United States Court of Appeals
For the First Circuit

No. 11-1595

IN RE: NEURONTIN MARKETING AND SALES PRACTICES LITIGATION

AETNA, INC.,

Plaintiff, Appellant,

v.

PFIZER, INC.; WARNER-LAMBERT COMPANY, LLC,

Defendants, Appellees.

APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

[Hon. Patti B. Saris, U.S. District Judge]

Before

Lynch, Chief Judge,
Souter,[*] Associate Justice,
and Lipez, Circuit Judge.

Peter D. St. Phillip, with whom Richard W. Cohen, Gerald Lawrence, and Lowey Dannenberg Cohen & Hart, P.C. were on brief, for appellant.

Mark S. Cheffo, with whom Katherine A. Armstrong and Skadden, Arps, Slate, Meagher & Flom LLP were on brief, for appellees.

[*] Hon. David H. Souter, Associate Justice (Ret.) of the Supreme Court of the United States, sitting by designation.

April 3, 2013

LYNCH, Chief Judge. In Kaiser Foundation Health Plan, Inc. v. Pfizer, Inc. (Kaiser), Nos. 11-1904, 11-2096 (1st Cir. ____ __, 2013), a related appeal in which we also issue an opinion today, we affirmed a court and jury verdict against Pfizer, Inc. ("Pfizer"), under section 1962 of the Racketeer Influenced and Corrupt Organizations Act (RICO), 18 U.S.C. §§ 1961-68, and a state statute, for fraudulent marketing of off-label uses of its drug Neurontin. The arguments presented in Kaiser and in another related appeal in which we issue an opinion today, Harden Manufacturing Co. v. Pfizer, Inc., No. 11-1806 (1st Cir. ____ __, 2013), on most issues are the same as or parallel to those presented in this appeal, which concerns the claims of Aetna, Inc. ("Aetna") against Pfizer. Many of the arguments made by Pfizer against Aetna in this case were rejected in Kaiser.

This case comes to us on Aetna's appeal from a grant of summary judgment in favor of Pfizer and against Aetna. In the Kaiser case, after trial, Pfizer lost. While the trial record in Kaiser was somewhat larger than the record here, the record on summary judgment in this case was very similar and included much the same expert and other evidence as to causation.

The outcome of this case turns on whether Aetna, a health insurer which makes claims of harm from third-party payments for its insureds' fraudulently induced prescriptions, is so differently situated from Kaiser that summary judgment was correctly entered

against it, thus precluding it from proving its case to a jury. The district court largely distinguished this case from Kaiser's on the basis that Kaiser had much stronger evidence of misrepresentations made directly to Kaiser and reliance by Kaiser on those misrepresentations in its formulary decisions.

We conclude that Aetna presented evidence of causation and damages sufficient to survive summary judgment on its RICO claim, and reverse the dismissal of this claim. We vacate the district court's dismissal of Aetna's claim under the Pennsylvania Insurance Fraud Statute (PIFS), 18 Pa. Cons. Stat. § 4117.

I.

We assume familiarity with the description of this case's procedural history and facts set forth in Kaiser, slip op. at 3-22. On February 1, 2005, Aetna filed a coordinated complaint with Kaiser Foundation Health Plan, Inc. and Kaiser Foundation Hospitals (together, "Kaiser") and Guardian Life Insurance Company of America ("Guardian") in the U.S. District Court of Massachusetts against Pfizer and Warner-Lambert Company (together, "Pfizer"). The coordinated plaintiffs asserted that they had suffered injury from the fraudulent marketing of Neurontin for off-label uses, and alleged violations of, inter alia, RICO and the PIFS. The coordinated complaint was part of a multidistrict litigation ("MDL") which had been consolidated in the District of Massachusetts on November 24, 2004.

