UNITED STATES COURT OF APPEALS
FOR THE SECOND CIRCUIT

August Term, 2009

(Argued: December 8, 2009 Decided: September 10, 2010)

Docket No. 09-0222-cv

UFCW LOCAL 1776 and participating employers health and welfare fund, ERIC TAYAG and MID-WEST NATIONAL LIFE INSURANCE COMPANY OF TENNESSEE, on behalf of themselves and others similarly situated, LOCAL 28 SHEET METAL WORKERS, on behalf of themselves and others similarly situated, SERGEANTS BENEVOLENT ASSOCIATION HEALTH AND WELFARE FUND, on behalf of themselves and others similarly situated,

Plaintiffs-Appellees,

— v.—

ELI LILLY AND COMPANY,

Defendant-Appellant,

TEXAS DEPARTMENT OF STATE HEALTH SERVICES,

Defendant.[*]

B e f o r e:

KATZMANN, LIVINGSTON, and LYNCH, *Circuit Judges*.

---

[*] The Clerk of Court is directed to amend the official caption in this case to conform to the listing of the parties above.

Plaintiffs-appellees brought a putative class action against Eli Lilly, manufacturer of the drug Zyprexa. The putative class asserted a civil RICO violation predicated on mail fraud, conspiracy to violate RICO, violation of state consumer protection laws, common-law fraud, and unjust enrichment based on Lilly's alleged misrepresentations about Zyprexa's efficacy and safety. Lilly seeks review of a certification of a plaintiff class and denial of its motion for summary judgment by the United States District Court for the Eastern District of New York (Jack B. Weinstein, *Judge*).

Reversed and remanded for further proceedings.

SAMUEL ISSACHAROFF, New York, New York; James R. Dugan, Stephen Murray, Jr., Douglas R. Plymale (*on the brief*), Murray Law Firm, New Orleans, Louisiana; Thomas M. Sobol, Lauren G. Barnes, Kristen J. Parker (*on the brief*), Hagens Berman Sobol Shapiro LLP, Cambridge, Massachusetts; Andrea Bierstein (*on the brief*), Hanly Conroy Bierstein Sheridan Fisher & Hayes LLP, New York, New York, *for Plaintiffs-Appellees*.

ROBERT A. LONG (Michael X. Imbroscio, Jonathan L. Marcus, Mark W. Mosier, *on the brief*), Covington & Burling LLP, Washington, D.C.; Nina M. Gussack, Thomas E. Zemaitis, Anthony Vale, Paul V. Avelar (*on the brief*), Pepper Hamilton LLP, Philadelphia, Pennsylvania, *for Defendant-Appellant*.

GERARD E. LYNCH, *Circuit Judge*:

Plaintiffs-appellees ("plaintiffs"), unions and insurers who act as third-party payors

("TPPs") who underwrite the purchase of prescription drugs by their members or insureds, brought this putative class action against Eli Lilly and Company ("Lilly"), manufacturer of the drug Zyprexa, alleging that Lilly had misrepresented Zyprexa's efficacy and side effects to physicians. The putative class is composed of TPPs, such as insurance providers, that paid for Zyprexa prescriptions. Plaintiffs argued that class members were injured in two ways: first, by paying for Zyprexa prescriptions that would not have been issued but for the alleged misrepresentations; and second, by paying a higher price for Zyprexa than would have been charged absent the alleged misrepresentations. The district court certified a class of TPPs under the second theory. This appeal followed.

BACKGROUND

I. Facts

A. Development and Approval of Zyprexa

Zyprexa, the brand name for the drug olanzapine, is a prescription medicine produced by Lilly. The FDA approved Zyprexa for treatment of schizophrenia in 1996, and later approved it for treatment of certain symptoms of bipolar disorder.

The first wave of medications commonly prescribed to treat schizophrenia are known as first-generation antipsychotics ("FGAs"). The FGAs are a group of about ten drugs first used in the 1950s. FGAs often cause significant side effects, such as a movement disorder called tardive dyskinesia, and have limited efficacy. Zyprexa is one

of a small group of medications known as second-generation antipsychotics ("SGAs"). The first SGA, approved by the FDA in 1989, was Clozaril, followed by Risperdal in 1993, and Zyprexa in 1996. After Zyprexa's approval, the FDA approved three additional SGAs: Seroquel in 1997, Geodon in 2001, and Abilify in 2002.

B. Side Effects and Efficacy

Plaintiffs allege that as Zyprexa was developed, Lilly became aware of harmful side effects associated with the drug that it did not disclose to patients once Zyprexa went on the market. Plaintiffs presented evidence to the district court that they argue supports this conclusion. For example, studies performed by Lilly in the early 1990s indicated that Zyprexa was strongly associated with weight gain, with participants in a 1993 study gaining on average 1.5 pounds per week. In a 1995 report prepared for submission to the FDA, Lilly noted that almost thirty percent of the patients in approximately fifty studies of Zyprexa reported significant weight gain.

Plaintiffs also allege that Lilly fraudulently claimed that Zyprexa was more effective than other SGAs on the market. In order to gain FDA approval, drug manufacturers need only show that a drug is more effective than a placebo in treating the indication for which approval is sought; it is not necessary to show superiority to other available drugs. Lilly submitted two studies to the FDA that showed that Zyprexa was better than a placebo in treating schizophrenia. Plaintiffs claim to have presented

evidence demonstrating that Lilly falsely marketed the drug to physicians as not merely effective, but as superior to other available medications for treating schizophrenia.

