UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

PAUL SANDERS, on behalf of himself and others similarly situated,	)	
Plaintiffs,	)	
v.	)	**Civil Action No. 13-11157-DJC**
AVEO PHARM., INC. et al.,	)	
Defendants.	)	
(IN RE AVEO PHARM., INC. SECURITIES LITIGATION)	)	

MEMORANDUM AND ORDER

CASPER, J. **March 20, 2015**

I. Introduction

Lead class action Plaintiffs Robert Levine and William Windham ("Plaintiffs") have filed this lawsuit against AVEO Pharmaceuticals, Inc. ("Aveo") and its former President, Chief Executive Officer and Director Tuan Ha-Ngoc ("Ha-Ngoc"), Chief Financial Officer David N. Johnston ("Johnston"), Chief Medical Officer William Slichenmyer ("Slichenmyer") and co-Founder and Director Ronald DePinho ("DePinho") (collectively, "Defendants"), alleging securities fraud in violation of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 ("Exchange Act") and Securities and Exchange Commission Rule 10b-5 ("Rule 10b-5"), promulgated thereunder, between January 3, 2012 and May 1, 2013 ("the Class Period"). D. 49; see 15 U.S.C. § 78j(b); 15 U.S.C. § 78t(a), 17 C.F.R. § 240.10b-5. Defendants have moved to

dismiss the Consolidated Amended Complaint. D. 55. For the reasons discussed below, the Court ALLOWS the motion to dismiss.

II. Factual Background

The Court acknowledges that there is a related case before this Court. Van Ingen v. Ha-Ngoc et al., 14-cv-11672-DJC (the "Derivative Litigation"). Although the facts alleged in the Derivative Litigation are substantially similar to those in the instant case, the Court must evaluate Plaintiffs' claims based upon the facts alleged in their complaint in this case and the applicable legal standards that apply in this direct action. The facts recited are as alleged in the Consolidated Amended Complaint, D. 49.

Plaintiffs are shareholders of Aveo, a "biopharmaceutical company focused on discovering, developing, and commercializing cancer therapies." D. 49 ¶¶ 1–2. Plaintiffs have brought this class action suit on behalf of "all persons other than defendants who purchased AVEO common stock between January 3, 2012 and May 1, 2013." Id. ¶ 1.

Aveo's lead product is tivozanib, an oral inhibitor of the vascular endothelial growth factor receptors. Id. ¶ 2. Aveo's goal was to commercialize tivozanib as a treatment for a prevalent form of kidney cancer called advanced renal cell carcinoma, to compete with established therapies such as chemotherapy. Id. ¶¶ 2, 51.

A. FDA Clinical Trial Protocol

The Food, Drug and Cosmetic Act ("FDCA") requires the Food and Drug Administration ("FDA"), which regulates pharmaceutical development and marketing, to refuse any drug application that does not meet specific safety standards. Id. ¶¶ 38-40. Those safety standards include "well-controlled clinical investigations," which are generally "double-blinded," such that

study participants and investigators do not know whether a participant was given the study drug or a placebo (or another recognized drug for comparison). Id. ¶ 40.

Companies that wish to market a pharmaceutical product, called "sponsors," are responsible for designing the clinical trials and their protocols, enrolling patients in the trials and demonstrating a benefit to the patient population for which approval of the drug is sought. Id. ¶¶ 38, 41-42. Trials for drugs intended to treat cancer generally measure both overall survival, the length of time the patient remains alive after starting treatment, and progression-free survival, the length of time the patient remains alive and the disease has not worsened, as assessed by the study researchers. Id. ¶ 3. According to the complaint, progression-free survival is often the favored endpoint by drug companies because the trials require fewer patients and are less expensive. Id. ¶ 5. Overall survival, an objective clinical endpoint, however, is the "gold standard" for clinical trials. Id. ¶ 4.

Federal law allows for sponsors to request from the FDA a "Special Protocol Assessment," whereby the FDA and the sponsor meet to discuss the sponsor's proposed protocols for the clinical trial and make any agreements in writing. Id. ¶ 41. Once a sponsor believes its clinical trials demonstrate sufficient efficacy and safety of the drug, the sponsor may file with the FDA a New Drug Application ("NDA") seeking approval to market the drug with a specific indication. Id. ¶ 44. Upon submission of an NDA, the FDA may choose to convene an advisory committee to provide it advice on the drug's approvability. Id. ¶ 48. The advisory committee is "the only forum in which the public can legally be advised by the FDA of the FDA's position and the FDA's interactions with the sponsor regarding the drug candidate." Id. ¶ 49.

