PRECEDENTIAL

UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

No. 25-2278

In re: AVANDIA MARKETING, SALES PRACTICES and PRODUCTS LIABILITY LITIGATION,

GlaxoSmithKline LLC,

Appellant

On Appeal from the United States District Court
for the Eastern District of Pennsylvania
(D.C. Civil Action No. 2:07-md-01871)
District Judge: Honorable Cynthia M. Rufe

Argued on February 26, 2026

Before: SHWARTZ, MONTGOMERY-REEVES, and AMBRO, *Circuit Judges*

(Opinion filed July 21, 2026)

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OPINION OF THE COURT

AMBRO, *Circuit Judge*

We do not presume in law that *x* caused *y* merely because *x* happened first. The connection might be causal. But it might be coincidental. Or some *z* might be responsible for *x* and *y* alike. As statisticians emphasize, correlation alone does not prove causation.

One method experts have developed for distinguishing true causation from mere correlation is multiple regression analysis. It can "define statistically the relationship between a dependent variable (*e.g.*, salary) and one or more independent variables (*e.g.*, education or work experience)," enabling us to conclude with confidence that the latter is the reason for the former (or is at least one reason). *Weisfeld v. Sun Chem. Corp.*, 84 F. App'x 257, 261 n.3 (Table) (3d Cir. 2004); *see also* 1 David L. Faigman *et al.*, Mod. Sci. Evidence § 6.1 (2025-2026 ed.). It can also enable us "to control for other independent variables" so we can rule out competing explanations (or at least rule them unlikely). *Id.* And it can quantify how much of a difference the cause makes to the effect. Thus, although it may be that "[t]he only empirical facts . . . we can discover about the world are facts about correlation," regression analysis can justify the "inference" of causation by "testing and attempted invalidation" of other "causal hypotheses." *See United States v. Mosley*, 454 F.3d 249, 266 (3d Cir. 2006).

This appeal raises this issue and more. Third-party payors ("TPPs") who covered prescriptions for the diabetes medication Avandia brought a putative class action against the manufacturer, GlaxoSmithKline LLC ("GSK"), for misrepresenting the drug's cardiovascular risks and benefits. GSK's misrepresentations, they claim, caused more health care

providers (we use "physicians," "prescribers," and similar terms interchangeably) to prescribe Avandia than cheaper alternatives. That, in turn, allegedly caused these TPPs to reimburse patients for Avandia that otherwise would not have been prescribed.

GSK challenges the District Court's certification of the class. It argues the proposed class is not ascertainable because there is not enough evidence to identify which TPPs reimbursed members for the drug. And it contends common issues do not predominate on causation because the plaintiffs lack class-wide evidence GSK's fraud caused them to cover more Avandia prescriptions than they would have otherwise. Their evidence, GSK contends, shows only correlation, not causation.

Though we hold the proposed class is ascertainable, we part with the District Court's ruling that common issues would predominate on causation. We join the other circuits that have addressed this issue—the First, Second, and Ninth—and conclude that plaintiffs in a pharmaceutical fraud RICO class action may use statistical evidence to prove the defendant was responsible for their injuries when the evidence can establish causation, not merely correlation. The Plans' statistical evidence does not satisfy this standard yet. After laying out the type of statistical evidence that may be used to prove causation in a case like this one, we vacate the District Court's certification of the class and remand for further fact-finding on predominance under the clarified standard.

I. BACKGROUND

In 1999, the Food and Drug Administration ("FDA") approved a new treatment for Type II diabetes: Avandia.[1] GSK, its developer, sold it for a higher price than the drug's older rivals, like metformin. But GSK said Avandia was worth the premium. According to the pharmaceutical company's marketing, Avandia would not help patients manage only their blood sugar. It would also reduce their cardiovascular risks. To diabetics, that mattered. Roughly two-thirds of diabetes patients die of cardiovascular conditions. So despite Avandia's higher cost, health insurers added it to their formularies and reimbursed patients. In the years following FDA approval, Avandia prescriptions soared. In 2006 alone, GSK sold $2.2 billion of the drug in the United States.

Meanwhile, GSK's own research began to suggest an inconvenient truth: the drug actually posed distinctive cardiovascular risks. In 2004, GSK began an internal meta-analysis, that is, a study of what existing clinical trials indicated about Avandia's cardiovascular profile. *See In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829, 856 (3d Cir. 1990) (defining as "meta-analysis" a study "combining the results of different . . . studies done by other scientists, and re-analyzing the combined data to see if the data, *in toto*, renders different results than the individual studies done with a smaller data sample"). That September, it completed its initial review of those trials, the precursor to the study later dubbed ICT-37.

[1] We limit our recitation of the facts, as we have recounted them in two prior precedential opinions in this case. *See In re Avandia Mktg., Sales Practices & Prod. Liab. Litig.*, 804 F.3d 633 (3d Cir. 2015); *In re Avandia Mktg., Sales Practices & Prod. Liab. Litig.*, 945 F.3d 749 (3d Cir. 2019), *cert. denied*, 141 S. Ct. 265 (Mem).

GSK did not complete the meta-analysis and present the results to its safety board as ICT-37 until a year later, September 2005. The conclusion: Avandia was associated with a statistically significant increase of serious ischemic events (compromises of the blood flow to the heart causing heart attack, disability, or death). GSK nonetheless did not immediately update the drug's label or ask the FDA for permission to do so.

In February 2006, GSK completed a new meta-analysis, reexamining the results of the clinical trials it examined in ICT-37 and evaluating five additional ones. This study, ICT-42, reached the same conclusion: Avandia posed serious cardiovascular risks. In August the same year, the company asked the FDA for permission to add a warning to Avandia's label, notifying patients that ICT-42 found the drug caused a statistically significant risk of an increase in myocardial ischemic events. In May 2007, GSK also asked to make that warning clearer and more prominent.

Then—before the FDA had ruled on either of these requests—the truth reached the public. The *New England Journal of Medicine* published a study of Avandia by Dr. Steve Nissen (the "Nissen study"). It found Avandia "was associated with a significant increase in the risk of myocardial infarction and with an increase in the risk of death from cardiovascular causes that had borderline significance." JA 443. The FDA denied GSK's requests to change the label, then demanded that it make more dramatic changes to address the Nissen study and other emerging research. By the end of 2007, the FDA had directed GSK to add a "black-box warning"[2] conveying that

[2] Though officially called a "boxed warning," the term refers to the FDA's most stringent safety alert communicated through

Avandia could cause or exacerbate congestive heart failure and increase the risk of myocardial ischemic events.

Prescriptions plummeted. Between 2004 and 2006, doctors prescribed Avandia about 1.2 million times per month. By the end of 2007, that number was below 500,000 prescriptions per month. After over 50 additional clinical trials, the FDA enhanced the black-box warning and restricted distribution of Avandia.[3]

Consequences followed. In 2012, GSK pled guilty to one count of failing to report clinical data to the FDA and agreed to pay a criminal fine of nearly $250 million. GSK also reached a civil settlement for misrepresenting Avandia's cardiac risks in violation of the False Claims Act, 31 U.S.C. § 3729, and agreed to pay the federal Government over $500 million.

United Food and Commercial Workers Local 1776 and Participating Employers Health and Welfare Fund ("UFCW"), along with J.B. Hunt Transport Services, Inc. ("J.B. Hunt"), provide prescription drug coverage to their members or employees. In 2010, they sued GSK on behalf of a proposed

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a bold, black-bordered notice atop a drug's label or package insert. *See generally* 21 C.F.R. § 201.57(c)(1) (explaining that black-box warnings reveal "[c]ertain contraindications or serious warnings, particularly those that may lead to death or serious injury").

[3] In 2013, the FDA relaxed these restrictions and removed the black-box warning for myocardial ischemic events (blocked blood vessels), but it retained the one for myocardial infarction (heart attack).

class of TPPs (the "Plans") that paid for Avandia, alleging violations of the Racketeer Influenced and Corrupt Organizations Act ("RICO"), 18 U.S.C. § 1962(c), and a host of state laws. Their cases were combined into the *In re Avandia Marketing, Sales Practices and Products Liability* multi-district litigation.

The Plans alleged GSK fraudulently misrepresented Avandia's true cardiovascular profile, marketing the drug for its supposed cardiovascular benefits while failing to disclose its real cardiovascular risks. In reliance on GSK's misrepresentations, they included Avandia on their formularies even though the drug cost more than the alternatives and covered more Avandia prescriptions than they would have absent the fraud.

GSK moved to dismiss the complaint for failure to state a claim, contending in relevant part that the Plans had failed to allege plausibly they suffered an economic injury and that GSK's alleged fraud was its proximate cause. *In re Avandia Mktg., Sales Practices & Prod. Liab. Litig.*, 804 F.3d 633, 637 (3d Cir. 2015) ("*Avandia I*"). The District Court denied the motion as to the RICO claim, holding the plaintiffs plausibly alleged GSK's misrepresentations about Avandia's cardiac benefits deprived them of "the substantial savings they would have experienced had they covered cheaper alternatives to Avandia." *Id.* We affirmed. *Id.* at 634.

In 2016, GSK moved for summary judgment on the grounds the federal Food, Drug, and Cosmetic Act, 21 U.S.C. Ch. 9, preempted the remaining state law claims and that the Plans had failed to create a genuine dispute of material fact about the existence of a RICO enterprise. *In re Avandia Mktg.,*

Sales Practices & Prod. Liab. Litig., 945 F.3d 749, 756 (3d Cir. 2019), *cert. denied*, 141 S. Ct. 265 (Mem). The District Court granted summary judgment for GSK. *Id.* We reversed the Court's order on the state law claims and vacated its order on the RICO claims, holding the Plans were entitled to discovery on the latter. *Id.* at 752–53.

In May 2023, the Plans moved to certify the following class:

> All entities in the United States of America and its territories, which indirectly purchased, and/or provided reimbursement for some or all of the purchase price for the drugs Avandia, Avandamet, and/or Avandaryl from May 25, 1999 until August 14, 2007.[4]
>
> Included in the Class are self-insured non-governmental entities and third-party payers that offer insured plans to private individuals and groups. Likewise third-party payers that offer insured plans to government entities including the Federal Employee Program, Managed Medicaid, and Medicare Part D are class members.