Prior to its approval of Zyprexa, the FDA recommended that Lilly include information about possible weight gain in the "Precautions" section of Zyprexa's label. Lilly successfully argued that weight gain should be listed instead in the "Adverse Reactions" sections, thus effectively deemphasizing the significance of weight gain as a possible side effect. Shortly after Zyprexa's launch, the FDA sent Lilly a warning letter stating that a teleconference led by Lilly's Research Laboratories Vice President Dr. Gary Tollefson, in which Dr. Tollefson implied that Zyprexa was more effective than other SGAs and had fewer side effects, was "false and misleading." The warning letter singled out as misleading a statement in which Tollefson argued that because the instances of weight gain occurred in many patients with relatively low starting weights, the weight gain was "a therapeutic recovery rather than an adverse event."

Four years later, Lilly sought and received FDA approval for Zyprexa as a treatment for bipolar disorder, and for expanding the contexts in which it could be prescribed to treat schizophrenia. The FDA approved Zyprexa for the treatment of bipolar disorder in early 2000, and for the ongoing maintenance of schizophrenia in October of the same year. As a condition of being approved for maintenance treatment of schizophrenia, the FDA required Lilly to articulate the narrow indications for which

Zyprexa was approved on the drug's label and to list "diabetic coma" under Adverse Reactions.

In early 2000, European regulatory agencies asked Lilly to provide information about Zyprexa's side effects. In May of that year, the FDA asked Lilly to review its studies and summarize information linking Zyprexa to hyperglycemia and diabetes. Confidential internal Lilly documents indicate that Lilly was aware that patients taking Zyprexa had an increased risk of hyperglycemia, although Lilly did not understand the mechanism of the association. Lilly was also aware that patients taking Zyprexa were more likely to gain weight, a problem given the connection between obesity and diabetes. In November 2000, the Malaysian Regulatory Authority requested that Lilly notify Malaysian physicians outlining the increased risk of hyperglycemia associated with Zyprexa.

In 2002, Japan's Ministry of Health and Welfare required Lilly to send an "Emergency Safety Information" letter to physicians in Japan alerting them to the risk of hyperglycemia and diabetic ketoacidosis among Zyprexa users. The Japanese agency also required that Zyprexa's label include instructions to physicians to monitor blood glucose levels. After the warning was included on the label, the number of new patients prescribed Zyprexa dropped by seventy-five percent. The same year, Mexico asked Lilly to change Zyprexa's package inserts regarding hyperglycemia, and Australia required

Zyprexa's label be changed to reflect the increased risk of diabetes.

In 2003, the FDA agreed that Lilly should add pancreatitis as an adverse reaction on Zyprexa's label. That same year, Zyprexa was approved for the treatment of bipolar mania in Canada with a statement specifically warning of increased risk of hyperglycemia, diabetes, and weight gain. European regulators also required that the European label be modified to highlight the risk of diabetes.

In September 2003, the FDA required Lilly and all other SGA manufacturers to add a warning concerning hyperglycemia and diabetes to SGA labels. In May 2005, the FDA required the manufacturers of the SGAs Zyprexa, Risperdal, Seroquel, and Abilify to add a black box warning to their labels concerning the increased risk of death in elderly patients taking those drugs for dementia.

C. Pricing

1. The Market for Prescription Drugs

The market for prescription drugs is quite inelastic, meaning that the price of a medication rarely has significant impact on the demand for that medication. This is particularly true of medications used to treat psychiatric disorders.

The initial price set by a pharmaceutical company is "sticky" in that the price does not respond to market demand. Rather, the price is generally increased over time as a routine matter by the manufacturer. The limited monopolies granted by patents on drugs

and brand loyalty of patients and physicians result in a core group of consumers who will buy a successful drug consistently. Even if negative information is released about a medication, the demand for the drug may go down, but the price generally remains the same. A drug company may even increase the price of a drug when it is expected that negative information will lower the demand, so that the price increase will compensate for the decrease in quantities sold and the overall profits of the company will not fall.

Lilly produced an expert witness before the district court to describe how manufacturers set the price of a new prescription drug. Dr. Eugene M. Kolassa established a set of pricing guidelines that have been widely adopted by drug manufacturers. According to Dr. Kolassa, drug manufacturers consider factors including the following:

1. The existence and price of competitive products and the pricing behavior of the firms that sell them (i.e., how competitor[s] respond to pricing actions).
2. The clinical, economic and social value offered by the medicine, both substantively and in economic terms.
3. Plaintiff population characteristics, such as age, common co-morbidities, and prescription drug coverage.
4. The factors that physicians will likely consider in determining whether to prescribe the medicine, and the degree to which the price may affect that decision.
5. Disease characteristics (e.g., chronic or acute; debilitating or cosmetic).
6. The reimbursement environment – how a product is likely to be reimbursed by payors – and issues in the specific market for the product.
7. Public relations and public policy concerns over pricing.

8. The needs and ability of the manufacturer, including overall corporate strategy, market positioning for future performance, and the availability of internal resources to support its pricing strategy.

Once the price of a new drug entering the market is established, individual transactions are also significantly different than transactions for typical consumer goods. The market for prescription drugs is unusual in that direct exchanges between consumers and producers are rare. An individual patient does not choose what drug to take; she is prescribed a drug by her physician. Nor does the individual patient always pay directly for that drug. Rather, a TPP, such as her insurance provider, often pays some or all of the drug's cost.

