No. 09-1156

IN THE
Supreme Court of the United States

MATRIXX INITIATIVES, *et al.*,
Petitioners,
v.

JAMES SIRACUSANO AND
NECA-IBEW PENSION FUND,
Respondents.

ON WRIT OF CERTIORARI TO THE
UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

BRIEF FOR THE PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA AND THE BIOTECHNOLOGY INDUSTRY ORGANIZATION AS AMICI CURIAE SUPPORTING PETITIONERS

MARK C. FLEMING
FELICIA H. ELLSWORTH
ADAM J. HORNSTINE
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

DAVID W. OGDEN
Counsel of Record
WILMER CUTLER PICKERING
HALE AND DORR LLP
1875 Pennsylvania Ave., NW
Washington, DC 20006
(202) 663-6000

QUESTION PRESENTED

Whether a plaintiff can state a claim under § 10(b) of the Securities Exchange Act and SEC Rule 10b-5 based on a pharmaceutical company's nondisclosure of adverse event reports even though the reports are not alleged to be statistically significant.

TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES

TABLE OF AUTHORITIES—Continued

Page(s)

TABLE OF AUTHORITIES—Continued

Page(s)

STATUTES AND REGULATIONS

OTHER AUTHORITIES

TABLE OF AUTHORITIES—Continued

TABLE OF AUTHORITIES—Continued

INTEREST OF AMICI CURIAE

The Pharmaceutical Research and Manufacturers of America (PhRMA) is a voluntary, nonprofit association that represents the country's leading research-based pharmaceutical and biotechnology companies.[1] PhRMA's members are dedicated to discovering medicines that enable patients to lead longer, healthier, and more productive lives. Member companies are the source of a majority of all new medicines. New medicines account for 40 percent of the increase in human lifespan between 1986 and 2000. *See* Lichtenberg, Nat'l Bureau of Econ. Research, Working Paper No. 9754, *The Impact of New Drug Launches on Longevity: Evidence From Longitudinal, Disease-Level Data From 52 Countries, 1982-2001*, at 21 (2003). Pharmaceutical companies, including PhRMA's members, have invested approximately $300 billion in the last decade to develop new medicines—including over $65 billion in 2009 alone. *See* PhRMA, *Pharmaceutical Industry Profile 2010*, at 26 (2010), at www.phrma.org/sites/phrma.org/files/attachments/Profile_2010_FINAL.pdf.

The Biotechnology Industry Organization (BIO) is the world's largest biotechnology organization, providing advocacy, business development, and communications services for more than 1,100 members worldwide.

---

[1] Counsel for both parties have filed letters consenting to the filing of all amicus briefs. No counsel for a party authored any part of this brief, and no person or entity other than members of or counsel for PhRMA and BIO made a monetary contribution to the preparation or submission of this brief. A list of PhRMA's members is available at http://www.phrma.org/member_company_list. A list of BIO's members is available at http://www.bio.org/members/biomembers.asp.

BIO members are involved in research and development of innovative healthcare technologies, as well as biotechnology applications in the agriculture, energy, and environmental sectors. Corporate members range from entrepreneurial companies developing a first product to Fortune 100 multinationals. BIO also represents state and regional biotechnology associations, service providers to the industry, and academic research centers.

PhRMA and BIO members closely monitor legal issues that affect the biopharmaceutical industry, and PhRMA and BIO have frequently participated in cases before this Court raising such issues. *See* Briefs filed by PhRMA and/or BIO in *Merck & Co.* v. *Reynolds*, 130 S. Ct. 1784 (2010) (No. 08-905); *Wyeth* v. *Levine*, 129 S. Ct. 1187 (2009) (No. 06-1249); *Warner-Lambert Co.* v. *Kent*, 128 S. Ct. 1168 (2008) (No. 06-1498); and *eBay Inc.* v. *MercExchange, LLC*, 547 U.S. 388 (2006) (No. 05-130).

The issue in this case is especially significant to PhRMA and BIO members because a number of members have borne the expense and burden of defending against securities fraud class actions in recent years. In 2008 and 2009, for example, over 40 such actions were filed against pharmaceutical and biotechnology companies. Dechert LLP, *Dechert Survey of Securities Fraud Class Actions Brought Against Life Sciences Companies* 2 (Mar. 2010), at www.dechert.com/library/3-10_WCSL_Kotler_Survey_of_Securities_Fraud_CA.pdf. These suits, which are often filed for their nuisance value, raise the already substantial costs and risks associated with the development of new medicines. The erroneous approach taken by the Ninth Circuit in this case is of serious concern to PhRMA and BIO members, as it makes it unnecessarily difficult, if

not impossible, for defendants in securities lawsuits to secure prompt dismissal of claims that rest only on a supposed failure to disclose information that would not affect the sales or profitability of the company. Such litigation accordingly threatens the ability of biopharmaceutical companies, including PhRMA's and BIO's members, to research and develop new medical advances.

SUMMARY OF ARGUMENT

A collection of adverse event reports that is not statistically significant does not permit a reasonable inference that a particular medicine actually *caused* the reported adverse event. Standing alone, such reports would not reasonably affect a biopharmaceutical manufacturer's earnings and, accordingly, are not material under the securities laws. Before the Ninth Circuit's decision, every Circuit to address the question presented had recognized as much. The decision below, however, departs from that well-reasoned principle while failing to supply any alternative standard whatsoever. The Ninth Circuit's ruling is all the more troubling because such a standardless test for materiality may compel manufacturers to over-disclose adverse event reports or studies that have no bearing on financial performance, lest they be accused of making misleading market statements about their products. In addition to being unduly burdensome, the resulting excessive disclosure of statistically insignificant adverse event reports will lead to investor confusion and stock fluctuation, which will harm manufacturers and their investors, as well as consumers and patients, who may be deterred from using safe and effective treatments.