They also proposed five exclusions:

> (i) governmental entities other than municipalities and/or local governments with self-funded prescription drug plans; (ii) fully

[4] We use Avandia throughout to refer to all three drugs.

> insured health plans, i.e., plans for which the insurer bears 100% of the risk for the reimbursement obligations to members; (iii) pharmacy benefit managers; (iv) natural person consumers; and (v) employees of [GSK], including its officers or directors, and subsidiaries and affiliates.

And they later agreed to narrow the class period to January 1, 2005 to August 14, 2007.

In support of their motion for class certification, the Plans moved to introduce two expert reports. The first, from Dr. Meredith Rosenthal, sought to prove causation. She offered two main opinions: (a) GSK's misrepresentations of Avandia's health benefits were responsible for a significant portion of the prescriptions the Plans covered; and (b) 41% of prescriptions in the class period would not have happened but for the fraud. Dr. Rosenthal based these conclusions on a multiple regression analysis performed to isolate the causal significance of GSK's misrepresentations on prescription volume.

The Plans introduced the second report, from Dr. Thomas McGuire, to prove damages. Using several models, he estimated damages totaling between $500 million and over $2 billion. As relevant here, one model—the Scenario 1 Step Down Adjustment—assumed the earlier publication of ICT-37 would have caused a similar decline in prescriptions as did the actual publication of the Nissen study. On that assumption, Dr. McGuire calculated damages by applying the percentage decline in prescriptions after that study to the earlier time period and estimated damages of around $1 billion.

GSK moved to exclude both reports. In October 2024, after a *Daubert* hearing, the District Court granted GSK's motion to exclude the Rosenthal report and granted in part and denied in part its motion to exclude the McGuire report. The Court found Dr. Rosenthal's opinions unreliable because her regression model deviated from the standards of her field and the deviations were consequential. The model appeared "results-oriented" and particularly susceptible to false positives. *In re Avandia Mktg., Sales Pracs. & Prods. Liab. Litig.*, No. 07-MD-1871, 2024 WL 4582876, at *10–11 (E.D. Pa. Oct. 25, 2024). For instance, not only did it show a statistically significant positive causal relationship between prescription volume and GSK's promotion of Avandia, it also indicated a statistically significant positive causal relationship between prescription volume and obviously irrelevant variables, like U.S. carbon emissions. So the District Court granted the motion to exclude it. The Court found one of Dr. McGuire's models unreliable because it depended on Dr. Rosenthal's opinions and rejected others as unreliable on their own merits. The Court nonetheless left one standing: the Scenario 1 Step Down Adjustment, explained above. The Plans did not appeal the District Court's evidentiary rulings.

In May 2025, the District Court granted the Plans' motion to certify the class. First, it held the proposed class satisfied the elements of Federal Rule of Civil Procedure 23(a): numerosity, commonality, typicality, and adequacy of representation. GSK did not contest any of the Rule 23(a) issues. Second, the Court ruled that the proposed class satisfied Rule 23(b)(3); in relevant part, it held the Plans established that common questions would predominate and that the proposed class was ascertainable.

GSK argued the Plans had not proven common questions would predominate on one element of their RICO claim: causation. The Plans advanced a quantity-effect theory of causation: that GSK's misrepresentations about Avandia's cardiac profile led doctors to issue more Avandia prescriptions, which in turn led the Plans to reimburse more prescriptions for this expensive drug. GSK claimed that individualized issues would predominate over common ones. It offered two arguments on this point.

First, GSK insisted, questions of reliance are typically individual questions: they turn on why particular doctors issued particular prescriptions to particular patients. Matters like that, it said, are not susceptible to proof by class-wide evidence. The District Court rejected GSK's argument. It held that the Plans had introduced enough common evidence to justify an inference of "class-wide reliance," emphasizing two forms of evidence. *In re Avandia Mktg., Sales Pracs. & Prods. Liab. Litig.*, No. 07-MD-1871, 2025 WL 1479618, at *7 (E.D. Pa. May 22, 2025). They had common evidence of the alleged uniform scheme to cover up the drug's dangers, like marketing materials touting Avandia's cardiac benefits and testimony from GSK employees about the success of that marketing. And they also had, the District Court found, statistical evidence that GSK's marketing mattered: internal GSK studies showed that some of its marketing campaigns increased prescriptions**.** Together, the Court determined, these two forms of common evidence could prove causation.[5]

[5] Along the way, it rejected GSK's argument that the individualized nature of providers' decision-making precluded an inference of reliance. As the Court saw the matter, "even though the decision to prescribe Avandia is not 'one-

Second, GSK argued, even if causation could be proven on a class-wide basis by these two forms of common evidence, the evidence here was insufficient. Specifically, according to GSK, its internal studies played a key role in the Plans' common evidence. But those studies did not isolate causation. And, without causation isolated, they could not serve as class-wide evidence capable of proving it. While the District Court acknowledged GSK's second argument, it did not articulate the reasons for rejecting it.

On ascertainability, the Plans proposed to identify members of the class through a combination of drug purchase records for GSK, a data publisher's list of entities that paid for Avandia, and a pharmaceutical database, supplemented by affidavits to confirm membership. GSK argued there would not be enough reliable evidence to determine which prospective class members had actually covered Avandia prescriptions. After a careful review of the record, the District Court rejected these concerns. So it held the class was ascertainable and granted the motion to certify.

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dimensional,' it is not so subjective that a provider's reliance cannot be inferred." *Avandia*, 2025 WL 1479618, at *8. It acknowledged "there are many factors that impact a provider's decision to prescribe one medication over another." *Id.* Yet it perceived "every provider's goal when considering whether to prescribe Avandia is largely the same—to treat a patient's diabetes without otherwise causing harm to their health." *Id.* And it thought "providers generally consider the same set of factors" with minimal patient-by-patient variation. *Id.*

In June 2025, GSK petitioned us for permission to appeal under Federal Rule of Civil Procedure 23(f). We granted it, and this appeal followed.

II. JURISDICTION AND STANDARDS OF REVIEW

The District Court had jurisdiction under 28 U.S.C. § 1331. We have jurisdiction under 28 U.S.C. § 1292(e) and Federal Rule of Civil Procedure 23(f). We review the certification of a class for abuse of discretion, "which occurs if the district court's decision rests upon a clearly erroneous finding of fact, an errant conclusion of law, or an improper application of law to fact." *In re Hydrogen Peroxide Antitrust Litig.*, 552 F.3d 305, 312 (3d Cir. 2008) (cleaned up).

III. DISCUSSION

GSK challenges the District Court's holdings that the class is ascertainable and that common issues would predominate on causation. We asked the parties to brief a third, threshold issue: the scope of our review of a Rule 23(f) appeal. That is where we begin.

A. We may limit the scope of our review under Rule 23(f).

Rule 23(f) provides that a "court of appeals may permit an appeal from an order granting or denying class-action certification under this rule." Fed. R. Civ. P. 23(f). The text does not expressly address whether a motions or merits panel may limit review to specific questions. No precedent of ours directly answers this question either. However, since Rule 23(f)'s inception, we have analogized it to another interlocutory appeal provision, 28 U.S.C. § 1292(b). Under that

subsection, we may choose which issues we review when we accept and decide an appeal. For this reason, we now hold we have the same discretion under Rule 23(f).

Rule 23(f) models § 1292(b). *Newton v. Merrill Lynch, Pierce, Fenner & Smith, Inc.*, 259 F.3d 154, 163 (3d Cir. 2001) (citing 7B Charles Alan Wright, Arthur R. Miller & Mary Kay Kane, Fed. Prac. & Proc. § 1802 (West Supp. 2000)). The statute authorizes us to permit an interlocutory appeal of a non-final order that "involves a controlling question of law as to which there is substantial ground for difference of opinion" where "an immediate appeal from the order may materially advance the ultimate termination of the litigation." 28 U.S.C. § 1292(b). As the Supreme Court has explained, "[c]ourts of appeals wield 'unfettered discretion' under Rule 23(f), akin to the discretion afforded circuit courts under § 1292(b). But Rule 23(f) otherwise 'departs from the § 1292(b) model,' for it requires neither district court certification nor adherence to § 1292(b)'s other 'limiting requirements.'" *Microsoft Corp. v. Baker*, 582 U.S. 23, 31 (2017) (quoting Comm. Note on Rule 23(f)). In short, Rule 23(f) is the class-action version of § 1292(b), save that it confers on courts of appeals even greater discretion.

Under § 1292(b), we may choose which issues to review. The Supreme Court has taken care to use permissive rather than mandatory language in characterizing appellate courts' power over the scope of our review in § 1292(b) appeals. *Yamaha Motor Corp., U.S.A. v. Calhoun* held that a court of appeals has appellate jurisdiction over the entire order certified for appeal because "it is the order that is appealable," not the certified question. 516 U.S. 199, 205 (1996) (emphasis omitted) (quoting 9 J. Moore & B. Ward, Moore's Federal

Practice ¶ 110.25[1], p. 300 (2d ed. 1995). The Court could have said a court of appeals *must* consider every question the parties raise. It did not. Instead, it consistently said that appeals courts *may* do that. *See, e.g.*, *id.* at 205.

We too have taken care to use permissive words like "may" and "can," rather than mandatory language like "must" or "shall," in the § 1292(b) context. *See, e.g.*, *Lundeen v. 10 W. Ferry St. Operations LLC*, 156 F.4th 332, 337 (3d Cir. 2025) ("Although the District Court certified a single question, our review *may* reach any matter 'fairly included within the certified order.'" (emphasis added) (quoting *Barbato v. Greystone All., LLC*, 916 F.3d 260, 264 (3d Cir. 2019))); *Gruber v. Price Waterhouse*, 911 F.2d 960, 963 (3d Cir. 1990) ("[S]ince we review orders and not isolated legal questions, we *may* consider all grounds that might require reversal of the order." (emphasis added) (citation omitted)); *see also McMunn v. Babcock & Wilcox Power Generation Grp.*, 869 F.3d 246, 266 (3d Cir. 2017) (noting "may" is permissive).