TPPs typically pay for a prescribed medication only if the drug is authorized under their formulary, a list of medications approved for payment. The formulary is usually managed by a Pharmacy Benefit Manager ("PBM"). PBMs manage approximately seventy-five percent of all outpatient drug claims. Drugs placed on a formulary are approved by the PBM's Pharmacy and Therapeutics Committee, made up of physicians and clinical pharmacists. PBMs maintain their formulary based upon publicly available clinical information, which is in large part produced and disseminated by the drug manufacturers themselves. TPPs have the right to customize their formulary beyond what the PBMs advise, but in practice TPPs rarely modify the recommendations of their PBMs. On the rare occasions when a TPP customizes its formulary, it generally does so in

consultation with the PBM's Pharmacy and Therapeutics Committee.

As the district court observed, in the market for prescription drugs three sets of price negotiations exist: "(1) retail pharmacies and nonretail providers negotiate with pharmaceutical manufacturers and wholesalers, (2) payors (often through PBMs) negotiate with pharmaceutical manufacturers and wholesalers, and (3) payors negotiate with retail pharmacies and nonretail providers." The negotiations over price, moreover, do not intersect with the therapeutic choice of what drug a patient should take, which is a decision made by a physician with only minimal input by her patient or the TPP. Physicians generally do not take the price of a drug into account when deciding among treatment options, and often do not even know the price of the drugs they prescribe. This is particularly true in the treatment of mental disorders, which is an extremely individualized process. Patients respond to antipsychotic drugs in an individualized manner, and patients with the same disease may respond to the same medication in very different ways. Even similar drugs – SGAs, for example – may have varying levels of success with the same patient. As a result, PBMs are reluctant to exclude antipsychotic drugs from their formularies, or to place financial conditions on their use. For example, state Medicaid plans often exempt antipsychotic drugs from requirements such as preferred drug lists and prior authorization provisions.

2. The Pricing of Zyprexa

At the time of Zyprexa's launch, the only other SGAs approved by the FDA were Clozaril and Risperdal. Clozaril, a very powerful antipsychotic, had serious, even potentially fatal, side effects. Risperdal caused a greater incidence than Zyprexa of so-called "extrapyramidal" side effects, causing symptoms such as muscle tremors, slurred speech, and other movement disorders. When Lilly considered what initial price to set for Zyprexa, it weighed Zyprexa's efficacy and side effects against those of Clozaril and Risperdal and set Zyprexa at a higher price. One doctor who discussed the launch price with Lilly before Zyprexa was put on the market recalled a Lilly senior employee explaining the higher price as "premium drug, premium price," meaning that Zyprexa's high price was justified by its assertedly superior performance as compared to the other antipsychotic drugs then on the market. Lilly set Zyprexa's initial prescription price $77 higher than the cost of either Clozaril or Risperdal.

After Zyprexa's launch, its per-prescription price was increased regularly, which was consistent with internal Lilly policies. Zyprexa's price increased from approximately $188 per prescription in 1996 to $292 in 2003 and $368 in 2006. Other SGAs did not increase their price at a similar rate – by the calculations of one expert witness presented to the district court, the difference between the cost of Zyprexa and that of its three main competitors increased from $77 per prescription in 1996 to $113 in 2003 and $150 in

2006.

D. Marketing and Off-Label Prescriptions

In late 2000, Lilly began marketing Zyprexa to primary-care physicians. This shift was important because previously Zyprexa had been targeted to – and was almost exclusively prescribed by – psychiatrists, who treat patients with severe mental disorders such as schizophrenia and bipolar disorder, the two indications for which Zyprexa was approved. Primary-care physicians, by contrast, treat patients for more common, and often less severe, disorders such as anxiety, depression, and dementia.

Although the FDA approves drugs for treatment of specific diseases, physicians may legally prescribe drugs, in their clinical judgment and discretion, for treatment of other diseases or disorders. This practice is known as "off-label" use. See Buckman Co. v. Plaintiffs' Legal Comm., 531 U.S. 341, 350 (2001). While off-label prescriptions are permitted within a physician's discretion, drug manufacturers are prohibited from promoting off-label uses in marketing a drug. Plaintiffs argue that Lilly shifted its marketing efforts to primary-care physicians with the intention of marketing off-label prescriptions of Zyprexa for such conditions as anxiety, depression, and dementia.

Lilly's marketing campaign targeting primary-care physicians was known as "Viva Zyprexa." Lilly internally announced "Viva Zyprexa" in March 2001. The campaign focused on prescribing Zyprexa to treat isolated symptoms not tied to a clinical diagnosis,

rather than treatment of the specific conditions – bipolar disorder and schizophrenia – for which Zyprexa had been approved by the FDA. For example, Lilly created profiles of hypothetical patients as examples of patients who could be treated with Zyprexa. One such hypothetical patient was Donna, "a single mom in her mid-30s appearing in your office in drab clothing and seeming somewhat ill at ease. Her chief complaint is that she feels anxious and irritable." Lilly suggested that sales representatives say that "when we look at efficacy in a patient like Donna, Zyprexa has been shown to improve mood, anxiety levels, and disrupted sleep patterns. . . . [W]hat Zyprexa will mean to a patient like Donna is that she will have less anxiety, less irritability and be able to sleep better." Notably, the materials do not state that Donna was diagnosed with bipolar disorder or schizophrenia, the two conditions that the FDA approved Zyprexa to treat.