B. Tivo-1 Clinical Trial Design and Implementation

In December 2008 and May 2009, Aveo met with the FDA regarding the design of a clinical trial for tivozanib. Id. ¶ 53. In those meetings, the FDA "expressly requested" that Aveo analyze the overall survival and progression-free survival of study participants. Id.

After the May 2009 meeting, Aveo specified a protocol for a Phase III clinical trial referred to as TIVO-1 ("Tivo"). Id. ¶ 54. Phase III clinical studies are "expanded studies 'performed after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling. Phase [III] studies usually include several hundred to several thousand subjects.'" Id. ¶ 43 (quoting 21 C.F.R. § 312.21).

The primary endpoint for Tivo, according to the protocol, was a statistically-significant improvement in progression-free survival, with a secondary endpoint of overall survival. Id. ¶ 54. The FDA explained in the advisory committee panel, however, that the overall survival comparison was to be the most important secondary endpoint and that the other secondary endpoints should not be analyzed unless an overall survival benefit was achieved. Id.

The Tivo protocol provided that study participants would be enrolled in 90 to 100 sites worldwide, in three major geographic groups: North America/Western Europe, Central/Eastern Europe and "the Rest of the World." Id. ¶ 55. Patients were randomized into one of two groups (or "arms"). Id. ¶ 9. The "control arm" received sorafenib, a drug approved by the FDA in 2005 for treatment of renal cell carcinoma. Id.

Aveo began enrolling patients for the trial in or around February 2010, completing enrollment in or around August 2010. Id. ¶ 57. Plaintiffs assert that the trial was faulty in three primary ways. Id. ¶¶ 10, 13, 57.

First, contrary to the Tivo protocol, which called for a "broad worldwide trial stratified across geographies, AVEO enrolled approximately 88% of TIVO-1 participants in Central and Eastern Europe, where enrollment and testing were cheaper." Id. ¶ 57.

Second, Plaintiffs assert that Defendants "confounded the study results by offering a crossover, or subsequent therapy, to one study arm without offering the same to the other study arm." Id. ¶ 10. Plaintiffs assert that when "a patient is crossed over to a subsequent therapy it is difficult and often impossible to determine whether that patient's survival benefit was attributable to the randomized therapy or the subsequent treatment." Id. ¶ 11. Under the Tivo crossover, patients assigned to the control arm were given the chance to switch (or "cross over") to tivozanib as a subsequent treatment, without cost. Id. ¶ 10. The tivozanib patients, however, were not offered a subsidized subsequent treatment. Id. Plaintiffs allege that the crossover was not included on the preliminary or final Tivo protocols or discussed with the FDA. Id.

Third, Plaintiffs allege that Defendants arranged for the dosages given to patients to be reduced at "materially different rates" for patients experiencing adverse reactions. Id. ¶ 13. Sorafenib dosages were reduced by fifty percent, while tivozanib rates were reduced by thirty-three percent. Id. Thus, Plaintiffs allege, "it was unclear whether patients in the sorafenib (control) arm who experienced disease progression after dose reduction did so because of the exaggerated dose reduction, or because there was a difference in the therapeutic effects of the compared drugs." Id.

Plaintiffs allege that by early January 2012, Aveo had gathered nearly sixteen months of data in the Tivo trial and was aware that "what initially began as an adverse trend in overall survival had . . . worsened." Id. ¶ 59. Plaintiffs also allege that "[i]t was clear by this time that that patients randomized to the tivozanib arm were dying more frequently than those randomized to the sorafenib (control) arm." Id.

