, Parke-Davis conducted interviews with 6 neurologists and 4 anesthesiologists who were selected as thought leaders in the field of pain. The survey found that physicians were only using Neurontin in the treatment of neuropathic pain “on a very limited basis.”

Ex. 193, WLC\_CBU\_095544

256. On September 28, 1995, Parke-Davis held an Advisory Board with physicians to discuss how to tap into the off-label market. The advisors were thought leaders mostly in the area of pain. The advisors suggested various tactics to communicate that Neurontin is an analgesic by using CMEs, conferences, symposia and publications that would create a “drumbeat in the literature.” The advisors also suggested techniques for “enriched enrollment,” a way to artificially make the study drug look more favorable by identifying “subjects who

Ex. 194, WLC\_CBU\_081517; Ex. 195, WLC\_CBU\_034813; Ex. 196, WLC\_FRANKLIN\_0000087284; Ex. 197, WLC\_FRANKLIN\_0000206531

respond best to the drug,” and then enrolling “only responders” in the clinical trial.

257. Several months later, on October 25, 1995, “[a] Decision Analysis meeting was held...to discuss indications for Neurontin related to the Life Cycle Plan. While initial analyses had favored bipolar disorders based on expected net present value (NPV) and the general location of the NPV distribution,” revised forecasts for neuropathic pain demonstrated that “it is difficult to distinguish between neuropathic pain and bipolar disorders on an expected NPV basis. Both bipolar disorders and neuropathic pain are recommended for inclusion in the Life Cycle Plan.”

Ex. 045, WLC\_CBU\_088676 at 088679.

258. On November 6, 1995, Parke-Davis convened a consultants meeting to discuss non-epileptic uses of Neurontin. Even though Parke-Davis lacked scientific evidence demonstrating Neurontin’s efficacy to treat pain, one of the purposes of the meeting was to explore “mechanisms by which we can disseminate the information which we currently have regarding the treatment of pain with gabapentin.”

Ex. 048, WLC\_FRANKLIN\_0000199668

259. One of the consultants, B.J. Wilder, proposed conducting CMEs where Neurontin was

Ex. 048, WLC\_FRANKLIN\_0000199668; Ex. 198, BJ\_Wilder\_Franklin Payment Register.pdf; Ex. 199,

discussed as a pain management drug. The CMEs could be sponsored by the Southern Clinical Neurological Society, an organization for which he was CME Director. B.J. Wilder would go on to earn well in excess of \$100,000 in speaking fees, many of them through events sponsored by the Southern Clinical Neurological Society using money received from Defendants.

BJ\_Wilder\_Betsy.pdf

2. Defendants' Intent to Suppress Negative Data

a. *Gorson Painful Diabetic Neuropathy Trial*

260. Dr. Gorson informed the Defendants that he was “planning to submit [a manuscript describing the results of his study] to *Neurology* as a first pass.”

Ex. 155,  
WLC\_FRANKLIN\_0000100272;  
Ex. 111,  
WLC\_FRANKLIN\_0000100273  
(emphasis in original).

261. The endpoints described in the abstract were: “mean change in McGill Pain Questionnaire (MPQ) scores, Visual Analogue Pain Scale (VAS), Present Pain Intensity (PPI) scale, and a global assessment of pain relief.”

Ex. 111,  
WLC\_FRANKLIN\_0000100273

262. The results described in the abstract of his manuscript were: “There was modest improvement in the MPQ score only...The mean change of the VAS and PPI and the number of patients who reported pain relief as moderate or excellent were similar for gabapentin and

Ex. 111,  
WLC\_FRANKLIN\_0000100273

placebo.”

263. The conclusion of Dr. Gorson’s abstract stated: “Gabapentin, at a dose of 900 mg/day, is probably no more effective than placebo in the treatment of painful diabetic neuropathy.”

Ex. 111,  
WLC\_FRANKLIN\_0000100273

264. On August 25, 1997, Phil Magistro, Associate Medical Director of NE CBU, and Leslie Magnus-Miller, M.D., Senior Director of Medical & Scientific Affairs, received Dr. Gorson’s manuscript entitled, “Low-Dose Gabapentin In The Treatment Of Painful Diabetic Neuropathy: A Placebo-Controlled, Double-Blind, Crossover Trial.”

Ex. 155,  
WLC\_FRANKLIN\_0000100272;  
Ex. 111,  
WLC\_FRANKLIN\_0000100273.

265. On January 7, 1998, Phil Magistro circulated an edited version of the August 25, 1997 Gorson manuscript to several Parke-Davis employees, including Oliver Brandicourt, Vice President of Product Planning, Elizabeth Garofalo and Leslie Magnus-Miller. In the cover memo, Phil Magistro spun Dr. Gorson’s findings: “While there were significant differences noted in the Neurontin treated group vs. baseline, a significant difference vs. placebo was noted only on the McGill Pain Questionnaire.”

Ex. 200,  
WLC\_FRANKLIN\_0000088375

266. In addition, the results described in

Ex. 200,  
WLC\_FRANKLIN\_0000088375

the abstract of the spun version of Dr. Gorson's manuscript were re-written to appear more favorable:

“There was substantial reduction in the mean MPQ, VAS and PPI scores in patients treated with gabapentin, but there was also significant improvement in the mean VAS score in patients treated with placebo. There was a mean reduction of 8.9 points in the MPQ score with gabapentin compared to 2.2 points with placebo (p = 0.03). The mean change of the VAS and PPI scores and the number of patients who reported pain relief as moderate or excellent were similar between gabapentin and placebo.”

267. The conclusion in the abstract of the spun version of the manuscript was: “Gabapentin may be effective in the treatment of painful diabetic neuropathy.”

268. On April 28, 1998 at the American Academy of Neurology annual meeting, the edited version of Dr. Gorson's manuscript, with its company-spun conclusions, was presented.

269. Gorson's study was not published as an original research article. Instead, it was published after the results of the Backonja study (945-210), as a

Ex. 200,  
WLC\_FRANKLIN\_00000088375

Ex. 201, Gorson KC, Schott C, Rand WM, Herman R, Ropper AH. Gabapentin In The Treatment Of Painful Diabetic Neuropathy: A Placebo-Controlled, Double-Blind, Crossover Trial. Neurology April, 1998; 50(Suppl.4): A103(Abstr. P02.055); Ex. 023, Abramson Report ¶145.

Ex. 202, Gorson KC, Schott C, Herman R, Ropper AH. Gabapentin In The Treatment Of Painful Diabetic Neuropathy: A Placebo Controlled, Double Blind, Crossover Trial. J Neurol Neurosurg Psychiatry. 1999

letter to the editor. Moreover, the misleading abstract was forwarded to Drugdex, a compendium of drug information which relies on drug companies to furnish them with abstracts of articles. Leslie Fierro, a Parke-Davis employee, was a member of the Drugdex “pharmaceutical advisory panel” and admitted that she “reviewed monograph information on Parke-Davis products that they were planning to put into their system.” Ms. Fierro has also admitted that “[i]f there was information missing from the [Drugdex] monograph I would provide [Drugdex] with the literature that I had available to me.”

b. *Backonja—Painful Diabetic Neuropathy Trial (945-210)*

270. Prior to the commencement of 945-210, Parke-Davis was aware that titration of Neurontin to doses resulting in higher side effects could result in an unblinding of patients on Neurontin, which would bias the results in the drug’s favor. Despite this knowledge, Defendants designed and utilized a forced titration up to dosages that greatly increased subjects’ side effects.

271. Prior to the publication of the results of 945-210, Parke-Davis employees admitted that “that patients with more severe AEs tend to believe that they are on a study drug (which would probably be a good

February; 66(2): 251–252 (“Gorson Letter”); Ex. 203, Drugdex Monograph; Ex. 204, Transcript of Deposition of Leslie Fierro taken on Oct. 4, 2002 in US ex rel. Franklin v. Pfizer et al., 96-11651-PBS (D. Mass.), at 115, 122-23.

Ex. 158, Miller RG, Moore D, Young LA, et al., Placebo-controlled trial of gabapentin in patients with amyotrophic lateral sclerosis. *Neurology*, 1996;47:1383-88; Ex. 159, <http://www.neurology.org/content/vol47/issue6/>; Ex. 023, Abramson Report ¶157 (internal citation omitted).

Ex. 161, Pfizer\_TMF\_CRF\_061889; Ex. 160, PFIZER\_LLAMOREAUX\_000905  
8

guess) and therefore tend to have better efficacy data, thus unblinding and corrupting the study.” For this reason, Parke-Davis recognized that additional analyses of efficacy and blind breaking data from the Backonja trial would be required. No such analysis can be found in Defendants’ documents.

272. The manuscript for 945-210 was actually written by Parke-Davis employees Judith Bammert Adams and Mark Aills, but the published article fails to list them as authors. Furthermore, the article went through two drafts before the listed authors ever saw it, and they only had ten days to provide Parke-Davis with comments. According to Dr. Abramson, it is clear “that the methodology used in the Backonja article to determine whether the experience of CNS-related adverse events had a significant effect on subjectively reported pain scores came directly from Defendants.” According to Drs. Jewell and Abramson, this methodology used in the published article was inadequate.

273. Even though Parke-Davis was aware of the results of the Gorson study when it drafted the Backonja manuscript, the published article makes no reference to the Gorson study or its negative results. To

Ex. 206, WLC\_CBU\_101546; Ex. 207, WLC\_FRANKLIN\_0000081976; Ex. 093, Backonja M, Beydoun A, Edwards KR, et al., Gabapentin for the symptomatic treatment of painful neuropathy inpatients with Diabetes Mellitus. *Journal of the American Medical Association*, 1998;280:1831-6 (“Backonja Article”); Ex. 023, Abramson Report ¶153.

Ex. 023, Abramson Report, ¶ 150.

the contrary, the Backonja manuscript denies the existence of the Gorson study and claims instead that “it was the first trial to evaluate gabapentin’s efficacy in [patients with painful diabetic peripheral neuropathy].”

c. *Morello Painful Diabetic Neuropathy Trial*

274. Because Morello was an outside study and the published article was written by authors outside of the company’s control, Parke-Davis could not suppress the results. Instead, the Defendants implemented a “two-pronged approach” to counter the negative results of the study. This included attacking alleged flaws in the study, and conducting a less scientific, open-label study known as the Dallocchio study, “which ultimately provided more favorable results.”

Ex. 166,  
Pfizer\_RGlanzman\_0040034

275. The published results of the Dallocchio study made no mention of the negative Morello study, even though the Dallocchio study was published 13 months after the Morello study.

Ex. 023, Abramson, ¶ 175.

d. *Reckless Painful Diabetic Neuropathy Trial (945-224)*

276. Despite the fact that the Patient Information Sheet for study 945-224 stated: “Information gained during this study may eventually benefit other persons with painful diabetic neuropathy,” Parke-Davis

Ex. 162, Research Report No. 720-04130; Ex. 023, Abramson Report ¶165.

had “a consistent strategy” of preventing the information gained from the study from becoming available to physicians, decision makers and the public.

277. The design of 945-224 was superior Ex. 023, Abramson Report ¶165.  
to the Backonja trial, using three times as many patients in the active treatment groups, and using fixed doses rather than a forced titration dosing.

278. Given this superiority, full and Ex. 163, Perry Report: Appendix -  
timely publication of the results of study 945-224 would Gabapentin Project Study detail  
have “fundamentally altered interpretation of the smaller summaries, Study No. 6 at 3.  
Backonja [protocol 945-210] trial and references to it!”

279. Nevertheless, Defendants’ emails Ex. 023, Abramson Report ¶165.  
reveal a campaign to suppress the negative results of 945-224.

280. On April 20, 2000, Dr. Beate Ex. 208,  
Roder, Defendants’ employee and the lead Parke-Davis PFIZER\_TMF\_CRF\_015313  
author on protocol 945-224, sent an email stating in part, (capitalizations in original); Ex.  
162, Research Report No. 720-  
04130  
“Although I would love to publish SOMETHING about  
945-224, Donna McVey [Parke-Davis Medical Director  
UK] made it clear that we should take care not to publish  
anything that damages Neurontin’s marketing success.  
So, I will rather not phone him [Dr. Reckless, the study’s  
lead investigator] until we have heard from Marketing

what they suggest.”

281. On April 20, 2000, Sarah Wensley, a Clinical Trials Monitor for protocol 945-224, sent an e-mail to Dr. Beate Roder recounting a conversation she had with Dr. Reckless on April 18, 2000. The e-mail stated “He [Dr. Reckless] felt that the data should be out in the public domain, especially that we have a license [UK approval] now. He is very keen for this data to be published and would like to speak to the drug director about this.”

Ex. 208,  
PFIZER\_TMF\_CRF\_015313

282. On April 20, 2000, Zina Eminton, Head of Clinical Monitoring and Analysis at Parke-Davis UK, sent an internal e-mail to several employees. The e-mail stated: “I don’t think we should be too hasty with this request [Dr. Reckless’s request to publish the results of protocol 945-224]. This clearly needs to be discussed with the Neurontin planning team and the marketing representatives from Europe.”

Ex. 208,  
PFIZER\_TMF\_CRF\_015313

283. On April 25, 2000, Sarah Jane-Bibby [CNS Clinical Trials Coordinator], in response to the April 20, 2000 e-mail from Dr. Roder, sent an internal e-mail to several employees. The e-mail stated: “It probably needs someone locally to go back to him [Dr.

Ex. 208,  
PFIZER\_TMF\_CRF\_015313

Reckless] and explain why at this time point we will not be publishing the data.” The e-mail also stated: “I agree that until we have our action plan agreed we don’t phone him to tell him that.”

284. On April 28, 2000, Dr. Reckless wrote to Defendants about publishing the results of protocol 945-224.

Ex. 208,  
PFIZER\_TMF\_CRF\_015313

285. On May 3, 2000, Sarah Jane Bibby sent an internal e-mail to several employees recounting that Sarah Wensley had told Dr. Reckless “that there were no plans at the current time to publish.”

Ex. 208,  
PFIZER\_TMF\_CRF\_015313

286. On June 20, 2000, Jenny Shaw, a Parke-Davis Medical Liaison Executive, sent an internal e-mail to several employees recounting her meeting with Dr. Reckless on June 19, 2000. The e-mail stated: “He [Dr. Reckless] also pointed out that he feels there are ethical reasons to write up the study - there is currently a movement to ensure that all trials are published and he feels that even if we [Defendants] don’t write the study up, the investigators should themselves.” This e-mail also stated: “He also wanted to start writing it up now but I have persuaded him to wait.” This e-mail also stated: “I didn’t miss the veiled threat in his words - if we don’t

Ex. 208,  
PFIZER\_TMF\_CRF\_015313

publish, they will (an option that doesn't reflect well on the investigators or ourselves).”

287. On June 21, 2000, in response to the June 20, 2000 e-mail from Jenny Shaw, Dr. Beate Roder sent an internal e-mail to several employees that stated: “If there is no threat to the marketing of gabapentin or maybe even some benefit (to correct misperceptions about the negative outcome), it might be worth pursuing publication in my mind.” The e-mail also stated that “Phil Magistro at some point offered money for a publication of the study results [of protocol 945-224]; I am not sure if he still supports this view after the results became known.”

Ex. 208,  
PFIZER\_TMF\_CRF\_015313

288. On June 26, 2000, in response to Jenny Shaw's June 20, 2000 e-mail, Sean Buckland wrote an internal e-mail to several employees. The e-mail stated: “It certainly sounds that, on balance we should write this paper up in time. We would need to have ‘editorial’ control, but would suggest we certainly involve Dr Reckless in the process, asking for his expert comment.”

Ex. 208,  
PFIZER\_TMF\_CRF\_015313

289. On June 26, 2000, several days after the merger between Parke-Davis and Pfizer, Sarah-Jane Bibby, in response to the e-mail from Sean Buckland,

Ex. 208,  
PFIZER\_TMF\_CRF\_015313

sent an internal e-mail to several employees. The e-mail stated: “PD [Parke-Davis] has ownership of the data, so Dr Reckless can publish his own centre data but that would need PD approval.”

290. By September 2000, Defendants’ chief concern with the negative results of protocol 945-224 was that they would upset the publicity blitz Defendants anticipated from two UK manuscripts that had been submitted to the *British Medical Journal*. One manuscript was for a study in PHN, while the other was based on study 945-306, which had been drafted in a way to make the study seem positive. On September 6, 2000, Pfizer employee Michael Rowbotham observed: “What is critical is that -224 is NOT submitted to any publication until we know WHEN the 2 UK studies are going to be published. This will allow us to ensure that 224 is not published before the UK studies.”

Ex. 209,  
PFIZER\_LCASTRO\_0002678

291. On September 6, 2000, Michael Rowbotham [a Neurontin team leader] reiterated the importance of not interfering with the publication of manuscripts with positive results in an internal e-mail sent to several employees. The e-mail stated: “I will be very interested to see the proposed timelines when they are

Ex. 209, Pfizer\_LCastro\_0002678

available so that we can ensure that they do not infringe on the NN25 and NN26 [the two UK studies] publication strategy.” At that point, it was still unknown when the two UK studies would be published.

292. On September 6, 2000, Michael Rowbotham further clarified Pfizer’s position as follows:

“What is critical is that -224 is NOT submitted to any publication until we know WHEN the 2 UK studies are going to be published. This will allow us to ensure that 224 is not published before the UK studies.” Dr. Roder responded to this e-mail stating: “I was aware that timing is crucial. Just let us keep in close contact to make sure the order of publication is respected.”

293. The next day, John Marino, Worldwide Marketing Team Leader for Neurontin, approved the decision to delay publication of 945-224, stating: “Michael [Rowbotham] has the right idea here. We must delay the publication of -224, as its results were not positive. Please work closely with him to make sure that this happens.”

294. On September 11, 2000, Michael Rowbotham conveyed this decision to other Pfizer employees. His e-mail message began with recognition

Ex. 209, Pfizer\_LCastro\_0002678 (capitalizations and underline in original).

Ex. 209, Pfizer\_LCastro\_0002678

Ex. 209, Pfizer\_LCastro\_0002678 (capitalization in original).

that: “Overall the study was not positive in terms of efficacy.” He wrote further: “The main investigator in the UK (Dr Reckless) is keen to publish but this will have several ramifications. The route that we have all agreed to now is that we will publish the study but NOT until we have published the results of NN25 and NN26.” Mr. Rowbotham also stated that study results would be “written up” by Synergy, a UK medical writing agency rather than the study investigators, and that Dr. Roder would coordinate this process.

295. On September 29, 2000, Michael Rowbotham further elaborated on the strategy, writing to other Pfizer employees: “I think that we can limit the potential downsides of the 224 study by delaying publication for as long as possible and also from where it is published. More importantly it will be more important to how WE write up the study. We are using a medical agency to put the paper together which we will show to Dr Reckless. We are not allowing him to write it up himself.”

Ex. 210,  
Pfizer\_LeslieTive\_0020985  
(emphasis in original).

296. By November 13, 2000, a ghostwritten draft of the results of protocol 945-224 was circulated. Dr. Beate Roder sent an internal e-mail to

Ex. 211,  
Pfizer\_LeslieTive\_0020922

several employees with the subject “Revised draft of publication for 945-224.” The e-mail stated: “please find attached some minor changes we would like to make to the revised draft you have forwarded to me on 24-Oct-2000.” The e-mail also stated: “Would you please return the revised draft to me after you have integrated our comments? I will then forward a copy of the draft publication to Dr. Reckless for review (in close co-operation with Dr. Uzman Azam [Pain Category Medical Manager for Pfizer-UK]).”

297. Dr. Kay Dickersin, an expert on publication bias, found that this manuscript, which was written by Parke-Davis, was biased in favor of Neurontin and departed from the company’s own internal findings. She found certain changes that “were likely to change the reader’s interpretation of at least one outcome,” while the conclusion that certain patients on Neurontin “experience an overall benefit from treatment despite the lack of a significant effect on pain scores” placed inappropriate emphasis on secondary findings over the negative primary results .

Ex. 117, Dickersin Report at 35-36 (citations omitted); Ex. 211, Pfizer\_LeslieTive\_0020922.

298. Angela Crespo [Senior Marketing Manager Neurontin Major Markets] immediately

Ex. 211, Pfizer\_LeslieTive\_0020922

forwarded the manuscript to Leslie Tive, Worldwide Medical Director for Neurontin, noting: “This is the negative study that we were talking about. I will inform Beate that you will contact her. As you can imagine, I am not in a hurry to publish it.”

299. The next day, a new letter was sent to the investigators. Dr. Dickersin found this letter to be bias towards Neurontin, noting that the letter “differed from the letter sent 8 March 2000, in that the results were interpreted more positively.” According to Dr. Dickersin, “Certain messages were written in bold; a reader focusing on the messages in bold could easily miss the message that the results were negative for the primary outcome variable...”

Ex. 117, Dickersin Report at 35; Ex. 164, Pfizer\_LeslieTive\_0020949.

300. The strategy to delay publication of 945-224 after publication of the two UK studies was tested when UK studies were rejected by the British Medical Journal (“BMJ”). On January 12, 2001, Dr. Usman Azam, a Pfizer UK employee, informed employees of the setback: “As you may be aware, the UK studies 225 and 226 are currently undergoing a second re write [*sic*] following the BMJ rejection. Are we still in agreement that 224 should be submitted after acceptance

Ex. 212, Pfizer\_LKnapp\_0053962

of the above or should we re evaluate [*sic*] this strategy.”

The e-mail also stated: “This decision is quite critical for the whole of the publication strategy in the UK and EU.”

Leslie Tive responded to this with the following: “My first instinct would be to continue to wait, for the same reasons you decided to wait initially.”

301. That same day, Dr. Roder sent an internal e-mail to several employees with the subject “Clearance for publication.” The e-mail was addressed to John Werth [Clinical Scientist Clinical Development, Experimental Medicine, Ann Arbor] and stated: “would you please initiate the internal clearance process for the attached publication of study results for 945-224? All company authors as well as the external lead author (Dr. Reckless) have reviewed the manuscript, and their comments are integrated.”

Ex. 212, Pfizer\_LKnapp\_0053962

302. Six months later, on July 18, 2001, Pfizer’s publication team, staffed with employees of Pfizer employees and its medical writing agent, Medical Actions Communications (MAC), met to discuss the 945-224 study. Even though the manuscript had been cleared earlier in the year, the team agreed that the manuscript “should not be pushed for publication.”

Ex. 213,  
Pfizer\_RGlanzman\_0044634

303. On February 14, 2002, Defendants submitted their ghostwritten manuscript of the results of 945-224 to *Diabetic Medicine*. The cover letter, signed by Dr. Beate Roder stated: “With respect to potential conflicts of interest, I would like to disclose that one of the authors [Pascal Maisonobe] is an employee of Pfizer GRD and that I am an employee of Pfizer GmbH.” The role(s) of the medical marketing vendors was not disclosed.

Ex. 214,  
Pfizer\_LeslieTive\_0020880

304. Dr. Dickersin found Defendants’ submission to *Diabetic Medicine* dishonest: “The covering letter [enclosing Defendants’ submission of the manuscript of the results of 945-224] sent with the submission emphasized, to an extent which I find dishonest, the study’s positive results.” This included the assertion that the results were “consistent with those seen in previous trials and further establish gabapentin as a useful and well-tolerated treatment option for painful diabetic neuropathy.”

Ex. 117, Dickersin Report at 36; Ex. 214, Pfizer\_LeslieTive\_0020880.

305. On May 13, 2002, an e-mail was sent from *Diabetic Medicine* to Dr. Roder. The e-mail stated that Defendants’ submission of the manuscript of the results of 945-224 “has not been accepted for publication.” Attached to the e-mail were the peer-

Ex. 214,  
Pfizer\_LeslieTive\_0020880; Ex. 117, Dickersin Report at 36-37.

reviewers' comments, which focused primarily on company bias and inappropriate statistics. Specifically, reviewers found that "the quality of the statistics appears to be poor, and hence the conclusions are not justified," that the authors needed to "perform an appropriate statistical analysis which should allow them to draw a less biased interpretation," that the most probable interpretation of the trial was that "NO statistical measures were positive," that with reanalysis and reinterpretation, the trial would be "considered a failure and the paper rewritten accordingly," that "there are many areas of company bias that need elimination," and that data from different groups were inappropriately combined, which is "one way of manipulating data to obtain desired results." Interestingly, one reviewer asked whether it was possible that patients taking Neurontin who experienced adverse events may have been unblinded.

306. Five months later, Defendants submitted their ghostwritten manuscript of 945-224 to *Diabetologia*. The cover letter that accompanied this submission was essentially identical to the one sent to *Diabetic Medicine*, including "the inappropriate and perhaps dishonest summary of findings." Once again, the

Ex. 215,  
Pfizer\_LeslieTive\_0020840; Ex.  
117, Dickersin Report at 37.

role(s) of any medical marketing vendors in preparing the manuscript, including the original ghost authorship by Synergy, were not disclosed.

307. On November 14, 2002, *Diabetologia*'s Editor-in-Chief sent a letter to Dr. Beate Roder informed her that the manuscript had been rejected. One peer-reviewer questioned the proffered claim of efficacy, noting:

- “There is no apparent dose-response curve”
- “No change in VAS or PPI normally gold standard measures of therapeutic efficacy in clinical trials of pain”
- “Is there a benefit in sleep scores, is this as a consequence of the side effect somnolence?”
- “Why did only 67 patients continue in the open-label study? If the drug is truly effective would you not expect more patients to have gone to open label.”

308. Another peer-reviewer noted the manuscript's pro-Neurontin bias, noting: “My concern that this is a pharmaceutical house prepared paper seems to be confirmed by my observation that reference 6 is even listed as a Parke-Davis study!” The reviewer also stated: “What is really needed is comparative trials of Gabapentin versus other known treatments for diabetic neuropathies.

Ex. 117, Dickersin Report at 37-38;  
Ex. 215,  
Pfizer\_LeslieTive\_0020840.

Ex. 215,  
Pfizer\_LeslieTive\_0020840.

It is surprising, therefore, that the authors fail to refer to the previous trial of Gabapentin versus Amitriptyline published by Morello et al. [which contained results negative for gabapentin], in the *Archives of Internal Medicine* two years ago.”

309. In late 2002, Pfizer made a decision to reference the 945-224 on the 9th page of an article that summarized the results of the Neurontin neuropathic pain trials, a practice known as bundling. In January 2003, the article appeared in *Clinical Therapeutics*. On January 26, 2003, Dr. Reckless sent an e-mail to Dr. Roder. The e-mail stated “I really think we should try to get this published, even if in a journal [*sic*] with a lower impact factor.”

Ex. 023, Abramson Report ¶220;  
Ex. 117, Dickersin Report, at \_\_\_\_;  
Ex. 216,  
Pfizer\_LeslieTive\_0020835.

310. On January 30, 2003, Dr. Roder forwarded Dr. Reckless’s January 26, 2003 e-mail to several of Defendants’ employees including Elizabeth Mutisya, Pfizer’s Medical Director for Major Markets. Dr. Roder’s e-mail stated: “please see Dr. Reckless’s reply below. If the NY team supports this approach, we should work with Fallon Medica to choose a new journal and revise the paper.”

Ex. 216,  
Pfizer\_LeslieTive\_0020835.

311. On February 3, 2003, Elizabeth

Ex. 216,  
Pfizer\_LeslieTive\_0020835; Ex.

Mutisya, responded to the e-mail, stating: “Unfortunately, given our limited budget for Neurontin this year, and the number of projects that Fallon Medica is currently handling for us, the agency will not be able to take the lead in revising the manuscript again. Dr. Reckless will have to take the lead this time,” a reversal of the prior policy limiting his involvement. In short, “Pfizer would not provide further financial and editorial *[sic]* support” to Dr. Reckless.

217,  
PFIZER\_LESLIETIVE\_0020834  
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312. On February 6, 2003, Dr. Reckless, responding to an e-mail from Dr. Roder informing him of the February 3, 2003 e-mail from Elizabeth Mutisya, sent an e-mail to Dr. Roder requesting “all the previous submissions, and copies of the background statistical analyses, and copies of the references used to date.”

Ex. 216,  
Pfizer\_LeslieTive\_0020835.

313. On February 11, 2003, Dr. Roder sent a letter to Dr. Reckless enclosing a binder “related to the publication of **gabapentin study 945-224**.” There is no evidence that the background statistical analyses Dr. Reckless requested were sent to him.

Ex. 216,  
Pfizer\_LeslieTive\_0020835  
(emphasis in original); Ex. 117,  
Dickersin Report at 38.

314. Over a three-year period, Defendants employed a “consistent strategy of preventing [the findings from 945-224], which contradicted the

Ex. 023, Abramson Report ¶165.

findings of the Backonja study, from becoming available to physicians, decision makers and the public.”

315. With regard to the Reckless study, Ex. 117, Dickersin Report at 33. Dr. Dickersin opines that “Study 945-224 is an example of suppression of negative results (publication bias), multiple forms of selective outcome reporting, spin, time lag bias, ghost authorship, and a form of citation bias.”

e. *Serpell Neuropathic Pain Trial (945-306)*

316. The research report for protocol Ex. 167, Protocol 945-306 at 22 (emphasis added); Ex. 167, Protocol 945-306, Appendix D.1 945-306 stated that “[t]he corresponding P-value from the analysis of raw data [before transformation] was P=0.06.” These results indicated that, for the primary endpoint, Neurontin *was no more effective* than placebo. This p-value, however, was never disclosed in the publication, even though it was a requirement of the protocol that “the results of original raw data ... will be displayed and discussed.”

317. Through Synergy (a medical Ex. 218, Pfizer\_LeslieTive\_0020631; Ex. 652, PFIZER\_TMF\_CRF\_068447. writing vendor), Defendants drafted a manuscript suggesting that the results of 945-306 were positive and submitted it to the *British Medical Journal*. The lead author was listed as Dr. Michael Serpell, even though he did not draft the manuscript. The manuscript was rejected

for several reasons among them; “badging” of the trial, i.e. “that two of the three named authors are from the sponsoring company and this put an overtly company favorable spin on the paper,” and because the trial results were skewed in favor of Neurontin when patients, who had previously tried gabapentin unsuccessfully, were excluded from the trial. Most importantly, the peer-reviewer found: “The study in its present format cannot justify gabapentin as first line treatment for neuropathic pain.”

318. Recognizing that even the favorable presentation of the Serpell trial fell short of the desired efficacy message for Neurontin, Pfizer and MAC [Medical Action Communications, a vendor hired to create publications] discussed ways to spin the Serpell trial. On September 20, 2002, David Cooper from MAC sent Angela Crespo of Pfizer an e-mail with the following subject line: “spinning Serpell.” Mr. Cooper warned that Pfizer and MAC should not “make up different ways of explaining away the results to different audiences.” The e-mail stated that it was MAC’s understanding that Pfizer had “publicized the study as supporting the use of gabapentin for these difficult mixed NeP [neuropathic

Ex. 219, MAC\_0003664; Ex. 117, Dickersin Report at 42-44.

pain] patients.”

319. In her response to the “spinning Serpell” e-mail, Angela Crespo indicated that something had to be done, because of all the neuropathic pain trial results that Defendants planned to present, “[t]he Serpell [trial] is the worst.”

Ex. 219, MAC\_0003664; Ex. 117, Dickersin Report at 42-44.

320. Still using the “spinning Serpell” subject line, Mr. Cooper responded to Angela Crespo stating “I understand your issue completely...If Pfizer wants to use, present, and publish this comparative data analysis in which 2 of 5 studies compared make the overall picture look bad, how [do]we make it sound better than it looks...”

Ex. 219, MAC\_0003664; Ex. 117, Dickersin Report at 42-44.

321. In October 2002, *Pain* published the results of Serpell which failed to properly report the results of the original raw data analysis.

Ex. 220, Serpell MG, Neuropathic Pain Study Group. *Pain* 2002;99:557-566 (“Serpell Article”); Ex. 221, <http://www.sciencedirect.com/science/journal/03043959>. Ex. 222, FAL\_0007867.

322. In November 11, 2002, *Pain* published a letter to the editor which commented on the Serpell Article. The letter explained that excluding patients who had previously not responded to gabapentin “must bias the results,” and, had these patients been included, it may have “pushed the P value, already tantalisingly [*sic*] close, above the 0.05 level.” The letter

stated: “To go on to state that the study ‘...provides further evidence of the clinical utility of gabapentin, with significant beneficial effects on overall pain scores...’ may at the very least be somewhat overstating a very modest reduction of borderline statistical significance.”

f. *POPP — Neuropathic Pain Trial (945-271)*

323. On September 11, 2001, just one month after Pfizer submitted the neuropathic pain sNDA to the FDA along with efficacy data from five trials, Dr. Mutisya sent an e-mail to several employees from Pfizer and MAC discussing the negative results from Defendants’ seventh study in neuropathic pain, this one examining neuropathic pain occurring post-operatively or post-traumatically (945-271 or “the POPP study”). Dr. Mutisya wrote: “We now have two studies that are negative for the primary efficacy parameter [referring to 945-224], both of which have authors who are eager to publish. The delay created by the completion of the substudy [POPP] would allow us to optimise timing between the release of the two studies.” Defendants never disclosed the negative results of POPP to the FDA.

Ex. 223,  
Pfizer\_LeslieTive\_0076417.

324. On September 13, Dr. Mutisya sent an e-mail to John Marino [Worldwide Team Leader for

Ex. 354, Pfizer\_JMarino\_0000809.

Neurontin] asking him whether it was correct to “assume that we would like to maximize the time interval between the Reckless paper [negative results from 945-224] and the POPP study [negative results from 945-271].” John Marino responded in an e-mail that Dr. Mutisya’s “assumptions were correct.” In his e-mail, John Marino stated: “these kind [sic] of things [delaying the negative results of studies] can always be a delicate issue, but I am sure that everyone can appreciate our desire to ‘take our time’ to review it [the POPP study] carefully.”

325. On September 14, 2001, Dr. Mutisya sent an internal e-mail to several employees that stated that “the POPP study has created challenges, and we need to agree on an acceptable approach to counter these.” Dr. Mutisya wrote that the investigators on the POPP study felt that Defendants had “a minimally effective drug” and “had only been able to demonstrate a slight difference between drug and placebo in other Pfizer trials because of the large size” of those studies. Finally, Dr. Mutisya mentioned two choices. The first was to continue to suppress the negative results and “hope that our competitors don’t notice the negative -224 study and this [POPP] study.” The second was to follow a similar

Ex. 166,  
Pfizer\_RGlanzman\_0040034.

approach, as what was used to counter the negative Morello study, and attack the flaws of the study while “design[ing] a study based on our experiences that may provide better results”

326. One year later, Pfizer and MAC prepared to submit a review article discussing Neurontin pain trials to *Clinical Therapeutics*. Initially, the plan was not to include either the POPP study or Reckless. However, it was recognized that the “real issue is deciding how to justify only reviewing 4 of the 6 randomized placebo controlled studies...” Actually, taking into account Gorson, there were 7 randomized studies. While Pfizer belatedly decided to partially include the results of the Reckless trial, it never considered including the negative results of the POPP trial.

