UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

NADIA SHASH and AMJAD KHAN, individually and on behalf of all others similarly situated,	*	
Plaintiffs,	*	
v.	*	Civil Action No. 1:21-cv-10479-IT
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 l7.5% 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