United States Court of Appeals
For the First Circuit

No. 16-2057

TERRY BRENNAN; RON KENNER;
KEVIN KOZIATEK; JEFFREY BUTERBAUGH;
DRAGON GATE MANAGEMENT, LTD; VINCENT RAMPE,

Plaintiffs, Appellants,

AVIAD BESSLER, individually and on behalf of all others similarly situated; THEODORE J. DALY,

Plaintiffs,

v.

ZAFGEN, INC.; THOMAS E. HUGHES,

Defendants, Appellees.

APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS
[Hon. F. Dennis Saylor, IV, U.S. District Judge]

Before

Kayatta, Circuit Judge,
Souter, Associate Justice,[*]
and Stahl, Circuit Judge.

Jeffrey C. Block, with whom Joel A. Fleming, Block & Leviton LLP, Jacob A. Goldberg, Gonen Haklay, and The Rosen Law Firm, P.A. were on brief, for appellants.

Deborah S. Birnbach, with whom Kevin P. Martin, Adam Slutsky, Kate MacLeman, Joshua Bone, and Goodwin Procter LLP were on brief, for appellees.

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

April 7, 2017

STAHL, **Circuit Judge**. Following a significant drop in the share price of Zafgen, Inc., a biopharmaceutical developer based in Boston, Massachusetts, its investors brought a securities fraud class action suit against the company and its Chief Executive Officer, Dr. Thomas Hughes ("defendants"), pursuant to Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, 15 U.S.C. §§ 78j(b) and 78(t)(a), and Securities and Exchange Commission Rule 10b-5, 17 C.F.R. § 240.10b-5. The investors' complaint[1] focuses on several allegedly misleading statements made by the defendants regarding Zafgen's anti-obesity drug Beloranib. Specifically, the complaint alleges that the defendants disclosed some, but not all, of the thrombosis-related adverse events that occurred during Beloranib's clinical trials. The investors claim that these partial disclosures caused Zafgen's common stock to trade at artificially-inflated prices -- prices that plunged after a clinical patient taking Beloranib died and the Food and Drug Administration ("FDA") placed the drug on a partial clinical hold.

Despite these allegations, the district court granted the defendants' motion to dismiss, concluding that the investors' complaint did not contain facts giving rise to a "cogent and compelling" inference of scienter as required under the Private

[1] The investors filed their original complaint on October 21, 2015, and amended that complaint on February 22, 2016. For the sake of clarity, we refer to this amended complaint as the "complaint" throughout this opinion.

Securities Litigation Reform Act of 1995 ("PSLRA"). Brennan v. Zafgen, Inc., 199 F. Supp. 3d 444, 471 (D. Mass. 2016) (quoting Tellabs, Inc. v. Makor Issues & Rights, Ltd., 551 U.S. 308, 324 (2007)). We agree, and therefore affirm.

I.

We recite the facts as alleged in the complaint, supplemented by certain "materials [the] defendants filed in the district court in support of their motion to dismiss." Fire & Police Pension Ass'n of Colo. v. Abiomed, Inc., 778 F.3d 228, 232 (1st Cir. 2015); see also Watterson v. Page, 987 F.2d 1, 3 (1st Cir. 1993) (noting that courts, when ruling on a motion to dismiss in securities fraud cases, often consider "documents the authenticity of which are not disputed by the parties," along with "official public records; . . . documents central to plaintiffs' claim[s]; [and] documents sufficiently referred to in the complaint").

Zafgen's stated goal is "to significantly improv[e] the health and well-being of patients affected by obesity and complex metabolic disorders." To that end, Zafgen has focused its efforts on developing Beloranib, a drug aimed at combating these conditions.[2] Hughes, as Zafgen's Chief Executive Officer, oversaw

[2] At all relevant times, Zafgen was a "one-drug company," meaning that Beloranib was Zafgen's only product candidate in clinical development.

Beloranib's clinical testing. While doing so, Hughes also steered Zafgen towards its initial public offering ("IPO"), which the company completed on June 19, 2014. The current dispute arises from the intersection of these two strategic endeavors.