This Court should endorse the approach taken by the Second Circuit and adopted by the First and Third

Circuits and several district courts: adverse event reports or studies known to a biopharmaceutical manufacturer, without more, cannot be material under the securities laws unless they establish a statistically significant link between the product and the adverse event. The statistical significance standard requires disclosure only once a correlation between an adverse event and the subject product can be reasonably inferred to be causal. It is only at that point that a manufacturer or regulatory body might react to adverse events, that a medicine's sales would be threatened, and that a rational investor might consider this information in making investment decisions.

The majority approach also properly recognizes that there may be limited circumstances in which statistically insignificant adverse event reports, together with other factors, demonstrate that a product's sales are threatened and a decline in sales of the drug would have a material effect on the biopharmaceutical manufacturer's earnings, such that the manufacturer is required to disclose adverse events that were not statistically significant. Absent such other indications of materiality, however, statistically insignificant adverse events standing alone are immaterial as a matter of law. Further, allegations of scienter also fail as a matter of law in such situations. A defendant can reasonably believe that statistically insignificant adverse event reports or studies (unaccompanied by additional indications of materiality) are immaterial.

This principle rests on the logical proposition that the sales and profitability of a medicine and the biopharmaceutical company that manufactures it are not threatened by adverse event reports from which no causal link can be inferred. Receipt of an adverse event report may be cause to investigate or inquire, but only

when adverse events become statistically significant is there a "substantial likelihood that the disclosure of the omitted fact would have been viewed by the reasonable investor as having *significantly altered* the total mix of information made available," thus requiring disclosure. *Basic Inc.* v. *Levinson*, 485 U.S. 224, 231-232 (1988) (emphasis added, internal quotation marks omitted). Assuming that the securities markets are efficient and rational, as this Court's jurisprudence requires, a reasonable investor will view statistically insignificant reports as the ordinary state of affairs, not as a significant change in the total mix of information bearing on a rational investment decision.

Recognizing the importance of statistical significance is all the more appropriate given that raw adverse event data are already publicly available. Adverse event reports submitted to the U.S. Food and Drug Administration (FDA) by patients, medical professionals, and manufacturers are catalogued and published on the FDA's website at regular intervals. Any potential investor can examine these reports, and the efficient market is presumed to be aware of this information. The rule adopted by the First, Second, and Third Circuits accepts that this information is already publicly disseminated, and thus manufacturers should not be forced to bury investors with additional public speculation regarding the meaning of each adverse event report.

The Ninth Circuit's decision improperly rejects this approach while providing no workable alternative to it. Its consequence would be to overwhelm the market with meaningless data and flood the courts with unproductive litigation, contrary to the purpose of the securities laws. *See TSC Indus., Inc.* v. *Northway, Inc.*, 426 U.S. 438, 448 (1976). The result will be not investor

protection but investor confusion, unduly burdensome over-disclosure of immaterial information, and the needless proliferation of unfounded concerns among patients and consumers regarding correlations that do not suggest causation. This Court should reverse.

ARGUMENT

I. A Reasonable Investor Would Not Base Investment Decisions On Statistically Insignificant Reports Of Adverse Events, Which Are Unlikely To Threaten A Drug's Sales

A. The Wide Range Of "Adverse Event Reports" In The Biopharmaceutical Industry

An "adverse event report" in the biopharmaceutical industry refers to any report of a negative event in which a biopharmaceutical product was used or involved. An adverse event report could be an anonymous electronic message submitted via a company website, a telephone call from any source to the FDA, or a published clinical study by reputable scientists. Reports vary widely in their detail, reliability, verifiability, and neutrality. The FDA receives hundreds of thousands adverse event reports every year—many of which are determined to have no causal association whatsoever with the product in question.

The FDA collects and analyzes reports of adverse events in order to monitor the continued safety of the products it regulates. The FDA's own definition of "adverse event" is extremely broad, including even events that result from the misuse or abuse of drug products:

> Any adverse event associated with the use of a drug in humans, *whether or not considered drug related*, including the following: An ad-

> verse event occurring in the course of the use of a drug product in professional practice; an adverse event occurring from drug overdose whether accidental or intentional; an adverse event occurring from drug abuse; an adverse event occurring from drug withdrawal; and any failure of expected pharmacological action.

21 C.F.R. § 314.80(a) (emphasis added). Adverse events can range from minor reactions, such as fevers, rashes, and mild patient discomfort, to severe side effects, including life-threatening complications or death. *See id.*

The FDA collects adverse event reports from several sources. The FDA receives adverse event reports directly from health care professionals such as physicians, pharmacists, and nurses; scientists conducting clinical studies; and members of the public, including patients, family members, and attorneys. *See* FDA, *Reports Received and Reports Entered into AERS by Year* (as of Mar. 31, 2010), at www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm070434.htm (*AERS Statistics*). Additionally, such individuals often choose to contact the drug manufacturer instead of the FDA: a consumer might spontaneously contact the manufacturer by telephone or over the Internet, or a health care professional might inform a manufacturer about adverse events experienced by one or more patients. Large drug manufacturers, including the members of PhRMA and BIO, receive thousands of such reports annually. *See id.*

Manufacturers are required by regulation to disclose adverse events to the FDA upon learning of them. *See* 21 C.F.R. § 314.80 (establishing post-marketing re-

porting of adverse drug experiences for manufacturers); *see also id.* § 600.80 (establishing similar reporting requirements for biologic products). Most adverse drug events are reported by manufacturers to the FDA on a quarterly basis; severe or unexpected adverse drug events must be transmitted to the FDA within fifteen days after the manufacturer learns of the adverse event. *See id.* § 314.80 (detailing periodic reporting requirements for adverse drug experiences); § 600.80 (detailing periodic reporting requirements for biologic products); *see also* Eng, *Drug Safety: It's a Learning Process*, 24 St. John's J. Legal Comment. 159, 176-182 (2009) (describing structure of adverse event reporting system and identifying limitations).