C. Aveo's Alleged Material Misstatements

Plaintiffs allege that during the Class Period Aveo "issued a press release announcing positive preliminary results from the Phase 3 TIVO-1 trial but omitting material adverse information regarding design defects so severe they rendered the results of that trial uninterpretable." Id. ¶ 60. Namely, Plaintiffs allege, Aveo's press release was misleading because it stated that "tivozanib demonstrated superiority over sorafenib in the primary endpoint of progression-free survival" in a "global, randomized Phase 3 clinical trial," but did not disclose certain adverse information, including:

1) TIVO-1 was conducted almost entirely in Central and Eastern Europe, which did not have comparable treatment with the United States for renal cell cancer;

2) the protocol was not followed and a "one-way crossover" was implemented, such that participants taking the control drug, sorafenib, received a different level of post-treatment therapy;

3) participants receiving sorafenib received weaker dosages following an adverse reaction;

4) these design defects rendered the trial results uninterpretable; and

5) tivozanib was "inferior to sorafenib in the most significant safety measure, risk of death as measured by overall survival."

Id. ¶¶ 60-61. Plaintiffs assert that these allegedly misleading results were reiterated in a number of forums during the Class Period, including an investor call and presentation, subsequent company press releases, reports filed to the SEC and a media interview. Id. ¶¶ 64-77, 81-86.

On or about May 16, 2012, Aveo issued a press release announcing preliminary information from the trial, including a one-year overall survival rate of 81 percent for the control group and 77 percent for the tivozanib group. Id. ¶ 78. Plaintiffs assert that Defendants "strongly encouraged investors to ignore these results" through alleged mischaracterizations and omissions." Id.

On or about this same date, Aveo held a meeting with the FDA regarding the NDA for tivozanib. Id. ¶ 79. In that meeting, "the FDA expressed concern that the Company's sole pivotal clinical trial demonstrated an adverse trend in overall survival." Id. ¶ 80. In an August 2, 2012 press release, Aveo allegedly made only a partial disclosure of the FDA's concerns. Id. ¶ 87. Still, Aveo's share price dropped about 27 percent, a drop Plaintiffs assert would have been more significant had Aveo disclosed the "full truth" about the FDA's concerns. Id. ¶ 88. "Namely, Defendants continued to omit that the FDA had recommended a second adequately-powered trial in a comparable population, that the agency questioned whether the NDA should be filed at all, and that the FDA had expressly warned that adverse overall survival trends could affect approvability." Id. Plaintiffs allege that Defendants continued to misrepresent the trial results and the FDA's concerns about the trial in SEC filings, investor presentations and press releases. Id. ¶¶ 89-102, 104-113.

D. FDA Advisory Committee Briefing and Aftermath

On April 30, 2013, the FDA released its advisory committee briefing document, disclosing for the first time that it "had expressly recommended that the Company conduct an additional clinical trial and highlight[ing] the regulatory history of Tivopath previously concealed by the Company, including the fact that the Company disregarded FDA recommendations for an additional clinical study . . . ." Id. ¶ 114. "The Briefing Document also

disclosed that the design of the TIVO-1 trial deviated significantly from that specified in trial protocol and discussed with the FDA in meetings in December 2008 and May 2009." Id. ¶ 115. For instance, the protocol did not include the one-way crossover and called for global patient enrollment. Id. The briefing document also, according to Plaintiffs, "disclosed flaws in the unproven hypothesis Defendants had offered to investors" that adverse overall survival rates for tivozanib were caused by post-study treatment methods, as opposed to long-term risks associated with use of tivozanib. Id. ¶ 116. After the briefing document was released, Aveo's share price fell by about 31 percent. Id. ¶ 117.

On May 2, 2013, at a hearing before the advisory committee, the FDA disclosed further information, which Plaintiffs characterize as "scientific misconduct that the Company had concealed during the Class Period." Id. ¶¶ 118-134. Following the hearing, Aveo's share price dropped by nearly 50 percent. Id. ¶ 135.

III. Procedural History

Plaintiff Paul Sanders brought a class action complaint on May 9, 2013. D. 1. The Court consolidated related actions, appointed lead Plaintiffs and approved selection of counsel on December 3, 2013. D. 44. Plaintiffs amended the complaint on February 3, 2014. D. 49. Defendants have moved to dismiss the amended complaint. D. 55. After a hearing, the Court took this motion under advisement. D. 64.