Ex. 355, MAC\_0004074. Ex. 023, Abramson Report ¶218.

327. Defendants successfully suppressed the results of the POPP study for more than seven years. The negative results of the POPP study were not submitted to a journal until April 22, 2007, well after this litigation was commenced and Defendants were made aware that Plaintiffs had discovered that the study had been suppressed.

Ex. 356, Gordh TE, Stubaug A, Jensen TS et al. Gabapentin in traumatic nerve injury pain: A randomized, double-blind, placebo-controlled, cross-over, multi-center study. *Pain*, 2008;138:255-66.

328. According to Dr. Dickersin: “Study Ex. 117, Dickersin Report at 39.

945-271 is an example of suppression of negative results (publication bias), time lag bias, and ‘spin’.”

3. Branding Guide Creation and Control of False and Misleading Key Messages

329. On October 11, 2000, the Pfizer approved the 2001 US Operating Plan for Neurontin. A “Key issue” for 2001 was “Unsatisfied Market in Emerging Uses.” One of the strategies to address that issue was to “Meet demand for Medical Education...” The medical education marketing plan included; “Weekend Symposia,” “Convention Symposia,” “Publications Enduring Materials,” and “Grand Rounds.” In support of neuropathic pain, Pfizer had 4 strategies: use of advisory boards, development of a diagnostic tool for neuropathic pain, “Presentation of new data at key congresses, and “Development of relationship with American Pain Society.” Pfizer lastly sought to implement a “Publication Strategy,” which included a tactic of ensuring “key message inclusion in all publications.”

Ex. 357,  
PFIZER\_RGLANZMAN\_0000650

330. In November 2000, Cline Davis & Mann, a medical marketing firm, began creating the Neurontin Global Branding Guide. The purpose of the Global Branding Guide, which was called “Brand Globally. Think Locally,” was to “maximize the

Ex. 358,  
PFIZER\_CGROGAN\_0016795 Ex.  
359,  
PFIZER\_LESLIETIVE\_0068419

worldwide success of NEURONTIN” through the use of core product positioning and key communication messages.” The global position of Neurontin for neuropathic pain was as follows: “Neuropathic pain--An ideal first-line therapy for all types of neuropathic pain providing a significant improvement in quality of life due to its proven efficacy...” Even though results of the Reckless trial, the Gorson trial, the Morello trial, and the concerns about unblinding in the Backonja study were known to Pfizer at the time, none of these issues are cited in the guide.

331. In early 2001, Pfizer formed a Publication Sub-Committee (PSC) in conjunction with Pfizer’s “Publication Strategy” in order to “Develop a Comprehensive Strategic Global Publications Plan” and “Ensure Key Message Inclusion in All Publications.”

Ex. 360, Pfizer\_THylan\_0002490

332. Owing to the extension of Neurontin’s patent exclusivity, Pfizer planned a “re-launch” of Neurontin to “capitalize” on the “published literature” in off-label uses, including neuropathic pain. Medical Action Communications was retained to assist Pfizer’s PSC (Publication Sub-committee) with the “challenge” of asserting “greater control over ongoing

Ex. 361, MAC\_E\_0018822

publications and data” and to “[e]nsure a consistent implementation of key medical and marketing messages in support of Neurontin for each target indication with the various target audiences.” In the case of neuropathic pain, the target audience consisted of neurologists, PCPs, pain specialists, diabetologists, sleep specialists, oncologists, psychiatrists, and psychologists.

333. The PSC efforts to re-launch Neurontin for neuropathic pain “resulted in a successful product transition,” which “[l]everaged PD/WL efforts surrounding Neurontin” and [f]illed the pipeline for aggressive transition into 2002 publication presence.”

Ex. 361, MAC\_E\_0018822

334. On September 13, 2001, in response to Dr. Mutisya’s e-mail from September 11, 2001, Kirk Taylor [Lyrica Medical Team Leader, Pfizer Medical and Regulatory Operations, PPG] sent an e-mail marked with “high” importance to several employees from Pfizer and MAC. The e-mail stated that Mr. Taylor “completely agree[d]” with Dr. Mutisya’s suggestions. The e-mail discussed “important” comments made at the investigators’ meeting, including that “Neurontin may be a drug for overall ‘well-being’ and not NeP,” a comment stemming from the “underlying negative halo about

Ex. 223,  
Pfizer\_LeslieTive\_0076417.

Neurontin's efficacy and the negative POPP study." The e-mail noted that opinion leaders felt that the efficacy seen in the JAMA papers was "slight," a "perception" that "must be corrected in terms of DPN and PHN." Mr. Taylor felt that "[j]ournal clubs with OL's [opinion leaders] and internal people may help."

335. With the help of Medical Action Communications, Pfizer began drafting key messages, which were due September 13, 2001. In August 2001, Leslie Tive, the Worldwide Medical Director for Neurontin, instructed MAC and other Pfizer employees that the "key messages" need not "be viewed solely as claims, but also of possible and desirable messages to develop for the future."

Ex. 224, MAC\_E\_0020147; Ex. 225, PFIZER\_LKNAPP\_0016491

336. A MAC document reveals that "key messages need not be true. Key messages could be "either statements that are currently supported by clinical data, or positions that the team would like to develop for the future." The latter type of key messages were referred to as "wish- list" messages and could be "included in earlier publications to encourage target audiences to watch for future studies." Allison Fannon testified that such unsupported messages were "aspirational key messages."

Ex. 226, MAC\_E\_0036778  
[Transcript of Deposition of Allison Fannon, June 19, 2007 at 292.

337. Allison Fanon admitted that “key messages” were a way to say promote Neurontin’s off-label uses: “Due to restrictions in the US label, the sales reps cannot promote this in the US. However, this message can be communicated in publications that sales representatives could not say.”

Ex. 227,  
PFIZER\_BPARSONS\_0162576;  
Ex. 228,  
PFIZER\_RGLANZMAN\_0121206

338. In February 2002, Cline Davis Mann prepared a revised Global Branding Guide for Neurontin called “Expanding the Global Brand.” The product position for Neurontin and neuropathic pain remained essentially the same: ‘NEURONTIN is an ideal first-line therapy for neuropathic pain, providing improvement in QOL, proven efficacy, favorable onset of action, excellent safety and tolerability, and convenience.’ The claim of “Proven efficacy in patients with neuropathic pain” was supported by “accumulating evidence.” However, neither Gorson, Reckless, Morello, POPP, nor the accurate results of Backonja and Serpell were cited.

Ex. 229,  
PFIZER\_LCASTRO\_0073188

339. On March 13, 2002, MAC proposed key messages for various indications, including neuropathic pain. One key messages was that Neurontin “[s]hould be considered a first choice of therapy for neuropathic pain” and that it had “proven efficacy in large,

Ex. 230,  
PFIZER\_RGLANZMAN\_0055248;  
Ex. 231,  
PFIZER\_RGLANZMAN\_0055189;  
Ex. 232, MAC\_E\_0051166

controlled, randomized studies.” Outside of PHN, the only support for the latter key message was the analysis of the Backonja study that failed to correct for unblinding of subjects. No mention was made of the negative Gorson, Reckless, POPP or Serpell studies. These key messages were approved by the Defendants’ PSC.

340. Pfizer’s 2003 Neurontin Operational and Tactical Plan indicated that pursuant to the Neurontin Branding Guidelines II, one of the “Key Selling Messages” would be Neurontin’s “Proven Efficacy” in neuropathic pain as demonstrated by “Four Large Scale Placebo Controlled Trials [Rowbotham, Backonja, Rice, Serpell]. No reference was made to the negative Gorson, Reckless, or POPP trials.

Ex. 233,  
PFIZER\_AMISHRA\_0002324

341. In early 2003, the PSC approved revised key messages, which included a key message that “Neurontin is effective in PHN, DPN, and in treating some NeP symptoms irrespective of etiology.” Fallon Medica, a subsidiary of Cline Davis & Mann, prepared tracking grids so that the insertion of key messages into journal article manuscripts could be monitored. These tracking grids were updated monthly.

Ex. 234,  
PFIZER\_LESLIETIVE\_0003830;  
Ex. 235,  
PFIZER\_LESLIETIVE\_0078566  
Ex. 250,  
PFIZER\_BPARSONS\_0202564

342. Pursuant to this marketing strategy,

Ex. 251,  
PFIZER\_RGLANZMAN\_0147404;

Defendants were able to publish the following false “key messages” in journal articles:

- Brodie, et al., *Epilepsia* (September 2002): “effective as monotherapy”
- Serpell et al., *Pain* (October 2002): “This study supports the evidence from PHN and painful diabetic neuropathy studies and provides further evidence of the clinical utility of gabapentin [in treating neuropathic pain]”
- Garcia-Borreguero, et al., *Neurology* (November 2002): “therapeutic activity...for several pain-related syndromes such as trigeminal neuralgia, post-herpetic pain, and diabetic neuropathy”
- Backonja and Glanzman, *Clinical Therapeutics* (January 2003): “Results of the randomized, placebo-controlled studies reviewed here indicate the efficacy and tolerability of gabapentin for the alleviation of a variety of pain symptoms,” which was designed to “reinforce the efficacy message of gabapentin in DPN, PHN and in treating neuropathic pain of many causes...”
- Thomas Guttuso, *Obstet. Gynecol.* (February 2003): “gabapentin has shown efficacy in

Ex. 252, MAC\_E\_0083628; Ex. 253, PFIZER\_CTAYLOR\_0007193; Ex. 254, PFIZER\_LESLIETIVE\_0038508; Ex. 255, MAC\_E\_0022741; Ex. 256, PFIZER\_BPARSONS\_0010171; Ex. 257, PFIZER\_AFANNON\_0016742.

controlled studies for neuropathic pain, migraine headache”

- McLean and Gidal, *Clinical Therapeutics* (May 2003): “published studies suggest maintenance dosages of 900 to 3600 mg/d will be efficacious for most adult patients”

4. Defendants’ Suppression of Expert Opinion

343. The target of Pfizer’s suppression Ex. 258, Pfizer\_LKnapp\_0070556  
efforts extended to the opinions of their own experts.  
After learning that one of its experts stated in meeting minutes that the “success of gabapentin is not due to its efficacy, it is less efficacious than Tricyclic antidepressants (TCA)...,” Larry Alphs, M.D., Ph.D., Director of Clinical Development CNS, wrote: “A larger concern that I have is that we need to be very sensitive how we write minutes of such meetings. Opinions are not the same as fact, but I have been deposed too many times and know that this type of statement fuels all kinds of fears and misperceptions. This statement comes across as being fact and is very prominently positioned as an undisputed truth. Such statements sometimes get out of the company and we can never adequately manage the damage that they do to our image.”

5. Defendants Rely on Faked Studies to Support Efficacy Claim

344. In June 2003, Dr. Robert Dworkin, a paid Pfizer consultant, contacted Lloyd Knapp and Douglas Shapiro, of Pfizer Global Research and Development, about an article authored by Dr. David Simpson with purportedly positive results. Dr. Dworkin expressed concerns about the validity and existence of Dr. Simpson's results. Lloyd Knapp told him that, unless it was determined that Defendants had sponsored the study he "would not touch" it. Dr. Dworkin was asked to review the article carefully. In response, he presented 21 concerns amounting to the fact that the study may have been faked and based on earlier circulated slide sets from Defendants.

Ex. 259, PFIZER\_LKNAPP\_0083145; Ex. 260, PFIZER\_LKNAPP\_0083148; Ex. 261, PFIZER\_LKNAPP\_0060187; Ex. 236, 0900000180114059.doc from Merlin Database; Ex. 163, Perry Report at 63-64.

Despite Defendants' knowledge of the very real possibility that this study was not genuine, the positive results appear in one of their "Dear Doctor" letters. Defendants did not share their suspicions with the Cochrane Collaboration who included the Simpson study in their 2005 review.

345. On October 1-3, 2004, Dr. Scott Reuben gave a presentation at the National Pain Forum on Neurontin and nociceptive pain. The slides used by Dr.

Ex. B, IMP\_0001008; Ex. C, IMP\_0001167; Ex. 668, [http://www.boston.com/news/health/articles/2009/03/11/doctor\\_accused\\_of\\_faking\\_studies/?page=full](http://www.boston.com/news/health/articles/2009/03/11/doctor_accused_of_faking_studies/?page=full)

Reuben contained false and miselading statements, including the misleading suggesting that Neurontin might be " a 'Broad-Spectrum' Analgesic," and a presentation of the results of a single trial of Neurontin in nociceptive pain, which omitted any reference to the Defendants' mutiple negative clinical trials. Subsqeuntly, Dr. Rebuen was discovered to have faked entire clinical trials for various drug companies. According to the Boston Globe "... the studies in question involved data about drugs made by pharmaceutical giant Pfizer Inc., including Celebrex, Lyrica, and Neurontin." Pfizer gave Reuben five research grants between 2002 and 2007, and as a member of Pfizer's speakers bureau he gave talks about Pfizer drugs to colleagues such as the one listed above.

6. Defendants' Developed Objection Handler to Address Complaints By Physicians that "Neurontin Doesn't Work"

346. Pfizer recognized that "Neurontin doesn't work" was the most frequent complaint received from physicians. Accordingly, Pfizer placed this as the top complaint in its "Objection Handler," a document designed to assist sales representatives in "answering objections about Neurontin concisely and confidently."

Ex. 262,  
PFIZER\_AZEUSCHER\_0013546

7. Defendants' Intent to Market Neurontin for Nociceptive Pain

347. In 1997, Parke-Davis filed several patent applications covering Neurontin’s use in non-neuropathic pain. In 1999, Parke-Davis issued a Clinical Development Plan for Neurontin’s use in nociceptive pain.

Ex. 669, U.S. Patent No. 6,329,429; Ex. 670, U.S. Patent No. 6,127,418; Ex. 671, PFIZER\_MPIERCE\_0002201; Ex. 672, PFIZER\_CTAYLOR\_0000285; Ex. 673, PFIZER\_JMARINO\_0002076.

Parke-Davis recognized that if Neurontin was found effective in a study for any single pain model, “There would be nothing to prevent you from promoting it for acute pain.” Even after the company learned the results of the multiple negative results in nociceptive pain, it nevertheless issued a “Marketing Needs Document,” which stated: “Following the creation of the new Pfizer the possibility exists to develop a combination of either Gabapentin or Pregabalin and a Cox-2, this combination would appear to match the unmet need in the back pain market identified in the market research... where it would be able to generate substantial sales.”

**C. False and Misleading Marketing of Neurontin for Pain**

1. Parke-Davis’s False and Misleading Statements Made During Class Period

a. *False and Misleading Statements-American Pain Society Annual Meeting—November 1995*

348. Between November 9 and 12, 1995, pursuant to the Marketing Assessment’s plan to have anecdotal data misleadingly pooled and presented by

Ex. 263, WLC\_FRANKLIN\_0000151184 Ex. 264, WLC\_FRANKLIN\_0000156836

various pain specialists, including Drs. Finkel and Mann of the University of North Carolina, Parke-Davis presented a poster misleadingly suggesting that it summarized the results of a trial of 82 patients, when in fact it was pooled anecdotal information that excluded patients that did not respond to Neurontin. The poster concluded that Neurontin was “efficacious” and proclaimed Neurontin “New Treatment for Chronic Pain.” Three months later, University of North Carolina received a check from Parke-Davis for \$30,000.

349. ACCME guidelines require that “[a]ll the recommendations involving clinical medicine in a CME activity must be based on evidence that is accepted within the profession of medicine as adequate justification for their indications and contraindications in the care of patients,” and a CME provider who seeks to provide “advocacy of unscientific modalities of diagnosis or therapy is not eligible to apply for ACCME accreditation.”

Ex. 265, ACCME guidelines.pdf

b. *False and Misleading Statements-1995-1996 “Home Study Course” CME*

350. Beginning in late 1995, Parke-Davis launched a misleading and deceptive CME “Home Study Course” program, which misleadingly represented that there was scientific evidence supporting Neurontin’s

Ex. 266,  
WLC\_FRANKLIN\_0000032920;  
Ex. 267,  
WLC\_FRANKLIN\_0000068832;E  
x. 268,  
WLC\_FRANKLIN\_0000164158;  
Ex. 269,  
WLC\_FRANKLIN\_0000068717;

use as a treatment for chronic pain. Specifically, Neurontin was listed as one of the treatments for chronic pain, and both of the fictionalized case studies—one for DPN and the other for RSD—involved patients dramatically improving their chronic pain symptoms by taking Neurontin after having failed other treatments. Physicians were told that the “Home Study Course,” including the “Home Study Course” participant workbook, were accredited by the ACCME, meaning that any reference to the use of Neurontin in treating chronic pain was “based on evidence that is accepted within the profession of medicine as adequate justification” for this use. Parke-Davis failed to inform physicians that the case studies were fictionalized, that there was, in fact, no scientific evidence supporting the use, and that physicians instead were being exposed to “advocacy of unscientific modalities of diagnosis.” In fact, one of the faculty members of the CME, Dr. Steven Schachter, admitted that at the time the CME content was created, there had only been one prior report (the Mellick case report) of Neurontin’s use for treating pain.

Ex. 270, WLC\_CBU\_054194;  
Ex 271,  
WLC\_FRANKLIN\_0000198590

351. The CME activity was sponsored by a division of Physicians World called Professional

Ex. 268,  
WLC\_FRANKLIN\_0000164158;  
Ex. 269,  
WLC\_FRANKLIN\_0000068717;

Postgraduate Services, without any disclosure that Physicians World and Parke-Davis had formed a “strategic partnership” to handle “several aspects of Medical Education: Independent & Promotional Symposia, Advisory Board Meetings, etc....” The faculty members for the “Home Study Course” included Dr. Schachter, who reported “[n]o significant financial interest or affiliation” with Parke-Davis, even though he was a regular speaker for Parke-Davis on Neurontin and routinely earned \$1000 per speaking engagement. Another faculty member, Dr. David Longmire, has stated that if he “had known of the Defendant’s illegal marketing scheme, he would not have placed his professional practice and reputation in jeopardy by accepting invitations to speak at meetings, the contents of which Defendant used as an important element in its illegal marketing scheme.”

Ex. 272,  
WLC\_FRANKLIN\_0000128008;  
Ex. 273, David Longmire v Pfizer  
Complaint.pdf.

352. In May and June 1996, Parke-Davis followed up its mailing of the CME “Home Study Course” with 32 dinner meetings held in 29 cities areas attended by 273 physicians. Parke-Davis also held 50 audio-conferences containing the “highlights” of these meetings, which allowed for hundreds of physicians in less urban

Ex. 274,  
WLC\_FRANKLIN\_0000015522;  
Ex. 266,  
WLC\_FRANKLIN\_0000032920;  
Ex. 275,  
WLC\_FRANKLIN\_0000032883

areas to participate.

c. *False and Misleading Statements-1996 Journal Article*

353. In March 1996, pursuant to the Ex. 276, WLC\_CBU\_001234 Marketing Assessment's plan to have anecdotal data misleadingly pooled and presented by various pain specialists, including Dr. Rosner in New York, Parke-Davis published an article by Rosner entitled "Gabapentin adjunctive therapy in neuropathic pain states" in the Clinical Journal of Pain. The article misleadingly suggested that it contained a "report of a trial of the new antiepileptic agent gabapentin." However, rather than the results of a scientific trial, what was presented was anecdotal information suggesting Neurontin's efficacy was misleadingly presented as being scientific evidence from a "trial."

d. *False and Misleading Statements-American Diabetes Association's Annual Meeting-June 1997*

354. In June 1997, Parke-Davis held a Ex. 280, WLC\_FRANKLIN\_0000079748 Satellite Symposium at the American Diabetes Association's annual meeting in Boston. At that meeting, the 350 attendees were presented with information suggesting Neurontin's utility in treating DPN, but were not informed about the negative results of the Gorson

study. Because the event was a CME, neither Parke-Davis nor its agents were supposed to control the content. Nevertheless, Parke-Davis marketing employees reviewed the presentations of the presenters beforehand, and expressed concerns to Cline Davis & Mann about the presentation of Dr. Vera Bril. According to CDM, “her abstract clearly illustrated that she was clearly not planning on presenting what had originally been agreed upon.” CDM immediately sought to formulate a plan to “counteract a possible ‘negative’ presentation.” First, CDM met with Dr. Bril and attempted to tell her the things that needed to be presented to give the attendees a “positive message.” When that didn’t work, CDM prepared pre-written questions designed to elicit favorable responses and counteract “negative comments” about Neurontin and planted an agent to ask those questions. CDM instituted internal guidelines so that “this type of situation does not occur again.”

e. *False and Misleading Statements-“Pain Weekend Meetings”-April-September 1997*

355. Between April and September 1997, Parke-Davis held ten “Pain Weekend” meetings in locations such as Ponte Vedra, FL, New York City, Rye

Ex. 281,  
WLC\_FRANKLIN\_0000066815;  
Ex. 282, WLC\_CBU\_180735; Ex.  
283,  
WLC\_FRANKLIN\_0000066770;  
Ex. 284,  
WLC\_FRANKLIN\_0000066773;

Brook, NY, Saratoga, NY, Rochester, NY, Newport, RI, Absecon, NJ, Philadelphia, PA, Hershey, PA, and Boston, MA. At these meetings, which were attended by a total of roughly 300 hundred physicians, Neurontin was presented in the “Key Presentation Slides” as “useful in a number of chronic pain situations.” The existence of Gorson’s study and its negative results were not presented at these meetings.

Ex. 285,  
WLC\_FRANKLIN\_0000066779;  
Ex. 286,  
WLC\_FRANKLIN\_0000066782;  
Ex. 287,  
WLC\_FRANKLIN\_0000066789;  
Ex. 288,  
WLC\_FRANKLIN\_0000066787;  
Ex. 289, WLC\_CBU\_179585.

f. *False and Misleading Statements-Journal Supplement-1997*

356. In November 1997, Parke-Davis mailed a 24-page CME “supplement” to the Journal of Internal Medicine to 56,000 physicians. This supplement suggested Neurontin’s efficacy to treat DPN yet omitted mention of the Gorson study.

Ex. 290,  
WLC\_FRANKLIN\_0000080451  
Ex. 291  
WLC\_FRANKLIN\_0000040543

g. *False and Misleading Statements-American Society of Regional Anesthesia’s 4th Annual Comprehensive Review of Pain Management-1997*

357. In November 1997, Parke-Davis prepared a syllabus for the American Society of Regional Anesthesia’s 4th Annual Comprehensive Review of Pain Management. The syllabus referred to Neurontin as a “new analgesic” which is an “attractive” treatment for “difficult patients,” but omitted any reference of the negative Gorson study.

Ex. 292,  
WLC\_FRANKLIN\_0000081948

h. *False and Misleading Statements-Case Study Series-1997*

358. In November 1997, Parke-Davis also mailed a CME case study series prepared by Cline Davis & Mann (“Cline Davis”) and Medical Education Resources, Inc. (“MER”) to the 350 attendees of the ADA Satellite Symposium held in Boston earlier that year. The goal of the case study series was to “convey a positive message about Neurontin in treating DPN, but omitted reference to the Gorson data.

Ex. 293,  
WLC\_FRANKLIN\_0000195502  
Ex. 294,  
WLC\_FRANKLIN\_0000080506

i. *False and Misleading Statements-www.pain.com-1997*

359. Beginning in 1997, Parke-Davis received a “substantial presence” on www.pain.com, a website hosted by the Dannemiller Memorial Educational Foundation, a CME-provider on topics relating to pain. The arrangement with the website allowed Parke-Davis to “suggest various content resources” and have Neurontin featured in the “Pain Expo,” a commercial site where product positioning was allowed. As a result of this access, Parke-Davis was able to post numerous misleading articles on the website. Examples of these articles include: Progress in Anesthesiology, Pharmacotherapy of Painful Peripheral Neuropathies, which was posted on the website in January 1999. This article, authored by Ahmad

Ex. 295,  
WLC\_FRANKLIN\_0000082494;  
Ex. 310,  
<http://web.archive.org/web/20000120044256/pain.com/freecme/beydoun/default.cfm>

Beydoun, made no reference to the negative results from the Gorson trial and described the results of the Backonja study without any disclosure of the potential corruption of the results due to unblinding.

j. *False and Misleading Statements-Annual Meeting of the Society of Pain Practice Management-1998*

360. In March 1998, Parke-Davis held a Neurontin neuropathic pain CME at the Annual Meeting of the Society of Pain Practice Management in Scottsdale, AZ, attended by more than 400 pain specialists. The CME program, entitled “The Pharmacologic Management of Neuropathic Pain,” featured content nearly identical to an original accredited article on “The Pharmacological Management of Neuropathic Pain” published in the February 1998 issue of Progress in Anesthesiology. The article omitted reference to the negative Gorson study.

Ex. 068,  
WLC\_FRANKLIN\_0000171583;E  
x. 296,  
WLC\_FRANKLIN\_0000082446;E  
x. 297,  
WLC\_FRANKLIN\_0000082462;E  
x. 298,  
WLC\_FRANKLIN\_0000178448;E  
x. 299, WLC\_CBU\_050411; Ex.  
300, WLC\_CBU\_146556

k. *False and Misleading Statements-Journal Article-1998*

361. On December 2, 1998, the Journal of the American Medical Association published Defendants’ manuscript of the results of protocol 945-210. The abstract’s conclusion was: “Gabapentin monotherapy appears to be efficacious for the treatment of pain and sleep interference associated with peripheral neuropathy

Ex. 093, Backonja M, Beydoun A, Edwards KR, et al., Gabapentin for the symptomatic treatment of painful neuropathy in patients with Diabetes Mellitus. Journal of the American Medical Association, 1998;280:1831-6 (“Backonja Article”).

and exhibits positive effects on mood and quality of life.”

362. The results of Dr. Gorson’s trial were not disclosed in the Backonja Article.

Ex. 093, Backonja M, Beydoun A, Edwards KR, et al., Gabapentin for the symptomatic treatment of painful neuropathy inpatients with Diabetes Mellitus. Journal of the American Medical Association, 1998;280:1831-6 (“Backonja Article”).

363. The Backonja Article “misleadingly stated” that “it was the first trial to evaluate gabapentin’s efficacy in this patient population [patients with painful diabetic peripheral neuropathy].”

Ex. 023, Abramson Report ¶150.

364. “Though not mentioned in the JAMA article, Gorson was the first trial to evaluate the efficacy of Neurontin in patients with painful diabetic neuropathy.”

Ex. 023, Abramson Report ¶159.

365. To test for the possibility that study participants had become unblinded by the occurrence of CNS adverse events, the authors of the Backonja Article “calculated separately whether each of the two most common side effects had a significant effect on the degree of pain relief reported. Thus, when patients experiencing dizziness were removed from the results, there was no significant impact on pain relief achieved by the remaining patients. And when these patients were put back into the mix and the patients experiencing

Ex. 023, Abramson Report ¶151;  
Ex. 093, Backonja Article.

somnolence were removed from the results, there was no significant impact on pain relief achieved by the remaining patients.”

366. The Backonja Article states:  
“inclusion of these patients [patients who experienced dizziness and somnolence as adverse events] central nervous system adverse effects in the original analysis did not account for the overall efficacy seen in the trial.”

Ex. 093, Backonja Article (internal citation omitted).

367. “Determination that pain relief was not significantly affected by removing those people experiencing single CNS side effects one at a time was inadequate to prove that the experience of CNS side effects *in toto* did not have a significant effect on the results.”

Ex. 023, Abramson Report ¶151.

368. Dr. Jewell reports that “[T]he entire apparent treatment effect reported in Backonja et al. disappears when data after the occurrence of treatment-related Central Nervous System (CNS) side effects [which could have alerted patients to the fact that they were taking Neurontin] is eliminated.”

Ex. 157, Jewell Report at 1.

369. Dr. Jewell concludes that the Backonja Article “provides no basis of any clinical efficacy of gabapentin over placebo in reducing pain.”

Ex. 157, Jewell Report at 1.

370. Dr. Dickersin finds that Protocol 945-210 and the Backonja Article contain the following biases: “Selective analyses - Analyses to examine possible association of side effects and primary outcome, requested by those outside and inside the company, were not produced; Design Bias - Investigators aware that CNS side effects at high doses could unmask patients to active intervention potentially biasing self-reported response.”

Ex. 117, Dickersin Report at 30 (internal reference omitted).

1. *False and Misleading Statements-JAMA Media Blitz-1999*

371. To increase public awareness of the publication of the Backonja article in JAMA and a companion study, Parke-Davis launched an unprecedented media blitz to “Establish Neurontin as the treatment of choice for post-herpetic neuralgia and diabetic neuropathy,” “generate interest in and coverage of gabapentin’s efficacy in chronic pain management,” and “Saturate trade and consumer media with a variety of telecommunications vehicles.” The campaign used multiple channels to disseminate the Backonja article, which failed to disclose the prior negative Gorson study or the corruption of the Backonja trial results due to unblinding.

Ex. 301, WLC\_CBU\_092879; Ex. 302, WLC\_CBU\_000221.

372. The target of this media blitz was

Ex. 301, WLC\_CBU\_092879; Ex. 302, WLC\_CBU\_000221; Ex. 095,

the entire medical community, including PCPs, Neurologists, Anesthesiologists, Nurse Practitioners, Pharmacists, Patients, Caregivers, Family, and the “Consumer and Trade Media.” Within 3 months, Parke-Davis’s media blitz created 85 million “impressions” across all major markets. In other words, the Parke-Davis sales message reached 85 million people by March 1999. By the end of 1999, the total number of media impressions was 128 million (71 million in print media, 40 million on TV, and 17 million on radio).

WLC\_CBU\_040534.

373. This media blitz, to disseminate the message that Neurontin was effective for pain, included the following activities:

- Use of the sales force to distribute copies of the Backonja article to physicians.

Ex. 301, WLC\_CBU\_092879; Ex. 302, WLC\_CBU\_000221.

- National Media Launch— Parke-Davis developed press releases and collateral materials that supported the Neurontin publicity campaign and targeted consumers and trade publications catering to medical professionals in the fields of diabetes and pain management.

Ex. 301, WLC\_CBU\_092879; Ex. 302, WLC\_CBU\_000221.

- Video News Release—In order to blanket the TV airwaves, Parke-Davis developed a canned video news release designed to appear as a genuine news report and was distributed to television stations in 79 different TV markets, including 8 of the top 10 key US markets, and 22 of the top 25. The ads ran on more than 100 TV stations, including: WCBS and WNBC in New York, WBZ in Boston, KNBC in Los Angeles, WGN and WMAQ in Chicago, KPIX and KGO in San Francisco, and WRC in

Ex. 301, WLC\_CBU\_092879; Ex. 302, WLC\_CBU\_000221.

Washington DC.

• Radio News Release—In order to reach the millions Americans that listen to the radio, Parke-Davis developed a 45-second canned radio news release (RNR) that was designed to sound like a genuine news report and was distributed to key radio stations across the country. The ads were run over three straight days nearly 1,200 on 595 radio stations, as well as four national networks covering another 600 radio stations.

Ex. 301, WLC\_CBU\_092879; Ex. 302, WLC\_CBU\_000221.

• Radio Health Journal—Parke-Davis also developed a 60-second Radio Health Journal (RHJ) spot to air unedited on stations around the country. The Radio Health Journal spot aired 1,700 times over a six-week period in all of the top 25 markets and 45 of the top 50.

Ex. 301, WLC\_CBU\_092879; Ex. 302, WLC\_CBU\_000221.

• Airline Video News Release—Parke-Davis also took advantage of the captive audiences in traveling in commercial aircraft by showing show short video segments to 2.9 million passengers of United Airlines and 200,000 passengers of TWA throughout the month of January 1999, and United Airlines and Northwest Airlines during the month of February 1999 as part of their in-flight entertainment.

Ex. 301, WLC\_CBU\_092879; Ex. 302, WLC\_CBU\_000221.

• Mat Release—In order to reach the millions of Americans who obtained their news from newspapers, Parke-Davis also developed a canned news article that was designed to appear as a genuine news story and was run unedited in daily and weekly newspapers and magazines around the country, including Business Week, the Washington Post, the Los Angeles Times, the Chicago Tribune, the San Francisco Chronicle, MSNBC.com, the AP and Reuters newswires.

Ex. 301, WLC\_CBU\_092879; Ex. 302, WLC\_CBU\_000221.

m. *False and Misleading Statements-Interactive CD Rom*

374. To assist sales representatives in detailing doctors on the results of Backonja (but not

Ex. 303, PFIZER\_TMARTIN\_0001306; Ex. 084, PFIZER\_DPROBERT\_0014027

Gorson), Parke-Davis prepared an “Interactive CD Rom” that the sales reps used to “navigate the physician through the audio visual aid...bringing up the appropriate information when an objection was raised or question was asked.” Sales representatives were trained to circumvent rules on off-label promotion in order to “communicate the use of Neurontin for the treatment of diabetic neuropathy.”

n. *False and Misleading Statements-Journal Article-1999*

375. In February 1999, the *Journal of Neurology, Neurosurgery and Psychiatry* published a letter to the editor from Dr. Gorson. The letter to the editor contained the content of the manuscript Dr. Gorson had faxed to Parke-Davis on August 23, 1997 and concluded: “The results of this study suggest that gabapentin is probably ineffective or only minimally effective for the treatment of painful diabetic neuropathy at a dosage of 900 mg/day.”

Ex. 311,  
<http://jnnp.bmj.com/content/vol66/issue2/>; Ex. 202, Gorson KC, Schott C, Herman R, Ropper AH. Gabapentin In The Treatment Of Painful Diabetic Neuropathy: A Placebo Controlled, Double Blind, Crossover Trial. *J Neurol Neurosurg Psychiatry*. 1999 February; 66(2): 251–252 (“Gorson Letter”);

376. Dr. Dickersin finds that the Gorson Letter contains the following biases: “Location Bias - Final (negative) results were published as Letter to the Editor and conference abstract/poster; Time lag bias - Internal memos indicate company delayed publication;

Ex. 117, Dickersin Report at 32 (internal citations omitted).