The FDA receives a significant number of adverse event reports every year. In 2009 alone, the FDA received 546,731 adverse event reports from manufacturers of drugs and biologic therapeutics. *See AERS Statistics*. Consumers and health care professionals lodged an additional 34,173 reports directly with the FDA. *Id.*

The FDA makes adverse event reports available to the public, including the investing community, through a variety of means. The FDA regularly releases raw adverse event report data through a database known as the Adverse Event Reporting System (AERS), which is accessible via the FDA's website and is designed to assist the FDA's post-marketing safety surveillance program for all approved drug and therapeutic biologic products. *See* FDA, *Adverse Event Reporting System*, at www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm (last updated Aug. 20, 2009) (*AERS Database)*. Information about certain post-market drugs is also available to the public through the FDA's Safety Information and Adverse Event Reporting Program, commonly

known as MedWatch. *See* FDA, *MedWatch: The FDA Safety Information and Adverse Event Reporting Program*, www.fda.gov/Safety/MedWatch/default.htm (last updated Aug. 25, 2010). The FDA also separately provides lists of any potential signals of serious risks or new safety information that it detects through its review of AERS. FDA, *Potential Signals of Serious Risks/New Safety Information Identified from the Adverse Event Reporting System*, at www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm082196.htm (last updated July 27, 2010) (*AERS Signals)*.[2]

Although manufacturers are required to relay each adverse event report they receive to the FDA, medical professionals and patients are under no parallel duty to report adverse events to manufacturers; point-of-care reporting is purely voluntary. Accordingly, a manufacturer may not even learn of adverse event reports associated with its products that are reported directly to the FDA before these reports are published in the AERS database.

---

[2] Similarly, the electronic Manufacturer and User Facility Device Experience (MAUDE) database is used to track adverse events associated with approved medical devices and is also available for viewing via the FDA's website. The FDA and the Department of Health and Human Services also track potential adverse reactions to vaccines through the electronic Vaccine Adverse Event Reporting System (VAERS) database. A small number of the adverse event reports received by the FDA are not entered in these databases, usually due to incomplete or missing information. Approximately 15% of the reports received by the FDA were not entered in the AERS database in 2009. *See AERS Statistics*.

Neither a manufacturer nor the FDA can determine the significance of an adverse event report standing alone. Nonetheless, the FDA and drug manufacturers constantly evaluate adverse event reports to determine whether a certain drug can be reasonably suspected of causing a previously unknown side effect. If there is a sufficient indication of a potential safety concern, the FDA may request further epidemiological studies or ask the manufacturer to investigate. Based on an evaluation of the drug's safety profile, the FDA may take significant regulatory action, such as requiring a manufacturer to update a product's labeling information (including warnings and precautions), restricting the use of the drug through a risk management program, communicating new safety information to the public, or, in rare instances, withdrawing the product's FDA approval. *See* 21 U.S.C. §§ 355-1 (risk management programs), 355(o) (labeling changes and postmarketing studies), 355(r) (FDA communication of new safety information), 355(e) (withdrawal of FDA approval); *see also* 42 U.S.C. § 262(j) (applying requirements of Federal Food, Drug, and Cosmetic Act to biologics). Often, however, the FDA finds that there is no connection between the medicine and reported adverse events.[3]

---

[3] Adverse event reports may also arise in the context of pre-approval products if a manufacturer becomes aware of adverse events experienced in the clinical trial or testing process. Although the pre-approval context is governed by different FDA regulations and requirements, the same general materiality standard governs for purposes of the securities laws, and the same issues of reliability and causation arise in connection with pre-approval adverse event reports as with post-approval reports. Equally present in the pre-approval context is the concern that the market will react unfavorably to disclosures of adverse events for

B. Adverse Event Reports Frequently Have No Causal Connection To The Product In Question

Importantly for purposes of this case, adverse event reports frequently do not even purport to identify a causal link between the event they report and any given drug product. In fact, as previously discussed, the FDA's definition of an adverse event includes events "associated with the use of a drug in humans, *whether or not considered drug related*." 21 C.F.R. § 314.80(a) (emphasis added).

The FDA recognizes that adverse event reports, many of which are anecdotal, have significant limitations. As the FDA correctly warns those reviewing adverse event reports via its public database, "there is no certainty that the reported event was actually due to the product." *AERS Database*. The FDA's regulations also recognize as much. *See* 21 C.F.R. § 314.80(k) ("A report or information submitted by an applicant … does not necessarily reflect a conclusion by the applicant or FDA that the report or information constitutes an admission that the drug caused or contributed to an adverse effect"); *id.* § 803.16 ("A report … and our release of that report or information, is not necessarily an admission that the device, or you or your employees, caused or contributed to the reportable event."). Even where the FDA has detected a "signal" of a potential

---

which there is no evidence of a causal relationship to the subject product. *See In re AstraZeneca Sec. Litig.*, 559 F. Supp. 2d 453, 470 (S.D.N.Y 2008) ("[P]articularly in the testing and development stage, the possible beneficial effects of a drug may be accompanied by adverse side effects, and there may be uncertainty as to how the risk-benefit balance ultimately turns out, and how it will be viewed by regulators.").

serious risk, it expressly warns that inclusion of a product on this list "*does not mean* that FDA has identified a causal relationship between the drug and the listed risk" and "emphasize[s] that the listing of a drug … does not mean that FDA is suggesting that healthcare providers should not prescribe the drug or that patients taking the drug should stop." *AERS Signals* (emphasis added).