Another hypothetical patient, "Martha," posited residents of nursing homes as ideal candidates for Zyprexa prescriptions. Lilly assigned 280 representatives to a "long-term care" sales force aimed at "driv[ing] the nursing home business." Internal documents stated that Lilly's number one strategy was to "establish Zyprexa as a first line choice in the treatment of the elderly patient who are *[sic]* experiencing behavior or cognitive symptoms." Lilly pursued this market, suggesting Zyprexa as beneficial for patients suffering from dementia, even though no evidence existed that Zyprexa was an effective treatment for dementia and Zyprexa had detrimental effects on the cognitive

functioning of patients with Alzheimer's.

Lilly also distributed a "Mood Disorder Questionnaire" ("MDQ") to primary-care physicians. The questionnaire asked a series of yes or no questions resulting in a positive or negative screen. Although screening tests are not diagnostic instruments and do not suggest treatment, and the MDQ was not sensitive enough to diagnose bipolar disorder (much less the limited types of bipolar disorder for which Zyprexa was approved), the MDQ became a significant source of Zyprexa prescriptions.

By 2002, almost two-thirds of Zyprexa prescriptions for bipolar disorder were for off-label uses. It is unlikely that TPPs paying for prescriptions were aware of the increased rate of off-label prescriptions at the time, as PBMs generally do not track off-label prescriptions of a drug. Such tracking is only possible if the drug is subject to a prior authorization program; such programs are in place for fewer than two percent of prescriptions (and are not common with respect to antipsychotic medication).

E. Sales

After the label change in September 2003, consumption of Zyprexa decreased. The peak of Zyprexa prescriptions occurred in 2003, when 11.092 million prescriptions were issued. In 2004, the number of Zyprexa prescriptions fell to 9.765 million, and prescriptions in 2006 were projected to fall still further to 6.901 million. A 2008 New York Times article stated that prescriptions of Zyprexa decreased fifty percent between

2003 and 2008. Plaintiffs offered evidence to show that the decline in Zyprexa prescriptions corresponds "almost entirely" to a drop in off-label prescriptions, leaving only the prescriptions for the approved indications.

II. Procedural Posture

On June 20, 2005, Mid-West National Life Insurance Company of Tennessee filed a putative class action against Lilly. Similar suits were brought by other TPPs and individuals in the following months. The plaintiffs ultimately brought five claims in a consolidated amended complaint: a civil RICO claim predicated on mail fraud, conspiracy to violate RICO, violation of state consumer protection laws, common-law fraud, and unjust enrichment. These claims were based on the plaintiffs' contention that Lilly made false statements and omitted material information concerning the safety and efficacy of Zyprexa. The plaintiffs asserted that Lilly withheld information concerning the risk of weight gain, hyperglycemia, and diabetes among people taking Zyprexa, and produced and disseminated false information minimizing or even denying those risks. The plaintiffs also argued that Lilly falsely claimed that Zyprexa was more effective than other available antipsychotics, and promoted off-label prescriptions for Zyprexa to treat conditions such as depression, anxiety, and dementia, for which there was no evidence that Zyprexa provided any effective treatment. These misrepresentations, the plaintiffs argued, resulted in a higher price and greater demand for Zyprexa than would have

existed had accurate information about Zyprexa's efficacy and risks been known.

The plaintiffs offered two theories of damages. First, the "quantity effect" theory posited that improper promotion of off-label use for Zyprexa resulted in more off-label prescriptions for Zyprexa than would otherwise have been written. The TPPs thus were harmed by paying for Zyprexa that would not have been prescribed but for Lilly's marketing efforts promoting Zyprexa as a treatment for conditions other than those for which Zyprexa had been approved by the FDA. Second, under the "loss-of-value" or "excess price" theory, the claimed harm was the monetary difference between what the plaintiff class was allegedly led to believe Zyprexa was worth and the actual economic value of Zyprexa, taking into account the lesser efficacy and greater harmful side effects allegedly hidden or misrepresented by Lilly. Dr. Meredith Rosenthal, plaintiffs' expert witness, estimated the damages under this excess price theory for the putative class period September 1, 1996 to December 31, 2006 as between $4 billion and $7.7 billion. Dr. Jeffrey E. Harris, another expert witness for the plaintiffs, estimated damages from both theories as approximately $5 billion.

Plaintiffs sought to certify a class to recover the value of their overpayments. They proposed one class – the Purchase Claim Plaintiff Class – comprising two subclasses: the Third-Party Payor Subclass and the Consumer or Direct Payor Subclass. The two subclasses could then be further subdivided based on off-label or "on-label" purchases.

Plaintiffs defined the proposed class as:

> All individuals and entities in the United States and its territories who, for purposes other than resale, purchased, reimbursed, and/or paid for Zyprexa during the period from September 1996 through the present. For purposes of the Class definition, individuals and entities "purchased" Zyprexa if they paid for some or all of the purchase price.

The Third-Party Payor Subclass was defined as:

> All private, non-government entities in the United States and its territories that are at risk, pursuant to a contract, policy, or plan, to pay or reimburse all or part of the cost of Zyprexa prescribed, provided, or administered to natural persons covered by such contract, policy, or plan during the period from January 1, 1996 to the present.