Spin - Conclusions modified between draft sent to Magistro and draft circulated internally by Magistro. Also, comments on why the study found negative results are different between the two drafts. In addition, conclusions differ between conference abstract, Gorson 1998 and letter to editor sent by Gorson 1999.”

377. Despite the results of the Gorson study as described above, the 2002 Diabetic Peripheral Neuropathy section of DrugDex reported that the Gorson study had shown that gabapentin was minimally effective rather than “probably no more effective than placebo”, cited only the significant result in one end point and included the false and misleading conclusion that: “[t]he authors suggest that higher doses of gabapentin are needed.”

o. *False and Misleading Statements—Journal Article-1999*

378. In March 1999, Parke-Davis distributed more than 10,000 copies of an article entitled “Pharmacology of Painful Peripheral Neuropathies,” appearing in the first-ever issue of Progress in Neurology. The author of the article was Dr. Beydoun. The article stated that Neurontin was “first line therapy for the treatment of painful peripheral neuropathies.” This article

Ex. 023, Abramson Report ¶146 (internal citations omitted); Ex. 203, Exhibit J to Affidavit of James E. Murray in support of Defendants’ Motion for Summary Judgment [Docket No. 295] filed in US ex rel. Franklin v. Pfizer et al., 96-11651-PBS (D. Mass. Apr. 14, 2003) (Drugdex Monograph.pdf)

Ex. 304, PFIZER\_DPROBERT\_0028487; Ex. 095, WLC\_CBU\_040534; Ex. 310, <http://web.archive.org/web/20000120044256/pain.com/freecme/beydoun/default.cfm>

was sent by Parke-Davis to all US neurologists, numbering more than 10,000. Other than substituting the word “Neurology” in place of “Anesthesiology,” the monograph was essentially a word-for-word copy of the Progress in Anesthesiology article posted at the www.pain.com website. The article fails to disclose the negative Gorson study or the potential corruption of the results of the Backonja study due to unblinding.

p. *False and Misleading Statements—Journal Article Supplement*

379. In March 1999, Parke-Davis distributed 50,000 copies of an article entitled “Management of Neuropathic Pain Syndromes” appearing as a supplement to Neurology Reviews. The supplement claimed Neurontin to be effective in treating neuropathic pain, but did not disclose the negative Gorson article or the unblinding of 945-210. This supplement was sent to 50,000 primary care physicians.

Ex. 305, WLC\_CBU\_021038;  
Ex. 095, WLC\_CBU\_040534.

q. *False and Misleading Statements—CME Meetings-1999*

380. Beginning in May, 1999, Defendants held various CME meetings, through the Dannemiller pain foundation, entitled “New Treatment Options for the Management of Pain,” where speakers (most often Dr. Beydoun), stated that Neurontin is “first

Ex. 306, WLC\_CBU\_175157; Ex. 307, MDL\_VENDORS\_067857

line therapy for the treatment of painful peripheral neuropathies” but failed to disclose the negative results of Gorson, or the unblinding of Backonja. Sales representatives distributed invitations to this event. Hundreds of physicians attended these events.

r. *False and Misleading Statements--Teleconferences*

381. Parke-Davis also held 50 teleconferences, which featured a 30-minute pre-recorded lecture and then a short question and answer period moderated by Ahmad Beydoun. The teleconferences’ audio script stated that Neurontin “should be used as first-line therapy for the treatment of painful neuropathies” but failed to disclose the negative results of Gorson, or the unblinding of Backonja.

Ex. 308,  
MDL\_VENDORS\_068131;  
Ex. F,  
SH\_0064555.0012039;  
Ex. 309,  
MDL\_VENDORS\_068193.

s. *False and Misleading Statements-CME Monograph*

382. Parke-Davis also prepared a CME monograph entitled “New Pharmacologic Options for the Management of Neuropathic Pain,” authored by Dr. Beydoun, which was essentially identical to his articles that appeared in Progress in Neurology and at the www.pain.com website, and made the same misleading presentation. Parke-Davis distributed 6,500 copies of the monograph to physicians. Sales representatives also

Ex. 312,  
PFIZER\_MDANA\_0002308; Ex.  
313, MDL\_VENDORS\_101225;  
Ex. 314, WLC\_CBU\_174914;  
Ex. 237, MDL\_VENDORS\_065967

distributed business reply cards to physicians who could request a copy of the monograph.

t. *False and Misleading Statements—2nd International Conference on Mechanisms and Treatment of Neuropathic Pain-1999*

383. On June 3, 1999, various Ex. 315, WLC\_CBU\_023248

misleading presentations were given at the Parke-Davis-sponsored 2nd International Conference on Mechanisms and Treatment of Neuropathic Pain in Washington, DC. In one lecture, Marco Pappagallo stated: “[t]he analgesic mechanism of gabapentin is unknown, but its efficacy for neuropathic pain has been established.” Pappagallo cited to the published Backonja article, but does not disclose that the apparent treatment effect was attributable to patient unblinding, nor did he disclose the results of the negative Gorson study. A different presentation misleadingly suggested Neurontin’s utility “acute inflammatory pain,” i.e. nociceptive pain.

u. *False and Misleading Statements-Grand Geneva Resort and Spa*

384. At a meeting of more than 1,500

physicians held at the Grand Geneva Resort and Spa in Lake Geneva, Wisconsin on June 11-13, 1999, Dr.

Backonja and other presenters stated that there were only two clinical trials relating to Neurontin and neuropathic

Ex. 316,  
MDL\_VENDORS\_103909; Ex.  
317, WLC\_CBU\_012710; Ex. 318,  
MDL\_VENDORS\_083903

pain, and that Neurontin’s efficacy in diabetic peripheral neuropathy and mixed neuropathic pains had been “demonstrated in double-blind studies.” The negative Gorson and Reckless studies were omitted from all presentations. The corruption of 945-210 due to unblinding of subjects was not disclosed either. Under the potential conflicts of interest and financial disclosures section, Dr. Backonja falsely stated “None.”

v. *False and Misleading Statements-350 CME Dinners and Grand Rounds-1999 and 2000*

385. In 1999 and 2000, Defendants held a series of more than 350 CME dinners and grand rounds entitled “Reevaluating Neuropathic Pain Treatment Algorithms,” which discussed the Backonja publication but omitted reference to corruption of results due to unblinding or to the negative Gorson study. The “target audience” of these events were:

Ex. 319, WLC\_CBU\_028526; Ex. 320, WLC\_CBU\_180318  
Ex. 095, WLC\_CBU\_040534.

- Primary Care Physicians
- Anesthesiologists
- Pain Management Specialists
- Neurologists
- Psychiatrists
- Endocrinologists

· Immunologists

· Infectious Disease Specialists

386. For this CME dinners and grand rounds series, Parke-Davis prepared the lecture content and trained the faculty, which consisted of more than 75 pain specialists from around the country. These faculty members were not informed about the negative results of the Gorson study or the unblinding of patients in 945-210. Speakers included: Dr. Ahmad Beydoun, Dr. Backonja, Dr. Schachter, and David A. Simpson.

Ex. 319, WLC\_CBU\_028526; Ex. 321, WLC\_CBU\_028618; Ex. 322, PFIZER\_RGLANZMAN\_0143484.

387. The slide set used in this CME initiative did not disclose the negative results of Gorson or the unblinding of Backonja's study due to side effects. A "prerecorded tele-session" featuring Dr. Beydoun was also used. This recording was available 24-hours a day by dialing a toll free number.

Ex. 322, PFIZER\_RGLANZMAN\_0143484; Ex. 303, PFIZER\_TMARTIN\_0001306; Ex. 238, WLC\_CBU\_000218.

w. *False and Misleading Statements—Internet-based CME Activity-1999*

388. Beginning in December 1999, physicians accessed, through Medscape, an internet-based CME activity created by Parke-Davis, to which 40,000 physicians were invited to participate. During the first three weeks it was available, over 7,400 health care professionals, including 2,700 physicians, logged in.

Ex. I, CDM0022284; Ex. 107, WLC\_CBU\_175353; Ex. 239, WLC\_CBU\_072218; Ex. 060, PFIZER\_LKNAPP\_0055357.

These physicians were then exposed to a misleading presentation entitled “Anticonvulsant Therapy in the Treatment of Neuropathic Pain CME,” presented by

Gary J. Bennett, PhD; Robert H. Dworkin, PhD; Bruce Nicholson, MD, which falsely stated that the “2 largest placebo-controlled clinical trials of anticonvulsants in patients with neuropathic pain were double-blind studies that examined gabapentin in postherpetic neuralgia and in painful diabetic neuropathy.” This statement falsely denied the existence of the much larger 945-224 study, which showed that Neurontin was no better than placebo in treating painful diabetic neuropathy. The presentation also fails to disclose the results of the negative Gorson study, and omits any reference to the Backonja study’s data being corrupted due to unblinding.

x. *False and Misleading Statements—CME “New Treatment Options for the Management of Pain”-2000*

389. Beginning on January 8, 2000, Defendants held 41 CME meetings, through the Dannemiller Memorial Educational Foundation, entitled “New Treatment Options for the Management of Pain,” where speakers (most often Dr. Beydoun), stated that Neurontin is “first line therapy for the treatment of painful peripheral neuropathies.” A total of 3,461 attendees were exposed to these statements but were not informed that the apparent treatment effect was attributable to patient unblinding, nor were they informed of the negative results of the Gorson study.

Ex. 240, MDL\_VENDORS\_068657  
Ex. 241, MDL\_VENDORS\_068649  
Ex. 242,  
MDL\_VENDORS\_072916; Ex.  
306, WLC\_CBU\_175157

2. Pfizer’s False and Misleading Statements Made During Class Period

390. In June 2000, the merger between Pfizer and Warner-Lambert became complete. However, the merger had no effect on existing contracts to market Neurontin.

Ex. 243, MDL\_VENDORS\_118884

a. *False and Misleading Statements—Journal Supplement “Mechanisms of Chronic Pain” -2000*

391. In September 2000, Pfizer distributed 10,751 copies of a supplement to the Clinical Journal of Pain entitled “Mechanisms of Chronic Pain.” According to the supplement, clinical trial evidence and systematic reviews “provide consistent support” for the efficacy of Neurontin, most notably in DPN. The supplement fails to disclose the negative Gorson study, nor the unblinding of the Backonja study.

Ex. 244,  
PFIZER\_LESLIETIVE\_0015887;  
Ex. 245,  
PFIZER\_LESLIETIVE\_0013973

b. *False and Misleading Statements—Journal Supplement “Progress in Pain Management” --2000*

392. In September 2000, Pfizer distributed a supplement called Progress in Pain Management for Primary Care Specialists which falsely stated that Neurontin “has been shown to be effective in the treatment of [DPN],” but made no mention of the negative Gorson study, the negative Reckless study, or the unblinding of the Backonja study. This supplement was sent to 50,000 primary care physicians.

Ex. 246,  
PFIZER\_DPROBERT\_0028502;  
Ex. 247  
PFIZER\_MDANA\_0000776

c. *False and Misleading Statements—Journal Article*

393. In October 2000, the *Journal of Pain and Symptom Management* published an article, sponsored by Defendants and authored by Dr. Dallochio et al., entitled: “Gabapentin vs. Amitriptyline in Painful Diabetic Neuropathy: An Open-Label Pilot Study.” Ex. 248, Dallochio C. et al. Gabapentin vs. amitriptyline in painful diabetic neuropathy: an open-label pilot study. *Journal of Pain and Symptom Management* 2000;20:280-5 (“Dallochio Article”).
394. “Like the Morello study, the Dallochio study compared the efficacy of Neurontin to amitriptyline for the treatment of painful diabetic neuropathy. The studies differed in one critically important way: instead of being a ‘gold standard’ double-blind RCT like the Morello study, the Dallochio study was *open-label* (patients and doctors knew which drug was being administered).” Ex. 023, Abramson Report ¶175 (internal footnote omitted, emphasis in original.)
395. “Despite the fact that the Dallochio study was published 13 months after the Morello study, it made no mention of the Morello findings or conclusion, nor the negative Gorson study or the unblinding of Backonja.” Ex. 023, Abramson Report ¶175.
396. Dr. Dickersin observes that the Dallochio Article contains the following biases: “Citation bias - Did not cite Morello, a randomized trial published one year before and showing no evidence of benefit; Ex. 117, Dickersin Report at 32.

Design Bias - Open label, designed to counter Morello.”

397. “Dr. Elizabeth Mutisya (a Pfizer medical director) explained Parke-Davis’s strategy to neutralize the effect of the Morello study: ‘When the negative UCSD gabapentin amitriptyline paper [Morello] was published, Parke-Davis had a two-pronged approach. Attack the flaws in the study, and sponsor another study which ultimately provided more favorable results (the Dallochio study).’”

Ex. 023, Abramson Report ¶175;  
Ex. 166,  
Pfizer\_RGlanzman\_0040034.

d. *False and Misleading Statements-American Academy of Pain Medicine (12 meetings) 2000*

398. In early 2001, Pfizer, under the aegis of the American Academy of Pain Medicine (AAPM) held a series of 12 meetings entitled “New Directions in the Understanding & Treatment of Chronic Pain” in various cities around the country. During those meetings, presentations such as the lecture by Dr. Beydoun entitled “Clinical Success Factors in Managing Neuropathic Pain” were made which stated that Neurontin was effective for treating neuropathic pain and speakers reviewed the published clinical trials on Neurontin but omitted reference to the negative Gorson, Reckless or POPP studies. An estimated 1,200 physicians attended

Ex. 249,  
MDL\_VENDORS\_068519; Ex.  
323, MDL\_VENDORS\_068511;  
Ex. 324,  
MDL\_VENDORS\_094647

these meetings.

399. During those same meetings, approximately 1,200 physicians in attendance also were exposed to a misleading presentation entitled “Practical Approaches to Treating Chronic Low Back Pain,” discussing Neurontin’s use in treating nociceptive pain. Neurontin was listed as an analgesic option for nociceptive low back pain, without disclosure of the multiple negative studies demonstrating Neurontin’s inefficacy for nociceptive pain.

Ex. 249, MDL\_VENDORS\_068519  
Ex. 323,  
MDL\_VENDORS\_068511; Ex.  
324, MDL\_VENDORS\_094647;  
Ex. A, SH\_0064559.0092769.

e. *False and Misleading Statements—Union and Employer Advisory Boards-2001*

400. In November 2001, Pfizer held two advisory boards targeting employer and union, mostly medical directors and benefits managers. The meetings were held in New York City and Arizona. The presentations contained a slide entitled “Clinical Data from Neuropathic Pain Trials” which omitted the negative Gorson, Reckless, Morello and POPP studies.

Ex. 325,  
PFIZER\_SDOFT\_0052466

f. *False and Misleading Statements-Advisory Boards Palm Beach, FL and Dallas, TX—2002*

401. On January 12, 2002, at a physician advisory board held at the Four Seasons Resort in Palm Beach, Florida, Leslie Tive repeated her presentation to

Ex. 326,  
PFIZER\_SDOFT\_0052543;  
Ex. 327,  
PFIZER\_SDOFT\_0052549; Ex.  
328, PFIZER\_SDOFT\_0052606;  
Ex. 329,

the union and employer advisory board referenced above.. The presentation contained a slide entitled “Clinical Data from Neuropathic Pain Trials” which omitted the Gorson, Reckless, Morello and POPP studies. Robert Glanzman gave an identical presentation on the same day to a different group of physicians. He repeated that presentation February 2002 at a physician advisory board held at the Mansion on Turtle Creek in Dallas, Texas. His presentation also contained a slide entitled “Clinical Data from Neuropathic Pain Trials” which omitted the negative results from the Gorson, Reckless, Morello and POPP studies. At all of these presentations, the Pfizer employees misleadingly stated that low back pain was a condition “associated with neuropathic pain,” This statement misleadingly suggested that Neurontin’s falsely claimed efficacy for neuropathic pain was applicable to low back pain. No disclosure was made of the multiple negative clinical trials.

PFIZER\_SDOFT\_0013666; Ex. 330, PFIZER\_SDOFT\_0013668; Ex. 163, Perry Report at 76.

g. *False and Misleading Statements—HMO/Managed Care Pain Advisory Boards--2002*

402. Leslie Tive repeated this same presentation on January 25, 2002 at an HMO/Managed Care pain advisory board at the Disney BoardWalk Resort

Ex. 331, PFIZER\_SDOFT\_0052567; Ex. 332, PFIZER\_SDOFT\_0052571; Ex. 333, PFIZER\_SDOFT\_0052573; Ex. 334, PFIZER\_SDOFT\_0052575; Ex.

in Orlando, Florida. A similar advisory board was held on March 4, 2002, and Leslie Tive once again gave the same presentation. A managed care and long term care advisory board was held on June 24, 2002, and the same slides were used. Again, the Defendants' presentation omitted the negative Gorson, Reckless, Morello and Popp studies.

335,  
PFIZER\_SDOFT\_0013811; Ex.  
336,  
PFIZER\_RGLANZMAN\_0149235

h. *False and Misleading Statements—Journal Article-2002*

403. In October 2002, Pfizer published the Serpell study in the journal *Pain*, which had a circulation of 7,660. The manuscript was written by Synergy, a medical writing company.

Ex. 220,  
Serpell MG, Neuropathic Pain Study Group. *Pain* 2002;99:557-566 (“Serpell Article”); Ex. 221, <http://www.sciencedirect.com/science/journal/03043959>.

404. The results of Defendants' raw analysis of protocol 945-306, which demonstrated that the findings for the primary endpoint of 945-306 were *not* statistically significant, were suppressed and not presented in the Serpell Article.

Ex. 220, Serpell Article.

405. The article contained the key promotional message that “Gabapentin is efficacious in treating neuropathic pain symptoms arising from a broad range of different pain syndromes”, referred to “evidence from large randomized trials in two types of neuropathic pain [DPN and PHN]” and stated that, “Case reports, pilot studies, and retrospective reviews also suggest efficacy

Ex. 220, Serpell Article; Ex. 337, PFIZER\_MPATEL\_0139889; Ex. 338, PFIZER\_RGLANZMAN\_0121216; Ex. 339, MAC\_E\_0049671

gabapentin in a variety of neuropathic pain syndromes...,”

The Defendants failed to disclose the negative Gorson, Reckless and POPP studies.

406. Dr. Dickersin finds that the Serpell Ex. 117, Dickersin Report at 31.  
Article contains the following biases: “Selective analysis -  
Use of transformation to obtain statistical significance;  
outcomes significant only for selected time points, not at  
time point specified in protocol; effectiveness in post-  
herpetic neuropathy population influences overall result;  
Selective analysis - Analyzed populations were different  
from those presented in the protocol; Citation bias -  
Citation of only positive findings in a conference poster;  
Ghost authorship - Full length article written by hired  
medical writers (Synergy); Spin - Negative findings  
reported to sound positive; Design bias - Excluded  
patients who were ‘non-responders’ to gabapentin in the  
past resulting in a selective study population.”

407. Dr. Dickersin opines that Protocol Ex. 117, Dickersin Report at 30.  
945-224 contains the following biases: “Publication bias -  
Final primary results not published in full article;  
Selective outcome reporting - Secondary outcomes  
reported (in selective meta-analysis) with greater emphasis  
and conclusions based on secondary outcomes; Selective

analysis - Study's findings used in selective meta-analysis by another author to show overall effectiveness; Time lag bias - Internal memos indicate company delayed publication; Ghost authorship - Both drafts written by unacknowledged commercial source to include "key messages."

i. *False and Misleading Statements-Journal Article -2003*

408. In January 2003, *Clinical Therapeutics* published Defendants' manuscript entitled "Gabapentin Dosing for Neuropathic Pain: Evidence from Randomized Placebo-Controlled Trials." The authors were Dr. Miroslav Backonja and Robert Glanzman, an employee of Pfizer. *Clinical Therapeutics* has 4,000 subscribers.

Ex. 340, Backonja M., Glanzman R. Gabapentin dosing for neuropathic pain: Evidence from randomized, placebocontrolled clinical trials. *Clinical Therapeutics* 2003; 25(1): 81-104 ("Backonja/Glanzman Dosing Article"), Ex. 339, MAC\_E\_0049671 at 175.

409. The article in *Clinical Therapeutics* contained promotional "Key Messages" to reinforce "the efficacy message" of Neurontin in DPN, and in treating neuropathic pain of many causes. While the article purported to review all significant clinical trials in neuropathic pain, it omitted any reference to the negative Gorson and POPP studies. The article also referenced the published data from Backonja and Serpell and did not disclose the unblinding problem or the lack of statistical

Ex. 341, PFIZER\_LALPHS\_0013849

significance that accompanied those trials respectively.

The article concluded: “[r]esults of the randomized, placebo-controlled studies reviewed here indicate the efficacy and tolerability of gabapentin for the alleviation of a variety of pain symptoms.” Defendants failed to disclose that the FDA had reviewed the same trials and reached the opposite conclusion.

410. “The fact that there was no significant difference between the gabapentin and placebo group in the primary endpoint of the Reckless study (the largest of the studies addressed other than post-herpetic neuralgia included in the review) is not mentioned until the ninth page. Even then, the positive findings in the secondary outcome measures were accentuated in a way that was criticized by reviewers of the twice rejected manuscript (see above). The review article failed to include the results from the Gorson study, which had been known to the Defendants four years earlier.”

Ex. 023, Abramson Report ¶220.

j. *False and Misleading Statements—“Dear Doctor Letters”*

411. From December 1998 through the present, Defendants mailed several versions of a “Dear Doctor” letter on “various pain conditions” to 7,891 physicians that falsely stated that “available data from

Ex. 085, Merlin

other studies... suggests that gabapentin should be considered in the treatment of neuropathic pain as first-line agents [sic],” while omitting any reference to the failed POPP, Gorson and Reckless clinical trials . The letter also cited to the study by Dr. Simpson, even though a senior Pfizer employee had stated that he “would not touch” the study and Pfizer’s outside pain expert had cited 21 reasons why the study was likely faked.

k. *False and Misleading Statements Influenced COCHRANE’s Review of Neurontin for Pain*

412. In April 2000, the first Cochrane review of gabapentin for neuropathic pain was issued stating: “While gabapentin is increasingly being used for neuropathic pain the evidence would suggest that it is not superior to carbamazepine.” The Cochrane collaboration did not have access to the suppressed results of protocol 945-224, nor did Defendants alert the authors to the unblinding of 945-210 that rendered it incapable of providing any basis for the efficacy of gabapentin for neuropathic pain.

Ex. 342, Wiffen P, Collins S, McQuay, et al., Anticonvulsant Drugs for Acute and Chronic Pain (Cochrane Review) , The Cochrane Library, Issue 1, 2002; Ex. 023, Abramson Report ¶¶193-194.

l. *False and Misleading Statements-Journal Article --2000*

413. In December 2000, the *Journal of Pain Symptom Management* published another review,

Ex. 343, Collins SL, Moore RA, McQuay HJ, Wiffen P, Antidepressants and anticonvulsants for Diabetic Neuropathy and Postherpetic Neuralgia: A

from the Pain Research Group at Oxford that concluded: “No difference in efficacy was demonstrated between gabapentin...and the older anticonvulsants phenytoin and carbamazepine.” The Defendants failed to inform the authors of this review that the results of study 945-210 had been comprised by unblinding, negating any basis for claiming that Neurontin was broadly effective for pain. Defendants also failed to furnish the authors with the negative results of study 945-224, which at that point were being suppressed pursuant to the Defendants’ publication strategy.

Quantitative Systematic Review, Journal of Pain Symptom Management, 2000;20:449-58; Ex. 023, Abramson Report ¶195.

m. *False and Misleading Statements—Use of Sales Representatives and Outcomes Research to Counter Negative External Reviews-2001*

414. Defendants carefully monitored external reviews of the scientific evidence concerning Neurontin, not to make sure that such external reviewers had access to all data, but rather to make sure that Neurontin would receive favorable reviews and any negative reviews would be blunted or countered. On January 3, 2001, in response to the negative external review published in the Journal of Pain Symptom Management, Defendants drafted a field letter to send to all sales representatives to assist in handling questions

Ex. 344, MAC\_0001296; Ex. 345, MAC\_E\_0020024; Ex. 346, PFIZER\_MGARCIA\_0002894; Ex. 347, PFIZER\_RGLANZMAN\_0146211; Ex. 348, Pfizer\_CGrogan\_0012128; Ex. 349, Pfizer\_CGrogan\_0012131

regarding Neurontin's inefficacy as a treatment for neuropathic pain. The letter discussed "ways that this study could be handled if customers raise the article." One of the suggested spins was to allude to studies that were soon to be published, including the misleading Serpell manuscript, which had already been rejected by the *BMJ* for reasons including inappropriate company bias and enrichment secondary to gabapentin-favorable exclusion criteria.

415. On March 16, 2001, the senior vice-president of Pfizer at the time [and current Chief Medical Officer] Joe Feczko sent an internal e-mail to several employees with the subject "Systematic Reviews/Metaanalyses." The e-mail expressed concern about external reviews of "Pfizer sponsored clinical and outcomes trials" and mentioned that Defendants had received "requests for individual level patient data" during the course of those reviews. Dr. Feczko stated that "these reviews have significant potential risk for global product positions and several recent reviews have had negative results due to incompleteness of data reviewed or a misunderstanding of the data." Dr. Feczko concluded his e-mail: "It is critical that all reviews have protocols that

Ex. 350,  
Pfizer\_LeslieTive\_0035819.

are reviewed and approved by Area Medical and Outcomes Research management” and that “[t]hese approvals should be obtained prior to any data release.”

416. On March 20, 2001, Michael Rowbotham responded to the March 16, 2001 e-mail from Dr. Feczko, stating: “we need to be very clear what we want to get out of the analysis and why. We also need to be clear what we believe the what [*sic*] the outcome will be from our understanding of the data.” Dr. Leslie Tive responded directly to Michael Rowbotham recommending that he “work closely with the outcomes research team on this initiative.”

Ex. 350,  
Pfizer\_LeslieTive\_0035819.

417. A Pfizer marketing team member warned of external reviewers’ increasingly common use of numbers needed to treat (NNT) as a measure for pain relief: “Essentially NEURONTIN does not come out favorably in the comparison if the raw numbers are listed on a slide as NEURONTIN has a high NNT and AMT [amitriptyline] has a low NNT. (lower is better!)... we should be aware how it is handled as on the surface it could not look good for NEURONTIN.”

Ex. 351,  
PFIZER\_DPROBERT\_0007559

418. Another Pfizer marketing team member, known only as “Z,” claimed credit for raising the

Ex. 346,  
PFIZER\_MGARCIA\_0002894

issue of NNTs with the result of his efforts are that the Neurontin marketing team and outcomes research became focused on finding ways to “counter” this type of meta-analysis.

n. *False and Misleading Statements—Journal Article—2002*

419. In January 2002, the *European Journal of Pain* published a review article, which Defendants had sponsored. No financial or conflict of interest disclosure was made. The review article failed to disclose the negative results from protocol 945-224, nor did it reveal that the results from protocol 945-210 had been compromised by unblinding, thus negating any basis for claiming that Neurontin was effective for pain. Finally, the article failed to disclose the negative results from protocol 945-271 (POPP).

Ex. 352, McQuay HJ, Neuropathic pain: evidence matters, *European Journal of Pain*, 2002; 6 (Suppl. A): 11-18; Ex. 363, [http://www.europeanjournalpain.com/issues/contents?issue\\_key=S1090-3801\(00\)X0009-2](http://www.europeanjournalpain.com/issues/contents?issue_key=S1090-3801(00)X0009-2); Ex. 023, Abramson Report ¶¶201.

o. *False and Misleading Statements—Cochrane Review, “Gabapentin for Acute and Chronic Pain”--2005*

420. The 2005 Cochrane review entitled “Gabapentin for acute and chronic pain” could have but did not include the negative results from 945-224 nor 945-271. “Hence, the Cochrane 2005 systematic review of gabapentin is irremediably compromised by “publication bias.” Defendants could have but failed to inform the

Ex. 353, Wiffen PJ, McQuay HJ, Rees J, Moore RA. Gabapentin for acute and chronic pain. *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD005452. DOI: 10.1002/14651858.CD005452.; Ex. 163, Perry Report at 23; Ex. 023, Abramson Report ¶¶202-204.

Cochrane Collaboration that the results of 945-210 had been compromised by unblinding, negating any basis for claiming that Neurontin was effective for pain.

p. *False and Misleading Statements—Cochrane Review, “Anticonvulsant Drugs for Acute and Chronic Pain”*

421. Similarly, the 2005 Cochrane review entitled “Anticonvulsant Drugs for Acute and Chronic Pain” did not include the negative results of protocols 945-224 and 945-271. Once again, Defendants failed to inform the Cochrane Collaboration that the results of 945-210 had been compromised by unblinding negating any basis for claiming that Neurontin was effective for pain.

Ex. 342, Wiffen PJ, Collins S, McQuay HJ, Carroll ID, Jadad A, Moore RA. Anticonvulsant drugs for acute and chronic pain. Cochrane Database of Systematic Reviews 2005, Issue 3. Art.No.: CD001133. DOI: 10.1002/14651858.CD001133.pub2 ; Ex. 023, Abramson Report ¶¶202-204.

422. The Cochrane reviews illustrate that, since “Defendants were not informing physicians of the Level 1 scientific evidence from their own studies, there is no possibility that practicing physicians could [have been] informed about or consider[ed] all the evidence in their clinical decision making.”

Ex. 023, Abramson Report ¶205.

#### **D. Results of the Fraudulent Marketing Campaign**

##### **1. Aggregate Results**

423. According to IMS NDTI data, the average number of uses of Neurontin for neuropathic pain

Ex. 138, Revised Conti Declaration, Figure 8 (Revised).

per quarter in 1995 was 4,663.

424. According to IMS NDTI data, the average number of uses of Neurontin for nociceptive pain per quarter in 1995 was 0.

Ex. 138, Revised Conti Declaration, Figure 9 (Revised).

425. According to IMS NDTI data, in the four quarters preceding July 1995, there were a total of 5,658 Neurontin uses for neuropathic pain. In the four quarters following July 1995, there were a total of 90,302 Neurontin uses for neuropathic pain. This represents an increase of 1600%.

Ex. 138, Revised Conti Declaration ¶28.

426. Scott-Levin's estimate was lower than IMS's, estimating only 1,000 total Neurontin uses for neuropathic pain in the 12 months prior to August 1995.

Ex. 205, WLC\_FRANKLIN\_0000033011

427. According to IMS NDTI data, 0% of neurologists' total uses of Neurontin were for pain until Q3 1995. In Q3 1995, only 4% of neurologists' total uses of Neurontin were for pain.

Ex. 138, Revised Conti Declaration, Figure 21 (Revised).

428. According to IMS NDTI data, in the four quarters preceding September 1995, there were a total of 0 Neurontin uses for nociceptive pain. In the four quarters following September 1995, there were a total of 21,110 Neurontin uses for nociceptive pain.

Ex. 138, Revised Conti Declaration ¶29.

429. In the four months following the

Ex. 277, WLC\_CBU\_095272

Neuropathic Pain Marketing Assessment, Neurontin prescriptions for pain “increased considerably.”

430. In May 1996, an internal Parke-Davis memorandum noted that Neurontin prescriptions for neuropathic pain constituted less than 1% of the overall market. However, the memorandum noted, “[n]ot surprisingly, Neurontin had the greatest growth rate over the last twelve months in terms of the anticonvulsants used to treat neuropathic pain.”

Ex. J,  
WLC\_FRANKLIN\_0000032365

431. According to IMS NDTI data, the average number of uses of Neurontin for neuropathic pain per quarter in 1996 was 30,099.

Ex. 138, Revised Conti Declaration, Figure 8 (Revised).

432. According to IMS NDTI data, the average number of uses of Neurontin for nociceptive pain per quarter in 1996 was 6,800.

Ex. 138, Revised Conti Declaration, Figure 9 (Revised).

433. According to IMS NDTI data, the average number of uses of Neurontin for neuropathic pain per quarter in 1997 was 30,099.

Ex. 138, Revised Conti Declaration, Figure 8 (Revised).

434. According to IMS NDTI data, the average number of uses of Neurontin for nociceptive pain per quarter in 1997 was 25,377.

Ex. 138, Revised Conti Declaration, Figure 9 (Revised).

435. According to IMS NDTI data, by 1997, 34% of neurologists' total uses of Neurontin were

Ex. 138, Revised Conti Declaration, Figure 21 (Revised).

for pain. This represents a 850% growth in neurologists uses' of Neurontin for pain since Q3 1995.

436. By August 1997, Neurontin was the most commonly used AED to treat neuropathic pain. Ex. 279, WLC\_CBU\_078961

437. Parke-Davis admitted that growth in off-label uses in 1996-1997 was “primarily driven by CME educational events, publications & clinical trials.” Ex. 362, WLC\_CBU\_050479

438. According to IMS NDTI data, the average number of uses of Neurontin for neuropathic pain per quarter in 1998 was 103,329. Ex. 138, Revised Conti Declaration, Figure 8 (Revised).

439. According to IMS NDTI data, the average number of uses of Neurontin for nociceptive pain per quarter in 1998 was 36,230. Ex. 138, Revised Conti Declaration, Figure 9 (Revised).

440. According to IMS NDTI data, by Q2 1998, 42% of neurologists' total uses of Neurontin were for pain and uses for pain had surpassed FDA-approved uses. Thereafter, neurologists had more uses of Neurontin for pain than for its FDA-approved uses. In fact, through the end of the class period (2004), one-half (50%) of neurologists' total uses of Neurontin were for pain. Ex. 138, Revised Conti Declaration, Figure 21 (Revised).

441. According to IMS NDTI data, the average number of uses of Neurontin for neuropathic pain Ex. 138, Revised Conti Declaration, Figure 8 (Revised).

per quarter in 1999 was 164,291.

442. According to IMS NDTI data, the average number of uses of Neurontin for nociceptive pain per quarter in 1999 was 61,907.

Ex. 138, Revised Conti Declaration, Figure 9 (Revised).

443. In early 2000, Parke-Davis admitted that publications and CME activity supported the growth of Neurontin. Parke-Davis also admitted that peer-to-peer interaction was the “backbone” of dissemination of product knowledge, and that “[e]ducational initiatives have driven sales in the US.” Accordingly, the company recognized that CMEs needed to be increased in order to “[c]reate advocates that will further disseminate messages.”

Ex. 419, PFIZER\_CGROGAN\_0018342; Ex. 420, WLC\_CBU\_076460

444. According to IMS NDTI data, the average number of uses of Neurontin for neuropathic pain per quarter in 2000 was 276,297.

Ex. 138, Revised Conti Declaration, Figure 8 (Revised).