This permissive language is no accident. It reflects the position we adopted around the same time we started writing on these discretionary terms: on a § 1292(b) appeal, "we are free to consider 'all grounds advanced in support of [reversal] and all grounds suggested for [affirmance].'" *See Miller v. Bolger*, 802 F.2d 660, 666 (3d Cir. 1986) (quoting *Struble v. N.J. Brewery Emps.' Welfare Tr. Fund*, 732 F.2d 325, 336 n.10 (3d Cir. 1984)). "In deciding whether to exercise that power, we are guided by prudential considerations"—not by any obligation to consider every challenge the appellant raises. *Id.*

Were there any doubt, in 1988 our full Court adopted these expressly permissive terms for § 1292(b) appeals,

providing that we "*may* consider all grounds that might require reversal of the order appealed from." *In re Data Access Sys. Sec. Litig.*, 843 F.2d 1537, 1539 (3d Cir. 1988) (*en banc*) (emphasis added) (citing *Merican, Inc. v. Caterpillar Tractor Co*., 713 F.2d 958, 962 n.7 (3d Cir. 1983)), *superseded on other grounds by statute as stated in In re Exxon Mobil Corp. Sec. Litig.*, 500 F.3d 189, 198 (3d Cir. 2007).

We have refused to consider a ground for reversal on a § 1292(b) appeal at least three times: in *Miller*, 802 F.2d at 666–67; *Resol. Tr. Corp. v. Cityfed Fin. Corp.*, 57 F.3d 1231, 1236 & n.6 (3d Cir. 1995), *vacated on other grounds sub nom. Atherton v. FDIC*, 519 U.S. 213 (1997); and most recently in this very case. A decade ago, we heard an appeal from the District Court's denial of GSK's motion to dismiss for failure to state a claim. *See Avandia I*, 804 F.3d at 637. GSK had moved to dismiss all of the Plans' claims, federal and state. *See id.* at 636–37 & n.9. The District Court certified for appeal three questions about its denial of the motion to dismiss the federal-law claims. *Id.* at 637. Even though GSK asked us to reverse on the state-law claims as well, we refused to consider them. *Id.* at 637 n.11.

The lesson of our § 1292(b) practice: we may circumscribe the scope of our review, refusing to consider asserted grounds for reversal. *See* 16 Charles Alan Wright, Arthur R. Miller & Edward H. Cooper, Fed. Prac. & Proc. § 3931.1 (3d. ed. 2026).

To be sure, in the more distant past we declared that "[o]n a Section 1292(b) appeal we consider all grounds which might require a reversal of the order appealed from." *Murphy v. Heppenstall Co.*, 635 F.2d 233, 235 n.1 (3d Cir. 1980); *see*

also Merican, 713 F.2d at 962 n.7 (same); *In re Sch. Asbestos Litig.*, 789 F.2d 996, 1002 & n.5 (3d Cir. 1986) (same). But these cases predate our 1988 *en banc* decision in *Data Access*. Since then, we have never repeated the arguably mandatory language. Instead, we have used the permissive version. *See, e.g.*, *Howard Hess Dental Lab'ys Inc. v. Dentsply Int'l, Inc.*, 424 F.3d 363, 368–69 (3d Cir. 2005) ("We *may* 'consider all grounds which might require a reversal of the order appealed from.'" (emphasis added) (quoting *Merican*, 713 F.2d at 962 n.7)).[6]

There are two caveats. First, we cannot set aside challenges to our subject matter jurisdiction. *See Fox v. Saginaw Cnty.*, 67 F.4th 284, 292 (6th Cir. 2023). Even if a motions panel purported to refuse review of a jurisdictional question, the merits panel not only may, but must, address it. *Cf. Council Tree Commc'ns, Inc. v. FCC*, 503 F.3d 284, 292

[6] There is also some language in *Katz v. Carte Blanche Corporation*, 496 F.2d 747 (3d Cir. 1974) (*en banc*), *cert. denied*, 419 U.S. 885 (1974), that one could read as requiring us to consider any argument that a district court erroneously certified a class, *see id.* at 756. Even if that were the right reading of *Katz*, it would not survive our decision in *Link v. Mercedes-Benz of North America, Inc.*, 550 F.2d 860 (3d Cir. 1977) (*en banc*). The case presented two questions: whether the District Court erred in certifying a class and whether it could bifurcate the trial and use separate juries for the liability phase and damages phase were liability found. *Id.* at 861–62. Even though a motions panel had granted permission to appeal these matters, *id.* at 862, the full Court declined to rule on either one, *id.* at 861, 864–65; *see also Sperling v. Hoffman-La Roche Inc.*, 862 F.2d 439, 443–44 (3d Cir. 1988).

(3d Cir. 2007). Second, as the history we have recounted reveals, although a motions panel is free to specify the issues for the merits panel to review, the merits panel may refuse to answer them. *See, e.g.*, *Link v. Mercedes-Benz of North America, Inc.*, 550 F.2d 860, 861, 864–65 (3d Cir. 1977) (*en banc*).

In sum, Rule 23(f) essentially mirrors § 1292(b). To the extent they differ, Rule 23(f) provides more discretion, not less. Under § 1292(b), we may limit the scope of our review of an order to select issues. We have exercised this discretion for decades. There is no reason to think we may not do the same on a Rule 23(f) appeal. Accordingly, we hold we may circumscribe review of a Rule 23(f) appeal to the issues we choose.

B. The proposed class is ascertainable.

Class certification is warranted when the putative class meets the requirements of Rule 23(a) and Rule 23(b)(1), (2), or (3). *See Reyes v. Netdeposit, LLC*, 802 F.3d 469, 482 (3d Cir. 2015). Here, there is no dispute the Plans satisfied Rule 23(a). What is disputed is whether they satisfy two requirements of Rule 23(b)(3): predominance and ascertainability. Although we do not believe the ascertainability issue presented in this case merits review, we briefly address it out of respect for the parties.

To establish ascertainability, the plaintiffs must prove that "(1) the class is defined with reference to objective criteria" and "(2) there is a reliable and administratively feasible mechanism for determining whether putative class members fall within the class definition." *In re Niaspan*

Antitrust Litig., 67 F.4th 118, 130 (3d Cir. 2023) (quoting *Hargrove v. Sleepy's LLC*, 974 F.3d 467, 469–70 (3d Cir. 2020)). That happens when membership can be determined from a combination of objective records and verifiable affidavits from potential members. *See Byrd v. Aaron's Inc.*, 784 F.3d 154, 171 (3d Cir. 2015); *Hargrove*, 974 F.3d at 480; *City Select Auto Sales Inc. v. BMW Bank of N. Am. Inc.*, 867 F.3d 434, 441 (3d Cir. 2017). The Plans intend to determine membership using this very combination of evidence: identifying potential members with Avandia purchase and reimbursement records, then confirming actual membership with an affidavit and proof of purchase.

GSK nonetheless advances two arguments that the Plans failed to prove there is a reliable and feasible mechanism for identifying class members. First, it contends there are no records of which putative members reimbursed Avandia prescriptions in the class period. Second, it asserts that even if those records existed, they would not indicate whether a putative member was an end-payor (thus eligible for class membership) or was fully insured (hence ineligible for class membership).

The District Court's finding that there are objective records of the Plans' reimbursements for Avandia prescriptions has no clear error. We note that two named plaintiffs—Allied Services Division Welfare Fund and United Benefit Fund ("UBF")—dropped out of the case when they could not obtain purchase records from their pharmaceutical benefit managers ("PBMs"). But, after receiving a subpoena, UBF's PBM provided the data, showing it has (or at least had) the records after all. Even if PBMs could not provide the requisite data, the District Court's finding that class members would be able to

corroborate their claims was not clearly erroneous because a potential class member's affidavit can be corroborated using multiple forms of documentation.

The District Court's finding the Plans will be able to distinguish end-payors from fully insured plans did not clearly err either. GSK claims that most TPPs will rely on PBM purchase records to establish their membership in the class. Generally, those documents do not identify whether a purchaser was an end-payor. *See Niaspan*, 67 F.4th at 136. The Plans, however, do not propose to rely on PBM data alone; the record contained ample evidence they would be able to use other resources to distinguish end-payors from fully insured TPPs.

In a final bid to prevent class certification, GSK frames the Plans' proposal as a dilemma. In its view, the proposal permits potential class members to identify themselves—violating our admonition that ascertainability cannot rest on mere say-so—or it depends on individualized evidence, risking the very mini-trials the ascertainability requirement exists to prevent. *See id.* at 130–31.

This dilemma is illusory. The Plans' proposal for distinguishing end-payors from fully insured plans does not rely on mere say-so. Each potential class member's payor status would be verified with documentation like receipts, claims data, plan documents, or public records. And using these records to confirm a TPP is an end-payor hardly constitutes a mini-trial. To the contrary, it is the "straightforward 'yes-or-no' review of existing records to identify class members" we have held "is administratively feasible even if it requires review of individual records with

cross-referencing of voluminous data from multiple sources." *Kelly v. RealPage Inc.*, 47 F.4th 202, 224 (3d Cir. 2022).

The Plans' proposal falls well within the bounds of our precedents, leaving no abuse of discretion in holding the class is ascertainable.

C. The record so far does not show that common issues would predominate.

Rule 23(b)(3) requires "questions of law or fact common to class members predominate over any questions affecting only individual members." *Reyes*, 802 F.3d at 482 (quoting Fed. R. Civ. P. 23(b)(3)). "An individual question is one where 'members of a proposed class will need to present evidence that varies from member to member,' while a common question is one where 'the same evidence will suffice for each member to make a prima facie showing [or] the issue is susceptible to generalized, class-wide proof.'" *Tyson Foods, Inc. v. Bouaphakeo*, 577 U.S. 442, 453 (2016) (alteration in original) (quoting 2 W. Rubenstein, Newberg on Class Actions § 4:50 196–97 (5th ed. 2012)).

"[T]he presence of individual questions does not *per se* rule out a finding of predominance." *In re Prudential Ins. Co. Am. Sales Prac. Litig. Agent Actions*, 148 F.3d 283, 315 (3d Cir. 1998). Common questions predominate so long as they "overwhelm individual issues." *Neale v. Volvo Cars of N. Am., LLC*, 794 F.3d 353, 371 (3d Cir. 2015) (citing *Amgen Inc. v. Conn. Ret. Plans & Tr. Funds*, 568 U.S. 455, 468–69 (2013)). In other words, "[w]hen one or more of the central issues in the action are common to the class and can be said to predominate, the action may be considered proper under Rule 23(b)(3) even

though other important matters will have to be tried separately, such as damages or some affirmative defenses peculiar to some individual class members." *Tyson*, 577 U.S. at 453–54 (cleaned up).