Lilly moved for summary judgment on the ground that plaintiffs could not satisfy the elements of any of their claims. Specifically, Lilly argued that plaintiffs' reliance on aggregate proof of reliance, rather than individualized proof, was impermissible, and that the plaintiffs could not show a sufficient causal link between Lilly's actions and the alleged overpricing harm.

The district court, addressing only plaintiffs' excess price theory, denied Lilly's motion for summary judgment on June 28, 2007. The court concluded that the "broad-based" nature of Lilly's alleged scheme, and Lilly's ability to "distort[] the general body of knowledge about Zyprexa," made aggregate proof of reliance permissible. The court also found triable issues of fact relating to causation because Lilly's allegedly false

representations and material omissions could have increased the price of and demand for Zyprexa by leading "doctors to continue to prescribe, and plaintiffs to continue to pay for, greater amounts . . . than they would have absent the fraud," ultimately resulting in additional costs to plaintiffs.

The district court held a hearing in early 2008 on plaintiffs' motion to certify a class. On September 5, 2008, the court certified a class of TPPs on the RICO claims predicated on the overpricing theory of damages, but refused to certify a class of individual payors or to certify a class as to the state consumer protection claims. The district court limited the class period from June 20, 2001 to June 20, 2005.

The court concluded that the proposed TPP class presented common questions of law and fact because "[t]he only difference among class third-party payors is how much of the total overcharge each shall receive in damages." The court first addressed whether the losses suffered by the class could be established with sufficient precision. The court concluded that

> Assuming fraud leading to a price differential has been established, damages may be estimated based on the difference between what was paid for Zyprexa and the actual value of the product. The computation requires (i) estimating the total out-of-pocket expenditures for the class members and (ii) using well-accepted techniques in applied economics to determine the actual value or appropriate launch price (plus minor increases) of Zyprexa.

The district court also found that reliance could be proven for the class because the

alleged fraud was "directed through mailings and otherwise at doctors who relied, causing damages in overpayments by plaintiffs." This, the district court concluded, could appropriately be shown by generalized proof, in contrast to the more abstract "fraud on the market" theory rejected in McLaughlin v. Am. Tobacco Co., 522 F.3d 215 (2d Cir. 2008).

After approving the plaintiff class, the district court certified its order denying summary judgment under 28 U.S.C. 1292(b), and Lilly moved for leave to appeal. Lilly also moved under Federal Rule of Civil Procedure 23(f) for leave to appeal the district court's order certifying the class. This Court granted Lilly's petition, and this appeal followed.

DISCUSSION

I. Standard of Review

We review denial of summary judgment de novo. See Tasini v. N.Y. Times Co., 206 F.3d 161, 165 (2d Cir. 2000). We review the district court's decision to certify a class for abuse of discretion. See Parker v. Time Warner Entm't Co., 331 F.3d 13, 18 (2d Cir. 2003). To the extent that the district court's decision as to class certification is premised on a finding of fact, we review that finding for clear error. See In re Initial Pub. Offerings Sec. Litig., 471 F.3d 24, 40-41 (2d Cir. 2006).

II. Class Certification

Under Rule 23(b)(3), Fed. R. Civ. P., "[a] class action may be maintained if Rule 23(a) is satisfied and if . . . the court finds that the questions of law or fact common to class members predominate over any questions affecting only individual members," and that a class action is superior to other methods of adjudication for fairness and efficiency. The parties agree that the requirements of Rule 23(a) are satisfied,[1] but dispute whether common questions "predominate." "Class-wide issues predominate if resolution of some of the legal or factual questions that qualify each class member's case as a genuine controversy can be achieved through generalized proof, and if these particular issues are more substantial than the issues subject only to individualized proof." Moore v. PaineWebber, Inc., 306 F.3d 1247, 1252 (2d Cir. 2002). To determine whether the proposed TPP class was properly certified, therefore, we must consider whether substantial elements of its claim against Lilly may be established by generalized, rather than individualized, proof.

We first briefly outline the substance of plaintiffs' claims against Lilly. The putative class of TPPs alleges that in the course of promoting off-label prescriptions of

[1] Under Rule 23(a), a proposed class must (1) be "so numerous that joinder of all members is impracticable," (2) present "questions of law or fact common to the class," (3) be represented by parties whose claims or defenses are "typical to the claims or defenses of the class," and (4) be represented by parties who "will fairly and adequately protect the interests of the class." See Fed. R. Civ. P. 23(a).

Zyprexa, Lilly engaged in mail and wire fraud by deliberately misrepresenting the drug's safety and efficacy. Plaintiffs claim that Lilly thereby conducted a racketeering enterprise, which they called "the Off-Label Promotion Enterprise," in violation of RICO. There is no real dispute that whether or not the substance of that claim is true, it is a unitary claim that is common to the putative class.