These warnings reflect a common-sense recognition that people who use FDA-approved drugs are often seriously ill and suffer adverse events that are frequently not caused by the drug. Many adverse events are the result of an underlying medical condition or something else altogether. Additionally, the amount of publicity that a drug receives may dramatically alter the number of adverse event reports submitted to manufacturers and the FDA. The veracity and accuracy of these reports are also inherently difficult to verify. For these reasons, the FDA cautions that anecdotal adverse event reports "cannot be used to calculate the incidence of an adverse event in the U.S. population." *AERS Database*.

Accordingly, it is not uncommon for the FDA to conclude that, notwithstanding the receipt of adverse event reports, no regulatory action is warranted regarding a particular drug. One example arose earlier this year when the FDA examined several adverse event reports for the drug Spiriva®, a drug co-marketed by Pfizer Inc. and Boehringer Ingelheim Pharmaceuticals, Inc., members of PhRMA and BIO. Spiriva treats breathing problems associated with chronic obstructive pulmonary disease. Certain adverse event reports correlated use of Spiriva with a possible increased risk of cardiovascular problems. The FDA concluded that the available data did not support an association between

the use of the drug and an increased risk for these serious cardiovascular events. *See* FDA, *Tiotropium (marketed as Spiriva HandiHaler)*, at www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm095076.htm (last updated Jan. 14, 2010).

As this example illustrates, the mere presence of adverse event reports, standing alone, without any scientific analysis, does not permit a logical inference that the reported events were caused by the subject drug. Adverse event reports may be mistaken, fabricated, or incomplete, and they also may identify a factual coincidence and not a causal relationship. At most, they are a prompt to further investigation and analysis. Moreover, the mere presence of adverse event reports is by no means an unusual occurrence. The broad definition of "adverse event" and the relative costlessness of providing a report to the FDA or a manufacturer ensures that virtually every drug will be the subject of numerous such reports, even where there is no scientific basis to believe that the drug caused the adverse event.

C. Statistically Insignificant Adverse Event Reports, Standing Alone, Are Immaterial Because They Do Not Threaten A Drug's Sales Or Profitability

Because adverse event reports take many forms and frequently offer no meaningful information about the drug in question, neither the FDA nor a manufacturer can or should base rational decisions on such reports without first determining whether they are statistically significant, *i.e.* "that the ill effects may be caused by—rather than randomly associated with—use of the drugs." *In re Carter-Wallace, Inc. Sec. Litig.*, 150 F.3d 153, 157 (2d Cir. 1998) ("*Carter-Wallace I*").

More often than not, adverse event reports do not lead to any formal FDA regulatory action such as a label change, a so-called "black box" warning advising that the drug may have serious side effects, or a recall. The few that do ultimately trigger such a regulatory response do so only after careful review by the FDA. Therefore, a drug's sales and profitability are likely to be altered only after concrete, scientific analysis takes place, and only at that point would such information (without more) potentially be "material" to a reasonable investor.

An omission is material when there is a "substantial likelihood that the disclosure of the omitted fact would have been viewed by the *reasonable investor* as having *significantly altered* the total mix of information made available." *Basic Inc.* v. *Levinson*, 485 U.S. 224, 231-232 (1988) (emphasis added, internal quotation marks omitted). But statistically insignificant adverse event reports are the normal state of affairs for marketed drug products, given the ease with which such reports can be made and the FDA's regulatory *requirement* that manufacturers disclose them regardless of causation. 21 C.F.R. § 314.80(a). Statistically insignificant reports do not alter, much less "significantly" alter, the total mix of information available to the investing public. Indeed, "[s]ome adverse events may be expected to occur randomly, especially with a drug designed to treat people that are already ill." *In re Carter-Wallace, Inc. Sec. Litig.*, 220 F.3d 36, 41 (2d Cir. 2000) ("*Carter-Wallace II*").

Courts have accordingly ruled that "the receipt of an adverse report does not in and of itself show a causal relationship between [a drug] and the illness mentioned in the report." *Carter-Wallace II*, 220 F.3d at 41. And where there is no scientifically reliable allegation of a

causal connection, there is *a fortiori* no materiality. Thus, in the absence of such statistically significant information, manufacturers are under no obligation to address such reports in their securities filings.