A. Beloranib and the FDA Approval Process

As part of the development process, the FDA requires that any new drug "go through a series of clinical trials before it can be approved for marketing and sales in the United States." N.J. Carpenters Pension & Annuity Funds v. Biogen IDEC Inc., 537 F.3d 35, 39 (1st Cir. 2008) (citation omitted). After a pharmaceutical developer finishes its initial testing of a drug on animals, it must then "submit[] an application to the FDA for approval to test the drug on humans." Id.; see also 21 C.F.R. § 312.20. If the FDA approves that request, human testing begins. Typically, such testing consists of three phases of clinical trials.[3] Biogen IDEC, 537 F.3d at 39; see also 21 C.F.R. § 312.21.

[3] Our decision in Biogen IDEC ably summarized the objectives of these three phases:

> Phase I studies generally involve twenty to eighty subjects, and are designed to determine how the drug works in humans and the side effects associated with increasing doses. Phase II studies usually involve no more than several hundred subjects, and are designed to evaluate the effectiveness of the drug, as well as common short-term side effects and risks. Phase III studies are large-scale trials, usually involving several hundred to several thousand subjects, and are intended to gather the information necessary to provide an

Each phase "requires the company to test the drug on a broader population and results in more stringent monitoring and evaluation." Biogen IDEC, 537 F.3d at 39. Throughout the course of these trials, "the drug company must report to the FDA and to all participating physicians any serious and unexpected adverse drug experiences that occur." Id. (citing 21 C.F.R. § 312.32(c)(1)(i)(A)).

At the time the investors first brought this suit, Zafgen had conducted three Phase I trials, four Phase II trials, and one Phase III trial. The investors' complaint, however, concentrates on Zafgen's ZAF-201 trial, a Phase II trial that consisted of 160 patients and lasted from August 2012 to May 2013. From this group of 160 patients, Zafgen treated 122 of them with Beloranib. As the ZAF-201 trial progressed, four of the patients given Beloranib suffered adverse "thrombotic," or blood-clotting, events of varying severity. Third-party clinical investigators classified two of these adverse events as "superficial" and the other two as "serious."[4] Zafgen disclosed the two serious adverse events in

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> adequate basis for labeling the drug. . . . After Phase III, the FDA considers the results of all the clinical trials in determining whether to approve a drug for market.

Id. (internal citations omitted).

[4] An adverse event is "serious" if "it results in . . . [d]eath, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of

advance of its IPO, noting their occurrence in its April 18, 2014 Form S-1 Registration Statement. The company did not, however, directly disclose the two superficial adverse events at that time.

B. Zafgen's Stock Price Declines

Zafgen's share price began to decline in October 2015. On October 12th, Zafgen's share price closed at $34.76. By the close of trading the next day, Zafgen's share price had dropped to $15.75. On October 14th, Zafgen announced that a patient in its ongoing Phase III trial had died, and confirmed on October 16th that the patient had been treated with Beloranib, not a placebo, and that the FDA had placed Beloranib on a partial clinical hold. During a conference call held that same day, Dr. Dennis Kim, Zafgen's Chief Medical Officer, likewise informed analysts that a total of six adverse thrombotic events had occurred throughout the course of Beloranib's clinical testing: two in the company's ongoing clinical trials and four in the completed ZAF-201 trial. Dr. Kim's comments marked the first time that Zafgen or any of its representatives had informed its investors of the two superficial adverse thrombotic events that had occurred in the ZAF-201 trial. By the close of trading on October 16th, Zafgen's share price

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the ability to conduct normal life functions, or a congenital anomaly/birth defect," or where it "may require medical or surgical intervention to prevent one of [these] outcomes." 21 C.F.R. § 312.32(a).

plummeted to $10.36 per share, a nearly 51% decline from the previous day's closing price.

C. Zafgen's Disclosures

Based on these events, the investors brought a class action suit against Zafgen and Hughes. The complaint asserted claims on behalf of a putative class consisting of all persons who purchased or otherwise acquired Zafgen common stock between June 19, 2014, the date of Zafgen's IPO, and October 16, 2015, the date the company announced the FDA's partial clinical hold. In the complaint, the investors claimed that the defendants made false or misleading statements concerning the results of the ZAF-201 trial, to wit:

> - As severely obese patients are at an increased risk for cardiovascular disease, we measured systemic biomarkers of cardiovascular disease risk, including low density lipoprotein cholesterol, HDL, CRP, triglycerides and blood pressure in trial participants, to determine [B]eloranib's impact on such biomarkers. The results of these biomarker measurements in this trial, as summarized below, **suggest that [B]eloranib treatment does not increase the risk of cardiovascular disease and may be associated with reduced cardiovascular disease risk.**
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> - There were no deaths or any SAEs ["serious adverse events"] deemed to be possibly, probably, or definitely related to [B]eloranib, although there were **two serious thrombotic adverse events** which, while not attributed to [B]eloranib treatment, may point to the utility of assessment of prior history of thrombotic events in patients enrolled in subsequent trials and added vigilance for AEs

> related to blood clotting during future clinical trials. The most commonly reported TEAEs ["treatment-emergent adverse events"] were gastrointestinal disorders, mainly nausea, diarrhea, or vomiting, nervous system disorders, mainly dizziness, and psychiatric disorders, mainly insomnia, sleep disorder, or abnormal dreams. TEAEs were generally mild in severity and transient. Other frequently reported TEAEs were headaches and injection site bruising/itching, although the incidences were comparable to placebo and not observed to be dose-related.

The investors alleged that Zafgen made these statements (and others that used substantially similar language) in ten different documents, all of which Hughes signed. These disclosures, the investors maintained, were materially misleading because "the FDA considers the frequency/rate of adverse events in determining whether a drug is causing those adverse events," meaning that the defendants should have disclosed even the superficial adverse thrombotic events. Similarly, the investors alleged that "[a]t all times during the Class Period, [d]efendants knew -- or were reckless in not knowing -- that there was a significant risk of thrombotic adverse events in future clinical trials of [B]eloranib."

In response to the investors' allegations, the defendants emphasize several other statements made by Zafgen in its Form S-1 and its subsequent SEC filings, claiming that these additional disclosures belie the investors' accusations of fraudulent intent:

- SAEs that are not characterized by clinical investigators as possibly related to [B]eloranib or SAEs that occur in small numbers may not be disclosed to the public until such time the various documents submitted to the FDA as part of the approval process are made public. We are unable to determine if the subsequent disclosure of SAEs will have an adverse effect on our stock price.

- Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late stage clinical trials after achieving positive results in early-stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, pre-clinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including previously unreported adverse events.

D. The District Court's Dismissal of the Complaint

On August 9, 2016, the district court granted Zafgen and Hughes's motion to dismiss on the ground that the investors had failed to adequately plead scienter.[5] With respect to the investors' Section 10(b) claim, the district court determined that the complaint's allegations were only marginally material, thus weakening any inference of scienter. The district court then also

[5] The district court found that the only materially misleading statements alleged in the complaint concerned the defendants' failure to disclose the non-serious adverse thrombotic events. Neither the investors nor the defendants dispute this feature of the district court's ruling.

dismissed the investors' Section 20(a) claim against Hughes. This appeal followed.

II.

The investors argue that the district court improperly heightened the PSLRA's pleading requirements, applied these heightened requirements to its complaint, and then mistakenly dismissed both their claims for failing to plead facts giving rise to a "strong inference" of scienter. We review whether a complaint meets the PSLRA's pleading requirements de novo, accepting all well-pled factual allegations as true and making all reasonable inferences in a plaintiff's favor. See Miss. Pub. Emps.' Ret. Sys. v. Bos. Sci. Corp., 523 F.3d 75, 85 (1st Cir. 2008). Even through this lens, we agree with the district court that the facts alleged in the investors' complaint do not give rise to a sufficiently strong inference of scienter.

A. Section 10(b) and Rule 10b-5

Section 10(b) of the Securities Exchange Act "forbids the 'use or employ, in connection with the purchase or sale of any security . . . , [of] any manipulative or deceptive device.'" Tellabs, Inc., 551 U.S. at 318 (alterations in original) (quoting 15 U.S.C. § 78j(b)). Pursuant to this statute, SEC Rule 10b-5 makes it unlawful to, among other things, "make any untrue statement of a material fact or to omit to state a material fact necessary in order to make the statements made, in the light of

the circumstances under which they were made, not misleading." 17 C.F.R. § 240.10b-5(b). Therefore, to state a claim for securities fraud under Section 10(b) and Rule 10b-5, "a plaintiff must allege: (1) a material misrepresentation or omission; (2) scienter, or a wrongful state of mind; (3) in connection with the purchase or sale of a security; (4) reliance; (5) economic loss; and (6) loss causation." In re Genzyme Corp. Sec. Litig., 754 F.3d 31, 40 (1st Cir. 2014).