445. According to IMS NDTI data, the average number of uses of Neurontin for nociceptive pain per quarter in 2000 was 82,433.

Ex. 138, Revised Conti Declaration, Figure 9 (Revised).

446. According to IMS NDTI data, the average number of uses of Neurontin for neuropathic pain per quarter in 2001 was 357,641.

Ex. 138, Revised Conti Declaration, Figure 8 (Revised).

447. According to IMS NDTI data, the

Ex. 138, Revised Conti Declaration, Figure 9 (Revised).

average number of uses of Neurontin for nociceptive pain per quarter in 2001 was 94,031.

448. According to IMS NDTI data, the average number of uses of Neurontin for neuropathic pain per quarter in 2002 was 323,235.

Ex. 138, Revised Conti Declaration, Figure 8 (Revised).

449. According to IMS NDTI data, the average number of uses of Neurontin for nociceptive pain per quarter in 2002 was 121,230.

Ex. 138, Revised Conti Declaration, Figure 9 (Revised).

450. According to IMS NDTI data, the average number of uses of Neurontin for neuropathic pain per quarter in 2003 was 396,281.

Ex. 138, Revised Conti Declaration, Figure 8 (Revised).

451. In its 2002 Operating Plan, Pfizer admitted that “detailing physicians drives prescribing,” and that “higher detailing frequency drives prescription growth.”

Ex. 421,  
PFIZER\_BPARSONS\_0022255

452. According to IMS NDTI data, the average number of uses of Neurontin for nociceptive pain per quarter in 2003 was 143,112.

Ex. 138, Revised Conti Declaration, Figure 9 (Revised).

453. According to IMS NDTI data, the average number of uses of Neurontin for neuropathic pain per quarter in 2004 was 427,021.

Ex. 138, Revised Conti Declaration, Figure 8 (Revised).

454. According to IMS NDTI data, the average number of uses of Neurontin for nociceptive pain

Ex. 138, Revised Conti Declaration, Figure 9 (Revised).

per quarter in 2004 was 137,522.

2. Individual Class Reps

a. *Gerald Smith*

455. Gerald Smith suffered from severe headaches and neuropathic pain. He took Neurontin over a period of nearly two years, and in that time period his headaches never got better.

Ex. 422, Deposition of Gerald Smith (“Smith Dep.”) at 27 – 28, 70 – 71.

456. Gerald Smith’s neurologist, Dr. Kylene Huler, was detailed hundreds of times by various Parke-Davis and Pfizer sales representatives from 1996 through 2004. During these details, she discussed off-label uses of Neurontin, such as migraine.

Ex. 423, Huler Sherlock and CMMS.

457. Dr. Huler was detailed roughly 27 times in the space of a year by a single sales representative, who recorded in his contemporaneous notes:

Ex. 423, Huler Sherlock and CMMS; Ex. 476, Huler Wolters Kluwer

Dr. Huler...is down with all of the Pfizer [products]...She is the Pfizer Queen (Zoloft, Neurontin) and she said as much...Dr. Huler really likes the fact that we know she is high on the list of Pfizer (zoloft, Neurontin) products... Feed her ego although she is a nicelady [sic] and not an megalomaniac , she likes being the #1 queen.

Prior to her first Neurontin prescription in July 1998, Dr. Huler had already been detailed more than 30 times by 3 different sales representatives.

Ex. 423, Huler Sherlock and CMMS.

b. *Lorraine Kopa*

458. Lorraine Kopa suffered chronic neck and back pain as a result of a car accident. She took Neurontin for roughly six months but did not benefit from the drug.

Ex. 424, Deposition of Lorraine Kopa at 30, 84, 103-106.

459. Ms. Kopa's prescribing physician was Dr. Vithalbhai Dhaduk, a trained Pfizer speaker who spoke regularly on Neurontin and earned significant fees.

Ex. 425, Deposition of Vithalbhai Dhaduk Dep. at 131 – 32, 135, 270, 289.

460. Dr. Dhaduk attended a Parke-Davis "Pain Weekend" seminar, an event series devoted to fraudulently marketing Neurontin for pain.

See ¶ \_\_ supra. [INSERT ¶ NO. FOR ¶ WHICH MENTIONS "PONTE VEDRA"]

461. Dr. Dhaduk's involvement with the Defendants directly related to other off-label uses, including the use of Neurontin at doses above 1800 mg per day, and epilepsy monotherapy. Dr. Dhaduk was a investigator in the STEPS study, a "seeding" trial designed to induce physicians to prescribe Neurontin at higher than approved doses through the use of kickbacks. (Dhaduk Dep. at 143:17-146:6.) Dr. Dhaduk had also agreed to serve as a speaker on monotherapy, even though monotherapy was never an approved use of Neurontin.

Ex. 426, WLC\_FRANKLIN\_0000066968.

462. Defendants also paid Dr. Dhaduk to attend their conferences and consultant meetings. At all times, Dr. Dhaduk's airfare, hotel and meals are also paid

Ex. 425, (Dhaduk Dep. at 127, 128, 141, 284 – 86).

for by Defendants.

463. Dr. Dhaduk has received hundreds of visits from Defendants' sales representatives and medical liaisons.

Ex. 425, (Dhaduk Dep. at 110, 117); Ex. 427, Dhaduk Sherlock and CMMS.

464. According to Pfizer's sales call database, a Pfizer sales representative asked Dr. Dhaduk to agree to increase the share his prescriptions for a Pfizer drug to 25% of his overall prescriptions. Dr. Dhaduk agreed, indicating "don't worry about it," and promising the sales rep that he increase his prescriptions

Ex. 427, Dhaduk Sherlock and CMMS.

c. *Carolyn Hollaway*

465. Carolyn Hollaway suffered from nociceptive pain, specifically chronic back pain resulting from a traumatic motor vehicle accident and "specific point tenderness in the lower back..." The accident caused inflammation which prompted Dr. Rogers to prescribe Bextra, a Pfizer COX-2 inhibitor used to treat nociceptive pain (until 2005, when Pfizer withdrew it from the U.S. market on recommendation by the FDA, citing an increased risk of heart attack and stroke. Pfizer agreed to pay \$894 million to settle various claims, including claims that Bextra was fraudulently marketed and that physicians were provided with information that was not truthful). Dr.

Ex. 428, Hollaway Ex. 8; Ex. 429, Hollaway Ex. 12; Ex. 430, [http://www.pfizer.com/news/press\\_releases/pfizer\\_press\\_releases.jsp?rsUrl=http://mediaroom.pfizer.com/portal/site/pfizer/index.jsp?ndmViewId=news\\_view&ndmConfigId=1010794&newsId=20081022006046&newsLang=en](http://www.pfizer.com/news/press_releases/pfizer_press_releases.jsp?rsUrl=http://mediaroom.pfizer.com/portal/site/pfizer/index.jsp?ndmViewId=news_view&ndmConfigId=1010794&newsId=20081022006046&newsLang=en); Ex. 431, [http://www.pfizer.com/news/press\\_releases/pfizer\\_press\\_releases.jsp?rsUrl=http://mediaroom.pfizer.com/portal/site/pfizer/index.jsp?ndmViewId=news\\_view&ndmConfigId=1010794&newsId=20081017005371&newsLang=en](http://www.pfizer.com/news/press_releases/pfizer_press_releases.jsp?rsUrl=http://mediaroom.pfizer.com/portal/site/pfizer/index.jsp?ndmViewId=news_view&ndmConfigId=1010794&newsId=20081017005371&newsLang=en) Ex. 552, Transcript of Hollaway Deposition at 18.

Rogers also prescribed Pfizer's Neurontin, but it was not effective for relieving her back pain.

466. Dr. Greg Rogers, Ms. Hollaway's physician, has admitted that he has "trouble distinguishing between [neuropathic pain and nociceptive pain]." In fact, Dr. Rogers incorrectly defined nociceptive pain as:

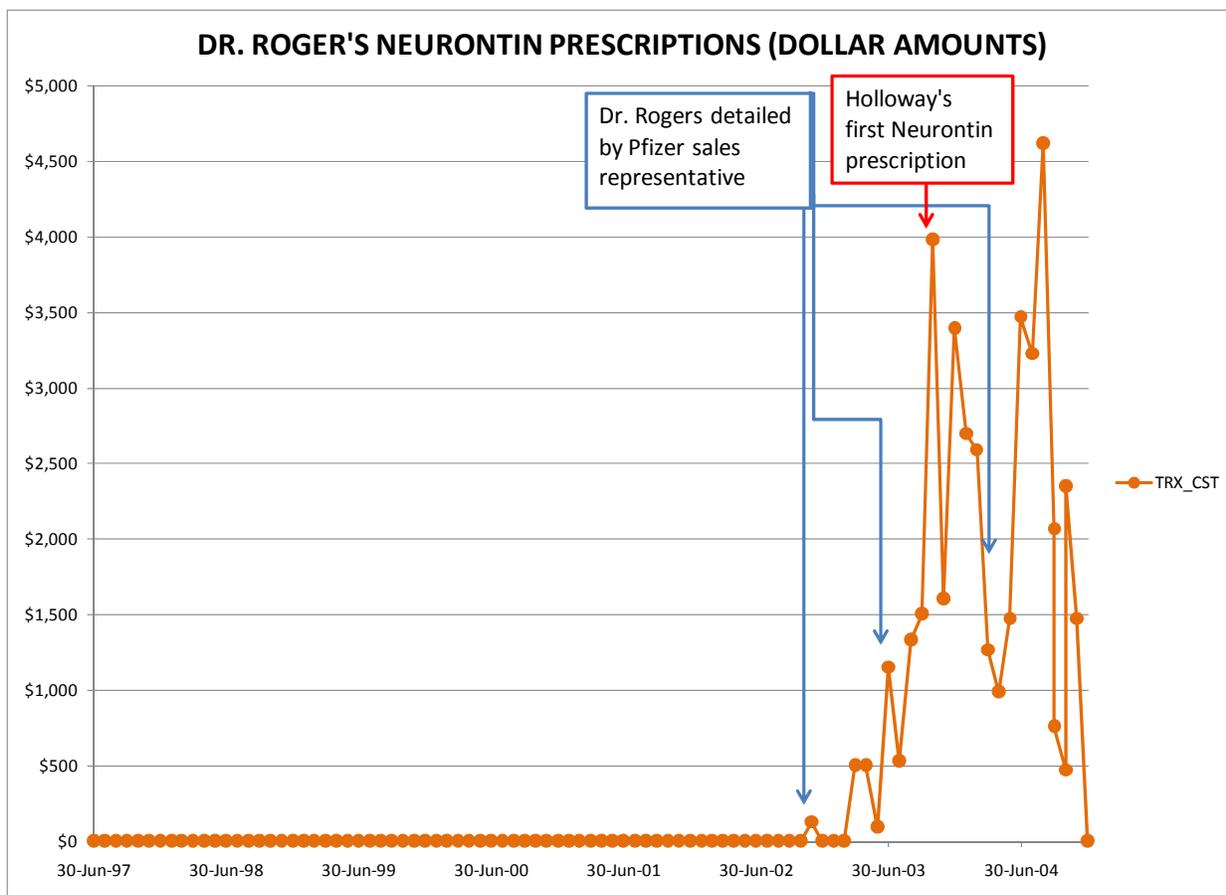
pain that's not really generated by a specific location such as an arm, a leg, a knee, an ankle. But the nerve that connects the brain to that location is being affected and is generating the pain that the brain perceives. And it's not really -- it may seem like it's knee pain, but it's really something involving the nerve between the knee and the brain. So if something in the brain stem goes wrong, you won't perceive it properly. If something -- if there's a herniated disc in the lumbar spine, it can affect it and cause the sensation of knee pain without the knee actually being injured. So that -- that would be sort of my description of it.

Dr. Rogers also prescribed Neurontin to Ms. Hollaway's husband for his arthritis, a type of nociceptive pain.

467. Dr. Rogers had never prescribed Neurontin until November 2002, the *same month* that he was *first* detailed by a Pfizer sales representative. He was detailed on Neurontin two more times by Pfizer.

Ex. 432, Deposition of Dr. Greg Rogers at 115, 124; Ex. 552, Transcript of Hollaway Deposition at 89-90.

Ex. 433, Rogers Sherlock; Ex. 434, Rogers Wolters Kluwer.



### III. FACTS RELATING TO MIGRAINE

#### A. Neurontin is Ineffective as a Treatment for Migraine

468. Defendants conducted three studies Ex. 117, Dickersin Report at 23. of Neurontin for the treatment of migraines (879-200, 945-217, and 945-220), all of which obtained negative results for the primary outcome examined.

##### 1. 879-200

469. By June 25, 1990, Defendants were Ex. 477, 4301\_00066\_(Official).pdf aware of the results of protocol 879-200, a double-blind, at 1; Ex. 478, McCrory Report at 7. placebo-controlled, parallel-group multicenter trial of Neurontin in prophylactic treatment of common migraine.

The study found no statistically significant difference in its primary efficacy measure, the adjusted mean reduction in migraine attack frequency, between the placebo and Neurontin treatment groups, or in the difference in attack frequency between the two groups.

2. 945-220

470. By March 10, 1998, Defendants were aware of the results of protocol 945-220, a double-blind, randomized, placebo-controlled, multicenter trial of Neurontin in migraine prophylaxis. The results showed no significant difference between gabapentin and placebo in the primary outcome measures HF at SP2 or change in HF from baseline to SP2 in the efficacy population.

Ex. 479, 995-00074\_(p1-366).pdf at 1; Ex. 478, McCrory Report at 10.

3. 945-217

471. By January 25, 1999, Defendants were aware of the results of protocol 945-217 a double-blind, randomized, placebo-controlled, multicenter trial of Neurontin in migraine prophylaxis, which in the primary outcome variables “did not show any statistically significant difference between gabapentin and placebo in either the efficacy population or the mITT population.”

Ex. 480, 995-00085.pdf at 1. Ex. 478, McCrory Report at 9.

4. Plaintiffs’ Expert Opinion Establishes Neurontin’s Inefficacy as a Treatment for Migraine

472. Dr. Douglas McCrory, a health

Ex. 478, McCrory Report at 1.

services researcher experienced in the evaluation of clinical trials, has reviewed the evidence-base on Neurontin's use in migraine and headache and concluded the following: "Based on my assessment of the published and unpublished reports from 4 unique double blind, placebo-controlled randomized trials of gabapentin for migraine prophylaxis, in my opinion, the total evidence does not meet the generally established criteria for efficacy. A single positive study is small, with a questionable analysis, and has failed to be replicated in several other larger better designed studies. The most notable studies are two negative trials performed by Parke-Davis, the primary analyses of which fail to reach statistical significance and have remained unpublished." Moreover, Dr. McCrory finds: "A meta-analysis of headache frequency data from 4 trials fails to show a statistically significant effect of gabapentin compared with placebo for migraine prophylaxis. In comparison with other widely used migraine preventive drugs, the estimated effect size for gabapentin not only fails to reach statistical significance, but also has a much lower magnitude of effect."

473. Dr. McCrory found that study 879-200 was negative in its primary efficacy measure, and “suffer[ed] from several deficiencies” including “differential contamination of the gabapentin arm with known effective cointerventions.” Ex. 478, McCrory Report at 8.

474. Dr. McCrory found study 945-220 to be “a negative trial.” The results showed no significant difference between gabapentin and placebo in the primary outcome measures HF at SP2 or change in HF from baseline to SP2 in the efficacy population. Ex. 478, McCrory Report at 10.

475. Dr. Abramson notes that the design of 945-220 “was flawed from the beginning because of its reliance upon the ‘efficacy evaluable population,’ which was a subset of the MITT population, which was in turn a subset of the intention-to-treat (ITT) population. Level 1 evidence from RCTs demands that analyses be conducted on the intention-to-treat population as a whole. The purpose of randomizing patients in the gold standard RCT study design is to eliminate to the greatest degree possible any systemic difference between the treatment and control groups. Modification of the ITT population diminishes the likelihood that significant differences in outcome measures between the study groups were due to actual Ex. 023, Abramson Report ¶184.

effect of the active drug. Relying upon any subset of the ITT population allows factors that might systematically skew patient outcomes after randomization to distort the results of the study.”

476. Dr. McCrory states that 945-217 Ex. 478, McCrory Report at 9.  
was “a negative study, since the analysis of the primary outcome variable in both the efficacy population and the mITT population failed to achieve statistical significance.”

477. In summary, Dr. McCrory’s expert Ex. 481, McCrory Affidavit, ¶ 3.  
opinion is that “Neurontin is ineffective for migraine prevention.”

**B. Defendants’ Intent to Fraudulently Market Neurontin for Migraine**

478. In July 1985, Defendants finalized Ex. 477, 4301-00066\_(Official).pdf  
protocol 879-200 entitled: “Gabapentin as prophylactic at 73.  
interval therapy in patients with migraine.”

479. By 1987, Dr. Wessely, the lead Ex. 483, Wessely P, Baumgartner  
investigator of the trial, reported “an interim analysis of C, Klingler D, Kreczi J, Meyerson  
study 879-200.” Although no p-value was disclosed, the M, Sailer L, et al. Preliminary  
investigators were aware that “the difference between results of a double-blind study with  
gabapentin and placebo [was] not statistically significant.” the new migraine prophylactic drug  
Gabapentin. Cephalalgia. 1987;  
7(Suppl 6):477-8 (“Wessely  
Abstract”) (DouglasC.McCrory-  
10.pdf); Ex. 478, McCrory Report  
at 8-9.

480. In March 1995, at a Core Marketing Ex. 184, WLC\_CBU\_100422.  
Team Meeting, it was noted that “The US will be  
conducting some preliminary qualitative research (focus

groups) with Neurologists during the American Academy of Neurologists to assess reactions to initial monotherapy use as well as exploring additional off-label uses (neuropathic pain, migraine)...”

481. At a consultants meeting in Boston held on September 28, 1995, Parke-Davis obtained feedback from various physicians on the best ways to communicate an efficacy message to physicians. The consultants recommended: “CME events,” “publications of seeding trials” to create a “drumbeat in the literature,” “speakers bureau,” and “monographs in journals.” The point Parke-Davis derived from this meeting is that “[o]nce Neurontin is proven effective in a controlled trial, its use will likely spread to other pain syndromes.”

Ex. 196,  
WLC\_FRANKLIN\_0000087284;  
Ex. 197,  
WLC\_FRANKLIN\_0000206531;  
Ex. 274,  
WLC\_FRANKLIN\_0000015522.

482. In December 1995, Parke-Davis made the decision to include migraine in its 1996 Operating Plan for Neurontin, which listed migraine alongside neuropathic pain as some of the drug’s “opportunities.”

Ex. 484, WLC\_CBU\_111454

483. On April 23, 1996, the Neurontin Development Team had adopted a formal plan to market Neurontin as a treatment for migraine. At that meeting, Leslie Magnus-Miller and John Knoop raised the

Ex. 274,  
WLC\_FRANKLIN\_0000015522;  
Ex. 485, WLC\_CBU\_088644.

possibility of pursuing “a study for migraine... since the study will give some entry to the pain indication.”

484. On May 8-9, 1996, it was reported to the Marketing Council that: “The US will start 2 studies in migraine prophylaxis. Product Planning (O. Brandicourt) will coordinate a marketing assessment with Portfolio Management to evaluate potential sales.”

Ex. 486, WLC\_CBU\_088639

485. On July 31, 1996, Parke-Davis’s Marketing Planning Department issued a Marketing Assessment for Neurontin in migraine prophylaxis. The Marketing Assessment reflected the decision to “conduct only publication study(ies) in the U.S. due to the current patent situation in the U.S....” and to publish the results only “if positive.” The Marketing Assessment noted that migraine represented “an attractive commercial opportunity” for Neurontin, despite the fact that “[t]here is no established preclinical rationale that would support the use of Neurontin in migraine prophylaxis.” The Marketing Assessment recommended that two trials be conducted, despite the fact that a clinical study had already been conducted in the 1980s which “revealed no statistically significant difference in the adjusted mean reduction in migraine attack frequency.” While the Marketing

Ex. 487,  
PFIZER\_JMARINO\_0001583.

Assessment references the negative 879-200 study, it contained no suggestion that the results of that negative study should be published.

486. On September 2, 1996, the Core Marketing Team Meeting ratified the Marketing Assessment's recommendation that "two additional publication studies [on migraine] be conducted in the U.S. since sales generated from these trials could generate additional revenue of \$20 to \$25 million in by patent expiration." It was noted, however, that "[t]he U.S. does not intend to file an sNDA for Migraine Prophylaxis."

Ex. 488, WLC\_CBU\_046363.

487. On December 4, 1996, Defendants approved protocol 945-217 entitled: "Double-Blind, Randomized, Placebo-Controlled, Multicenter Trial to Determine the Efficacy and Safety of Neurontin® (Gabapentin) in Migraine Prophylaxis." Defendants' putative migraine expert, Dr. Alan Rapoport was listed as an investigator for protocol 945-217.

Ex. 480, 995-00085.pdf at 1, 167.

488. On February 26, 1998, Defendants approved protocol 945-220 entitled: "Double-Blind, Randomized, Placebo-Controlled, Multicenter Trial to Determine the Efficacy and Safety of Neurontin® (Gabapentin) in Migraine Prophylaxis Administered in

Ex. 479, 995-00074\_(p1-366).pdf at 1, 152; Ex. 478, McCrory Report at 10.

Doses Divided Three Times a Day (TID).” Dr. Ninan Mathew and Defendants’ putative migraine expert, Dr. Alan Rapoport, were listed as investigators on protocol 945-220. The study design of protocol, with the exception of the higher dose of gabapentin used, was “essentially the same design as that of” protocol 945-217.

489. On March 30, 1998, Defendants amended protocol 945-217 including changes to the statistical evaluation plan, such as the definition of the “Evaluation for Efficacy” population, the population on which the primary analysis of protocol 945-217 was planned, as well as on the primary efficacy parameter.

Ex. 480, 995-00085.pdf at 167,188-89.

490. Protocol 945-217 contains the following bias: Publication bias - Final, “negative,” results not published.

Ex. 117, Dickersin Report at 24.

491. According to the 2001 Neurontin Situation Analysis, because the results of protocol 945-217 were negative, “[t]he team has delayed posting or dissemination of results and they have not been presented at any scientific meetings to date.” The 2001 Neurontin Situation Analysis misrepresents the results of 945-220 as favoring Neurontin. The results of 879-200 were not disclosed in the 2001 Neurontin Situation Analysis.

Ex. 142, Pfizer\_JMarino\_0002350.

**C. Defendants' False and Misleading Marketing of Neurontin for Migraine**

1. False Statements

a. *False and Misleading Statement—Journal Article—1987*

492. Although interim results from 879-200 were published in abstract form in *Cephalalgia*, the abstract is “not listed in MEDLINE,” and no publication was ever made of the final study results.

Ex. 483, Wessely P, Baumgartner C, Klingler D, Kreczi J, Meyerson M, Sailer L, et al. Preliminary results of a double-blind study with the new migraine prophylactic drug Gabapentin. *Cephalalgia*. 1987; 7(Suppl 6):477-8 (“Wessely Abstract”); Ex. 478, McCrory Report at 8-9; Ex. 489, McCrory Dep. at 148.

493. Protocol 879-200 and the Wessely

Ex. 117, Dickersin Report at 24.

Abstract contain the following biases: (1) “Publication bias - Final negative primary results not published; only positive preliminary results;” (2) “Selective outcome reporting - Outcome reported was not primary or secondary outcome;” (3) “Selective statistical analyses - Two nonrandomized patients assigned Neurontin were included with randomized. Reported numbers ‘investigated,’ failed to report number randomized.”

b. *False and Misleading Statement—Consultants’ Meeting—1995*

494. At a consultants meeting in Boston held on September 28, 1995, Parke-Davis gathered several influential and high-prescribing physicians, including Dr. Russell Portenoy, Director of Analgesic Studies at Memorial Sloan-Kettering Cancer Center, Dr. Ninan

Ex. 196,  
WLC\_FRANKLIN\_0000087284;  
Ex. 197,  
WLC\_FRANKLIN\_0000206531

Mathew, a prominent researcher in the field of migraine, and Dr. Steven Schacter, a high-volume Neurontin prescriber and a frequent paid speaker on Neurontin's off-label uses, to discuss "pain syndromes where [Neurontin] might be of clinical benefit." However, these physicians, including most notably Dr. Mathew, were not told of the negative results of 979-200. As a result, the physician-consultants recommended that "[l]arge controlled trials should be done in...frequent migraine."

c. *False and Misleading Statements—CME "Home Study Course"—1995*

495. In late 1995, Parke-Davis launched a misleading and deceptive CME "Home Study Course" program, which presented case studies of successful treatment of migraine with Neurontin and suggested there was scientific evidence suggesting Neurontin was helpful in "chronic daily headaches," but failed to disclose the negative results of study 879-200.

Ex. 268,  
WLC\_FRANKLIN\_0000164158;  
Ex. 268,  
WLC\_FRANKLIN\_0000068717;

d. *False and Misleading Statements—Speakers' Bureau and Consultant Meetings—1996*

496. Beginning in 1996, Parke-Davis held various speakers bureau and consultants meetings where a misleading set of slides were used showing purportedly scientific evidence that Neurontin "reduced

Ex. 490,  
WLC\_FRANKLIN\_0000016148

severity and frequency of headaches...” but failed to disclose the negative results of the 879-200 study.

e. *False and Misleading Statements—American Academy of Neurology Meeting—1996*

497. At the American Academy of Neurology Meeting held on March 23-26, 1996 in San Francisco, Parke-Davis, whose goal it was to “attend and dominate” the proceedings, gave a presentation of the preliminary analysis of open-label data suggesting Neurontin’s efficacy to treat migraine, but suppressed the negative results of study 879-200.

Ex. 491,  
WLC\_FRANKLIN\_0000096359;  
Ex. 492,  
WLC\_FRANKLIN\_0000036427

f. *False and Misleading Statements—“Medi-Fax” to 11,200 Physicians*

498. As a follow-up to the meeting, Parke-Davis hired the Medical Education Network to mail a “Medi-Fax” news bulletin to more than 11,200 physicians that falsely claimed that Neurontin “appears to be an effective, well tolerated agent for migraine,” without disclosing that clinical trial results showed that Neurontin did not appear to be an effective agent for migraine.

Ex. 415,  
WLC\_FRANKLIN\_0000039567;  
Ex. 416,  
WLC\_FRANKLIN\_0000041545,  
Ex. 414,  
WLC\_FRANKLIN\_0000067667.

g. *False and Misleading Statements—Consultants’ Meeting, Aspen, CO—1996*

499. On April 19-20, 1996, Parke-Davis held a consultants meeting in Aspen, CO, attended by 120 physicians. The meeting featured a talk by Dr. Mathew

Ex. 493,  
WLC\_FRANKLIN\_0000015627;  
Ex. 494,  
WLC\_FRANKLIN\_0000212402;  
Ex. 495,  
WLC\_FRANKLIN\_0000015445

entitled “Clinical and Scientific Reports on other Uses for Neurontin: Migraine,” which had the following as its conclusion: “So in summary, gabapentin appears to be an effective, well-tolerated prophylactic agent in migraine and in transformed migraine. Double-blind, placebo-controlled studies are being planned to confirm this preliminary observation.” Dr. Mathew did not disclose the existence of a trial 879-200 or its negative results because Parke-Davis failed to disclose the trial to him at that consultants meeting in Boston in September 1995.

h. *False and Misleading Statements—Consultants’ Meeting, Jupiter Beach, FL—1996*

500. On April 19-20, 1996, Parke-Davis also held a consultants meeting in Jupiter Beach, FL, attended by 74 physicians. Once again, preliminary data suggesting Neurontin’s efficacy for migraine was presented in the absence of any disclosure of the negative results of 879-200. In fact, the existence of a prior clinical trial was repeatedly denied. Dr. Schachter did not disclose the existence of a trial 879-200 or its negative results because Parke-Davis failed to disclose the trial to him at that consultants meeting in Boston in September 1995. One attendee asked directly: “Is there data using it

Ex. 496,  
WLC\_FRANKLIN\_0000107015;  
Ex. 478, McCrory Report at 23; Ex.  
497,  
WLC\_FRANKLIN\_0000205213

[gabapentin] as a prophylactic agent?" The speaker replied, "I think right now, there's ... I don't know of any ... any properly controlled studies on that yet." Once again, Parke-Davis failed to disclose the existence of 879-200 to the attendees of its consultant meeting.

i. *False and Misleading Statements—CME “Home Study Course” and Audio-Conferences--1996*

501. In May and June 1996, Parke-Davis followed up its mailing of the CME “Home Study Course” with 32 dinner meetings held in 29 cities areas attended by 273 physicians. Parke-Davis also held 50 audio-conferences containing the “highlights” of these meetings, which allowed for hundreds of physicians in less urban areas to participate.

Ex. 274,  
WLC\_FRANKLIN\_0000015522;  
Ex. 266,  
WLC\_FRANKLIN\_0000032920;  
Ex. 275,  
WLC\_FRANKLIN\_0000032883

j. *False and Misleading Statements—Consultants’ Meeting—Philadelphia, PA—1996*

502. On May 4, 1996, Parke-Davis held another consultants meeting in Philadelphia, attended by 25 physicians. Once again, preliminary data suggesting Neurontin’s efficacy for migraine was presented in the absence of any disclosure of the negative results of 879-200.

Ex. 498,  
WLC\_FRANKLIN\_0000064068 at  
-229; Ex. 499,  
WLC\_FRANKLIN\_0000062555

k. *False and Misleading Statements—Consultants’ Meeting—Boston, MA—1996*

503. Defendants also failed to disclose study 879-200 at a similar consultants meeting in Boston on May 10, 1996 with 39 physicians in attendance.

Ex. 500, WLC\_CBU\_157708; Ex. 501, WLC\_FRANKLIN\_0000107231; Ex. 502, WLC\_CBU\_158008

1. *False and Misleading Statements—Advisory Board Meeting—1996*

504. On May 25, 1996, Parke-Davis held an advisory board meeting to discuss “Gabapentin in the Management of Migraine.” The meeting was attended by several influential, high-prescribers, including Dr. Ninan Mathew. There were also several Parke-Davis employees in attendance, including John Boris, who was preparing the migraine assessment at the time and thus was aware of the negative migraine study from the 1980s. At the advisory board meeting, Parke-Davis suppressed any reference to study 879-200. In fact, Leslie Magnus-Miller, Parke-Davis’s Medical Affairs Director was directly asked, “But do you have any data [relating to Neurontin and migraine]?” Dr. Magnus-Miller, who knew or should have known about the negative migraine study, responded: “We didn’t...No, not really, because we didn’t capture headache baseline.” Edda Guerrero added: “Unfortunately we did not, not even in monotherapy I think. Right?” John Boris did not correct this misstatement.

Ex. 503, WLC\_FRANKLIN\_0000116885

m. *False and Misleading Statements—“Pain Weekend” Meetings—1997*

505. Between April and September 1997, Parke-Davis held numerous “Pain Weekend” meetings in locations such as Ponte Vedra, FL, New York City, Rye Brook, NY, Saratoga, NY, Rochester, NY, Newport, RI, Absecon, NJ, Philadelphia, PA, Hershey, PA, and Boston, MA. AT these meetings, which were attended hundreds of physicians, Neurontin was presented as a treatment for migraine. No mention was made of negative clinical data from 879-200.

Ex. 282, WLC\_CBU\_180735; Ex. 283, WLC\_FRANKLIN\_0000066770; Ex. 284, WLC\_FRANKLIN\_0000066773; Ex. 285, WLC\_FRANKLIN\_0000066779; Ex. 286, WLC\_FRANKLIN\_0000066782; Ex. 287, WLC\_FRANKLIN\_0000066789; Ex. 289, WLC\_CBU\_179585.

n. *False and Misleading Statements—American Pain Society Annual Meetings—1997 and 1998*

506. At the American Pain Society’s 1997 and 1998 annual meetings, Parke-Davis presented a poster of interim results of 945-220 that misleadingly stated that the study demonstrated statistically significant reduction in headaches, even though 945-220 failed to find such a reduction. Moreover, the poster failed to mention the negative results of 879-200.

Ex. 504, WLC\_CBU\_107310

o. *False and Misleading Statements—Monograph 1997*

507. In March 1998, Parke-Davis distributed a monograph containing the proceedings of the Epilepsy and Related Disorders Symposium held in

Ex. 505, WLC\_FRANKLIN\_0000167320.

November 1997 in Monte Carlo. In that monograph, misleading statements suggesting Neurontin's efficacy in treating migraine were made, with no disclosure of the failed study from the 1980s.

p. *False and Misleading Statements—American Pain Society's Annual Meeting—1998*

508. In November 1998, the results from Ex. 506, MDL\_Vendors\_026372. protocol 945-220 were falsely presented as positive at the American Pain Society's annual meeting in San Diego. The results of the primary analysis of protocol 945-220, as documented in the August 1999 research report were negative.

q. *False and Misleading Statements—“Dear Doctor Letters—1998-2000*

509. Between December 1998 and July Ex. 507, WLC\_CBU\_018759; Ex. 085, Merlin 2000, Defendants distributed a false and misleading “Dear Doctor” to 1,140 physicians. The letter stated falsely that: “Parke-Davis is conducting placebo-controlled studies investigating the safety and efficacy of Neurontin for the treatment of migraine headaches,” even though the company had already completed three trials. Each of these three trials was negative, crucial facts which are misleadingly omitted from the letter.

r. *False and Misleading Statements—Journal Article—1999*

510. In 1999, Parke-Davis published a misleading review article entitled “Nonepileptic Uses of Gabapentin” in *Epilepsia* by Leslie Magnus-Miller, a Parke-Davis employee. The article references only a single open label study of Neurontin in migraine, but fails to list the two negative randomized double blind placebo-controlled clinical trials that were available at the time: 879-200 and 945-220. As an author of the research report that summarized the results of 945-220, Leslie Magnus-Miller was aware that study 945-220 had been concluded.