A securities plaintiff might state a claim by plausibly alleging (among other elements) that a company intentionally failed to disclose adverse event reports that a reliable source—such as the FDA, the company's own internal safety professionals, or a clinical study committee—had concluded were statistically significant, because such a conclusion would be likely to harm a drug's future sales. But it is only when reported adverse events rise to that level of statistical significance—thus permitting a *sound* inference of causation between drug and event—that such reports, without more, could become material for purposes of the securities laws.[4]

---

[4] Moreover, although alleging statistical significance is necessary for a plaintiff to plead a securities fraud claim based solely on undisclosed adverse event reports, such an allegation is not sufficient to survive a motion to dismiss where it is unsupportable or the plaintiff's theory is implausible. Thus, it would not be sufficient for a plaintiff to assert, in a conclusory fashion and without supporting factual allegations, that certain adverse event reports were statistically significant. *See Ashcroft* v. *Iqbal*, 129 S. Ct. 1937, 1949 (2009) (to survive a motion to dismiss, the complaint must have "facial plausibility," *i.e.*, "factual content that allows the court to draw the reasonable inference that the defendant is liable for the misconduct alleged"); *Bell Atl. Corp.* v. *Twombly*, 550 U.S. 544, 570 (2007) (complaint must "state a claim to relief that is plausible on its face"); *Oran* v. *Stafford*, 226 F.3d 275, 284 (3d Cir. 2000) (Alito, J.) (requiring that the allegedly withheld data be able to "demonstrate[] a[] medically conclusive link in light of the millions of prescriptions written" for the drug in question); *see also New Jersey Carpenters Pension & Annuity Funds* v. *Biogen IDEC Inc.*, 537 F.3d 35, 49-50 (1st Cir. 2008) (allegations must provide a

This approach is all the more sensible given that most adverse event data are already made available to the public by the FDA through its MedWatch system, the AERS database, and other FDA sources, data of which investors are presumed to be aware. *See In re Zyprexa Prods. Liab. Litig.*, 549 F. Supp. 2d 496, 534 (E.D.N.Y. 2008) (investors are presumed to know about "available medical research, media coverage … and securities analyst reports"); *Yanek* v. *Staar Surgical Co.*, 388 F. Supp. 2d 1110, 1126 (C.D. Cal. 2005) ("both the information about the recalls and the MAUDE printouts were available through the FDA and thus were publicly known or available information"). A requirement that manufacturers report adverse event information not only to the FDA but also in a company's SEC filings would therefore be redundant and unduly burdensome. And, as this Court has frequently noted, the "market price of shares traded on well-developed markets reflects all publicly available information." *Basic*, 485 U.S. at 246.[5]

"basis to conclude" that "the[] results ... were statistically significant").

[5] The fact that raw adverse event information is publicly available also calls into question whether a plaintiff making claims like Respondents' claim here could plead or prove loss causation, because the allegedly material information was already available to the public. Loss causation is a separate element of a Rule 10b-5 claim that requires plaintiffs to show "a causal connection between the material misrepresentation and the loss." *Dura Pharm., Inc.* v. *Broudo*, 544 U.S. 336, 342 (2005). To establish this connection, plaintiffs must show that a previously hidden truth is revealed through a disclosure that corrects a prior statement. *Id.* This "corrective disclosure" must at least reveal to the market that the prior representation was false. *Lentell* v. *Merrill Lynch & Co.*, 396 F.3d 161, 175 n.4 (2d Cir. 2005). In scenarios involving adverse

Some courts have incorrectly questioned this concept, suggesting that the market could be misled by a manufacturer's failure to disclose in a securities filing information that was already in the market by virtue of the company's FDA submissions. *See In re Pfizer Inc. Sec. Litig.*, 584 F. Supp. 2d 621, 636-637 (S.D.N.Y. 2008) (disagreeing with the "presum[ption] that disclosure to the FDA is equivalent to disclosure to the market" even though "it is likely the FDA would highlight or require disclosure of material negative safety information about a drug"). This Court has made clear that this is not how the efficient market functions. *Basic*, 485 U.S. at 247 ("publicly available information is reflected in market price"). The market is presumed to have assimilated information that is in the public domain; this would certainly include information available through a searchable government database such as AERS, in published medical journals, or in the news media. Indeed, it would seem incongruous to allow plaintiffs to claim, on the one hand, that they relied on information in the market (positive statements made by a publicly traded company about its drugs) while simultaneously disavowing knowledge of other readily available information (the adverse event report data made available by the FDA).

---

event reports, however, the information contained in a manufacturer's disclosure to the SEC of material adverse event reports will merely confirm information previously disclosed to the FDA, and a plaintiff will have a difficult time establishing loss causation. *See In re Retek Inc. Sec. Litig.*, 621 F. Supp. 2d 690, 705 (D. Minn. 2009) ("[C]onfirmatory information—that information already known to the market—may not constitute such a corrective disclosure" (internal quotation marks omitted)).

In the *Carter-Wallace* cases, a company withdrew its product (an epilepsy drug) from the market when it concluded the drug was causing deaths. The Second Circuit upheld the dismissal of securities fraud claims notwithstanding numerous earlier adverse event reports, because

> [d]rug companies need not disclose isolated reports of illnesses suffered by users of their drugs until those reports provide statistically significant evidence that the ill effects may be caused by—rather than randomly associated with—use of the drugs and are sufficiently serious and frequent to affect future earnings.

Carter-Wallace I, 150 F.3d at 157. Absent such evidence, the company's projections of increased sales were not materially misleading. *Id.*; *see also Carter-Wallace II*, 220 F.3d at 40 (rejecting allegations of fraud even though plaintiffs alleged that the adverse reports were "extremely serious" and the "number of incidents was … statistically unacceptable").