IV. Standard of Review

For allegations of securities fraud brought under Sections 10(b) and 20(a) of the Securities Exchange Act, plaintiffs "must plead the circumstances of the fraud with particularity, pursuant to Rule 9(b)." Hill v. Gozani, 638 F.3d 40, 55 (1st Cir. 2011) (citation omitted). The PSLRA further requires plaintiffs to "specify each statement alleged to have been misleading

[and] the reason or reasons why the statement is misleading." Id. (alteration in original) (citation and quotations omitted). "[I]f an allegation regarding the statement is made on information and belief, the complaint shall state with particularity all facts on which that belief is formed." In re Cabletron Sys., Inc., 311 F.3d 11, 27 (1st Cir. 2002) (citation omitted).

The complaint must also, with "respect to each [alleged] act or omission . . . state with particularity facts giving rise to a strong inference that the defendant acted with the required state of mind. Hill, 638 F.3d at 55 (alteration and omission in original) (citation and emphasis omitted). Plaintiffs are not required, however, to plead evidence. Id. (citation omitted).

Still, as with any Rule 12(b)(6) motion, the Court must "accept well-pleaded factual allegations in the complaint as true and view all reasonable inferences in the plaintiffs' favor." Id. (citation omitted).

V. Discussion

To state a Section 10(b)-5 claim, Plaintiffs must plead: "(1) a material misrepresentation or omission; (2) scienter, or a wrongful state of mind; (3) a connection with the purchase or sale of a security; (4) reliance; (5) economic loss; and (6) loss causation." Hill, 638 F.3d at 55 (citation omitted). Defendants challenge the adequacy of the complaint as to actionable misrepresentations or omissions and scienter. D. 56 at 20, 31. The Court addresses each of these arguments.

A. Plaintiffs Have Sufficiently Pleaded Actionable Statements

While Defendants assert that Plaintiffs have pleaded no actionable statement, the Court agrees with Plaintiffs that they have sufficiently alleged material misrepresentations or omissions. Generally, Plaintiffs assert that Defendants: (1) were aware of safety concerns the FDA expressed in a May 2012 meeting, but failed to inform investors of these concerns when

discussing the drug's safety and efficacy; (2) were aware that Tivo was not being conducted in conformance with the prescribed protocol in several important ways that could affect the trial's integrity and thus, the drug's approvability, but failed to disclose these deviances to investors; and (3) misrepresented Tivo's preliminary safety findings.

1. Allegations Concerning May 2012 Meeting with FDA

a. Duty to Disclose FDA's Concerns to Investors

"[A] corporation does not commit securities fraud merely by failing to disclose all nonpublic material information in its possession. The corporation must first have a duty to disclose the nonpublic material information." Gross v. Summa Four, Inc., 93 F.3d 987, 992 (1st Cir. 1996) (citing Roeder v. Alpha Indus. Inc., 814 F.2d 22, 26 (1st Cir. 1987)). "[A] duty to disclose arises only where both the statement made is material, and the omitted fact is material to the statement in that it alters the meaning of the statement." In re Boston Tech., Inc. Sec. Litig., 8 F. Supp. 2d 43, 53 (D. Mass. 1998). Thus, "[w]hen a corporation does make a disclosure – whether it be voluntary or required – there is a duty to make it complete and accurate." Rosenbaum Capital LLC v. Boston Commc'ns Grp., Inc., 445 F. Supp. 2d 170, 175-76 (D. Mass. 2006) (quoting Roeder, 814 F.2d at 26). Statements cannot be "so incomplete as to mislead." Id. at 176 (quoting Backman v. Polaroid Corp., 910 F.2d 10, 16 (1st Cir. 1990)).

Here, Plaintiffs have pleaded that in a May 2012 pre-NDA meeting with "the Company and certain executives and advisors," the FDA "expressed a concern about the adverse trend in overall survival" and that the "FDA recommended that the sponsor conduct a second adequately-powered randomized trial in a population comparable to that in the U.S." D. 49 ¶¶ 14, 76, 78-80. The FDA further requested that the NDA submission be postponed so that it could include results from the overall survival analysis. Id. ¶¶ 79, 80.

