22-1773

IN THE

United States Court of Appeals

FOR THE FIRST CIRCUIT

NADIA SHASH, individually and on behalf of all others similarly situated;
AMJAD KHAN, individually and on behalf of all others similarly situated,

Plaintiffs-Appellants,

VICTOR D. MENASHE,
individually and on behalf of all others similarly situated,

Plaintiff,

—v.—

BIOGEN INC.; MICHEL VOUNATSOS; ALFRED W. SANDROCK, JR.;
SAMANTHA BUDD HAEBERLEIN,

Defendants-Appellees,

JEFFREY D. CAPELLO; MICHAEL R. MCDONNELL,

Defendants.

ON APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

BRIEF FOR PLAINTIFFS-APPELLANTS

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REASONS WHY ORAL ARGUMENT SHOULD BE HEARD

Plaintiffs respectfully request oral argument. This case presents important and novel questions concerning the proper application of the federal securities laws to misleading statements about clinical trial results. The record is lengthy and complex, with an operative Complaint over 100 pages long and several hundred pages of exhibits filed with the motion to dismiss briefing. Oral argument would assist the Court in resolving the appeal.

PRELIMINARY STATEMENT

This case concerns Biogen's misleading disclosures about clinical trial results for its Alzheimer's drug, Aduhelm. In an effort to prove the drug's efficacy, Biogen ran two Phase III clinical trials known as Study 301 and Study 302. Biogen's independent monitor terminated both studies early when it appeared that neither would succeed. Further review of Study 302 showed that its results might be passable after all. But Study 301 was a clear failure. Biogen needed some way to explain away that failure if it was to obtain approval.

Biogen tasked its legions of statisticians with reanalyzing the Study 301 data to find some way to explain away the failure. The theory they came up with was that Study 301 failed because it had fewer patients taking Aduhelm at the highest dose. Both studies included "carriers" of a gene that presents a greater risk of side effects; Biogen originally gave carriers a reduced dose. But Biogen modified its protocol partway through the trials so carriers could receive the full dose. Because Study 301 began sooner, it included more carriers who were treated under the old protocol and therefore received a lower dose. Biogen seized on that difference as the explanation for Study 301's failure. It told investors that "all" of its data was consistent with that theory: "***[Y]ou really need to get to the higher dose***. And I think ***our data are all consistent with that***." A108-09 ¶191 (emphasis altered).

In fact, Biogen's data was not "all consistent with that." Biogen's own Study 302 refuted its explanation: In that study, carriers who received the higher dose did ***worse*** than carriers who received the original dose. And non-carriers, who always received the higher dose, performed poorly in ***both*** studies. Contrary to its past practice, Biogen withheld that critical data from the public.

An FDA statistician, Dr. Tristan Massie, sounded the alarm. An advisory committee then voted ***ten to zero*** against approval. But Biogen and its allies at the FDA pushed the drug through anyway — a decision one advisory committee member described as "probably the worst drug approval decision in recent U.S. history." A156 ¶322(a). Congress opened an investigation. Medicare refused to cover the drug. Biogen ultimately ceased all commercial marketing of the drug and replaced its CEO.

Plaintiffs now seek compensation for the massive losses they suffered as a result of Biogen's misleading statements. The district court dismissed the suit after adopting a near-categorical rule that statements interpreting clinical trial data are not actionable. That holding has no basis in the law.

This Court should reverse.

JURISDICTIONAL STATEMENT

The district court had jurisdiction under 28 U.S.C. § 1331. A63 ¶37. The court entered a final order dismissing all claims on September 12, 2022. Add.42. Plaintiffs timely appealed on October 10, 2022. A1096-98. This Court has appellate jurisdiction under 28 U.S.C. § 1291.

ISSUES PRESENTED

1. Whether the Complaint adequately alleges that Biogen made materially misleading statements abouts its Phase III clinical trials for Aduhelm.

2. Whether the Complaint adequately alleges scienter based on Biogen's willful manipulation of statistical data, departures from past disclosure practices, and other indicia of knowing or reckless conduct.

3. Whether the Complaint fails to allege loss causation merely because the named plaintiffs purchased Biogen stock shortly after the disclosure of Dr. Massie's report, but before the market digested its contents.

STATEMENT OF THE CASE

Plaintiffs brought this class action against Biogen and three of its senior officers under Section 10(b) of the Securities Exchange Act, 15 U.S.C. § 78j(b), and other provisions. A51-174. Plaintiffs appeal from the district court's order dismissing the action. Add.42; A1096-98.

I. BACKGROUND

A. The FDA's Requirements for Clinical Trials

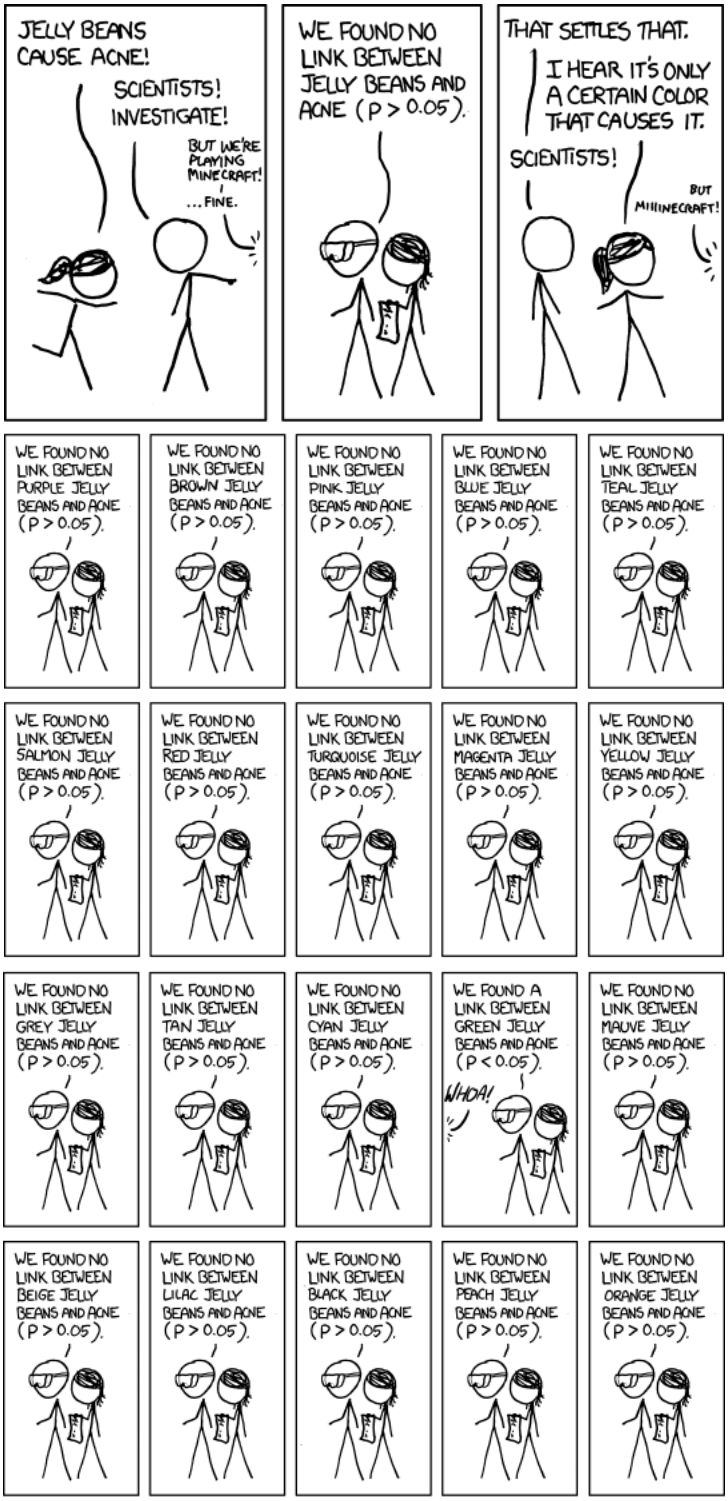
The Food and Drug Administration ("FDA") requires a new drug to go through a series of clinical trials before it can be approved for marketing. 21 C.F.R. §312.21. During those trials, the drug is tested on increasingly broad populations for safety and efficacy. *Id.* "[T]he FDA considers the results of all of the clinical trials in determining whether to approve a drug for market." *N.J. Carpenters Pension & Annuity Funds v. Biogen IDEC Inc.*, 537 F.3d 35, 39 (1st Cir. 2008); *see* 21 C.F.R. §§314.125-126.

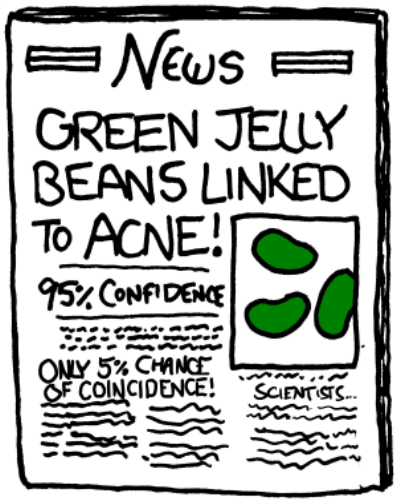
The FDA has promulgated extensive guidance on clinical trials. One important requirement is that the plan for evaluating the trial's success or failure in meeting its objectives (the "endpoints") must be specified in advance. *See* Food & Drug Admin., *Guidance on Statistical Principles for Clinical Trials*, 63 Fed. Reg. 49,583, 49,585 (Sept. 16, 1998) (analysis plan should be "clearly specified in a protocol written before the trial begins"); Food & Drug Admin., *Adaptive Designs for Clinical Trials of Drugs and Biologics Guidance for Industry* 8 (2019) (plan must be "completely specified prior to initiation of the trial"); A85 ¶134. The analysis plan must be registered in advance with the FDA, which publishes it on a public website. 42 C.F.R. §11.28(a)(1), (2)(i)(W)-(X); A86 ¶139.

That requirement reflects basic statistical principles. Scientists analyzing clinical trial data calculate the probability (the "p-value") of seeing the observed results in the absence of any correlation between the drug and the clinical outcomes. *See* Russell Katz, *FDA: Evidentiary Standards for Drug Development and Approval*, 1 NeuroRX 307, 310 (2004); Fed. Jud. Ctr., *Reference Manual on Scientific Evidence* 357 (2d ed. 2000). For example, if the difference in outcomes between patients taking a drug and patients taking a placebo has a p-value of 0.25, there is a 25% chance of observing the difference purely by chance. Scientists typically label results "statistically significant" when the p-value is less than 0.05. Katz, *supra*, at 310-11; Fed. Jud. Ctr., *supra*, at 357-58. The low p-value makes it less likely the results occurred by chance and more likely they occurred because the drug actually works.

P-values are an important benchmark, but they are vulnerable to manipulation by "p-hacking." "P-hacking is the act of misusing data analysis to show that patterns in data are statistically significant, when in reality they are not. This is often done by performing multiple tests on data and only focusing on the tests that return results that are significant." Sam Lau, Joey Gonzalez & Deb Nolan, *Principles and Techniques of Data Science* §18.5 (2020). In other words, p-hacking involves "repeatedly running different statistical tests on the same dataset, but then only reporting the most interesting results." Michael Kearns & Aaron Roth, *The Ethical*

Algorithm: The Science of Socially Aware Algorithm Design 144-45 (2019); A85 ¶135. As one author illustrates the concept:





Randall Munroe, *Significant*, xkcd, https://xkcd.com/882/.

Absent "stringent recording and disclosure requirements," p-hacking "tend[s] to be invisible" and "virtually guarantees a researcher statistically significant (and therefore publishable) evidence for a false hypothesis." Edith Beerdsen, *Litigation Science After the Knowledge Crisis*, 106 Cornell L. Rev. 529, 549-51 (2021); *see also* Regina Nuzzo, *Scientific Method: Statistical Errors*, 506 Nature 152 (2014); A86 ¶138. The FDA's prespecification requirement forces researchers to "commit[] to analytic steps without advance knowledge of the research outcomes." Brian A. Nosek et al., *The Preregistration Revolution*, 115 Procs. Nat'l Acad. Sci. 2600, 2601-02 (2018); *see* A86 ¶139.

B. Biogen's Clinical Trials for Aduhelm

Biogen disregarded those principles in clinical trials of its Alzheimer's drug, Aduhelm. This case arises out of Biogen's misleading descriptions of the results of its analysis.

1. *Biogen's Phase III Clinical Trials*

Many scientists have hypothesized that Alzheimer's disease is caused by the build-up of "amyloid plaques" that interfere with connections in the brain. A67-68 ¶¶53-58. In 2011, Biogen began investigating a new drug — known generically as "aducanumab" and by its brand name "Aduhelm" — which sought to treat Alzheimer's disease by targeting and destroying those plaques. A68-70 ¶¶59-62, 66. Biogen conducted early clinical trials over the next few years. A70 ¶¶67-69.

Biogen then designed two identical Phase III clinical trials, known as Study 301 ("ENGAGE") and Study 302 ("EMERGE"), that began in 2015. A72 ¶¶76-77. Both studies ran in parallel, although Study 301 began a month earlier and remained ahead in enrollment. A72 ¶¶77-81. The studies compared the effects of taking Aduhelm against a placebo over an 18-month period, with some patients taking a "high dose" and others a "low dose." A75 ¶90.

As required by the FDA, Biogen specified the endpoints for its clinical studies in advance. A73 ¶82. The primary endpoint sought to evaluate the impact of the drug on clinical outcomes by measuring memory, orientation, and judgment/ problem-solving. A73 ¶¶83-84. Separately, Biogen would use brain scans to study the level of plaque reduction and examine whether that reduction correlated with better clinical outcomes. A75 ¶89. Biogen planned to conduct separate analyses on the high-dose, low-dose, and placebo groups. A120 ¶218.

Some patients ("carriers") have a gene that places them at greater risk of side effects from Aduhelm. A70-71 ¶¶71-73. Biogen initially gave carriers lower doses of the drug. A75 ¶¶91-93. But in March 2017, after reviewing additional safety data, Biogen amended its protocol so that carriers in the high-dose group received the same high dose as non-carriers. A77 ¶¶99-100. Because enrollment in Study 301 was slightly ahead of Study 302, that amendment resulted in more Study 302 patients receiving the full high dose. A90 ¶149.

Both studies provided for a "futility analysis" that would end the studies early if the drug appeared unlikely to succeed. A77 ¶101. An independent data monitoring committee analyzed the data collected by December 2018 to assess whether the studies had a 20% chance of meeting their primary endpoints. A78 ¶¶105, 107-108. The committee found that Study 301 had a 0% chance of success and Study 302 had only a 12% chance. A78 ¶107. Biogen thus terminated both studies on March 21, 2019. A78 ¶108.

2. *Biogen's P-Hacking of Its Clinical Trial Data*

Biogen's early termination of the trials was a disaster for the company. Analysts feared that the failure "left Biogen dead." A80 ¶112. Desperate to recover, "Biogen tasked 49 of its statisticians to pore over the Phase III results and salvage any data that could support aducanumab's approval." A81 ¶118.

That is what Biogen's statisticians did. Although the futility analysis was based on data collected through December 2018, Biogen had continued to collect data until it terminated the studies in March 2019. A81 ¶118. Biogen's statisticians re-ran the analysis with that additional data and found that Study 302 was "just barely statistically significant." A57 ¶7.

Study 301, by contrast, was ***still*** a failure. A57 ¶8. That failure was a big obstacle: The FDA had told Biogen in 2014 that it would not approve the drug with one failure and one success. A82 ¶124. Biogen needed a way to explain away Study 301's failure. A89 ¶¶146-147.

Biogen thus went back and reanalyzed its Study 301 data yet again. Biogen found that patients in Study 301 who had received higher doses because of the March 2017 protocol amendment achieved clinical outcomes similar to patients in Study 302. A90 ¶150. Biogen thus claimed that the reason Study 301 failed while Study 302 succeeded was that Study 301 included more patients who enrolled before the amendment and thus more patients treated at the lower dose. A90 ¶¶149-150. Once those patients were excluded, Biogen asserted, Study 301 produced results consistent with Study 302. *Id.*

The problem with that theory was that the rest of Biogen's clinical trial data refuted it. The ***Study 302*** data showed that the higher doses did ***not*** improve outcomes: Carriers who received the higher dose following the protocol amendment

fared ***worse*** than carriers who received the lower dose. A92-93 ¶¶157-159. Moreover, non-carriers, who always received the higher dose, performed poorly in ***both*** studies, with a margin over the placebo group that was "virtually nil." A91 ¶¶152-153. Those results were irreconcilable with Biogen's theory that the reason Study 301 failed was that it had fewer high-dose patients.

Biogen engaged in similar re-engineering of its plaque reduction data. Biogen's prespecified analysis plan called for it to analyze the low-dose and high-dose groups separately for each of the two studies to measure the correlation between plaque removal and better clinical outcomes. A120 ¶¶217-218. Those results were essentially random. All four subgroups showed correlation coefficients well below 0.3, the threshold that statisticians consider a "fair" correlation. A114 ¶206; A121 ¶220; Y.H. Chan, *Biostatistics 104: Correlational Analysis*, 44 Sing. Med. J. 614, 614 (2003) (A846-51). Two subgroups had a negative or virtually no correlation. A121 ¶220. The subgroup with the negative correlation was the ***high-dose*** group from Study 302 — another inexplicable result for Biogen's attempt to explain away the failure of Study 301. A121 ¶220.

Faced with those results, and despite having already performed extensive analysis, Biogen changed its analysis plan in 2020 by aggregating the low-dose and high-dose data. A120-21 ¶¶215, 218-220. That aggregation helped Biogen obscure

the inconsistent results that showed no meaningful positive correlation for half the subgroups, including a ***negative*** correlation for high-dose patients in Study 302:

Correlation coefficient between amyloid beta levels and clinical outcomes	Low dose	High dose	Pooled
Study 301	0.009	0.135	0.026
Study 302	0.165	-0.036	0.105
Pooled	0.083	0.084	0.066

A121 ¶220.

C. Biogen's Misleading Descriptions of Its Trial Results

Throughout the class period from October 22, 2019 to November 6, 2020, Biogen made misleading statements that touted the results of its new statistical analyses while concealing the contradictory data. A55 ¶1; A100-11 ¶¶171-196; A121-26 ¶¶221-232.

On an October 22, 2019 earnings call, for example, Biogen's Chief Medical Officer, Defendant Alfred W. Sandrock Jr., laid out Biogen's new explanation for why Study 301 failed: "Our primary learning from these data is that ***sufficient exposure to high dose aducanumab*** reduced clinical decline . . . ." A100 ¶171 (emphasis altered). "This reduction in clinical decline was statistically significant in [Study 302], and . . . the data from patients who achieved sufficient exposure to high dose aducanumab in [Study 301] support the findings of [Study 302]." *Id.* "[P]atients included in the futility analysis were those who had enrolled early in

the trials and those early enrolling patients had a lower average exposure to aducanumab . . . ." *Id.* Biogen's Vice President of Clinical Development, Defendant Samantha Budd Haeberlein, agreed: "I think what we have learned clearly is that dose is very important, but that if individuals do receive [the high dose] then they do have an efficacious response." A103 ¶179.

Sandrock repeated that claim on Biogen's January 30, 2020 earnings call: "[D]ata from [Study 301] did not meet the primary endpoint, although we do believe that data from patients who achieve sufficient exposure to high dose aducanumab in [Study 301] support the findings of [Study 302]." A105-06 ¶185. Budd Haeberlein agreed on an April 4, 2020 call: "In a post hoc analysis [of Study 301], data from subs[ets] of patients, the [post-amendment] population who had the opportunity to be exposed to high dose did support the positive findings of [Study 302]." A106-07 ¶187.