Similarly, in *Oran* v. *Stafford*, 226 F.3d 275 (3d Cir. 2000) (Alito, J.), the Third Circuit rejected securities fraud claims based on the nondisclosure of adverse patient data concerning a combination of diet drugs, including 55 reports of heart-valve disorders in patients taking the drugs and a report by the Mayo Clinic raising "significant concern that this combination … has important implications regarding valvular disease." *Id.* at 279-280, 282 (internal quotation marks omitted). The Third Circuit held that "[b]ecause the link between the … drugs and heart-valve disorders was never definitively established during the relevant period … [defendant's] failure to disclose this data cannot render its statements about the inconclusiveness of the relation-

ship materially misleading." *Id.* at 284. The court also reasoned that, in the absence of statistically significant data establishing a link between the drugs and the adverse events, it was speculative whether the company would be exposed to significant product liability claims, and there was no duty to disclose information concerning the extent of any such claims. *Id.* at 285-286.

Likewise, in the recent decision of *In re Medtronic Inc., Securities Litigation*, a district court dismissed a securities fraud claim based on a failure to disclose statistically insignificant adverse event information where a physician informed the defendant that adverse events might indicate a potential safety issue with a particular product, after which the defendant commissioned a broader study. 618 F. Supp. 2d 1016, 1026, 1030 (D. Minn. 2009), *appeal pending*, *Detroit Gen. Ret. System* v. *Medtronic, Inc.* (8th Cir. No. 09-2518). The company concluded that the adverse events were not statistically significant but might become so later, decided to suspend distribution of the product voluntarily, and announced this decision promptly to the public and the market. In a securities class action suit similar to the one at issue here, the district court concluded that the company's handling of this situation was entirely appropriate and dismissed the plaintiffs' complaint because no *rational* investor would have believed that the statistically insignificant reports about the product would have had any effect on the company's stock price. 618 F. Supp. 2d at 1026 ("failure to disclose additional statistically insignificant information cannot have been materially misleading").[6]

---

[6] *See also, e.g., In re Elan Corp. Sec. Litig.*, 543 F. Supp. 2d 187, 213 (S.D.N.Y. 2008) ("Even if scientists suspected that [the

In *New Jersey Carpenters Pension & Annuity Funds* v. *Biogen IDEC Inc.*, 537 F.3d 35 (1st Cir. 2008), the First Circuit adopted the statistical significance test of *Carter-Wallace* and *Oran* in the different but related context of scienter. The First Circuit ruled that "[a] statement cannot be intentionally misleading if the defendant did not have sufficient information at the relevant time to form an evaluation that there was a need to disclose certain information and to form an intent not to disclose it." *Id.* at 45. In other words, a manufacturer cannot intentionally or recklessly mislead the markets by failing to disclose statistically insignificant adverse event reports, because the manufacturer can reasonably believe such information to be immaterial. Accordingly, mere awareness of statistically-insignificant reports cannot give rise to a cogent inference of scienter. *Tellabs, Inc.* v. *Makor Issues & Rights, Ltd.*, 551 U.S. 308 (2007); *see also Biogen*, 537 F.3d at 50 ("There is no plausible inference from the reports of just five [adverse events] that the defendants knew of any causal relationship between the use of [the drug] and the [adverse events], and then intentionally withheld data."); *Carter-Wallace II*, 220 F.3d at 41 (the absence of a material omission itself negates any

---

drug at issue] might cause adverse events and Defendants knew of these suspicions, these facts would not have required Defendants to conclude that these effects were real before such a relationship was established using accepted statistical methods and standards of proof."); *In re Bayer AG Sec. Litig.*, No. 03-1546, 2004 WL 2190357, at *4 (S.D.N.Y. Sept. 30, 2004) (even though the company was "inundat[ed]" with increasing numbers of adverse event reports, it had no duty to disclose them prior to a meeting of its safety executives where a "consensus … emerged" that the data concerning the drug's dangers was "putting the brand at risk" (internal quotation marks omitted)).

finding of scienter, because it cannot be willful or reckless not to disclose immaterial adverse event reports).[7]

Contrary to the Ninth Circuit's reasoning, the use of statistical significance in this context does not run afoul of this Court's caution regarding "bright-line rule[s]." *Basic*, 485 U.S. at 236. This Court did not reject general principles that could be used to determine materiality, and it certainly did not hold that a dispute regarding materiality must always survive a motion to dismiss. Rather, the Court warned against treating "ease of application alone" as "an excuse for ignoring the purposes of the Securities Acts and Congress' policy decisions," noting that an approach that "designates a single fact or occurrence as *always determinative* of an inherently fact-specific finding such as materiality, must necessarily be overinclusive or underinclusive." *Id.* (emphasis added).

But nothing in the *Carter-Wallace* cases, *Oran*, or the numerous other decisions that take a similar approach suggests that statistical significance is *always*

---

[7] *See also*, *e.g.*, *Elan*, 543 F. Supp. 2d at 218 (failure to allege that "Defendants knew of any statistically significant or causal relationship" between drug and adverse effect undercut plaintiffs' allegations of scienter); *In re Bausch & Lomb, Inc. Sec. Litig.*, 592 F. Supp. 2d 323, 350 (W.D.N.Y. 2008) (dismissing complaint for failure to plead scienter where plaintiffs failed to allege that "anyone at [defendant company] believed during the Class Period that there was a causal link between [product] and [adverse event], much less that [the company] had reached an internal consensus at odds with its public statements concerning [product's] safety"); *AstraZeneca*, 559 F. Supp. 2d at 461 (dismissing complaint for failure to plead scienter where pharmaceutical company received adverse medical reports about a pre-market drug but continued to issue positive press releases stating, inter alia, that its drug had a "positive benefit-risk profile")

