UNITED STATES COURT OF APPEALS
FOR THE SECOND CIRCUIT

August Term 2014

(Argued: June 25, 2015 Decided: November 13, 2015)

No. 14-2318-cv

SERGEANTS BENEVOLENT ASSOCIATION HEALTH AND WELFARE FUND, NEW ENGLAND CARPENTERS HEALTH BENEFITS FUND, ALLIED SERVICES DIVISION WELFARE FUND,
Plaintiffs-Appellants,

STATE OF LOUISIANA, CITIZENS OF THE STATE OF LOUISIANA, LOUISIANA DEPARTMENT OF HEALTH AND HOSPITAL, AND ON BEHALF OF ALL OTHERS SIMILARLY SITUATED, CHARLES C. FOTI, JR., IN HIS OFFICIAL CAPACITY AS THE ATTORNEY GENERAL FOR THE STATE OF LOUISIANA AS PARENS PATRIAE ON BEHALF OF,
Plaintiffs,

-v.-

SANOFI-AVENTIS U.S. LLP, SANOFI-AVENTIS U.S., INC.,
Defendants-Appellees.

Before: CABRANES, LIVINGSTON, and DRONEY, *Circuit Judges*.

Appeal from the March 30, 2011 and May 12, 2014 orders of the United States District Court for the Eastern District of New York (Sandra L. Townes, *Judge*) denying Plaintiffs-Appellants' motion to certify a proposed class and

granting Defendants-Appellees' motion for summary judgment. Plaintiffs sought to certify a class of health insurance plans that paid for prescriptions of Defendants' antibiotic drug Ketek, arguing that Defendants violated the Racketeer Influenced and Corrupt Organizations Act, 18 U.S.C. § 1961 *et seq.*, by making misrepresentations that underplayed Ketek's safety risks. Relying on our decision in *UFCW Local 1776 v. Eli Lilly & Co.*, 620 F.3d 121 (2d Cir. 2010), the district court denied class certification, and later granted summary judgment to Defendants, on the ground that Plaintiffs could not prove causation by generalized evidence. We agree that, because Plaintiffs cannot show causation by generalized evidence and have offered no individualized evidence, Plaintiffs' claims may not be litigated as a class action, and Defendants were entitled to summary judgment on Plaintiffs' individual claims. Accordingly, we AFFIRM the orders and the judgment below.

THOMAS SOBOL (Lauren Barnes and Jessica R. MacAuley, *on the brief*), Hagens Berman Sobol Shapiro, LLP, Cambridge, MA, *for Plaintiffs-Appellees*.

WILLIAM N. WITHROW JR. (Lindsey B. Mann and J. Nick Phillips, *on the brief*), Troutman Sanders LLP, Atlanta, GA, *for Defendants-Appellees*.

DEBRA ANN LIVINGSTON, *Circuit Judge*:

Plaintiffs-Appellants are three health-benefit plans ("HBPs") that brought suit under the Racketeer Influenced and Corrupt Organizations Act, 18 U.S.C. § 1961 *et seq.* ("RICO"), and various state laws, claiming that Defendants-Appellees sanofi-aventis U.S. LLP and sanofi-aventis U.S., Inc. (collectively,

"Aventis") engaged in a pattern of mail fraud by failing to disclose the true risks of the antibiotic drug telithromycin, marketed as "Ketek." Plaintiffs sought to certify a class of all HBPs that paid for Ketek prescriptions on the theory that such HBPs were injured as a result of paying for Ketek prescriptions that would not have been written if Aventis had not concealed Ketek's safety risks. The United States District Court for the Eastern District of New York (Sandra L. Townes, *Judge*), denied Plaintiffs' motion for class certification, relying on our decision in *UFCW Local 1776 v. Eli Lilly & Co.*, 620 F.3d 121 (2d Cir. 2010) ("*Zyprexa*"), to hold that the individual decisions of prescribing physicians thwarted Plaintiffs' effort to prove class-wide causation using generalized proof. The district court subsequently granted Aventis summary judgment on all claims, again citing *Zyprexa* and Plaintiffs' inability to prove causation with generalized evidence.

Although we agree with Plaintiffs that *Zyprexa* does not foreclose class certification for all RICO mail-fraud claims brought against a drug manufacturer, we nevertheless conclude that *Zyprexa*'s reasoning applies to *this* case, and bars Plaintiffs' attempt to certify a class. While it may be possible for a class of plaintiffs to prove the causation element of a pharmaceutical fraud claim such as

this one with generalized proof, Plaintiffs have failed to offer such proof here. Class certification was therefore correctly denied. Our class certification decision, moreover, necessarily disposes of the summary judgment question as well: if Plaintiffs' RICO claims cannot be proved by generalized proof and Plaintiffs have adduced no *individualized* proof (which they have not), Plaintiffs' claims cannot survive summary judgment. We also agree with the district court's dismissal of Plaintiffs' state-law claims. Accordingly, we affirm the district court's orders denying class certification and granting Aventis's motion for summary judgment on all claims.

BACKGROUND

A. Antibiotic Treatment Options for Respiratory Tract Infections

The human respiratory tract—comprising the sinuses, throat, and lungs—is highly susceptible to invading microorganisms. These microscopic invaders are the cause of the sniffling, sneezing, congestion, and coughing that most laypeople identify as symptoms of "a cold" or "the flu." The medical community classifies such symptoms as those of either upper respiratory infections—the common cold and sinusitis being the most common examples—or lower respiratory infections—of which bronchitis and pneumonia are the most familiar.

See Patrick R. Murray et al., *Medical Microbiology* 6-7, 153-54 (7th ed. 2013). Respiratory tract infections may be caused by bacteria or by viruses; most cases are caused by viruses. Ctrs. for Disease Control & Prevention, *Get Smart: Know When Antibiotics Work (What Everyone Should Know)*, http://www.cdc.gov/getsmart/community/about/should-know.html (last visited Nov. 12, 2015) [hereinafter CDC, *Get Smart*].

Antibiotic drugs were first produced for widespread use in the 1940s, and their discovery was one of the greatest medical advances in history. Ctrs. for Disease Control & Prevention, *About Antimicrobial Resistance*, http://www.cdc.gov/drugresistance/about.html (last visited Nov. 12, 2015) [hereinafter CDC, *Antimicrobial Resistance*]. One of the first antibiotic drugs was penicillin, which was a member of a class of antibiotics known as beta-lactams. *Pneumonia: In-Depth Report (Antibiotic and Antiviral Drug Classes)*, N.Y. Times, http://www.nytimes.com/health/guides/disease/pneumonia/antibiotic-and-antiviral-drug-classes.html (last visited Nov. 12, 2015). Other beta-lactam antibiotics include amoxicillin, which, with the addition of clavulanic acid, is marketed under the name Augmentin. *Id.* In addition to the beta-lactams, the most common classes of antibiotic drug used to treat respiratory infections are

macrolide drugs, such as azithromycin (Zithromax) and clarithromycin (Biaxin), and the most recent major class of antibiotics to come on the market, fluoroquinolones. *Id.* All categories of antibiotic drug have their own benefits and risks. Antibiotics in all categories, however, are only effective against bacteria, and not against viral infections. Thus, because most respiratory tract infections are viral in nature, most such infections are unaffected by antibiotics. CDC, *Get Smart*.

For a variety of reasons, doctors nonetheless frequently prescribe antibiotic drugs to patients with respiratory tract infections, even if they have no evidence that the infection in question is caused by a bacteria rather than a virus. This kind of over-prescription of antibiotic drugs, as well as the widespread use of antibiotic therapies in general, has given rise to a phenomenon known as antibiotic resistance. CDC, *Antimicrobial Resistance*. Antibiotic resistance occurs when bacteria mutate to become impervious to the antibacterial action of a particular antibiotic drug; this resistant bacterial strain then multiplies and spreads, becoming more prevalent as antibiotic drugs wipe out its competitor strains. *Id.* Many of the bacteria commonly responsible for respiratory tract infections, such as *Streptococcus pneumoniae*, exist in strains that have developed

resistance to beta-lactam antibiotics or to macrolide antibiotics. Ctrs. for Disease Control & Prevention, *Antibiotic Resistance Threats in the United States* 79 (2013) ("*S. pneumonia* has developed resistance to drugs in the penicillin and erythromycin groups," causing 19,000 excess hospitalizations and 7,000 deaths every year.). Some strains have developed resistance to multiple classes of antibiotic drugs: these are known as multi-drug-resistant strains, or MDRS.

Although the various classes of drugs used to treat respiratory infections exhibit similar effectiveness and thus offer a similar benefit, each class has different downsides. Beta-lactams such as penicillin and amoxicillin are not suitable for patients with penicillin allergies, and Augmentin (amoxicillin with clavulanic acid) is a well-known cause of liver injury. In addition, resistance to both beta-lactams and to macrolide antibiotics is high. Macrolides can cause serious allergic reactions, impaired liver function, and sometimes-fatal heart problems. Fluoroquinolones can cause serious side effects in the central and peripheral nervous system, and can cause heart problems. Although all antibiotics can cause colitis by killing the normal, healthy microorganisms in a patient's body that protect us from the dangerous bacterium *Clostridium difficile*, or *C. dif*, *see* Ctrs. for Disease Control & Prevention, *Making Health Care Safer:*

Stopping C. difficile Infections, http://www.cdc.gov/vitalsigns/HAI/StoppingCdifficile/index.html (last visited Nov. 12, 2015), fluoroquinolones are particularly prone to this effect, because they attack a broader spectrum of bacteria, and thus kill more healthy gut bacteria than other drugs. All antibiotic drugs can have dangerous side effects; antibiotics are responsible for approximately twenty percent of all emergency room visits for adverse drug events. CDC, *Get Smart*.