"Class certification is proper only 'if the trial court is satisfied, after a rigorous analysis, that the prerequisites' of Rule 23 are met." *Hydrogen Peroxide*, 552 F.3d at 309 (quoting *Gen. Tel. Co. of Sw. v. Falcon*, 457 U.S. 147, 161 (1982)). "Factual determinations necessary to make Rule 23 findings must be made by a preponderance of the evidence." *Id.* at 320. This requires resolving "every dispute that is relevant to class certification" before it can be granted. *Ferreras v. Am. Airlines*, 946 F.3d 178, 183 (3d Cir. 2019).

We "analyze predominance in the context of Plaintiffs' actual claims" because "the nature of the evidence that will suffice to resolve a question determines whether the question is common or individual." *Neale*, 794 F.3d at 371–72 (quoting, in second passage, *Hydrogen Peroxide*, 552 F.3d at 311). That means class-wide evidence of each element of the cause of action must predominate over evidence particular to individual class members. *See Reyes*, 802 F.3d at 482–83, 489; *see also Hydrogen Peroxide*, 552 F.3d at 311 ("If proof of the essential elements of the cause of action requires individual treatment, then class certification is unsuitable." (cleaned up)). Accordingly, here predominance is "satisfied if each element of the alleged RICO violation involves common questions of law and fact capable of proof by evidence common to the class." *Reyes*, 802 F.3d at 489 (emphasis omitted).

"Establishing liability under [§ 1962(c)] of the RICO statute requires (1) conduct (2) of an enterprise (3) through a

pattern (4) of racketeering activity, plus an injury to business or property." *Id.* (alteration in original) (quoting *In re Ins. Brokerage Antitrust Litig.*, 579 F.3d 241, 269 (3d Cir. 2009)). Implicit is a requirement that the racketeering activity was the but-for cause of the alleged injury. *Id.* "The simplest statement of the concept of but-for causation is that event A is a but-for cause of event B if event B could not happen without event A happening first." *Mosley*, 454 F.3d at 266.

"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." *Sergeants Benevolent Ass'n Health & Welfare Fund v. Sanofi-Aventis U.S. LLP*, 806 F.3d 71, 87 (2d Cir. 2015) *cert. denied*, 580 U.S. 825 (2016).

> 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.

Id.

Because "reliance is nearly always an individualized question," *Harnish v. Widener Univ. Sch. of L.*, 833 F.3d 298, 309 (3d Cir. 2016), establishing predominance on causation in

a putative RICO class action can be challenging. Yet if a reasonable jury could find reliance based on class-wide evidence, then common questions predominate. *See Sergeants Benevolent*, 806 F.3d at 92–94.

In this case, the predominance question is whether the Plans can prove by class-wide evidence that they covered more Avandia prescriptions by reason of GSK's fraud. To do so, they must prove prescribers relied on GSK's misrepresentations. That is because the Plans propose a quantity-effect theory of third-party reliance: they claim GSK's fraud caused them to reimburse more prescriptions for Avandia because the fraud swayed physicians to prescribe it. And the District Court agreed. But it did not fully address all disputes relevant to class certification. Even if it had, certain of the evidence proved correlation not causation, and the remaining evidence has not yet been analyzed.

We have not addressed whether TPPs in a RICO pharmaceutical fraud action can prove reliance by statistical evidence. We hold it is possible, but the Plans have not done it to date. Statistical evidence can prove reliance. But not just any data will do. Proof of correlation is not enough. Proof of causation is required. One form such proof may take is a regression analysis or comparably robust quantitative study that is sufficiently reliable to pass muster under *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993).

1. All disputes relevant to class certification need resolution, so we must vacate.

The District Court mentioned three possible regression or statistical analyses that the Plans could have leaned on as

class-wide evidence: Dr. Rosenthal's analysis, Dr. McGuire's analysis, and GSK's own internal statistical analyses. The Court, however, held that only one of these analyses could be used to prove reliance: GSK's internal statistical analyses.

GSK argued to the District Court that these analyses could not isolate causation and thus could not reliably serve as a form of class-wide evidence. And the Court acknowledged that argument in its opinion. JA 16 ("GSK argues that because its own internal statistical analyses do not isolate the effect of their marketing regarding Avandia's cardiovascular profile specifically, they cannot be used to demonstrate class-wide reliance on that marketing."). But, as explored more below, it never grappled with this concern despite the direct bearing on the adequacy of key statistical evidence purporting to serve as class-wide evidence. That unresolved dispute requires us to vacate.

"Rule 23 requires rigorous consideration of all the evidence and arguments offered by the parties." *Hydrogen Peroxide*, 552 F.3d at 321; *see also Byrd*, 784 F.3d at 163 (noting that "a court evaluating a motion for class certification is obligated to probe behind the pleadings when necessary . . . to determine whether the Rule 23 certification requirements are satisfied"). This is because its requirements "must be *met*," not just supported by some evidence or conditionally met. *Hydrogen Peroxide*, 552 F.3d at 321 (emphasis added) (cleaned up). Thus, "[p]rior to certifying a class, a district court must resolve every dispute that is relevant to class certification." *Ferreras*, 946 F.3d at 183. Not to do so presents a problem for an affirmance. *See id.*; *Hydrogen Peroxide*, 552 F.3d at 320 ("[A] district court exercising proper discretion in deciding whether to certify a class will . . . hav[e] considered

all relevant evidence and arguments presented by the parties."). "[T]he party proposing class-action certification bears the burden of affirmatively demonstrating by a preponderance of the evidence her compliance with the requirements of Rule 23." *Byrd*, 784 F.3d at 163.

2. We part from the District Court's rationale for holding common issues would predominate.

As alluded above, the District Court held the Plans established predominance on the causation issue by introducing two forms of class-wide evidence that would justify an inference of class-wide reliance: "evidence of a common scheme to deceive" and "statistical or econometric models that show the allegedly unlawful promotion caused an increase in prescriptions" during the class period. *Avandia*, 2025 WL 1479618, at *7–9. Despite our deep respect for the Court's thoughtful work on this challenging case, we part ways. As to the first, we take a different view of the law. As to the second, we take a different view of the record.

a. The Plans did not seek, and the record does not warrant, an inference of "class-wide reliance."

Before proceeding to those two points, we begin by trying to understand what the District Court meant when it found that the Plans' evidence justified an "inference of class-wide reliance." *See generally Avandia*, 2025 WL 1479618, at *8–9 (repeatedly using variations of the phrase "inference of class-wide reliance"). It cannot have meant that *every member of the class* relied on GSK's misrepresentations. The Plans could not have shown *every* member of the class relied on

GSK's fraud, for they have not even alleged *any* member relied on it. They offered a different theory: that every member of the class was injured because prescribers relied on the misrepresentations.

Perhaps, then, the District Court meant that the Plans justified an inference that *every physician* relied on the fraud or that *every prescription* was made in reliance. That would make sense as to the heart of its reasoning: that it could infer reliance from the supposed fact that every prescription decision turned on the same considerations. So it is tempting to think the Court meant that it could infer all physicians relied, because all of them would have made their prescribing decisions in light of GSK's claims about Avandia's cardiac profile. But that doesn't work either. The Court expressly found the Plans' evidence could *not* support an inference that, but for GSK's fraud, no prescriptions would have been made. *Avandia*, 2025 WL 1479618, at *8.

The Plans offer a third interpretation of the opinion: the District Court meant that *many* physicians relied on the fraud—enough to infer every member of the class covered at least one prescription made in reliance. That would match the Plans' theory. But the Court did not say that.

b. The evidence of a common scheme, without more, did not warrant an inference of reliance in this case.

Next, we turn to the significance of the evidence of a common scheme to defraud. As the District Court noted, "courts may infer class-wide reliance when a plaintiff presents evidence of a common scheme to deceive." *Id.* at *7 (citing *In*

re Cmty. Bank of N. Va. Mortg. Lending Pracs. Litig., 795 F.3d 380, 408 (3d Cir. 2015)). But our cases do not support a broad, uniform rule that courts may infer class-wide reliance any time plaintiffs propose to prove the defendant committed fraud. True, we have endorsed the position that "where proof of the RICO violation is demonstrated through common evidence of a common scheme, reliance may be inferred on a classwide basis." *Cmty. Bank*, 795 F.3d at 408. But as noted earlier, we also have warned, in a case where the proof of the violation came from common evidence of a common scheme, that "reliance is nearly always an individualized question." *Harnish*, 833 F.3d at 309. So how should we distinguish cases where common evidence of a unified scheme justifies an inference of reliance from cases where it does not?

Several considerations distinguish this one. First, there is no fraud exception to the requirement of proving predominance. Decades ago, the Supreme Court observed that "[p]redominance is a test readily met in certain cases alleging consumer or securities fraud or violations of the antitrust laws." *Amchem Prods., Inc. v. Windsor*, 521 U.S. 591, 625 (1997). But since then we have emphasized that "it does not follow that a court should relax its certification analysis, or presume a requirement for certification is met, merely because a plaintiff's claims fall within one of those substantive categories." *Hydrogen Peroxide*, 552 F.3d at 322. "'[A]ctual, not presumed, conformance' with the Rule 23 requirements remains necessary." *Id.* (alteration in original) (quoting *Newton*, 259 F.3d at 167).

Second, aside from *Harnish*, the only two cases of ours the District Court relied on for this part of its decision come up short. One, *In re Warfarin Sodium Antitrust Litig.*, 391 F.3d

516 (3d Cir. 2004), shows that evidence of a common scheme to defraud can establish predominance when the theory of causation does not turn on reliance at all. There, "individual reliance on the misrepresentations was irrelevant to liability." *Id.* at 529. Here, however, the Plans' theory of causation requires that physicians relied on GSK's misrepresentations.

The other, *Community Bank*, the District Court described as governing cases where the plaintiffs allege the fraud concerned the only factor that mattered to the decision that resulted in their injuries, *see Avandia*, 2025 WL 1479618, at *8 n.56. The Second Circuit explained the point well:

> 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.