Most strikingly, on Biogen's July 22, 2020 earnings call, Sandrock stated that "***all***" of Biogen's data was consistent with this explanation: "We believe that data from [Study 301] . . . support the analysis that we did with [Study 302]. . . . [T]he lower doses did not show much of an effect. So consistent with the findings from [Study 301] and [Study 302], ***you really need to get to the higher dose***. And I think ***our data are all consistent with that***." A108-09 ¶191 (emphasis altered).

Nowhere during any of those calls did Biogen disclose that its other data refuted its explanation for why Study 301 failed. A91-93 ¶¶152-153, 157-159.

Biogen made similarly misleading statements about whether its clinical trials showed a correlation between plaque reduction and better outcomes. On Biogen's October 22, 2019 earnings call, for example, Sandrock stated: "[I]f you give enough of the high dose, you can achieve a certain amount of amyloid removal and that certain amount is what's required to see the reduction in clinical decline in an 18-month study." A122-23 ¶223. Biogen's Chief Executive Officer, Defendant Michel Vounatsos, made even starker claims during an October 23, 2019 interview: "What we demonstrate is that [aducanumab] . . . is able to erode and eliminate the plaque ***leading to the benefits we see in terms of cognition for the patients***. It reduces basically the decline and we can see effects such as on memory orientation, language, but also functionally the ability to take care of oneself." A124 ¶227 (emphasis altered).

None of those statements disclosed that Biogen's clinical trials showed no substantial correlation between plaque removal and better outcomes and a ***negative*** correlation for high-dose patients in Study 302. A114 ¶206; A121 ¶220. Nor did Biogen disclose that it abandoned its prespecified plan in favor of aggregated data. A120-21 ¶¶215-219.

Analysts asked Biogen to release the data from its clinical trials, as it had done in the past, so they could draw their own conclusions. *See, e.g.*, A164-65 ¶¶346-347 ("[T]here was so much presented but also so much not presented perhaps. And

I couldn't tell why. So could you speak to what the carrier and noncarriers look like?"). Sandrock responded by admitting that Biogen's withholding of data was a departure from past practice but asserted that the company had "nothing to hide": "***[Y]ou're right, I mean, typically, we do present a lot of things, subgroups included, in the past. You're right, we did do that.*** There's a time and a place for everything. And look, this will soon be under review at regulatory authorities. And so for that reason, we're very sensitive about what we want to present now. ***We have nothing to hide.***" A164-65 ¶346 (emphasis altered). Sandrock did not explain why the FDA's forthcoming review of the company's drug application would be a good reason to withhold clinical trial data from the public.

D. Biogen's Efforts To Obtain FDA Approval

Sandrock has a longstanding professional relationship with Dr. Billy Dunn, the head of the FDA's Office of Neurology and its top regulator for Alzheimer's drugs like Aduhelm. A61 ¶21; A177-78. In May 2019, about two months after Biogen terminated its studies for futility, Sandrock and Dunn attended the annual meeting of the American Academy of Neurology in Philadelphia. A61 ¶21. Sandrock arranged a secret, "off-the-books" meeting with Dunn at which he persuaded Dunn to move forward with Aduhelm's approval despite the termination of the studies. *Id.* That meeting violated FDA policy, which requires regulators to meet with drugmakers in documented settings. A81 ¶121; A178.

Dunn agreed to help find a way to approve Aduhelm. A82 ¶123. In June 2019, Dunn presented Biogen with "five different pathways to approval." A83 ¶128. Dunn agreed to push for Aduhelm's approval so long as Biogen could explain the failure of Study 301. A89 ¶¶145-146.

The FDA ultimately scheduled a public meeting for November 6, 2020, at which an advisory committee of independent experts would answer questions the agency posed about whether to approve the drug. A60 ¶16; A136-37 ¶272. The FDA uses advisory committees to "provide independent advice that will contribute to the quality of the agency's regulatory decision-making and lend credibility to the product review process." Food & Drug Admin., *Advisory Committees: Critical to the FDA's Product Review Process* (May 4, 2016); *see* 21 C.F.R. §14.5(a). As analysts noted, however, the FDA's questions about Aduhelm were "leading questions designed to support approval." A136-37 ¶272.

Two days before the advisory committee meeting, on November 4, 2020, the FDA publicly released briefing materials on Aduhelm that it had jointly prepared with Biogen. A135 ¶262. Those materials were highly unusual: The FDA almost never releases joint briefing materials with a drugmaker. A135 ¶265; A139 ¶276(g). The materials were also effusive: The FDA stated that "[t]he effect of aducanumab in Study 302 is robust and ***exceptionally persuasive*** on several of the instruments used to evaluate efficacy." A135-36 ¶¶264-269 (emphasis added).

Analysts interpreted the joint briefing materials as evincing a "clear bias in favor of approval." A138 ¶276; *see* A139 ¶276(g) ("[W]e've never really seen anything like that before, where the FDA is just working that closely with a company. They went to the [advisory committee] basically saying, 'This drug's getting approved.'"). By the end of the day on November 4, 2020, Biogen's stock price had soared to $355.63. A141 ¶278.

Buried at the back of the briefing materials, nearly 250 pages in, was a report marked "draft" by an FDA statistician, Dr. Tristan Massie. A137 ¶273; A197-294. That draft report was highly technical, with nearly 100 pages of statistical analysis of raw clinical trial data. A60 ¶16; A137 ¶274; A197-294.

Analysts did not initially appreciate the significance of the Massie report, focusing instead on the effusive joint briefing materials. A138-41 ¶¶276-277. Several analysts did not mention the report, and others downplayed its significance. *Id.* One stated: "It's going to take us most of the day to go through it all." A140-41 ¶277(b).

In fact, the Massie report was damning. Relying on the raw data that Biogen had submitted to the FDA but withheld from the public, the report revealed that, in Study 302, the protocol amendment that increased doses for carriers did ***not*** improve outcomes, and that non-carriers performed poorly in ***both*** studies — refuting Biogen's attempt to explain away the failure of Study 301. A60 ¶16; A138 ¶275;

A226-27, A284. The report also revealed that Biogen's claims about a correlation between plaque removal and better outcomes relied on an after-the-fact analysis plan, and that the high-dose group in Study 302 showed a ***negative*** correlation. A60 ¶16; A114 ¶206; A120 ¶215; A244-45.

The next day, November 5, Biogen's stock price began to fall as investors digested the Massie report. A142 ¶279. By the end of the day, the price had fallen to $328.90, down 7.5%. *Id.*

E. The Advisory Committee's Vote Against Aduhelm

The advisory committee met as scheduled on November 6, 2022. A142-43 ¶281. On the critical question whether it was "reasonable to consider Study 302 as primary evidence of effectiveness" in light of Study 301's poor results, the committee voted ***ten to zero*** against the drug, with one "uncertain." A142-43 ¶281. Explaining their rationales, committee members repeatedly referred to the Massie report and its damaging findings. A143-44 ¶¶283-292.

Trading of Biogen's stock was halted all day on November 6 (a Friday) due to the advisory committee meeting. A142 ¶280. The next trading day, November 9, Biogen's stock price plummeted. It opened at $230.82 and closed at $236.26, down 28.2% from the $328.90 close on November 5. A60 ¶19; A145 ¶294.

F. The Aftermath

Undeterred by the advisory committee's disastrous vote, Biogen and Dunn plowed ahead. In March and April 2021, Dunn appeared before the FDA's Medical Policy and Program Review Council to push for approval. A61 ¶22; A153 ¶¶309-310. The "vast majority" voted against the drug. A153 ¶311.

Biogen and Dunn therefore took a different tack. FDA regulations allow the agency to grant "accelerated approval" to a drug based on a "surrogate endpoint," even without clinical trials proving efficacy, so long as the FDA believes that the surrogate endpoint makes it "reasonably likely . . . to predict clinical benefit." 21 C.F.R. §314.510; A148 ¶300. For Aduhelm, the "surrogate endpoint" would be the drug's ability to reduce amyloid plaque. A149-50 ¶304.

The FDA had previously told Biogen that there was no scientific consensus to support using amyloid plaque removal as a surrogate endpoint. A149 ¶303. The FDA had reiterated that position in public guidance as recently as 2018. A148-49 ¶301. Dunn told the advisory committee that the FDA was not using plaque reduction as a surrogate for efficacy. A150 ¶305. Nonetheless, on April 26, 2021, an FDA official convened a meeting to consider approving Aduhelm on that theory. A153-54 ¶¶313-314. Among the officials who voted were the head of the FDA's Office of Oncology and the head of its vaccine program — officials who had nothing

to do with Alzheimer's disease. A153-54 ¶¶313-314. A majority voted to grant accelerated approval. A154 ¶315.

That decision to approve Aduhelm despite the advisory committee's lopsided vote proved exceptionally controversial. Three of the advisory committee's nine permanent members resigned. A156-57 ¶322. One criticized the approval as "probably the worst drug approval decision in recent U.S. history." A156 ¶322(a). Another observed that "[t]his was the first time that nobody voted for approval of this drug — nobody — and [the FDA] went against that." A157 ¶322(c).

Multiple congressional committees launched an investigation. A157-58 ¶325. The Secretary of Health and Human Services insisted that its Inspector General's Office investigate too. A158 ¶327. Upon learning of Biogen's relationship with Dunn, the FDA even called for an investigation of itself. A159 ¶330. A survey of neurologists found that "80% had lost confidence in the FDA." A63 ¶34.

Some of the nation's largest insurance companies refused to cover Aduhelm. A159-160 ¶331. Some of the largest health systems refused to stock or administer the drug, citing concerns over the "integrity of the FDA-Biogen relationship." A160 ¶332. In April 2022, the Centers for Medicare & Medicaid Services announced that Medicare would not cover Aduhelm (except for clinical trials) because there was "not currently enough evidence . . . demonstrating improved health outcomes." Ctrs. for Medicare & Medicaid Servs., *CMS Finalizes Medicare Coverage Policy for*

Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (Apr. 7, 2022) (A900-03). In response, Biogen "substantially eliminate[d] its commercial infrastructure supporting ADUHELM" and "beg[an] a search for a new Chief Executive Officer." Biogen Inc., *Biogen Reports First Quarter 2022 Results* 3, 6 (May 3, 2022) (A974-91).

On December 29, 2022, the congressional committees investigating the FDA's decision released a scathing report. *See* Staffs of the H. Comm. on Oversight & Reform and H. Comm. on Energy & Commerce, *The High Price of Aduhelm's Approval: An Investigation into FDA's Atypical Review Process and Biogen's Aggressive Launch Plans* (Dec. 2022) ("House Staff Report"). The report found that "FDA's approval process was rife with irregularities." *Id.* at 15. There was "atypical collaboration and interactions between FDA and Biogen," and "FDA failed to follow its own documentation protocol." *Id.* at 15-18. In addition, "FDA and Biogen inappropriately collaborated on a joint briefing document . . . that did not adequately represent differing views within FDA." *Id.* at 19. Even "FDA's own internal review found that this approach . . . was inappropriate . . . given the substantial disagreement between FDA reviewers." *Id.* at 21.[1]

[1] This Court may take judicial notice of the congressional report because its contents "can be accurately and readily determined from sources whose accuracy cannot reasonably be questioned." Fed. R. Evid. 201(b)(2), (d); *see United States ex rel. Winkelman v. CVS Caremark Corp.*, 827 F.3d 201, 207-08 (1st Cir. 2016)

II. PROCEEDINGS BELOW

A. The Investors' Complaint

Following the advisory committee vote on November 6, 2020, an investor filed a securities class action against Biogen in the Central District of California. A9-34. The court appointed Nadia Shash as lead plaintiff and transferred the case to the District of Massachusetts. A37-44; A45-48. On August 4, 2021, Nadia Shash and Amjad Khan filed the operative Second Amended Complaint (the "Complaint") against Biogen, Vounatsos, Sandrock, and Budd Haeberlein. A64-65 ¶¶42-46.

Plaintiffs represent a putative class of all investors who purchased Biogen stock between October 22, 2019 and November 6, 2020. A55 ¶1. The Complaint alleges that defendants violated Section 10(b) of the Securities Exchange Act, 15 U.S.C. §78j(b), and SEC Rule 10b-5, 17 C.F.R. §240.10b-5, by making false and misleading statements about the Aduhelm clinical trial data. A169-71 ¶¶360-369.

(congressional testimony and CRS report); *Stasiukevich v. Nicolls*, 168 F.2d 474, 479 (1st Cir. 1948) (congressional committee report). Even apart from the truth of its contents, the report is relevant because it is "supportive of the plausibility of [the complaint's] claims." *Insulate SB, Inc. v. Advanced Finishing Sys., Inc.*, 797 F.3d 538, 543 n.4 (8th Cir. 2015). The Medicare coverage decision (A900-03) and Biogen's press release (A974-91) are subject to judicial notice for similar reasons. The district court disagreed because those documents post-date the class period. Add.14-15. But the documents confirm the misleading nature of Biogen's earlier statements regardless of their timing. *See Rothman v. Gregor*, 220 F.3d 81, 92 (2d Cir. 2000) (post class period evidence relevant to scienter).

It also alleges that the three individual defendants are liable as control persons under Section 20(a), 15 U.S.C. § 78t(a). A171-72 ¶¶370-375.

B. The District Court's Decision

On September 12, 2022, the district court granted defendants' motion to dismiss. Add.1-41.

Misleading Omissions. The district court first held that Biogen's statements were not materially misleading. Add.15-33. The court deemed the statements "more akin to opinions than conclusive findings." Add.18. It acknowledged that "classifying a statement as an opinion does not categorically preclude" liability. *Id.* But it adopted a broad rule that effectively exempted interpretations of clinical trial data from liability: "'[I]nterpretations of clinical trial data are considered opinions' and . . . disagreements with the scientific conclusions drawn from those opinions are ***not actionable***." Add.17 (emphasis added).

With respect to Biogen's efforts to explain away the failure of Study 301, the court reasoned that it was "widely known" that Study 301 had not met its prespecified endpoint and that Biogen had engaged in "post hoc analysis." Add.23. The court acknowledged that Biogen's other data was "inconsistent" with its conclusions. Add.24. But it asserted that "nothing in the complaint establishes the primacy of the sub-group level analysis." *Id.* The court claimed that "the FDA had endorsed Biogen's statistical model" and that the dispute was therefore "one of

genuine scientific debate." Add.25. "[T]hough Plaintiffs make a strong case for why Biogen's conclusions may have been flawed, Biogen's failure to disclose the contradicting studies was not misleading." Add.27.

The district court reached a similar conclusion for the plaque reduction claims. The court did not dispute that Biogen's prespecified analysis plan showed inconsistent results, including a ***negative*** correlation for high-dose patients in Study 302. Add.27; A121 ¶220. But it held that Biogen's statements were not actionable because they included comments like "we're still learning as we look at the data." Add.28. The court described Biogen's statements as "optimistic responses" or "educated speculation." Add.28-29. In its view, "Plaintiffs are again asking the court to declare one post hoc analysis superior to another." Add.30. And it asserted that "[t]he FDA ultimately endorsed Biogen's methodology and conclusions." *Id.*

Scienter. The district court also held that the Complaint did not adequately allege scienter. Add.33-38. It acknowledged that the fact that "Biogen conducted a rigorous analysis could be sufficient to show Biogen was aware of [the] countervailing analyses" in the Massie report. Add.34. But that did not prove that "Biogen believed its own conclusions were wrong." *Id.* "This is particularly true here where the FDA collaborated with Biogen to conduct the post hoc analysis, expressed support for Biogen's conclusions . . . and publicly endorsed Biogen's statistical methodology . . . ." Add.35.

The court held that "Plaintiffs fail to plead facts that demonstrate Defendants' omission of the sub-group data or related analysis was highly unreasonable." Add.36. That "the data was under review by the FDA," it asserted, was "a plausible explanation for withholding the information from the public." *Id.* And "[n]o reasonable investor" would interpret Biogen's statement that it had "nothing to hide" to mean that "the sub-group data supported Biogen's conclusion." Add.37. In fact, "Biogen's avoidance of the topic and suggestion that it had 'nothing to hide' should spark a reasonable investor's curiosity." *Id.* Finally, "the fact that Biogen had been working closely with the FDA and that the FDA has endorsed [its] post hoc analysis . . . is strong evidence against finding scienter." Add.38.

Loss Causation. The district court likewise rejected the allegations of loss causation. Add.38-40. The named plaintiffs purchased Biogen stock on November 4 or 5, 2020, shortly after the FDA released its effusive joint briefing materials and the Massie report on November 4. Add.39. The court held that those facts precluded loss causation. In its view, loss causation "is not tied to when the market reacts to information, but rather when that information became available to the public." Add.40. Because "the Massie Report . . . was published before Plaintiffs purchased Biogen stock, the complaint fails." *Id.*

SUMMARY OF ARGUMENT

I. Biogen's statements about its clinical trial results are actionable because they omitted information "necessary 'to make . . . statements made, in the light of the circumstances under which they were made, not misleading.'" *Matrixx Initiatives, Inc. v. Siracusano*, 563 U.S. 27, 44 (2011). The statements are actionable whether they are classified as facts or opinions. Even an opinion "convey[s] facts . . . about the speaker's basis for holding that view." *Omnicare, Inc. v. Laborers Dist. Council Constr. Indus. Pension Fund*, 575 U.S. 175, 188 (2015).

The district court adopted a seemingly per se rule that "'[i]nterpretations of clinical trial data are considered opinions' and . . . disagreements with the scientific conclusions drawn from those opinions are ***not actionable***." Add.17 (emphasis added). That is not the law. Statements about clinical trials that misleadingly omit crucial information are subject to the same standards as any others.

Biogen made two categories of misleading statements here. First, Biogen tried to explain away the failure of Study 301 on the ground that, because that trial started sooner, it had fewer high-dose patients than Study 302. Biogen claimed that "all" of its data was consistent with that explanation: "***[Y]ou really need to get to the higher dose***. And I think ***our data are all consistent with that***." A108-09 ¶191 (emphasis altered). Biogen concealed glaring facts that were ***not*** consistent with its explanation: In Study 302, patients who received higher doses as a result of Biogen's

protocol amendment did ***worse*** than lower-dose patients; and in both studies, non-carriers who received the full dose showed hardly any effect. Those facts make it far more likely that Biogen's explanation for Study 301's failure reflects, not a genuine correlation between dosage and outcomes, but p-hacking.

Second, Biogen claimed that its studies showed a correlation between plaque reduction and better outcomes. In fact, Biogen's data was essentially random. For high-dose patients in Study 302, the correlation was ***negative***. Biogen secretly modified its analysis plan to obscure those details.

II. The Complaint alleges facts supporting an inference of scienter that is "cogent and at least as compelling as any opposing inference." *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 551 U.S. 308, 324 (2007). Several facts suggest that Biogen intentionally misled investors — or at least recklessly disregarded that risk.

First, Biogen's bad faith statistical manipulation and selective reporting of clinical trial results makes it more likely that Biogen knowingly or recklessly violated its disclosure obligations. Second, Biogen departed from past practice by withholding its clinical trial data. Third, Biogen colluded with the FDA in an approval process fraught with irregularities. And finally, the importance of Aduhelm to Biogen's financial success confirms that Biogen's managers would have closely scrutinized the results.

III. Finally, the Complaint adequately pleads loss causation. Even efficient markets may take a day or two to digest complex information. *See In re Xcelera.com Sec. Litig.*, 430 F.3d 503, 513 n.11 (1st Cir. 2005). The Complaint reasonably alleges a delayed reaction here: The Massie report was a nearly impenetrable statistical analysis buried behind 250 pages of glowing FDA commentary.