B. The FDA Approval Process for Ketek

1. Aventis's Original Application for FDA Approval for Ketek

On February 28, 2000, Aventis submitted a New Drug Application ("NDA") to the Food and Drug Administration ("FDA") seeking approval to sell and market Ketek as a treatment for four types of respiratory infections: acute bacterial sinusitis ("ABS"), acute exacerbation of chronic bronchitis ("AECB"), tonsillopharyngitis, and community-acquired pneumonia ("CAP"). In support of the NDA, Aventis submitted data from *in vitro* testing of Ketek against various bacteria in a controlled lab setting, data from animal testing, and data from small human safety and efficacy trials. The *in vitro* data demonstrated that Ketek was capable of killing strains of common bacterial pathogens that were resistant to

other antibiotics, including MDRS, though *in vitro* results cannot always be replicated in clinical trials.

At the time when the FDA was considering the Ketek application, the FDA used a non-inferiority standard to assess the efficacy of antibiotic drugs in treating respiratory tract infections. This means that the FDA accepted, as conclusive proof of a drug's effectiveness, trials demonstrating that a new drug was no worse at treating a particular illness than existing, approved drugs—or, at least, was not so much worse than existing drugs that it fell below a set statistical threshold. The FDA did *not* require, and there was thus no incentive for a manufacturer to conduct, studies comparing the effectiveness of the new drug to the effectiveness of a placebo. In other words, manufacturers were merely required to prove that their product was no worse than similar products, even though—because minor respiratory infections like sinusitis and bronchitis usually go away on their own even without medication—the FDA did not know whether any of those similar products actually improved patient outcomes. This odd situation arose mostly by historical accident: because antibacterial drugs were discovered so long ago and represented such a major advance in treatment, "antibacterial therapy was incorporated into clinical practice . . . before clinical

trial design had become more sophisticated." J.A. 4448. There was also an ethical concern regarding giving sick patients placebos instead of real drugs.

Aventis's Ketek application was evaluated by the FDA's Anti-Infective Drug Advisory Committee ("AIDAC"), a panel of experts tasked with assessing an antibiotic drug's risk/benefit profile and making an approval recommendation to the FDA. The agency usually follows the recommendation of such a committee, but it is not bound by it. On April 26, 2001, the AIDAC met and voted to recommend limited approval of Ketek only for treatment of CAP—the most serious of the four conditions considered. The committee also recommended that further studies be performed to assess Ketek's potential side effects, known in the medical community as "adverse events." Specifically, the AIDAC members were concerned that Ketek might have serious but rare side effects that the small-scale clinical trials conducted thus far might not have revealed. Following this meeting, the FDA sent Aventis a letter finding its application for CAP, AECB, and ABS (though not tonsillopharyngitis) "approvable"—subject to the performance of a large-scale clinical study. Such a study would ideally reveal rarer side effects that might not have appeared in trials of only a few hundred or few thousand subjects. In other words, the study recommended by the AIDAC

would be a microcosm of what could be expected to happen if Ketek were approved and entered the marketplace.

2. Study 3014

Aventis agreed to perform such a study, and enlisted Pharmaceutical Product Development, Inc. ("PPD") to create the study protocol for and oversee the operation of what Aventis dubbed "Study 3014." Study 3014 was designed to enroll 24,000 patients, half of whom would be treated with Ketek, and half of whom would be treated with Augmentin. Patients were to be randomly assigned to one or the other drug. PPD was charged with recruiting physicians, who would be paid $400 for every patient of theirs who completed the study. The study required that each patient be diagnosed with ABS, AECB, or CAP at an initial appointment, at which baseline labs would be drawn and one of the two study medications would be prescribed. The protocol then required two follow-up visits.

Study 3014 was a fiasco. Dr. David Ross, who was the primary FDA safety reviewer responsible for review of Ketek, testified before a congressional hearing that the fraud in Study 3014 was "unprecedented . . . at this scope and scale." J.A. 4213. "[O]ut of 10 [study] sites that were inspected [by the FDA], all had serious

problems that made their data completely unreliable. . . . [E]very single one was found to have significant violations of what are called Good Clinical Practices, the rulebook for conducting clinical trials. Four of the 10—40 percent—were referred for criminal investigation." *Id.* Most egregiously, the study's largest enroller by far—Dr. Anne Kirkman-Campbell, who enrolled 407 patients—fabricated data on a vast scale. In the end, FDA investigators determined that she had only administered the study drugs to fifty patients, and that the other 350 patients were fictitious. Another study site regularly failed to report adverse events, while yet another site submitted suspiciously similar records for multiple subjects, including nearly identical blood test results. A site that enrolled 160 patients was run by a doctor who was ignorant of the study guidelines or the Good Clinical Practices rules, "argumentative about complying with the guidelines," and "[un]interested in learning about" them. J.A. 3798-99.

As a result of this widespread fraud and incompetence, the FDA Division of Scientific Investigations ("DSI") concluded that "[t]he integrity of data from all sites involved in Study 3014 cannot be assured with any degree of confidence." J.A. 643. "[I]f these sites, which were high-enrolling sites, where supposedly the company had been keeping close tabs on the doctors, were unreliable, the rest of

the sites couldn't be relied on either." J.A. 4213. Ultimately, because "the integrity of data from all of the 1,800 investigative sites . . . could not be assured," the FDA "did not rely on those data to take a regulatory action." J.A. 4539; *see also* J.A. 4387 ("Although the FDA did not rely on study 3014 to support approval, we reviewed the study for safety findings that would have counted 'against the drug,' as is consistent with good review practice."). Thus, Study 3014's ultimate conclusion—that Ketek was comparable to Augmentin in safety and effectiveness—was worthless.

3. FDA Approval of Ketek

On July 24, 2002—before the FDA had reason to suspect fraud in Study 3014—Aventis filed its amended NDA, including data from Study 3014, and post-marketing safety data from countries in Europe and South America, where Ketek had already been approved for sale. Aventis's report about Study 3014 omitted any mention of the study's data integrity problems. On October 15, 2002, DSI began its investigation of Dr. Kirkman-Campbell's involvement in Study 3014, which led swiftly to discovery of her fraud.

On January 8, 2003, the AIDAC met for a third time to discuss the Ketek application. The committee was missing crucial information, however—the FDA

did not reveal to the AIDAC members any information relating to DSI's ongoing investigation of Study 3014. Unaware of the unreliability of Study 3014's results, the AIDAC recommended that the FDA approve Ketek for ABS, AECB, and CAP. The FDA, armed with the information the AIDAC lacked, did not accept the committee's recommendation, but instead requested additional information from Aventis concerning both Study 3014 and post-marketing safety data from countries where Ketek was already in use.

Finally, on April 1, 2004, the FDA approved Ketek for three indications: ABS, AECB, and CAP. Because the agency was aware that Study 3014 was unreliable, and Aventis had conducted no other large-scale safety studies, the FDA relied almost entirely on post-marketing safety reports from other countries in approving the drug. This was highly unusual. *See* J.A. 4231 (Dr. David Graham, associate director for science and medicine in FDA's Office of Surveillance and Epidemiology, testified that he could not "think of a single other example where FDA used such data as the primary basis for the approval of a drug['s] safety.").

At congressional hearings later convened on the topic of Ketek's approval, witnesses put forth different explanations for the FDA's decision. Dr. Ross

pointed to "a culture of approval" at the FDA, J.A. 4199, and "a fear of being seen as holding up new products," J.A. 4220. Dr. John Powers, former lead medical officer for antimicrobial drug development at the FDA, noted that there were "economic issues regarding antibiotic development that were pressuring FDA from the outside"—namely, drug companies "had decided to stop antibiotic discovery" because the market for antibiotics is flooded with generic competitors, and because antibiotics are not as lucrative as drugs like antidepressants or statins, which are taken continuously for months or years. J.A. 4200-02. This slowdown in the development of new antibiotic drugs, according to Dr. Powers, was especially dangerous given the need for new drugs to replace older antibiotics to which antibiotic resistance had developed. In this environment, "if [the] FDA made any moves to increase the rigor of scientific studies in the area of antibiotics," there was a fear that "it would be perceived as a . . . disincentive" to the development of new drugs. J.A. 4201. Dr. Andrew von Eschenbach, then-commissioner of the FDA, testified that Ketek's approval was based on "the need for newer, more effective antibiotics" to "overcome resistance" and add to the "antibiotic armamentarium." J.A. 4298.

The label agreed upon by Aventis and the FDA for Ketek noted that there was some risk of liver failure associated with the drug, but this information was not included in the "Warnings" section, nor was any indication included therein that Ketek should not be prescribed to patients with a history of liver problems. J.A. 3934-35. No information from Study 3014 appeared on the Ketek label. The FDA's approval of Ketek, like FDA approval of any other drug, *see Zyprexa*, 620 F.3d at 127, permitted doctors to prescribe Ketek not only for its approved indications (ABS, AECB, and CAP), but also for any other disease or symptom for which an individual physician thought it might be effective. Prescription of a drug for an indication other than the indications approved by the FDA is called "off-label" prescription or "off-label" use. *Id.*

C. Ketek in the Marketplace

1. The Marketplace for Antibiotic Drugs

A prescription for antibiotic drugs, like any prescription, involves three main actors: the patient, who takes the medication and often assumes some share of the cost; the doctor, who prescribes the drug but is not involved with the financial side of the prescription; and the payer, who covers the majority of the drug's cost. For insured patients, the payer is a health-benefit plan ("HBP"),

which pays whatever cost the patient's co-pay does not cover. Plaintiffs in this case are all HBPs. Most HBPs contract out their prescription drug benefit coverage to pharmacy benefit managers ("PBMs"), and all three named plaintiffs here did so. PBMs manage approximately seventy-five percent of all outpatient prescription drug claims, and the three largest PBMs—Medco, Caremark, and Express Scripts—handle about two-thirds of those claims, or about half of all retail prescriptions.