On March 2, 2009, Pfizer filed a motion seeking summary judgment on all of the coordinated plaintiffs' pending claims. On January 8, 2010, the district court granted Pfizer's motion in part, dismissing the claims of Guardian and Aetna, but denying summary judgment as to Kaiser's claims. See In re Neurontin Mktg. & Sales Practices Litig. (Neurontin Coordinated SJ), 677 F. Supp. 2d 479, 499 (D. Mass. 2010). The court entered judgment against Guardian and Aetna and in favor of Pfizer on February 9, 2011, and on April 20, 2011, the court denied Aetna's motion to alter or amend judgment and motion for reconsideration. On May 19, 2011, Aetna timely filed a notice of appeal as to the district court's judgment against Aetna and the court's denial of Aetna's motion for reconsideration.

II.

We review a district court's grant of summary judgment de novo, "drawing all reasonable inferences in favor of the non-moving party while ignoring 'conclusory allegations, improbable inferences, and unsupported speculation.'" Sutliffe v. Epping Sch. Dist., 584 F.3d 314, 325 (1st Cir. 2009) (quoting Sullivan v. City of Springfield, 561 F.3d 7, 14 (1st Cir. 2009)). We must reverse a grant of summary judgment if we find that "the nonmovant has 'established a genuine issue of material fact that a reasonable jury could resolve in their favor.'" Rockwood v. SKF USA Inc., 687 F.3d 1, 9 (1st Cir. 2012) (emphasis omitted) (quoting Collins v.

Univ. of N.H., 664 F.3d 8, 19 (1st Cir. 2011)). We assume familiarity with the background facts concerning Neurontin's development and FDA approval described in Kaiser, slip op. at 7-8. These were not disputed at summary judgment. We describe only the facts relevant to Aetna's appeal.

A. Neurontin's Effectiveness for Off-Label Uses

As the district court noted, Aetna presented studies showing that Neurontin was not more effective than a placebo in treating certain off-label indications. These studies included: four clinical studies regarding bipolar disorder, Neurontin Coordinated SJ, 677 F. Supp. 2d at 489; six clinical trials regarding neuropathic pain, id.; four clinical trials regarding nociceptive pain, id. at 490; three studies regarding migraine, id.; and three clinical trials regarding doses above 1800 mg per day, id. at 490-91.

B. Defendants' Marketing of Neurontin for Off-Label Uses

Beginning in late 1995 and early 1996, Parke-Davis, a subsidiary of Warner-Lambert, began marketing Neurontin as an effective treatment for bipolar disorder and other mood disorders, neuropathic and nociceptive pain, migraines and other headaches, and doses above 1800 mg per day, though the FDA had not approved Neurontin for these off-label uses. These marketing efforts continued after Pfizer purchased Parke-Davis in 2000, through at least 2001, and are described in Kaiser, slip op. at 8-9.

As the district court stated, Aetna "presented evidence that Defendants communicated half truths that are actionable under the RICO statute" in conducting this marketing, including by "suppressing negative information while submitting for publication in monographs positive information about off-label indications." Neurontin Coordinated SJ, 677 F. Supp. 2d at 492; see also id. at 495, 498-99. Pfizer does not argue to the contrary on appeal.

C. Defendants' Targeting of Third-Party Payors ("TPPs"), Including Aetna

Defendants' efforts to promote Neurontin, for both on-label and off-label uses, demonstrated their understanding that TPPs, including Aetna, would both play a role in determining demand for Neurontin (by managing access to formularies, or lists of drugs for which TPPs would pay) and ultimately pay for most prescriptions of Neurontin.

In 1993, Parke-Davis listed Aetna as the number four managed care plan it intended to target to encourage the use of Neurontin as an anticonvulsant. In 1994, Parke-Davis commissioned a survey of the pharmacy directors of ten managed care plans, including Aetna. This study concluded that these plans, including Aetna, were unlikely to place formulary restrictions on anticonvulsants. A 1998 Parke-Davis business plan stated that, "[i]n general, formulary access is not an issue for Neurontin so share building programs can be carried out unrestricted." Pfizer prepared a marketing business plan regarding Aetna in 2002 that

noted that Pfizer's "sales representatives have open access to the providers" in Aetna's network. That same year, Pfizer established a Neurontin Outcomes Research Task Force that sought to support the marketing of Neurontin for neuropathic pain and to prepare "for a more vigorous defense of reimbursement" to managed care plans. In 2003, as Neurontin's patent neared expiration, defendants commissioned a study by a market research company of how TPPs would react to a new tablet form of the drug intended to compete with generic forms of the drug. The market research company conducted focus groups with TPP representatives, including representatives from Aetna. Pfizer prepared "HMO Opportunity Reports" for Neurontin that tracked formulary status, projected annual sales and prescriptions, potential profits, and market share for various HMOs, including Aetna. Pfizer also tracked sources of revenue for Neurontin sales; in 2001, Pfizer recorded that 69% of its Neurontin revenues came from TPPs.