Sergeants Benevolent, 806 F.3d at 88 (quoting Richard A. Nagareda, *Class Certification in the Age of Aggregate Proof*, 84 N.Y.U. L. Rev. 97, 121 (2009)). For example, when plaintiffs allege the defendant fraudulently overbilled them, a court may presume they paid too much in reliance on the defendant's misrepresentation about the amount due because there is generally no other reason plaintiffs would pay more than they owed. *Id.* at 89 (citing *In re U.S. Foodservice Inc. Pricing Litig.*, 729 F.3d 108, 120 (2d Cir. 2013), *cert. denied*,

572 U.S. 1087 (2014)); *see also Klay v. Humana, Inc.*, 382 F.3d 1241, 1259–60 (11th Cir. 2004), *abrogated in part on other grounds by Bridge v. Phoenix Bond & Indem. Co.*, 553 U.S. 639 (2008).

It is in this context we last declared that "where proof of the RICO violation is demonstrated through common evidence of a common scheme, reliance may be inferred on a classwide basis." *Cmty. Bank*, 795 F.3d at 408. There, the plaintiffs asserted "class-wide evidence demonstrate[d] that [the defendant] performed no services in exchange for settlement charges." *Id.* We held that "on this record and in this context"—where the plaintiffs had alleged the defendant charged them for services it falsely claimed to have provided—we "d[id] not believe that the District Court abused its discretion in accepting the Plaintiffs' position" that their evidence of a class-wide scheme justified an inference they paid for those nonexistent services in reliance on the alleged misrepresentations. *Id.* When the decision is one-dimensional, reliance may be treated as one-dimensional.

Community Bank does not apply here because, as the District Court acknowledged, whether to prescribe Avandia was not a one-dimensional decision. The Court thought it could rely on it anyway because, "even though the decision to prescribe Avandia is not 'one-dimensional,' it is not so subjective that a provider's reliance cannot be inferred." *Avandia*, 2025 WL 1479618, at *8. The record does not justify that inference. The Court's portrayal of prescribers' decision-making process did not cite a single page of the several-thousand-page record. This speculation about how providers make decisions is not the "rigorous analysis" required for class

certification. *See Hydrogen Peroxide*, 552 F.3d at 309 (quoting *Gen. Tel. Co.*, 457 U.S. at 161).

In this context, the Plans could not prove reliance with their evidence of GSK's scheme alone. The law did not permit that inference.

c. The District Court did not adequately justify its finding that GSK's marketing studies warranted an inference of reliance.

Last, we turn to the statistical evidence. To repeat, the District Court found the Plans could justify an inference of class-wide reliance because they had introduced "statistical or econometric models that show the allegedly unlawful promotion caused an increase in prescriptions." *Avandia*, 2025 WL 1479618, at *7, *9. That evidence is crucial because their theory of but-for causation is that they were injured because physicians "relied on [GSK's] misrepresentation[s]." *See Sergeants Benevolent*, 806 F.3d at 87. In our view, the District Court did not provide the necessary analysis of this point to establish that the prerequisites of Rule 23 are met. *See Hydrogen Peroxide*, 552 F.3d at 309.

The Court stated that the Plans introduced internal GSK studies showing a few of its marketing campaigns caused an increase in prescriptions. *Avandia*, 2025 WL 1479618, at *9. On their own, they may not be evidence that GSK's purportedly "*unlawful* promotion" caused an increase in prescriptions, *id.* at *7 (emphasis added), because they did not isolate the cardiovascular messaging from other messaging about Avandia as the cause of increased prescriptions.

The Court, while acknowledging GSK raised this concern, defended its determination that the internal marketing research could establish "class-wide reliance" by citing cases holding that, in general, such an inference can be justified by statistical or aggregate evidence a RICO defendant's fraud caused the plaintiffs' injuries. *See Avandia*, 2025 WL 1479618, at *9. That is true. But it does not resolve GSK's concern. If the GSK studies showed its allegedly fraudulent claims about Avandia's cardiac effects caused an uptick in prescriptions, then the cases the District Court cited would provide a legal foundation for putting them to work here. But as far as we can tell from the expert reports describing the studies, they did not identify the distinctive consequences of GSK's allegedly *fraudulent* marketing as opposed to its marketing generally. Even if they could show physicians relied on what GSK said about Avandia, they may not be able to show doctors were swayed by its alleged misrepresentations about its cardiac effects in particular. Similarly, even if the problem is that all of GSK's marketing omitted the truth about Avandia's cardiac profile, the data in the record may not explain how much of its efficacy arose from that omission.

If the District Court understood the actual scope of the studies but reasoned they sufficed to justify an inference of class-wide reliance, an error of law crept in: what the studies can prove is a legal matter, not a factual one. *See Comcast Corp. v. Behrend*, 569 U.S. 27, 36 n.5 (2013) ("[W]hile the data contained within a . . . model may well be 'questions of fact' in the relevant sense, what those data prove is no more a question of fact than what our opinions hold."). Even by the lights of the cases the District Court cited, only a report that attempts to isolate the effects of the alleged fraud could warrant that inference. *See In re Celexa & Lexapro Mktg. & Sales*

Pracs. Litig., 915 F.3d 1, 13–14 (1st Cir. 2019) (discussing *In re Celexa & Lexapro Mktg. & Sales Pracs. Litig.*, 315 F.R.D. 116, 126–29 (D. Mass. 2016)); *Sergeants Benevolent*, 806 F.3d at 91–93; *In re Neurontin Mktg. & Sales Pracs. Litig.* ("*Neurontin III*"), 712 F.3d 60, 68 (1st Cir. 2013); *cf. Comcast*, 569 U.S. at 32, 35 (holding a damages model must at least attempt to isolate the effects of each of the plaintiffs' independent theories of liability, at least where some have been rejected).

And if the District Court incorrectly understood what the data concerned, its factual error was a clear one. *See Reyes*, 802 F.3d at 483. Nothing in the record indicated the studies isolated the effects of GSK's fraudulent marketing from the effects of its marketing in general. And the Plans disavow using these studies for that purpose. Further, because these studies do not seem to speak to the issue at hand, combining them with the common evidence of GSK's alleged scheme does not yield an adequate basis for the District Court's decision either.

3. The Plans' alternative basis for holding common issues would predominate does not work either.

The Plans claim they can show reliance differently: by introducing statistical evidence of a correlation between the Nissen study's exposure of the fraud and the subsequent decline in prescriptions, then using circumstantial evidence to show that the earlier exposure of the fraud would have led to the same decline—thus closing the gap between correlation

and causation.[7] In their view, if the public had learned the truth about Avandia's cardiovascular profile at the start of the class period in 2005, prescriptions would have declined in the same way they did after the Nissen study exposed that information in 2007.

We disagree. A few courts have permitted TPPs in similar RICO class actions to prove reliance with class-wide evidence when the evidence includes both statistical and circumstantial evidence of causation. But we are not aware that any court has permitted a putative class of TPPs to prove providers' reliance by class-wide evidence without statistical evidence the defendant's conduct *caused* the injuries. The Plans could have cleared the bar if they had introduced statistical evidence of causation, like a regression analysis. They tried. But the District Court struck that evidence after a *Daubert* hearing. Without it, the Plans have only statistical evidence of correlation and circumstantial evidence of causation. In this context, where their theory depends on establishing the fraud caused enough prescriptions to make it likely the fraud injured the entire class, that is not enough. TPP pharmaceutical fraud class action plaintiffs can prove causation by class-wide statistical evidence. But doing so takes more rigorous statistics than the Plans so far have presented.

Every circuit to address this question has held or suggested that statistical evidence of causation may prove a

[7] The Plans claim the District Court considered and endorsed this theory. Yet they do not—and cannot—point to a single page of the District Court's class-certification opinion where it did. Instead, they cite only a couple of remarks it made during a prior hearing.

drug manufacturer's fraud injured a class of TPPs. Begin with the First Circuit. In three related decisions, it held that multiple regression analysis suggesting a causal relationship between a drug maker's illegal marketing and an increase in prescriptions can help prove the fraud injured a TPP. *See In re Neurontin Mktg. & Sales Pracs. Litig.* ("*Neurontin I*"), 712 F.3d 21, 29–30, 40, 46 (1st Cir. 2013); *In re Neurontin Mktg. & Sales Pracs. Litig.* ("*Neurontin II*"), 712 F.3d 51, 56–58 (1st Cir. 2013); *Neurontin III*, 712 F.3d at 68. These cases were RICO actions health insurers brought against Pfizer for illegally promoting its drug Neurontin for off-label use. *Neurontin I*, 712 F.3d at 25–26; *Neurontin II*, 712 F.3d at 52–53; *Neurontin III*, 712 F.3d at 61–62, 68–69. Across these cases, the but-for causation question was whether Pfizer's unlawful marketing caused the insurers to reimburse more Neurontin prescriptions than they otherwise would have because physicians issued more prescriptions in reliance on the messaging. *Neurontin I*, 712 F.3d at 25–26, 40–42; *Neurontin II*, 712 F.3d at 52–53, 57; *Neurontin III*, 712 F.3d at 61–62, 68.

The TPPs tried to answer that question by introducing class-wide statistical evidence and circumstantial evidence. *Neurontin I*, 712 F.3d at 42–45; *Neurontin II*, 712 F.3d at 56; *Neurontin III*, 712 F.3d at 63–64. The primary statistical evidence was the analysis of expert Dr. Rosenthal, who performed a regression analysis that "found a causal connection between the fraudulent marketing and the quantity of prescriptions written for off-label indications." *Neurontin I*, 712 F.3d at 29–30; *see also Neurontin II*, 712 F.3d at 56; *Neurontin III*, 712 F.3d at 63. Her analysis also identified "the percentage of prescriptions caused by Pfizer's fraudulent off-label marketing." *Neurontin I*, 712 F.3d at 30.