Most PBMs use formularies to outline which drugs are covered by a particular plan and what type of coverage each drug receives. Many formularies are "tiered," often using a three-tier system which separates generics (Tier 1), "preferred" brand name drugs (Tier 2), and "non-preferred" brand name drugs (Tier 3). J.A. 1138-39. Tier 1 drugs require the smallest co-pay, and may even be free, while Tier 2 and Tier 3 drugs will be progressively more expensive for the patient. J.A. 68. Formularies may also place freestanding restrictions on their coverage of a drug—for example, they may refuse to cover a particular drug until a preferred alternative has been tried, and has failed. It is rare for a PBM to remove an FDA-approved drug from its formulary, although PBMs regularly move particular drugs up or down a tier based on new information about a drug.

Although HBPs implement tiered formularies and otherwise classify drugs in order to incentivize patients to request cheaper, safer, and more effective drugs over more expensive, dangerous, or ineffective ones, the ultimate decision regarding which drug will be prescribed to a patient rests entirely with the patient's doctor. The parties to this case agree that a variety of factors contribute to a physician's decision, including both patient-specific factors and the physician's own experience with, and knowledge about, the various options. Those factors include, in the case of antibiotics: the patient's age and sex, the possibility of pregnancy, drug allergies, success of prior courses of treatment in this patient, other medications the patient is taking, other illnesses the patient is experiencing, family history, drug compliance tendencies (whether the patient is likely to take and finish the course of treatment as prescribed), patient preferences, side effects from previous antibiotics, the likelihood of antibiotic resistance in the patient, the profile of antibiotic resistance in the region, and, of course, the drug's safety and efficacy.

There are many antibiotic drugs available to treat respiratory tract infections, including AECB, ABS, and CAP. As discussed above, each class of drug, and each individual drug within that class, comes with its own particular

risks and benefits, including the type and severity of potential side effects, the existence of resistant organisms, and whether the drug targets a broad or narrow spectrum of bacteria. Ketek's competitors also vary significantly in cost. Zithromax, in the timespan shortly after Ketek's entrance into the market, cost $39.54 for a full course of therapy, while Levaquin (a fluoroquinolone) cost $62.09 for a course of treatment for AECB and $124.18 for a course of treatment for ABS. Amoxicillin clavulanate cost $75.77 for a full course of therapy for both diseases. Generic competitors like penicillin cost much less. Ketek was priced close to Zithromax, which Aventis considered its main competitor: $46.15 per course of therapy for both ABS and AECB.

Following FDA approval, HBPs placed Ketek on their formularies. At the time relevant to this action, two of the named plaintiffs, New England Carpenters Health Benefits Fund ("NEC") and Allied Services Division Welfare Fund ("ASD"), employed a three-tiered formulary; Sergeants Benevolent Association Health and Welfare Fund ("SBA"), the third named plaintiff, did not employ a tiered formulary at all. It is not clear in which tier ASD's PBM classified Ketek during the relevant time period; all that is known is that, as of March 2010, ASD's PBM listed Ketek as "Tier 2," which is the tier for preferred brand-name

drugs. NEC covered Ketek at Tier 2 until December 2006, at which point it moved Ketek to Tier 3. SBA, which does not employ a tiered formulary, has covered Ketek at the same level from the time of its original FDA approval through the date of the district court's summary judgment decision.

2. Ketek's Market Performance

After FDA approval in April 2004, Ketek entered the market in July 2004 and became an immediate commercial success. Even though Ketek only became available halfway through the year, Ketek was prescribed 859,696 times in 2004. Ketek sales grossed $209 million in 2005 alone, and Dr. Ross estimated that, in 2006, a Ketek prescription was written "every four or five seconds." J.A. 4202. CAP represented only eight percent of Ketek prescriptions; the rest were for ABS, AECB, or off-label indications.

Ketek entered a market that was in a significant state of flux. Zithromax, the market leader, and the drug that Aventis considered Ketek's true rival, was scheduled to go off-patent in the fourth quarter of 2005. Biaxin, another popular macrolide antibiotic, was scheduled to go generic in the second quarter of 2005. Cefzil, a less popular competitor, was going off-patent in the third quarter of 2005, and Levaquin and Tequin, two of the first fluoroquinolone drugs, were

scheduled to go off-patent in 2007. In other words, Ketek entered a market which was dominated by brand-name drugs facing off against other brand-names, but which likely would not remain that way for long. Ketek had to be able to compete even when its most popular rivals became cheaper and more widely available than ever before.

Ketek's sales peaked in the winter months and dropped in the summer months, which is typical for drugs treating seasonal illnesses like sinusitis and pneumonia. After the peak sales of winter 2005-06, however, sales dropped much more steeply than they had following the first winter peak in 2004-05; sales ultimately fell to about 60,000 prescriptions in July 2006, far below the July 2005 low of about 140,000 prescriptions. Ketek's numbers then began to rise again, as expected in the fall and winter, but on a much smaller scale. Indeed, Ketek's peak for the 2006-07 winter was only about 130,000 prescriptions—lower than Ketek's summer 2005 "low" of about 140,000. In short, Ketek's sales took an unmistakable dive starting in early-to-mid-2006. The reason or reasons for this precipitous decline are intensely disputed by the parties.

3. Ketek's Post-Marketing Safety History

The FDA maintains a publicly available database of spontaneous reports of adverse drug reactions, known as the Adverse Event Reporting System, or "AERS." In March 2005, slightly less than a year after Ketek was approved, the FDA Center for Drug Evaluation and Research asked the Division of Drug Risk Evaluation ("DDRE") to evaluate reports appearing in AERS related to Ketek — specifically, reports of "visual disturbances, automobile accidents, liver events, and syncope/loss of consciousness." J.A. 2230. After assessing the AERS reports in detail and determining that a number of the reported hepatic adverse events were caused by something other than Ketek, DDRE concluded that the hepatic adverse event reports were "consistent with those seen prior to approval in worldwide experience and as described in the current labeling." *Id.* DDRE recommended only "including a statement in the **PRECAUTIONS** section [of the Ketek label], following the current statement about hepatic dysfunction, that the hepatic dysfunction may be severe (as [was] currently stated in [other parts of the label])." *Id.*

By the end of January 2006, Ketek had been prescribed approximately four and a half million times, and ten cases of serious hepatic adverse events closely associated with Ketek had been reported to AERS, including two deaths. On

January 20, 2006, the medical journal Annals of Internal Medicine published a short article describing a cluster of three Ketek-associated hepatic adverse events that occurred in North Carolina. All three patients were previously healthy; one patient died, one spontaneously recovered, and one required a liver transplant. On the same date that the article was published online, and prompted by the publication of said article, the FDA issued a Public Health Advisory regarding Ketek. The Public Health Advisory affirmed that earlier studies had suggested "that the risk of liver injury with [Ketek] was similar to that of other marketed antibiotics," but nevertheless recommended that healthcare providers "monitor patients taking [Ketek] for signs or symptoms of liver problems." J.A. 3984-85.

The year 2006 saw a spike in reports of hepatic adverse events associated with Ketek. The six months from January 2006 to June 2006 saw twenty-five cases of serious hepatic side effects reported as associated with Ketek—more than twice as many as had been reported in the entire eighteen months that Ketek had previously been on the market. The six months from June 2006 to December 2006 saw an additional eighteen reported serious adverse hepatic events, for a total of fifty-three such events since Ketek came on the market. DDRE noted in an October 2006 report on Ketek that "the rising trend of reporting rates

associated with [Ketek] is of concern," J.A. 3855, but also noted that the rise in reporting of hepatic events associated with Ketek was potentially "stimulated" reporting prompted by the Annals of Internal Medicine article in January 2006, J.A. 3866. Stimulated reporting occurs when press coverage of a particular adverse event associated with a drug prompts healthcare providers to notice and report similar drug-event pairings with greater frequency; when it occurs, this phenomenon makes it difficult to compare reporting rates for different drugs, because a higher reported rate of liver failure associated with one drug as opposed to another may simply reflect greater public salience rather than greater risk. The October 2006 DDRE report noted that the domestic reporting rate for Ketek-associated serious hepatic adverse events was 23 per 10 million prescriptions and recommended "consideration of regulatory actions for [Ketek] such as restricted use for only patients who have failed other antibiotic treatments or even market withdrawal." J.A. 3869. On June 29, 2006, Aventis (with the FDA's approval) changed Ketek's label to include additional warnings about liver toxicity and sent a Dear Healthcare Professional letter to prescribers alerting them to the change. On the same date, the FDA issued a press release cautioning that many antibiotics may pose a risk of liver failure, and that "as

drug usage becomes more widespread, it is expected that rare adverse events may be detected or reported in greater numbers." J.A. 3061-62. On September 12, 2006, the AIDAC voted to reject an NDA for the fluoroquinolone gemifloxacin, targeted at ABS, in part because clinical trials demonstrated only non-inferiority; the manufacturer could not prove that gemifloxacin was more effective than a placebo. On October 23, 2006, the FDA effectively announced a new superiority requirement for antibiotic trials by rejecting an NDA for another anti-infective aimed at respiratory infections, faropenem, and raising no safety concerns but instead advising the manufacturer to conduct superiority trials.