B. Scienter and the PSLRA

Scienter encompasses a "mental state embracing [an] intent to deceive, manipulate, or defraud." Ernst & Ernst v. Hochfelder, 425 U.S. 185, 193 n.12 (1976). At the pleading stage, the PSLRA requires plaintiffs to "state with particularity facts giving rise to a strong inference that the defendant acted with" scienter. 15 U.S.C. § 78u-4(b)(2)(A); see also ACA Fin. Guar. Corp. v. Advest, Inc., 512 F.3d 46, 58 (1st Cir. 2008) (describing the PSLRA's pleading standard for scienter as "rigorous"). In the current setting, scienter encompasses both a "conscious intent to defraud" and, alternatively, a "high degree of recklessness." ACA Fin. Guar. Corp., 512 F.3d at 58 (quoting Aldridge v. A.T. Cross Corp., 284 F.3d 72, 82 (1st Cir. 2002)). Specifically, recklessness involves "a highly unreasonable omission" that involves "not merely simple, or even inexcusable, negligence, but an extreme departure from the standards of ordinary care, and which

presents a danger of misleading buyers and sellers that is either known to the defendant or is so obvious that the actor must have been aware of it." Greebel v. FTP Software, Inc., 194 F.3d 185, 198 (1st Cir. 1999) (quoting Sundstrand Corp. v. Sun Chem. Corp., 553 F.2d 1033, 1045 (7th Cir. 1977)).[6]

Meanwhile, "[t]o qualify as 'strong' . . . an inference of scienter must be more than merely plausible or reasonable -- it must be cogent and at least as compelling as any opposing inference of nonfraudulent intent." Tellabs, 551 U.S. at 314. When evaluating a complaint for compliance with this demanding standard, a court "must consider the complaint in its entirety . . . [Courts must ask] whether all the facts alleged, taken collectively, give rise to a strong inference of scienter, not whether any individual allegation, scrutinized in isolation, meets that standard." Id. at 322-23. To that effect, we have found the standard met where a complaint "contains clear allegations of admissions, internal records or witnessed discussions suggesting that at the time they made the statements claimed to be misleading, the defendant[s] were aware that they were withholding vital information or at least were warned by others that this was so."

[6] "Even if plaintiffs wish to prove scienter by 'recklessness,' they still must allege, with sufficient particularity, that defendants had full knowledge of the dangers of their course of action and chose not to disclose those dangers to investors." Maldonado v. Dominguez, 137 F.3d 1, 9 n.4 (1st Cir. 1998).

In re Bos. Sci. Corp. Sec. Litig., 686 F.3d 21, 31 (1st Cir. 2012). Likewise, a plaintiff "may combine various [other] facts and circumstances indicating fraudulent intent," including those demonstrating "motive and opportunity," to satisfy the scienter requirement. Aldridge, 284 F.3d at 82.

Here, the investors maintain that they met the PSLRA's requirements for pleading scienter. They hinge this argument on their allegations that the defendants (1) knew, or were reckless in not knowing, about news and scientific articles that purportedly established a "link" between Beloranib and the occurrence of thrombotic adverse events; and (2) had a motive to commit securities fraud, as shown by Zafgen's compensation structure and the "heavy" insider sales that occurred before the patient death. We find these arguments unpersuasive, and therefore hold that the complaint's allegations, viewed holistically, do not support a strong inference of scienter under either a conscious intent or recklessness theory.

1. News and Scientific Articles

To start, the investors' reliance on news and scientific articles analyzing the effects of angiogenesis inhibitors, the class of drug to which Beloranib belongs, is misplaced. "The key question in this case is not whether defendants had knowledge of certain undisclosed facts, but rather whether the defendants knew or should have known that their failure to disclose those facts"

risked misleading investors. City of Dearborn Heights Act 345 Police & Fire Ret. Sys. v. Waters Corp., 632 F.3d 751, 758 (1st Cir. 2012) (internal citation omitted). Here, though the articles may suggest that the defendants had an awareness of some connection between Beloranib and thrombotic events, they do not show that the defendants deliberately or recklessly risked misleading investors by not disclosing the two superficial adverse thrombotic events from the ZAF-201 study until October 16, 2015. See In re NVIDIA Corp. Sec. Litig., 768 F.3d 1046, 1060 (9th Cir. 2014) (noting that the articles cited by the plaintiffs did not contribute to a strong inference of scienter, in part because they "d[id] not reflect [the defendants'] knowledge" at the time of the alleged misstatements).