D. Aetna's Decision to Pay for Neurontin Prescriptions

Aetna, a large TPP, provides health payment benefits to more than 13 million people across the country. Aetna added Neurontin to its formulary -- a list of drugs it agreed to pay for under its member contracts -- soon after the FDA approved Neurontin in 1993 for use as an add-on therapy in the treatment of epilepsy.

Aetna had a formulary development team comprised of pharmacists who developed clinical reviews of drug classes to

present to Aetna's Pharmacy and Therapeutics Committee ("P & T Committee"). These reviews presented all the clinical information available to Aetna about a drug class, and included all the drugs within a class used for a particular therapeutic purpose. The formulary development team looked at package inserts, drug compendia, and online collections of clinical research, and also met with drug manufacturers to get information that had not been published.

Aetna's P & T Committee met monthly to determine what would be included on formularies, as well as appropriate coverage restrictions on drug classes, by majority vote. The Committee reviewed clinical drug reviews, previous clinical policy bulletins the Committee had issued, and any other formulary documents (such as formulary guides disseminated to doctors). The Committee considered the safety, efficacy, on-labeled indications, and off-label indications of drugs, as well as cost information and the other drugs within a class. To control drug prescriptions, Aetna used formulary controls and mailings to physicians.

Aetna initially decided not to place formulary restrictions on the anticonvulsant drug class, which included Neurontin. In late 2003, however, Aetna decided to manage the class of anticonvulsants because it wanted to encourage the use of first-line monotherapy drugs. Neurontin was moved to "non-preferred" status. That is, Aetna imposed quantity (i.e.,

dose) limits on Neurontin prescriptions in 2004, and step edits (under which other drugs needed to be tried before Neurontin could be prescribed) in 2006. Some other anticonvulsants were moved to non-preferred status at the same time.

Michael Brodeur, the head of formulary development and clinical pharmacy policies at Aetna, had communications with Pfizer and Warner-Lambert, but did not remember any specific communications about Neurontin. Aetna conceded that defendants, in any communications to Aetna about Neurontin, had not made any direct misrepresentations to it, its P & T Committee, or its formulary development team. Before January 2004, Aetna did not manage the drug class which included Neurontin. But Brodeur stated that, had the facts concerning the manufacturers' misleading marketing campaign surfaced earlier, he believed this would have led Aetna to start to manage this drug class at an earlier date.

E. Statistical Evidence of Causation

The summary judgment record included the statistical evidence presented by experts Dr. Meredith Rosenthal, Ph.D., and Dr. Raymond Hartman, Ph.D., that we described in Kaiser, slip op. at 13-16, 19-20. For the reasons stated in Kaiser, that evidence could be found by a reasonable factfinder to show that Pfizer's marketing of Neurontin for off-label indications caused a sharp increase in the number of prescriptions that Aetna paid for or reimbursed.

Dr. Rosenthal, an associate professor of health economics and policy at the Harvard School of Public Health, submitted an expert report in which she used "standard econometric methods" to quantify the impact of defendants' promotional activities on the number of off-label prescriptions of Neurontin written. Dr. Rosenthal's data on promotional spending included defendants' expenditures on detailing and advertising in professional journals. Her database included prescriptions paid for by Aetna, as did Dr. Hartman's.