D. FDA Withdrawal of Approval

In December 2006, the FDA convened a joint meeting of the AIDAC and the Drug Safety and Risk Management Advisory Committee ("DSRMAC") to consider whether the agency should (1) withdraw, limit, or modify Ketek's approval for some or all of its three indications; (2) require changes to Ketek's label; or (3) issue an official restriction on Ketek's use. The meeting included both voting and non-voting attendees, and those voting included members of both committees, as well as Special Government Employee Consultants and Federal Employee Consultants. The attendees voted, *inter alia*, on the specific question,

"If superiority studies are conducted with Ketek, would that be sufficient evidence to support [the conclusion that] benefit outweighs risk?" J.A. 4395-96.

The meeting's introductory comments, delivered by the Director of the FDA's Office of Surveillance and Epidemiology, Dr. Gerald Dal Pan, noted "concerns that non-inferiority trials cannot determine if the observed clinical success rate" of drugs treating respiratory infections "is due to the drug or to the natural history of the condition." J.A. 4432-33. Similar concerns about the continued viability of non-inferiority trials recurred throughout the meeting. The meeting also featured an FDA statistical analysis of the Ketek-related reports appearing in AERS, which concluded that Ketek displayed a "fairly high" propensity to cause hepatic failure but noted that its propensity to cause both hepatic failure and hepatitis was statistically similar to that of another leading antibiotic drug, Augmentin. J.A. 4664-65. An epidemiological analysis of Ketek's connection to hepatic adverse events by the FDA's Office of Surveillance and Epidemiology concluded that the "reporting rate for [Ketek]-associated [liver failure] . . . was found to be similar to . . . reporting rates for selected comparators [in the quinolone family] . . . given variation inherent in spontaneous adverse event reporting." J.A. 4753.

Regarding the deficiencies of Study 3014, one attending consultant remarked that, although "[m]uch has been made . . . out of the fact" that Study 3014 had been improperly conducted and could not be considered in connection with Ketek's risks, "a clinical trial . . . is not a great way to get an answer to a question that involves a very low event rate," because "for the event rates we are talking about, a 24,000-patient trial isn't going to show much." J.A. 4844-45. Another attendee agreed, asking, "how much power would a study of 12,000 patients exposed to [Ketek] . . . [have] to tell us about liver injuries that are occurring at" a "potential rate of 1 in 20,000 to 1 in 30,000." J.A. 4848. A third attendee pointed out that "one other major limitation to clinical trials in terms of safety data . . . is that the majority of clinical trials . . . don't enroll very sick people," which is precisely the group of patients most likely to develop adverse drug reactions once a drug is prescribed widely in the general population. J.A. 4854-55.

At the end of the meeting, the attendees voted to withdraw Ketek's approval for ABS and AECB. Asked to state their rationale along with their votes, a number of members cited safety concerns, explaining that they would "need to know more about the risks" before allowing Ketek back on the market, J.A. 2277,

or that they were "concerned about the possibility that the level of toxicities we see right now may herald an increasing prevalence that may occur in the future," J.A. 2284. But many members cited effectiveness instead, noting that, in the absence of superiority trials, Ketek might well be no better than a sugar pill. Several attendees expressly explained their votes in terms of the shift from non-inferiority trials to superiority trials. Two attendees voted to continue Ketek's approval based on fairness concerns, arguing that Ketek and its competitors had been approved when non-inferiority trials were considered acceptable, and that it was "unfair to single out a single drug company because we have shifted the playing grounds." J.A. 2280. Finally, the voting attendees unanimously voted "Yes" on the question "If superiority studies are conducted with Ketek, would that be sufficient evidence to support [the conclusion that] benefit outweighs risk?" J.A. 4396.

The FDA accepted the attendees' recommendation that Ketek's approval for ABS and AECB be withdrawn, and that Ketek continue to be approved for CAP. The attendees also recommended that Ketek's label be amended with a "black box warning" and expressed concern that foreign postmarketing data indicated that Ketek exacerbated the rare neurological disorder myasthenia

gravis in patients already suffering from the disease, resulting in hospitalization and sometimes death. The black box warning ultimately added to Ketek's label in 2007 indicated that "Ketek is contraindicated in patients with myasthenia gravis" and referenced this data. Shortly after learning of the agency's decision, Aventis decided to terminate its rebate contracts[1] for Ketek and to stop promoting Ketek in the United States.

The withdrawal of Ketek's approval for ABS and AECB took effect on February 9, 2007. On February 13, 2007, the House Energy and Commerce Subcommittee on Oversight and Investigations began hearings on the FDA's drug-approval process, focused in large part on the FDA's decision to approve Ketek, the widespread fraud in Study 3014, antibiotic resistance, and the issue of non-inferiority versus superiority trials for drugs that address self-resolving infections like ABS and AECB. Ketek's domestic sales, already declining, continued their downward trend after the withdrawal. Ketek is still available for sale in the United States, but is rarely prescribed here. Sales remain brisk abroad.

E. Procedural History

[1] Rebate contracts are agreements through which drug manufacturers provide financial rebates to PBMs either to gain access to a particular formulary tier or as an incentive to increase a drug's market.

Plaintiffs filed the original complaint in this action on January 14, 2008, alleging violations of state consumer protection laws and unjust enrichment.[2] On June 4, 2008, Plaintiffs filed a second amended complaint, alleging for the first time a substantive RICO violation under 18 U.S.C. § 1962(c) and a RICO conspiracy in violation of 18 U.S.C. § 1962(d). The substantive RICO claim alleged that the "association-in-fact" between Aventis and PPD, the supervisor of Study 3014, constituted a criminal enterprise with a common purpose to enable Aventis "to fraudulently represent that Ketek had valid regulatory approval for broad antibiotic uses." Special App. 69. The predicate acts alleged were mail fraud, wire fraud, tampering with witnesses, and use of interstate facilities to conduct unlawful activity. *Id.* Plaintiffs sought class-wide refund damages of $195.1 million and class-wide unjust enrichment damages of $224 million. If Plaintiffs' RICO claims were successful, they stood to recover treble damages of nearly $600 million, not including any recovery for unjust enrichment.

In May 2010, Plaintiffs moved to certify a class including all HBPs that paid or incurred costs for Ketek between April 1, 2004, when the drug received

[2] The State of Louisiana and its instrumentalities were also originally named as plaintiffs in the complaint, but they voluntarily dropped out of the litigation on May 21, 2008.

FDA approval, and February 12, 2007, when it lost such approval for ABS and AECB. Plaintiffs argued, *inter alia*, that Ketek was so dangerous that no physician would have prescribed Ketek if Aventis had not concealed its true safety risks; every Ketek prescription, according to Plaintiffs, was thus traceable to Aventis's alleged fraud. Magistrate Judge Ramon Reyes issued a Report and Recommendation recommending that class certification be denied because Plaintiffs could not establish through generalized proof that Aventis's alleged RICO violations caused Plaintiffs' injuries. *Sergeants Benevolent Ass'n Health & Welfare Fund v. Sanofi-Aventis U.S. LLP*, No. 08-cv-0179 (SLT) (RER), 2011 WL 824607 (E.D.N.Y. Feb. 16, 2011) ("*Sergeants I*"). Judge Reyes reasoned that this case is virtually identical to *Zyprexa*, in which this Court held that RICO claims brought by HBPs against Eli Lilly ("Lilly") under the theory that Lilly misrepresented Zyprexa's safety and efficacy were not susceptible to generalized proof, because physicians' individual treating decisions disrupted the causal chain. *Id.* at *15. That Report and Recommendation was adopted by the district court on March 30, 2011. *Sergeants Benevolent Ass'n Health & Welfare Fund v. Sanofi-Aventis U.S. LLP*, No. 08-cv-0179 (SLT) (RER), 2011 WL 1326365 (E.D.N.Y. Mar. 30, 2011) ("*Sergeants II*"). Plaintiffs petitioned this Court for immediate

appeal of the class certification decision, but their petition was denied on July 28, 2011.

On December 22, 2011, Aventis moved for summary judgment with respect to all four causes of action alleged in the second amended complaint, arguing that Plaintiffs could not prove causation under RICO or prove that they suffered an injury, and arguing that Plaintiffs' state-law claims failed because Plaintiffs could not prove a violation of any of the state consumer protection statutes listed in the second amended complaint or make out an unjust enrichment claim under the law of their home states. On January 4, 2012, the district court again referred the matter to Magistrate Judge Reyes, who recommended that Aventis's motion for summary judgment be granted in its entirety. *Sergeants Benevolent Ass'n Health & Welfare Fund v. Sanofi-Aventis U.S. LLP*, No. 08-cv-0179 (SLT) (RER), 2012 WL 4336218 (E.D.N.Y. Sept. 17, 2012) ("*Sergeants III*").

On May 12, 2014, the district court adopted Judge Reyes's Report and Recommendation except to the extent that Judge Reyes recommended limiting the state-law causes of action to claims brought pursuant to the laws of Plaintiffs'

home states.[3] *Sergeants Benevolent Ass'n Health & Welfare Fund v. Sanofi-Aventis U.S. LLP*, 20 F. Supp. 3d 305 (E.D.N.Y. 2014) ("*Sergeants IV*"). The district court expressed concern that "the causal connection between [Aventis]'s alleged wrongdoing and Plaintiffs[']injury might be too attenuated to meet RICO's [proximate] causation requirement," but ultimately based its causation holding on *Zyprexa*'s statements to the effect that physicians' prescribing decisions are too independent to allow proof of causation through generalized proof. *Id.* at 327. The district also held that, "[e]ven assuming that the decline in Ketek sales was caused exclusively by safety considerations, one cannot use generalized proof to determine the injury to Plaintiffs caused by [Aventis]'s misconduct," because Plaintiffs could not prove which antibiotics would have been prescribed in the place of Ketek and whether those drugs would have been less expensive than Ketek. *Id.* at 327-28.