In *Neurontin I* and *Neurontin II*, the First Circuit held this statistical evidence, combined with circumstantial evidence, sufficed to permit a jury to find Pfizer's fraud caused the plaintiff insurers' injuries. *Neurontin I*, 712 F.3d at 45–47; *Neurontin II*, 712 F.3d at 57–58. The Court observed that "regression analysis is a well recognized and scientifically valid approach to understanding statistical data." *Neurontin I*, 712 F.3d at 42. It also noted that courts permit plaintiffs to prove causation with regression analysis in multiple legal domains, including Title VII claims, Sixth Amendment claims about whether a jury pool reflects a reasonable cross-section of the community, and antitrust claims. *Id.* (citations omitted). The antitrust precedents were particularly significant because "RICO has drawn many of its causation principles" from antitrust law, though antitrust law generally does not require proof of reliance. *Id.* at 44. The Court further considered and set aside Pfizer's contention that some individual doctors might have prescribed Neurontin for off-label uses without relying on the illicit marketing. *Id.* at 45. "The existence of some doctors who purportedly were not influenced by Pfizer's misinformation would not defeat the inference that this misinformation had a significant influence on prescribing decisions which injured" the plaintiff insurers—and that inference was all the plaintiffs needed. *Id.* Finally, Dr. Rosenthal's regression analysis proved causation, not just correlation, particularly when combined with the circumstantial evidence. *Id.* at 46.

Most relevantly, in *Neurontin III* the First Circuit vacated a denial of class certification on the same ground. 712 F.3d at 62, 68, 70. Echoing the prior analysis, it held "that the Rosenthal report is capable of providing proof of but-for causation." *Id.* at 68. "[R]egression analysis is a widely

accepted method of showing causation under several causes of action," the Court explained, and it saw "no reason to reach a different conclusion for a specific subset of RICO claims based on fraudulent pharmaceutical marketing." *Id.* at 69. Because the trial court's denial of class certification "pivoted on the determination that the Rosenthal report could not provide proof of causation," that denial could not stand. *Id.* at 70. Class-wide statistical evidence capable of distinguishing causation from correlation, such as a regression analysis, may prove common questions predominate on RICO but-for causation.

The First Circuit later reaffirmed that this reasoning applies to the predominance analysis of class certification. In another RICO class action brought by TPPs against a drug manufacturer, it explained that the plaintiffs' "clinical and statistical evidence, if believed, could establish causation and injury at least for any TPP who paid for more than a handful of different patients' prescriptions." *Celexa*, 915 F.3d at 14. The Court emphasized that the record featured the testimony of two experts, who opined not only that the drug company's promotional spending was *correlated* positively with sales, but also that its allegedly unlawful promotions *caused* 76 percent and 54 percent, respectively, of the off-label prescriptions for the relevant two drugs. *Id.* at 13. From these figures, one of the experts estimated that if a TPP covered as few as five prescriptions, there was a 98 percent chance at least one resulted from the illicit marketing. *Id.* The plaintiffs bolstered that statistical evidence with direct and circumstantial evidence the fraud caused their injuries, like evidence the pharmaceutical company's sales representatives had called or visited physicians who subsequently issued the off-label prescriptions at issue. *Id.* In the First Circuit, then, a TPP in a pharmaceutical fraud RICO case may prove causation by class-

wide evidence where that evidence includes statistical analysis that isolates the effects of the fraud from other variables and shows it is likely the fraud injured each TPP.

A pair of Second Circuit decisions contemplated the same approach. The first, *UFCW Local 1776 v. Eli Lilly & Co.* ("*Zyprexa*"), 620 F.3d 121 (2d Cir. 2010), was a RICO class action brought by a putative class of TPPs against Eli Lilly and Company for misrepresenting the efficacy and side effects of Zyprexa. *Id.* at 123, 129. The TPPs advanced the now-familiar theory that Eli Lilly's fraud increased the number of Zyprexa prescriptions doctors made, which in turn increased the number members of the putative class covered. *Id.* at 135. However, as the Court later explained in a separate case discussing *Zyprexa*, "[t]o prove that doctors had, in fact, relied on Lilly's misrepresentations in making their prescription decisions, the [*Zyprexa*] plaintiffs primarily offered evidence that the number of Zyprexa prescriptions fell after the drug's weight- and diabetes-related side effects were disclosed." *Sergeants Benevolent*, 806 F.3d at 89–90. That evidence of a correlation between the exposure of the truth and a decline in prescriptions could not prove the fraud caused more pre-exposure prescriptions, the Court explained, because there were "any number[ ]of a multitude of reasons" a doctor might have prescribed Zyprexa. *Id.* at 90. "The fact that Zyprexa prescriptions declined markedly following the disclosure of the previously concealed information was not sufficient to support this necessary inference [of causation]." *Id.* "[B]ecause 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." *Id.*

A few years later, the Second Circuit rejected a similar attempt to establish predominance on causation for the same reason, while clarifying what would suffice. In *Sergeants Benevolent*, 806 F.3d 71 (2d Cir. 2015), the plaintiffs "sought to certify a class of all [TPPs] that paid for Ketek prescriptions on the theory that such [TPPs] 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." *Id.* at 74. The Court acknowledged that "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," but it held the plaintiffs "failed to offer such proof" there. *Id.* at 74–75.

Like the *Zyprexa* plaintiffs, the *Sergeants Benevolent* plaintiffs tried to prove causation by presenting evidence prescriptions "dropped precipitously" after the truth was exposed. *See id.* at 91. And like the *Zyprexa* plaintiffs, they introduced the testimony of an expert—again, Dr. Rosenthal—that "this unprecedented drop must have been caused entirely by the disclosure of Ketek's post-marketing safety data." *Id.* However, as in *Zyprexa*, the expert testimony was not accompanied by statistical proof of causation, like a regression analysis; it instead assumed the causal link the plaintiffs needed to prove. *Id.* at 91–92, 95. "Plaintiffs [thus] made no attempt to control for [potential confounding variables], 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." *Id.* at 92. Because "mere correlation does not demonstrate causation," evidence of "a simple correlation between the safety disclosure and the decline in prescriptions," *id.*, "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," *id.* at 95.

The Court then went out of its way to note "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." *Id.* at 94 (emphasis omitted). Even if the plaintiffs had advanced such a theory, evidence of correlation would have been insufficient to prove causation because it did not "isolate[] the relative causal effect of the numerous variables bearing on the decline in Ketek's sales." *Id.* at 95–96. The Court distinguished the evidence before it from Dr. Rosenthal's regression analysis in *Neurontin*, which controlled for other variables. *Id.* at 96 (citing *Neurontin I*, 712 F.3d at 30). Although Dr. Rosenthal was also an expert in *Sergeants Benevolent*, she had not performed a regression analysis. *Id.* at 95.

The Court pointedly concluded by observing "*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." *Id.* at 97. In short, what the plaintiffs needed to add was a regression analysis or some other evidence "firmer than speculation" that prescriptions were written in reliance on the fraudulent marketing. *Id.* at 95.

Last year, the Ninth Circuit joined this nascent consensus. *Painters & Allied Trades Dist. Council 82 Health Care Fund v. Takeda Pharm. Co.*, No. 23-55742, 2025 WL 1683472 (9th Cir. June 16, 2025). Certifying a class of TPPs in a RICO class action against a pharmaceutical company, a district court had held that "a statistical regression . . . can establish but-for causation for a civil RICO claim, especially when used in tandem with other circumstantial or direct evidence." *Painters & Allied Trades Dist. Council 82 Health Care Fund v. Takeda Pharm. Co.*, 674 F. Supp. 3d 799, 827 (C.D. Cal. 2023). The Circuit Court affirmed, explaining that the expert report the TPPs submitted could prove causation because it "used regression models to show that the decline in prescriptions was caused by the failure to disclose," even accounting for possible confounding variables. *Painters*, 2025 WL 1683472, at *2 (footnote omitted). The upshot (again): TPPs can prove providers relied on a drug manufacturer's misrepresentations by introducing statistical evidence of causation—like a regression model—supplemented by circumstantial evidence.

We too conclude that, in a RICO pharmaceutical fraud action, TPPs may use class-wide statistical evidence to prove physicians' reliance, and hence but-for causation, so long as the evidence can distinguish correlation from causation. That evidence may take the form of a regression analysis or any comparably robust statistical method.[8]

[8] Whether other types of evidence could prove common questions would predominate on causation in this case is not before us.

As a general matter, the Supreme Court and our Court have held plaintiffs may use statistical evidence to prove causation. *See, e.g.*, *Texas Dep't of Housing and Cmty. Affairs v. Inclusive Cmtys. Project*, 576 U.S. 519, 542–43 (2015); *Watson v. Fort Worth Bank & Tr.*, 487 U.S. 977, 994 (1988); *Bazemore v. Friday*, 478 U.S. 385, 400–03 (1986) (Brennan, J., concurring in part); *In re Linerboard Antitrust Litig.*, 305 F.3d 145, 153–55 (3d Cir. 2002).

In this context, using statistical evidence to prove but-for causation would satisfy the Supreme Court's general criteria for using such evidence in predominance analysis. Although the Court has declined to adopt "broad and categorical rules governing the use of representative and statistical evidence in class actions," it has identified two criteria which, if jointly met, permit us to find common questions predominate. *See Tyson*, 577 U.S. at 454–60.

First, statistical evidence may be used to show predominance only if a reasonable jury could have relied on it to find each class member proved the element at issue in an individual action. *Id.* at 455. "[W]here representative evidence is relevant in proving a plaintiff's individual claim, that evidence cannot be deemed improper merely because the claim is brought on behalf of a class." *Id. Tyson* itself held the plaintiffs in a Fair Labor Standards Act collective action could use evidence of how long a representative sample of employees spent donning and doffing protective gear to prove how long each worker spent. *Id.* at 454, 456–59. That was because an individual worker could have deployed the same representative evidence to prove the same point in an individual action where his or her employer had failed to keep adequate records. *See id.* at 455–57. In this situation, "[r]ather than absolving the

employees from proving individual injury, the representative evidence . . . was a permissible means of making that very showing." *Id.* at 457.

Second, statistical evidence can support class-wide liability when the defenses to it are also class-wide. *Id.* at 457. *Tyson* met that criterion because, in the absence of employer records of how long each employee worked, the "primary defense" available to the employer "was to show that [the] study was unrepresentative or inaccurate"—a defense "common to the claims made by all class members." *Id.*

In a case like ours, statistical evidence of causation could meet both criteria. As the *Neurontin* Court recognized in its two non-class-action decisions, an individual TPP may use statistical evidence, combined with circumstantial evidence, to prove a pharmaceutical manufacturer's fraud caused it to reimburse more prescriptions than it otherwise would have. *See Neurontin I*, 712 F.3d at 45–47; *Neurontin II*, 712 F.3d at 57–58. GSK cites no authority holding otherwise.