Plaintiffs allege, however, that when subsequently discussing this meeting with investors and the media, the Defendants omitted these and certain other aspects of the meeting with the FDA. On June 4, 2012, Aveo, Ha-Ngoc and Slichenmyer made a presentation to investors at the annual American Society of Clinical Oncology meeting. Id. ¶ 83. While safety was discussed, Slichenmyer stated that overall survival information was "not sufficiently mature" to discuss, failing to mention that the FDA had specifically expressed concerns about overall survival in the Tivo trial and approvability of the drug. Id. ¶¶ 83-85. On June 5, 2012, Aveo and Johnston presented to investors at the Jeffries & Co. Health Care conference. Id. ¶ 85. There, Johnston stated that "TIVO also showed superior safety when compared to sorafenib in this trial," again failing to disclose that the FDA had specifically expressed concerns about overall survival. Id. ¶¶ 85-86.

Defendants cite a number of cases to support the proposition that "medical researchers may well differ over the adequacy of given testing procedures and in the interpretation of test results, but the difference does not show fraud." D. 56 at 22, 25-26 (citations and quotations omitted). For instance, Defendants cite In re Alkermes Sec. Litig., No. 03-cv-12091-RCL, 2005 WL 2848341, at *16 (D. Mass. Oct. 6, 2005), to support their argument that Aveo "was not required to disclose the FDA recommendation or AVEO's scientific disagreement with it." D. 56 at 26. The holding in Alkermes provided that the defendant company never "guaranteed FDA approval" and thus, was not required to disclose to investors that the FDA requested additional pre-clinical studies. Alkermes, 2005 WL 2848341, at *16. Further, the defendants in that case did not conduct the actual clinical trials and there was "no allegation that the [d]efendants made any statement whatsoever to the market regarding test results." Id. The court highlighted that there were "no facts alleged in the complaint regarding what, if any, information

the Defendants (as opposed to [the company that conducted the trials]) even had to disclose." Id. Such is not the case here. To the contrary, Plaintiffs have pleaded that in the May 2012 pre-NDA meeting, the FDA specifically requested that Aveo postpone its NDA submission because it was concerned about the adverse trend in overall survival from the Tivo trial. As the Alkermes court noted, "[w]hen reasonable investors are led to believe that regulatory approval is a 'when not if' proposition," as was arguably the case here, "'subjective scientific disagreement over the efficacy' of the drug should be disclosed to investors." Id. (quoting In re Transkaryotic Therapies, Inc., Sec. Litig., 319 F. Supp. 2d 152, 160 (D. Mass. 2004)). The Plaintiffs in the instant case have alleged sufficient facts that the Defendants misled investors by failing to disclose the FDA's concerns about tivozanib's safety and approvability when describing the drug as superior to sorafenib.

Defendants also contend that Plaintiffs rely on "hindsight" because "there is no basis to conclude that Aveo made any statement about Tivo safety that was misleading when made." D. 56 at 23-24.[1] As discussed above, however, Plaintiffs have sufficiently pleaded that Defendants

[1] After hearing on the motion, Defendants filed notice of supplemental authority, In re Sanofi Sec. Litig., No. 13-cv-08806-PAE (S.D.N.Y. Jan. 28, 2015), to argue that Defendants had no duty to disclose interim communications with the FDA. D. 70. In Sanofi, the court held that the defendants' positive statements regarding a clinical trial were not materially misleading where defendants did not disclose FDA concerns about a single-blind study. Sanofi, 2015 WL 365702, at *23-28. In considering whether the Sanofi defendants were required to disclose FDA feedback, however, the court noted that "much of the information conveyed to [the defendant] was publically available" and that "the FDA had publicly stated, including in federal regulations, its preference for double-blind studies." Id. at *24. Therefore, the court concluded that "a reasonable investor had reason to know that the design of the [] clinical trials fell short of the FDA's gold standard." Id. at *25. Furthermore, the Sanofi court found that the FDA statements did not indicate that the drug "would not obtain timely FDA approval." Id. at *26. Rather, the court found only that the FDA statements "explained that a heightened showing of proof was needed to compensate for the less reliable testing methodology used." Id. Notably, the FDA subsequently approved the drug at issue there. Id. at *8. Here, in contrast, Plaintiffs allege that the FDA expressed specific concerns that Aveo's "sole pivotal clinical trial demonstrated an adverse trend in overall survival," D. 49 ¶ 80, that the FDA recommended a second trial, that the