ARGUMENT

I. STANDARD OF REVIEW

This Court reviews *de novo* an order granting a motion to dismiss. *See Constr. Indus. & Laborers Joint Pension Tr. v. Carbonite, Inc.*, 22 F.4th 1, 6 (1st Cir. 2021). The Court "accept[s] well-pleaded factual allegations in the complaint as true and, while cognizant of the requirements for pleading scienter, [the Court] view[s] all reasonable inferences in the plaintiff's favor." *Id.*

II. PLAINTIFFS SUFFICIENTLY ALLEGED THAT BIOGEN MADE MISLEADING STATEMENTS AND OMISSIONS

A securities fraud plaintiff must ordinarily allege a "material misrepresentation or omission." *Matrixx Initiatives, Inc. v. Siracusano*, 563 U.S. 27, 37 (2011). Under the Private Securities Litigation Reform Act ("PSLRA"), the Complaint must "specify each statement alleged to have been misleading" and "the reason or reasons why the statement is misleading." 15 U.S.C. § 78u-4(b)(1); *see also* Fed. R. Civ. P. 9(b). The Complaint easily meets those standards here.

Biogen made two categories of misleading statements. First, Biogen purported to explain away the failure of Study 301 on the ground that it had fewer high-dose patients, while concealing that its other data contradicted that explanation. Second, Biogen described its plaque reduction data as supporting the drug's efficacy, while concealing that the data was essentially random and that it had secretly changed its analysis plan to obscure those results. The district court rejected both claims only by ignoring the governing legal standards.

A. The District Court Erroneously Carved Out a New Exception for Misleading Statements About Clinical Trials

Even absent a freestanding duty to disclose, a company may not omit material information that is "necessary 'to make . . . statements made, in the light of the circumstances under which they were made, not misleading.'" *Matrixx*, 563 U.S. at 44 (quoting 17 C.F.R. § 240.10b-5(b)). "[L]iteral accuracy is not enough: An issuer must as well desist from misleading investors by saying one thing and holding back another." *Omnicare, Inc. v. Laborers Dist. Council Constr. Indus. Pension Fund*, 575 U.S. 175, 192 (2015).

Those principles apply to opinions no less than statements of fact. "[A] reasonable investor may . . . understand an opinion statement to convey facts about how the speaker has formed the opinion — or, otherwise put, about the speaker's basis for holding that view. And if the real facts are otherwise, but not provided, the opinion statement will mislead its audience." *Omnicare*, 575 U.S. at 188. In

particular, "a statement in the form of an opinion . . . may convey three facts: that the speaker has such a belief; that the belief fairly aligns with the facts known to the speaker; and . . . that the speaker has made the type of inquiry that a reasonable investor would expect given the circumstances." *Carbonite*, 22 F.4th at 7. A misstatement or omission about ***any one*** of those facts is thus actionable.

The district court failed to apply those principles. Instead, it adopted a novel rule of immunity for clinical trials: "'[I]nterpretations of clinical trial data are considered opinions' and . . . disagreements with the scientific conclusions drawn from those opinions are ***not actionable***." Add.17 (emphasis added). That holding has no support in the law.

Neither the Exchange Act nor Rule 10b-5 includes any carve-out for statements about clinical trials. 15 U.S.C. §78j(b); 17 C.F.R. §240.10b-5. The Supreme Court's cases setting forth the governing standards contain no suggestion that courts may create ad hoc exemptions for particular subjects like clinical trials. *See, e.g.*, *Omnicare*, 575 U.S. at 183-87. And the district court's rule ignores numerous precedents applying ordinary standards to statements about clinical trials or other medical data.

In *Matrixx*, for example, the Supreme Court held that a drugmaker was required to disclose that a handful of patients had lost their sense of smell from its cold remedy, even though the company urged that the results were not statistically

significant. 563 U.S. at 38-47. Rejecting the company's assessment of the importance of this data, the Court held that its statements were misleading because "reasonable investors" would consider the information consequential. *Id.* at 43.

In *In re Ariad Pharmaceuticals, Inc. Securities Litigation*, 842 F.3d 744 (1st Cir. 2016), this Court allowed a claim against a drugmaker for misleading statements about its cancer drug. Based on clinical trial data, the company asserted that pancreatitis was the "most prevalent serious adverse event," even though the FDA had expressed concerns about a different problem, cardiovascular events. *Id.* at 752-53. The Court found that omission "misleading" and had "little difficulty" concluding that investors would consider it material. *Id.* at 753.

Other circuits agree. In *Schueneman v. Arena Pharmaceuticals, Inc.*, 840 F.3d 698 (9th Cir. 2016), a company predicted that its drug would be approved "based on the Phase II data, the Phase I data, the preclinical studies that [were] done, [and] all the animal studies that have been completed." *Id.* at 702. The company did not disclose one rat study that showed increased cancer rates; it believed that the results presented no safety issues, but the FDA had expressed concerns and required more analysis. *Id.* at 701-02. The Ninth Circuit held that omission misleading: "[O]nce defendants chose to tout [the drug's] likely approval by referencing allegedly positive animal and pre-clinical studies, they were bound to do so in a manner that

wouldn't mislead investors [by withholding] potentially negative information within their possession." *Id.* at 707-08 (alterations omitted).

Similarly, in *Abramson v. Newlink Genetics Corp.*, 965 F.3d 165 (2d Cir. 2020), after a clinical trial showed that a company's pancreatic cancer drug achieved a 24-month survival rate, the company touted the result by claiming that "all the major studies" show typical rates less than 20 months. *Id.* at 170. The Second Circuit found the statement misleading because many studies showed longer survival rates. *Id.* at 176-77. "When omitted contrary facts substantially undermine the conclusion a reasonable investor would reach from a statement of opinion," the court held, "that statement is misleading and actionable." *Id.* at 177.[2]

This Court has reached similar results in analogous contexts involving technical data. In *Lucia v. Prospect Street High Income Portfolio, Inc.*, 36 F.3d 170

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[2] *See also Khoja v. Orexigen Therapeutics, Inc.*, 899 F.3d 988, 1010 (9th Cir. 2018) ("[O]nce Orexigen chose to tout the apparently positive . . . interim results, Orexigen had the obligation also to disclose that they were likely unreliable."); *SEB Inv. Mgmt. AB v. Endo Int'l, PLC*, 351 F. Supp. 3d 874, 900 (E.D. Pa. 2018) (statements about clinical trial data misleading when they "painted a favorable picture" while omitting "details that would have presented a complete and less favorable one"); *In re Delcath Sys., Inc. Sec. Litig.*, 36 F. Supp. 3d 320, 331 (S.D.N.Y. 2014) (statements misleading where company "disclosed data regarding the number and percentage of [adverse events] in the Drug Group, but did not disclose comparable information for the Control Group"); *Frater v. Hemispherx Biopharma, Inc.*, 996 F. Supp. 2d 335, 340-45 (E.D. Pa. 2014) ("cherry-pick[ed]" statements actionable); *In re Merck & Co. Sec., Deriv. & ERISA Litig.*, No. 05-1151, 2011 WL 3444199, at *7, *15 (D.N.J. Aug. 8, 2011) (benign explanation for increase in heart attacks misleading where company concealed data attributing heart attacks to drug).

(1st Cir. 1994), fund promoters claimed that junk bonds had outperformed Treasury securities over a ten-year period, but failed to disclose that they ***underperformed*** over the most recent six years. *Id.* at 173. The Court found that omission misleading: "[W]e think that a six-year comparison favoring Treasury securities is substantial enough to cast some doubt on the reliability of the reported ten-year figure." *Id.* at 176. "[A] reasonable shareholder [c]ould consider the six-year comparison important to the investment decision." *Id.*

The district court's reasoning cannot be reconciled with those precedents. By adopting a sweeping rule that "[i]nterpretations of clinical trial data" are "not actionable," A1070, the court stacked the deck in Biogen's favor. Statements about clinical trials are subject to the same standards that govern other statements, and if Biogen touted positive data while misleadingly concealing other data that refuted its assertions, plaintiffs are entitled to proceed.

B. Biogen's Explanation for Why the First Clinical Trial Failed Was Misleading

Under the correct standard, the Complaint sufficiently alleges that Biogen misled investors by claiming that Study 301 failed because it had fewer high-dose patients, while concealing the results that refuted that claim.

Biogen repeatedly told investors that Study 301 failed because it had fewer high-dose patients. "Our primary learning from these data is that ***sufficient exposure to high dose aducanumab*** reduced clinical decline . . . ." A100 ¶171

(emphasis altered). Study 301 failed because patients "who had enrolled early in the trials," before Biogen amended the protocol to increase the doses for carriers, "had a lower average exposure." *Id.* "[W]hat we have learned clearly is that dose is very important," and "if individuals do receive [the high dose] then they do have an efficacious response." A103 ¶179. "[A]ll" of Biogen's data supposedly supported that conclusion: "[Y]ou really need to get to the higher dose. And I think ***our data are all consistent with that***." A108-09 ¶191 (emphasis altered).

What Biogen failed to mention was that its other results — shared with the FDA but withheld from the public — refuted that explanation. In Study 302, carriers who received the higher dose fared ***worse*** than carriers who received the original dose. A92-93 ¶¶157-159. And non-carriers, who always received the higher dose, performed poorly in ***both*** studies. A91 ¶¶152-153. Those data contradicted Biogen's attempt to explain away the failure of Study 301: Fewer high-dose patients could not be the reason Study 301 failed if higher doses do not improve outcomes.

That concealed information was clearly material. A fact is material if "there is a substantial likelihood that a reasonable [investor] would consider it important." *Omnicare*, 575 U.S. at 196. The concealed data drastically undercut Biogen's explanation for Study 301's failure. The data made it far more likely that Biogen's attempt to explain away Study 301's failure was an artifact of p-hacking: Having

abandoned its prespecified analysis plan, Biogen kept reanalyzing its data until it stumbled across a theory that made the results look benign.

Analyst reactions confirm the information's materiality. Once analysts digested the Massie report, they derided Biogen's analysis as "unscientific, statistically inappropriate, and misleading." A140-41 ¶277(b). Biogen's explanations "just look[ed] ridiculous" and "don't make any sense at all." A97-98 ¶168. The company's stock price plummeted — a reaction that is itself evidence of materiality. A142 ¶279; *see Kleinman v. Elan Corp.*, 706 F.3d 145, 155 (2d Cir. 2013) ("A drop in stock price, if relevant, tends to establish materiality . . . .").

Biogen thus omitted material information necessary to render its statements not misleading. *See Matrixx*, 563 U.S. at 44. That is true whether the statements are classified as facts or opinions. Even if the statements were opinions, they are actionable because they did not "fairly align[] with the facts known to the speaker" or reflect "the type of inquiry that a reasonable investor would expect." *Carbonite*, 22 F.4th at 7. "When omitted contrary facts substantially undermine the conclusion a reasonable investor would reach from a statement of opinion, that statement is misleading and actionable." *Abramson*, 965 F.3d at 177.

Biogen's statements were at least as misleading as the defendant's statement in *Ariad* that pancreatitis was the "most prevalent serious adverse event," while omitting the FDA's concerns about a different problem. 842 F.3d at 752-53. They

closely resemble the statements in *Lucia*, where the defendants touted that junk bonds had outperformed Treasuries over a ten-year period, while omitting that they had underperformed over the most recent six years. 36 F.3d at 176.

Moreover, Sandrock's statement that "all" of Biogen's data supported its explanation — that "our data are ***all*** consistent with that," A108-09 ¶191 (emphasis altered) — is strikingly similar to the statement in *Schueneman* that "***all*** the animal studies" supported the drug's approval, 840 F.3d at 702 (emphasis added), and the statement in *Abramson* that "***all*** the major studies" showed survival rates less than 20 months, 965 F.3d at 176-77 (emphasis added). In reality, Biogen's data was ***not*** "all consistent with that." Biogen's own data — for carriers in Study 302 and for non-carriers in both studies — refuted its explanation. *See also In re PTC Therapeutics, Inc. Sec. Litig.*, No. 16-1124, 2017 WL 3705801, at *11-15 (D.N.J. Aug. 28, 2017) (statement that "totality" of data supported clinical benefit was misleading where "only a fraction of patients" reported benefit); *In re OSI Pharm., Inc. Sec. Litig.*, No. 04 Civ. 5505, 2007 WL 9672541, at *8 (E.D.N.Y. Mar. 31, 2007) (statement that drug "improved survival in all subsets" misleading where drug did not improve survival in some subsets).

None of the district court's responses supports Biogen's position. The court reasoned that Biogen's statements could not be misleading because it was "widely known" that Biogen engaged in "post hoc analysis." Add.23. But plaintiffs are not

accusing Biogen of committing securities fraud merely by engaging in post hoc analysis. Rather, Biogen committed fraud by offering an explanation for why Study 301 failed while concealing facts that refuted that explanation. Biogen's p-hacking was merely relevant context — context that made it more, not less, important that Biogen disclose information investors needed to evaluate its explanation.

The district court urged that "nothing in the complaint establishes the primacy of the sub-group level analysis." Add.24. But Biogen itself injected subgroup analysis into the dialogue by claiming that Study 301 failed because it had more patients who enrolled before Biogen increased the doses for carriers. A100 ¶171. In any event, the question is not the "primacy" of one analysis over the other, but whether Biogen's selective reporting made its statements misleading. Investors plainly thought so. A140-42 ¶¶277-279; A145 ¶294.

Finally, the district court asserted that the fact that "the FDA had endorsed Biogen's statistical model" meant the dispute was "one of genuine scientific debate and therefore not actionable." Add.25. But the FDA never endorsed Biogen's analysis: Dr. Dunn's office, which supported approval, and Dr. Massie's office, which opposed it, are both part of the FDA. And in the end, the FDA granted ***accelerated*** approval precisely because Biogen's clinical trials did ***not*** show that Aduhelm was effective. A154-55 ¶316.

In any case, the district court's theory ignores the Complaint's detailed allegations about the reasons for the FDA's actions: Biogen's Chief Medical Officer had a longstanding relationship with the head of the FDA's Office of Neurology, and the two colluded to push the drug through. A61 ¶21; A177-78; A138-39 ¶276; A139 ¶276(g). Numerous allegations confirm that the FDA review process was irregular. The plan was hatched at an "off-the-books" meeting that violated FDA policy. A61 ¶21. The agency formulated "leading questions" for the advisory committee that were "designed to support approval." A136-37 ¶272. The agency issued effusive joint briefing materials. A136 ¶265; A138-39 ¶276. And for the first time in FDA history, the agency approved the drug despite a ***ten to zero*** advisory committee vote against it. A142 ¶281; A157 ¶322(c). Multiple congressional committees investigated. A157-58 ¶325. And when the FDA learned of Biogen's relationship with Dunn, the agency called for an investigation of itself. A159 ¶330.[3]

The FDA's support for Aduhelm was not evidence of "genuine scientific debate" — it was evidence of regulatory capture. Add.25. Even under the PSLRA,

[3] The recent House Staff Report provides even more grounds to question the proceedings. That report reveals that, "while certain members of the FDA review team worked closely with Biogen to prepare a joint briefing document," Dr. Massie's office was "excluded from the process" and received a draft only "two to three days before comments were needed." House Staff Report at 20. The report also explains that, although a different FDA office had occasionally issued joint briefing materials in the past, it had done so only when there was internal consensus, which clearly was not the case here. *Id.* at 19-21.

a court must credit well-pled factual allegations and draw all inferences in plaintiffs' favor. *See Aldridge v. A.T. Cross Corp.*, 284 F.3d 72, 78 (1st Cir. 2002). The district court ignored that rule.

C. Biogen's Description of Its Plaque Reduction Data Was Misleading

Biogen also misled investors by claiming that its data showed a correlation between plaque reduction and better patient outcomes. Biogen told investors that Aduhelm "is able to erode and eliminate the plaque leading to the benefits we see in terms of cognition for the patients." A124 ¶227. "[I]f you give enough of the high dose, you can achieve a certain amount of amyloid removal and that certain amount is what's required to see the reduction in clinical decline." A122-23 ¶223.

Biogen concealed facts that cast those claims in a completely different light. Biogen's prespecified analysis plan called for separate statistical tests on low-dose and high-dose patients. A120 ¶¶217-218. Those results showed nothing approaching a fair correlation for ***any*** subgroup. A114 ¶206; A121 ¶220. The results looked random: There was virtually no correlation for low-dose patients in Study 301, and a ***negative*** correlation for high-dose patients in Study 302 — the group that should supposedly benefit the most. A121 ¶220. Rather than disclose those inconsistent results, Biogen secretly changed its plan and pooled the data. *Id.* Biogen did so even though its explanation for why Study 301 failed was that patients needed the high dose for the drug to work.

That undisclosed information was material because "there is a substantial likelihood that a reasonable [investor] would consider it important." *Omnicare*, 575 U.S. at 196. The fact that Aduhelm removes amyloid plaque is irrelevant unless plaque reduction benefits patients. Biogen's prespecified analysis plan produced inconsistent results, with the worst results for high-dose patients in Study 302. The advisory committee highlighted those facts in voting against approval. A143-44 ¶¶283-287. The fact that Biogen changed its plan in 2020, after already having collected the data and spent months analyzing it, shows that Biogen's results were the product of more p-hacking.

Analyst commentary confirms that materiality. Before the draft Massie report, analysts wrote that Aduhelm showed "a consistent association between [plaque] reduction . . . and clinical response." A118 ¶211(i). Once the truth emerged, analysts changed their tune: "Weak correlation between plaque reduction and [clinical outcomes]. The correlation between plaque reduction . . . and the primary endpoint . . . has an R^2 value of just 0.13 [sic], which calls into question the amyloid hypothesis entirely if it wasn't questioned enough already." A140-41 ¶277.

The district court held that Biogen's statements were not misleading because they included comments like "we're still learning as we look at the data." Add.28. But whatever Biogen was "still learning" could not change what it already knew. The results from its prespecified analysis plan showed no meaningful positive

correlation for half the subgroups, including a ***negative*** correlation for high-dose patients in Study 302. A121 ¶220.

The court also dismissed Biogen's statements as mere "optimistic responses" or "educated speculation." Add.28-29. That is not a fair characterization. Vounatsos, for example, said that Aduhelm "is able to erode and eliminate the plaque leading to the benefits we see in terms of cognition for the patients." A124 ¶227. That is an unambiguous claim of correlation.

Plaintiffs are not "asking the court to declare one post hoc analysis superior to another." Add.30. The problem was that Biogen suppressed its own ***prespecified*** plan and used post hoc analysis without disclosing the change. A121 ¶220. Finally, the claim that "[t]he FDA ultimately endorsed Biogen's methodology and conclusions" is no more persuasive here than it was above. Add.30. The FDA's approval was an inside job. The district court simply ignored the Complaint's allegations in favor of its own preferred narrative.

III. PLAINTIFFS SUFFICIENTLY ALLEGED SCIENTER

The district court also erred by rejecting the Complaint's allegations of scienter. "[A] plaintiff may satisfy the scienter requirement with a showing of either conscious intent to defraud or 'a high degree of recklessness.'" *ACA Fin. Guar. Corp. v. Advest, Inc.*, 512 F.3d 46, 58 (1st Cir. 2008). Recklessness requires "an extreme departure from the standards of ordinary care . . . which presents a danger

of misleading buyers . . . that is either known to the defendant or is so obvious the actor must have been aware of it." *Ariad*, 842 F.3d at 750.

Under the PSLRA, a complaint must "state with particularity facts giving rise to a strong inference that the defendant acted with the required state of mind." 15 U.S.C. §78u-4(b)(2)(A). A strong inference "need not be irrefutable, *i.e.*, of the 'smoking-gun' genre, or even the 'most plausible of competing inferences.'" *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 551 U.S. 308, 324 (2007). But it must be "cogent and at least as compelling as any opposing inference." *Id.* The Court must analyze "all of the facts alleged, taken collectively," not "any individual allegation, scrutinized in isolation." *Id*. at 322-23.