For example, two of the cited articles simply analyze the general effects of angiogenesis inhibitors. Three other articles, meanwhile, examine clinical trials conducted for drugs other than Beloranib which were used to treat cancer, not severe obesity. Moreover, developers often administered these other drugs at significantly higher dosage levels compared to those dispensed in the ZAF-201 study.[7] Of those articles that did discuss Beloranib, several suggested that lower doses of the drug reduced

[7] For instance, doses in the cancer trials often exceeded 50 mg of angiogenesis inhibitors, while Beloranib doses in the 2012-2013 ZAF-201 clinical trial, ranged from 0.6 mg to 2.4 mg.

the risk of potential thrombotic-related side effects in patients being treated for obesity-related ailments.

Taken together, the articles do not add much support for the complaint's allegation that the defendants knew, or were reckless in not knowing, that they risked misleading investors unless they disclosed the two superficial adverse thrombotic events. See In re Ariad Pharm., Inc. Sec. Litig., 842 F.3d 744, 751 (1st Cir. 2016) (noting 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" (alteration in original) (quoting Biogen IDEC, 537 F.3d at 45)). This conclusion is especially warranted where, as here, the complaint contains no specific facts about any "warnings by subordinates or expressions of concern by executives" regarding the propriety of allegedly deceptive disclosures. See Auto Indus. Pension Tr. Fund v. Textron Inc., 682 F.3d 34, 39 (1st Cir. 2012).[8]

[8] This is not to say that a plaintiff in a securities case governed by the PSLRA must plead the existence of direct evidence of scienter to avoid dismissal. As the investors point out, an investor's access to such information prior to discovery will often be limited at best. Nonetheless, it stands to reason that where a complaint is devoid of any direct-evidence allegations, the indirect-evidence allegations in the complaint will need to do more work to carry the burden of raising a "strong inference of scienter" on their own. See Local No. 8 IBEW Ret. Plan & Tr. v. Vertex Pharm., Inc., 838 F.3d 76, 83 n.9 (1st Cir. 2016)

2. Motive and Insider Trading Allegations

The complaint's motive allegations are similarly deficient. First, the investors focus on Zafgen's compensation structure, namely that "a significant portion of [its] executives' annual compensation consists of 'Option Awards' and 'Non-Equity Incentive Plan Compensation' (i.e., 'performance-based cash bonuses')." They allege that this structure resulted in Zafgen insiders, armed with undisclosed information regarding the ZAF-201 study results, selling substantial amounts of company shares in September 2015. Hughes, for instance, sold 22,500 of his Zafgen shares on September 17, 2015, and another 23,126 shares on September 18, 2015, generating approximately $1.8 million in personal proceeds.

Of course, even "weak[]" insider trading allegations provide "some support against the defendants' motion to dismiss." Miss. Pub. Emps.' Ret. Sys., 523 F.3d at 92 (quoting Shaw v. Dig. Equip. Corp., 82 F.3d 1194, 1224 (1st Cir. 1996)). Still, "[t]he vitality of the inference to be drawn depends on the facts, and can range from marginal to strong." Greebel, 194 F.3d at 197-98 (internal citations omitted). Here, the district court found that

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(acknowledging that "prior to discovery, few plaintiffs will be in a position to make specific allegations about the form of internal documents" or discussions, but also noting that Congress has nonetheless "deliberately raised the entry bar to discovery . . . through the PSLRA's heightened pleading standards" (alteration in original) (quoting Textron, 682 F.3d at 40)).

the insider trading alleged in the complaint was insubstantial. On appeal, the investors do not challenge the district court's finding to that effect, instead arguing that the district court erroneously drew a negative inference against scienter based on the weakness of their allegations. Not so. Rather, the district court observed that the insider trading allegations in this case "are relatively weak" and therefore found that the allegations "d[id] not alter the conclusion that the complaint as a whole fails to raise a strong inference of scienter." Brennan, 199 F. Supp. 3d at 468.