Ex. 508, PFIZER\_NMANCINI\_0024603; Ex. 509, MAC\_E\_0050010; Ex. 479, RR 995-00074.pdf.

s. *False and Misleading Statements—Multimedia Educational Program, “Advances in the Preventative Treatment of Migraine”*

511. Starting in June 1999, Parke-Davis launched a multimedia educational program on Neurontin and migraine entitled “Advances in the Preventative Treatment of Migraine.” Program materials were mailed to 20,000 neurologists and 5,000 primary care physicians. Parke-Davis also distributed audiocassettes featuring the voice of Dr. Ninan Mathew and provided an (800) number where callers who could not participate in the above heard a condensed version of the Mathew audiotape edited by the medical marketing firm Cline Davis & Mann. All of these program components made false or misleading

Ex. 510, WLC\_CBU\_135183; Ex. 511, WLC\_CBU\_013059; Ex. 512, WLC\_CBU\_013073; Ex. 513, MDL\_VENDORS\_008194; Ex. 514, MDL\_VENDORS\_008274; Ex. 515, MDL\_VENDORS\_008400.

statements suggesting Neurontin is effective to treat migraines, while omitting reference to the negative clinical trials on migraine. Parke-Davis distributed at least 10,000 copies of a summary monograph, which claimed that Neurontin “has been shown to be effective in a randomized double-blind placebo-controlled trial for migraine prophylaxis,” but made no mention of the negative results of three randomized double-blind placebo-controlled trials that were available at the time. Despite the available negative evidence showing Neurontin’s inefficacy in treating migraine, Parke-Davis recognized that “the monograph very favorably mentions Neurontin.”

512. At the conclusion of the program, Ex. 516, WLC\_CBU\_013057. Cline Davis & Mann offered “to work with Parke-Davis to research and track prescriptions for those physicians who completed the program. This additional investment could be worthwhile to track the ROI for the program.” See WLC\_CBU\_013057.

t. *False and Misleading Statements—Journal Article—1999*

513. In June 1999, Parke-Davis created a Ex. 517, WLC\_CBU\_014199 journal supplement entitled “Diagnosis and Modern Treatment of Migraine,” under the Progress in Neurology

series that had been created for the company by the Dannemiller Memorial Education Foundation. In the supplement, the author, Dr. Mathew falsely stated that Neurontin “has been shown to be effective in a randomized double-blind placebo-controlled trial for migraine prophylaxis,” but made no mention of the negative results of three randomized double-blind placebo-controlled trials that were available at the time.

- u. *False and Misleading Statements—Meetings, “New Directions in the Understanding & Treatment of Chronic Pain”—1999-2001*

514. Between late 1999 and early 2001, Ex. 108, RELATOR02281

Pfizer held dozens of meetings entitled “New Directions in the Understanding & Treatment of Chronic Pain.”

These meetings contained lectures called “Effective treatment of hard to treat migraine” where physicians were exposed to presentations where Neurontin was stated to be “preventative” for migraine

- v. *False and Misleading Statements—Treating the Elderly CMEs—1999*

515. In May and June 1999, Parke-Davis Ex. 518, PFIZER\_TMARTIN\_0000850; Ex. 519, SH\_0064559.0096785. held half a dozen CMEs called “Treating the Elderly: New

Options for Pain \* Psychiatry \* Epilepsy \* Stroke.” Even though the results of 879-200, 945-217, and 945-220 were known to the company, speakers at these events stated

that, with respect to Neurontin, “clinical trials have demonstrated efficacy in the clinical treatment of ... migraine prophylaxis...”

w. *False and Misleading Statements-Grand Geneva Resort and Spa*

516. At the conference held at the Grand Geneva Resort and Spa in Lake Geneva, Wisconsin on June 11-13, 1999, Dr. Backonja gave a presentation to the roughly 1,500 physicians in attendance, including Dr. Kyle Huler, that misleadingly suggesting Neurontin’s efficacy for migraine and headache, but affirmatively denied the existence of any negative clinical trials. Under the potential conflicts of interest and financial disclosures section, Dr. Backonja falsely stated “None.”

Ex. 520, MDL\_SM\_000350; Ex. 521, WLC\_CBU\_012710; Ex. 318, MDL\_VENDORS\_083903; Ex. 316, MDL\_VENDORS\_103909

x. *False and Misleading Statements—Advisory Boards—1999-2000*

517. In late 1999 and early 2000, Defendants held numerous “off-label Advisory Board meetings” coordinated through Sudler & Hennessey where hundreds of attendees were falsely told that Neurontin’s “efficacy and “potential usefulness” for migraine, but were not were not told of the negative results of studies 879-200, 945-217, and 945-220. These meetings were explicitly limited to a discussion of Neurontin’s “off-label” uses, they were “classified as promotional.” The

Ex. 444, WLC\_CBU\_175636; Ex. 521, WLC\_CBU\_134383; Ex. 522, MDL\_VENDORS\_111857; Ex. 523, MDL\_VENDORS\_057958; Ex. 524, WLC\_CBU\_013274; Ex. 449, WLC\_CBU\_164376; Ex. 525, MDL\_VENDORS\_057687; Ex. 526, MDL\_VENDORS\_057701; Ex. 527, MDL\_VENDORS\_057705; Ex. 528, MDL\_VENDORS\_057727; Ex. 529, MDL\_VENDORS\_057743; Ex. 387, WLC\_CBU\_164409.

moderators for these events, usually Ahmad Beydoun, received \$2,000 per event. While the attendance for some meetings was roughly 20 physicians, one meeting in Scottsdale, Arizona on January 21, 2000 had 98 physician-attendees.

y. *False and Misleading Statements—Pain CMEs—1999-2000*

518. In 1999 and 2000, Defendants held more than 100 CMEs with more than 7,000 attendees entitled “New Treatment Options for the Management of Pain: The Role of Anticonvulsants,” at various cities around the country. Ahmad Beydoun chaired most of the meetings and was the program’s overall program director. Attendees of these CMEs were falsely told that Neurontin had been “shown effective in migraine prophylaxis,” and the existence of the negative studies 879-200, 945-217, and 945-220 were suppressed.

Ex. 530, MDL\_VENDORS\_056827; Ex. 531, MDL\_VENDORS\_072756; Ex. 532, MDL\_VENDORS\_072304; Ex. 533, MDL\_VENDORS\_101216.

z. *False and Misleading Statements—CME Monograph—2000*

519. In April 2000, Defendants distributed 6,000 copies of a CME Monograph entitled “Spectrum of Uses of Antiepileptic Drugs: New Treatments, New Strategies”—5,000 to physicians through the mail, and an extra 1,000 copies that were handed out to physicians sales representatives—falsely

Ex. 110, MDL\_Vendors\_055236; Ex. D, SH\_0064555.0012057

stated that Neurontin had “efficacy” migraine, and failed to disclose the three negative trials (879-200, 945-217, and 945-220) that contradicted such statement.

aa. *False and Misleading Statements—Pain CMEs—2001*

520. In 2001, Defendants held a dozen CMEs entitled “New Directions in the Understanding & Treatment of Chronic Pain,” held through the American Academy of Pain Medicine. The meetings drew roughly 1,000 attendees, who were exposed to a misleading slide presentation listing Neurontin as a preventative treatment for migraine, with no disclosure of the existence of three negative clinical trials. Gabapentin is a second-generation antiepileptic drug (AED) that has been shown to be effective in double-blind studies.

Ex. 534, SH\_0064559.0092830; Ex. 249, MDL\_VENDORS\_068519; Ex. 323, MDL\_VENDORS\_068511; Ex. 324, MDL\_VENDORS\_094647.

bb. *False and Misleading Statements—Neurobehavioral Working Group Meetings—2001*

521. In 2001, Pfizer held 20 half-day meetings through the supposedly independent Neurobehavioral Working Group, a disguised marketing organization created by Defendants, which attempted to convince the roughly 2000 physicians who attended that Neurontin was effective for a variety of inter-related neurobehavioral disorders. The group concocted a premise that migraine, epilepsy, neuropathic pain,

Ex. 535, MDL\_VENDORS\_052600; Ex. 536, MDL\_VENDORS\_095923;

psychiatric disorders, and sleep disorders were highly comorbid and therefore treatments that are effective for all these conditions, not surprisingly Neurontin, should be used. To help physicians remember this, a mnemonic phrase was developed: MENDS (**M**igraine, **E**pilepsy, **N**europathic pain, **p**sychiatric **D**isorder, and **S**leep disorders). The standard slide deck created for and used at these meetings false stated that Neurontin “has been shown to be effective in double-blind studies.”

cc. *False and Misleading Statements—Mathew Article—2001*

522. In February 2001, Headache published the submitted manuscript of the results of 945-220. Dr. Ninan Mathew and Dr. Alan Rapoport were the first two authors.

Ex. 537, Mathew NT, Rapoport A, Saper J, Magnus L, Klapper J, Ramadan N, et al., Efficacy of gabapentin in migraine prophylaxis. Headache. 2001 Feb;41(2):119-28 (“Mathew Article”)( 2001 Mathew Headache.pdf); Ex. 538, <http://www3.interscience.wiley.com/journal/119014514/issue>. Ex. 537, Mathew Article; Ex. 478, McCrory Report at 11;

523. The Mathew Article, purportedly presenting the results of Defendants’ protocol 945-220, falsely states that “the primary outcome measure was the 4-week migraine rate during stabilization period 2 ([SP2] the last 4 weeks of the stable-dosing period) for patients who had received a stable dose of 2400 mg/day.” The Mathew Article misleadingly reports the results of a post hoc analysis as the primary efficacy results: “At the end of

the 12-week treatment phase, the median 4-week migraine rate was 2.7 for the gabapentin-treated patients maintained on a stable dose of 2400 mg/day and 3.5 for the placebo-treated patients (P=.006), compared with 4.2 and 4.1, respectively, during the baseline period. Additionally, 26 (46.4%) of 56 patients receiving a stable dose of 2400 mg/day gabapentin and 5 (16.2%) of 31 patients receiving placebo showed at least a 50% reduction in the 4-week migraine rate (P=.008).”

524. The difference between the negative Ex. 478, McCrory Report at 13-14. results of protocol 945-220 and the positive results of the Mathew Article (supposedly presenting the results of protocol 945-220) was achieved through “redefining the study population by limiting it to those patients on a stable 2400mg daily dose.” The Mathew Article defined the population reported on as the mITT population which was “misleading because it [was] in fact a subgroup analysis. There was no mention of a planned subgroup analysis based on dose received” in protocol 945-220. “[T]his was an unplanned or post hoc subgroup analysis...to give the false impression that this was a positive study supporting the claim that gabapentin [was] effective. Calling this post hoc subgroup analysis a mITT analysis seems [to

have been] designed to give the impression that the intention-to-treat principle was being followed; however, this analysis consider[ed] a smaller, more select population than even the original efficacy population, not a broader population more like those initially randomized as the mITT language implies.” This is “an enormous misrepresentation of the study...which portrays this as a positive study by presenting the few positive secondary analyses as if they were the primary end points and major findings.”

525. The results of protocols 879-200 and 945-217 were not disclosed in the Mathew Article.

Ex. 537, Mathew Article; Ex. 023, Abramson Report ¶187.

“Thus, physicians reading the misrepresented results of study 945-220 in a peer-reviewed journal were further misled by the Defendants’ withholding of the rest of the scientific evidence in their possession showing that Neurontin was not effective for the prophylaxis of migraine headache.”

526. The design of protocol 945-220 was similar to the design of protocol 945-210 (forced titration).

Ex. 023, Abramson Report ¶179.

“The frequency of somnolence and dizziness in the study participants was similar to that experienced in the Backonja study. The manuscript for the Mathew article

was submitted to Headache October 2, 2000, and therefore Defendants were well aware...of the potential unblinding effect of the increased frequency of CNS-related side effects in those taking Neurontin and the statistical steps that would have determined whether or not the increased frequency of side effects effectively unblinded the trial and confounded the results. But potential unblinding was neither mentioned nor corrected for in the Headache article.”

527. “Readers of [the Mathew] article (including the authors of the Cochrane review on migraine prophylaxis and other review articles...) had no way of knowing that this [the primary outcome reported in the Mathew Article] was not the primary outcome measure identified in Defendants’ research report.” Ex. 023, Abramson Report ¶183.

528. The Mathew Article contains the following biases: (1) “Selective analyses - Reported only the analysis with major patient exclusions. Definition of ‘evaluable patients’ in publication different from research report, for the primary outcome;” (2) “Primary outcome redefined in publication - Primary outcome changed to reduce the number of evaluable patients, result is that p-value and findings in research report are not the same as Ex. 117, Dickersin Report at 24-25.

publication;” (3) “Multiple publication - The 2 conference abstracts, presented at different times, are nearly duplicates. Neither cited the other abstract;” (4) “Time lag bias - Three years to publication from end of study;” (5) “Citation Bias - No mention of other negative results (eg Wessely 1987, 945-217);” (6) “Spin - Conclusions do not match actual study findings per research report.”

529. The authors of the studies repeated Ex. 538, WLC\_CBU\_008134 the same misrepresentations of their results in slide presentations to doctors that were shown in person at various events.

dd. *False and Misleading Statements—Other Journal Articles—2001-2003*

530. In November 2001, Headache Ex. 539, Mathew NT, Antiepileptic Drugs in Migraine Prevention, published an article authored by Dr. Ninan Mathew Headache, 2001; 41 Suppl 1:S18-24 (Antiepileptic Drugs in Migraine Cluster Headache and Mood Disorders.pdf); Ex. 540, entitled “Antiepileptic Drugs in Migraine Prevention.” [http://www3.interscience.wiley.com/journal/119014638/issue.](http://www3.interscience.wiley.com/journal/119014638/issue) There is no financial disclosure listed. The article falsely states that the “only double-blind, placebo-controlled study of gabapentin for migraine prevention” was trial described in the Mathew Article. Dr. Mathew’s review misrepresents the negative results of protocol 945-220 as positive and does not disclose the suppressed negative results of 945-217 or 879-200.

531. In this review article, “[n]o mention Ex. 023, Abramson Report ¶12.

is made of the other two Defendant-sponsored RCTs, both of which had shown—like the Mathew et al. article should have shown—that Neurontin is not effective for migraine prophylaxis. Because the Defendants’ two negative trials were not included in Mathew’s review, and because the Defendants’ third negative trial was misrepresented as positive, Mathew’s review article comes to an erroneous conclusion: “The double-blind trials of divalproex, gabapentin, and topiramate demonstrate their effectiveness in migraine prevention.”

532. In October 2003, Clinical Therapeutics published an article authored by Marco Pappagallo entitled “Newer Antiepileptic Drugs: Possible Uses in the Treatment of Neuropathic Pain and Migraine.” The Mathew Article was cited as evidence of Neurontin’s efficacy for the treatment of migraine. The author of this review article did not have access to the suppressed negative results from protocol 945-220, the suppressed negative results from protocol 945-217, nor the suppressed negative results from 879-200.

Ex. 541, FAL\_0000737

533. In November 2003, the Journal of Managed Care Pharmacy published a review article entitled: “Examination of the Evidence for Off-Label Use

Ex. 542, Mack A, Examination of the Evidence for Off-Label Use of Gabapentin, J Man Care Pharm, 2003;9:559-68 (PFIZER\_LKNAPP\_0057719); Ex. 023, Abramson Report, ¶ 216.

of Gabapentin.” The article concluded that gabapentin should be used “where randomized controlled clinical trials have demonstrated gabapentin efficacy” offering migraine headaches as an example. The article cites to the misleading Mathew Article which misrepresents the results of protocol 945-220 as favoring gabapentin and “shows that positive information available to physicians was dominated by Defendants’ misrepresented study 945-220.”

534. In December 2003, Defendants published an article through authors Spira and Beran in Neurology which falsely stated that Neurontin “has been found to be of benefit in a variety of painful disorders including...migraine,” and cited to the misleading Mathew Article as support for the proposition that Neurontin had been “found to be effective” for migraine in a DBRCT. The authors failed to disclose the true results of the 945-220, and did not reference the negative 879-200 and 845-217 studies. Pfizer was aware that of these misrepresentations, as Bruce Parsons, a Pfizer medical director, and Allison Fannon, a Pfizer marketing manager, had been assigned as lead reviews of the draft manuscripts that had been submitted and re-submitted to

Ex. 543, DouglasC.McCrory-9.pdf; Ex. 544, PFIZER\_CWOHLHUTER\_0011973; Ex. 545, MAC\_0002476; Ex. 546, MAC\_E\_0012008.

Neurology prior to publication. One of Allison Fannon's responsibilities was to develop Pfizer's key messages.

One of the key messages developed was that Neurontin had "[p]roven effective against a wide range of neurologic and psychiatric conditions."

ee. *False and Misleading Statements—Drugdex*

535. Despite her testimony that she would send information to Drugdex if it were missing from the Drugdex monograph, Parke-Davis employee Leslie Fierro, who was also a member of the Drugdex editorial board, never forward to Drugdex the results of 879-200 or 945-217. Moreover, Drugdex references the false and misleading conclusion of Neurontin's efficacy for migraine from 945-220 planted in the Mathew Article, rather than the truthful conclusion stated in Pfizer's internal research report. Both Pfizer and Drugdex were made aware of the omission of negative clinical trial data in the Franklin litigation. However, by 2004, neither Leslie Fierro nor any other Pfizer employee ever forwarded these negative trials to Drugdex. As a result, Drugdex concludes that Neurontin is "effective" for migraine prophylaxis.

Ex. 203, Drugdex monograph.pdf; Ex. 204, Transcript of Deposition of Leslie Fierro taken on Oct. 4, 2002 in US ex rel. Franklin v. Pfizer et al., 96-11651-PBS (D. Mass.), at 115, 122-23; Ex. 547, PFIZER\_CPACELLA\_0039845.

2. Concealing Information From Cochrane

536. In 2002, one the authors of the Cochrane systematic review on anticonvulsants for migraine prevention, Wim Mulleners, sent out a letter to all companies known to have a product for migraine in the Netherlands requesting any and all data on the efficacy of anticonvulsants for migraine prevention. Among the companies to whom the letter was sent is Pfizer Netherlands. Dr. Mulleners reported to Plaintiffs' migraine expert, Dr. McCrory, that he received a reply from the Dutch representative from Pfizer who said he had forwarded the request the US headquarters. Dr. Mulleners never received any further reply or any of the requested data.

Ex. 478, McCrory Report at 19.

537. On March 15, 2002, Angela Crespo sent an internal e-mail to several employees asking whether reviews on gabapentin and migraine could be sent to Cochrane. Angela Crespo reiterated her question in an internal e-mail on April 3, 2002.

Ex. 548,  
Pfizer\_RGlanzman\_0140655

538. On April 5, 2002, in response to Angela Crespo's e-mail, Dr. Elizabeth Mutisya sent an internal e-mail to several employees stating that Pfizer "would not be able to provide them with our databases which is what they [Cochrane] ultimately are interested

Ex. 548,  
Pfizer\_RGlanzman\_0140655

in.”

539. On April 9, 2002, in response to Dr. Mutisya’s e-mail, Dr. Leslie Tive sent an internal e-mail to several employees which stated: “I don’t understand why Cochrane cant [sic] do a search to find the literature they want. If they are looking for unpublished data, I would be reluctant to send it. I would not even send actual articles.” Ex. 548, Pfizer\_RGlanzman\_0140655

540. On April 9, 2002, in response to Dr. Tive’s April 9, 2002 e-mail, Marino Garcia (Director/Team Leader, Major Markets, Neurontin) sent an internal e-mail to several employees. The e-mail began that “it would be useful if the whole team could understand who they [Cochrane] are and what their motivation is.” Marino Garcia suggested to “have someone from medical just tell them that we are not indicated for this condition [migraine] and that we are only aware of two double-blind placebo controlled trials done independently of Pfizer and which we have no involvement and send them the reference.” Marino Garcia concluded his e-mail: “We definitely will not supply any internal data, we all agree on that.” The two trials Marino Garcia referenced were 945-220, which Defendants Ex. 548, Pfizer\_RGlanzman\_0140655

conducted and a small Italian trial authored by Di Trapani et al.

541. The Cochrane Collaboration published their review entitled “Anticonvulsant drugs for migraine prophylaxis.” The review relied on the misleading Mathew Article, which inaccurately reported the negative results of protocol 945-220. The review did not have access to the suppressed negative results from protocol 945-217. The review did not have access to the suppressed negative results of 879-200.

Ex. 549, Chronicle E, Mulleners W, Anticonvulsant drugs for migraine prophylaxis (Review), The Cochrane Library, 2005, Issue 4.

### 3. Expert Conclusions

542. “Pfizer’s strategy of withholding unpublished studies and internal data from Cochrane reviewers was successful. Neither of the Defendants’ two negative RCTs is mentioned in the Cochrane review. Furthermore, the fact that study 945-220 was negative for the pre-specified outcome measures remained invisible—it was presented in the Cochrane review as a positive study, as it was originally published in *Headache*. The evidence from clinical trials presented in the Cochrane review of migraine prophylaxis about Neurontin is positive—and differentiates Neurontin from other AEDs. With access to the Defendants’ documents, it is clear that

Ex. 023, Abramson Report ¶192.

the weight of evidence from clinical trials is overwhelmingly negative, yet physicians a) are misled by the Cochrane review because evidence has been withheld and misrepresented, b) don't have access to any more evidence than the Cochrane reviewers could get, and c) cannot be expected to distrust one of their most trustworthy sources of information or engage in independent searches for unknown missing or misrepresented evidence.”

543. Within Defendants' trials of migraine, “[m]ultiple reporting biases are present and it appears data have been manipulated by re-defining the primary outcome. Three studies were conducted but the final results were only published for one (Mathew). The final results for all three studies were negative. Nevertheless, positive preliminary results were published for one study, and one study was published in full, after a long time lag. In this study (945-220), statistically significant primary results were presented in the article and this was not consistent with the findings in the research report. It appears this positive result was obtained by redefining the primary outcome as it applied only to a select group of patients (those who had received

Ex. 117, Dickersin Report at 23-24.

a stable dose of 2400 mg/day). Thus, the number analyzed in the Neurontin group was greatly reduced from the number randomized.”

544. Protocol 945-220 “was a negative trial, yet the scientific record, because of the noted manipulations, reflected a positive trial.” Ex. 023, Abramson Report ¶183.

#### **D. Results**

##### **1. Aggregate Results**

545. According to IMS NDTI data, the average number of uses of Neurontin for migraine per quarter in 1995 was 476. Ex. 138, Revised Conti Declaration, Figure 10 (Revised).

546. By July 1996—even after the inception of the migraine marketing—Neurontin’s use for migraine was 0.14% of the entire migraine prescription drug market. Ex. 462, WLC\_Franklin\_0000038571.

547. According to Dr. Conti, there was virtually no use of Neurontin for migraine prior to the proposed commencement of the migraine class period. Ex. 138, Revised Conti Declaration ¶30.

There were a total of 1,904 uses of Neurontin for migraine over the four quarters prior to the proposed commencement of the migraine class period. There were a total of 21,989 uses of Neurontin for migraine in the four

quarters after the proposed commencement of the migraine class period.

548. According to IMS NDTI data, the average number of uses of Neurontin for migraine per quarter in 1996 was 10,892.

Ex. 138, Revised Conti Declaration, Figure 10 (Revised).

549. According to IMS NDTI data, the average number of uses of Neurontin for migraine per quarter in 1997 was 11,608.

Ex. 138, Revised Conti Declaration, Figure 10 (Revised).

550. According to IMS NDTI data, the average number of uses of Neurontin for migraine per quarter in 1998 was 23,783.

Ex. 138, Revised Conti Declaration, Figure 10 (Revised).

551. According to IMS NDTI data, the average number of uses of Neurontin for migraine per quarter in 1999 was 22,480.

Ex. 138, Revised Conti Declaration, Figure 10 (Revised).

552. According to IMS NDTI data, the average number of uses of Neurontin for migraine per quarter in 2000 was 36,278.

Ex. 138, Revised Conti Declaration, Figure 10 (Revised).

553. According to IMS NDTI data, the average number of uses of Neurontin for migraine per quarter in 2001 was 67,946.

Ex. 138, Revised Conti Declaration, Figure 10 (Revised).

554. According to IMS NDTI data, the average number of uses of Neurontin for migraine per quarter in 2002 was 44,969.

Ex. 138, Revised Conti Declaration, Figure 10 (Revised).

555. According to IMS NDTI data, the average number of uses of Neurontin for migraine per quarter in 2003 was 40,800.

Ex. 138, Revised Conti Declaration, Figure 10 (Revised).

556. According to IMS NDTI data, the average number of uses of Neurontin for migraine per quarter in 2004 was 31,348.

Ex. 138, Revised Conti Declaration, Figure 10 (Revised).

## 2. Gerald Smith

557. Gerald Smith suffered from severe headaches. He took Neurontin over a period of nearly two years, and in that time period his headaches never got better.

(Ex. 422, Deposition of Gerald Smith (“Smith Dep.”) at 27 – 28, 70 – 71).

558. Gerald Smith’s neurologist, Dr. Kylene Huler, was detailed hundreds of times by various Parke-Davis and Pfizer sales representatives from 1996 through 2004. During these details, she discussed off-label uses of Neurontin, such as migraine.

Ex. 423, Huler Sherlock and CMMS.

559. Dr. Huler was detailed roughly 27 times in the space of a year by a single sales representative, who recorded in his contemporaneous notes:

Ex. 423, Huler Sherlock and CMMS.

Dr. Huler...is down with all of the Pfizer [products]...She is the Pfizer Queen (Zoloft, Neurontin) and she said as much...Dr. Huler really likes the fact that we know she is high on the list of Pfizer (zoloft, Neurontin) products... Feed her ego although she is a nicelady [sic] and not an megalomaniac , she

likes being the #1 queen.

560. Prior to her first Neurontin prescription in July 1998, Dr. Huler had already been detailed more than 30 times by 3 different sales representatives.

Ex. 423, Huler Sherlock and CMMS; Ex. 476, Huler Wolters Kluwer.

561. According to their own detail records, Defendants never disclosed the negative results of 879-200, 945-217 or 945-220.

Ex. 423, Huler Sherlock and CMMS.

562. Nor did Dr. Backonja or the other paid speakers disclose the results of these negative trials to Dr. Huler or the other 1,500 physicians who attended the “Advances in Epilepsy and AEDs” Conference held at Grand Geneva Resort and Spa in Lake Geneva, Wisconsin on June 11-13, 1999. Instead, Dr. Backonja and the other speakers gave misleading presentations suggesting Neurontin’s efficacy for migraine and headache.

Ex. 317, WLC\_CBU\_012710; Ex. 316, MDL\_VENDORS\_103909

#### **IV. FACTS RELATING TO DOSES ABOVE 1800 MG PER DAY**

##### **A. Neurontin Has No Greater Efficacy at Doses Above 1800 mg per day**

###### **1. Epilepsy Studies**

563. Neurontin was approved by the FDA in 1993 to treat epilepsy at doses ranging from 900-1800 mg per day.

Ex. 364, WLC\_FRANKLIN\_0000151674

564. Defendants conducted three trials of Ex. 365, Alldredge Report at 9.

Neurontin for the treatment of epilepsy at doses reaching or exceeding 1800 mg/day. These trials were conducted according to protocols, 945-77, 945-82 and 945-88. None of these trials demonstrated any enhanced efficacy of Neurontin at dosages above the FDA-approved limit of 1800 mg/day.

a. *945-082*

565. By no later than February 23, 1995, Defendants were aware of the results of study 945-082, a 26-week, double-blind, dose-controlled, study of Neurontin in fixed doses of 600, 1200 and 2400 mg/day. Study 945-082 did not provide evidence of enhanced efficacy of gabapentin at dosages above the FDA-approved limit of 1800 mg/day. In fact, the results of 945-082 demonstrated that Neurontin did not “demonstrate a dose-response relationship for the drug.”

Ex. 366, 720-03495\_945\_082\_(Official).pdf at 1; Ex. 365, Alldredge Report at 12.

b. *945-088*

566. On August 9, 1995, Defendants completed protocol 945-088, a study which compared low-dose Neurontin at 300 mg per day to high-dose Neurontin at 3600 mg per day. Protocol 945-088 did not provide evidence of enhanced efficacy of gabapentin at dosages above the FDA-approved limit of 1800 mg/day,

Ex. 367, 720-03675\_(Official).pdf at 1; Ex. 365, Alldredge Report at 14.

because 1800 mg was not studied. In fact, because no other doses within the effective range were studied, study 945-088 found no “dose-response relationship.”

c. 945-077

567. By no later than March 1997, Defendants knew the results of study 945-77, a randomized, double-blind study compared three doses of gabapentin 300, 900, and 1800 mg/day and open-label carbamazepine in patients with newly diagnosed epilepsy. Because this trial did not include gabapentin dosages above 1800 mg/day, the efficacy of the drug above this dosage limit cannot be addressed. However, study data showed that patients in the 1800 mg/day group were either equally or more likely to result in treatment failure than the lower dosage groups.

Ex. 435, RR 720-03779; Ex. 365, Alldredge Report at 10-11.

## 2. Pain Studies

568. Defendants conducted six trials of Neurontin at dosages higher than 1800 mg/day for the treatment of neuropathic pain. Two of these trials, 945-224 and 945-295, failed to demonstrate any enhanced efficacy of Neurontin at dosages above the FDA-approved limit of 1800 mg per day. The remaining trials, 945-210, 945-211, 945-306 and a9451008, were incapable of

Ex. 365, Alldredge Report at 14.

demonstrating any enhanced efficacy at dosages above 1800 mg/day because the trial failed to use fixed-dose groups.

a. 945-224

569. By no later than September 7, 1999, Ex. 162, 720-04130.pdf at 1; Ex. 365, Alldredge Report at 18. Defendants were aware of the results of study 945-224, a double-blind, placebo-controlled trial of Neurontin in DPN using 3 fixed dose groups of 600, 1200 and 2400 mg per day. Defendants were aware that, unlike 945-210 and -211, the fixed-dose parallel group design of this trial is appropriate to gather information to inform the dose-response effect of Neurontin. However, the results of this trial clearly demonstrated that Neurontin was not effective and that no dose-response effect was seen. Thus, 945-224 did not provide substantial evidence of increased efficacy of gabapentin at dosages above the FDA-approved limit of 1800 mg/day.

b. 945-295

570. By December 17, 1999, Defendants Ex. 368, 430-00124.pdf at 1; Ex. 365, Alldredge Report at 18-19. were aware of the results of 945-295, a double-blind, placebo-controlled trial of Neurontin in PHN using 3 fixed dose groups of 1800 and 2400 mg per day. According to Parke-Davis, the fixed-dose rather than forced titration

design “was employed to gather data regarding the dose-response effect of gabapentin.” However, the results of the study clearly showed that “no dose-response effect for gabapentin was found.” Therefore, 945-295 did not provide substantial evidence of increased efficacy of gabapentin at dosages above the FDA-approved limit of 1800 mg/day.

c. *945-210*

571. On March 20, 1997, Defendants completed study 945-210, a double-blind placebo-controlled trial of Neurontin in DPN using a forced titration design up to 3600 mg per day. Since fixed dose groups were not used, this protocol could not address “the dose-response relationship of gabapentin in this condition.” The study design of protocol 945-210 was not adequately sufficient “for establishing a dose-response relationship,” even where the reported results were not entirely compromised by the unblinding of participants due to the occurrence of CNS side effects. Defendants were aware that protocol 945-210 provided no basis for the efficacy of Neurontin.

Ex. 156, 720-03908\_Vol\_1.pdf at 1;  
Ex. 365, Alldredge Report at 16;  
Ex. 160,  
Pfizer\_LLamoreaux\_0009058.

d. *945-211*

572. On July 14, 1997, Defendants

Ex. 369, 995-00070\_945-211\_(Part\_1).pdf at 1; Ex. 365,

completed study 945-211, a similarly designed trial of Neurontin in PHN also using a forced titration design. As with 945-210, the forced titration design of study 945-211 rendered it “insufficient to establish a dose-response relationship” for gabapentin. Thus, 945-211 “does not provide substantial evidence of increased efficacy of gabapentin” at dosages above the FDA-approved limit of 1800 mg/day.

Allredge Report at 16-17.

e. *945-306*

573. On February 8, 2000, Defendants completed study 945-306, a trial of Neurontin in exhibiting symptoms from various types of neuropathic pain. The study did not use fixed dose groups, meaning that “it is not possible to draw any conclusions regarding a dose-response effect of gabapentin.” Therefore, 945-306 did not provide substantial evidence of increased efficacy of gabapentin at dosages above the FDA-approved limit of 1800 mg/day.

Ex. 167, 430-00125.pdf at 1; Ex. 220, Serpell MG, et al. Gabapentin in neuropathic pain syndromes: a randomized, doubleblind, placebo-controlled trial. Pain 2002;99:557-66; Ex. 365, Allredge Report at 19-20.

f. *a9451008*

574. On November 11, 2003 Defendants completed study a9451008, a 15 week, randomized, double-blind, placebo-controlled study of Neurontin in DPN. As with 945-210 and -211, the study used a forced

Ex. 370, Pfizer\_LKnapp\_0062214; Ex. 371, Pfizer\_LCastro\_0008182; Ex. 365, Allredge Report at 20.

titration design, meaning that no conclusions regarding gabapentin dose-response relationship could be drawn. Thus, a9451008 did not provide substantial evidence of increased efficacy of gabapentin at dosages above the FDA-approved limit of 1800 mg/day.

3. FDA Rejections of Defendants' Claims of Greater Efficacy at Doses Above 1800 mg Per Day

575. On two separate occasions, the FDA specifically rejected Defendants' efforts to increase the recommended dose above 1800 mg per day.

576. On September 13, 1996, Defendants submitted a supplemental New Drug Application (sNDA) to the FDA. The sNDA included "an increase in the effective dose range to include 3600 mg/day" and "an increase in the maximum recommended dose to 4800 mg/day."

Ex. 373,  
WLC\_FRANKLIN\_0000090128

577. On August 26, 1997, the FDA rejected Defendants' request to change the effective and maximum recommended dose of gabapentin. In a letter to Defendants, FDA Director of Division of Neuropharmacological Drug Products Dr. Paul Leber wrote: "experience gained at these higher doses in monotherapy trials cannot support the safety of these

Ex. 373,  
WLC\_FRANKLIN\_0000090128;  
Ex. 374, Kessler Report ¶41.

doses when given as adjunctive therapy, the only currently approved condition of use” and “that the evidence from controlled trials fails to provide evidence that higher doses of Neurontin are more effective than those recommended.”

578. Similarly, in 2002, the FDA rejected Defendants’ submitted dosing instructions of gabapentin for PHN which stated: “The dose can subsequently be titrated up as needed for pain relief to a maximum daily dose of 3600 mg” and that there was “greater efficacy with increasing dose.” In its place, the FDA required that the following statement be inserted into the label: “Additional benefit of using doses greater than 1800 mg/day was not demonstrated.”

Ex. 436, Pfizer LCastro 0011868;  
Ex. 437, Pfizer MPatel 0077867;  
Ex. 438, Pfizer LCastro 0011563;  
Ex. 374, Kessler Report ¶41.