In *Matrixx*, for example, the Supreme Court found allegations of scienter sufficient where the inference of knowing or reckless misconduct was at least as compelling as "the inference that [the company] simply thought the [loss-of-smell] reports did not indicate anything meaningful." 563 U.S. at 49. In *Ariad*, this Court found allegations sufficient where the company expressed optimism about its drug's chances for approval despite knowing of "recent troubling developments [that] created an impermissible risk of misleading investors." 842 F.3d at 753. And in *Schueneman*, the Ninth Circuit found allegations sufficient where the company "express[ed] confidence by claiming that all of the data was running in [the drug's] favor" when, in fact, "[i]t was not." 840 F.3d at 707-09.

The district court departed from those principles. It acknowledged that the fact that "Biogen conducted a rigorous analysis could be sufficient to show Biogen was aware of [the] countervailing analyses" in the Massie report. Add.34. But it saw no sufficient allegations that "Biogen believed its own conclusions were wrong." *Id.* In fact, there are multiple indicia that Biogen intentionally sought to obscure the unfavorable aspects of its clinical trial results. At the very least, Biogen disregarded serious risks that its incomplete portrayals would mislead investors.

A. Biogen's Willful Manipulation of Clinical Trial Data Supports an Inference of Scienter

Biogen's p-hacking, selective reporting, and other statistical abuses support an inference of scienter. Biogen's willingness to manipulate statistical data makes it more likely that Biogen acted intentionally or recklessly when it presented misleading results to the public.

In *Alaska Electrical Pension Fund v. Pharmacia Corp.*, 554 F.3d 342 (3d Cir. 2009), for example, a drug company published data from the first six months of its 13-month clinical trial, but intentionally withheld the remainder, which would have made the drug look worse. *Id.* at 344-45. The Third Circuit held that the selective reporting supported an inference of scienter: "While it is true that a legitimate disagreement over scientific data does not give rise to a securities fraud claim, . . . a ***bad faith misrepresentation of scientific data*** . . . [is] sufficient to withstand the '[e]xacting pleading requirements' of the PSLRA." *Id.* at 352 (emphasis added).

Similarly, in *In re Merck & Co. Securities, Derivative & ERISA Litigation*, No. 05-1151, 2015 WL 2250472 (D.N.J. May 13, 2015), a drug company manipulated its clinical trial data by "chang[ing] the endpoint" from its "pre-specified . . . analysis." *Id.* at *22. The defendant argued that there were "legitimate scientific reasons for the decisions." *Id.* at *23. But the court found that "bad faith misrepresentation of scientific data" sufficient to infer scienter. *Id.*

So too here. The FDA requires analysis plans to be specified in advance. Food & Drug Admin., *Guidance on Statistical Principles for Clinical Trials*, 63 Fed. Reg. 49,583, 49,593 (Sept. 16, 1998). Yet when Biogen's prespecified plan failed to yield the desired results, Biogen resorted to p-hacking: It "tasked 49 of its statisticians to pore over the Phase III results" and find some way to make them look better. A81 ¶118. Biogen then selectively reported results while concealing data that refuted its explanation. A91-93 ¶¶152-153, 157-159.

Biogen's manipulation of its plaque removal data was similarly egregious. Biogen had a prespecified analysis plan that separately evaluated the high-dose and low-dose groups. A120 ¶216-218. But after Biogen received the trial data, it changed its plan, obscuring the inconsistent results. A120-21 ¶¶218, 220.

Biogen's pattern of manipulating clinical trial data and presenting only the favorable results to investors supports an inference of scienter.

B. Biogen's Departure from Past Practice in Withholding Its Clinical Trial Data Supports an Inference of Scienter

Biogen's refusal to disclose its Phase III clinical trial data, contrary to its practice for prior studies, likewise supports an inference of scienter.

Courts have repeatedly held that a defendant's changes in reporting practices that conceal negative information support an inference of scienter. In *Dahhan v. OvaScience, Inc.*, 321 F. Supp. 3d 247 (D. Mass. 2018), for example, a company's decision to stop reporting quarterly data supported an inference that it was intentionally concealing poor sales. *Id.* at 255-56. And in *In re Ebix, Inc. Securities Litigation*, 898 F. Supp. 2d 1325 (N.D. Ga. 2012), a company's decision to stop reporting separate revenue figures for legacy and acquired businesses supported an inference that it was recklessly concealing poor organic growth. *Id.* at 1346; *see also In re St. Jude Med., Inc. Sec. Litig.*, 836 F. Supp. 2d 878, 899 (D. Minn. 2011) (defendant "changed its practice" to avoid documentation).

Likewise here, Biogen changed its reporting practices. When Biogen conducted an earlier clinical trial on Aduhelm, it made the raw data available to researchers. A165 ¶347. But Biogen refused to make that data available for its Phase III trials. A165 ¶348. Analysts questioned Biogen about the specific subgroups at issue and pleaded with Biogen to release the data. A164-65 ¶346 ("So could you speak to what the carrier and noncarriers look like?"). But Biogen refused, even while admitting that its actions were a break from precedent: "[Y]ou're right,

I mean, typically, we do present a lot of things, subgroups included, in the past. You're right, we did do that." *Id.* Biogen's uncharacteristic decision to withhold the Phase III data supports an inference of scienter: Biogen kept that data under wraps because it knew the subgroup data — particularly the crucial Study 302 data for patients affected by the dose increase — would expose its flawed explanation for Study 301's failure.

The district court dismissed those allegations because Sandrock justified the change on the ground that the drug would "soon be under review at regulatory authorities." A163-65 ¶346; *see* Add.36. But that explanation was hardly exonerating. A jury could readily infer from Sandrock's statement that Biogen withheld the data because it was worried that the public reaction would jeopardize FDA approval. That rationale only reinforces that Biogen intentionally concealed material information.

Sandrock's assurance that "***[w]e have nothing to hide***" compounds the inference of scienter. A164-65 ¶346. Sandrock's statement falsely reassured investors that Biogen was withholding the data only for regulatory reasons, not because the data undercut information Biogen did disclose. Biogen ***did*** have something to hide, and Sandrock's overly defensive and gratuitous comment suggests he knew it — the classic case of a speaker who "doth protest too much." *Cf. Ghorbani v. Pac. Gas & Elec. Co. Grp. Life Ins.*, 100 F. Supp. 2d 1165, 1168

(N.D. Cal. 2000). The district court opined that "Biogen's avoidance of the topic and suggestion that it had 'nothing to hide' should spark a reasonable investor's curiosity," as if that somehow cut ***against*** a finding of scienter. Add.37. The opposite is true: Sandrock's comment confirms that Biogen was hiding the ball.

C. The FDA's Irregular Approval Process Supports an Inference of Scienter

Still more evidence of scienter comes from Biogen's role in the FDA's irregular approval process for Aduhelm. Biogen and its allies at the FDA colluded to put Aduhelm on a predetermined path to approval, blowing past agency policies and conventions along the way. Biogen's witting role in that process makes it more likely that Biogen would take bad faith steps of its own to ensure approval.

Failure to comply with standards and procedures can support an inference of scienter. In *Aldridge v. A.T. Cross Corp.*, 284 F.3d 72 (1st Cir. 2002), for example, this Court held that a company's violation of accounting standards supported an inference of scienter. *Id.* at 83. And in *Singer v. Reali*, 883 F.3d 425 (4th Cir. 2018), the Fourth Circuit held that a company's illegal coaching of surgeons to mislabel procedures for reimbursement supported an inference of scienter. *Id.* at 443-44.

The Complaint alleges that Biogen colluded with FDA insiders to get Aduhelm approved through a process fraught with irregularities. Sandrock and his longtime ally Dunn hatched the plan at an "off-the-books" meeting that violated FDA policy. A61 ¶21. The FDA and Biogen then colluded to issue effusive and

highly atypical joint briefing materials. A135 ¶265. The FDA submitted blatantly leading questions to its advisory committee. A136-37 ¶272. It approved the drug even though that committee voted ***ten to zero*** against approval. A142-43 ¶281. Some of the officials who voted for approval had no background in Alzheimer's at all. A154 ¶314. Biogen was an eager partner in that scheme. Its willingness to bend the rules to obtain approval makes it more likely that it gave short shrift to its disclosure obligations too.

The district court asserted that "the fact that Biogen had been working closely with the FDA and that the FDA has endorsed [its] post hoc analysis . . . is strong evidence against finding scienter." Add.38. But that theory ignores, yet again, the Complaint's well-pled allegations. Even under the PSLRA, a court must draw all reasonable inferences in plaintiffs' favor. *Aldridge*, 284 F.3d at 78. The jury could readily find from the FDA's controversial and unprecedented actions that the agency supported Aduhelm because Biogen and its allies were steering the drug toward approval no matter what. Biogen's role in that collusion supports rather than refutes an inference of scienter.[4]

[4] Once again, the House Staff Report confirms those allegations. That report reveals that "FDA and Biogen engaged in at least 115 meetings, calls, and substantive email exchanges concerning the application process," including at least 45 meetings with Dr. Dunn and Defendant Budd Haeberlein. House Staff Report at 15. After Dr. Massie's team expressed concerns, they were "not invited to further working group meetings," "were not consulted on final details of models used," and "received a

D. The Importance of Aduhelm to Biogen's Financial Success Supports an Inference of Scienter

Finally, the importance of the concealed information confirms the inference of scienter. Aduhelm was critical to Biogen's financial success. That fact supports the inference that Biogen's management either knew about the adverse clinical trial data or were reckless for not inquiring about it.

This Court has made clear that "the importance of a particular item to a defendant can support an inference that the defendant is 'paying close attention' to that item," and thus support an inference of scienter if "close attention would have revealed an incongruity so glaring as to make the need for further inquiry obvious." *Carbonite*, 22 F.4th at 9. Such facts suggest that management "either inquired about [the product] before deciding to promote it to investors or were reckless in failing to do so." *Id.* at 10.

Aduhelm was critical to Biogen. If successful, the drug would be "the most profitable treatment ever approved by the FDA." A55-56 ¶2. As one analyst put it: "[Aduhelm's approval is] make-or-break for the company. I can't think of more of a defining event for a large-cap company." A69 ¶63. "[Biogen] lives and dies by how aducanumab plays out." A80 ¶116. News about Aduhelm had a major impact

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draft [of the joint briefing materials] '***two to three days*** before comments were needed.'" *Id.* at 20 & n.80 (emphasis added). Those events strongly suggest that Biogen colluded with the FDA to shield Aduhelm from critical scrutiny within the agency and then intentionally sandbagged Dr. Massie at the last moment.

on Biogen's stock price. *See, e.g.*, A78 ¶¶108-109 (29% drop upon futility announcement); A144-45 ¶¶293-294 (28% drop upon advisory committee vote).

Aduhelm's importance suggests that management was closely focused on the clinical trials. Sandrock's statement that "our data are all consistent with that" implies that management had in fact considered all the data. A108-09 ¶191. Other executives confirmed that they had "looked very closely" at the data. A127 ¶238. Dr. Massie's analyses were based on the data Biogen provided. A60 ¶16. The district court agreed that Biogen's "rigorous analysis could be sufficient to show Biogen was aware of [the] countervailing analyses." Add.34.[5]

Focused so closely on their blockbuster drug, Biogen's management must have known that the narrative they were spinning on why Study 301 failed was contrary to their own data. If they did not — if they simply gave that explanation without even checking whether their data contradicted it — they were reckless.

IV. PLAINTIFFS SUFFICIENTLY ALLEGED LOSS CAUSATION

Finally, the district court erred by rejecting plaintiffs' allegations of loss causation. Loss causation is the "causal connection between the material misrepresentation and the [investor's] loss." *Dura Pharm., Inc. v. Broudo*, 544 U.S. 336, 342 (2005). Plaintiffs often establish loss causation by showing a "corrective

[5] The House Staff Report confirms that Dr. Massie's team "conveyed their reservations regarding the evidence to . . . Biogen in Type C meetings" starting in late 2019. House Staff Report at 20 n.80.

disclosure." *Mass. Ret. Sys. v. CVS Caremark Corp.*, 716 F.3d 229, 237 (1st Cir. 2013). A plaintiff can also establish loss causation by showing a materialization of the risk the fraud concealed. *See Abramson*, 965 F.3d at 178-80.

Here, plaintiffs' theory was straightforward. Biogen concealed that its own clinical trial data undermined its attempt to explain away Study 301's failure as well as its claims about plaque reduction's correlation to better outcomes. A91 ¶¶152-153; A92-93 ¶¶157-159; A119-21 ¶¶213-220. Those misleading statements artificially inflated Biogen's stock price. A170 ¶366. The Massie report, released on November 4, 2020, revealed the truth. A60 ¶16; A120 ¶215; A138 ¶275; A197-294. Because that report was a dense technical document tucked behind 250 pages of effusive briefing materials, the market did not react immediately. A137-41 ¶¶273-278. The stock price started to decline on November 5. A142 ¶279. But it was only after the advisory committee voted against the drug on November 6, based largely on Dr. Massie's criticisms, that the stock price tumbled, dissipating the artificial inflation. A142-45 ¶¶280-294.

Plaintiffs purchased their stock on November 4 or 5, 2020, shortly after the FDA released the Massie report, but well before the market finished digesting that information. A35-36; A49-50; A457-66. Plaintiffs suffered losses caused by the fraud as the market incorporated Dr. Massie's revelations, causing the stock price to

fall. Those allegations establish loss causation: Investors suffered losses because of disclosure of the very facts Biogen concealed.

The district court disagreed based on a categorical rule that loss causation "is not tied to when the market reacts to information, but rather when that information became available to the public." Add.40. Because "the Massie Report . . . was published before Plaintiffs purchased Biogen stock, the complaint fails." *Id.* That holding is wrong for several reasons.

A. Corrective Disclosures Need Not Have an Immediate Impact on Stock Price To Support Loss Causation

First, the district court's per se rule ignores precedent holding that markets may take more than one day to absorb new information.

In *In re Xcelera.com Securities Litigation*, 430 F.3d 503 (1st Cir. 2005), for example, this Court endorsed an event study that measured the effect of new information on a stock's price, not only over a one-day window, but also over "longer windows of two, three, and five days." *Id.* at 513 n.11. The Court cited authority for the point that a "two-day window" was sufficient to show "a cause and effect relationship between company-specific announcements and stock price." *Id.* (citing *Lehocky v. Tidel Techs., Inc.*, 220 F.R.D. 491 (S.D. Tex. 2004); and Jonathan R. Macey et al., *Lessons from Financial Economics: Materiality, Reliance, and Extending the Reach of Basic v. Levinson*, 77 Va. L. Rev. 1017 (1991)).

In *Lormand v. US Unwired, Inc.*, 565 F.3d 228 (5th Cir. 2009), the Fifth Circuit held that "[t]he market could plausibly have had a delayed reaction; a delayed reaction can still satisfy the pleading requirements for 'loss causation' though proof of causation would be more difficult when significant time elapses before the market allegedly reacts." *Id.* at 266-67 n.33 (collecting cases). And in *In re DVI, Inc. Securities Litigation*, 639 F.3d 623 (3d Cir. 2011), the Third Circuit held that the fact that "some information took two days to affect the price does not undermine a finding of [market] efficiency." *Id.* at 635.

The Complaint alleges numerous reasons why the market took time to digest the Massie report. The report was highly technical, with nearly a hundred pages of dense statistical analysis. A137-38 ¶¶274-275; A197-294. It was buried after nearly 250 pages of "effusive" joint briefing materials. A135 ¶¶263-264. And unlike those materials, it bore a prominent "DRAFT" watermark. A137 ¶273; A197-294.

Analyst coverage corroborates those allegations. Several analysts did not mention the draft Massie report at all and instead focused on the effusive briefing materials. A138-39 ¶276. Others mentioned the report but "downplayed" its significance. A140 ¶277. Only later did they publish follow-up reports that highlighted Dr. Massie's revelations. *Id.*

The amount of delay here was not substantial: The FDA released the report during the trading day on November 4, 2020, A135 ¶262; the stock price fell

somewhat on November 5, A142 ¶279; trading was halted all day on November 6, A142 ¶280; and the stock price had already collapsed when the market opened on November 9, A145 ¶294. Plaintiffs' claims thus entail only a one to two trading day delay — well within precedent. *See Xcelera.com*, 430 F.3d at 513 n.11 (two days).

The Complaint reasonably alleges that plaintiffs suffered losses because the stock price went down in response to Dr. Massie's revelations. That the market did so over the course of two trading days, rather than instantaneously, does not sever that well-pled causal connection.

B. The Advisory Committee Decision Was a Corrective Disclosure

The Complaint also alleges another basis for loss causation: The November 6, 2020 advisory committee decision was itself a corrective disclosure. Committee members repeatedly referenced Dr. Massie's revelations. A143-44 ¶¶283-292. The advisory committee vote was thus a corrective disclosure for the same reason as the Massie report.

That the Massie report was already public when the committee voted does not preclude loss causation. "A disclosure based on publicly available information can . . . constitute a corrective disclosure," so long as "the alleged corrective disclosure provided new information to the market that was not yet reflected in the company's stock price." *In re BofI Holding, Inc. Sec. Litig.*, 977 F.3d 781, 795 (9th Cir. 2020).

Information might not already be reflected in the stock price if it is "complex[]" or if "great effort [is] needed to locate and analyze it." *Id.* at 795.

In *In re Gilead Sciences Securities Litigation*, 536 F.3d 1049 (9th Cir. 2008), for example, the FDA accused a drug company of "improper off-label marketing" in a public warning letter. *Id.* at 1051. Two months later, the company reported reduced demand, and its stock price plummeted. *Id.* at 1054. Despite that gap, the court held that the allegations of loss causation from the off-label marketing were sufficient because "the public failed to appreciate [the letter's] significance." *Id.* at 1058; *see also Pub. Emps. Ret. Sys. of Miss. v. Amedisys, Inc.*, 769 F.3d 313, 323 (5th Cir. 2014) ("[C]omplex economic data understandable only through expert analysis may not be readily digestible by the marketplace.").

Likewise here, the Complaint explains that the Massie report was "dense to the point of being impenetrable" and was "written for world-renowned experts who sat on the Advisory Committee, not investors." A137 ¶274. It was not until the advisory committee analyzed the report and voted against Aduhelm that the market fully appreciated its significance. A144 ¶293. The Complaint thus adequately alleges that the advisory committee vote itself was a corrective disclosure.

C. The Advisory Committee Decision Was a Materialization of Risk

Finally, the Complaint adequately alleges loss causation based on a materialization of concealed risk. Under that theory, the stock price decline need

not result from a disclosure of the fraud itself. It is sufficient that "the risk that caused the loss was within the zone of risk ***concealed*** by the [fraud]." *Lentell v. Merrill Lynch & Co.*, 396 F.3d 161, 173 (2d Cir. 2005). The plaintiff need only "demonstrat[e] that 'the ***subject*** of the fraudulent statement or omission was the cause of the actual loss suffered.'" *In re Vivendi, S.A. Sec. Litig.*, 838 F.3d 223, 261 (2d Cir. 2016).

By concealing clinical trial results that undermined its statements about Aduhelm's efficacy, Biogen concealed the ***risk*** of adverse regulatory actions. That is what happened when the advisory committee voted against Aduhelm. The subject of the fraud was the cause of the losses shareholders suffered when Biogen's stock price plummeted. For that reason too, plaintiffs pled loss causation.[6]

[6] The district court dismissed the Section 20(a) claim solely for failure to plead a Section 10(b) violation. Add.41. Reversal of the latter ruling thus also requires reversal of the former.