Dr. Rosenthal's analysis demonstrated that defendants' marketing of Neurontin for the off-label indications of bipolar, neuropathic pain, nociceptive pain, migraine, and doses over 1800 mg per day caused 43 million off-label prescriptions of Neurontin between 1995 and 2004. This total included prescriptions for Neurontin for these uses paid for by Aetna. She concluded that nationally during this period, defendants' off-label marketing caused 99.4% of the Neurontin prescriptions written by psychiatrists for bipolar; 27.9% of the Neurontin prescriptions written by neurologists for migraine; 70.0% of the Neurontin prescriptions for neuropathic pain; 84.7% of the Neurontin prescriptions for nociceptive pain; and 37.5% of the Neurontin prescriptions for doses exceeding 1800 mg per day.

III.

In ruling on defendants' motion for summary judgment, the district court concluded that Aetna had "presented evidence that Defendants communicated half truths that are actionable under the RICO statute," Neurontin Coordinated SJ, 677 F. Supp. 2d at 492, and that plaintiffs "presented sufficient evidence to support [their] RICO claim that Neurontin was ineffective for the off-label indications," so that they sustained injury from paying for off-label prescriptions of Neurontin, id. at 498.

However, the court also determined that:

> There is no evidence in the record that Guardian or Aetna at any point directly relied on Pfizer's "half truths," communicated through its alleged manipulation and withholding of studies that suggested Neurontin's ineffectiveness for off-label indications. Rather, their causation argument is wholly dependent on individualized proof that their members' prescribing physicians relied on defendants' misrepresentations. Because the Court has concluded that the evidence provided in support of this theory, namely the aggregate evidence presented in Dr. Meredith Rosenthal's report, is legally insufficient to effectively segregate damages caused by Defendants' misrepresentations from damages caused by other sources, Guardian and Aetna cannot rely solely on the aggregate evidence to prove causation. Accordingly, the motion for summary judgment with respect to Guardian and Aetna will be allowed.

Id. at 497 (emphasis added) (footnote omitted). The district court determined that "[w]hile each of the Coordinated Plaintiffs can prove through aggregated proof that the fraudulent marketing campaign likely caused them injury, they cannot prove which doctor's prescriptions were caused by Defendants' alleged

fraudulent misrepresentations or omissions and which were not." Id. at 495. Because Aetna did not present proof of its direct reliance upon defendants' misrepresentations,[1] as Kaiser did, the court concluded that Aetna's evidence of but-for causation -- which relied largely on aggregate statistical evidence -- was insufficient as a matter of law. The district court granted defendants' motion for summary judgment as to Guardian and Aetna's claims, including Aetna's claim under the PIFS (though the court did not discuss this claim separately). Id. at 499.

Aetna argues on appeal that the district court erred in rejecting its aggregate evidence of causation and damages under RICO and in requiring Aetna to present stronger evidence of direct misrepresentations and reliance as to its formulary. Aetna also argues that the court erred in dismissing its claim under the PIFS. Defendants respond that the court correctly rejected Aetna's aggregate evidence and PIFS claim, and that Aetna's RICO claim was further doomed by its failure to present evidence of proximate causation or injury.

[1] Aetna argues on appeal that in addition to its aggregate evidence of but-for causation, it presented Brodeur's testimony as to the effect of Pfizer's suppression of negative information about Neurontin's off-label effectiveness on Aetna's decision not to impose restrictions on Neurontin in its formulary. Because we conclude that Aetna's aggregate evidence of but-for causation was sufficient to survive summary judgment, we need not separately consider the adequacy of Brodeur's testimony.

A. RICO: But-For Causation and Aggregate Evidence

The but-for causation question in this case is "whether, absent Pfizer's fraud, [a plaintiff TPP] would have paid for fewer off-label Neurontin prescriptions." Kaiser, slip op. at 24. In Kaiser, we noted "the use of . . . aggregate evidence to show causation under several causes of action" and concluded that there was "no reason to reach a different conclusion for the specific subset of RICO claims based on fraudulent marketing." Id. at 54. We believe the evidence Aetna presented on but-for causation -- that in the absence of Pfizer's alleged fraud, Aetna would have paid for fewer off-label prescriptions of Neurontin -- survives summary judgment.[2] Aetna's evidence of but-for causation included not only aggregate statistical evidence, but circumstantial evidence, such as the increase in off-label prescriptions of Neurontin following the initiation of Pfizer's alleged fraudulent marketing efforts, and the fact that Pfizer embarked on these efforts in order to increase sales of Neurontin for off-label uses. The absence of evidence from individual doctors in this record does not defeat our conclusion that summary judgment was inappropriately