Aveo, Johnston, Slichenmyer, Ha-Ngoc were misleading in failing to inform investors of the FDA's concerns as to overall survival. For instance, although it is correct that the ultimate FDA disapproval of tivozanib could not have been known at the time of the statements and/or omissions, certainly the FDA had expressed concerns about the adverse trend shown in trial, the specter of another trial and connected these concerns to the prospect of the drug's approvability. That is, downplaying and/or failing to disclose these concerns at the time was, as alleged, misleading as to the prospects of approval. As to Aveo and Slichenmyer, Plaintiffs have alleged that these Defendants had direct knowledge of the FDA's May 2012 concerns and that Slichenmyer subsequently admitted as much in a June 11, 2013 conference call. D. 49 ¶¶ 80, 138. Moreover, Johnston, in an August 16, 2012 investor meeting referenced "[w]hen we met with the FDA in our pre-NDA meeting" that he was aware that the FDA expressed concerns with overall survival. Id. ¶¶ 91, 99. Accordingly, their public statements omitting these concerns were false or misleading at the time made. As to Ha-Ngoc, the Court agrees with Plaintiffs that pleadings are sufficient in this regard as to this defendant as well as to the details of the trial and meaning of data from same, as alleged by Plaintiffs. D. 49 ¶¶ 53, 101 (detailing and specifying overall survival rate of trial and features of trial without disclosing FDA's concerns regarding same).

The Court, however, disagrees that Plaintiffs have made sufficient allegations about whether the statement made by DePinho is actionable. Plaintiffs have alleged that on May 20, 2012, DePinho offered in a media interview about another topic that Aveo had a "very effective drug" with a "superior safety profile" and that he did so despite the fact that the FDA had specifically expressed concerns about overall survival in the Tivo trial and approvability of the

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FDA "questioned whether the NDA should be filed at all" and that the FDA "expressly warned that adverse overall survival trends could affect approvability." Id. ¶ 88.

drug. Id. ¶¶ 81-82. They do not, however, allege his basis for knowing about the FDA concerns and do not allege later statements or evidence suggesting knowledge of same. For these reasons, the Court concludes that sole statement by DePinho is insufficient for stating a claim against him, particularly in light of the absence of scienter, as discussed below.

b. Materiality

The Court recognizes that to survive a motion to dismiss, the Defendant's alleged misrepresentations and omissions must also be material. "Information is material if a reasonable investor might have considered [it] important in the making of [the investment] decision." Roeder, 814 F.2d at 25 (alteration in original) (citation and quotations omitted). That is, a company need not "disclose all nonpublic material information in its possession," Gross, 93 F.3d at 992 (citation omitted), but need only "disclose enough accurate information and not omit pertinent information to allow investors to make an informed decision about whether to invest." ACA Fin. Guar. Corp. v. Advest, Inc., 512 F.3d 46, 61 (1st Cir. 2008). "When information merely creates a possibility that an event affecting the company will later occur, materiality will depend at any given time upon a balancing of both the indicated probability that the event will occur and the anticipated magnitude of the event in light of the totality of the company activity." In re Boston Scientific Corp. Sec. Litig., 686 F.3d 21, 27 (1st Cir. 2012) (citations, quotations and emphasis omitted). It is, however, "ultimately a question for the trier of fact . . . whether statements are false or misleading so as to be actionable under 10b–5," Geffon v. Micrion Corp., 249 F.3d 29, 34 n.6 (1st Cir. 2001), and allegations need only "raise a reasonable expectation that discovery will reveal evidence" to satisfy materiality. Matrixx Initiatives, Inc. v. Siracusano, __ U.S. __, 131 S. Ct. 1309, 1323 (2011). The Court, therefore, examines only whether the

complaint provides a "plausible jury question of materiality." Baron v. Smith, 380 F.3d 49, 53 (1st Cir. 2004) (citation omitted).