CONCLUSION

The district court's judgment should be reversed.

January 12, 2023

Respectfully submitted,

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/s/ Robert K. Kry
Robert K. Kry

ADDENDUM

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Add. 1

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

NADIA SHASH and AMJAD KHAN, individually and on behalf of all others similarly situated,	*	
Plaintiffs,	*	Civil Action No. 1:21-cv-10479-IT
v.	*	
BIOGEN INC.; MICHEL VOUNATSOS; ALFRED W. SANDROCK, JR.; and SAMANTHA BUDD HAEBERLEIN,	*	
Defendants.	*	

MEMORANDUM & ORDER

September 12, 2022

TALWANI, D.J.

Plaintiffs Nadia Shash and Amjad Khan bring this securities fraud putative class action against Defendants Biogen Inc. ("Biogen") and its executives Michel Vounatsos, Alfred W. Sandrock, Jr., and Samantha Budd Haeberlein. Plaintiffs allege Defendants misled investors about the efficacy of Biogen's nascent Alzheimer's drug, aducanumab, in violation of Sections 10(b) and 20(a) of the Securities Exchange Act and implementing regulations. Pending before the court is Defendants' Motion to Dismiss [Doc. No. 60] the Second Amended Complaint [Doc. No. 58], Plaintiffs' Motion to Strike [Doc. No. 65] and Plaintiffs' two Requests for Judicial Notice [Doc. Nos. 71, 73]. For the reasons that follow, Plaintiffs' motion to strike is GRANTED in part and DENIED in part, Plaintiffs' requests for judicial notice are DENIED, and Defendants' motion to dismiss is GRANTED.

I. Procedural Background

This action was initiated in the Central District of California on behalf of persons or

entities who purchased or otherwise acquired publicly traded Biogen securities between October 22, 2019, and November 6, 2020 (the "Class Period"). That court appointed Nadia Shash lead plaintiff and transferred the action to the District of Massachusetts. Order on Appointment [Doc. No. 30]; Mot. to Transfer [Doc. No. 34]; Dkt Minutes [Doc. No. 36].

Following transfer, Plaintiffs filed the first amended complaint and, after Defendants timely moved to dismiss, the operative Second Amended Complaint [Doc. No. 58]. Defendants responded with the pending Motion to Dismiss [Doc. No. 60] and in support submitted the Declaration of William Trach [Doc. No. 62] with twenty-three exhibits [Doc. Nos. 62-1 through 62-23]. Plaintiffs opposed and moved to strike certain of these exhibits. Opp'n [Doc. No. 63]; Mot. to Strike [Doc. No. 65].

Plaintiffs subsequently filed two requests for judicial notice. First, Plaintiffs sought judicial notice of a decision by the Center for Medicare and Medicaid Services regarding its coverage of aducanumab. First Request for Notice [Doc. No. 71]. Plaintiffs' second request concerned a Biogen press release announcing upcoming leadership changes. Second Request for Notice [Doc. No. 73]. Defendants opposed both requests. See Opp'ns to Requests for Notice [Doc. Nos. 72, 74]. The court heard oral argument on the pending motions.

II. Factual Background as Alleged in the Second Amended Complaint

A. Alzheimer's Disease

Alzheimer's disease is a neurodegenerative disease defined by brain degeneration and progressive loss of cognitive function. Sec. Am. Compl. ¶ 52 [Doc. No. 58]. While the progression of the disease is well understood, the cause of Alzheimer's remains largely unknown. Id. at ¶ 52. The leading theory, known as the amyloid hypothesis, posits that Alzheimer's is caused by the build-up of amyloid plaque in the brain, which blocks neuron

pathways and damages the synaptic connections, causing the loss of cognition associated with the disease. Id. at ¶¶ 52–57. As a result, significant resources have been committed to the research and development of therapies aimed at targeting this potentially harmful plaque. Id. at ¶ 57. Despite these efforts, no successful amyloid related treatment had been developed. Id.

B. Biogen and Aducanumab

Biogen is a publicly traded biopharmaceutical company focused on developing treatments for neurological and neurodegenerative diseases and autoimmune and hematologic disorders. Id. at ¶ 42. Biogen invested significant resources in the development of a highly anticipated Alzheimer's treatment called aducanumab. Id. at ¶ 66, Ex. 1, Stat Article [Doc. No. 58-1]. Aducanumab is an amyloid beta targeting monoclonal antibody designed to delay clinical decline in patients with Alzheimer's disease and if successful would be the first Alzheimer's drug capable of slowing the progression of the disease. Id. at ¶¶ 3, 59–60.

Biogen designed aducanumab to avoid the failures of other Alzheimer's therapies. Id. at ¶¶ 57–58, 61. Unlike failed amyloid-based treatments, aducanumab targets only harmful aggregated amyloid beta. Id. at ¶¶ 61–62. Biogen claimed that "[b]y more precisely targeting aggregated amyloid beta . . ., aducanumab can be given in doses high enough to be clinically effective" without confronting the toxicity concerns that constrained earlier treatments. Id. at ¶ 61.

C. Aducanumab Clinical Trials

To study the effects of aducanumab on Alzheimer's patients and generate data necessary to seek full approval of the drug, Biogen submitted an investigational new drug application to the FDA in 2011 and began phase I clinical trials shortly thereafter. Id. at ¶ 66. What followed was the standard sequence of clinical trials aimed first at toxicity and then at safety and efficacy. Id.

at ¶¶ 77-78. In 2012, Biogen commenced Study 103 or PRIME, a Phase 1b/2 clinical trial to evaluate safety and tolerability. Id. at ¶¶ 68-69. Secondary and exploratory endpoints of the PRIME study also included aducanumab's effect on amyloid plaque in the brain and the sensitivity of the study's clinical efficacy measures. Id. at ¶ 75. The exploratory PRIME data showed "10 mg/kg as the most effective dose of aducanumab" and "a correlation between removal of amyloid plaque and better clinical outcomes." Id. at ¶ 199. These positive findings informed Biogen's design of the phase III clinical trials. Id. at ¶¶ 76, 90.

In 2015, Biogen commenced aducanumab's phase III clinical trial, designed to evaluate aducanumab's safety and efficacy using prespecified endpoints. Id. at ¶¶ 77, 81. The phase III trial was conducted as two independent but identically designed studies—Study 301 (ENGAGE) and Study 302 (EMERGE)—that started about one month apart, with ENGAGE beginning first and remaining ahead in enrollment throughout. Id. at ¶¶ 77, 81, 149–50. In addition to evaluating the effect of aducanumab on cognition, the studies tracked certain biomarkers to assess aducanumab's effect on brain pathology, including on amyloid plaque reduction. Id. at ¶ 89.

About two thirds of the patients enrolled in the phase III trial had a protein producing gene called APOE4. Id. at ¶ 10. Individuals with APOE4 ("Carriers") have an increased risk of developing Alzheimer's disease and make up a disproportionate percentage of Alzheimer's patients. Id. Carriers are also predisposed to developing Amyloid Related Imaging Abnormalities ("ARIA"), an aducanumab side effect that can cause serious neurological complications. Id. To minimize study participants' risk, Biogen initially restricted Carriers to low doses of aducanumab. Id. at ¶ 91. Over the life of the phase III trial, Biogen altered the dosing protocols for the Carrier population twice, increasing the dosage available to Carriers each time. Id. at ¶ 96. After the second protocol amendment, all high dose patients—regardless of Carrier status—

received the proscribed 10mg/kg dose. Id. at ¶¶ 92–100.[1] Because enrollment in EMERGE (Study 302) began later and proceeded at a slower pace than enrollment in ENGAGE (Study 301), more patients in EMERGE received the full dose and for a longer percentage of the trial period. Id. at ¶¶ 149–50.

Pursuant to the Phase III pre-established protocol, an independent monitoring committee conducted an interim futility analysis of data pooled from both studies once half the enrolled patients had reached week 78 of the trial. Id. at ¶ 101. The futility analysis showed that meeting the primary endpoints at the end of the trial was unlikely. Id. at ¶ 105. Based on these results, the independent committee determined that continuing the trial would be futile and recommended early termination. Id. at ¶¶ 101–02, 104, 107. On March 21, 2019, Biogen accepted the committee's conclusion and publicly announced the termination of both studies on futility grounds. Id. at ¶ 108.

D. Biogen's Post Hoc Analysis

Following termination of the aducanumab phase III trial, Biogen conducted its own review of the phase III data. Id. at ¶ 118. Biogen's data scientists analyzed the futility dataset plus an additional three months of data that was collected after the futility dataset closed but before Biogen terminated the trial on March 21, 2019. Id. When Biogen disaggregated the data and analyzed ENGAGE and EMERGE independently, "[the data] showed that in EMERGE, the high dose reduced clinical decline as measured by the primary and secondary endpoints," but

[1] The first modification allowed patients to resume their original aducanumab dose after resolution of an ARIA event. Id. at ¶¶ 95–96. The second modification eliminated the 6mg/kg dose restriction for Carriers and set the high dose for all trial participants at 10mg/kg. Id. at ¶¶ 99–100.

that the topline ENGAGE data showed "aducanumab did not reduce the clinical decline" among the high dose population. Id. at ¶ 181. However, when the Biogen team narrowed its analysis to "data from patients who achieved sufficient exposure to high dose aducanumab in ENGAGE," the results "support[ed] the findings of EMERGE." Id. at ¶ 171. Biogen shared these findings with the FDA, prompting the formation of an FDA/Biogen collaborative group focused on analyzing the phase III data. Id. at ¶¶ 21, 133.

Biogen also shared these findings with shareholders. On October 22, 2019, during its quarterly earnings call, Biogen reported that "[a]fter consultation with the FDA, [Biogen] believe[d] that the totality of these data support a regulatory filing." Id. at ¶ 171. On that call, Biogen told shareholders that the "primary learning from these data is that sufficient exposure to high dose aducanumab reduced clinical decline across multiple clinical endpoints," a finding that "was statistically significant in EMERGE" and supported by "the data from patients who achieved sufficient exposure to high dose aducanumab in ENGAGE." Id. Biogen posited to investors that ENGAGE's negative result stemmed from its faster enrollment pace, which meant that fewer participants benefited from the mid-study protocol amendments. Id.

The next day, October 23, 2019, Defendant Vounatsos appeared on MSNBC to discuss aducanumab. Id. at ¶ 227. During the interview, Vounatsos told viewers that he was convinced "more than ever" that beta-amyloid was the key to dealing with Alzheimer's, explaining that the data shows aducanumab binds to targeted plaque and "is able to erode and eliminate the plaque leading to the benefits we see in terms of cognition for the patients." Id. at ¶ 227.

Next, on December 5, 2019, Defendants presented the top line phase III results on two separate occasions: first, at the Clinical Trials on Alzheimer's Disease Conference and second during an investor Q&A regarding Biogen's phase III topline results. Id. at ¶ 51. At these

presentations, and numerous times over the subsequent year, Defendants made specific factual statements explaining their interpretations of the clinical trial data, repeating these two conclusions: that Biogen's post hoc analyses showed that aducanumab was dose and exposure dependent and that its effect on reducing amyloid plaque was evidence of efficacy. During each of these discussions, Defendants reiterated that data from ENGAGE offered no evidence that aducanumab had a positive effect, consistent with the futility findings, while the EMERGE data showed aducanumab produced a statistically significant effect based on the satisfaction of the prespecified primary and secondary endpoints.

Biogen repeated these findings that the topline results of the post hoc analysis showed that aducanumab was dose and exposure dependent and effective in reducing amyloid plaque on a January 30, 2020 Q4 2019 earnings call, during an April 2, 2020 encore presentation of its aducanumab phase III topline results, on Biogen's July 22, 2020 Q2 2020 earnings call, during a July 29, 2020 presentation of the topline results at the Alzheimer's Association International Conference, and during a September 19, 2020 presentation of the topline results at the 23rd Chinese National Conference of Neurology. Id.

Additionally, on the December 5, 2019 investor Q&A, Defendant Budd Haeberlein stated "we believe" neither geography nor demographics were "driving the overall outcomes that we see or the differences that we see between the studies." Id. She also noted that "it's the breadth of endpoints having [a]n effect on [each measure of cognitive change], which is encouraging rather than any one of them or pieces thereof." Id. at ¶ 248.

E. Biogen's Application, the FDA Advisory Committee & the Massie Report

Relying on its post hoc analysis, Biogen applied for full FDA approval of aducanumab—to be marketed as Aduhelm—in July 2020. Ex. 1, Stat Article, at 13 [Doc. No. 58-1].

The FDA empaneled an advisory committee to assist in its review of Biogen's application (the "Advisory Committee"). Sec. Am. Compl. ¶ 259 [Doc. No. 58]. "The primary role of an advisory committee is to provide independent advice that will contribute to the quality of the agency's regulatory decision-making and lend credibility to the product review process." Id. Given the controversial nature of the clinical trials and uncertainty around the results, stock analysts recognized the Advisory Committee's decision would be a critical factor in determining the fate of aducanumab. Id. at ¶¶ 260–61.

In advance of the Advisory Committee meeting, Biogen and the FDA jointly prepared briefing materials (the "Briefing Materials"), which the FDA published on its website during the trading day on November 4, 2020. Id. at ¶¶ 262–63. The Briefing Materials largely mirrored Biogen's public statements concerning aducanumab's efficacy and the statistical basis for its conclusion. In the Briefing Materials, the FDA provided an "effusive" endorsement of Biogen's post hoc analysis, methodology, and conclusions. Id. at ¶ 264.

The Briefing Materials set out Biogen's position and the FDA's responses, the majority of which expressed agreement with Biogen's position. Id. ¶ 265. The FDA concluded in the Briefing Materials that "the results of Study 302 [EMERGE] are highly persuasive and the study is capable of providing the primary contribution to a demonstration of substantial evidence of effectiveness of aducanumab," that the "results of Study 103 [PRIME Phase 1b] are appropriately viewed as supportive evidence of the effectiveness of aducanumab," and that the "effect of aducanumab in Study 302 [EMERGE] is robust and exceptionally persuasive on several of the instruments used to evaluate efficacy." Id. at ¶¶ 266–69.

Attached as Appendix 2 to the Briefing Materials, and published alongside it, was a dissenting report (the "Massie Report") prepared by Tristan Massie, the FDA's statistical

reviewer on aducanumab's application. Id. at ¶¶ 16, 263, 273; Ex. 3, Massie Report [Doc. No. 58-3]. The Massie Report makes several statistical counterarguments challenging the Briefing Material's support for approval.[2] Massie concludes that "the totality of the data does not seem to support the efficacy of the high dose" and that "[i]nconsistency on many levels summarizes the final clinical efficacy data" related to aducanumab. Massie Report 253, 255 [Doc. No. 58-3].

On November 4, 2020, the day the Briefing Materials, including the Massie Report, were published, Biogen's stock price increased from $253.20 at the open to $355.63 per share. The market's initial reaction to the Briefing Materials was "focused on the laudatory position the FDA took in the Briefing Materials" and considered "[t]he briefing documents for aducanumab [] a landslide win for [Biogen]" with the effect of "increase[ing] the likelihood of aducanumab approval substantially." Sec. Am. Compl. ¶¶ 276–77 [Doc. No. 58]. "[I]t was plain that even analysts whose job was to cover Biogen had not read the Draft Massie Report but had noticed the FDA's clear bias in favor of approval[.]" Id. However, by close on the following trading day after investors had begun to digest the Massie Report's findings, Biogen's stock price had fallen 17.5% to $328.90 per share. Id. at ¶ 279. Trading in Biogen shares was suspended Friday, November 6, 2020, while the Advisory Committee convened. Id. at ¶ 280. Late that night, the Advisory Committee reported its almost unanimous vote against finding it "reasonable to

[2] The Massie Report revealed that: (a) the effects on Non-Carriers was essentially nil; (b) PV4 had no impact on Carriers in Study 302; (c) in both Studies 301 and 302, Carriers whose titration was interrupted by ARIA experienced better clinical outcomes than Carriers whose titration was not interrupted and so received more 10mg/kg doses; (d) the number of 10mg/kg doses had no impact on Carriers in Study 302; (e) there was no correlation between the amount of amyloid plaque removed and clinical outcomes; (f) there was wide variation in treatment effect between countries and the U.S. performed poorly; (g) younger patients and those whose Alzheimer's disease was less advanced achieved worse outcomes; and (h) the multiple endpoints were closely correlated.

consider Study 302 as primary evidence of effectiveness of aducanumab for the treatment of Alzheimer's disease." Id. at ¶ 281. Massie's analysis had cast doubts on Biogen's conclusions by illuminating inconsistencies in the data that one would not expect to see where there is a strong efficacy signal. Id. at ¶ 283. The only question where the Advisory Committee voted in favor of a Biogen's position (with 5 votes answering yes, 6 votes uncertain, and no votes against) was that "the Applicant presented strong evidence of a pharmacodynamic effect on Alzheimer's disease pathophysiology [i.e., does aducanumab reduce amyloid plaque?]." Id. at ¶ 281. The Advisory Committee's vote made approval seem unlikely, but not impossible. Id. at ¶ 296. When trading resumed on November 9, 2020, Biogen stock opened at $230.82 per share. Id. at ¶ 294. When the market closed that day, Biogen was at $236.26, down 28.2% from the last close on November 5th. Id.

III. Standard of Review

When evaluating a motion to dismiss for failure to state a claim, the court assumes "the truth of all well-pleaded facts" and draws "all reasonable inferences in the plaintiff's favor." Nisselson v. Lernout, 469 F.3d 143, 150 (1st Cir. 2006). To survive dismissal, a complaint must contain sufficient factual material to "state a claim to relief that is plausible on its face." Bell Atl. Corp. v. Twombly, 550 U.S. 544, 570 (2007). "While a complaint attacked by a Rule 12(b)(6) motion to dismiss does not need detailed factual allegations . . . [f]actual allegations must be enough to raise a right to relief above the speculative level . . . ." Id. at 555 (internal citations omitted). "A claim has facial plausibility when the plaintiff pleads factual content that allows the court to draw the reasonable inference that the defendant is liable for the misconduct alleged." Ashcroft v. Iqbal, 556 U.S. 662, 678 (2009).

"Exhibits attached to the complaint are properly considered part of the pleading for all purposes, including Rule 12(b)(6)." Trans-Spec Truck Service, Inc. v. Caterpillar Inc., 524 F.3d 315, 321 (1st Cir. 2008) (internal citations and quotations omitted). In ruling on a motion to dismiss, "a judge can mull over 'documents incorporated by reference in [the complaint], matters of public record, and other matters susceptible to judicial notice.'" Lydon v. Local 103, Int'l Bhd. of Elec. Workers, 770 F.3d 48, 53 (1st Cir. 2014) (quoting Giragosian v. Ryan, 547 F.3d 59, 65 (1st Cir. 2008)) (alteration in original). A court may consider extrinsic documents "without converting the motion into one for summary judgment" where "the relevant entirety of a document is integral to or explicitly relied upon in the complaint" and thus incorporated by reference. Clorox Co. P.R. v. Proctor & Gamble Comm. Co., 228 F.3d 24, 32 (1st Cir. 2000) (internal quotations omitted). That a complaint mentions a document, or even repeatedly refers to a document, however, is not enough; a complaint incorporates a document by reference only where the allegations are "expressly linked to – and admittedly dependent upon – a document (the authenticity of which is not challenged)" such that the "document effectively merges into the pleadings and the trial court can review it in deciding a motion to dismiss under Rule 12(b)(6)." Beddall v. State St. Bank & Trust Co., 137 F.3d 12, 17 (1st Cir. 1998); see also Alt. Energy, Inc. v. St. Paul Fire and Marine Ins. Co., 267 F.3d 30, 33 (1st Cir. 2001). If other matters outside the pleadings are presented to the court, the court may exclude such matters or may treat the motion as one for summary judgment, with all parties given a reasonable opportunity to present all the material that is pertinent to the motion. Fed. R. Civ. P. 12(d); see also Trans-Spec Truck Serv., Inc., 524 F.3d at 321 (if materials outside the complaint are considered, the motion ordinarily "must be decided under the more stringent standards applicable to a Rule 56 motion for summary judgment").