determinative. *See Elan*, 543 F. Supp. 2d at 210 ("[T]his Court agrees … that *Carter-Wallace I* does not establish a bright-line rule for the materiality of information regarding drug safety risks."). On the contrary, it is possible that, in certain limited circumstances, statistically insignificant adverse event reports may arise together with *other* information that, when viewed as a whole, establishes that drug sales are threatened and a drop in sales of the drug would have a material effect on the manufacturer's future earnings. *See*, *e.g.*, *Medtronic*, 618 F. Supp. 2d at 1026 (considering possible "other indications" of materiality beyond statistical significance but finding that none "demonstrat[ed] that the undisclosed information was a sufficiently serious threat to Medtronic's future earnings so as to require disclosure"); *Bausch & Lomb*, 592 F. Supp. 2d at 350 (statistically insignificant information could "become material even in the absence of statistically significant evidence in light of other indications that the risk associated with adverse drug events is legitimate and serious enough to threaten drug sales"); *Bayer*, 2004 WL 2190357, at *9-10 (adverse event reports lacking statistical significance, when considered in conjunction with an internal corporate "consensus" that a drug's "potential dangers were putting the brand at risk," were enough to find materiality; adverse event reports, "coupled with other evidence," can demonstrate that "defendants viewed the adverse event reports as sufficiently serious and frequent to affect future earnings").

In this case, the Ninth Circuit did not rely on any allegations of additional indications of materiality. Rather, it denied the motion to dismiss because the presence of adverse event reports *alone*—with no allegation of statistical significance or *any other* contextual information suggesting causation—could, in the court's

view, be found to have significantly altered the total mix of information available to a reasonable investor.[8] That was error—not because the court failed to apply a "bright-line rule," but because it failed to recognize that the mere allegation of undisclosed adverse event reports was insufficient to allege a material omission.[9]

Further, even once reported adverse events are found to be statistically significant, it does not necessarily follow that these events are "material" for purposes of the securities laws. The underlying reporting may be inaccurate, or the nature of the adverse events may be too minor to have any effect on the drug's commercial success. The affected drug must also be suffi-

---

[8] Even the case upon which the Ninth Circuit most heavily relied, *In re Pfizer Inc. Securities Litigation*, recognized that the standard for pleading the materiality of adverse events is based on statistical significance. 584 F. Supp. 2d at 633. However, the district court in *Pfizer* nonetheless denied the defendants' motion to dismiss, concluding that it could not ascertain on the pleadings or by judicial notice whether two clinical studies cited in the complaint demonstrated a statistically significant link between two of Pfizer's prescription pain medications and cardiovascular events, even though the FDA had determined that the studies showed no such link. The *Pfizer* court concluded that "statistical significance is a question of fact." *Id.* at 635-636. That decision was erroneous because plaintiffs had the burden of pleading that, at the time of the alleged nondisclosures and misstatements, the studies at issue demonstrated a statistically significant causal link between the drugs and the adverse cardiovascular events, and the court failed to address whether plaintiffs met their burden.

[9] PhRMA and BIO take no position on whether Respondents *could* allege sufficient additional facts to permit a reasonable jury to conclude that the adverse event reports on which they rely were material. Under the Ninth Circuit's ruling, Respondents were not required to make such an allegation; that is in itself sufficient grounds to reverse in this case.

ciently profitable and represent a significant enough portion of the company's earnings or future products that a drop in sales would have a material effect on the manufacturer's overall financial position. *See Carter-Wallace I*, 150 F.3d at 157 (statistically significant adverse events must be "sufficiently serious and frequent to affect future earnings"); *Medtronic*, 618 F. Supp. 2d at 1030 ("[T]here is nothing to suggest that such undisclosed information constituted a sufficiently serious threat to Medtronic's stock price as to render such information material."); *see also Parnes* v. *Gateway 2000, Inc.*, 122 F.3d 539, 547 (8th Cir. 1997) (statements or omissions are not material where they "present or conceal such insignificant data that … [they] simply would not matter to a reasonable investor").

II. THE JUDGMENT BELOW WOULD EFFECTIVELY REQUIRE MANUFACTURERS TO FLOOD THE MARKETS WITH DISCLOSURES OF ADVERSE EVENT REPORTS, TO THE DETRIMENT OF INVESTORS AND PATIENTS

The Ninth Circuit's ruling has an additional flaw: if allowed to stand, it would require a company to disclose in its securities filings statistically insignificant adverse event reports, which would in effect require it to disclose adverse event reports for all products. This would result in the inclusion of literally thousands of such reports per year in biopharmaceutical companies' securities filings. *See AERS Statistics*. The Ninth Circuit's ruling would require biopharmaceutical companies to "report on every conjecture, rumor or adverse claim," an outcome that would "unnecessarily burden the industry." *In re Carter-Wallace, Inc. Sec. Litig.*, No. 94-5704, 1999 WL 1029713, at *1 (S.D.N.Y. Nov. 10, 1999), *aff'd*, 220 F.3d 36 (2d Cir. 2000). Nor does the Ninth Circuit "clearly explain how the accumulation of additional anecdotal data, short of statistical signifi-

cance," adds anything to the disclosures already made to the investing public by biopharmaceutical manufacturers. *Oran*, 226 F.3d at 284. Such a disclosure regime contravenes this Court's command that issuers not "bury the shareholders in an avalanche of trivial information." *TSC Indus. Inc.* v. *Northway, Inc.*, 426 U.S. 438, 448 (1976).[10]