Regarding Plaintiffs' state-law claims, as relevant here, the district court held that: (1) Plaintiffs' claims under New York General Business Law § 349(a), Massachusetts General Law chapter 93A, and the Illinois Consumer Fraud and

[3] Plaintiffs subsequently chose to dismiss their claims brought pursuant to the laws of sixteen other states in order to permit the immediate appeal of the district court's summary judgment decision.

Deceptive Business Practices Act all failed because Plaintiffs could not prove that they suffered an injury as a result of Aventis's actions; (2) that Plaintiffs' Illinois unjust enrichment claim failed because Plaintiffs have an adequate remedy at law; and (3) that Plaintiffs' Massachusetts and New York unjust enrichment claims failed because it was not inequitable for Aventis to retain the money it was paid in exchange for an antibiotic that provided value to patients by effectively treating their diseases. *Id.* at 334-37; 339-40. Plaintiffs timely appealed both the class certification and the summary judgment orders.

DISCUSSION

We review a district court's denial of class certification for abuse of discretion. To the extent that the court's decision was based on conclusions of law, we review such conclusions *de novo*, and to the extent that its decision was based on findings of fact, we review such findings for clear error. *See Zyprexa*, 620 F.3d at 130-31. Our review of a district court's denial of summary judgment is *de novo*. *Id.* Summary judgment is properly granted if "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a).

I.

Plaintiffs seek class certification under Federal Rule of Civil Procedure 23(b)(3). They must therefore demonstrate, *inter alia*, that "questions of law or fact common to class members predominate over any questions affecting only individual members."[4] Fed. R. Civ. P. 23(b)(3). "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 to individualized proof." *Zyprexa*, 620 F.3d at 131 (quoting *Moore v. PaineWebber, Inc.*, 306 F.3d 1247, 1252 (2d Cir. 2002)).

Plaintiffs' claim is brought under RICO § 1964(c). To prevail on such a claim, 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*,

[4] In every case, a plaintiff seeking to certify a class must also satisfy all the prerequisites listed in Rule 23(a). *See* Fed. R. Civ. P. 23(a) (requiring (1) that the "class [be] so numerous that joinder of all members is impracticable," (2) that "there are questions of law or fact common to the class," (3) that "the claims or defenses of the representative parties are typical of the claims or defenses of the class," and (4) that "the representative parties will fairly and adequately protect the interests of the class"). The parties and the district court agree that the Rule 23(a) factors are met here.

Inc., 541 F.3d 425, 439 (2d Cir. 2008), *rev'd on other grounds sub nom. Hemi Grp. v. City of New York*, 559 U.S. 1 (2010) (quoting 18 U.S.C. § 1964(c)).

The statute's "by reason of" language "require[s] a showing that the defendant's violation not only was a 'but for' cause of his injury, but was the proximate cause as well," which mandates "some direct relation between the injury asserted and the injurious conduct alleged" that is not "too remote." *Holmes v. Sec. Inv. Prot. Corp.* 503 U.S. 258, 268 (1992). Accordingly, a plaintiff seeking to certify a class of plaintiffs in a § 1964(c) suit cannot succeed unless the proposed class can demonstrate by generalized proof that the defendant's misconduct was both the but-for cause and the proximate cause of each class member's injury. *See Zyprexa*, 620 F.3d at 131-32 (explaining that in the context of RICO claims such as Plaintiffs', Rule 23(b)(3) predominance requires the putative class "to prove its theory of injury through generalized proof").

The core of the substantive RICO violation alleged by Plaintiffs is a pattern of mail fraud, which occurs "whenever a person, 'having devised or intending to devise any scheme or artifice to defraud,' uses the mail 'for the purpose of executing such scheme or artifice or attempting to do so.'" *Bridge v. Phoenix Bond & Indem. Co.*, 553 U.S. 639, 647 (2008) (quoting 18 U.S.C. § 1341). The parties do

not dispute that Aventis "use[d] the mail" in connection with its alleged fraud and thus (for purposes of this appeal) focus primarily on whether Aventis's alleged fraud caused an injury to Plaintiffs and other class members, rather than on whether Aventis's alleged conduct actually constituted a "scheme or artifice to defraud" within the meaning of the mail-fraud statute. The district court determined that common issues did not predominate, rendering class certification unavailable, because Plaintiffs could not establish using generalized proof that each putative class member suffered an injury "by reason of" Aventis's alleged fraud. Because that decision was not an abuse of discretion, we affirm the district court's order denying class certification.

A.

Although reliance on the defendant's alleged misrepresentation is not an element of a RICO mail-fraud claim, the plaintiffs' theory of injury in most RICO mail-fraud cases will nevertheless depend on establishing that someone—whether the plaintiffs themselves or third parties—relied on the defendant's misrepresentation. *See Bridge*, 553 U.S. at 658-59; *In re U.S. Foodservice Inc. Pricing Litig.*, 729 F.3d 108, 119 n.6 (2d Cir. 2013), *cert. denied*, 134 S. Ct. 1938 (2014). That is because reliance will typically be a necessary step in the causal chain linking

the defendant's alleged misrepresentation to the plaintiffs' injury: if the person who was allegedly deceived by the misrepresentation (plaintiff or not) would have acted in the same way regardless of the misrepresentation, then the misrepresentation cannot be a but-for, much less proximate, cause of the plaintiffs' injury.[5] *See Bridge*, 553 U.S. at 658-69.

Because proving causation will ordinarily require proving reliance, and because of the difficulty of proving reliance using "generalized proof," *Zyprexa*, 620 F.3d at 131-32, it is quite difficult, though not impossible, to certify a class in a RICO mail-fraud case. To set out some helpful guideposts for our inquiry in this case, we first examine several cases involving "first-party reliance"—i.e., cases where proving causation requires proof that the plaintiffs themselves had relied on the defendant's misrepresentations. *Cf. Halliburton Co. v. Erica P. John Fund, Inc.*, 134 S. Ct. 2398, 2408 (2014) (observing, in the context of a securities fraud class action, that "[i]f every plaintiff had to prove direct reliance on the defendant's misrepresentation, 'individual issues then would . . . overwhelm[]

[5] Even if the plaintiff's or a third-party's reliance on the defendant's misrepresentation does, in fact, render that misrepresentation a but-for cause of the plaintiffs' injury, the relationship between the misrepresentation and the injury must still be "direct" enough for proximate causation to be satisfied. *See Hemi Grp.*, 559 U.S. at 7-14.

the common ones,' making certification under Rule 23(b)(3) inappropriate" (second and third alterations in original) (quoting *Basic Inc. v. Levinson*, 485 U.S. 224, 242 (1988))).

In *McLaughlin v. American Tobacco Co.*, 522 F.3d 215 (2d Cir. 2008), the putative class consisted of cigarette smokers allegedly induced to purchase "light" cigarettes by a tobacco company's misrepresentations that light cigarettes were healthier than regular ones. The plaintiffs' theory of injury thus required proving that each class member would not have bought light cigarettes but for the misrepresentation. *See id.* at 227. We held that the plaintiffs could not do so by generalized proof: "Individualized proof is needed," we explained, "to overcome the possibility that a member of the purported class purchased Lights for some reason other than the belief that Lights were a healthier alternative—for example, if a Lights smoker was unaware of that representation, preferred the taste of Lights, or chose Lights as an expression of personal style." *Id.* at 223.

For essentially the same reasons, the Ninth Circuit denied certification in *Poulos v. Caesars World, Inc.*, 379 F.3d 654 (9th Cir. 2004), to a putative class of plaintiffs who were allegedly induced to gamble by a casino's misrepresentations about their odds of winning. The court explained: "Some players may be

unconcerned with the odds of winning, instead engaging in casual gambling as entertainment or a social activity. Others may have played with absolutely no knowledge or information regarding the odds of winning such that the appearance and labeling of the machines is irrelevant and did nothing to influence their perceptions. Still others, in the spirit of taking a calculated risk, may have played fully aware of how the machines operate." *Id.* at 665-66. For gamblers who did not rely on the casino's misrepresentations in deciding whether to gamble, the alleged fraud simply played no causal role in their injury; and because there was no way to establish through generalized proof that each individual class member had, in fact, relied on the casino's misrepresentations, certification was improper. *See id.* at 666.

We have recognized, however, that plaintiffs may be able to prove class-wide causation based on first-party reliance *without* an individualized inquiry into whether each class member relied on the defendant's misrepresentation if "circumstantial evidence" generates a sufficiently strong inference that all class members did, in fact, rely. *McLaughlin*, 522 F.3d at 225 n.7. In certain factual contexts, it may well be reasonable to infer that each class member would only have taken the action leading to its injury if it had relied on the defendant's

alleged misrepresentation. Such an inference may be available if, for example, the class members all faced "the same more-or-less one-dimensional decisionmaking process," such that the alleged misrepresentation would have been "essentially determinative" for each plaintiff. Richard A. Nagareda, *Class Certification in the Age of Aggregate Proof*, 84 N.Y.U. L. Rev. 97, 121 (2009). Although deciding whether to smoke light cigarettes and deciding whether to gamble are not one-dimensional decisions, a plaintiff class may be able to convince a jury that other decisions are.