4. Plaintiffs’ Expert Opinion Establishes Neurontin’s Inefficacy to Provide Additional Benefit at Doses Above 1800 mg Per Day

579. Dose-response information describes the relationship between the amount of a drug that is given to a person and the clinical effects of that drug on the individual. These clinical effects can be both therapeutic (i.e., an improvement in a medical condition) or toxic (i.e., adverse effects of the medication).

Ex. 365, Alldredge Report at 6.

Understanding the dose-response relationship of a given

medication is often of paramount importance in determining the safety and effectiveness of a drug. For drugs that are shown to be safe and effective, prescribers (e.g., physicians) rely on dose-response information to determine the optimal dosages for use by their patients – that is, the dosage that is most likely to benefit the individual and least likely to cause unacceptable adverse effects.”

580. According to Plaintiffs’ expert on Ex. 365, Alldredge Report at 7. dose, Dr. Brian Alldredge, “The standards for establishing a scientifically valid dose-response relationship are quite high. In this regard, data derived from randomized, double-blind, controlled clinical trials in which subjects are assigned to receive various fixed doses of a drug (“fixed dose, parallel group studies”) are often of greatest value in establishing a scientifically valid dose-response relationship. In general, open-label studies, non-randomized studies, and studies that do not employ fixed doses are of much lesser value in establishing a true dose-response relationship.”

581. Dr. Alldredge opines that, a “fixed- Ex. 365, Alldredge Report at 27-28. dose, parallel group study is the most appropriate design to establish a dose response effect. Studies 945-05, 945-

77, 945-82, 945-88, 945-224, and 945-295 are examples of this study design.” The results from all four of these studies “fail to support a dose-response relationship for gabapentin” at dosages above the FDA-approved limit of 1800 mg/day.

582. Dr. Alldredge concludes that these studies, which represent the “highest quality evidence,” failed to establish a dose-related effect (i.e., “continued improvement in efficacy [of Neurontin]”) at dosages above 1800 mg/day. Ex. 365, Alldredge Report at 1.

583. Dr. Alldredge also found that the Defendants used study designs that provide evidence of lesser quality, including open-label studies (with the potential for introduction of bias), studies with non-random assignment to different dosages, and studies during which dosage is adjusted in a fixed-titration or optional titration manner. Ex. 365, Alldredge Report at 1.

584. Studies 945-210, 945-211 and a9451008 are examples of “forced titration” study design. According to Dr. Alldredge, such a study design is “suboptimal” for determining a dose-response relationship. Studies 945-210, 945-211 and a9451008 do not provide evidence to support a dose-response Ex. 365, Alldredge Report at 28.

relationship for gabapentin at dosages above the FDA-approved limit of 1800 mg/day.

585. Studies 945-306, 945-411, the open-label extensions and the STEPS study are examples of “optional titration” study design which is a “poor choice for establishing a dose-response relationship.” Dr. Alldredge found that studies 945-306, 945-411, the open-label extension of 945-082, and the STEPS study did not provide evidence to support a dose-response relationship for gabapentin at dosages above the FDA-approved limit of 1800 mg/day.

Ex. 365, Alldredge Report at 29.

586. Based on a review of all the relevant studies, Dr. Alldredge concludes: “There is insufficient evidence to demonstrate enhanced efficacy of gabapentin (Neurontin) at doses above 1800 mg per day.” Accordingly, Dr. Alldredge concludes that “Neurontin is not more effective at doses greater than 1800 mg per day when compared to doses of 1800 mg per day and less....In plain language, [the negative studies] demonstrate that dosing Neurontin above 1800 mg per day is ineffective as a strategy to improve therapeutic response.

Ex. 365, Alldredge Report at 30;  
Ex. 553, Alldredge Declaration, ¶¶  
6-7.

5. Defendants’ Own Admissions Regarding Neurontin’s Inefficacy to Provide Additional Benefit at Doses Above 1800 mg Per Day

587. On September 28, 1995 at a Neurontin Core Marketing Team meeting in Munich, Germany, Defendants discussed how 954-082 would be “considered negative by regulatory authorities due to lack of statistical significance between” the dose groups.

Ex. 554, WLC\_CBU\_104929.

588. On April 8, 1997, at a Neurontin Core Marketing Team Meeting, Defendants discussed the fact that their clinical trials indicated that Neurontin demonstrated no enhanced efficacy at dosages above the FDA-approved limit of 1800 mg/day. Specifically, Defendants discussed that protocol 945-082 had “failed to establish a significant difference between the doses” and that protocol 945-088 had also not provided evidence of a dose response for Neurontin.

Ex. K, WLC\_CBU\_045802.

589. Defendants were aware that the forced titration design of 945-210 rendered it incapable of assessing a dose-response relationship for gabapentin. This was discussed in Defendants’ meeting with the French Drug Agency on June 18, 1998: “[t]here was only one dosage of Neurontin in [protocol 945-210], it is thus difficult to analyze the impact of the dosage on efficacy.”

590. The Defendants were aware that the use of an “optimal dose design” 945-306 meant that “it is

Ex. 167, 430-00125.pdf at 1; Ex. 220, Serpell MG, et al. Gabapentin in neuropathic pain syndromes: a randomized, doubleblind,

not possible to draw any conclusions regarding a dose-response effect of gabapentin.”

placebo-controlled trial. Pain 2002;99:557-66.

**B. Intent to Fraudulently Market Neurontin at Doses Above 1800 mg per day**

591. At an August 31, 1994 Neurontin Development Team Meeting, Oliver “Brandicourt expressed his concern regarding gabapentin pricing if a high dose treatment is needed for gabapentin monotherapy. He felt that if the price per day of gabapentin has to increase due to the high dose treatment requirement, it will be difficult to promote the product.”

Ex. 377, WLC\_CBU\_088734.

592. On November 23, 1994, the Portfolio Management Department circulated a memorandum containing its marketing goals for 1995. The memorandum called for a “more aggressive” positioning message for Neurontin and concluded that one of the “Key Must-Do’s [sic]” for 1995 was to “[l]aunch new Neurontin campaign – efficacy titration message.”

Ex. 378,  
WLC\_FRANKLIN\_0000197106

593. On December 15, 1994, Defendants held a Marketing Power Hour teleconference during which a key 1995 activity was discussed: “[c]larify for physicians ‘titration to effect.’”

Ex. 379, WLC\_CBU\_116896.

594. In February 1995, Defendants finalized protocol 945-193 known as the STEPS study.

Ex. 380, 995-00057\_(Official).pdf at 341; Ex. 365, Alldredge Report at 38-39; Ex. 381, WLC\_Franklin\_0000093580; Ex.

The Neurontin STEPS study was a seeding trial used to increase Neurontin prescriptions and to promote the false message of enhanced efficacy at dosages above the FDA-approved limit of 1800 mg/day. Physicians were paid \$300.00 per enrolled subject. Selected centers and physicians were “offered” larger or smaller numbers of enrollments based on their influence. In fact, some physicians were offered as many as 50 patients for a total of \$15,000.00. An additional \$50.00 was offered to physicians for each patient who continued Neurontin at the end of the trial. Physicians enrolled in the STEPS trial had their prescriptions tracked pre- and post-exposure to the “high dose” message.

382, WLC\_Franklin\_0000069350;  
Ex. 383,  
WLC\_Franklin\_0000039745; Ex.  
384, WLC\_Franklin\_0000069499.

595. The goal of the STEPS study was to “teach physicians to titrate Neurontin to clinical effect” and cause an “[increase in the] Average Dosage/Day.”

Ex. 385,  
WLC\_FRANKLIN\_0000037793  
Ex. 386,  
WLC\_FRANKLIN\_0000055261

596. The STEPS study was presented at various Speakers Bureau meetings as evidence that higher dosages of Neurontin were needed for efficacy.

Ex. 387, WLC\_CBU\_164409; Ex.  
388, MDL\_Vendors\_064551; Ex.  
365, Alldredge Report at 40.

597. On March 10, 1995, at an Epilepsy Disease Team Meeting, it was noted that physicians prescribed Neurontin most often at 900 mg/day and were not titrating to effect. In fact, in July 1994, fewer than 5%

Ex. 389,  
WLC\_Franklin\_0000036620; Ex.  
365, Alldredge Report at 35.

of dosages of Neurontin were above 1800 mg/day.

598. On March 10, 1995, in a briefing to Anthony Wild, President of Parke-Davis, it was noted that the average daily dose of Neurontin prescriptions was 1140 mg per day and that “[p]hysicians are not titrating to effect.” One week later, at a Core Marketing Team Meeting, it was agreed that “...the message must continue to focus on...’Titration to effect.’” The briefing anticipated that marketing efforts to increase the doses of Neurontin would be successful, but recognized that this success would require “managing pricing as average dose increases.”

Ex. 390,  
WLC\_FRANKLIN\_0000055473;  
Ex. 184, WLC\_CBU\_100422.

599. In May 1995, the average wholesale price of 1800 mg of Neurontin per day was slightly more than \$4.30. The average consumer took only 1140 mg per day and thus paid only \$3.30 per day. If consumers were to increase their daily dosage of Neurontin to 3600 mg per day, the daily cost of Neurontin would balloon to \$9.72 per day.

Ex. 391,  
WLC\_FRANKLIN\_0000055458.

600. At the September 13, 1995 Neurontin Tactics Planning Meeting the top strategies of 1995 were discussed including using the STEPS trial whose purpose was “to give neurologists the opportunity

Ex. 384,  
WLC\_Franklin\_0000069499.

to titrate to higher doses (>1800mg).”

601. On November 8, 1995 at the first meeting of the Defendants’ Northeast Customer Business Unit Antiepileptic Advisory Board, John Krukar provided a presentation with the goal of providing an overview of Neurontin marketing in 1995. The slides presented a marketing message that went through several iterations from “Push the dose!” to “Labeling recommended too low a dose to see efficacy” to “efficacy usually starts at 1800 mg” to “most pts [patients] controlled on dose between 2400-3600 mg” to “Titrate to clinical effect.” The dialog accompanying this slide stated that, in response to noticing that physicians were using lower doses of Neurontin, “[w]e therefore went on an aggressive campaign to try to convince the doctors to push the dose of Neurontin up into the 2400 to 3600mg range.” The negative results of study 945-082 were not presented at this meeting.

Ex. 392,  
WLC\_Franklin\_0000071334.

602. A key issue identified in the 1996 Epilepsy Business Plan was that the average dose of Neurontin was 1200 mg and that physicians were “not titrating.”

Ex. 384,  
WLC\_Franklin\_0000069499.

603. On May 8-9, 1996, at a Marketing

Ex. 393, WLC\_CBU\_049708.

Council Meeting, a formal decision was made to reject the Core Marketing Team's proposal of capping Neurontin's use at 2400 mg per day. Defendants would continue efforts to market Neurontin at doses up to and including 3600 mg, regardless of "pricing considerations" and regardless of the clinical trials that had demonstrated that there was no enhanced efficacy of Neurontin at dosages above the FDA-approved limit of 1800 mg/day.

604. The 1997 Neurontin Tactical Plan called for "High dose meetings" with the objective of encouraging titration to higher doses through "peer-to-peer influence." The fora suggested for such meetings were dinner meetings and teleconferences. The meetings were aimed at low usage neurologists and high decile PCPs.

Ex. 394,  
WLC\_Franklin\_0000112204; Ex.  
365, Alldredge Report at 37.

605. In 1997, Defendants proposed holding "High Dose" meetings to "encourage titration to higher doses through peer-to-peer influence." Defendants also developed case reports to disseminate to physicians to "[u]se peer-to-peer influence to give nonusers reassurance that Neurontin can be safely titrated to higher doses." Defendants authorized the case reports to be based on "[r]eal cases...[or] [a]lternatively on fictionalized case

Ex. 394,  
WLC\_FRANKLIN\_0000112204.

histories [that] could be written based on real situations.”

606. On July 27, 1998, Defendants met with Cline Davis & Mann for a Neurontin Strategy Meeting. At that meeting, the broad strategies and tactics for 1999 were discussed. In particular, it was stated that: “[p]hysicians will be encouraged to titrate to higher daily doses.” Defendants would benefit from this strategy through the “increasing sales due to physicians increased willingness to titrate to higher daily dose.”

Ex. 395, WLC\_CBU\_074575.

607. On July 31, 2001, Marino Garcia sent an e-mail to numerous Pfizer employees and several MAC employees discussing “key messages.” Marino Garcia wrote: “One key message I would like to see supported is ‘1800mg by week 2 of therapy before evaluating patient response.’” The e-mail stated that 1800 mg/day was “the minimum optimal effective dose in NeP [neuropathic pain]” and that “any publication we can provide input on should make this point clear.”

Ex. 396, Pfizer\_LKnapp\_0035987.

608. On April 4, 2001, Defendants held a training meeting for Pfizer sales representatives in Puerto Rico entitled “Dosing Messages for Improved Efficacy in Pain and Epilepsy: Review of the publications and clinical data supporting ‘Start fast, go high’”

Ex. 397, Pfizer\_LKnapp\_0023336;  
Ex. 365, Alldredge Report at 37.

presented by Pfizer employees Angela Crespo, Dr. Robert Glanzman and David Probert. Presentations to sales reps discussed the perception that Neurontin was a safe, but ineffective drug, that this was due to “starting too slow, stopping too low.” Sales reps were instructed to deliver the key message to titrate Neurontin to 3600 mg/day for greater efficacy for pain and epilepsy. The trials presented at this meeting did not provide any evidence to support these key messages. The negative results of studies 945-082 and 945-224 were not presented at this meeting.

609. Beginning in August 2001, Pfizer began planting its marketing messages in “articles that Pfizer will be submitting for prints in journals.” Pfizer referred to these marketing messages as “key messages that Pfizer/Neurontin Team will be targeting to display to the audience directly or indirectly in the article that is produced.” Two of the “key messages” involved titrating Neurontin above 1800 mg per day. In pain, the “key message” was to use a “dose above 1800 mg/day as tolerated to achieve maximum efficacy.” In epilepsy, the “key message” was that “doses up to 3600 mg/day” provided “incremental improvements in efficacy.” These messages were in direct contradiction to the results from

Ex. 398, PFIZER\_JSU\_0032011;  
Ex. 399,  
PFIZER\_LESLIETIVE\_0014606.

clinical trials which had demonstrated that there was no enhanced efficacy of gabapentin at dosages above the FDA-approved limit of 1800 mg/day.

610. On August 23, 2001, Angela Crespo sent an e-mail to several Pfizer and MAC employees regarding the twin dosing papers that would eventually be published in *Clinical Therapeutics* in 2003 and possible authors to whom MAC's ghostwritten article could be attributed. Defendants' proffered dose expert in this litigation, Dr. Michael McLean, was suggested as a possibility for the epilepsy paper, because he was "so pro-Neurontin" and would "support our claim" that Neurontin was (a) effective for neuropathic pain and (b) required high-doses. Allison Fannon responded to this e-mail stating that "Dr. McLean is an advocate of higher doses" and will be "able to deliver a good message on why and how Neurontin should be used at higher doses." Defendants concern with choosing Dr. McLean as the ostensible author of the ghostwritten article was based on "how much he speaks for us."

611. On August 24, 2001, Stephen Valerio of MAC sent an e-mail to several Pfizer and MAC employees discussing the dosing articles. The e-mail

Ex. 400,  
Pfizer\_RGlanzman\_0133526; Ex.  
365, Alldredge Report at 49.

Ex. 400,  
Pfizer\_RGlanzman\_0133526.

stated that MAC would be sending Pfizer's Angela Crespo outlines for the articles. "Once the outlines have your approval we will be able to contact the authors to discuss their interest."

612. The October 11, 2001 Neurontin Global Operating Plan included a goal to achieve "Message and Dosing Alignment." Defendants felt the average daily dose of Neurontin prescriptions was "too low" and desired a message that "Max efficacy with good safety is 3600 mg/day." Evidence from clinical trials had determined that there was no enhanced efficacy of Neurontin at dosages above the FDA-approved limit of 1800 mg/day. Despite this, Defendants' Global Operating Plan called for a "Publication strategy to increase average dose."

Ex. 401, Pfizer\_JMarino\_0000094  
at Pfizer\_JMarino\_00000112.

613. In an October 17, 2002 e-mail to Pfizer and MAC employees, Alison Fannon confirmed that "[i]n the major markets, we have been promoting rapid titration." The e-mail further states: "Due to restrictions in the US label [regarding dose], the sales reps cannot promote this [doses higher than 1800 mg/day] in the US. However, this message can be communicated in publications." In response to this e-mail, Dr. Leslie Tive

Ex. 227, Pfizer\_BParsons\_0162576;

wrote: “As long as the messages are supported by the trials [which they were not] and do not go beyond what has been studied [which they did] I think this is fine.”

614. Increasing dose remained Pfizer’s goal for 2003. A key strategy contained in the company’s 2003 Medical Operating Plan was to “increase the average daily dose.”

Ex. 402,  
Pfizer\_RGlanzman\_0148325.

615. Pfizer’s vice presidents of sales, and the regional managers who reported to them, made sure that the dosing message was communicated to the Pfizer sales force. In the Neurontin VP/RM Action Plan Playbook prepared in 2003, which served as a guide for the semi-annual sales “action plans,” contained the message that “...1800mg is still only ½ of max dose...like running on ½ tank of gas...” The 2003 action plan that followed instructed sales reps to urge doctors to “[t]itrate to a minimum of 1800 mg.” The action plan in 2004 revealed that the “core strategy” was to “[i]ncrease dose more often to 1800mg or higher.”

Ex. 403, Pfizer\_DGruber\_0000287;  
Ex. 404, Pfizer\_KBrett\_0003846;  
Ex. 405,  
PFIZER\_AMISHRA\_0007030

616. Neurontin’s 2004 Operating Plan outlined the same strategy of urging physicians to titration to effect, but merely euphemized the strategy as “optimizing dose,” as the “optimal” dose was defined to

Ex. 406, Pfizer\_SPiron\_0011527 at  
Pfizer\_SPiron\_0011535, -550,

be “1800mg/day and above.” The plan stated incorrectly that the majority of physicians were not reaching an efficacious dose, even though the average prescription dose by that point was already at or above 1800 mg per day. Neither 945-082 nor 945-224, which showed that there was no additional benefit of dosing beyond 1800 mg per day, were disclosed in the 2004 Operating Plan.

**C. False and Misleading Marketing of Neurontin for Doses Greater Than 1800 mg Per Day**

617. On March 4, 1995, Defendants conducted a STEPS “telebroadcast,” a videoconference directed to the 1,542 physicians who were either STEPS investigators or potential STEPS investigators. This videoconference, shown to physicians in Boston, New York, Washington DC, Chicago, Atlanta, St. Louis, Dallas, San Francisco, and Los Angeles, were promotional in nature, as the company tracked the DACON [average daily dosing] of both the investigators as well as “attendees who will not become investigators.”

Ex. 407, WLC\_CBU\_115481;  
Ex. 389,  
WLC\_FRANKLIN\_0000036620.

618. The STEPS telebroadcast was deemed to be “successful,” in large part because “[t]he titrate to effect message was clearly communicated by the advisory panel to the investigators.” Defendants thereafter

Ex. 408,  
WLC\_FRANKLIN\_0000052175;  
Ex. 384,  
WLC\_FRANKLIN\_000006949 Ex.  
383, WLC\_Franklin\_0000039745.

monitored the effect of the event by tracking the investigators' average daily dose. This tracking showed that the number of physicians exposed to the STEPS telebroadcast who were prescribing Neurontin over 2000 mg per day had increased 34% only two months after the broadcast. In that same interval, the number of physicians whose prescriptions were exceeding 3600 mg per day had increased 525%. Based on this tracking analysis, Defendants concluded that "[e]ducation about titration... appears to have had a positive impact on the physicians exposed to it."

619. In May 1995, Defendants held various promotional dinner meetings where discussion scripts called for the moderator to tell attendees that "Neurontin doses should be pushed [above 1800 mg per day] to get more efficacy," and that Neurontin should be "titrated as needed."

620. In May 1995, Defendants mailed a Medi-Fax report to thousands of physicians in connection with the American Academy of Neurology's annual meeting. The Medi-Fax contained the false and misleading heading "Efficacy of Gabapentin Is Increased in Doses Higher than 1800 mg/Day." The text contained

Ex. 409,  
WLC\_FRANKLIN\_0000060466.

Ex. 410,  
WLC\_Franklin\_00000041586  
(emphasis in original); Ex. 365,  
Alldredge Report at 52.

false and misleading statements attributable to Defendants' proffered dose expert, Dr. Michael McLean, including that, with the higher doses used in the open-label extension trials of gabapentin, more efficacy was "being perceived" and that gabapentin "was underdosed in the clinical trials." The Medi-Fax falsely stated "many physicians are using much higher doses [than 1800 mg/day]," a fact belied by Defendants' own data and knowledge.

621. As of July 1995, Defendants had enrolled more than 1800 investigators in the STEPS seeding trial.

Ex. 411,  
WLC\_FRANKLIN\_0000220793.

622. In the summer of 1995, Defendants held five seminars (one per CBU) on Mastering Epilepsy, including one on July 7, 1995 in South Carolina, where attendees were told that about the need to titrate to effect but were not informed that studies had shown that there was no enhanced efficacy of Neurontin at higher dosages.

Ex. 412,  
WLC\_FRANKLIN\_0000033115.

623. On December 15-17, 1995, Defendants held a weekend advisory board meeting in New York where Dr. Michael McLean, Defendants proffered dose expert in this litigation, told more than 25 high prescribing physicians at some of the most influential

Ex. 413,  
WLC\_FRANKLIN\_0000164694.

teaching hospitals that many Neurontin patients “require doses higher than 2400 mg/day,” and that “it is abundantly clear that doses exceeding 4800 mg/day may be needed to achieve optimum results, even monotherapy.” The contradictory results of 945-082 were not disclosed.

624. In March 1996, Defendants sponsored another Medi-Fax Report relating to the 1996 annual meeting of the American Academy of Neurology. This Medi-Fax, which was mailed to more than 11,200 neurologists, contained the false and misleading heading “Increased Efficacy Seen with Gabapentin Doses above 2400 mg/Day.” The Medi-Fax falsely claimed that “there was evidence that higher doses of gabapentin can enhance effectiveness.” The Medi-Fax cited data from uncontrolled and open-label trials. The Medi-Fax omitted the fact that the DBRCT 945-082 had demonstrated that gabapentin was ineffective as monotherapy for epilepsy and, therefore, had not demonstrated any benefit of higher-dose of gabapentin.

Ex. 414,  
WLC\_Franklin\_0000067667; Ex.  
415,  
WLC\_FRANKLIN\_0000039567; E  
x. 416,  
WLC\_Franklin\_0000041545; Ex.  
365, Alldredge Report at 52-53

625. In 1996, Defendants—in one CBU alone—held 14 CMEs and other events attended by more than 450 neurologists, which were “[d]esigned to emphasize the need to titrate to 3,600 mg or higher if

Ex. 417, WLC\_CBU\_165674.

necessary.” Although studies had demonstrated that there was no enhanced efficacy of Neurontin at higher dosages than the FDA-approved limit of 1800 mg/day, Defendants concealed this information.

626. In June 1997, Defendants distributed a Pain Medicine Supplement for the AAPM, which stated that there was “no plateau” of efficacy at 1800 mg per day, and that “incremental anticonvulsant efficacy has been suggested at higher doses.” These statements were directly contradicted by the results of clinical trials which had demonstrated that there was no enhanced efficacy at dosages above the FDA-approved limit of 1800 mg/day.

Ex. 418, WLC\_CBU\_004837.

627. The Autumn 1997 issue of the STEPS NewsLine highlighted unheard of seizure-free rates of nearly 50% as well as slides implying a dose-response relationship of Neurontin and enhanced efficacy at dosages above the FDA-approved limit of 1800 mg/day. The fact that patients taking less than 1800 mg/day had a greater reduction in seizure frequency than those taking greater than 1800 mg/day was not highlighted. This is an example of the selective outcome reporting from the STEPS trial.

Ex. 439,  
WLC\_Franklin\_0000130292; Ex.  
365, Alldredge Report at 40-41.

628. Between July and October 1998, Defendants sponsored a CME activity entitled “New Frontiers in Social Phobia and Bipolar Disorder.” This CME recommended dosages of gabapentin up to 4800 mg/day, but failed to disclose the results of clinical trials that showed no enhanced efficacy at higher doses.

Ex. 071, WLC\_CBU\_028064; Ex. 023, Abramson Report ¶¶255-256.

629. In a transcript from a 1998 video series, sponsored by Defendants, entitled “Adjunctive Use of Neurontin for Effective Management of Partial Epileptic Seizures,” Defendants’ proffered dose expert in this litigation, Dr. Michael McLean, suggested the use of Neurontin at high doses based on the STEPs study, without disclosing that the STEPS study was not capable of supporting such an efficacy claim.

Ex. 440, WLC\_Franklin\_0000177155; Ex. 365, Alldredge Report at 43.

630. Between January 11 and 18, 1999, Defendants held teleconferences for physician participants to promote their higher-dose message through the use of the STEPS and NEON studies, both of which were not designed, and were not sufficient, to provide evidence of a dose-response. The speakers at these teleconferences were Dr. Ahmad Beydoun and Dr. Jack Pellock. Post-meeting summary reports described the false messages given, which included that for many patients it was

Ex. 441, WLC\_CBU\_012963; Ex. 365, Alldredge Report at 45-46.

appropriate to go beyond 1800 mg/day up to 4-5000 mg/day, that Neurontin was effective at higher doses than 1800 mg/day, that effectiveness was “really seen” at doses of 5-6000 mg/day, that dosing of Neurontin “should go to at least 3600” to provide an adequate trial, that one “[n]eed[s] to push the dose,” that “higher doses are effective where 1800 mg may not bring effective results,” that “[a]s the dose increase[s], you get greater beneficial effect” and that the STEPS and NEON trials had showed that 1800 mg was the “beginning dose.” Studies of high-dose gabapentin had demonstrated that there was no enhanced efficacy at dosages above the FDA-approved limit of 1800 mg/day.

631. Between January and March 1999, Parke-Davis held 5 advisory board meetings where attendees were informed about the “optimal dose” of Neurontin and the “efficacy results from the STEPS [trial]” were discussed, even though STEPS was not suitable to support an efficacy claim. Moreover, there was no disclosure of the negative results of 945-082.

Ex. 442,  
WLC\_FRANKLIN\_0000177446.

632. On June 4, 1999, Defendants sponsored a symposium held in Montreaux, Switzerland entitled “Broadening the spectrum of clinical use of

Ex. 443, McLean\_0003873; Ex. 365, Alldredge Report at 47-48.

antiepileptic drugs.” The proceedings were later published in the International Congress and Symposium Series. The proceedings included an article authored by Defendants’ proffered dose expert in this litigation, Dr. Michael McLean, entitled “Management of convulsive disorders with the newer antiepileptic drugs: a current review.” In this paper, Dr. McLean falsely and misleadingly stated that “[t]he studies that led to gabapentin’s approval were performed at doses that are now considered to be too low” and that “in the hands of physicians willing to use high doses - > 3600 mg, well described in the literature – greater efficacy can be obtained.” Studies of gabapentin at doses higher than the FDA-approved limit of 1800 mg/day had demonstrated that there was no enhanced efficacy of Neurontin at higher doses.

633. On December 1, 1999, Defendants held an advisory board meeting in Houston, Texas. During this meeting, Dr. Ahmad Beydoun presented the STEPS and NEON studies. Dr. Beydoun stated that the usual range for refractory epilepsy patients of Neurontin went up to “4800mg.” Studies of higher doses of gabapentin than the FDA-approved limit of 1800 mg/day

Ex. 444, WLC\_CBU\_175636; Ex. 365, Alldredge Report at 44.

had demonstrated that there was no enhanced efficacy at higher doses. The fact that protocol 945-224 had demonstrated no dose response for gabapentin was not disclosed at this meeting.

634. Defendants' proffered dose expert, Dr. Michael McLean, authored a chapter on gabapentin for the textbook *The Treatment of Epilepsy: Principles & Practice*. Dr. McLean's chapter contains several false and misleading statements including that in the open-label extension of 945-082 "3600 mg/day or more was necessary to sustain success as monotherapy [for epilepsy]," that "[d]oses up to 3600 mg/day may be required to benefit patients with seizures," that "[a]chieving maximal efficacy may require trying doses of 3600-4800 mg/day" and that the "package insert includes 3600 mg/day as effective." Studies of Neurontin at doses above the FDA-approved limit of 1800 mg/day had demonstrated that there was no enhanced efficacy of Neurontin at higher doses. The last statement omits that Neurontin's label actually states, as required by the FDA, that "[a]dditional benefit of using doses greater than 1800 mg/day was not demonstrated" and that "[t]he effective dose of Neurontin is 900 to 1800 mg/day."

Ex. 445, Neurontin Label at 25; Ex. 446, McLean\_0012596.

635. In 2000, Defendants sponsored a CME activity entitled “Management of Neuropathic Pain Syndromes.” In this CME, Dr. Charles Argoff suggested that it was not appropriate to stop gabapentin at doses of 1800 mg/day, referencing study 945-211 as evidence of efficacy at higher doses. As 945-211 did not demonstrate that there was enhanced efficacy of Neurontin at dosages above the FDA-approved limit of 1800 mg/day, this statement is false and misleading. The fact that protocol 945-224 had demonstrated no dose response for gabapentin was not disclosed.

Ex. 448, WLC\_CBU\_076620; Ex. 365, Alldredge Report at 45.

636. On March 15, 2000, Defendants held an advisory board meeting in Denver, Colorado. During this meeting, Dr. Ahmad Beydoun presented the STEPS and NEON studies. Dr. Beydoun stated: “The usual efficacious range is around 1800-4800mg.” Studies of higher doses of gabapentin than the FDA-approved limit of 1800 mg/day had demonstrated that there was no enhanced efficacy at higher doses.

Ex. 449, WLC\_CBU\_164376; Ex. 365, Alldredge Report at 44.

637. On April 12, 2000, Defendants held an advisory board meeting in Houston, Texas. At this meeting, Defendants’ proffered dose expert, Dr. Michael McLean, stated, during a presentation of the NEON and

Ex. 450, WLC\_CBU\_175606; Ex. 365, Alldredge Report at 43.

STEPS studies, that “[i]n terms of efficacy as add-on therapy, as you go to higher doses, you get better results, especially up at 3600 mg/day.” Studies of higher doses of gabapentin than the FDA-approved limit of 1800 mg/day had demonstrated that this was not true.

638. On April 13, 2000, Defendants held an advisory board meeting in St. Louis, Missouri.

Ex. 451, MDL\_Vendors\_057666;  
Ex. 365, Alldredge Report at 43-44.

Defendants’ proffered dose expert, Dr. Michael McLean, without support, stated “therapeutic efficacy skyrockets when you increase the dosage” and “the useful dose range is about 900-4800 mg/day.” Dr. McLean also encouraged titrating up to 3600 mg/day. Studies of higher doses of gabapentin than the FDA-approved limit of 1800 mg/day had demonstrated that there was no enhanced efficacy at higher doses.

639. On September 16, 2000, at a speaker training meeting entitled “Neurology Breakthroughs in the Millennium” held at the Watergate hotel in Washington DC, Pfizer falsely told 49 of its speakers: “the PI [FDA-approved package insert] dosing was not high enough. The STEPS study proved that dosing had to go higher than 1st expected to get the effect needed. In 1995, pain data came out saying that 2400-

Ex. 388,  
MDL\_VENDORS\_064551.

3600 was an effective dose and then they came out with 600 and 800 mg tablets.”

640. In December 2000, Pfizer developed a sales piece which directed sales representatives to falsely inform physicians that the “STEPS trial demonstrated an efficacy rate” that was higher than the efficacy rate of the labeled dose.

Ex. 452,  
MDL\_VENDORS\_079295.

641. Plaintiffs’ expert, Dr. Alldredge, reviewed Defendants’ marketing documents and found that “promoting the use of doses up to 3600 mg/day was a primary goal of the marketing campaign,” a message that was “in direct conflict with the highest quality evidence, both in epilepsy and in pain conditions, regarding the dose response effect of gabapentin.”

Ex. 365, Alldredge Report at 37-38.

642. According to Dr. Alldredge, “the fundamental marketing message – that, higher doses (above 1800 mg/day) are necessary for greater efficacy – was misleading (it advocated a dose response relationship for which there was no strong, scientifically sound, evidence) and incomplete (it de-emphasized randomized controlled trial data that did not support the message, as well as FDA judgment regarding the lack of increasing efficacy above 1800 mg/day).”

Ex. 365, Alldredge Report at 38.

643. On June 2, 2001, Defendants sponsored a CME activity entitled “New Directions in the Understanding & Treatment of Chronic Pain” which included a lecture entitled “Effective Management of the Hard-to-Treat Migraine” that advocated Neurontin at dosages of up to 4800 mg/day for migraine prevention.

Ex. 453, MDL\_Vendors\_094765.

644. In June 29, 2001, Defendants received a Notice of Violation (NOV) from the FDA’s Division of Drug Marketing, Advertising, and Communications (DDMAC) regarding misleading promotional claims made based on the NEON (Neurontin Evaluation of Outcomes in Neurological Practice) study which the FDA did not consider high quality evidence. The FDA recommended immediate discontinuation of the promotional materials. Defendants recognized the similarities between the NEON study and the STEPS study and that “DDMACs comments also applied to the use of STEPS efficacy and tolerability data.” As a result, Defendants planned to only use “STEPS data if presentation on efficacy and tolerability was balanced with a similar presentation of the pivotal clinical trial data.” There was “[n]o agreement at RC level regarding discontinuing use of STEPS data in promotion.” Thus

Ex. 454, Pfizer\_AGarrity\_0002142;  
Ex. 455, Pfizer\_LCastro\_0006580;  
Ex. 456,  
Pfizer\_RGlanzman\_0054596.

Pfizer continued to promote STEPS as an efficacy trial even after becoming aware that the FDA would consider such promotion to be misleading.

645. In a July 2, 2001 e-mail discussing Ex. 454, Pfizer\_AGarrity\_0002142. the Notice of Violation, Lucy Castro wrote that “all our [high-dose] promotional materials are based on these two [STEPS and NEON] studies. Without these data, we only have the pivotal data for promotion and that data is weak.”

646. The manuscript for protocol 945- Ex. 457, Pfizer\_LKnapp\_0026472. 411 (completed on December 4, 2001) was ghostwritten by MAC. On October 31, 2001, Lloyd Knapp sent an e-mail to Pfizer and MAC employees. The e-mail stated: “My recommendation is to select Dr Francisco Gomez Prez [*sic*] as lead author as he is the head of the most famous Diabetic Clinic in the country” and “Dr Gomez Perez is [a] well known an[d] respected Diabetologist. This will help with the commercial aspects of the indication.”