In any event, we agree with the district court that the strength of the insider trading allegations drifts toward the marginal end of that spectrum because Hughes and all other Zafgen insiders kept the vast majority of their Zafgen holdings. After accounting for Hughes's vested options, he retained at least 93% of his Zafgen holdings even after the September 2015 sales, and every other insider identified in the complaint retained at least 85%. See Waters Corp., 632 F.3d at 760-61 ("In calculating the percent of holdings sold, . . . it is appropriate to consider not only the shares of stock that [the defendants] held prior to their sales, but also the shares that they could have sold through the exercise of options . . . ."). Moreover, all of the insider sales happened before the patient death that occurred during Zafgen's Phase III testing. As the district court noted:

> During the October 16 conference call, which occurred almost a month after the final insider sale on September 18, Hughes stated that Zafgen disclosed the patient death to the FDA approximately two weeks earlier, and "well within" the one week requirement from the death to the FDA disclosure. Thus, even liberally construed, the complaint's allegations support an inference that the patient death occurred at least a week after the final insider sale.

Brennan, 199 F. Supp. 3d at 469. Therefore, neither the timing nor the amount of insider sales is particularly unusual or suspicious.[9]

Second, the complaint asserts that Zafgen was a one-drug company, meaning Zafgen and Hughes had a motive to "shade the truth" since all of the company's hopes, and a significant portion of Hughes's compensation, hinged on Beloranib's success. However, such "catch-all allegations," which merely assert the existence of a motive and an opportunity to engage in fraudulent behavior, do not satisfy the PSLRA "without something more." In re Cabletron Sys., Inc., 311 F.3d 11, 39 (1st Cir. 2002) (quoting Greebel, 194 F.3d at 197); see also Aldridge, 284 F.3d at 83 (noting that generalized financial incentive allegations are relevant to the scienter analysis only if they "go far beyond the usual arrangements of compensation based on the company's earnings").

[9] We decline to address the parties' arguments concerning the defendants' 10b5-1 trading plans, see 17 C.F.R. § 240.10b5-1(c), because the investors' allegations regarding the purported insider trading are insufficient even without considering those plans.

Here, the complaint only identifies "the usual concern by executives to improve financial results." Cabletron, 311 F.3d at 39. Given that we must take into account the opposing inferences stemming from a complaint's allegations, we find it difficult to infer fraudulent intent simply because the defendants' compensation structure rewards the achievement of corporate goals. See In re Rigel Pharm., Inc. Sec. Litig., 697 F.3d 869, 884 (9th Cir. 2012) (noting that "it is common for executive compensation . . . to be based partly on the executive's success in achieving key corporate goals" and that it would be improper to "conclude that there is fraudulent intent merely because a defendant's compensation was based in part on such successes"). Consequently, we assign these allegations little weight in the scienter calculus.

3. Other Considerations

Several other considerations also bolster our conclusion that the complaint's allegations do not give rise to a sufficiently strong inference of scienter. To start, the marginal materiality of the two superficial adverse thrombotic events undermines such a finding. As we have previously noted, "the materiality and scienter inquiries are linked," Abiomed, 778 F.3d at 240, since "the marginal materiality of an omitted fact 'tends to undercut the argument that the defendants acted with the requisite intent . . . in not disclosing' it," Ariad, 842 F.3d at 750 (citing Abiomed, 778 F.3d at 242). Thus, we must consider whether there

is "a substantial likelihood that" a reasonable investor would have viewed the disclosure of the two superficial adverse thrombotic events "as having significantly altered the total mix of information made available." Basic Inc. v. Levinson, 485 U.S. 224, 231-32 (1988).

The investors' arguments to this effect are unconvincing. "Adverse event reports are daily events in the pharmaceutical industry." Matrixx Initiatives, Inc. v. Siracusano, 563 U.S. 27, 43 (2011). To be sure, these reports may be material even if they "d[o] not provide statistically significant evidence of a causal link." Id. at 44. Nonetheless, it remains unlikely that a reasonable investor in this case would have viewed the two superficial adverse thrombotic events, at the time they occurred, as having significantly altered the information available to them. Zafgen forthrightly disclosed the two serious adverse thrombotic events to investors, and third-party investigators never linked any of the adverse events, including the serious ones, to Beloranib. Indeed, the superficial adverse thrombotic events took on the bulk of their significance only after the patient death. See ACA Fin. Guar. Corp., 512 F.3d at 62 ("A plaintiff may not plead 'fraud by hindsight'; i.e., a complaint 'may not simply contrast a defendant's past optimism with less favorable actual results' in support of a claim of securities fraud." (quoting Shaw, 82 F.3d at 1223)).