The Eleventh Circuit's decision in *Klay v. Humana, Inc.*, 382 F.3d 1241 (11th Cir. 2004), illustrates this point. In *Klay*, a putative class of doctors claimed that a number of HMOs had misrepresented in their contracts with the doctors that the HMOs would provide reimbursement for all necessary medical expenses provided to the doctors' patients. The Eleventh Circuit upheld class certification, rejecting the HMOs' contention that the plaintiffs could not show class-wide reliance using generalized proof: "It does not strain credulity," the court said, "to conclude that each plaintiff . . . relied upon the defendants' representations and assumed they would be paid the amounts they were due." *Id.* at 1259. Thus, "[a] jury could quite reasonably infer that guarantees concerning physician pay—the

very consideration upon which those agreements are based—go to the heart of these agreements, and that doctors based their assent upon them." *Id.* This Court relied on similar logic in *U.S. Foodservice*, where we affirmed certification of a class of plaintiffs who alleged that they had been overbilled by a food-service company. "In cases involving fraudulent overbilling," we reasoned, "payment may constitute circumstantial proof of reliance based on the reasonable inference that customers who pay the amount specified in an inflated invoice would not have done so absent reliance upon the invoice's implicit representation that the invoiced amount was honestly owed." 729 F.3d at 120.

Similar principles apply in cases involving "third-party reliance"—i.e., cases in which proving the necessary causal connection between the defendant's misrepresentation and the plaintiffs' injury requires proving that someone other than the plaintiffs relied on the defendant's alleged misrepresentations. *See, e.g.*, *Bridge*, 553 U.S. at 658-59. Just as in cases involving first-party reliance, the individualized nature of the reliance inquiry can make it difficult to prove causation using generalized proof. Nonetheless, it may be possible in certain circumstances for a putative class to prove causation on a class-wide basis by offering sufficient circumstantial proof—analogous to that offered in *Klay* and

U.S. Foodservice—to permit the reasonable inference that the third parties in question *must* have relied on the defendant's misrepresentation.

Our decision in *Zyprexa* illustrates the difficulty of proving class-wide causation in a RICO mail-fraud case using generalized proof of third-party reliance. There, a putative class of HBPs sued the pharmaceutical company Eli Lilly, alleging that Lilly had violated RICO by making false representations about the antipsychotic medication Zyprexa, which the FDA had approved to treat schizophrenia and bipolar disorder. 620 F.3d at 124. The plaintiffs alleged that Lilly had concealed evidence of Zyprexa's tendency to cause serious weight gain and diabetes, and had unlawfully marketed Zyprexa for "off-label" conditions such as depression, dementia, and anxiety disorder for which there was no evidence of effectiveness. *Id.* at 124-25, 127-28.

The *Zyprexa* plaintiffs advanced two theories of injury, which we termed the "quantity effect" theory and the "excess price" theory. *Id.* at 129. The former theory—like Plaintiffs' theory of injury in the present case against Aventis—argued that Lilly's misrepresentations caused the HBPs to pay for prescriptions that would not otherwise have been written; the latter theory maintained that Lilly's misrepresentations caused the HBPs to pay more for Zyprexa than they

otherwise would have. *Id.* Both theories depended on the premise that doctors, as opposed to the HBPs themselves, had relied on Lilly's alleged misrepresentations in choosing to prescribe Zyprexa to their patients. To prove that doctors had, in fact, relied on Lilly's misrepresentations in making their prescription decisions, the plaintiffs primarily offered evidence that the number of Zyprexa prescriptions fell after the drug's weight- and diabetes-related side effects were disclosed by a revision to its label in 2003. *Id.* at 128; *see also id.* at 135 (noting that the plaintiffs' expert "assum[ed] that the decline in the number of Zyprexa prescriptions following the [disclosure of Zyprexa's risks] . . . was due almost entirely to a decrease in the number of off-label Zyprexa prescriptions," and also "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").

This Court held that neither of the plaintiffs' two theories was susceptible to generalized proof of causation on the facts presented, and we therefore reversed the district court's certification of the plaintiff class. With respect to the quantity effect theory in particular (the theory primarily relevant here), we concluded—relying heavily on *McLaughlin*—that the plaintiffs' attempt to show

causation through generalized proof was "thwart[ed]" by the individualized nature of physicians' prescribing decisions. *Id.* As we explained:

> 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. . . . 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 . . . .

Id. at 135-36. In other words, we viewed a doctor's decision to prescribe Zyprexa as roughly analogous to a smoker's decision to smoke light cigarettes: because the decision could have been made for any numberof a multitude of reasons, we could not reasonably infer that Lilly's misrepresentations were, in fact, a but-for cause (much less the proximate cause) of the excess prescriptions paid for by the plaintiffs. The fact that Zyprexa prescriptions declined markedly following the disclosure of the previously concealed information was not sufficient to support this necessary inference, especially in light of evidence that "at least some doctors were not misled by Lilly's alleged misrepresentations." *Id.* at 135. Thus, because a reasonable jury would be unable to find RICO causation satisfied for

each class member based on the generalized proof offered by the plaintiffs, common questions did not predominate, and class certification under Rule 23(b)(3) was therefore inappropriate.

B.

Here, as in *Zyprexa*, Plaintiffs' theory of injury requires them to prove third-party reliance by doctors on Aventis's alleged misrepresentations in order to establish that those misrepresentations caused HBPs to pay for Ketek prescriptions that would not have been written otherwise. Aventis argues, and the district court held, that *Zyprexa* controls this case and forecloses class certification. We agree. As explained below, the proof offered by Plaintiffs here does not differ in any meaningful way from that offered by the *Zyprexa* plaintiffs, and *Zyprexa* accordingly establishes that Plaintiffs' generalized proof is insufficient to establish RICO causation for each member of the putative class. We therefore conclude that the district court did not abuse its discretion in denying class certification under Rule 23(b)(3).

1.

Plaintiffs' attempt to show class-wide causation through generalized proof centers on the premise that, unlike the prescribing decisions described in

Zyprexa—which were multifaceted and therefore called for individualized determinations as to whether the prescriptions had in fact been written because of Lilly's alleged fraud—physicians' prescribing decisions regarding Ketek were "more-or-less one-dimensional." Nagareda, *supra*, at 121. In other words, Plaintiffs argue that this case is more like *Klay* and *U.S. Foodservice* than it is like *Zyprexa*, *McLaughlin*, and *Poulos*. Plaintiffs contend that safety is the preeminent consideration in prescribing an antibiotic, so that had physicians known about Ketek's "true" risks, none of them would have prescribed it. On this logic, any Ketek prescription written without notice of the safety information allegedly withheld by Aventis was necessarily written in reliance on Aventis's nondisclosure of that information. This argument is not persuasive, and it entirely fails as a basis for distinguishing *Zyprexa*.[6]

[6] There are numerous other problems with Plaintiffs' theory of causation, which we largely set to the side for the purposes of our analysis—which assumes, as the district court did, that Aventis "allegedly violated RICO by fraudulently exaggerating the safety and efficacy of a prescription antibiotic in order to boost sales and revenues." *Sergeants IV*, 20 F. Supp. 3d at 323. Among these problems is the fact that the only safety information allegedly withheld by Aventis was a piece of data from Study 3014 purportedly showing that Ketek was three times more dangerous than Augmentin. Plaintiffs' theory appears to be that Aventis withheld this result from the FDA, rendering Aventis's marketing materials for Ketek misleading to the extent that those materials suggested that Ketek had "valid" regulatory approval. However, the record indicates both that the FDA was aware of Study 3014—including the specific piece of data mentioned by Plaintiffs, which was included in a report on Study 3014 that Aventis

Plaintiffs purport to demonstrate the one-dimensional nature of a physician's decision to prescribe Ketek by presenting evidence showing that sales of Ketek dropped precipitously after the FDA's public health advisory and Ketek's label revisions in 2006. According to Plaintiffs, this sequence of events illustrates that doctors *must* have prescribed Ketek in reliance on Aventis's misrepresentations prior to the new safety disclosures, because they stopped prescribing Ketek upon learning of that new information. Plaintiffs' expert, Dr. Meredith Rosenthal, testified that the drop in Ketek's sales was so precipitous that she had never seen anything like it—that even a drug's loss of patent protection generally did not cause such a slide in sales. J.A. 1134-35. Despite testifying that Ketek's sales history was unique in her experience, Dr. Rosenthal nonetheless opined that, "[i]n [her] experience," this unprecedented drop must have been caused entirely by the disclosure of Ketek's post-marketing safety data. J.A. 1135.

The decline in Ketek sales, combined with Dr. Rosenthal's testimony, cannot support an inference that all pre-disclosure Ketek prescriptions were

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submitted to the FDA—and that the FDA did not rely on it in approving Ketek for ABS, AECB, and CAP. It is difficult to understand, then, how Ketek did not have "valid" regulatory approval.

written in reliance on Aventis's alleged fraud, because we have already addressed precisely this kind of generalized proof in *Zyprexa* and held that it was insufficient to show class-wide RICO causation. There, too, the plaintiffs' expert simply "assumed" that a downturn in Zyprexa's sales was attributable to the disclosure of the previously hidden safety risks, thereby illustrating (in his view) that the difference between the number of prescriptions written before and those written after the disclosure was attributable to Lilly's alleged fraud. 620 F.3d at 135. We held that this generalized proof—which showed a simple correlation between the safety disclosure and the decline in prescriptions—was not enough for the plaintiffs to prove that each class member was injured by Lilly's alleged misrepresentations, in light of the multifaceted and individualized nature of physicians' prescribing decisions.

The same is true here: Ketek's declining sales may have been correlated with the issuance of the FDA's public health advisory and with Ketek's label revisions, but mere correlation does not demonstrate causation. *See, e.g.*, *Brown v. Entm't Merchs. Ass'n*, 131 S. Ct. 2729, 2739 (2011). Moreover, the weakness of the correlation-based inference that Plaintiffs ask us to draw is particularly stark in light of the fact that Ketek's lower sales were *also* correlated with significant

larger changes in the market for anti-infectives, including some of the dominant market players moving off-patent, as well as a growing scientific consensus that the entire field of anti-infective drugs was of dubious efficacy in treating Ketek's most popular indications, ABS and AECB.[7] Plaintiffs made no attempt to control for these other factors, or to supply any other information that might render reasonable the inference that the drop in sales was actually attributable to the safety disclosures, as opposed to other factors.