647. On November 2, 2001, in response Ex. 457, Pfizer\_LKnapp\_0026472. to Lloyd Knapp’s October 31, 2001 e-mail, Dr. Elizabeth Mutisya sent an e-mail to several Pfizer employees and Jeremy Mierop of MAC informing Mr. Mierop that “[w]e are all in agreement that Francisco Gomez Perez should be

the lead author” of the MAC-written manuscript of protocol 945-411.

648. At a 2002 Neuropathic Pain advisory board meeting entitled “Focus on the Specialist,” Defendants stated that primary care physician “titration patterns tend to be very conservative. A misleading graph was displayed containing the doses used in “pivotal studies.” Defendants actively suppressed the results of studies 945-224 and 945-271, both of which had negative results for gabapentin. Thus, they were not included in this advisory board. Defendants created the impression that primary care physicians were underdosing their patients. The clinical trial evidence had demonstrated that there was no benefit of high-dose gabapentin.

Ex. 023, Abramson Report ¶¶288-291; Ex. 458, Pfizer\_RGlanzman\_0059497.

649. In January 2003, *Clinical Therapeutics*, which has a circulation of 4,000 subscribers, published Defendants’ first of two ghostwritten manuscripts about dosing, entitled “Gabapentin Dosing for Neuropathic Pain: Evidence from Randomized Placebo-Controlled Trials.” The ostensible authors were Dr. Miroslav Backonja and Dr. Robert Glanzman.

Ex. 340, Backonja M., Glanzman R. Gabapentin dosing for neuropathic pain: Evidence from randomized, placebo-controlled clinical trials. *Clinical Therapeutics* 2003; 25(1): 81-104 (“Backonja/Glazman Dosing Article”); Ex. 339, MAC\_E\_0049671 at 175.

650. The Backonja/Glanzman Dosing

Ex. 340, Backonja/Glanzman Dosing Article; Ex. 023, Abramson

Article misleadingly recommended the titration of gabapentin to 1800 mg/day over 2 weeks based on the studies reviewed. The studies reviewed, protocols 945-210, 945-211, 945-306, 945-224 and 945-295 (note: Defendants did not include the suppressed negative results of protocol 945-271), did not provide evidence of enhanced efficacy of gabapentin at dosages above the FDA-approved limit of 1800 mg/day. In fact, these protocols did not even provide evidence for gabapentin's efficacy outside of PHN.

Report ¶¶115-116.

651. The Backonja/Glanzman Dosing Article falsely stated that “further dose escalation of gabapentin up to 3600 mg/day may be necessary” and that “doses between 1800 and 3600 mg/day have been found to be effective in achieving” greater improvement in pain scores. These statements were false, as the studies reviewed in this article did not reveal any enhanced efficacy of gabapentin at dosages above the FDA-approved limit of 1800 mg/day.

Ex. 340, Backonja/Glanzman Dosing Article; Ex. 023, Abramson Report ¶¶225-228.

652. The Backonja/Glanzman Dosing Article falsely states: “This recommendation [that studies had demonstrated that 3600 mg/day may be necessary] is consistent with the 1800 to 3600 mg/range of gabapentin

Ex. 340, Backonja/Glanzman Dosing Article; Ex. 023, Abramson Report ¶231; Ex. 445, <http://www.fda.gov/cder/foi/label/2005/20235s029,20882s015,21129s016lbl.pdf> (“Neurontin Label”) at 25; Ex. 365, Alldredge Report at 51.

approved by the FDA for the treatment of PHN.” The article also misleadingly states: “gabapentin can be titrated up to 3600 mg/d as required over the following weeks to achieve a maximal response with good tolerability.” The FDA-approved product label states: “Additional benefit of using doses greater than 1800 mg/day was not demonstrated.” The implication that response improves above 1800 mg/day is misleading as studies of gabapentin at high-doses had demonstrated that there was no greater efficacy at dosages above the FDA-approved limit of 1800 mg/day.

653. The Backonja/Glanzman Dosing Article is an example of the use of publications as “information laundering” to allow “a marketing-driven key message to be integrated as the core message of a drug company written article that is published in a medical journal.”

Ex. 023, Abramson Report ¶119.

654. Defendants developed the key messages for the Backonja/Glanzman Dosing Article before either author was even involved. The article was written by MAC. The first page of the third draft of the article, summarizing the key messages that would be included in the article, including the following false

Ex. 459, Pfizer\_LKnapp\_0023646 (underline in original to denote changes from first draft); Ex. 023, Abramson Report ¶233; Ex. 365, Alldredge Report at 50.

messages: (1) “Gabapentin is an anticonvulsant that has [been] proven effective in the treatment of neuropathic pain;” (2) “1800 mg/d is the recommended dose for patients with neuropathic pain [600 mg tablet 3 times daily]; however, some patients may require doses as high as 3600 mg/d;” (3) “Gabapentin doses up to 3600 mg/d have been proven well tolerated and effective in clinical studies;” and (4) “Based on these findings, it is recommended [th]at, after a 3-day titration to 900 mg/d, additional titration is performed to 1800 mg/d. Doses up to 3600 mg/d may be necessary in some patients.”

655. “Physicians had no reason to believe that this [the Backonja/Glanzman Dosing] article, recommending doses of Neurontin up to 3600 mg/day for neuropathic pain, did not accurately and fairly represent the best available scientific evidence. Yet the history and development of this article...show that its primary purpose was to influence ‘major markets.’ Both science and FDA regulations were sacrificed to the demands of marketing.”

Ex. 023, Abramson Report ¶121.

656. “[T]he key messages for the Backonja/Glanzman review article about dosing for neuropathic pain were developed before either author was ‘on board.’ The purpose of the article was commercial not

Ex. 023, Abramson Report ¶236.

scientific. The article presented a biased view of the science in order to convince readers of the efficacy of Neurontin for neuropathic pain—a conclusion that Defendants’ own consultants and the FDA had recently rebuked. The article also presented a biased view of the science to justify recommendations for higher than FDA-approved doses. And finally, the plan to capitalize on the commercial opportunity created by the publication of this review is clearly articulated in Defendants’ e-mails.”

657. On January 7, 2003, Angela Crespo, Dr. Robert Glanzman and Joan Kaplan sent an e-mail to all “Neurontin Product Champions” informing them that the Backonja/Glanzman Dosing Article was now available on *Clinical Therapeutics* website. The e-mail stated that “one of the problems with physicians’ use of Neurontin for pain is under dosing, resulting in less than optimal efficacy.” The e-mail discussed how the article contained a key promotional message to titrate to 1800 mg/day within 2 weeks and increase to 3600 mg/day “to achieve maximal benefit.” The e-mail stated that “[b]ecause this is a key publication for NEURONTIN, information from this study should be used in all neuropathic pain initiatives, subject to your local

Ex. 341, Pfizer\_LAlphs\_0013849;  
Ex. 023, Abramson Report ¶235.

regulations.” Activities included “Promotional detail aids,” “Speakers programs,” “Regional promotional and scientific meetings” and “Public relations programs.” Finally, the e-mail stated that representatives could start using the false and misleading Backonja/Glanzman Dosing Article “in direct promotion.”

658. Defendants hired MAC to ghostwrite another article containing their false and misleading high-dose marketing message. The article’s attributed author was Defendants’ proffered dose expert in this litigation, Dr. Michael McLean, even though he was not the actual author. Early drafts of the manuscript outlined false and misleading key messages that Defendants wanted to appear in the article, including that “[t]itrating up to 3600 mg/day is recommended,” as “3600 mg/day has better efficacy than lower doses,” that, in high-dose trials, “[h]igher doses were typically more efficacious than lower doses, as expected from the trend towards increased efficacy with higher gabapentin doses” and that “[d]oses of 3600 mg/day has [sic] better efficacy than lower doses.”

Ex. 460, MAC\_E\_0026749; Ex. 365, Alldredge Report at 51-52.

659. In May 2003, *Clinical Therapeutics* published the ghostwritten McLean dosing article

Ex. 475, McLean MJ, Gidal BE. Gabapentin dosing in the treatment of epilepsy. *Clin Ther* 2003;25:1382-406; Ex. 365,

containing the false and misleading high-dose marketing message. The McLean dosing article falsely states: “[t]he

effective dosage range is 900 to 3600 mg/d.” Dr.

Allredge reviewed the article and found it to be

“incomplete, and misleading.” High-quality randomized

fixed-dose comparison studies had demonstrated that there

was no enhanced efficacy of Neurontin at dosages above

the FDA-approved limit of 1800 mg/day. The McLean

dosing article fails to disclose them. *Clinical*

*Therapeutics* has a circulation of 4,000 subscribers.

Allredge Report at 51-52; Ex. 445, Neurontin Label at 25; Ex. 339, MAC\_E\_0049671 at 175.

660. Plaintiffs’ expert Dr. Allredge

reviewed Defendants’ marketing documents and found

that “promoting the use of doses up to 3600 mg/day was a

primary goal of the marketing campaign,” a message that

was “in direct conflict with the highest quality evidence,

both in epilepsy and in pain conditions, regarding the dose

response effect of gabapentin.”

Ex. 365, Allredge Report at 37-38.

661. According to Dr. Allredge, “the

fundamental marketing message – that, higher doses

(above 1800 mg/day) are necessary for greater efficacy –

was misleading (it advocated a dose response relationship

for which there was no strong, scientifically sound,

evidence) and incomplete (it de-emphasized randomized

Ex. 365, Allredge Report at 38.

controlled trial data that did not support the message, as well as FDA judgment regarding the lack of increasing efficacy above 1800 mg/day).”

662. The message repeatedly presented at advisory boards, mostly by Defendants’ proffered dose expert in this litigation, Dr. Michael McLean, as well as Dr. Ahmad Beydoun, indicated that there was enhanced efficacy at dosages above the FDA-approved limit of 1800 mg/day. This message was contradicted by the studies of high-dose gabapentin. Therefore, this message was “incomplete and misleading.”

Ex. 365, Alldredge Report at 44.

663. In summary, Dr. Alldredge found that: “the marketing materials/practices used by Defendants/Pfizer with regard to efficacy claims for gabapentin doses above 1800 mg/day were incomplete and misleading. The studies from which data were presented to support efficacy at doses above 1800 mg/day lacked scientific rigor; and many presentations of these data were not balanced by the inclusion of higher quality evidence that failed support the “higher dosage / higher efficacy” message.”

Ex. 365, Alldredge Report at 55.

**D. Results of Fraudulent Marketing Campaign**

664. According to IMS NDTI data, the

Ex. 138, Revised Conti Declaration, Figure 24.

average number of high-dose [ $>1800$  mg/day] uses per quarter in 1994 for indications other than epilepsy was 0.

665. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 1994 for epilepsy was 4,561.

Ex. 138, Revised Conti Declaration, Figure 23.

666. “[O]verdosing of Neurontin for epilepsy indications counts for approximately 10,000-20,000 uses per quarter between January 1995 and January 2003 and the majority of this use appears to be in the 2400+ mg per day range.”

Ex. 138, Revised Conti Declaration ¶48.

667. “[O]verdosing of Neurontin for non-epilepsy indications counts for under approximately 20,000 uses per quarter through the last quarter of 1997. The uses of Neurontin for daily dosages exceeding 1800 mg began to rise around January 1998 and increased to a peak of about 100,000 per quarter around January 2003. Uses above 2400 mg per day appear to constitute approximately half of all use over 1800 mg per day beginning in January 2002.”

Ex. 138, Revised Conti Declaration ¶49.

668. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 1995 for indications other than epilepsy was 475.

Ex. 138, Revised Conti Declaration, Figure 24.

669. According to IMS NDTI data, the average number of high-dose [>1800 mg/day] uses per quarter in 1995 for epilepsy was 12,828.

Ex. 138, Revised Conti Declaration, Figure 23.

670. Internal Parke-Davis tracking memoranda demonstrate the effects of exposure to the misleading information presented to investigators in the STEPs trial to their prescriptions during 1995. In just three months of the initial STEPS telebroadcast, there was a 38% increase in the number of Neurontin prescriptions written by exposed physicians, as well as a 10% increase in the average mg/day written in just three months. Near the end of 1995, the percentage of prescriptions written above 1800 mg per day increased 73%. The tracking showed that “Neurontin prescriptions written at average daily doses of between 2800mg and 3600mg showed the most significant gains.” The share of prescriptions above 2800 mg per day increased 156%; the share of prescriptions above 3600 mg per day increased 925%. And while STEPS investigators had never prescribed Neurontin above 4800 mg per day prior to the telebroadcast, after the broadcast the share of prescriptions above this level grew steadily. Based on this tracking analysis, Defendants concluded that “[e]ducation about

Ex. 408,  
WLC\_FRANKLIN\_0000052175;  
Ex. 384,  
WLC\_FRANKLIN\_0000069499;  
Ex. 383,  
WLC\_Franklin\_0000039745; Ex.  
461,  
WLC\_FRANKLIN\_0000038491

titration... appears to have had a positive impact on the physicians exposed to it.”

671. As a result of the “titrate to effect” campaign, from May 1995 to April 1996, Defendants were able to triple the number of patients taking Neurontin above 1800 mg per day. For patients taking Neurontin at doses of up to 3600 mg per day, there was 400% increase.

Ex. 391,  
WLC\_FRANKLIN\_0000055458.

672. According to IMS NDTI data, the average number of high-dose [>1800 mg/day] uses per quarter in 1996 for indications other than epilepsy was 4,122.

Ex. 138, Revised Conti Declaration,  
Figure 24.

673. According to IMS NDTI data, the average number of high-dose [>1800 mg/day] uses per quarter in 1996 for epilepsy was 23,534.

Ex. 138, Revised Conti Declaration,  
Figure 23.

674. According to the 1997 Neurontin Situation Analysis, Marketing Strategy #1 from 1996 included “Positioning and Focus Promotional Message on Titration to Higher Doses.” The STEPS trial had been a key activity for the implementation of this strategy. Market research conducted at the American Academy of Neurology meeting confirmed that the campaign was working, that physicians were titrating to higher doses.

Ex. 462,  
WLC\_Franklin\_0000038571.

675. According to IMS NDTI data, the

Ex. 138, Revised Conti Declaration,  
Figure 24.

average number of high-dose [ $>1800$  mg/day] uses per quarter in 1997 for indications other than epilepsy was 8,202.

676. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 1997 for epilepsy was 19,389.

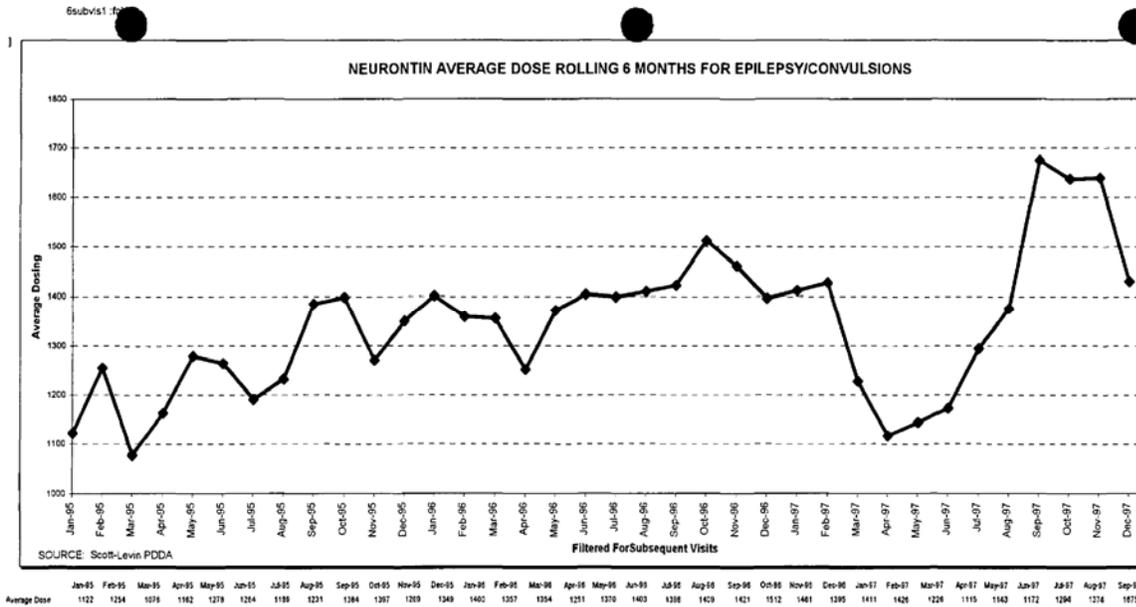
Ex. 138, Revised Conti Declaration, Figure 23.

677. According to Scott-Levin PDDA data, by September 1997, the average daily dose of Neurontin for epilepsy/convulsions had surpassed 1800 mg/day. This meant that any above-average prescribers were prescribing Neurontin at levels well above 1800 mg per day.

Ex. 463, WLC\_CBU\_132501.

678. Defendants' internal tracking analysis, shown below, demonstrates how successful the titrate-to-effect campaign was in causing physicians to raise the average daily dose of Neurontin prescriptions to almost 1800 mg per day by September 1997. However, at that point, the FDA rejected the company's application to tout higher doses, and thus Defendants temporarily scaled back the marketing of higher doses, causing the average daily dose to return towards pre-fraud levels.

Ex. 463, WLC\_CBU\_132501.



679. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 1998 for indications other than epilepsy was 29,963.

Ex. 138, Revised Conti Declaration, Figure 24.

680. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 1998 for epilepsy was 23,052.

Ex. 138, Revised Conti Declaration, Figure 23.

681. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 1999 for indications other than epilepsy was 42,277.

Ex. 138, Revised Conti Declaration, Figure 24.

682. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 1999 for epilepsy was 19,686.

Ex. 138, Revised Conti Declaration, Figure 23.

683. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 2000 for indications other than epilepsy was 59,772. Ex. 138, Revised Conti Declaration, Figure 24.

684. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 2000 for epilepsy was 13,574. Ex. 138, Revised Conti Declaration, Figure 23.

685. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 2001 for indications other than epilepsy was 86,282. Ex. 138, Revised Conti Declaration, Figure 24.

686. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 2001 for epilepsy was 19,272. Ex. 138, Revised Conti Declaration, Figure 23.

687. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 2002 for indications other than epilepsy was 103,087. Ex. 138, Revised Conti Declaration, Figure 24.

688. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 2002 for epilepsy was 18,310. Ex. 138, Revised Conti Declaration, Figure 23.

689. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses Ex. 138, Revised Conti Declaration, Figure 24.

per quarter in 2003 for indications other than epilepsy was 117,400.

690. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 2003 for epilepsy was 9,429.

Ex. 138, Revised Conti Declaration, Figure 23.

691. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 2004 for indications other than epilepsy was 108,265.

Ex. 138, Revised Conti Declaration, Figure 24.

692. According to IMS NDTI data, the average number of high-dose [ $>1800$  mg/day] uses per quarter in 2004 for epilepsy was 10,351.

Ex. 138, Revised Conti Declaration, Figure 23.

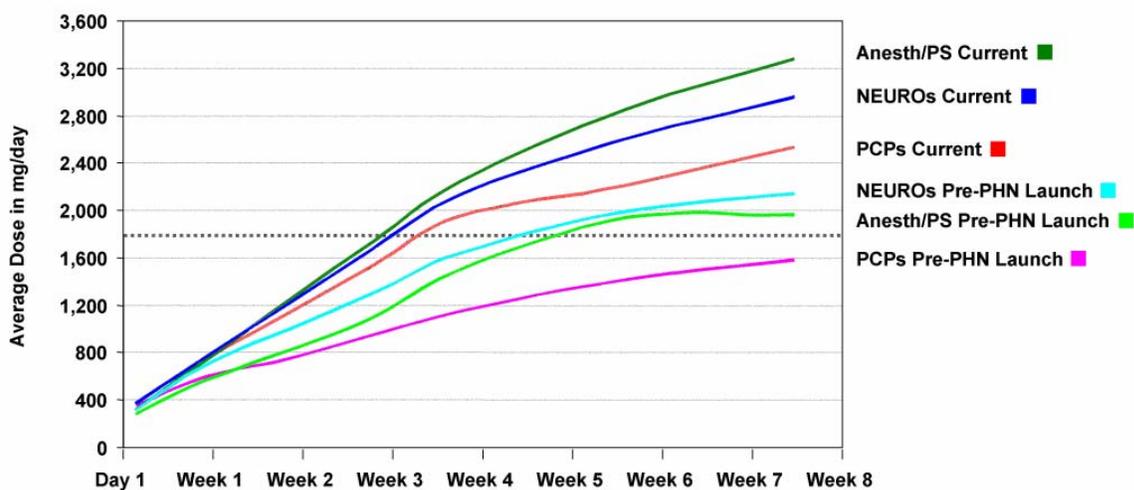
693. By 2003, Defendants' high-dose marketing of Neurontin had significantly raised the average daily dose well above 1800 mg/day for all major specialty groups.

Ex. 464, Pfizer\_BParsons\_0179305 (See chart at 0179314.)

# Physicians Titrating to 1800mg/day Quicker

Pfizer\_BPParsons\_0179314

## Mean Daily Dose of NEURONTIN Over 8 Weeks of Therapy



Source: Ziment PHN Tracking Study, December 2003



1. Jeanne Ramsey

694. Ms. Ramsey's insurance copay Ex. 465, Ramsey Depo Ex. 5.

required her to pay for half the amount of the prescription at the point of sale.

695. Ms. Ramsey first saw Dr. Ex. 466, Ramsey Depo Ex. 3.

Waldo for her reflex sympathetic dystrophy (RSD), a form of neuropathic pain in March 2000. On March 13, 2000, Dr. Waldo prescribed Neurontin at a daily dose of 900 mg per day.

696. Ms. Ramsey's co-pay for this Ex. 465, Ramsey Depo Ex. 5.

prescription was \$46.44.

697. Two weeks later, on March 31, 2000, Ms. Ramsey saw Dr. Haynsworth, who had earlier that month been detailed for his first time on Neurontin. Within just one month of this detail, Dr. Haynsworth raised her Neurontin prescription to 2400 mg per day, and then 3200 mg per day.

Ex. 467, Ramsey Depo Ex. 4; Ex. 468, Ramsey Depo Ex. 6; Ex. 469, Haynsworth Sherlock.

698. Ms. Ramsey's co-pay for this prescription was \$124.60.

Ex. 465, Ramsey Depo Ex. 5.

699. On July 25, 2000, Dr. Waldo saw Ms. Ramsey and reduced her Neurontin back under 1800 mg per day.

Ex. 470, Ramsey Depo Ex. 7.

700. On September 12, 2000, Ms. Ramsey saw Dr. Haynsworth again. Dr. Haynsworth, who had been detailed on Neurontin in July and August, raised her prescribed dose of Neurontin once again back above 1800 mg per day, to 2400 mg per day.

Ex. 471, Ramsey Depo Ex. 9; Ex. 469, Haynsworth Sherlock.

701. Ms. Ramsey's co-pay for this prescription was \$124.60.

Ex. 465, Ramsey Depo Ex. 5.

702. By December 2000, Dr. Waldo lowered Ms. Ramsey's Neurontin dosage to back below 1800 mg per day. Even at high doses,

Ex. 472, Ramsey Depo Ex. 12; Ex. 465, Ramsey Depo Ex. 5; Ex. 555, Ramsey Transcript at 35-36.

Neurontin did not control Ms. Ramsey's pain, and she stopped taking Neurontin at the end of 2000. She did not take Neurontin again until 2003.

703. In total, Ms. Ramsey spent a total of \$898.40 on Dr. Haynsworth's 4 Neurontin prescriptions in 2000, while she only spent \$157.58 for the 4 prescriptions written by Dr. Waldo during that same time period.

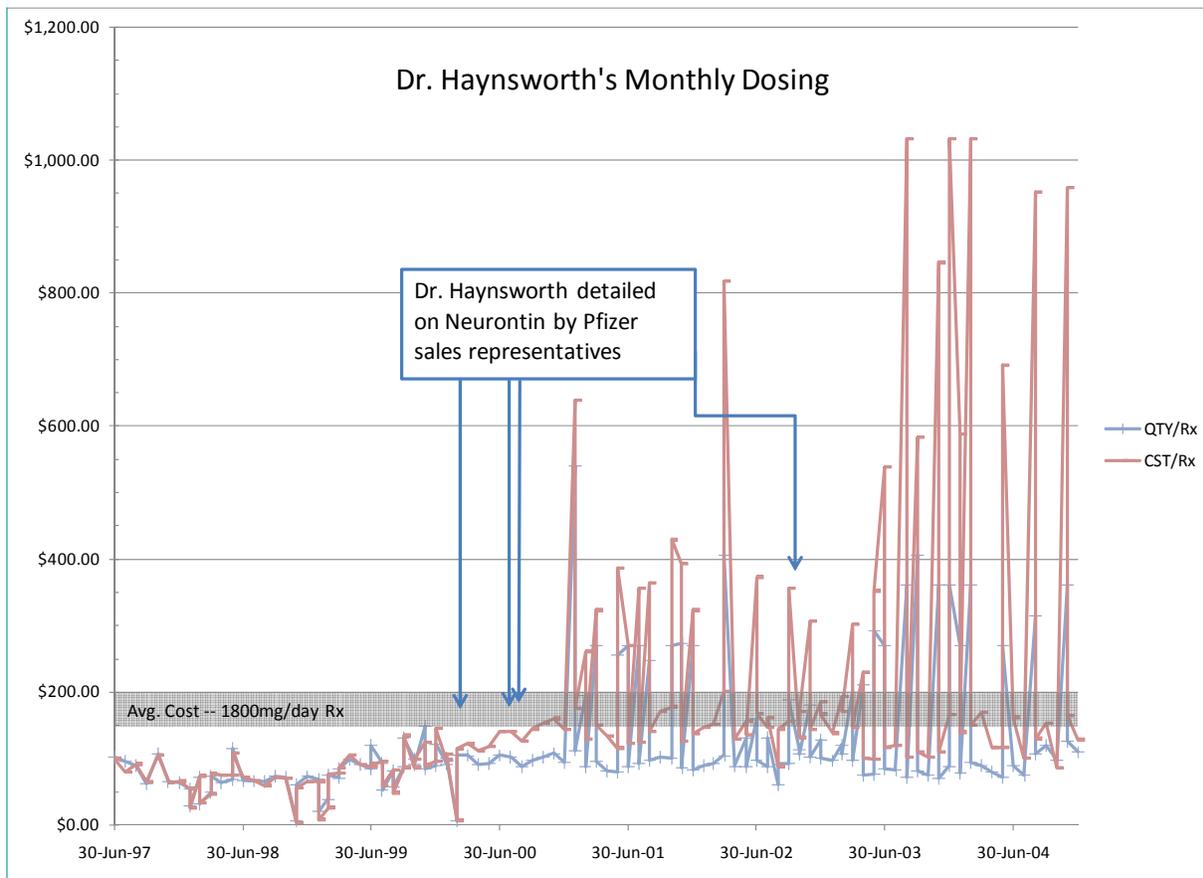
Ex. 465, Ramsey Depo Ex. 5.

704. In 2000, Dr. Haynsworth was detailed heavily during the time that he was treating Ms. Ramsey.

Ex. 469, Haynsworth Sherlock S2

705. During that time, the cost of an average Neurontin prescription written by Dr. Haynsworth surged from well below \$200 (roughly what 1800 mg per day costs per month) to a more than \$200. In some cases, Dr. Haynsworth's average prescription greatly exceeded \$1800 mg per day.

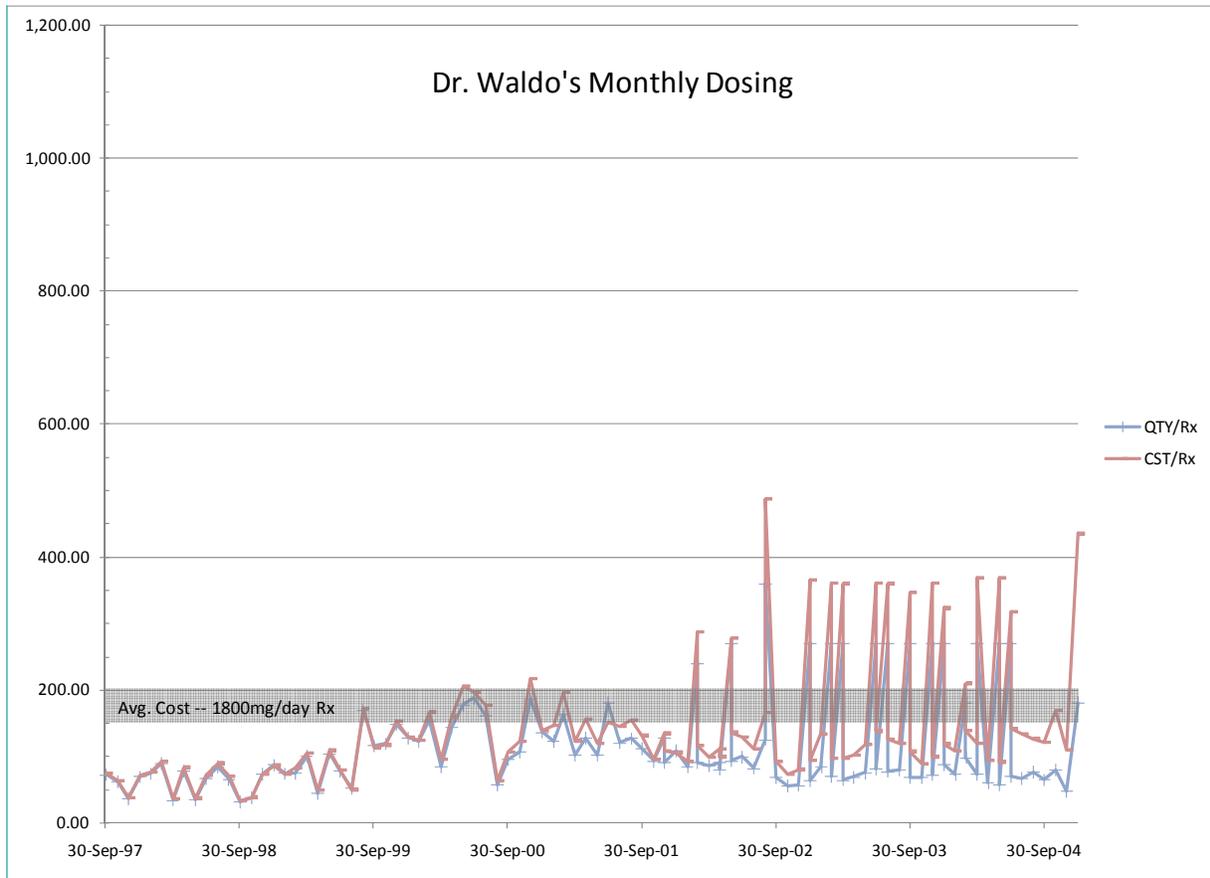
Ex. 473, Haynsworth Wolters Kluwer



706. In contrast, Neurontin

Ex. 474, Waldo Wolters Kluwer.

prescriptions written by Dr. Waldo, who never prescribed more than 1800 mg per day to Ms. Ramsey, remained at a level below 1800 mg per day during that time.



**V. LOUISIANA HEALTH SERVICE INDEMNITY COMPANY D/B/A BLUECROSS  
BLUESHIELD OF LOUISIANA (“BCBSLA”) AND ASEA**

707. BCBSLA is a not-for-profit mutual company, owned by its policy holders. Ex. 556, Deposition of Sabrina Heltz (“Heltz Tr.”) at p. 64:5-10

708. In 1994, BCBSLA had about 300,000 to 400,000 covered lives. Ex. 562, Deposition of Dr. James Gengelbach (“Gengelbach Tr.”) at p. 25:16-25

709. By 2003, BCBSLA had over one million covered lives. *Id.*

710. BCBSLA offers preferred provider organization (“PPO”), health maintenance organization (“HMO”), preferred provider, point of Ex. 557, Heltz Tr. at pp. 23:24-26:3

service, Medicare choice and supplement, administrative services only (“ASO”), dental, cancer, and serious disease products, all of which usually include a pharmacy benefit.

711. The PBM who processed claims for BCBSLA was Paid Prescriptions, Inc. (“PAID”) and National Rx Services, Inc. of Texas (“NATIONAL”) from April 1, 1995 through April 1, 1998.

Ex. 575, Louisiana Health Service Indemnity Company d/b/a Bluecross/Blueshield of Louisiana’s Objections and Response to Defendants’ First Set of Interrogatories at ¶ 2.

712. Merck-Medco (“Medco”) acquired PAID and NATIONAL and was BCBSLA’s PBM from April 1, 1998 until April 1, 2004.

Id.

713. In 1998 BCBSLA renewed its contract with Medco.

Ex. 576, Deposition of J. Richard Williams (“Williams Tr.”) at p. 42:17

714. Express Scripts, Inc. (“ESI”) became BCBSLA’s PBM on April 1, 2004.

Ex. 575, Louisiana Health Service Indemnity Company d/b/a Bluecross/Blueshield of Louisiana’s Objections and Response to Defendants’ First Set of Interrogatories at ¶ 2; Ex. 579, Deposition of Imelda Coleman (“Coleman Tr.”) at p. 37:10-13

715. Approximately 80,000 members remained on the manual paper claims system when Medco was hired in 1995; these members’ pharmacy claims processing was taken over by Medco in 1998.