In order to recover damages under RICO, however, a plaintiff must show "(1) a substantive RICO violation under § 1962; (2) injury to the plaintiff's business or property, and (3) that such injury was by reason of the substantive RICO violation." City of New York v. Smokes-Spirits.com, Inc., 541 F.3d 425, 439 (2d Cir. 2008), overruled on other grounds by Hemi Group, LLC v. City of New York, 130 S. Ct. 983 (2010) (internal quotation marks omitted) (holding that City's asserted injury – inability to collect taxes due to failure by out-of-state cigarette sellers to file records with state officials as required by federal law – did not give rise to RICO claim because injury was not caused by reason of allegedly fraudulent conduct). Plaintiffs argue that Lilly injured them because (1) they paid for Zyprexa prescriptions that would not have been written absent the fraud (the quantity effect theory) and (2) they paid too much for Zyprexa prescriptions because Lilly relied upon the fraud to set an excessively high price (the excess price theory). While there is no dispute that the existence of a RICO violation is a question common to all class members, Lilly disputes that the second and third elements required to recover

damages – proof of an injury and proof that such injury was by reason of the RICO violation – are common to the proposed class.

In order to pursue their claims as a class rather than as individual plaintiffs, the putative class must be able to prove its theory of injury through generalized proof. Here, the district court found that the plaintiff class could appropriately use generalized proof to show that Zyprexa was overpriced as a result of Lilly's "excessive claims of utility as well as disavowal of adverse secondary effects" of Zyprexa.

To show injury by reason of a RICO violation, a plaintiff must demonstrate that the violation caused his injury in two senses. First, he must show that the RICO violation was the proximate cause of his injury, meaning "there was a direct relationship between the plaintiff's injury and the defendant's injurious conduct." First Nationwide Bank v. Gelt Funding Corp., 27 F.3d 763, 769 (2d Cir. 1994). Second, he must show that the RICO violation was the but-for (or transactional) cause of his injury, meaning that but for the RICO violation, he would not have been injured. See Holmes v. Sec. Investor Prot. Corp., 503 U.S. 258, 268 (1992).

Until recently, this Court required a RICO plaintiff asserting predicate acts of fraud to show first-person reliance – "that he relied on the defendant's misrepresentation" – in order to demonstrate but-for causation. McLaughlin, 522 F.3d at 222. In Bridge v. Phoenix Bond & Indemnity Co., however, the Supreme Court held that a plaintiff alleging a RICO mail fraud is not required to show first-person reliance. 128 S. Ct. 2131, 2134

(2008). The Court rejected reliance as an element of the RICO fraud claim, either to show but-for causation or to establish a direct relationship between the defendant's conduct and the plaintiff's injury sufficient to demonstrate proximate causation. Id. at 2144. The Court explained further:

> Of course, none of this is to say that a RICO plaintiff who alleges injury "by reason of" a pattern of mail fraud can prevail without showing that *someone* relied on the defendant's misrepresentations. In most cases, the plaintiff will not be able to establish even but-for causation if no one relied on the misrepresentation. . . .
>
> Accordingly, it may well be that a RICO plaintiff alleging injury by reason of a pattern of mail fraud must establish at least third-party reliance in order to prove causation. "But the fact that proof of reliance is often used to prove an element of the plaintiff's cause of action, such as the element of causation, does not transform reliance itself into an element of the cause of action." . . . Proof that the plaintiff relied on the defendant's misrepresentations may in some cases be sufficient to establish proximate cause, but there is no sound reason to conclude that such proof is always necessary.

Id., quoting Anza v. Ideal Steel Supply Corp., 547 U.S. 451, 478 (2006) (Thomas, J., concurring in part and dissenting in part) (internal citation omitted).

Plaintiffs argue that there is therefore *no* reliance requirement under RICO. We recently addressed whether RICO requires a showing of reliance by any party:

> [T]he Supreme Court noted that "it may well be that a RICO plaintiff alleging injury by reason of a pattern of mail fraud must establish at least third-party reliance in order to prove causation," and that there may be situations where the "complete absence of reliance may prevent the plaintiff from establishing proximate cause." Here, there is no question that the City has alleged third-party reliance . . . .

> Thus, as we find that the City has adequately alleged proximate cause and third-party reliance, we need not address the question of whether an allegation of proximate cause fails where there are absolutely no allegations of reliance.

Smokes-Spirits.com, 541 F.3d at 444 n.24, quoting Phoenix Bond & Indem. Co., 128 S. Ct. at 2144-45 (internal citation omitted). We find ourselves in a similar position here: while reliance may not be an element of the cause of action, there is no question that in this case the plaintiffs allege, and must prove, third-party reliance as part of their chain of causation. Plaintiffs allege an injury that is caused by physicians relying on Lilly's misrepresentations and prescribing Zyprexa accordingly. Because reliance is a necessary part of the causation theory advanced by the plaintiffs, we must ask whether reliance can be shown by generalized proof.

A. Excess Price Theory

The district court granted class certification on the theory that plaintiffs could use generalized proof to show that Zyprexa was overpriced as a result of Lilly's "excessive claims of utility" and "disavowal of [the drug's] adverse secondary effects." Because we conclude that plaintiffs' excess price theory is not susceptible to generalized proof with respect to either but-for or proximate causation, class certification based on this theory was an abuse of discretion.

1. But-for Causation

Two years ago, we held that reliance on a misrepresentation made as part of a nationwide marketing strategy "cannot be the subject of general proof." McLaughlin, 522 F.3d at 223. In McLaughlin, the alleged misrepresentation arose from the marketing of light cigarettes as healthier than full-flavored cigarettes. We concluded that because each individual consumer might have purchased light cigarettes for any number of reasons other than the purported health claim, individualized proof was necessary to show the causal link between the misrepresentation that light cigarettes were healthier and the injury to the consumers who smoked light cigarettes and suffered the same ill health effects as if they had smoked regular cigarettes. Id.