Securities fraud allegations are held to heightened pleading requirements under Federal Rule of Civil Procedure 9(b) and the Private Securities Litigation Reform Act of 1995 ("PSLRA"). 15 U.S.C. § 78u–4(b)(2); see In re Boston Sci. Corp. Sec. Litig., 686 F.3d 21, 27, 30 (1st Cir. 2012); see N. Am. Catholic Educ. Programming Found., Inc. v. Cardinale, 567 F.3d 8, 15 (1st Cir. 2009) (holding that the particularity requirement applies not only to actual fraud claims but also to "associated claims where the core allegations effectively charge fraud"). As with all allegations of fraud, a complaint must be dismissed unless it "state[s] with particularity facts giving rise to a strong inference that the defendant acted with the required state of mind." 15 U.S.C. § 78u–4(b)(2).

IV. Motion to Strike

Plaintiffs argue that Defendants improperly submitted and relied on extrinsic evidence and that the impermissible evidence should be struck from the record and not considered in evaluating the sufficiency of their complaint. Mot. to Strike [Doc. No. 65].

First, Plaintiffs argue that documents published on the FDA's website (Exhibits B, K, L, M. N, and P to the Trach Declaration [Doc. No. 62]) may not be considered for the truth of the contents and, to the extent Defendants' arguments do so, such references must be struck from the record. Both parties agree, however, that the court may take judicial notice that the FDA published each of the challenged exhibits, and that at this stage the court is precluded from considering these documents for the truth of their contents. Mem. in Supp. of Mot. to Strike 2–3 [Doc. No. 67]; Opp'n to Mot. to Strike 3–5 [Doc. No. 68]. Accordingly, the court finds no basis for striking these exhibits from the record but considers them only for the fact that they exist and not the truth of their contents.

Second, Plaintiffs move to exclude the FDA's full 343-page joint briefing book prepared for the Advisory Committee meeting (Exhibit A of the Trach Declaration [Doc. No. 62]) and to strike Defendants' reliance on it. Plaintiffs contend that the report is extrinsic evidence not reviewable in support of a motion to dismiss; Defendants argue that Plaintiffs incorporated the report into the Second Amended Complaint [Doc. No. 58] by reference and therefore that the court may review it.

The joint Briefing Materials contain three parts: (i) the FDA's report conveying its support for Biogen's conclusions concerning aducanumab's efficacy; (ii) Appendix 1, a clinical review of the aducanumab data; and (iii) Appendix 2, the dissenting Massie Report. Plaintiffs heavily cite and substantially rely on Appendix 2 in their complaint and incorporate it in full as an exhibit. While there may be merit to Defendants' argument that by attaching the Massie Report to the complaint and citing it—and other portions of the larger, unattached, 343 page joint Briefing Materials—the court finds that in this case it need not reach this question. Like the other FDA publications, the court takes judicial notice of the full Briefing Materials and considers it only for the fact that it exists and not for the truth of its contents.[3]

V. Requests for Judicial Notice

The saga surrounding the FDA's ultimate approval of aducanumab continued after the Class Period. Plaintiffs have described in some details the events from the end of the class period

[3] Plaintiffs do not oppose the consideration of the remaining exhibits, including the full transcripts from the calls and slides from the presentations where Defendants made the allegedly false and misleading statements at issue in the complaint (Trach Exs. D, O, Q, R [Doc. Nos. 62-4, 62-15, 62-17, 62-18]). To the extent review of these records is necessary to fully contextualize the challenged statements, these documents may be considered. See Clorox Co., 228 F.3d at 32 (allowing consideration of extrinsic documents where "the relevant entirety of a document is integral to or explicitly relied upon in the complaint" and thus incorporated by reference).

through the filing of the complaint. Briefly, after the advisory committee declined to endorse aducanumab's application for full FDA approval, the FDA began reviewing aducanumab as a candidate for accelerated approval. Id. at ¶¶ 312–14.[4] On April 26, 2021, the FDA granted accelerated approval to aducanumab for the treatment of Alzheimer's disease, based on the surrogate endpoint of reducing amyloid beta plaque and with the approval of the majority of attendees. Id. at ¶¶ 314–15. The FDA's approval memorandum states, however, that "residual uncertainty remains about aducanumab's clinical benefit" and that the FDA therefore required Biogen "to conduct a postapproval trial to verify benefit" as a component of the grant of accelerated approval. Id. at ¶ 316. Upon news of approval, Biogen's stock price immediately shot up." Id. at ¶ 317. Plaintiffs now ask the court to take judicial notice of an April 7, 2022 press release from the Center for Medicare and Medicaid Services ("CMS") announcing it would not cover aducanumab except for patients engaged in clinical trials, Request for Judicial Not. [Doc. No. 71], and a May 3, 2022 Biogen press release announcing the company's "substantial elimination of Biogen's global commercial infrastructure supporting [aducanumab]" and decision to search for a Chief Executive Officer to replace Michael Vounatsos, Request for Judicial Not. [Doc. No. 73], Ex. 1, Biogen Press Release 4 [Doc. No. 73-1].This new information, together with the allegations in the complaint concerning the FDA's ultimate

[4] Accelerated approval is a mechanism the FDA may use to approve drugs based on their effectiveness on surrogate, rather than primary, endpoints. Id. at ¶ 300. In granting accelerated approval, the FDA approves drugs based on their promise for producing clinical outcomes, not based on evidence of clinical outcomes themselves. Id. The FDA had communicated accelerated approval as a possible path for approval to Biogen in the June 2019 meeting "based on [aducanumab's] effect on reducing brain amyloid." Id.

approval of aducanumab, fall outside the presumptive class period, and therefore the court finds no basis to consider them here.

VI. Count I – Violation of Section 10(b) of the Exchange Act and Rule 10b-5

To state a claim for securities fraud under Section 10(b) and Rule 10b–5, a plaintiff must sufficiently allege "(1) a material misrepresentation or omission; (2) scienter; (3) a connection with the purchase or sale of a security; (4) reliance; (5) economic loss; and (6) loss causation." In re Boston Sci. Corp. Sec. Litig., 686 F.3d 21, 27 (1st Cir. 2012) (quoting Miss. Pub. Empls.' Ret. Sys. v. Boston Sci. Corp., 523 F.3d 75, 85 (1st Cir. 2008)). Defendants challenge the sufficiency of the allegations as to the first, second, fourth and sixth elements.

A. Materially False Misstatements or Omissions

The complaint alleges that throughout the Class Period, Biogen made material misstatements or omissions through the individual Defendants concerning four topics related to Biogen's post hoc analyses of the aducanumab phase III clinical trial data: (1) Defendants' assertion that patients in ENGAGE (Study 301) experienced a dose dependent response to aducanumab; (2) Defendants' assertion that amyloid plaque reduction *led to* positive clinical outcomes; (3) Defendants' minimization of regional variation affecting clinical outcomes; and (4) Defendants' assertion that the breadth of positive secondary endpoints in EMERGE (Study 302) was evidence of efficacy. Defendants argue that the challenged statements convey Biogen's genuine conclusions concerning its post hoc analyses of the phase III data and are unactionable statements of opinion.

For a Section 10(b) complaint to survive a motion to dismiss, it must allege a materially "false, or misleadingly omitted, statement of [material] fact." Constr. Indus. & Laborers Joint Pension Tr. v. Carbonite, Inc., 22 F.4th 1, 7 (1st Cir. 2021). To plead falsity under the PSLRA, a

plaintiff must "specify each statement alleged to have been misleading [and] the reason or reasons why the statement is misleading." Hill v. Gozani, 638 F.3d 40, 55 (1st Cir. 2011) (alteration in original) (quoting 15 U.S.C. § 78u-4(b)(1)). A fact or omissions is material where "there is a substantial likelihood that a reasonable investor would have viewed it as significantly altering the total mix of information made available." Fire and Police Pension Ass'n v. Simon, 778 F.3d 228, 240 (1st Cir. 2015) (internal quotations omitted). But even where the omitted "information is material, there is no liability . . . unless there was a duty to disclose it." Roeder v. Alpha Indus., Inc., 814 F.2d 22, 26 (1st Cir. 1987). Thus, Section 10(b) "do[es] not create an affirmative duty to disclose any and all material information," just what is necessary to prevent statements, when viewed "in the light of the circumstances under which they were made," from being "so incomplete as to mislead." In re Bos. Sci. Corp., 686 F.3d at 27 (quoting Matrixx Initiatives, Inc. v. Siracusano, 563 U.S. 27, 44 (2011)); Thant v. Karyopharm Therapeutics Inc., 43 F.4th 214, 226 (1st Cir. 2022) ("we have conclusively established that a company is not, by virtue of making some disclosures about its products, obligated to disclose all potentially interesting information."); City of Bristol Pension Fund v. Vertex Pharms. Inc., 12 F. Supp. 3d 225, 236 (D. Mass. 2014) ("A disclosure of certain facts may trigger a duty to disclose others where necessary to avoid making a misleading statement."). Further, "[i]t follows that '[i]t is not a material omission to fail to point out information of which the market is already aware.'" Thant, 43 F.4th at 226 (quoting Baron v. Smith, 380 F.3d 49, 57 (1st Cir. 2004)).

"[T]he most significant difference between statements of fact and expressions of opinion is that 'a statement of fact ("the coffee is hot") expresses certainty about a thing, whereas a statement of opinion ("I think the coffee is hot") does not.'" Constr. Indus. & Laborers, 22 F.4th at 7 (quoting Omnicare, Inc. v. Laborers Dist. Council Constr. Indus. Pension Fund, 575 U.S.

175, 183 (2015)). While "[w]ords like 'I think' or 'I believe' can play a role in demonstrating a lack of certainty," they do not immunize the speaker from liability where the speaker is false or misleading as to a material fact. Constr. Indus. & Laborers, 22 F.4th at 7; Corban v. Sarepta Therapeutics, Inc., 868 F.3d 31, 38 (1st Cir. 2017). Likewise, the substance and context of a statement may indicate an opinion even where no qualifying language is used. Credit Suisse First Bos. Corp., In re, 431 F.3d 36, 47 (1st Cir. 2005) (finding "although [stock] ratings are based to some degree on objective facts, they ultimately convey an opinion about a stock's prospects").

Analytical conclusions are generally understood to convey opinions where "two knowledgeable analysts, each acting in the utmost good faith" could reasonably interpret the data differently. Id.; see Karyopharm Therapeutics Inc., Sec. Litig., 552 F. Supp. 3d 77, 89 (D. Mass. 2021) (finding discrepancy between FDA's and defendants' results due to using different statistical methods and assumptions when analyzing the data constitutes a non-actionable scientific disagreement even where "defendants' view of the data may have been erroneous"), aff'd sub nom. Thant, 43 F.4th 214.

Several circuits have made explicit that "[i]nterpretations of clinical trial data are considered opinions" and that disagreements with the scientific conclusions drawn from those opinions are not actionable. City of Edinburgh Council v. Pfizer, Inc., 754 F.3d 159, 170–71 (3d Cir. 2014); see Kleinman v. Elan Corp., plc, 706 F.3d 145, 153 (2d Cir. 2013) (alleged misstatements about a drug's efficacy "are little more than a dispute about the proper interpretation of data"); see also In re Adolor, 616 F. Supp. 2d 551, 567 (2009) (holding disagreements about the proper methodology and conduct of clinical studies are insufficient to establish falsity); In re Sanofi Sec. Litig., 87 F. Supp. 3d 510, 543 (S.D.N.Y. 2015) ("courts have repeatedly held 'publicly stated interpretations of the results of various clinical studies' to be

'opinions' because 'reasonable persons may disagree over how to analyze data and interpret results, and neither lends itself to objective conclusions'"), aff'd sub nom. Tongue v. Sanofi, 816 F.3d 199, 214 (2d Cir. 2016).

The allegations here center on how Biogen conducted its post hoc review of the aducanumab trial data and the validity of the conclusions about aducanumab's efficacy that Biogen drew from it. Plaintiffs object on grounds that "the final determination of efficacy must be made based on the pre-specified clinical endpoints as analyzed in the pre-specified statistical plan" and that "[d]ata from clinical trials can be analyzed in multiple ways" and when not bound by pre-specified methodologies or endpoints can lead to data manipulation. Sec. Am. Compl. ¶¶ 134–35 [Doc. No. 58]. But it is widely understood that unbounded post hoc analyses produce less reliable results. And where Biogen acknowledged that its conclusions are drawn from unprescribed post hoc analyses, they are more akin to opinions than conclusive findings. Accordingly, because Biogen's statements "express a view, not a certainty" about the meaning of the phase III data, the court treats them as opinions. Omnicare, 575 U.S. at 185.

However, classifying a statement as an opinion does not categorically preclude "the possibility that the statement as a whole may still mislead as to some fact." Constr. Indus. & Laborers, 22 F.4th at 7. A statement of opinion may convey three facts: "that the speaker has such a belief; that the belief fairly aligns with the facts known to the speaker; and . . . that the speaker has made the type of inquiry that a reasonable investor would expect given the circumstances." Id.; see Omnicare, 575 U.S. at 186; Tongue, 816 F.3d at 214. An opinion that materially misleads as to any of these facts—either through admission or omission—is actionable. Here, Plaintiffs do not directly challenge the sincerity of Defendants' statements. Accordingly, the court considers whether (1) Biogen's conclusions concerning aducanumab did

not align with the facts known to Defendants when the statements were made or (2) Biogen failed to conduct the type of inquiry a reasonable investor would have expected under the circumstances before making the challenged statements.

Where a complaint pleads multiple misstatements, falsity is judged statement-by-statement, not "on the basis of the general flavor derived from an issuer's collective statements over a long period of time." In re Bos. Tech., Inc. Sec. Litig., 8 F. Supp. 2d 43, 56 (D. Mass. 1998). But the actual language must be considered in "[t]he immediate context of each statement—namely, the balance of what was said on the particular occasion, and the immediate circumstances in which the particular statement was made." Id. at 55. Because here the "statements are closely related and may be grouped together for consideration without diminishing the individualized attention needed to be given to each," the court proceeds by assessing each of four topics in turn. Urman v. Novelos Therapeutics, Inc., 796 F. Supp. 2d 277, 282 (D. Mass. 2011).

1. Statements about Aducanumab's Dose Dependent Response

The complaint alleges Defendants falsely reported that aducanumab was effective in patients who received a 10mg/kg dose for ten or more weeks. Sec. Am. Compl. ¶ 150 [Doc. No. 58]. Defendants contend that these statements are not actionable because they convey scientific conclusions reasonably supported by Biogen's post hoc analyses.

The substance of the challenged statements about aducanumab's dose response is exemplified by Defendant Sandrock's statement on Biogen's October 22, 2019 quarterly earnings call:

> Our primary learning from these data is that sufficient exposure to high dose aducanumab reduced clinical decline across multiple clinical endpoints. This reduction in clinical decline was statistically significant in EMERGE, and we believe that patients – that the data from

> patients who achieved sufficient exposure to high dose aducanumab in ENGAGE support the findings of EMERGE. After consultation with the FDA, we believe that the totality of these data support a regulatory filing.
>
> Importantly, patients included in the futility analysis were those who had enrolled early in the trials and those early enrolling patients had a lower average exposure to aducanumab in large part due to two protocol amendments that occurred sometime after the start of the trials. These two protocol amendments were put in place precisely to enable more patients to reach high dose aducanumab, and for a longer duration. As a consequence, the larger dataset available after trial cessation included more patients with sufficient exposure to high dose aducanumab.

Id. at ¶ 171.

Defendant Sandrock elaborated: "what I'm saying is that there is a very sort of sharp dose response, if you will, you have to get to high dose of aducanumab and intermediate dosing at least in an 18-month trial is not enough." Id. at ¶ 173. Defendant Budd Haeberlein followed that dosing was "a complex combination of duration, magnitude and no interruptions" and that "you need to achieve high dose for long enough, but also have no interruptions, and so that's a more complex calculation between the two studies." Id. at ¶ 175. She concluded: "I think what we have learned clearly is that dose is very important, but that if individuals do receive 10 milligrams per kilogram then they do have an efficacious response." Id. at ¶ 179. Defendant Budd Haeberlein explained that these results were not drawn exclusively from EMERGE, the positive study and that "[a]lthough the primary and secondary endpoints were not met in ENGAGE in post analysis, the subset of patients who received sufficient exposure to 10 milligram per kilogram aducanumab in this case, at least 10 doses of 10 milligram per kilogram showed similar results to the comparable population from EMERGE, in terms of both amyloid plaque reduction and reduced clinical decline on CDR-SB." Id. at ¶ 177.

Defendants repeated these two points—that EMERGE showed statistically significant evidence that aducanumab was effective at high doses and sufficient exposure and that data from ENGAGE supported this conclusion—numerous times over the following year.

The challenged statements from the two December 5, 2019 presentations of the topline results—the Clinical trials on Alzheimer's Disease Conference and Biogen's Q&A with investors—contain largely the same information as was shared on the October 22, 2019 earnings call. At the conference, Defendant Budd Haeberlein told attendees:

> To summarize, the aducanumab Phase III top line results. Following study termination based on futility, we analyzed a larger dataset. And this showed that in EMERGE, the high dose reduced clinical decline as measured by the primary and secondary endpoints. In ENGAGE, aducanumab did not reduce the clinical decline. In a post-hoc analysis, data from a subset of patients exposed to the high dose of aducanumab support the positive findings of EMERGE. I'm (going to) read this. In sub studies of biomarkers, aducanumab showed an effect on those disease-related biomarkers.

Id. at ¶ 181. On the investor Q&A that same day, Defendant Budd Haeberlein explained: [t]oday, though, we shared a new post hoc analysis, which is what we've called those – that subgroup of individuals who were able to have the opportunity for the intended dosing regimen, the so-called Protocol Version 4 group. And in that subset of patients, aducanumab did support the positive findings of EMERGE and ENGAGE." Id. at ¶ 183.

Budd Haeberlein repeated this sentiment in April 2020 during a Biogen investor call, which Plaintiffs also challenge. Id. at ¶ 187. And she repeated it again in a challenged statement made during a conference presentation on July 29, 2020.[5] Id. at ¶ 193.

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[5] "To understand the difference between the studies and the impact of changing the protocol, we defined population by a randomized cohort, who had the opportunity for all 14 doses of 10 milligram per kilogram, and this is termed the post Protocol Version 4 or PV4 population. If we compare the ITT population with the post-PV4 population, we can see that the post PV4 population in ENGAGE is consistent with the overall ITT population in EMERGE."

Plaintiffs also challenge a statement made by Sandrock during Biogen's January 2020 Q4 2019 earnings call, which repeated Budd Haeberlein's October and December 2019 statements concerning data from ENGAGE supporting the positive findings from EMERGE:

> Final analysis of these data showed that EMERGE was a positive study with the high dose regimen of aducanumab achieving statistical significance on both the pre-specified primary endpoint of CDR Sum of Boxes as well as on all three pre-specified secondary endpoints. On the other hand data from the ENGAGE study did not meet the primary endpoint, although we do believe that data from patients who achieve sufficient exposure to high dose aducanumab in ENGAGE support the findings of EMERGE.

Id. at ¶ 185.