The "primary defense" against this common evidence would also apply class-wide. *Tyson*, 577 U.S. at 457. "[T]he question is whether [the drug maker's] misrepresentations caused an injury to each [TPP], and because each [TPP] paid for numerous [drug] prescriptions, each would have been injured . . . so long as at least some of the prescriptions for which it paid were written in reliance on those misrepresentations." *Sergeants Benevolent*, 806 F.3d at 94 (emphasis omitted). Because it is enough for the TPPs to show "*some* prescriptions paid for by each class member were written based on the defendant's alleged misrepresentations," *id.* (emphasis in text), "[t]he existence of some doctors who

purportedly were not influenced by [the defendant's] misinformation would not defeat the inference that this misinformation had a significant influence on prescribing decisions which injured [the plaintiff]," *Neurontin I*, 712 F.3d at 45. The theme: proving any particular doctor prescribed Avandia without relying on GSK's misrepresentations would not disprove the Plans' theory of the case. Their claim is true regardless whether any specific physician prescribed Avandia in reliance on GSK's fraud, so long as enough doctors relied to justify the inference each class member covered at least one prescription that *was* made in reliance. That is the sort of claim statistical evidence is all about. As in *Tyson*, the defendant's "primary defense [is] to show that [the] study was unrepresentative or inaccurate"—a defense "common to the claims made by all class members." *Tyson*, 577 U.S. at 457.

All that said, not just any statistical evidence will do. As we have recognized, correlation does not imply causation. *See City of Hoboken v. Chevron Corp.*, 45 F.4th 699, 709–10 (3d Cir. 2022); *Linerboard*, 305 F.3d at 153. We do not see how a reasonable jury could find that a drug maker's fraud injured a TPP in an individual action with nothing more than evidence of a correlation between the exposure of the fraud and a decline in prescriptions market-wide. Evidence of mere correlation leaves causation speculative, particularly regarding quantitative questions like how much of the prescription volume the fraud caused or the probability that every member of the class covered at least one relevant prescription. The point is not that a jury might not believe the data. It is that there is a limit to what the data, if believed, can prove. *See Comcast*, 569 U.S. at 36 n.5.

Informed by the First, Second, and Ninth Circuits, we hold that TPPs in a pharmaceutical fraud RICO action may prove but-for causation with class-wide statistical evidence so long as that evidence is sufficiently rigorous to show causation, not just correlation. Statistical evidence has such rigor if, like a regression analysis, it can distinguish the causal significance of the variable at issue and justify the rejection of competing explanations.

We turn to the evidence in this case. It is much more like the evidence that fell short in *Zyprexa* and *Sergeants Benevolent* than the evidence that courts indicated would suffice in the *Neurontin* cases, *Celexa*, and *Painters*. The Plans have about the same circumstantial evidence the plaintiffs had in all those cases. But that evidence boils down to a graph showing Avandia prescriptions fell sharply after the Nissen study exposed the drug's true cardiac profile. They have no regression analysis or expert testimony to distinguish causation from correlation by isolating other potential variables; the expert concluding that each TPP likely paid for Avandia in reliance on the fraud was offered only for damages. No appellate court has yet held TPPs established predominance on RICO but-for causation with as weak statistical evidence as the Plans so far put forward here. We will not be the first.

The Plans refer to four forms of statistical evidence of causation: GSK's internal marketing studies, the Rosenthal report, the McGuire report, and the post-Nissen study drop in Avandia prescriptions. None alone holds up. As discussed in our review of the District Court's analysis, GSK's internal marketing studies cannot show its fraud caused the Plans' injuries because it appears they do not even purport to isolate the causal effects of its allegedly illicit marketing from those

of its marketing as a whole. The regression analysis the Plans commissioned from Dr. Rosenthal, which purported to show GSK's fraudulent marketing caused TPPs to pay for Avandia prescriptions, was excluded after the *Daubert* hearing. The Plans have not appealed that ruling. Whatever the McGuire report may be able to prove, the Plans may not use it to prove causation in this appeal. They did not offer it to prove causation in the pre-trial proceedings, and the District Court expressly declined to consider the report for purposes of establishing reliance—and thus, causation—in its class-certification decision. *Avandia*, 2025 WL 1479618, at *9 n.64.

That leaves the post-Nissen study drop—the heart of the Plans' alternative basis for affirmance. They introduced data showing that when the Nissen study came out in 2007, Avandia prescriptions sharply declined. Their aim was to use "Nissen's publication in 2007 as a natural experiment to show *exactly* what would have happened to Avandia prescriptions had GSK published the same information in 2005." Answering Br. 35 (emphasis in text). Just as Avandia prescriptions plummeted after the Nissen study revealed the drug's true cardiac risks, they say, so prescriptions would have fallen had ICT-37 exposed the danger earlier.

The post-Nissen study drop data is the very sort of statistical evidence the Second Circuit found insufficient in *Zyprexa* and *Sergeants Benevolent*. Recall what that Court said about *Zyprexa*: "To prove that doctors had, in fact, relied on Lilly's misrepresentations in making their prescription decisions, the [*Zyprexa*] plaintiffs primarily offered evidence *that the number of Zyprexa prescriptions fell after the drug's weight- and diabetes-related side effects were disclosed*." *Sergeants Benevolent*, 806 F.3d at 89–90 (emphasis added).

The Second Circuit described the *Sergeants* evidence in much the same way, reporting that the plaintiffs "present[ed] evidence showing that *sales of Ketek dropped precipitously after the FDA's public health advisory and Ketek's label revisions in 2006*," and argued "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." *Id.* at 91 (emphasis in first quotation added; emphasis in second quotation in text). That is what the Plans have here—evidence that, after the publication of the Nissen study, Avandia prescriptions declined. In fact, the Plans have even less rigorous evidence than the plaintiffs who fell short in *Sergeants*. At least there the insurers had an expert's testimony "that she had never seen anything like" Ketek's post-disclosure decline. *Id.* Here, that is absent.

The Plans' statistical evidence thus far is also weaker than that in *Painters*, *Celexa*, and the *Neurontin* cases. In *Painters*, the Ninth Circuit held the TPPs' statistical evidence was sufficiently rigorous to prove causation class-wide because the expert's regression analysis accounted for alternative explanations to explain prescription volume, enabling the Court to confirm the exposure of the fraud caused the ensuing decline. *See Painters*, 2025 WL 1683472, at *2–3. Similarly, in *Celexa* the First Circuit thought the TPPs' statistical evidence could support causation because two expert analyses quantified the portion of prescriptions attributable to the fraud and the odds that a given class member had reimbursed its insureds for one of those prescriptions. *See Celexa*, 915 F.3d at 13. And in the *Neurontin* cases the statistical evidence sufficed because the expert's regression analysis isolated the causal significance of the fraud. *See*

Neurontin I, 712 F.3d at 30. Here the Plans lack the crucial evidence that can sift out causation from correlation. Indeed, the *Neurontin* and *Sergeants Benevolent* Courts were so dismissive toward bare correlation data like the Plans' Nissen study drop evidence that they did not even characterize it as statistical evidence at all, but as circumstantial evidence (that is, facts that imply, rather than directly prove, a result). *See Neurontin II*, 712 F.3d at 57; *Sergeants Benevolent*, 806 F.3d at 92. We agree—by the standards of the First, Second, and Ninth Circuits, the Plans' Nissen study drop data alone does not prove causation.

The Plans insist "[t]his case is largely indistinguishable from *Neurontin*, with the only distinction being that plaintiffs' 'aggregate evidence' is the natural experiment of Nissen instead of a regression analysis." Answering Br. 32. But that distinction makes all the difference. The problem is not with their natural experiment approach, but with their class-wide evidence. The Plans' logic is straightforward: A caused C; B is relevantly similar to A; so if B had happened, then C would have happened. According to the Plans, the Nissen study caused a steep decline in Avandia prescriptions; the publication of ICT-37 would have exposed the drug's cardiac effects in the same way Nissen's report did; therefore, if ICT-37 had been published, Avandia prescriptions would have declined as much as they did after publishing the Nissen study. This argument is sound only if the first premise is true. And the bare fact that Avandia prescriptions fell after the Nissen study came out does not alone prove it is. A "natural experiment" is no substitute for a regression analysis (or comparably robust evidence of causation) because its first premise requires one to establish a causal link.

The Plans cite cases where courts accepted natural experiments as evidence. However, in all of those cases, the first premise—that A either caused or did not cause C—was backed up by expert analysis, not presumed from a bare correlation. *See In re Nat'l Collegiate Athletic Ass'n Athletic Grant-in-Aid Cap Antitrust Litig.*, 958 F.3d 1239, 1249–50 (9th Cir. 2020); *In re Flonase Antitrust Litig.*, 284 F.R.D. 207, 220, 222–23 (E.D. Pa. 2012); *In re Namenda Indirect Purchaser Antitrust Litig.*, 338 F.R.D. 527, 562–63 (S.D.N.Y. 2021). If there were evidence the Nissen study *caused* the post-Nissen drop, then perhaps we could infer that the exposure of the same information a few years earlier would have caused a similar drop. But that argument cannot get off the ground without it.

The Plans also claim they have put forward the very case *Sergeants* contemplated. They have not. When the *Sergeants* Court said "reliance can be proved to a jury with sufficiently powerful aggregate evidence," it was referring to evidence capable of distinguishing causation from correlation. *See* 806 F.3d at 96–97. While it entertained the possibility that a precipitous decline in prescriptions alone could justify an inference of reliance, it expressly cabined that to the "extraordinary case" of "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." *Id.* at 92. Avandia is not that drug.