McLaughlin also rejected the theory that the cigarette manufacturers "distorted the body of public information" as a whole. Id. at 223-24. In advancing this theory, the McLaughlin plaintiffs invoked the fraud-on-the-market presumption established in the context of the securities market. Because misrepresentations by securities issuers affect the price of those securities when they are traded on the open market, and because investors view the market price of securities as an accurate measure of value, investor reliance upon public misrepresentations by securities issuers is presumed. McLaughlin refused to extend this presumption into the consumer market for cigarettes, explaining that the market for consumer goods "is anything but efficient," as demonstrated by the fact that publication of monographs explaining that light cigarettes were no healthier than

regular cigarettes "produced no change in either the sales or the price" of light cigarettes. Id. at 224.

The district court believed that McLaughlin was distinguishable from the present case and that here "the evidence supports a finding of an overcharge based on the fraud on doctors, third-party payors, and others." In re Zyprexa Prods. Liab. Litig., 253 F.R.D. 69, 194 (E.D.N.Y. 2008). "The fraud was directed to prescribing doctors. The overpayments were made by third-party . . . payors." Id. at 191.

However, the evidence in the record, as discussed above, supports the conclusion that prescribing doctors do not generally consider the price of a medication when deciding what to prescribe for an individual patient. Any reliance by doctors on misrepresentations as to the efficacy and side effects of a drug, therefore, was not a but-for cause of the price that TPPs ultimately paid for each prescription.

2. Proximate Causation

Even assuming but-for causation, plaintiff's theory of liability does not permit proximate cause to be shown by generalized proof. The TPP plaintiffs, who unlike the doctors were in a position to negotiate the prices of drugs in their formularies, paid the full price set by Lilly. The TPP plaintiffs draw a chain of causation in which Lilly distributes misinformation about Zyprexa, physicians rely upon that misinformation and prescribe Zyprexa for their patients, and then the TPPs overpay. This narrative skips

several steps and obscures the more attenuated link between the alleged misrepresentations made to doctors and the ultimate injury to the TPPs. In fact, if plaintiffs' factual allegations are correct, the chain of causation runs as follows: Lilly distributes misinformation about Zyprexa, physicians rely upon the misinformation and prescribe Zyprexa, TPPs relying on the advice of PBMs and their Pharmacy and Therapeutics Committees place Zyprexa on their formularies as approved drugs, TPPs fail to negotiate the price of Zyprexa below the level set by Lilly, and TPPs overpay for Zyprexa. Thus, in this case "the conduct directly causing the harm was distinct from the conduct giving rise to the fraud." Hemi Group, 130 S. Ct. at 990. Plaintiffs' "theory of liability rests on the independent actions of third and even fourth parties," id. at 992, as physicians, PBMs, and PBM Pharmacy and Therapeutics Committees all play a role in the chain between Lilly and TPPs.

Crucially, the TPPs do not allege that *they* relied on Lilly's misrepresentations – the misrepresentations at issue were "directed through mailings and otherwise at doctors." In re Zyprexa, 253 F.R.D. at 193. Because only the TPPs were in a position to negotiate the price paid for Zyprexa, however, the only reliance that might show proximate causation with respect to price is reliance by the TPPs, not reliance by the doctors.

Furthermore, the failure of most TPPs to negotiate Zyprexa's price demonstrates why generalized proof cannot show proximate causation in this context. There is

evidence that at various times, individual TPPs began to request rebates from Lilly or restrict usage of Zyprexa for some indications. Even after the side effects of Zyprexa became publicly known, however, most TPPs continued to pay the full price when Zyprexa was prescribed to treat symptoms of schizophrenia, even as payment for other indications were limited. Because these varying actions prompt questions about why certain TPPs negotiated Zyprexa's price where others didn't, and why approval of Zyprexa for some indications was limited by some TPPs, generalized proof of reliance by doctors cannot complete the causation chain.[2] The district court's certification of the plaintiff class was thus in error.

B. Quantity Effect Theory

Alternatively, plaintiffs seek to resurrect the quantity effect theory of injury. Plaintiffs themselves appear to have abandoned this theory before the district court as a basis for class certification, recognizing the unworkable complexity of joining as a single class of plaintiffs some individuals who they argue should never have been prescribed Zyprexa and some individuals who they argue were properly prescribed Zyprexa, but paid too much for it. At a hearing before the district court, plaintiffs stated that they did "not

[2] There is also a question whether individual TPPs offer different benefits or cover populations of patients with salient characteristics that could impact injury or damages or that might allow aggregate proof of an individual TPP's patients and prescriptions. The district court did not analyze any such data, so we express no view as to whether such differences further undermine the ability of the TPPs to establish either injury or reliance by generalized proof.

seek to get all of the money back for the people who otherwise would not have bought the product." Accordingly, the district court certified a class of TPPs seeking only damages for overpayments, and not for excess prescriptions.