[2] Defendants argue on appeal that "[a]ggregate proof of reliance in these circumstances is impermissible for the additional reason that it represents a back-door attempt to invoke the 'fraud on the market' doctrine, which is limited to the securities context and cannot be applied to Plaintiffs' RICO claims." As we explained in Kaiser, slip op. at 29 n.9, the analogy between the fraud-on-the-market doctrine and the use of aggregate evidence in civil RICO cases is inapt.

granted.[3] It should have been left to a jury to weigh the aggregate and circumstantial evidence of causation presented by Aetna against any failure to present individualized testimony from doctors.

While Aetna did have the burden of "segregat[ing] damages caused by Defendants' misrepresentations from damages caused by other sources," Neurontin Coordinated SJ, 677 F. Supp. 2d at 497, this did not mean that Aetna was required to "prove which doctor's prescriptions were caused by Defendants' alleged fraudulent misrepresentations," id. at 495, as the district court concluded. Quantifying the damages caused by defendants' alleged fraud belongs to the damages phase of Aetna's RICO case, and "[o]n that phase of the case the plaintiff has a more relaxed burden of proof." BCS Servs., Inc. v. Heartwood 88, LLC, 637 F.3d 750, 759 (7th Cir. 2011).

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[3] Defendants argue that Aetna failed to make an adequate showing of but-for causation because it "did not produce a single doctor who claimed to have 'relied on a misrepresentation or omission in prescribing Neurontin for an off-label indication.'" Defs.' Br. at 19 (quoting Neurontin Coordinated SJ, 677 F. Supp. 2d at 495). Aetna's failure to present the form of but-for causation evidence that defendants would have favored does not mean that the evidence Aetna did present was insufficient for a jury to conclude that Aetna showed the needed causation. Moreover, as we noted in Kaiser, slip op. at 50, relying on physicians' individual recollections as to their prescribing decisions might have been an unreliable approach.

B. RICO: Proximate Causation

Pfizer also argues that summary judgment was, in any event, appropriate because there was inadequate evidence of proximate causation. For reasons similar to those we enunciated in Kaiser, we conclude that Aetna made a sufficient showing of proximate causation to withstand summary judgment.

Regarding Pfizer's argument that Aetna, unlike Kaiser, has not shown direct reliance on Pfizer's misrepresentations, direct reliance is not an element of proximate cause in a private RICO claim predicated on mail fraud. See Bridge v. Phoenix Bond & Indem. Co., 128 S. Ct. 2131, 2134 (2008). Moreover, Aetna's aggregate statistical evidence of causation did not rely upon the theory that direct misrepresentations by Pfizer influenced Aetna's management of its formulary. Instead, Dr. Rosenthal demonstrated a causal relationship between Pfizer's alleged fraudulent marketing to doctors and Aetna's payment for off-label prescriptions of Neurontin. Aetna did not have to show direct reliance to establish proximate or but-for causation.

A jury could have found that Aetna, like Kaiser, was "the primary and intended victim[] of the scheme to defraud," id. at 2139, and that the injury suffered was a "foreseeable and natural consequence" of the fraudulent scheme, id. at 2144. Because TPPs ultimately paid for most prescriptions of Neurontin, Pfizer monitored TPPs' management of Neurontin on their formularies, kept

track of sales to TPPs, and targeted TPPs as Neurontin customers, with respect to both on-label and off-label sales of the drug. Defendants particularly monitored sales to Aetna, targeted Aetna as a Neurontin customer, and sought information from Aetna about its formulary management practices and willingness to pay for Neurontin instead of generic gabapentin. Pfizer prepared a marketing business plan targeting Aetna. A reasonable jury could have concluded based on this evidence that Aetna was the intended victim of defendants' fraudulent scheme and that Aetna's economic injury was a "foreseeable and natural consequence" of this scheme. That is so even if the scheme involved making misrepresentations to doctors about Neurontin's off-label effectiveness instead of making those misrepresentations directly to Aetna itself.