Though but-for causation is generally provable by statistical evidence, the evidence the Plans have here is not yet sufficient.[9]

* * *

[9] Our concurring colleague observes that one District Court in our Circuit granted class certification in a pharmaceutical case without a regression analysis. *See In re Flonase Antitrust Litig.*, 284 F.R.D. 207, 221 (E.D. Pa. 2012). But *Flonase* differs in two important respects. First, it was not a RICO case. *Id.* at 210–11. That matters, because predominance turns on whether each element of the cause of action is provable by common evidence. *See Neale*, 794 F.3d at 371–72. And in this context the causation requirement of a RICO fraud claim requires establishing reliance on the defendant's misrepresentations. *See Sergeants Benevolent*, 806 F.3d at 87. Because *Flonase* was not a RICO case, the plaintiffs were not required to prove reliance—the showing for which we seek a regression here. Second, predominance in *Flonase* turned on whether there was common evidence the defendant's alleged conduct—delaying the entry of a generic—led the plaintiffs to pay higher prices. *See Flonase*, 284 F.R.D. at 221. As we have acknowledged before, a price-effect theory like that does not require proof of reliance, for its premise is that the defendant's conduct caused the plaintiffs' injuries by raising prices across the market, which the plaintiffs then paid in the ordinary course. *See Harnish*, 833 F.3d at 311–12. In sum, our opinion is consistent with *Flonase* because our holding concerns the sort of common evidence that can establish reliance in a RICO fraud action—a question *Flonase* did not pose, let alone answer.

We summarize as follows: we may limit the scope of our review under Rule 23(f); the District Court soundly determined the class is ascertainable; and the Court has not resolved all class-certification disputes. Even if it had, the Plans have yet to satisfy the predominance requirement. The District Court understood the Plans as seeking an inference that every member of the class, or every doctor, relied on GSK's fraud. We cannot treat GSK's studies of the effects of its marketing campaigns in general as studies of the effects of its fraudulent marketing specifically. And the Court thought the law permits an inference of reliance under broader circumstances than it does.

The Plans' alternative ground for affirmance cannot fix the problem. Their overarching theory is that the 2007 publication of the Nissen study caused Avandia prescriptions to decline because it exposed the drug's real cardiac profile, so a 2005 publication of similar facts by GSK would have caused a similar drop. The problem is that the Plans' statistical evidence shows only that Nissen's publication in 2007 was followed by a decline in prescriptions. That alone does not prove causation. The First and Ninth Circuits have held TPPs in a pharmaceutical fraud RICO action may prove common questions predominate on but-for causation with class-wide evidence where the statistical evidence speaks to actual causation rather than mere correlation. The Second Circuit has suggested it favors the same position. We agree with them. But as noted, the Plans have not met that requirement at this time. Without a regression analysis or other causation evidence, they currently do not have enough to get from correlation to causation.

However, it may yet be possible for the Plans to clear the bar. They now claim the McGuire report can prove causation. Answering Br. 29; Oral Argument Tr., Dkt. No. 70, at 16-17. And the District Court reserved judgment on that question. *Avandia*, 2025 WL 1479618, at *9 n.64. Other evidence the Court may allow might prove relevant as well.

With this understanding of the governing law in our Circuit, we vacate the District Court's certification of the class and remand for proceedings consistent with this opinion. *Cf. Hydrogen Peroxide*, 552 F.3d at 326–27; *Hargrove*, 974 F.3d at 481 n.8. On remand, the Court may reopen discovery on predominance under Federal Rule of Civil Procedure 16(b) if good cause is shown.

SHWARTZ, J., concurring in part and concurring in the judgment.

I agree with my colleagues that a motions panel has the authority to select the issues worthy of interlocutory review under Federal Rule of Civil Procedure 23(f) and that the proposed class is ascertainable, so I join those portions of the Majority's opinion in full. As to the predominance issue, however, I join only Part III(C)(1), which explains that remand is required to allow the District Court to address specific issues. Therefore, I concur in the judgment.

I first address my reasons for joining Section III(C)(1) and then explain why I decline to join my colleagues' announcement that a regression analysis is almost always needed in a case like this.

I

In RICO putative class actions, we evaluate whether a district court fulfilled its obligation when considering predominance under Rule 23 by determining whether the court acted within its discretion in finding that the plaintiffs demonstrated, by a preponderance of the evidence, that their RICO claim is "capable of common proof at trial." See In re Lamictal Direct Purchaser Antitrust Litig., 957 F.3d 184, 190-92 (3d Cir. 2020); In re Hydrogen Peroxide Antitrust Litig., 552 F.3d 305, 325 (3d Cir. 2008), as amended (Jan. 16, 2009) (stating that the predominance inquiry asks whether the elements of the claim are "susceptible to proof at trial through available evidence common to the class").

Here, the Plans presented evidence that Avandia prescriptions plummeted after the 2007 Nissen study disclosed cardiovascular risks that had been known to GSK for about two years and were particularly consequential to diabetics, although an expert opined that GSK marketed Avandia as having cardiovascular benefits.

The Plans also told us that they will offer "GSK marketing analyses showing the impact of" the marketing that portrayed Avandia as having cardiovascular benefits. Appellee Br. at 28. Although those marketing analyses are not in the record on appeal, the District Court (1) apparently relied on them to conclude that the Plans had offered "statistical or econometric models that show the allegedly unlawful promotion caused an increase in prescriptions," In re Avandia Mktg., Sales Pracs. & Prods. Liab. Litig., No. 07-MD-1871, 2025 WL 1479618, at *7, *9 (E.D. Pa. May 22, 2025) (discussing arguments concerning GSK's "own internal statistical analyses"), and (2) rejected GSK's argument that those analyses did not isolate the fraudulent marketing as the cause of increased sales, id. at *9.

The District Court, however, did not explain how (1) the analyses isolated fraudulent marketing as a cause for the prescription increase, or (2) if they did not isolate such a cause, how the analyses still served as common evidence that fraudulent marketing caused prescription volume to increase. See id. Our precedent requires the Court to provide the reason for its conclusion. See Hydrogen Peroxide, 552 F.3d at 321.

Furthermore, the District Court seemed to conclude that the predominance requirement was met only because evidence of individual reliance by every prescribing doctor was not

required. See Avandia, 2025 WL 1479618, at *9. Although individualized evidence is not required, the District Court did not explain why this view shows that the Plans presented sufficient common evidence from which to decide whether GSK's scheme caused the drop.

In short, the District Court must provide its view on the Plans' theory that prescriptions would have dropped by the same amount they did after the Nissen study if GSK had disclosed what it knew years before and not fraudulently marketed Avandia. Although the District Court mentions GSK's marketing materials and planning documents as evidence of GSK's scheme to deceive, id. at *8, it does not explain how these materials lead to its conclusion.

For those reasons, I join the Majority to the extent it concludes that a remand is warranted to allow the District Court to address these matters and others the Majority identifies in Part III(C)(1).

II

I also write separately to explain why I depart from my colleagues' view that a regression analysis is almost always required to prove causation in a case like this. I view our responsibility at this phase to determine whether there is sufficient common evidence in the record from which a fact finder could make a finding on the elements of the cause of action.

Here, the record contains common evidence, including (1) the post-Nissen decline in prescriptions, (2) expert testimony that the risks disclosed by the Nissen Study were the

same ones GSK should have disclosed in 2005, (3) internal GSK documents acknowledging that the Nissen Study was consistent with GSK's own conclusions reached in 2005, (4) evidence that diabetes patients were particularly vulnerable to cardiovascular disease, and (5) expert testimony that GSK marketed Avandia as having cardiovascular benefits. In addition, and notably, GSK has offered no explanation for the plummeting prescriptions after the Nissen study's publication aside from the revelation of its fraud. See Oral Arg. Tr. at 44-46. Together, this may constitute sufficient common evidence upon which a jury could decide whether the Plans have proven that GSK's actions caused their injury. While it is circumstantial, it could support an inference that at least some Avandia prescriptions written before the drop were written in reliance on the fraudulent marketing, particularly in view of GSK's failure to offer an alternative explanation for the drop. Through this proof, the Plans (subject to District Court's consideration of the items described in Part I) may well have shown that causation is "susceptible to proof at trial through" common evidence. Hydrogen Peroxide, 552 F.3d at 318, 325.[1]

My colleagues essentially assert that a regression analysis is necessary to satisfy the predominance element and certify the class, but this seems to exceed the requirements for

[1] The District Court's determination that the Plans have offered sufficient common evidence for causation at class certification does "not bind the fact-finder on the merits," so a jury would still be free to find that the Plans have not met their burden if it is not convinced that this evidence shows that GSK's fraud caused the Plans' injuries. In re Hydrogen Peroxide Antitrust Litig., 552 F.3d 305, 318 (3d Cir. 2008), as amended (Jan. 16, 2009).

class certification. Although I recognize that the evidence must ultimately prove causation and not correlation, that seems to be a different question from whether sufficient common evidence exists concerning a matter each class member, through the named plaintiffs, must prove, namely whether the Plans have adduced sufficient common evidence to support an inference of causation.

Although a regression analysis may be strong evidence of causation, and the Majority opinion cites many cases where the presence or absence of a regression analysis was dispositive, such proof is not required. Indeed, in In re Flonase Antitrust Litigation, no regression was offered to support the conclusion that purchasers who switched to a generic version of a drug would have switched earlier if the generic had been available earlier. 284 F.R.D. 207, 220-22 (E.D. Pa. 2012). There, circumstantial evidence, including the fact that those purchasers switched to the generic when it became available and an expert's conclusion that the generic would have been cheaper than the brand-name if released earlier, provided common evidence from which a jury could reasonably conclude that those purchasers would have switched earlier, which was sufficient. Id.; see also In re Namenda Indirect Purchaser Antitrust Litig., 338 F.R.D. 527, 562-63 (S.D.N.Y. 2021) (concluding that every TPP class member likely reimbursed someone who would have switched to a generic based on (1) expert evidence that people did not often file claims with one TPP, and (2) "massive switching from brand to generics following generic launch"). Although Flonase was not a RICO case and was based on a price-effect theory, it exemplifies the propriety of drawing an inference about causation from strong circumstantial evidence in the absence of statistical evidence directly supporting the inference.

The strong common circumstantial evidence here may similarly provide a basis upon which a factfinder could decide whether GSK's conduct caused the Plans' injury, including expert reports that Nissen revealed the exact health risks, which were consequential to diabetic patients, that GSK concealed. Combined with the stark drop in prescriptions after the Nissen study revealed Avandia's cardiovascular risks, for which GSK offers no alternative explanation, this evidence may well be sufficient for a jury to find that the fraudulent marketing caused the Plans to pay for some Avandia prescriptions that they otherwise would not have.

Because I nevertheless agree that the District Court should evaluate the items described here in Part I and the Majority's opinion in Part III(C)(1), I concur in the judgment on the predominance issue.