Sandrock repeated a version of this explanation in another challenged statement made during the July 2020 Q2 earnings call.[6] Id. at ¶ 191. Defendant Budd Haeberlein repeated this conclusion in her presentation of the aducanumab phase III analysis at the Chinese National Conference of Neurology on September 19, 2020, which Plaintiffs also challenge.[7] Id. at ¶ 195.

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[6] "I think – look, the filing is based on these 3 studies, EMERGE, ENGAGE and PRIME. EMERGE is the first study to show in effect, not only on the primary endpoint, but all 3 prespecified secondary endpoints. We believe that data from ENGAGE – that portions of the data from ENGAGE, a negative study, that portions of it do support the analysis that we did with EMERGE. And then I'll say in also PRIME, which was published, shows even though the clinical endpoints were exploratory endpoints, on the highest dose, there was an effect on MMSE as well as CDR sum of boxes. And again, very similar that the lower doses did not show much of an effect. So consistent with the findings from ENGAGE and EMERGE, you really need to get to the higher dose. And I think our data are all consistent with that . . . . So we submitted all the data from those 3 studies that I mentioned: EMERGE, ENGAGE and PRIME. And what the FDA chooses to look at is – that's their purview. We – I will say that in terms of the negative study, ENGAGE, we do – we have analyses that show that those who received the highest dose over a sustained period of time do show evidence of efficacy similar to what we found in EMERGE. And so that's the data we presented to CTAD and AD/PD, and that's why we believe there's supportive evidence coming from ENGAGE."

[7] "So in summary, following study termination based on futility, there was an analysis of a larger data set. In EMERGE, the high dose aducanumab reduced clinical decline as measured by both the primary and secondary endpoints. In ENGAGE, aducanumab did not reduce the clinical decline. However, in a post-hoc analysis, data from a subset of patients exposed to high dose

Plaintiffs do not dispute that the challenged statements accurately reported the results of Biogen's post hoc analyses and that the post hoc results support the inference that aducanumab showed signs of effectiveness at higher doses. Plaintiffs contend, however, that statements about aducanumab's dose dependent response were false and misleading because Biogen's post hoc analysis itself was unreliable and Defendants' conclusions were irreconcilable with other alternative post hoc analyses that considered patient-level and sub-group level data.

First, Plaintiffs contend that Biogen manipulated the topline results by running different post hoc analyses on the phase III trial population until one "yield[ed] a statistically significant result" that supported the conclusion that aducanumab worked as intended. Id. at ¶ 135. But post hoc analyses are exploratory by nature. They lack the constraints of rigid pre-specified analyses, but also lack the presumption of reliability. Kleinman v. Elan Corp., PLC, 706 F.3d 145, 153 n.11 (2d Cir. 2013) ("Referring to post-hoc analysis as 'exploratory,' the FDA has cautioned that '[a]ny conclusion of treatment efficacy (or lack thereof) or safety based solely on exploratory subgroup analyses is unlikely to be accepted'" (quoting FDA Center for Drug Evaluation and Research, E9 Statistical Principles for Clinical Trials, 63 Fed.Reg. 49583, 49595 (Sept. 16, 1998))).

Thus, where "it is clear that a post-hoc analysis is being used, it is understood that those results are less significant and should therefore have less impact on investors." Id. at 154. The aducanumab post hoc results were no exception. It was widely known that EMERGE (Study 302) had met its pre-specified primary endpoint and that ENGAGE (Study 301) had not. See

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aducanumab support the positive findings of EMERGE. In sub-studies, aducanumab also showed an effect on disease-related biomarkers."

Sec. Am. Compl. ¶¶ 171, 177, 185, 191 [Doc. No. 58]. Biogen was transparent that the goal of the post hoc analyses was to look for evidence of efficacy to support FDA approval and Biogen further disclosed that its post hoc analyses were aimed at using alternative statistical analyses to identify different, non-specified, indicators of effectiveness. Investors too understood that Biogen's post hoc analyses were designed to see if Biogen could identify data from ENGAGE that supported the conclusions in EMERGE. See Hill, 638 F.3d at 60 n.5 ("In circumstances where some level of risk materializes, we have not required complete disclosure of all of the details when the overall risk is disclosed and the nature of the future risk remains uncertain."). And that is precisely what Biogen did. At bottom, Plaintiffs complain that Biogen was "able to tout positive results only because they deviated from the established protocol (which called for a linear analysis) and changed the metrics by which data was analyzed." Sec. Am. Compl. ¶ 154 [Doc. No. 58]. But this allegation amounts to Plaintiffs having "a problem with using post-hoc analysis as a methodology in pharmaceutical studies," not with Biogen's specific methodology. Kleinman, 706 F.3d at 154. Accordingly, the topline results of Biogen's post hoc analysis—which revealed patients who received sufficient exposure to the 10mg/kg dose of aducanumab had better clinical outcomes as compared to patients in the control group—were not themselves unreliable.

Next, Plaintiffs allege Biogen's statements asserting that aducanumab produced a dose dependent response were false because an alternative post hoc analysis—focused on patient subgroups—produced results inconsistent with Biogen's topline conclusions. But nothing in the complaint establishes the primacy of the sub-group level analysis. Though the complaint provides support for crediting the sub-group level scientific conclusion over Biogen's topline conclusions, the facts as alleged do not support a finding that Biogen's interpretation of the data

was objectively false. To the contrary, the complaint alleges that the FDA had endorsed Biogen's statistical model over the one Plaintiffs contend should supersede it here. On its face, this demonstrates that the proper statistical method for analyzing the topline results is one of genuine scientific debate and therefore not actionable under the PSLRA. Karyopharm Therapeutics Inc., 552 F. Supp. 3d 77 at 89 (finding discrepancy between FDA's and defendants' results due to using different statistical methods and assumptions when analyzing the data constitutes a non-actionable scientific disagreement even where "defendants' view of the data may have been erroneous").

Finally, Plaintiffs contend that Defendants' failure to reveal the countervailing analyses was misleading because it artificially inflated the significance of Biogen's conclusions. But the court has already concluded that Biogen's understanding that aducanumab was effective at a high enough dose had a reasonable basis in its topline post hoc results. And while the sub-group analysis casts doubt on the strength of Biogen's conclusion, investors "do[] not expect that *every* fact known to an issuer supports its opinion statement," and it "is not necessarily misleading when an issuer knows, but fails to disclose, some fact cutting the other way." Omnicare, 575 U.S. at 183, 195. This was particularly true here where "an investor reads each statement within such a document . . . in light of all its surrounding text, including hedges, disclaimers, and apparently conflicting information." Id. at 196. Defendants never made sweeping statements about aducanumab's efficacy. Because investors knew Biogen's conclusions were drawn from its post hoc analyses, and the caveats implicit in doing that, and were "aware of the company's use of the [subset] population," the company may lawfully "defend use of the [subset] population and cast its trial results in a positive light." Corban v. Sarepta Therapeutics, Inc., 2015 WL 1505693, at *6 (D. Mass. Mar. 31, 2015), aff'd, 868 F.3d 31, 39 (1st Cir. 2017).

Moreover, Defendants limited their discussion to the topline (placebo v. active groups) and the PV4 group. When Defendants made broad statements about efficacy, the statements all refer to the positive EMERGE study whereas when Defendants discussed ENGAGE, they consistently framed the support as qualified and applying to just a portion of the patient data. See Id. ("That the company ... cast its trial results in a positive light does not detract from [its] disclosure[s], as a defendant does not have a duty to cast the descriptions of its business in the most negative light." (internal quotation marks omitted)). And "securities laws do not . . . require that companies who report information from imperfect studies include exhaustive disclosures of procedures used, . . . [or] various opinions with respect to the effects of these choices on the interpretation of the outcome data." Padnes v. Scios Nova Inc., 1996 WL 539711, at *5 (N.D. Cal. Sept. 18, 1996).

Moreover, Biogen has no affirmative duty to disclose all information in its possession in which an investor may have an interest, nor does Rule 10-b "mean that by revealing one fact about a product, one must reveal all others that, too, would be interesting, market-wise; a company must reveal only those facts 'that are needed so that what was revealed would not be so *incomplete as to mislead*.'" See Hill, 638 F.3d at 56–57 (emphasis added in Hill); see Cooperman v. Individual, Inc., 171 F.3d 43, 49 (1st Cir. 1999) ("[T]he mere possession of material[,] nonpublic information does not create a duty to disclose it." (quoting Backman v. Polaroid Corp., 910 F.2d 10, 16 (1st Cir. 1990) (en banc))). Considering the context of Biogen's statements characterizing its post hoc analysis—even without always using qualifying language—reasonable investors would "understand[], and take[] into account, the difference we have discussed . . . between a statement of fact and one of opinion. . . . and grasp[] that [indicia of opinion] convey some lack of certainty as to the statement's content." Omnicare, 575 U.S. at

187. Accordingly, though Plaintiffs make a strong case for why Biogen's conclusions may have been flawed, Biogen's failure to disclose the contradicting studies was not misleading given that Biogen expressed its conclusions as reasonable opinions. See City of Edinburgh, 754 F.3d at 170 (holding a "[c]ompany's failure to accurately disclose clinical trial data may be actionable under the securities laws" but only where allegations contain plausible allegations of affirmative false statements about the drug's efficacy and safety, not just misrepresentations).

2. Plaque Reduction and Clinical Outcomes

Next, the complaint alleges that Defendants misled investors in statements asserting that reduction in amyloid plaque in patients' brains—caused by high dose of aducanumab—was correlated to positive clinical outcomes. Sec. Am. Compl. ¶¶ 221–32 [Doc. No. 58].

Plaintiffs do not dispute that Biogen's post hoc analysis showed aducanumab produced statistically significant, dose-dependent reductions in amyloid plaque when compared to placebo. Rather, Plaintiffs contend Defendants' statements assigning such a correlation were not reasonably rooted in the facts known to them. Plaintiffs assert that alternative post hoc analyses, based on patient-level—not topline—data was inconsistent with Biogen's conclusion because (1) high dose patients in EMERGE had a negative correlation between plaque removal and clinical outcomes and (2) of the four groups (high / low in each study), the correlation was strongest in EMERGE patients who received the low dose of aducanumab. Id. at ¶ 220.

During the October 22, 2019 quarterly earnings call, Defendant Vounatsos explained, in reference to the positive EMERGE study (Study 302), that "the new analysis of the larger dataset, which was conducted in consultation with the FDA, showed that aducanumab had a dose-dependent effect on the underlying pathology as measured by amyloid-PET imaging and reduced clinical decline in patients with early Alzheimer's disease as measured by the pre-

specified primary and secondary endpoints." Id. at ¶ 221. Plaintiffs allege this statement is misleading because in the high-dose arm of EMERGE, there was a slight negative relationship between removal of amyloid plaque and clinical outcomes and therefore, even if there had been any reduction in clinical decline in patients with early Alzheimer's disease, the reduction would have been unconnected to the reduction in amyloid plaque. Id. at ¶ 222. But the facts alleged are insufficient to support this conclusion. Not only is Vounatsos's statement based on Biogen's topline results, which compare the performance of the treatment group against the placebo group without differentiating among high and low dose populations, but throughout the call the individual Defendants also reiterated that "we're still learning as we look at the data." Id. at ¶ 223. Moreover, on that same October 2019 earnings call, Defendant Budd Haeberlein stated that "we have the exploratory analysis that we disclosed to explain what it is we learned around the importance of dose, but there is no perfect number of doses that are required, it's not binary." Id. That statement, coupled with Biogen's articulated belief that even where a large amount of amyloid is removed "there is a little bit of a lag" "for the biological activity to have an effect on clinical outcomes," presents a plausible explanation for why the data on amyloid reduction was not necessarily correlated with positive clinical outcomes. Id. Sandrock also explained that the Phase I PRIME data was consistent with their theory that a lag exists between the plaque removal and clinical improvement which may not be fully captured in an eighteen-month trial, further complicating how to interpret the data. Id. The remaining statements challenged by Plaintiffs are opinions consisting of either optimistic responses to questions soliciting the

speaker's perspective[8] or educated speculation.[9] Both lack the sufficient certainty to mislead. These statements constitute the kind of "vague optimism about a product's future" that the First Circuit has held "cannot constitute a material misstatement for purposes of the pleading requirements set by the PSLRA," even when—like here—the statements are "touting 'successful' or 'compelling' clinical support." Thant, 43 F.4th 214 at 223.

Accordingly, although the sub-group analysis provides insightful context, the fact that Defendants did not share this alternative view of the data does not make Biogen's conclusion, which was transparently based on the topline results and reasonably supported by them, misleading.

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[8] "**Interviewer**: So [aducanumab] is a monoclonal antibody that actually is designed to go after beta amyloid plaques which are seen in some Alzheimer's patients. You're telling me that it actually removes the plaques. There was some speculation that maybe that's not it; could be that you get Alzheimer's and the plaques then come about as a result of Alzheimer's, it's not an actual cause. You're convinced beta-amyloid is the key to dealing with –

Defendant Vounatsos: More than ever. What we demonstrate is that [aducanumab] who's binding to the right part of the amyloid-beta, the aggregated form of amyloid beta, is able to erode and eliminate the plaque leading to the benefits we see in terms of cognition for the patients. It reduces basically the decline and we can see effects such as on memory orientation, language, but also functionally the ability to take care of oneself." Id. at ¶ 227.

[9] "[T]he difference between EMERGE and ENGAGE actually is significant. And I think [Budd Haeberlein] pointed out this morning that in the EMERGE trial, the reduction was what we had expected based on the PRIME data. But ENGAGE fell short. And that's the reason why we started to focus on exposure because it looked like the amyloid reduction in ENGAGE was not quite what we had expected. And that's what led us down this track of looking at drug exposure." Id. at ¶ 229. "As part of an explanation for the negative ENGAGE results, [Defendant] Sandrock indicated to us that the amyloid lowering effect in ENGAGE underperformed expectations. He believes that the effect may have been partly responsible for the confounding results (e.g. due to less target engagement)." Id. at ¶ 231. "[W]e believe, having looked very closely at the baseline demographics and characteristics, that none of these are driving the overall outcomes that we see or the differences that we see between the studies." Id. at ¶ 238.

Rather, Plaintiffs are again asking the court to declare one post hoc analysis superior to another. But it is not "[the court's] job to evaluate the use of post-hoc analysis generally," "nor are [d]efendants required to adopt (and disclose) [plaintiffs'] view of the data" where [d]efendants' conclusions are reasonably supported by their own analyses. Kleinman, 706 F.3d at 154–55. Scientific conclusions "cannot be misleading merely because the FDA disagreed with the conclusion—so long as [d]efendants conducted a 'meaningful' inquiry and in fact held that view, the statements did not mislead in a manner that is actionable." Tongue, 816 F.3d at 214.

Here, the complaint alleges that Biogen disclosed to investors that it had been conducting its post hoc analyses in collaboration with the FDA. The FDA ultimately endorsed Biogen's methodology and conclusions before the Advisory Committee. Accordingly, Plaintiffs do not plead facts that Biogen did not conduct a meaningful inquiry. Moreover, Biogen had a reasonable basis for asserting a correlation existed. The topline results showed a statistically significant effect in the phase III population. There was also a positive correlation between amyloid beta levels and clinical outcomes across the clinical trials, as well as in both ENGAGE and EMERGE independently, id. at ¶ 220, though Plaintiffs allege that the correlation was not strong enough to support Defendants' scientific conclusion, particularly when isolating high-dose patients in EMERGE, id. at ¶¶ 206–08. But disagreement with the company's findings is not enough to find them misleading. City of Edinburgh Council, 754 F.3d at 170 (finding where "the Phase 2 interim results showed circumstantial evidence of efficacy for one important patient subgroup, the disagreement . . . with the company's interpretation of the interim results is not sufficient to show defendants' interpretation lacked a reasonable basis"). Here, like in Kleinman, Plaintiffs "may take issue with [the] [d]efendant's researchers and scientists, but where a

defendant's competing analysis or interpretation of data is itself reasonable, there is no false statement." Kleinman, 706 F.3d at 154.

3. Correlation of Endpoints

Plaintiffs challenge Defendants' statement that the positive endpoints in EMERGE (Study 302) was an "encouraging" sign of the drug's effectiveness where a separate post hoc analysis showed that the performance of the endpoints was correlated and thus a positive result on one is likely to produce a positive result on all. Sec. Am. Compl. ¶¶ 247–48, 251 [Doc. No. 58]. While evidence of correlation does detract from the significance of the data showing multiple positive endpoints, it does not preclude Biogen's conclusion that multiple positive endpoints are an encouraging sign for the drug's effectiveness. As discussed above, the existence of data that may cut against Biogen's conclusions does not itself make Biogen's analyses false or misleading. And here Biogen's post hoc analysis of the EMERGE data revealed the study was positive on all endpoints. Therefore, regardless of their correlation, it is not misleading to describe those results as encouraging, particularly because "words like 'encouraging' are the type of 'expressions of puffery and corporate optimism' that do not generally 'give rise to securities violations.'" Kleinman, 706 F.3d at 153 (quoting Rombach v. Chang, 355 F.3d 164, 174 (2d Cir. 2004)). Accordingly, Biogen's statement assigning significance to the multiple positive endpoints in EMERGE (Study 302) cannot serve as a basis for liability here.

4. Importance of Regional Variation

Finally, Plaintiffs allege that Biogen misled investors about the effect of regional variation among patients on the clinical outcomes in each study.

Specifically, Plaintiffs challenge an exchange between Budd Haeberlein and an analyst during the December 5, 2019 Q&A. The analyst observed that the clinical outcomes for high-

dose patients in ENGAGE (Study 301) "c[aught] up with" patients in EMERGE (Study 302), and asked Budd Haeberlein whether she was "certain that there isn't anything related to study sites, geography, or any other variation that could explain the breadth of the improvement other than just the exposure to the higher dose." Def. Ex. O, Q&A Call Tr. 3 [Doc. No. 62-15]; Sec. Am. Compl. ¶ 238 [Doc. No. 58]. Budd Haeberlein responded that "we believe, having looked very closely at the baseline demographics and characteristics, that none of these are driving the overall outcomes that we see or the difference between the studies." Sec. Am. Comp. ¶ 238 [Doc. No. 58]. Plaintiffs allege that this statement was misleading because "there were statistically significant differences between countries in the effect of aducanumab," and because patients who received high dose aducanumab in the United States performed 20% less well against the placebo compared to the global population, though in both cases the high dose group did better than the placebo. Id. at ¶¶ 240–44.

But Defendants did not say there was no variation in performance based on characteristic or demographic differences. Rather, Budd Haeberlein expressed her opinion that any differences in outcomes among these groups were "driving the overall outcomes . . . or the difference between the studies." Id. at ¶ 238. And Plaintiffs do not allege facts demonstrating that these differences were in fact driving outcomes. Rather, they allege disparate sub-group analyses that show there was some variation in clinical outcomes based on geography and demographics. This does not, however, compel the conclusion that it was these differences that explain why the two studies produced such different results. See Corban, 868 F.3d at 40 ("[S]imply pointing us to omitted details, as the plaintiffs have done, and failing to explain how the omitted details rendered the particular disclosures misleading, misses the mark."). Because Plaintiffs have failed to allege facts showing the demographic and geographical differences in the studies

meaningfully impacted the studies' overall outcomes, Budd Haeberlein's statement is not actionable here against the Defendants.

In sum, Plaintiffs have not alleged facts sufficient to show that the statements at issue were false or misleading. That alone warrants dismissal of the Second Amended Complaint [Doc. No. 58].