The functional tests for proximate cause articulated in Holmes v. Securities Investor Protection Corp., 503 U.S. 258, 269-70 (1992), further favor the conclusion that Aetna made an adequate proximate causation showing. A jury could have ascertained the amount of Aetna's damages based on Dr. Rosenthal's and Dr. Hartman's expert reports; Aetna alone suffered the damages it alleged, so there was no risk of multiple recoveries; and as the party directly injured, Aetna was best placed to act as a private attorney general. Id.

The "individualized decisions made by thousands of physicians who decided to prescribe Neurontin" do not introduce

such attenuation into Aetna's causal theory as to prevent a reasonable jury from finding proximate causation, as defendants contend. A reasonable jury could have concluded, based on the evidence, that defendants' scheme relied upon the expectation that fraudulent off-label marketing to doctors would induce them to act in a foreseeable fashion -- i.e., to write off-label prescriptions for Neurontin that would be paid for by Aetna.

C. RICO: Economic Injury

Defendants argue on appeal that the district court's grant of summary judgment may also be affirmed on the alternate theory, rejected by the district court, that Aetna failed to present evidence of economic injury. Defendants argue that, to establish the economic injury needed to make out its civil RICO claim, Aetna was required to prove that Neurontin was always ineffective for the off-label uses at issue,[4] and that Aetna failed to produce evidence of ineffectiveness at summary judgment. Defendants are incorrect. Aetna presented evidence at summary

[4] Defendants argue that Aetna "expressly disavowed any burden" to prove Neurontin's ineffectiveness, and instead opposed summary judgment based on a purportedly invalid "cheaper alternative" theory of economic injury. That misrepresents Aetna's arguments that it could prove economic injury based either on a "cheaper alternative" theory or on a theory of Neurontin's ineffectiveness. See Coordinated Pls.' Mem. Law in Opp'n to Defs.' Mot. Summ. J. at 18-21 & n.16. Because we conclude that Aetna presented sufficient evidence of Neurontin's ineffectiveness to survive summary judgment, we need not pass on the viability of the "cheaper alternative" theory of injury.

judgment[5] that multiple clinical trials had demonstrated that Neurontin was no more effective than placebo in treating the off-label conditions at issue. A reasonable jury could have found from the evidence on the summary judgment record that Neurontin was ineffective for these uses,[6] as the district court correctly concluded. Neurontin Coordinated SJ, 677 F. Supp. 2d at 498 ("The Court finds that [plaintiffs have] presented sufficient evidence to support [their] RICO claim that Neurontin was ineffective for the off-label indications . . . .").

D. Aetna's PIFS Claim

Coordinated plaintiffs asserted a PIFS claim pursuant to 18 Pa. Cons. Stat. § 4117(a)(2). The district court denied Aetna's PIFS claim without separate discussion. Id. at 499. In light of our holding on the RICO claim, we vacate and leave the matter for further consideration on remand.

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[5] Defendants devote much of their argument on this point to the evidence presented at the trial on Kaiser's claims, and to the district court's findings with respect to Kaiser's state law claim, rather than examining the evidence of ineffectiveness plaintiffs presented at summary judgment. In this case "we review the record as it existed at the time the district court rendered its ruling." Lewis v. City of Boston, 321 F.3d 207, 214 n.7 (1st Cir. 2003). Further, on the fuller trial record, we rejected Pfizer's argument.

[6] Defendants argue that "Aetna had the burden of proving that none of its members derived any benefit from the defendant's drug," but they offer no authority in support of this contention, and it is plainly incorrect. As we noted in Kaiser, slip op. at 57, "due to the placebo effect, some patients would report improvements regardless of whether the drug was scientifically effective for their conditions."

IV.

The judgment of the district court is reversed as to Aetna's RICO claim, and vacated as to Aetna's PIFS claim. We remand for further proceedings consistent with this opinion.