To be sure, it is possible (as the district court recognized) to envision a drug so dangerous that no physician would ever prescribe it to treat a non-fatal condition if that physician were aware of its true risks. And, in such an extraordinary case, a reasonable jury might well be able to infer solely from a precipitous drop-off in sales that any prescription for the drug was necessarily written in reliance on the defendant's concealment of the drug's risks. *See Sergeants IV*, 20 F. Supp. 3d at 327 ("Obviously, in situations where the health

[7] Plaintiffs concede that Ketek's final drop-off in sales was partly caused by Aventis's decision to stop actively promoting Ketek and to terminate its rebate contracts with PPMs, but argue that these are dependent rather than independent variables—that Aventis only stopped promotion and rebating because it had given up on Ketek's success. Even if we accept this premise, however, it merely begs the question *why* Aventis believed Ketek could no longer be a market success; Plaintiffs, of course, contend that Aventis gave up on Ketek because of the disclosure of post-marketing safety data, but this is merely their same *post hoc* argument over again.

risks of a drug are extremely severe, safety considerations might be the sole determinant of a physician's decision."). After all, the multitude of factors recognized in *Zyprexa* as entering into individual physicians' prescribing decisions—e.g., the age and sex of the patient, the availability of generics, or the patient's past reactions to a drug—would be irrelevant if a physician knew that the drug would cause certain death or, to take a less extreme example, if the physician knew that a drug meant to treat acne would cause blindness in a tenth of the patients who took it. The tradeoff simply would never be worth the risk. In such a case, the dangerousness of the drug would speak for itself, leaving open the possibility of proving class-wide RICO causation through "circumstantial proof," *McLaughlin*, 522 F.3d at 225 n.7, such as a precipitous drop-off in sales, rather than through individualized inquiries as to physicians' actual reliance. *Zyprexa* did not involve an extremely dangerous drug, so its class certification holding has little to say about cases that *do*.

Plaintiffs suggest that this *is* such a case—that Ketek is so dangerous that no reasonable physician would have prescribed it if the safety information allegedly withheld by Aventis had been known. But the record simply does not support this conclusion. The evidence adduced by Plaintiffs shows that Ketek

had risks. But it also shows that all antibiotics prescribed to treat respiratory infections have risks, and that Ketek's risks, while perhaps higher than those of most of its competitors, were well within the range of dangerousness typical of similar anti-infectives.[8] By the end of June 2006, after more than six million domestic Ketek prescriptions, only four deaths and approximately fifty-three serious hepatic adverse events had been linked to Ketek. Even assuming widespread underreporting of adverse drug events, that rate of adverse events is simply not enough to support an inference that Ketek was so seriously dangerous that no physician would ever have prescribed it had the safety information allegedly withheld by Aventis been made public earlier. Furthermore, as the district court observed, had doctors' prescribing decisions truly been one-dimensional, one would expect sales of Ketek to cease entirely after the new safety information was made available. But Ketek's "[s]ales did not

[8] Even the drugs that we consider most benign can carry surprisingly serious risks. *See, e.g.*, Food & Drug Admin., *Acetaminophen Overdose and Liver Injury—Background and Options for Reducing Injury* (2009), http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM164897.pdf (noting that acetaminophen (a drug found in numerous over-the-counter products, including Tylenol) "was the leading cause of acute liver failure in the United States," *id.* at 2, in part because "[c]onsumers may consider acetaminophen a familiar product [and] assume that the medicine is completely safe," *id.* at 4).

drop to zero immediately after the FDA issued a public health advisory relating to Ketek's liver toxicity in January 2006. Rather, sales declined in a manner consistent with the cyclical manner in which sales had declined during the same months the previous year." *Sergeants IV*, 20 F. Supp. 3d at 327.

Plaintiffs point to two sources of evidence supporting their argument that no doctor would have prescribed Ketek if its true risks had been known earlier. First, Plaintiffs argue that the FDA's withdrawal of approval for two of Ketek's indications and imposition of a black box warning demonstrate Ketek's dangers. But the record shows that the vote at the December 2006 joint committee meeting to withdraw those indications was not motivated purely or even predominantly by safety: many voting attendees did not mention safety at all, but rather explained their votes on the basis of effectiveness, citing concerns that Ketek might not be any better than a placebo at treating ABS and AECB. And the black-box warning added to Ketek's label had nothing to do with Ketek's hepatic risks: it was imposed in connection with Ketek's tendency to exacerbate the symptoms of patients afflicted with the rare neurological disorder myasthenia gravis. *See* J.A. 1725.

Second, Plaintiffs argue that data from Study 3014—data that they claim Aventis withheld from the FDA—revealed that Ketek was three times more likely than Augmentin to cause serious hepatic adverse events. But Plaintiffs' position throughout this litigation, including on appeal, has been that Study 3014 was plagued with fraud and therefore unreliable. And on this point, Plaintiffs are absolutely correct. The doctors responsible for conducting Study 3014 invented patients out of whole cloth, among a host of other failures that tainted the data with "fraud." J.A. 647, 6498. Plaintiffs' assertion that a specific Study 3014 result would have revealed the true danger of Ketek if only it had been disclosed to the FDA therefore strains credulity. The Study 3014 numbers reveal nothing, because they are utterly unreliable and probably fictional. Plaintiffs cannot describe Study 3014 as fraudulent when it is to their advantage while simultaneously arguing that its findings are material and would have changed the FDA's approval decision—and physicians' prescribing decisions—if made public. Accordingly, the alleged "three times as dangerous" result also does not show that no doctor would have prescribed Ketek absent Aventis's alleged misrepresentations.

2.

As the foregoing discussion illustrates, Plaintiffs' theory in this case is effectively all-or-nothing: Plaintiffs seek to persuade us that *every* individual physician's decision to prescribe Ketek was truly a "one-dimensional" decision based entirely on safety, and that the safety information allegedly withheld by Aventis was so significant that it would dictate *every* physician's decisionmaking, based on nothing more than a decline in Ketek's sales figures. We have explained why this theory fails: on this record (as in *Zyprexa*), given the number of factors that enter into doctors' prescribing decisions, it is simply not reasonable to infer from just that decline in sales that all pre-decline Ketek prescriptions were written in reliance on the alleged misrepresentations about Ketek's safety. In contrast to the hypothetical case of an extremely dangerous drug, the record here does not suggest that the safety information allegedly withheld by Aventis—which revealed Ketek to be at most marginally more dangerous than comparable antibiotics—would reasonably be expected to have such a significant impact on the number of prescriptions written. This strongly suggests that something other than Aventis's alleged misrepresentations was at least partly responsible for the decline in sales, which in turn suggests that physicians' pre-decline prescription

decisions were not, in fact, based solely on their misperception of Ketek's relative safety. Plaintiffs' all-or-nothing theory thus simply does not hold up.

We wish to note, however, that it may be possible to demonstrate class-wide RICO causation in a case such as this one by adducing generalized proof from which a reasonable jury could conclude that only *some* prescriptions paid for by each class member were written based on the defendant's alleged misrepresentations. In other words, not all claims of this type must necessarily be all-or-nothing claims. In cases in which *first*-party reliance is a necessary part of the plaintiffs' chain of causation—as in *McLaughlin* and *Poulos*—the plaintiff class has no choice but to show through generalized proof that *each one* of them relied on the defendant's alleged misrepresentations; otherwise, the misrepresentations could not have caused an injury to each class member. The situation is arguably somewhat different in a third-party reliance case like this one. Here, the question is whether Aventis's misrepresentations caused an injury to *each HBP*, and because each HBP paid for numerous Ketek prescriptions, each would have been injured by Aventis's misrepresentations so long as at least some of the prescriptions for which it paid were written in reliance on those misrepresentations. While a RICO plaintiff must always show that the

defendant's conduct caused an "*actual*, quantifiable injury," *McLaughlin*, 522 F.3d at 227, the precise number of excess prescriptions paid for by each HBP would seem to bear on the damages suffered by each class member, and not on the separate question whether Aventis's misrepresentations caused each class member to suffer an injury.[9] *See In re Neurontin Mktg. & Sales Practices Litig.*, 712 F.3d 21, 34 (1st Cir. 2013) (asking whether "absent [the defendant's] fraud, [the plaintiff] would have paid for fewer . . . prescriptions"); *BCS Servs., Inc. v. Heartwood 88, LLC*, 637 F.3d 750, 759 (7th Cir. 2011) (finding that "[t]he [district court] . . . confused proof of causation with proof of amount of damages and so denied the plaintiffs the benefit of the easier burden of proving damages than of causation").

Even if we were to read Plaintiffs' claim to be of this more nuanced type, requiring only a showing that Aventis's alleged misrepresentations caused each

[9] As an alternative argument in favor of affirming the district court's class-certification decision, Aventis claims that the damages model proffered by Plaintiffs is insufficient to demonstrate damages on a class-wide basis. *See Comcast Corp. v. Behrend*, 133 S. Ct. 1426, 1433-35 (2013) (reversing a lower court's certification of a class on the basis of this argument). We do not reach this alternative argument because we conclude that Plaintiffs cannot prove class-wide causation using generalized proof for the reasons given in the text. But unlike in this case, in which Plaintiffs have sought damages on a class-wide basis, it may be possible in other cases to certify a class as to liability while leaving damages to be ascertained on an individualized basis—in which case *Comcast*'s guidance on aggregate damages would be largely irrelevant. *See Butler v. Sears, Roebuck & Co.*, 727 F.3d 796, 800 (7th Cir. 2013).