In response, the investors claim that because the FDA looks to the overall frequency of adverse thrombotic events when evaluating a drug's safety, all adverse thrombotic events must be material. This argument, however, ignores the Supreme Court's observation that "the mere existence of reports of adverse events -- which says nothing in and of itself about whether the drug is causing the adverse events -- will not satisfy" the materiality standard. Matrixx Initiatives, 563 U.S. at 44. Instead, "[s]omething more is needed." Id. In this case, neither "the source, content, [nor] context of the reports" provides that "[s]omething more." Id. Although a pharmaceutical developer must report all adverse events when filing a New Drug Application with the FDA, it need not disclose every superficial adverse event until it reaches that stage of clinical development. See 21 C.F.R. § 312.33(b)(1) (stating that developers, in their annual reports to the FDA, must disclose summary information "showing the most frequent and the most serious" adverse events observed during that year's clinical and nonclinical drug investigations). Thus, even the accuracy of the investors' core assumption, that the FDA cared about the superficial adverse thrombotic events at the time they occurred, seems doubtful, further diminishing the materiality of these events to reasonable investors. See Bos. Sci. Corp., 686 F.3d at 31 (stating that "marginal materiality not only defeats any independent inference of deliberate withholding but also makes

the pled facts insufficient for a fact finder to find the 'extreme recklessness in not disclosing the fact' that is the least that is required to establish scienter" (quoting Waters Corp., 632 F.3d at 757)).

We also note that Zafgen's own disclosures both before and during the class period weaken the complaint's scienter showing. The defendants disclosed to investors the two serious adverse thrombotic events, and noted on several occasions that the company was not going to disclose all the adverse events as they occurred. Although "[f]ragmentary information may be as misleading . . . as active misrepresentation," V.S.H. Realty, Inc. v. Texaco, Inc., 757 F.2d 411, 414-15 (1st Cir. 1985) (alteration in original) (citation omitted), the facts alleged in the complaint at the very least support a strong competing inference that the defendants disclosed what they considered to be, at the time, the most relevant information about Beloranib's clinical trials.

The investors respond by pointing to literature from the Centers for Disease Control and Prevention ("CDC") that they claim suggests that it is merely "fortuitous" for a blood clot to be non-serious. According to the investors, this report, coupled with the defendants' statement acknowledging the possible "utility of assessment of prior history of thrombotic events . . . and added vigilance for [adverse events] related to blood clotting during future clinical trials," shows that their decision to not disclose

the two non-serious thrombotic events was made intentionally or recklessly. However, while the CDC's language cited in the complaint suggests that it may be true that "[h]ow a clot affects the body depends on the type and location of the clot," it does not mean that good fortune is all that separates a superficial thrombotic adverse event from a more serious one. Instead, the FDA's regulations, which do not require the disclosure of all thrombotic events, see 21 C.F.R. 312.33(b)(1), and the defendants' own disclosures, which informed investors of the most serious adverse events and warned investors that Zafgen would not disclose all adverse events as they occurred, undercut the investors' efforts to make this showing.

In short, although the investors maintain that Zafgen's statements prove the company acknowledged that even superficial adverse events were important to investors, the totality of the company's disclosures produces a compelling counter-inference that the company wished to "provide investors with warnings of risks," actions which "generally weaken the inference of scienter." Waters Corp., 632 F.3d at 760 (quoting Ezra Charitable Tr. v. Tyco Int'l, Ltd., 466 F.3d 1, 8 (1st Cir. 2006)). Thus, the defendants' disclosures both before and during the class period further "undercut any inference of fraudulent intent on the part of defendants." Genzyme Corp., 754 F.3d at 42.

III.

The investors concede that their Section 20(a) claim against Hughes is derivative of their Section 10(b) and Rule 10b-5 claim. Because we hold that the complaint, considered as a whole, does not present allegations giving rise to a "cogent and compelling" inference of scienter, Tellabs, 551 U.S. at 324, we conclude that the district court properly dismissed both claims. Therefore, the judgment of the district court is **affirmed**.