B. Scienter

Even if Plaintiffs had alleged actionable statements or omissions, Plaintiffs' failure to adequately plead scienter is dispositive. Under the PSLRA, a plaintiff must "state with particularity facts giving rise to a strong inference" of scienter. 15 U.S.C. § 78u-4(b)(2). Scienter is "a mental state embracing intent to deceive, manipulate, or defraud." Matrixx Initiatives, Inc., 563 U.S. at 48 (quoting Ernst & Ernst v. Hochfelder, 425 U.S. 185, 193 n.12 (1976)). It requires "a showing of either conscious intent to defraud or a high degree of recklessness." ACA Fin. Guar. Corp. v. Advest, Inc., 512 F.3d 46, 58 (1st Cir. 2008) (quotation marks and citations omitted).[10]

"[A]n 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, Inc. v. Makor Issues & Rights, Ltd., 551 U.S. 308, 324 (2007); see ACA Fin. Guar. Corp., 512 F.3d at 59. A plaintiff must plead "the basis for inferring scienter." N. Am. Catholic Educ. Programming Found, 567 F.3d at 13. And while it "need not be ironclad, it must be persuasive."

[10] Under the PSLRA, if the alleged misstatement or omission is a "forward-looking statement," the required level of scienter is "actual knowledge." Matrixx Initiatives, Inc., 563 U.S. at 48 n.14 (quoting 15 U.S.C. § 78u–5(c)(1)(B)).

In re Credit Suisse First Bos. Corp., 431 F.3d at 48–49. This is a holistic inquiry. The court must consider "whether *all* of the facts alleged, taken collectively, give rise to a strong inference of scienter . . . ." Tellabs, 551 U.S. at 322–23. "While under Rule 12(b)(6) all inferences must be drawn in plaintiffs' favor, inferences of scienter do not survive if they are merely reasonable, as is true when pleadings for other causes of action are tested by motion to dismiss under Rule 12(b)(6)." ACA Fin. Guar. Corp., 512 F.3d at 58–59 (quoting Greebel v. FTP Software, Inc., 194 F.3d 185, 195 (1st Cir. 1999)). Scienter may be established through facts alleging intent to deceive or a high degree of recklessness.

1. Intent to Deceive

The facts alleged do not support the inference that Defendants acted with an intent to deceive investors. Fire and Police Pension Ass'n, 778 F.3d at 231 ("Not all claims of wrongdoing by a company make out a viable claim that the company has committed securities fraud."). Plaintiffs' scienter allegations are based primarily on the presumption that Defendants' post hoc analysis of the discordant phase III data should have disclosed that Biogen's conclusions were incompatible with the findings of Massie's sub-group level analysis, therefore revealing the falsity of Biogen's efficacy claims. The key question, however, 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. 2011) (internal citation omitted). Here, that Biogen conducted a rigorous analysis could be sufficient to show Biogen was aware of countervailing analyses, but it does not establish the primacy of Massie's conclusions, nor does it support the conclusion that Biogen believed its own conclusions were wrong. Accordingly, Biogen's presumed awareness of Massie's conclusions

does not show Defendants deliberately or recklessly risked misleading investors by not disclosing the countervailing analyses.

In other words, Plaintiffs cannot allege intent to deceive shareholders based solely on the inference that a defendant "must have had" knowledge that an alternative or conflicting view existed. Maldonado v. Dominguez, 137 F.3d 1, 9–10 (1st Cir. 1998) (dismissing complaint where it lacked allegations that anyone at the company was aware of facts contrary to the allegedly misleading public statements). This is particularly true here where the FDA collaborated with Biogen to conduct the post hoc analysis, expressed support for Biogen's conclusions—with full visibility into the underlying data—and publicly endorsed Biogen's statistical methodology and ultimate position that the Phase III data showed aducanumab was effective at 10mg/kg with sufficient exposure.

Plaintiffs next point to allegations that Biogen committed significant resources to its continued pursuit of aducanumab approval as evidence that aducanumab's success was important for the financial health of the company. But without more, the company's focus on aducanumab cannot serve as evidence of scienter. Corban, 868 F.3d at 39 ("[w]e require something more than the ever-present desire to improve results, such as allegations that that the very survival of the company w[as] on the line" (internal quotations omitted)). Rather, the facts as alleged support the more plausible inference that Biogen—at the FDA's suggestion and under its regulator's guidance—conducted the post hoc analysis and revealed its conclusions in a genuine attempt to obtain FDA approval to bring aducanumab to market. In other words, the more plausible explanation based on the facts as alleged is that Biogen was pursuing a non-artificial means of increasing its stock price—approval and ultimate marketing of aducanumab.

Plaintiffs also point out that "when Biogen presented the Study 103 results, it made the raw data available to researchers," and argue that Biogen's failure to do so with the phase III data was evidence of scienter. Sec. Am. Compl. ¶ 347 [Doc. No. 58]. But this "out of character decision" not to release the raw data does not confer fraudulent intent. Biogen is not obligated to disclose the data and investors may interpret this decision themselves. Because Biogen's own analysis of the data is not fully discredited by sub-group data presented in the Massie report, Biogen's decision not to release the raw phase III data does not create an inference of scienter. See Constr. Indus. & Laborers, 22 F.4th at 10.

2. Recklessly Mislead

Plaintiffs also fail to demonstrate that Defendants' allegedly misleading statements and omissions were reckless. To establish scienter by recklessness, a plaintiff must show that defendants made "a highly unreasonable omission, involving 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 or sellers that is either known to the defendant or is so obvious the actor must have been aware of it." City of Dearborn Heights, 632 F.3d at 757. This form of recklessness is "closer to a lesser form of intent" than it is to ordinary negligence. Greebel, 194 F.3d at 199; Loc. No. 8 IBEW Ret. Plan & Tr. v. Vertex Pharms., Inc., 838 F.3d 76, 80 n.6 (1st Cir. 2016) ("allegations of merely unreasonable conduct do not sufficiently plead scienter").

Here, Plaintiffs fail to plead facts that demonstrate Defendants' omission of the sub-group data or related analysis was highly unreasonable. First, within the allegedly misleading statements is a plausible explanation for withholding the information from the public: that the data was under review by the FDA. Sec. Am. Compl. ¶ 346 [Doc. No. 58]. Biogen also disclosed

to investors that it was not releasing or providing an analysis of the underlying sub-group data sets and did not imply that its own conclusions were based on any such analysis. Id. The market knew the data was being drawn from a study that had been terminated early due to futility and that Biogen was mining the data to uncover evidence of aducanumab's efficacy. No reasonable investor would interpret Biogen's acknowledgement that it was not releasing data related to "a lot of things, sub-groups included," but that it "had nothing to hide" to mean the sub-group data supported Biogen's conclusion. In fact, in this exchange, Biogen refrained from making any assurances or conclusory statements regarding the sub-group analysis. Rather, Biogen's avoidance of the topic and suggestion that it had "nothing to hide" should spark a reasonable investor's curiosity.

Second, missing from the allegations is any contention that any Defendant viewed the topline results as incompatible with the sub-group analysis, or that anyone conveyed such skepticism to any Defendant. See Vertex Pharms., Inc., 838 F.3d at 82 (finding no scienter where "complaint does not even allege that scientists in general, much less those at Vertex, regarded the reported results as implausible"). By contrast, courts have repeatedly rejected the inference that a company would continue to invest in a therapy when it supposedly knows it does not work. See Cozzarelli v. Inspire Pharmaceuticals Inc., 549 F.3d 618, 627 (10th Cir. 2008) (finding it "improbable that [defendant] would stake its existence on a drug and a clinical trial that the company thought was doomed to failure"); Nguyen v. Endologix, Inc., 962 F.3d 405, 415 (9th Cir. 2020) (affirming dismissal on scienter grounds because theory that defendants would express optimism about FDA approval despite knowledge to the contrary "does not make a whole lot of sense" and has "no basis in logic or common experience"). This is particularly true here where Biogen was submitting its analysis to the FDA for marketing approval.

And finally, the fact that Biogen had been working closely with the FDA and that the FDA has endorsed the post hoc analysis and conclusions that were then presented to the Advisory Committee is strong evidence against finding scienter. Moreover, even if Biogen were aware of the Massie Report's conclusion, "when defendants do not divulge the details of interim 'regulatory back-and-forth' with the FDA, that alone cannot support an inference of scienter under the PSLRA when the defendants do provide warnings in broader terms." Kader v. Sarepta Therapeutics, Inc., 887 F.3d 48, 59 (1st Cir. 2018) (internal quotations omitted). Here, Defendants initially told investors that Biogen was collaborating with the FDA on its analysis of the phase III data, but in July 2020, after Biogen submitted its application seeking regulatory approval for aducanumab to the FDA, Defendant Sandrock explicitly told investors "we submitted all the data from those 3 studies that I mentioned: EMERGE, ENGAGE and PRIME" and while Biogen does "have analyses that show that those who received the highest dose over a sustained period of time do show evidence of efficacy similar to what we found in EMERGE . . . and that's why [Biogen] believe[s] there's supportive evidence coming from ENGAGE," "what the FDA chooses to look at is – that's their purview." Sec. Am. Compl. ¶ 191 [Doc. No. 58]. If anything, Biogen likely went into November 6, 2020—the date of the Advisory Committee—thinking aducanumab was likely to be approved.

Accordingly, having considered the facts alleged as a whole, the court finds that Plaintiffs have not met the PSLRA's pleading standard with respect to scienter. N.J. Carpenters Pension & Annuity Funds v. Biogen IDEC Inc., 537 F.3d 35, 45 (1st Cir. 2008).

C. Economic Loss and Loss Causation

Additionally, Defendants contend dismissal is warranted on the theory that the complaint does not plead facts connecting the allegedly artificial stock increase—or subsequent drop—to

Biogen's misstatements. To plead loss causation, a plaintiff must allege facts establishing a "causal link between the alleged misconduct and the economic harm ultimately suffered." In re Alkermes Sec. Litig., 2005 WL 2848341, at *10 (D. Mass. Oct. 6, 2005). Whether allegations of loss causation must conform to the heightened specificity standard for fraud claims pursuant to Fed. R. Civ. P. 9(b) or the typical plausibility standard under Fed. R. Civ. P. 8 remains an open question in the First Circuit. See Massachusetts Ret. Sys. v. CVS Caremark Corp., 716 F.3d 229, 239 n.6 (1st Cir. 2013) (expressly declining to decide the issue because allegations satisfied both standards, explaining "[i]t is unclear whether a plaintiff may plead loss causation with 'a short and plain statement of the claim showing that the pleader is entitled to relief,' or if there is a heightened standard akin to the rule that 'a party must state with particularity the circumstances constituting fraud'").

Here, similar to Massachusetts Ret. Sys., the allegations fail under both standards and thus the court need not determine which one applies. Plaintiffs purchased Biogen stock on November 4, 2020, at a price they contend Biogen artificially inflated through misleading investors about aducanumab's efficacy. Sec. Am. Compl. ¶¶ 262, 276 [Doc. No. 58]. After Biogen's stock price dropped on November 9, 2020, the first day of trading following the Advisory Committee's November 6, 2020 votes, Plaintiffs sold their Biogen stakes resulting in the loss amounts at issue here. Id. at ¶¶ 19, 280. But "[i]t is not enough to allege that [d]efendants made false statements on the one hand and that some announcement caused a stock drop on the other;" the complaint must allege facts to demonstrate the trading loss was caused by information that corrects the alleged misstatements. Coyne v. Metabolix, Inc., 943 F. Supp. 2d 259, 273 (D. Mass. 2013). Plaintiffs argue that once investors digested the appended Massie Report, they realized Biogen had mislead investors about aducanumab's efficacy and adopted a more

pessimistic view of the drug's prospects for approval, causing the price to fall. But causation is not tied to when the market reacts to information, but rather when that information became available to the public. Therefore, even assuming the Massie Report was a corrective disclosure, where it was published before Plaintiffs purchased Biogen stock, the complaint fails to sufficiently allege a corrective disclosure that "*connect[s]* the current, present, negative information to the earlier false or misleading statement." Id. (emphasis in original). Accordingly, because the complaint lacks facts demonstrating that the challenged conduct caused their losses, Plaintiffs have not adequately pled the loss causation necessary to state a claim for securities fraud.

D. Reliance and Standing

Finally, Defendants contend Plaintiffs did not sufficiency plead reliance and therefore also failed to allege facts sufficient to support their standing. Defendants argue that as a matter of law, Plaintiffs could not have reasonably relied on the alleged misrepresentations and omissions where they purchased Biogen stock after public disclosure of the information they now allege had been concealed. For the same reasons, Defendants argue Plaintiffs lack standing to bring their claims.

It is undisputed that Plaintiffs purchased their stock after the Massie Report had been published and thus after the alleged corrective disclosure was made. Generally, "[a] plaintiff who purchased after a corrective disclosure was made would have no standing," because (1) "relying on the earlier misrepresentation would no longer be reasonable in light of the new information," and (2) "the market is assumed to have processed the correction, which would be reflected in the stock price." City of Bristol Pension Fund, 12 F. Supp. 3d at 235. Here, reliance—and by extension standing—therefore hinges on whether it was reasonable for Plaintiffs to rely on the

challenged statements in the hours after the Massie Report was published. Defendants contend reliance was unreasonable where Plaintiffs purchased Biogen stock after the Massie Report was published, and thus corrective information had already been disclosed. Plaintiffs counter, where financial analysts could not immediately recognize the Massie Report's corrective nature due to its highly technical analysis and where Plaintiffs purchased Biogen stock within hours of the Massie Report's publication—before the market had processed the information as a correction—that their reliance was reasonable. The court, however, need not address this question where it has already found dismissal warranted on several other grounds.

VII. Count II – Violation of Section 20(a) of the Exchange Act

Finally, Plaintiffs assert claims for control person liability against the individual Defendants pursuant to Section 20(a) of the Exchange Act. Section 20(a) imposes joint and several liability on any person who, "directly or indirectly, controls any person liable" under Section 10(b) and Rule 10b-5. 15 U.S.C. § 78t(a). Because the Second Amended Complaint [Doc. No. 58] fails to allege an underlying violation of federal securities law, the Section 29(b) claims must be dismissed. See Greebel, 194 F.3d at 207.

VIII. Conclusion

For the foregoing reasons, Plaintiffs' Motion to Strike [Doc. No. 65] is GRANTED in part and DENIED in part, Plaintiffs' two Requests for Judicial Notice [Doc. Nos. 71, 73] are DENIED, and Defendants' Motion to Dismiss [Doc. No. 60] is GRANTED.

IT IS SO ORDERED.

September 12, 2022

/s/ Indira Talwani
United States District Judge

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

NADIA SHASH and AMJAD KHAN, individually and on behalf of all others similarly situated,	*	
Plaintiffs,	*	Civil Action No. 1:21-cv-10479-IT
v.	*	
BIOGEN INC.; MICHEL VOUNATSOS; ALFRED W. SANDROCK, JR.; and SAMANTHA BUDD HAEBERLEIN,	*	
Defendants.	*	

ORDER OF DISMISSAL

September 12, 2022

TALWANI, D.J.

Pursuant to the court's Memorandum and Order [Doc No. 76] allowing Defendants' Motion to Dismiss [Doc. No. 60], the Second Amended Complaint [Doc. No 58] is hereby DISMISSED. This case is CLOSED.

IT IS SO ORDERED.

/s/ Indira Talwani
United States District Judge

RELEVANT STATUTORY PROVISIONS

Section 10 of the Securities Exchange Act of 1934, codified as amended at 15 U.S.C. § 78j, provides in relevant part:

> **Manipulative and deceptive devices**
>
> It shall be unlawful for any person, directly or indirectly, by the use of any means or instrumentality of interstate commerce or of the mails, or of any facility of any national securities exchange—
>
> . . . .
>
> (b) To use or employ, in connection with the purchase or sale of any security registered on a national securities exchange or any security not so registered, or any securities-based swap agreement, any manipulative or deceptive device or contrivance in contravention of such rules and regulations as the Commission may prescribe as necessary or appropriate in the public interest or for the protection of investors.

Section 20 of the Securities Exchange Act of 1934, codified as amended at 15 U.S.C. § 78t, provides in relevant part:

> **Liability of controlling persons and persons who aid and abet violations**
>
> **(a) Joint and several liability; good faith defense**
>
> Every person who, directly or indirectly, controls any person liable under any provision of this chapter or of any rule or regulation thereunder shall also be liable jointly and severally with and to the same extent as such controlled person to any person to whom such controlled person is liable (including to the Commission in any action brought under paragraph (1) or (3) of section 78u(d) of this title), unless the controlling person acted in good faith and did not directly or indirectly induce the act or acts constituting the violation or cause of action.

Section 101(b) of the Private Securities Litigation Reform Act of 1995, codified as amended at 15 U.S.C. § 78u-4, provides in relevant part:

> **Private securities litigation**
>
> . . . .
>
> **(b) Requirements for securities fraud actions**
>
> **(1) Misleading statements and omissions**
>
> In any private action arising under this chapter in which the plaintiff alleges that the defendant—
>
> (A) made an untrue statement of a material fact; or
>
> (B) omitted to state a material fact necessary in order to make the statements made, in the light of the circumstances in which they were made, not misleading;
>
> the complaint shall specify each statement alleged to have been misleading, the reason or reasons why the statement is misleading, and, if an allegation regarding the statement or omission is made on information and belief, the complaint shall state with particularity all facts on which that belief is formed.
>
> **(2) Required state of mind**
>
> **(A) In general**
>
> Except as provided in subparagraph (B), in any private action arising under this chapter in which the plaintiff may recover money damages only on proof that the defendant acted with a particular state of mind, the complaint shall, with respect to each act or omission alleged to violate this chapter, state with particularity facts giving rise to a strong inference that the defendant acted with the required state of mind.
>
> . . . .

Securities and Exchange Commission Rule 10b-5, codified as amended at 17 C.F.R. § 240.10b-5, provides:

> **Employment of manipulative and deceptive devices**
>
> It shall be unlawful for any person, directly or indirectly, by the use of any means or instrumentality of interstate commerce, or of the mails or of any facility of any national securities exchange,
>
> (a) To employ any device, scheme, or artifice to defraud,
>
> (b) To 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, or
>
> (c) To engage in any act, practice, or course of business which operates or would operate as a fraud or deceit upon any person,
>
> in connection with the purchase or sale of any security.

United States Court of Appeals
For the First Circuit

No. 22-1773

NADIA SHASH, individually and on behalf of all others similarly situated; AMJAD KHAN, individually and on behalf of all others similarly situated,

Plaintiffs - Appellants,

VICTOR D. MENASHE, individually and on behalf of all others similarly situated,

Plaintiff,

v.

BIOGEN INC.; MICHEL VOUNATSOS; ALFRED W. SANDROCK, JR.; SAMANTHA BUDD HAEBERLEIN,

Defendants - Appellees,

JEFFREY D. CAPELLO; MICHAEL R. MCDONNELL,

Defendants.

APPELLEE'S BRIEFING NOTICE

Issued: January 13, 2023

Appellee's brief must be filed by **February 13, 2023**.

The deadline for filing appellant's reply brief will run from service of appellee's brief in accordance with Fed. R. App. P. 31 and 1st Cir. R. 31.0. Parties are advised that extensions of time are not normally allowed without timely motion for good cause shown.

Presently, it appears that this case may be ready for argument or submission at the coming **May, 2023** session.

The First Circuit Rulebook, which contains the Federal Rules of Appellate Procedure, First Circuit Local Rules and First Circuit Internal Operating Procedures, is available on the court's

website at www.ca1.uscourts.gov. Please note that the court's website also contains tips on filing briefs, including a checklist of what your brief must contain.

Failure to file a timely brief in compliance with the federal and local rules could result in the appellee not being heard at oral argument. See 1st Cir. R. 45.0.

Maria R. Hamilton, Clerk

UNITED STATES COURT OF APPEALS
FOR THE FIRST CIRCUIT
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