HBP to suffer an injury, Plaintiffs' generalized proof in this case still falls short. At least where (as here) there is no basis for inferring that the drug in question was so dangerous that no doctor would prescribe it if its true risks were disclosed, *Zyprexa* establishes that mere correlation between a decline in prescriptions and a disclosure of allegedly withheld information is insufficient to prove class-wide RICO causation on the theory that the defendant's withholding of safety information caused doctors to write excess prescriptions. To ultimately find a defendant liable, a jury must be able to base its decision on something firmer than speculation. *See Anderson v. Liberty Lobby*, 477 U.S. 242, 247-52 (1986). As in *Zyprexa*, the kind of correlation evidence presented here does not furnish a sound basis to find causation on a class-wide basis.

Plaintiffs did not attempt to offer anything beyond mere correlation that might support a reasonable inference that Aventis's alleged withholding of safety information played a legally sufficient causal role in the number of Ketek prescriptions written. Significantly, Dr. Rosenthal conceded that she had not been asked by Plaintiffs' counsel to perform the kind of regression analysis that might have isolated the relative causal effect of the numerous variables bearing on the decline in Ketek's sales. *See* J.A. 1163 ("Q: [Y]ou haven't attempted in this

case, to undertake a cause-and-effect analysis relating to the various factors that could have led to the decline in Ketek's sales . . . , correct?" "A: That's correct. . . . I was not asked to conduct a specific regression analysis which might be the kind of analysis that an economist would undertake.").[10] Regression models are a well-known and widely accepted tool of economic analysis, and while they "cannot explicitly determine causation or prove causality between . . . variables," they can strongly support a causal relationship between two variables (here, safety disclosures and sales) by ruling out or limiting the influence of other variables, or by demonstrating that those other variables are themselves merely a

[10] When asked how much of the decline in Ketek's sales was attributable to normal seasonal patterns, Dr. Rosenthal responded that she "ha[d]n't been asked to quantify specifically the effects of the diffusion of information over this period separately from other effects." J.A. 2930. She also stated that she "ha[d] not quantified the effect of [contracting or rebating changes] on total sales," J.A. 2931, and had "not been asked to quantify" the effects of the January 2006 public health advisory versus the effects of the withdrawal of two of Ketek's indications in February 2007, and thus could not "analyze them separately," J.A. 2924. Finally, Dr. Rosenthal did not "make any attempt to analyze the impact of the entry of authorized generics in the market and the impact that may have had on Ketek sales." J.A. 2929. Although Dr. Rosenthal testified that "the literature in pharmaceutical economics . . . shows that generic entry for a therapeutically equivalent product has little, if any effect on a given brand name drug," J.A. 1155, she also conceded that the entry of an authorized generic drug into the market "could have had an impact," albeit "[a]n undefined small percentage," J.A. 1166. Whether this "small percentage" for each new generic would be multiplied for each of the five anti-infectives that became available as generics during Ketek's sales period or not, and whether the effect of a drug going off-patent remains small even if that drug, like Zithromax, was the market leader, are questions that Dr. Rosenthal did not address.

function of one of the first two. Andrew Dick & Peter Boberg, *Regression Analysis*, Antitrust 89 (Fall 2005). "At no time did Dr. Rosenthal say that a regression analysis could not be performed due to the lack of data or some other problem, or that a regression analysis would be inappropriate in this case." *Sergeants I*, 2011 WL 824607, at *10 n.16.

The simplistic nature of Dr. Rosenthal's analysis here distinguishes this case from the First Circuit's decision in *In re Neurontin Marketing & Sales Practices Litigation*—another case in which Dr. Rosenthal served as the plaintiffs' expert. In *Neurontin*, the plaintiffs were HBPs who alleged that the pharmaceutical company Pfizer had violated RICO by fraudulently marketing the drug Neurontin, which had only been approved by the FDA for the treatment of seizures, as an effective off-label treatment for bipolar disorder, neuropathic pain, and migraines. 712 F.3d at 27-28. The First Circuit's decision did not involve class certification, but in the course of affirming a jury verdict in the plaintiffs' favor, the court rejected Pfizer's contention that the plaintiffs had offered insufficient proof that Pfizer's misrepresentations caused doctors to write excess prescriptions paid for by the plaintiffs. The plaintiffs did not rely on individualized evidence that doctors had, in fact, relied on Pfizer's

misrepresentations, and instead presented an aggregate "regression analysis" performed by Dr. Rosenthal "on sales information against promotional spending on detailing, professional journal advertising, and the retail value of samples, while controlling for other variables." *Id.* at 30. The First Circuit concluded that Dr. Rosenthal's analysis, which determined that "Pfizer's [off-label] marketing had a causal effect on prescribing behaviors," *id.* at 45, was sufficient to support the jury's finding of RICO causation, *id.* at 45–47. Significantly, the *Neurontin* court stressed the differences between Dr. Rosenthal's analysis there and the mere correlation evidence relied upon by the plaintiffs in *Zyprexa*, which did "not come close to resembling Dr. Rosenthal's evidence." *Id.* at 46; *see also id.* (noting that in *Zyprexa*, "the plaintiffs' aggregate evidence of causation . . . involv[ed] only an extrapolation from the fact that the number of off-label prescriptions for Zyprexa fell after Eli Lilly's fraud became known").

As noted, the First Circuit did not address class certification in *Neurontin*, so it did not have occasion to hold squarely that a class of HBPs could succeed in proving class-wide RICO causation based on a regression analysis. In particular, the First Circuit was not required to decide whether Dr. Rosenthal's analysis—which it held was sufficient to support a finding that the specific HBPs before the

court had suffered an injury caused by Pfizer's misrepresentations—would also be sufficient to support the broader finding (necessary when class certification is at issue) that all HBPs in a class had suffered an injury caused by those misrepresentations. Nonetheless, *Neurontin* does indicate that where individual physicians' reliance on a pharmaceutical company's misrepresentations forms a necessary link in the causal chain between those misrepresentations and the plaintiffs' injury, such reliance can be proved to a jury with sufficiently powerful aggregate evidence, as opposed to individualized inquiries as to each prescribing physician's actual decisionmaking.

In any event, we need not (and do not intend to) express any view here on whether or when an aggregate regression analysis similar to the one deployed in *Neurontin* might be sufficient to prove causation on a class-wide basis in other pharmaceutical-marketing cases alleging a pattern of mail fraud actionable under RICO. Here, Plaintiffs' causation evidence—apparently by their own choice—is akin to the simplistic proof introduced by the *Zyprexa* plaintiffs, and not to the far more sophisticated proof offered in *Neurontin*. Because *Zyprexa* controls, we conclude that Plaintiffs are unable to show RICO causation by generalized proof,

and we accordingly conclude that the district court did not err in denying Plaintiffs' class-certification motion.

II.

The district court granted summary judgment to Aventis on Plaintiffs' RICO claims, relying on *Zyprexa* to hold that generalized proof of causation was impossible because of the intervening actions of prescribing physicians. As explained above, this conclusion—that Plaintiffs cannot prove third-party reliance, and thus causation, by generalized proof—is sound. On appeal, Plaintiffs do not criticize the district court's decision on any grounds particular to summary judgment, but rather continue to argue, as they did in the class certification context, that they can prove their claim by generalized evidence. As we have explained, they cannot.

This might be the end of the inquiry, but we observe that *Zyprexa* declined to extend its class certification holding regarding the quantity effect theory to also decide Lilly's motion for summary judgment: "while that theory cannot support class certification," the *Zyprexa* Court noted, "it is not clear that the theory is not viable with respect to individual claims by some [HBPs] or other purchasers." 620 F.3d at 136. The *Zyprexa* court thus "decline[d] to consider

whether summary judgment with respect to the quantity effect theory is appropriate in the first instance." *Id.*

In keeping with the distinction drawn in *Zyprexa*, we reaffirm that a plaintiff is not necessarily foreclosed from bringing a RICO claim merely because its attempt to certify a class using generalized proof has failed. As noted, moreover, it may be possible for a plaintiff to establish its own claim (as opposed to the claims of each class member) using aggregate statistical proof—i.e., without having to show the individual reliance of thousands of prescribing doctors—provided that such proof is more robust, and therefore more probative of causation, than the simplistic correlation evidence presented here.[11] *See, e.g.*, *Neurontin*, 712 F.3d at 45-47. But the correlation evidence offered by Plaintiffs here is no more probative as to whether Aventis's alleged fraud caused Plaintiffs themselves to suffer an injury than it is as to whether that alleged fraud caused an injury to each HBP in the putative class. Nor have Plaintiffs offered any other kind of proof that might show that they themselves, if not all class members, suffered an injury by reason of Aventis's alleged fraud. *See Sergeants IV*, 20 F.

[11] We do not express any view on what evidence Plaintiffs might have presented in order to succeed on their individual claims, as Plaintiffs neither assert that they have put forth such proof nor challenge the district court's conclusion that they have not done so.

Supp. 3d at 328-29 ("Since Plaintiffs do not argue that they are prepared to offer individualized proof, . . . Defendants are entitled to summary judgment on the RICO claims."). Accordingly, Plaintiffs cannot prove the causation element of their RICO claims, and we therefore affirm the district court's grant of summary judgment to Aventis on those claims.

III.

We affirm the dismissal of Plaintiffs' state-law claims for substantially the reasons stated by the district court in its well-reasoned opinion.

CONCLUSION

We have considered Plaintiffs remaining contentions and find them to be without merit. For the foregoing reasons, we **AFFIRM** the orders of the district court denying Plaintiffs' motion for class certification and granting Aventis's motion for summary judgment.