The decision below also disregards this Court's admonition that plaintiffs "with a largely groundless claim" should not be able "to simply take up the time of a number of other people, with the right to do so representing an *in terrorem* increment of the settlement value, rather than a reasonably founded hope that the [discovery] process will reveal relevant evidence." *Dura Pharm., Inc.* v. *Broudo*, 544 U.S. 336, 347 (2005) (quoting *Blue Chip Stamps* v. *Manor Drug Stores*, 421 U.S. 723, 730, 741 (1975)). Plaintiffs should not be permitted to file a securities fraud suit "with only a faint

[10] The disclosure rule contemplated by the Ninth Circuit would effectively require companies to address every adverse event report in a quarterly SEC filing to fend off securities claims for failure to disclose. As one court has observed, this potential for overly broad disclosure could expose manufacturers to securities fraud claims for making "misleading" *over*-disclosures. *See In re Medimmune, Inc. Sec. Litig.*, 873 F. Supp. 953, 966 (D. Md. 1995) (noting that premature disclosure without statistical significance could "cause … stock to decline in value [and then] rise … again"). Under this theory, if a company discloses an isolated adverse event report as "material," and the report later proves to have been specious, the report's disclosure would needlessly drive down the stock price. Investors might then claim to have been misled by this over-disclosure, exposing the company to securities lawsuits in both directions. *Id.* The securities laws should not be construed to expose publicly-traded companies to lawsuits every time their share price dips.

hope" that the expensive and time-consuming discovery process might ultimately reveal some plausible evidence of materiality. *Id.* (citation omitted). At the very least, plaintiffs seeking to base their allegation of causation solely on undisclosed adverse event reports should be required to plead specific facts that, if proven, would show that those reports were statistically significant.[11]

The approach followed by the First, Second, and Third Circuits, by contrast, prevents plaintiffs from forcing manufacturers into expensive and time-consuming discovery on the strength of anecdotal reports that permit no plausible inference of materiality.

---

[11] Indeed, the *Pfizer* securities litigation reveals the danger of allowing plaintiffs to pass the motion to dismiss stage without pleading that, at the time of the alleged nondisclosure or misstatement, there was statistically significant evidence linking a drug to adverse events. Since the motion to dismiss was denied in that case—and the mandatory stay of discovery under the Private Securities Litigation Reform Act lapsed—900 hours of deposition testimony have been ordered, millions of pages of documents have been produced, and the parties have engaged in costly expert discovery that culminated in a full *Daubert* hearing. *See In re Pfizer Inc. Sec. Litig.*, No. 04-9866, 2010 WL 1047618 (S.D.N.Y. Mar. 22, 2010). At the time of the alleged nondisclosures, both of the drugs at issue had been extensively tested on thousands of patients in studies conducted before and after they went on the market, and these studies showed no statistically significant link between the drugs and the adverse cardiovascular events. Despite this extensive testing—and the FDA's decision to take no action after receiving its results, which the FDA found did not demonstrate a statistically significant link between the drugs and the adverse events—Pfizer has been forced to expend millions of dollars to conduct discovery and defend the litigation. These substantial costs are borne directly by the company and its shareholders and indirectly by Pfizer's patients.

That approach is not an additional rule; it simply implements Congress's practical and necessary judgment that nondisclosure of immaterial information should not ground potentially abusive securities litigation. *See Dura*, 544 U.S. at 345 (noting that the securities laws are not "broad insurance against market losses").

The Ninth Circuit's rule would also effectively require manufacturers to disclose to the investing public information that the FDA and manufacturers have concluded does not warrant a warning to patients or health care professionals (apart from making the raw information publicly available via the FDA's website). Essentially, the Ninth Circuit's interpretation of the securities laws would require manufacturers to place an imprimatur of legitimacy on every adverse event anecdote received, effectively characterizing these reports as material through their disclosure—irrespective of reliability or verifiability—even though federal and state public health laws deem it immaterial for patients using the treatment or health care professionals prescribing it. But over-disclosure is disfavored in the public health context for good reason: it can lead patients and health care professionals to avoid or discontinue using beneficial, perhaps life-saving, treatments.

A paradigmatic example of the risk of over-disclosure arose with respect to implantable cardiac defibrillators—medical devices that are implanted in patients at risk of sudden cardiac death due to heart rhythm abnormalities. In 2004 and 2005, several defibrillator manufacturers reported a potential short-circuiting defect to the FDA. The potential defect was rare and appeared only under certain specific conditions. Nonetheless, after media coverage of a specific adverse event, the manufacturers issued advisories to health care professionals. As a result of the ensuing

publicity, many patients elected to replace their implanted devices. A scientific study later concluded that the elective replacements were in fact riskier than the potential defect. Gould & Krahn, *Complications Associated with Implantable Cardioverter-Defibrillator Replacement in Response to Device Advisories*, 295 J. Am. Med. Ass'n 1907, 1907-1911 (2006) (describing a study of patient outcomes from replacement surgery in response to device advisories); *see also* von Biela, *A Disclosure Dilemma: What You Don't Know Can Kill You, But So Can What You Do Know*, 65 Food & Drug L. J. 317 (2010) (describing various situations in which adverse event reports with no proven causal connection to the treatment in question led to over-warning by FDA and manufacturers, with results detrimental to public health). The Ninth Circuit's rule will only increase the frequency of such harmful and unnecessary reactions.

CONCLUSION

The judgment of the court of appeals should be reversed.

Respectfully submitted.

DAVID W. OGDEN
Counsel of Record
WILMER CUTLER PICKERING
HALE AND DORR LLP
1875 Pennsylvania Avenue, N.W.
Washington, D.C. 20006
(202) 663-6000

MARK C. FLEMING
FELICIA H. ELLSWORTH
ADAM J. HORNSTINE
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

AUGUST 2010