Ex. 577, Williams Tr. at p. 40:24-41:24

716. BCBSLA hired its first staff pharmacist in 1999.

Ex. 563, Gengelbach Tr. at p. 31:14-27

717. Prior to this time, the pharmacy benefit was basically not managed, and the long-term goal of hiring a pharmacist was to manage the pharmacy benefit because the cost of pharmacy claims was increasing faster than the cost of medical claims. Ex. 564, Gengelbach Tr. at pp. 32:21-33:13; Ex. 565, Gengelbach Tr. at p. 35:14-24
718. In 1999, BCBSLA formed its P & T committee. Ex. 566, Gengelbach Tr. at pp. 36:23-37:1
719. BCBSLA maintains an open formulary, meaning that they pay for all FDA approved drugs regardless of the formulary status of the drug. Ex. 610, Deposition of Milam Ford (“Ford Tr.”) at pp. 129-130; Ex. 580, Coleman Tr. at pp. 76:23-25; Ex. 581, Coleman Tr. at p. 77:3-7; Ex. 614, Deposition of Susan Hoomaian (“Hoomaian Tr.”) at p. 14:14-24
720. Prior to 2000, BCBSLA adopted the Medco formulary, which was entirely controlled by Medco and Medco’s P & T committee. Ex. 615, Hoomaian Tr. at pp. 14-16, Ex. 616, Hoomaian Tr. at pp. 28:25-29:6, Ex. 617, Hoomaian Tr. at p. 41:3-9, Ex. 618, Hoomaian Tr. at pp. 148:20-149:10-17; Ex. 567, Gengelbach Tr. at pp. 35:25-36:22; Ex. 578, Williams Tr. at pp. 36:23-37:11
721. Neurontin was listed as a preferred drug on the BCBSLA formulary between 1998 and 2004. Ex. 619, Id. at pp. 135:8-15
722. The formulary for BCBSLA was not used to prevent or limit the payment of drugs prescribed for off-label uses. Ex. 620, Id. at pp. 139:4-7
723. BCBSLA did not seek to remove Neurontin from its formulary between 1998 and 2004. Ex. 621, Id. at pp. 140:5-7
724. From February 1999 through February Ex. 627, Transcript of deposition testimony of Armando Ramirez, conducted January 14, 2008 (“Ramirez

2002, BCBSLA had no input into the scope of prescription drug coverage.

Tr.”) at p. 16:10-18

725. From February 1999 through February 2002, BCBSLA had no involvement with formulary management. Formulary management functions were performed by Medco.

Ex. 628, Id. at p. 16:19-21; Ex. 639, Transcript of deposition testimony of Elizabeth Rose Boudreaux as 30(b)(6) witness for Express Scripts, Inc. conducted November 8, 2006 (“Boudreaux Tr.”) at pp. 13:8-13

726. From February 1999 through February 2002, BCBSLA performed retrospective drug utilization reviews, however no action was taken on the results, as Medco was responsible for managing the formulary.

Ex. 629, Ramirez Tr. at pp. 29:15 – 30:1

727. From February 1999 through February 2002, there were no step therapy cost containment programs in place for Neurontin.

Ex. 630, Id. at p. 31:16-10

728. From February 1999 through February 2002, BCBSLA had no individual or entity that was responsible for off-label use or the consideration of off-label use of drugs.

Ex. 631, Id. at p. 59:9-15

729. Medco provided the BCBSLA P&T Committee with information and reporting on Medco’s actions, the P&T Committee did no independent research or review.

Ex. 632, Id. at pp. 60:1 – 61:7

730. From February 1999 through February

Ex. 633, Id. at p. 63:3-22

2002, the P&T Committee at BCBSLA made no decisions on drugs, but was a token committee, existing to comply with Blue Cross regulations.

731. BCBSLA was unaware if drugs were being prescribed off label as they did not have information about what was happening at the point of sale and there was no diagnosis indicated on prescriptions.

Ex. 634, Id. at pp. 67:21 – 68:2; Ex. 635, Id. at p. 69:7-13

732. From February 1999 through February 2002, drugs were considered for addition to the BCBSLA formulary every six months.

Ex. 636, Id. at p. 71:19-22

733. Drugs were not removed from the BCBSLA formulary, but rather were moved to different tiers.

Ex. 637, Id. at pp. 71:24 – 72:10

734. From February 1999 through February 2002, changes were unilaterally made to the formulary by Medco. BCBSLA offered opinions and if it objected to changes, Medco exercised its right under the contract to make changes notwithstanding BCBS's opinions.

Ex. 638, Id. at pp. 37:9 – 38:10

735. Medco's P & T committee reviewed new drugs coming out on the market, new drug indications, and classification switches of drug for

Ex. 622, Hoomaian Tr. at p. 35:11-17

inclusion on Medco's formulary.

736. BCBSLA basically still used Medco's existing formulary, and BCBSLA's P & T committee would review new drugs to determine at which tier a drug would be placed, e.g. whether it would be a preferred brand or a nonpreferred brand.

Ex. 568, Gengelbach Tr. at pp. 38:7-39-12; Ex. 582, Coleman Tr. at pp. 25:23-27:3

737. After 2000, BCBSLA's P & T committee still relies heavily on the PBM and only reviews new drugs or classes of drugs.

Ex. 611, Ford Tr. at pp. 149-150

738. BCBSLA's P & T committee did not review Neurontin because it was already included on the Medco formulary.

Ex. 612, Ford Tr. at p. 445; Ex. 569, Gengelbach Tr. at p. 80:14-22

739. BCBSLA's P&T Committee would meet four times each year before Medicare Part B, then six times per year afterwards.

Ex. 583, Coleman Tr. at p. 27:5-11, Ex. 584, Coleman Tr. at pp. 72:18 – 73:3

740. The P&T Committee would do a very short presentation and make a recommendation whether or not to add and at what tier to put a new drug on.

Id.

741. BCBSLA's formulary was always an open formulary under Medco, and BCBSLA still maintains an open formulary, in which all drugs are covered, unless they are specifically excluded in the

Ex. 614, Hoomaian Tr. at p. 14:14-24, 51:18-22; Ex. 585, Coleman Tr. at p. 75:3-14

member contract.

742. BCBSLA switched to ESI from Medco in 2004. Ex. 570, Gengelbach Tr. at pp. 83:19-84:8; Ex. 639, Boudreaux Tr. at pp. 13:8-13

743. The contract between Express Scripts and BCBSLA entitled Managed Prescription Drug Program Agreement became effective between the parties from April 1, 2004 through December 31, 2007. Ex. 640, Boudreaux Tr. at pp. 29:17-25 and Ex. 641, Boudreaux Tr. at p. 30:1-5

744. Express Scripts has its own P&T committee whose purpose is to evaluate drugs that come on the market as well as other classes of drugs to determine the clinical effectiveness in order to include it on a formulary. Ex. 642, Id. at pp. 38:7-9 and Ex. 643, Boudreaux Tr. at p. 39:13-18

745. The only communication about Neurontin between Express Scripts and BCBSLA that directly affected client benefits was a request to make Neurontin nonformulary when the generic became available. Ex. 644, Id. at pp. 54:2-8

746. The generic version of Neurontin is gabapentin which became available in certain strengths in 2004. Ex. 645, Id. at pp. 54:12-24

747. A closed formulary is a formulary where the drugs on formulary are covered, typically Ex. 613, Milam Ford Tr. at pp. 27:25 – 28:15

without restriction or with very little restriction, but drugs that are off formulary are restricted and require authorization or proof of medical necessity.

748. BCBSLA considered implementing a closed formulary when implementing Medicare Part D in January 2006.

Ex. 558, Heltz Tr. at pp. 75:4-23

749. A closed formulary created too many complications operationally and was not competitive in the Louisiana marketplace, so BCBSLA switched to an open formulary for Medicare Part D.

Ex. 559, Heltz Tr. at pp. 39:10-11; Ex. 560, Heltz Tr. at pp. 43:10-45:15; Ex. 558, Heltz Tr. at pp. 75:4-23

750. Generally for prescription drug claims, BCBSLA's PBM pays the pharmacy a negotiated rate for prescriptions, the pharmacy collects the co-pay from the member, and BCBSLA reimburses the PBM on a regular basis for amounts the PBM has paid to the pharmacy.

Ex. 575, Plaintiff Louisiana Health Service Indemnity Company d/b/a Bluecross Blueshield of Louisiana's Objections and Responses to Defendants' First Set of Interrogatories at ¶ 4

751. BCBSLA has always paid for Neurontin prescriptions for its insureds who have a pharmacy benefit.

Id.

752. BCBSLA has never considered excluding any drugs based on efficacy because it presumes that a drug is efficacious for its FDA approved indication.

Ex. 571, Gengelbach Tr. at p. 44:12-23

753. BCBSLA does not use step therapy. Ex. 586, Coleman Tr. at p. 59:5-12
754. BCBSLA has always been directly marketed to by pharmaceutical sales representatives, managed care representatives, and medical liaisons including those of Defendants such as Pfizer representative Jennifer Comeaux from 2000 to 2003, Cher Rezor, and Paula Roads among others. Ex. 572, Gengelbach Tr. at pp. 63:14-64:4, Ex. 573, Gengelbach Tr. at p. 87:12-25, Ex. 561, Heltz Tr. at pp. 71:12-72:15; Ex. 587, Coleman Tr. at pp. 27:4-19; Ex. 588, Coleman Tr. at pp. 139:2-140:2
755. BCBSLA relies on all information it receives from drug manufacturers, including published data, sales and marketing information to be complete and truthful. Ex. 589, Coleman Tr. at pp. 142:4-143:17
756. BCBSLA's Clinical Pharmacist, was detailed regularly by Parke-Davis sales representatives regarding off-label uses of Neurontin prior to her joining BCBSLA. Ex. 590, Coleman Tr. at pp. 100:11-102:25, Ex. 591, 128:11-130:13
757. While at her previous employment at Ochsner healthcare, BCBSLA's Clinical Pharmacist, Imelda Coleman, was detailed by Parke-Davis sales representatives, including Kathy Tugwell, about off-label uses of Neurontin, she was regularly provided unsolicited material from Parke-Davis medical liaisons, including Sarah LeCroix, regarding off-label uses of Neurontin, and at times was coerced by Parke-
- Id.

Davis sales representatives into signing requests for materials regarding off-label uses of Neurontin.

758. Ms. Coleman was paid by Parke-Davis to attend one of its Speakers Bureau training seminars. Ex. 592, Coleman Tr. at pp. 131:23-133:11

759. Ms. Coleman has been invited to and attended Pfizer advisory board meetings, including one managed care advisory board meeting on pregabalin, prior to that drug's approval, where Neurontin and its use in treating neuropathic pain was discussed. Ex. 593, Coleman Tr. at pp. 133:22-136:8, Ex. 594, Coleman Tr. at p. 137:8-15

760. Pfizer paid for Ms. Coleman's airfare, food, lodging and paid her an honorarium for attending these meetings. Ex. 595, Coleman Tr. at p. 136:9-13

761. Some Advisory Board meetings that Ms. Coleman has attended were purely marketing events. Ex. 596, Coleman Tr. at pp. 145:19-146:9

762. While previously employed, BCBSLA's Clinical Pharmacist would frequently receive letters regarding off-label studies from medical science liaisons. Commonly the representative would ask a leading question to elicit a response that would lead to the representative triggering a letter response. Occasionally unsolicited letters were sent as well. Ex. 597, Id. at p. 128:3-21

763. Ms. Coleman's husband is a podiatrist, Ex. 598, Coleman Tr. at p. 101:6-15

William Coleman, whom specializes in diabetic neuropathy.

764. In addition to detailing Ms. Coleman at Ex. 598, Coleman Tr. at p. 101:6-15 her prior job with Ochsner, Parke-Davis sales representatives detailed Ms. Coleman in an effort to reach and influence her husband to prescribe Neurontin for off-label uses.

765. One time, Ms. Coleman and her Ex. 599, Coleman Tr. at p. 143:4-22 husband were treated to dinner by Parke-Davis sales representative Kathy Tugwell and medical liaison Sarah LeCroix, during which they not only discussed but were supplied with studies regarding using Neurontin for the off-label treatment of diabetic peripheral neuropathy.

766. Because he was told by Parke-Davis Ex. 600, Coleman Tr. at pp. 118:17-119:2 sales representatives that Neurontin was effective for treating diabetic peripheral neuropathy, Mr. Coleman Ex. 601, Id. at pp. 122:8-123:7 tried prescribing Neurontin for his diabetic neuropathy patients. He no longer does because he never had any success in treating his diabetic neuropathy patients with Neurontin.

767. BCBSLA does not know the indication Ex. 574, Gengelbach Tr. at p. 65:6-11 for which a drug is prescribed.

768. Because BCBSLA processes hundreds of thousands of prescription claims per month, for thousands of different drugs, many of which have multiple indications, all without diagnosis codes, it is not practical to know if a drug was being prescribed for an off-label use.

Id.

769. Medco provided BCBSLA with bi-weekly claims data, which include the ingredient cost of the drug, the dispensing fee, the co-pay, all the member information, member identifying information, the pharmacy information and if there was a prior authorization on the drug, but do not contain the indication that the drugs are prescribed for.

Ex. 624, Hoomaian Tr. at pp. 55:13-56:2, Ex. 625, Hoomaian Tr. at p. 96:11-24

770. Electronic pharmacy claims data conform to a standardized format in the U.S. which is set by The National Council for Prescription Drug Programs, Inc. (NCPDP), a not-for-profit ANSI-Accredited Standards Development Organization consisting of over 1,500 members representing virtually every sector of the pharmacy services industry.

Ex. 626,. Id. at pp. 126:8-127:16; Ex. 646, [www.ncdp.org](http://www.ncdp.org)

771. The indication for which a drug is prescribed is not a field in the standard electronic

Ex. 602, Coleman Tr. at p. 127:17-19

claims data format set by NCPDP.

772. BCBSLA's pharmacy claims data are not integrated with its medical claims data.

Ex. 603, Coleman Tr. at p. 33:3-22; Ex. 647, Affidavit of Gayle Carpenter September 11, 2007

773. BCBSLA's pharmacy claims data for the proposed class period, 1994 through 2004, are stored in 4 distinct datasets: one dataset for the claims data from each of BCBSLA's three PBMs, PCS, Medco, and ESI, and one dataset for the in-house BCBSLA medical claims database ("Legacy dataset") that was used to process pharmacy claims during the period when BCBSLA did not use a PBM, and for pharmacy claims that are occasionally processed as part of a medical claim.

Ex. 647, Affidavit of Gayle Carpenter September 11, 2007 at ¶ 3

774. The identification system for each policy holder in the claims databases changed several times over the proposed class period, including a revision of the identification requirements to comply with HIPAA.

Ex. 647, Affidavit of Gayle Carpenter September 11, 2007 at ¶ 4; Ex. 607, Coleman Tr. at pp. 127:20-128:6

775. For the three PBM datasets, the indication and diagnostic code are not captured, and the prescribing physician is not always captured.

Ex. 647, Id. at ¶ 15

776. By 2003, anticonvulsants, driven primarily by Neurontin sales, had become one of the

Ex. 604, Coleman Tr. at p. 99:3-21

top five therapeutic classes in terms of cost for BCBSLA, which did not make sense, given the population of patients that had the condition for Neurontin's approved indication.

777. Neurontin is more expensive than other drugs used to treat diabetic peripheral neuropathy, more expensive than first generation antipsychotic drugs that are used to treat bi-polar disorder, and more expensive than other drugs used for migraine prophylaxis.

Ex. 605, Coleman Tr. at pp. 111:12-22, Ex. 606, 137:23-138:23

778. For the period from January 1, 1994 through July 2, 2005, BCBSLA paid for 111,501 prescriptions of Neurontin costing BCBSLA, after deducting co-pays, co-insurance, and deductibles, and including tax, a total of \$11,154,458.32.

779. Defendants' call notes document fraudulent and misleading off-label marketing of Neurontin to physicians who wrote prescriptions for Neurontin that BCBSLA paid for.

780. Fernando Alemany-Lopez, an internal medicine physician in Opelousas, Louisiana, wrote Neurontin prescriptions that were paid for by BCBSLA from 2001 through 2004. Dr Alemany-

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana's Objections and Responses to Defendants' First Set of Interrogatories at ¶ 6

Exhibit L, CMMS Data

Lopez was initially detailed in February and then August of 2000. Call notes show a discussion of “use in bipolar and mood stabilization Use in adolescents with these psychiatric disorders?” as well as “articles and abstracts use in peripheral neuropathies, psychiatric disorders, and migraine” and “ABSTRACTS REPORTS USE OF NEURONTIN IN PSYCHIATRIC DISORDERS: BIPOLAR, MANIA, ANXIETY, SOCIAL PHOBIA AND MIGRAINE TX.” In August of 2000, literature on “use in anxiety-related disorders” was sent to Dr. Al-Asahi from Pfizer Medical Affairs. BCBSLA claims data reveals that soon afterwards, in the first quarter of 2001, BCBSLA began paying for Neurontin prescriptions written by Dr. Alemany-Lopez. Details of Dr. Alemany-Lopez continued through at least 2003 and claims data from BCBSLA show the he continued writing prescriptions for Neurontin through 2004.

781. Lacie Alfonso, a New Iberia physical medicine and rehabilitation physician, wrote Neurontin prescriptions that were paid for by BCBSLA in 2004. Dr. Alfonso was visited by Pfizer sales representatives ten times from January through

Exhibit L, Merlin Data

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

Id.

Exhibit L, Sherlock S2 Data

May of 2004, during which time she was repeatedly detailed on Neurontin and agreed to at least one dinner. Towards May, the sales representative notes; “L-Using more Neuro business picking up. A-Cont 1st line F-Cont reinf.”

782. Brian Babiak, a Shreveport psychiatrist, wrote Neurontin prescriptions that were paid for by BCBSLA from 2003 through 2004. Dr. Babiak was detailed by a Pfizer representative in October of 1999 at which time off-label psychiatric uses were discussed. Immediately afterwards, literature on “treatment of bipolar depression and mood disorder” and “use in social phobia” was sent to Dr. Babiak from Pfizer Medical Affairs.

783. Carolyn Baker, a Baton Rouge neurologist, wrote Neurontin prescriptions that were paid for by BCBSLA from the end of 1996 through 2005. She was regularly detailed on Neurontin, often given samples and beginning in March of 1999, call notes reveal that she was invited to CMEs as well as speakers bureaus, and given sweets. Her prescriptions for Neurontin steadily increased from 1999 through 2002.

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

Exhibit L, CMMS Data

Exhibit L, Sherlock Data

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

Exhibit L, Sherlock S2 Data

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

784. Timothy Best, a Lake Charles neurologist, wrote Neurontin prescriptions that were paid for by BCBSLA from 2001 through 2004. Sales representatives began detailing Dr. Best on Neurontin in the fall of 1999, leaving articles about off-label uses, cookies, and invitations to CME programs and meetings. He was regularly detailed and given samples throughout the four year period, during which time his Neurontin prescriptions for BCBSLA patients increased fourteen fold.

785. Guy Brannon, a Shreveport psychiatrist, wrote Neurontin prescriptions that were paid for by BCBSLA from the end of 1999 through 2004. After a few sales calls in 1998, Dr. Brannon began to write Neurontin prescriptions in 1999 and began to receive regular sales calls that Fall. On September 13, 1999 a Pfizer sales representative discussed the possibility of Dr. Brannon becoming a Neurontin speaker and immediately afterwards, literature on “use in social phobia” was sent to Dr. Brannon from Medical Affairs. Payments from BCBSLA increased fivefold from the initial prescriptions in 1999 before peaking in the Fall of

Id.

Exhibit L, Sherlock S2 Data

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

Id.

Exhibit L, CMMS Data

Exhibit L, Sherlock S2 Data

Exhibit L, Merlin Data

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

2001.

786. Dr. Gregory Brown, a Shreveport psychiatrist, wrote Neurontin prescriptions that were paid for by BCBSLA from 1999 through 2004. Dr. Brown had written two prescriptions in early 1999 before being detailed by a Pfizer sales representative in early October of that year, which coincided with a six-fold increase in his Neurontin prescriptions. After that call, he was detailed monthly for the next year. The most notable of these calls was on December 7 of 1999, when Defendants' sales representative noted that Dr. Brown "Doesn't see the need to use Neurontin now. He says he is having good results with Depakote and believes that anticonvulsants are over used in the psychiatry area. Asked for info on if Neurontin has a mood stabilizing effect." Immediately afterwards, literature on "use in mood disorders" was sent to Dr. Brannon from Medical Affairs. Afterwards, he was detailed ten times for Neurontin in a period of nine months and continued writing prescriptions that were paid for by BCBSLA. The last Neurontin sales call made to this psychiatrist was in October of 2002.

787. Michael Cooper, a Thibodaux family

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana's Objections and Responses to Defendants' First Set of Interrogatories at ¶ 6

Id.

Exhibit L, Sherlock S2 Data

Exhibit L, Merlin Data

Exhibit L, CMMS Data and Exhibit L, Sherlock S2 Data

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana's Objections and Responses to Defendants' First Set of Interrogatories at ¶ 6

Exhibit L, Sherlock S3 Data

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of

practitioner, wrote Neurontin prescriptions that were paid for by BCBSLA from 1999 through 2006. Dr. Cooper was detailed once a year prior to 1999, but beginning in January of 1999 he was visited by a sales representative monthly for nearly two years, during which time he was a regular prescriber of Neurontin for BCBSLA patients. That January of 1999, use of Neurontin for treatment of chronic pain was discussed during a sales call, followed by calls with more discussion of off-label use, with articles sometimes left behind. On February 18, 2000, during a sales call, Dr. Cooper was invited to a pain symposium. Immediately afterwards, literature on “treatment of restless leg syndrome and periodic limb movement disorder of sleep” and “treatment of migraine headaches” was sent to Dr. Cooper from Medical Affairs.

788. Robert Dahmes, a New Orleans psychiatrist, wrote Neurontin prescriptions that were paid for by BCBSLA from 1999 through 2004. He was heavily detailed, no less than fifty times from January of 1999 to October of 2000. During that time, sales representatives promoted off-label uses,

Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

Exhibit L, Sherlock S2 Data, Exhibit L, CMMS Data

Exhibit L, Sherlock S2 Data

Id.

Exhibit L, Merlin Data

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

Exhibit L, Sherlock S2 Data, Exhibit L, CMMS Data

Exhibit L, Merlin Data

evidenced by their following-up on sales calls with materials from Medical Affairs on March 2, 1999 for “treatment of bipolar depression and mood disorder,” “treatment of movement disorders,” “treatment of anxiety-related illness,” and “treatment of various pain conditions,” followed by “use in anxiety-related disorders” on July 31, 2000.

789. Thomas Donner, a Thibodaux neurosurgeon, wrote Neurontin prescriptions that were paid for by BCBSLA from the last quarter of 1999 through 2004. Dr. Donner received his first sales call in October of 1999 and was again detailed on November 8, 1999 where he was “Left STEPS elderly tolerability study and gummy bears” by a Pfizer sales representative. This coincides with the time in which he began regularly and increasingly prescribing Neurontin to BCBSLA patients.

790. Gerard Dynes, a Baton Rouge neurologist, wrote Neurontin prescriptions that were paid for by BCBSLA from the last quarter of 1999 through 2006. Dr. Dynes received his first sales call in October of 1999 at which time he discussed use of Neurontin for neuropathy and dose. He was again

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Exhibit L, CMMS Data, Exhibit L, Sherlock Data

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

Id.

Exhibit L, Sherlock S2 Data

Id.

Exhibit L, Sherlock S2 Data, Exhibit L, Merlin Data, Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections

visited in November, and then again in December at which time the sales representative left cookies and the NEON study. That Fall he began writing Neurontin prescriptions for BCBSLA patients. Over the next several months he was regularly detailed, invited to a pain symposium, a CME, and dramatically increased his prescriptions. Call notes databases reveal that Dr. Dynes was continually called on by sales representatives from 1999 to 2004.

791. Charles Eberly, a Baton Rouge neurologist, wrote Neurontin prescriptions that were paid for by BCBSLA from the third quarter of 1997 through 2006. Dr. Eberly was an occasional prescriber of Neurontin in the months prior to his first sales call in February of 1998, but along with the monthly details complete with literature on the NEON study, an invitation to a CME, cookies and other gifts, came increasing prescriptions for BCBSLA patients. As late as July 30, 2003 Pfizer representatives discussed off-label Neurontin uses with Dr. Eberly, when he was “Asked about what he uses for prophylactic treatment of migraines. Uses TCAs, CC Blockers, Depakoate and some Neurontin. Send MI on

and Responses to Defendants’ First Set of Interrogatories at ¶ 6

Exhibit L, Sherlock S2 Data, Exhibit L, CMMS Data, Exhibit L, Sherlock S3 Data, Exhibit L, Sherlock S31 Data

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Exhibit L, Wolters Kluwer Data

Exhibit L, Sherlock S2 Data, Exhibit L, Merlin Data, Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

Exhibit L, Sherlock S31 Data

Neurontin for migraines. Quick reminder on Relpax.

Will be at pain symposium.”

792. Kenneth Gaddis, a Thibodaux neurologist, wrote Neurontin prescriptions that were paid for by BCBSLA from the end of 1996 through the beginning of 2006. Dr. Gaddis had been detailed many times and had been prescribing Neurontin for several years, but Defendants’ sales call records show a push beginning in 1998, which correlates with the increasing prescriptions that Dr. Gaddis wrote for BCBSLA patients. Medical Affairs records show that Dr. Gaddis was sent materials on March 24, 1999 for “treatment of various pain conditions,” “treatment of movement disorders,” “treatment of anxiety-related illness,” and “treatment of bipolar depression and mood disorder.” Further evidence of off-label sales efforts can be found in the December 8, 1999 sales note that reveals Dr. Gaddis was “Not using Neurontin for epilepsy. Has not had success using N for restless leg. Will start using it for sundowning syndrome in Alzheimer's patients. Does not use SSRI's but left info on it. Will see about using N for migraines.”

793. William Gladney, a Baton Rouge

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Exhibit L, Sherlock S2 Data, Exhibit L, CMMS Data, Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

Exhibit L, Merlin Data

Exhibit L, Sherlock S2 Data

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of

neurologist, wrote Neurontin prescriptions that were paid for by BCBSLA from 1996 through the beginning of 2006. Dr. Gladney was regularly detailed for Neurontin throughout that time and wrote many prescriptions for Neurontin. It is clear that on several occasions off-label uses were the subject of sales calls. On September 22, 1999, sales call notes reflect discussion of migraine use, and on October 19, 1999 call notes state; “Wants more Neurontin. Told him about sundowning syndrome.” This was at the time that Dr. Gladney was being regularly detailed and was nearing his peak of Neurontin prescriptions for BCBSLA patients. As late as the Spring of 2003, Dr. Gladney was still discussing Neurontin as a treatment for headache with Pfizer sales representatives.

794. Richard Lieux, a Baton Rouge internal medicine physician, wrote Neurontin prescriptions that were paid for by BCBSLA from the end of 1999 through 2004. Dr. Lieux had been detailed only once a year in the two years preceding 1999, when Defendants’ sales calls began picking up in the fall of that year. He was detailed three times that fall and winter, coinciding with BCBSLA’s initial payments

Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

Exhibit L, Sherlock S2 Data

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

Exhibit L, Sherlock S31 Data

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Exhibit L, CMMS Data, Exhibit L, Sherlock S2 Data, Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

for Neurontin prescriptions that he wrote. Off-label sales efforts by sales representatives are evidenced by a February 22, 2000 Medical Affairs record showing the delivery of materials for “treatment of restless leg syndrome and periodic limb movement disorder of sleep” and “treatment of migraine headaches” to Dr. Lieux immediately following a sales call on that day.

Exhibit L, Merlin Data

795. Charles Patout, a Baton Rouge physical medicine and rehabilitation physician, wrote Neurontin prescriptions that were paid for by BCBSLA in 2000. Dr. Patout was a reluctant prescriber, but Pfizer sales representatives were persistent. He was detailed six times before he finally began writing Neurontin prescriptions. On the third sales call, on February 28, 2000 it is recorded that he “Said that he would start trying Neurontin and wanted to stick with the 100 mgs to start out with,” which triggered delivery of materials for “treatment of various pain conditions” from Medical Affairs. But it would take three more sales calls before he began prescribing Neurontin in August of 2000.

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Exhibit L, Merlin Data, Exhibit L, Sherlock S2 Data

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

796. Anil Prasad, a Opelousas neurologist, wrote Neurontin prescriptions that were paid for by

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of

BCBSLA from 1997 through 2004. In February of 1999, Pfizer sales representatives began a series of sales calls to Dr. Prasad that bore fruit in increased Neurontin prescriptions. Off-label promotion is evidenced by Medical Affairs sending materials on “treatment of bipolar depression and mood disorder,” “treatment of movement disorders,” “treatment of various pain conditions,” and “treatment of anxiety-related illness” after a sales call on March 2, 1999. In October of 1999, a sales call included a social phobia article, starting dose study, and an invitation to a NSB meeting. November 1999’s detail included the STEPS study. April and June 2000 details included gifts and an invitation to Branson, Missouri for a family trip.

797. Steven Snatic, a Lafayette neurologist, wrote Neurontin prescriptions that were paid for by BCBSLA from 1996 through 2006. Prior to the highpoint of Dr. Snatic’s Neurontin prescriptions for BCBSLA patients, he was detailed frequently and given off-label materials on several occasions. On March 2, 1999, materials on “treatment of bipolar depression and mood disorder,” “treatment of various

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Exhibit L, Merlin Data

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Exhibit L, Sherlock S31 Data

Exhibit L, Merlin Data

pain conditions,” “treatment of movement disorders,” and “treatment of anxiety-related illness” were ordered. The next month, on April 5, 1999, the same materials were re-ordered from Medical Affairs. Months later, Dr. Snatic was invited to an NSB meeting and a Speakers Bureau. As late as August 12, 2003, Dr. Snatic was being detailed for off-label uses of Neurontin. Call notes from that day state that “Has used Neuro for prophylactic treatment of migraines. Send him data on this.” and Medical Affairs records confirm that two days later, materials for “use in the treatment of migraine headaches” were ordered for Dr. Snatic.

798. Lee Stevens, a Shreveport psychiatrist, wrote Neurontin prescriptions that were paid for by BCBSLA from 1999 through 2003. Dr. Stevens began writing these prescriptions immediately after his first detail, in January 1999, and continued while he was regularly detailed for off-label uses. On September 3, 1999 a sales representative ordered materials on “use in social phobia” after a detail. This was followed by another order for “use in social phobia” as well as “treatment of bipolar depression and mood disorder”

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after a September 21, 1999 detail. Similarly, on October 19, 1999 “treatment of anxiety-related illness” and on March 21 “use in mood disorders” and “treatment of various pain conditions” materials were ordered after details.

799. Sudar Tanga, a Bossier City pain management specialist, wrote Neurontin prescriptions that were paid for by BCBSLA from 2000 through the beginning of 2006. Dr. Tanga’s early details were accompanied by cookies or invitations to programs, but as late as April 13, 2004, during a detail, Dr. Tanga and a Pfizer sales representative discussed speaking opportunities for off-label uses; “Great teleconference. Seven cases studies on where using Neuro and alot come from neuro pain from cancer and radiation or surgery. Explore speaking opp here.”

800. Ronald Taravella, a Baton Rouge psychiatrist, wrote Neurontin prescriptions that were paid for by BCBSLA from late 2001 through 2004. Dr. Taravella was detailed eight times before writing his first Neurontin prescription, in September of 1999. All eleven call records reported for Dr. Taravella indicate that the topic of discussion was “INFO

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Exhibit L, Sherlock S31 Data

Ex. 575, Louisiana Health Service Indemnity Company d/b/a BCBSLA of Louisiana’s Objections and Responses to Defendants’ First Set of Interrogatories at ¶ 6

Exhibit L, Sherlock S3 Data

RE:TX W/NEUR FOR BIPOLAR DISEASE &  
MANIA.”

801. Mark Zielinski, a Baton Rouge psychiatrist, wrote Neurontin prescriptions that were paid for by BCBSLA from 1999 through early 2005.

Dr. Zielinski was detailed once before beginning to write Neurontin prescriptions, and was then regularly detailed for off-label psychiatric uses. On February 22, 1999, soon after a detail, materials on “treatment of bipolar depression and mood disorder” were ordered from medical affairs. This occurred again in October, 1999, not long after a call, in which it is reported that Dr. Zielinski “... Uses some Neurontin for Bipolar Disorder. Showed him the social phobia article. He has signed up for Nov 7 CME program.”

802. Robert Alberts, an Anchorage psychiatrist, wrote Neurontin prescriptions that were paid for by ASEA in 2002. Dr. Alberts was detailed twice before writing Neurontin prescriptions. First in April, then in May of 1999, immediately after which

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Exhibit L, Sherlock S2 Data, Exhibit L, CMMS Data, Exhibit L, Merlin Data

Exhibit M, ASEA/AFSCME Local 52 Health Benefit Trust’s Neurontin Prescription Records

Exhibit L, Sherlock S2 Data, Exhibit L, CMMS Data, Exhibit L, Merlin Data

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<sup>1</sup> ASEA/AFSCME Local 52 Health Benefit Trust’s Objections and Response to Defendants’ First Set of Interrogatories at ¶ 6.

<sup>2</sup> ASEA/AFSCME Local 52 Health Benefit Trust’s Objections and Response to Defendants’ First Set of Interrogatories at ¶ 6.

he was sent materials on “treatment of bipolar depression and mood disorder” from Medical Affairs. In June he began prescribing Neurontin. After his fifth detail, on August 3, 1999, “treatment of bipolar depression and mood disorder” materials were again ordered.

803. Lauri Dahms, a Palmer family practice physician, wrote Neurontin prescriptions that were paid for by ASEA in 2002. Dr. Dahms was detailed once before beginning to prescribe Neurontin. Within weeks of her first prescription, she was being detailed on Neurontin and within yet another week a third detail that resulted in materials from Medical Affairs on “treatment of various pain conditions” and “treatment of bipolar depression and mood disorder” being ordered on May 17, 1999.

Exhibit M, ASEA/AFSCME Local 52 Health Benefit Trust’s Neurontin Prescription Records

Exhibit L, Sherlock S2 Data, Exhibit L, CMMS Data, Exhibit L, Merlin Data

804. Cary Jasper, an Anchorage family practice physician, wrote Neurontin prescriptions that were paid for by ASEA from 2002 through 2004.<sup>1</sup> Shortly after his first prescriptions for Neurontin, Dr. Jasper was detailed on November 14, 1999 and sent materials from Medical Affairs for “treatment of various pain conditions.”

Exhibit M, ASEA/AFSCME Local 52 Health Benefit Trust’s Neurontin Prescription Records

Exhibit L, Sherlock S2 Data, Exhibit L, CMMS Data, Exhibit L, Merlin Data

805. Ramzi Nassar, an Anchorage psychologist, wrote Neurontin prescriptions that were paid for by ASEA from 2002 through 2004.<sup>2</sup> On May 26, 1999, the month before Dr. Nassar began prescribing Neurontin, he was detailed by a sales representative who immediately ordered materials on “treatment of bipolar depression and mood disorder” from Medical Affairs. Once he began writing Neurontin prescriptions in June of 1999, Dr. Nassar was detailed monthly.

Exhibit M, ASEA/AFSCME Local 52 Health Benefit Trust’s Neurontin Prescription Records

Exhibit L, Sherlock S2 Data, Exhibit L, CMMS Data, Exhibit L, Merlin Data

Dated: April 15, 2009

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