Even if plaintiffs had not abandoned reliance on the quantity effect theory, however, that theory suffers from many of the same faults as the excess price theory. An examination of plaintiffs' theory of causation makes this apparent. Dr. Harris, plaintiffs' expert, estimated damages under the quantity effect theory by assuming that the decline in the number of Zyprexa prescriptions following the label change and "Dear Doctor" letter in 2003 and 2004 was due almost entirely to a decrease in the number of off-label Zyprexa prescriptions. Dr. Harris then assumed that, but for Lilly's alleged misrepresentations, sales of Zyprexa would never have risen above the number of sales in 2006, after more accurate information about Zyprexa's side effects became public. Dr. Harris thus postulated that every prescription above the number of prescriptions written in 2006 was an "excess" prescription, and plaintiffs should recover the full cost of every excess prescription.

Having removed the variable of price, the chain of causation is in one sense simpler: TPPs place Zyprexa on their formularies as approved drugs, Lilly distributes misinformation about Zyprexa, physicians rely upon the misinformation and prescribe Zyprexa, and TPPs pay for too many Zyprexa prescriptions.

The nature of prescriptions, however, means that this theory of causation is interrupted by the independent actions of prescribing physicians, which thwarts any attempt to show proximate cause through generalized proof. Plaintiffs argue that "the ultimate source for the information on which doctors based their prescribing decisions was Lilly and its consistent, pervasive marketing plan." Lilly was not, however, the *only* source of information on which doctors based prescribing decisions. An individual patient's diagnosis, past and current medications being taken by the patient, the physician's own experience with prescribing Zyprexa, and the physician's knowledge regarding the side effects of Zyprexa are all considerations that would have been taken into account in addition to the alleged misrepresentations distributed by Lilly.

Furthermore, additional variables interfere further with plaintiffs' theory of causation. As the district court noted, the evidence showed that at least some doctors were not misled by Lilly's alleged misrepresentations, and thus would not have written "excess" prescriptions as identified by the plaintiffs. This makes general proof of but-for causation impossible.

In addition, showing injury by general proof is precluded by uncertainty about what the alternatives to an "excess" prescription would have been, and how they would have been distributed amongst the plaintiffs. Dr. Harris limits his definition of excess prescriptions to off-label prescriptions, and seems to imply that the alternative to an off-

label prescription is no prescription at all. But, as plaintiffs argue, Lilly promoted Zyprexa as treatment for disorders such as anxiety, depression, and dementia. Plaintiffs have not presented any evidence to show that, had Zyprexa not been prescribed, *no* medication would have been prescribed, nor that possible alternatives, such as antidepressants, would have been less expensive than Zyprexa. Similarly, each TPP and its PBM had to approve Zyprexa's placement on a formulary. Even now, TPPs pay for Zyprexa and for the most part have not implemented close control or review of Zyprexa prescriptions. Each TPP, moreover, covers a different group of insured patients. Given the patterns of off-label Zyprexa prescriptions, it seems likely that individual TPPs paid for different numbers of off-label prescriptions. For example, plaintiffs presented evidence that Lilly specifically targeted elderly patients suffering from dementia as candidates for Zyprexa. The average age of the population served by an individual TPP, therefore, would have strong bearing on the damages incurred.

All of these variables show that the quantity effect theory is no more demonstrable with generalized proof than the excess price theory. Plaintiffs cannot use generalized proof when individual physicians prescribing Zyprexa may have relied on Lilly's alleged misrepresentations to different degrees, or not at all, when some excess prescriptions may not have actually caused loss, given the likelihood of substitute prescriptions for other drugs, and when different TPPs may have paid for different "excess" quantities of

prescriptions. See Hemi Group, 130 S. Ct. at 992; McLaughlin, 522 F.3d at 226. We therefore decline to affirm class certification based on the quantity effect theory.

III. Summary Judgment

Before the district court certified the class, it denied Lilly's motion for summary judgment dismissing the complaint. In denying summary judgment, the district court cited Schwab v. Philip Morris USA, Inc., 449 F. Supp. 2d 992 (E.D.N.Y. 2006), which was overturned by McLaughlin, upon which much of our analysis above rests. The district court acknowledged, when certifying the denial of summary judgment along with the class certification for interlocutory appeal, that "[r]ecent appellate decisions may call into question some aspects of the decision." This is plainly true: Schwab was a class action alleging that Philip Morris misrepresented light cigarettes as less harmful than other cigarettes and thus charged an artificially inflated price for light cigarettes. McLaughlin reversed, holding that reliance on the misrepresentation could not be shown by general proof and decertifying the class. 522 F.3d at 222-24, 234.

The district court denied Lilly's motion for summary judgment on the understanding that "[b]oiled down, this is an overpricing claim." After Hemi Group, it is clear that plaintiffs' overpricing theory is too attenuated to "meet RICO's requirement of a direct causal connection between the predicate offense and the alleged harm." 130 S. Ct. at 990 (internal quotation marks omitted). The quantity effect theory, however, is less

attenuated, and while that theory cannot support class certification, it is not clear that the theory is not viable with respect to individual claims by some TPPs or other purchasers. Because the district court did not consider individual claims under the quantity effect theory when it ruled on Lilly's motion for summary judgment, we decline to consider whether summary judgment with respect to the quantity effect theory is appropriate in the first instance. We therefore vacate the denial of summary judgment insofar as the district court failed to grant summary judgment on the pricing theory, and remand for further proceedings, including possible further consideration of summary judgment, with respect to plaintiffs' quantity effect theory.

CONCLUSION

For the foregoing reasons, we REVERSE the class certification order, we VACATE the order denying Lilly's motion for summary judgment with respect to plaintiffs' overpricing claims, and we REMAND for further proceedings not inconsistent with this opinion.