The Court agrees with other district courts that a "failure to disclose FDA's serious criticism is a material omission." See, e.g., In re Transkaryotic Therapies, Inc. Sec. Litig., 319 F. Supp. 2d 152, 161 (D. Mass. 2004). Here, at least on the facts as pleaded, a factfinder could reasonably conclude that the Defendants were misleading in their public discussions of the drug's safety and efficacy, which occurred shortly after a May 2012 meeting with the FDA, where the FDA expressed concerns as to a secondary endpoint regarding survival (an endpoint the FDA had specifically requested Aveo include) and requested that Aveo postpone NDA submission because it wanted results from that endpoint. Further, the FDA requested that Aveo conduct a second clinical trial. A factfinder could consider the FDA's feedback to be "serious criticism" and thus, material information for investors, particularly when promoting the drug's purported superiority over the control drug.

Considering the First Circuit's test as articulated in Boston Scientific, 686 F.3d at 27, also compelling here is the fact that when Aveo disclosed in a press release that the FDA "expressed concern regarding the OS trend in [Tivo] and has said that it will review these findings at the time of the NDA filing as well as during the review of the NDA," D. 49 ¶ 87, Aveo's stock price dropped 27 percent. Id. ¶ 88. Further, in its April 30, 2013 briefing document, the FDA noted that Aveo disregarded its recommendation to conduct a second clinical trial, id. ¶ 114, ultimately concluding on May 2, 2013 that Tivo's results were "uninterpretable." Id. ¶¶ 118, 124. Shortly thereafter, Aveo's stock price dropped by $2.61 a share. Id. ¶ 135.

2. Allegations Concerning Tivo Protocol

Plaintiffs have alleged that Tivo deviated from its protocol in several significant ways, amounting to what Plaintiffs describe as "scientific misconduct," D. 60 at 28, and that Defendants should have disclosed these deviances from the protocol to investors.

First, contrary to the Tivo protocol, which called for "a broad worldwide trial stratified across geographies, Aveo enrolled approximately 88% of TIVO-1 participants in Central and Eastern Europe, where enrollment and testing were cheaper." D. 49 ¶ 57. Second, Plaintiffs assert that Defendants "confounded the study results by offering a crossover, or subsequent therapy, to one study arm without offering the same to the other study arm." Id. ¶ 10. Third, Plaintiffs allege that Defendants arranged for the dosages given to patients to be reduced at "materially different rates" for patients experiencing adverse reactions. Id. ¶ 13.

Defendants argue that "statements referring to clinical studies do not have to address study design in detail." D. 56 at 20 (citing Padnes v. Scios Nova Inc., No. 95-cv-1693-MHP, 1996 WL 539711 at *5 (N.D. Cal. Sept. 18, 1996); In re MELA Sciences, Inc. Sec. Litig., No. 10-cv-8774-VB, 2012 WL 4466604 at *13 (S.D.N.Y. Sept. 19, 2012)). Making misleading statements as to a drug's efficacy by relying on results of a trial conducted with methodological errors is, however, actionable. See Frater v. Hemispherx Biopharma, Inc., 996 F. Supp. 2d 335, 346 (E.D. Pa. 2014) (concluding that a "factfinder could easily determine that announcements that [] studies demonstrated [a drug's] effectiveness implied those studies' empirical validity and analytic soundness. To the extent that the cited conclusions were the product of statistically unsound analyses of empirically defective trials, statements lauding those conclusions would be misleading"). Specifically here, Plaintiffs allege that Slichenmyer conceded that he and Aveo "anticipat[ed] that the off-protocol crossover might distort overall survival," D. 49 ¶ 130 (alteration in original), with overall survival being, as discussed above, an important endpoint for

the FDA. Moreover, Aveo and the other Defendants allegedly issued a number of statements without mentioning the crossover or the potential effects the crossover could have on the study results. See, e.g., id. ¶¶ 83-84 (Ha-Ngoc and Slichenmyer's June 4, 2012 investor presentation), 85-86 (Johnston's June 5, 2012 investor presentation). A factfinder could therefore conclude that, at least as to Defendants' statements that omitted mention of the off-protocol crossover, Defendants' statements were materially misleading.

3. Safety Findings

Plaintiffs also argue that Defendants were misleading about tivozanib's safety profile. D. 60 at 30. Namely, Plaintiffs allege that Aveo's own data showed that tivozanib patients were dying at a "higher clip" than were the control patients. Id. Defendants argue that "[t]his does not state a claim because plaintiffs lack a factual basis to assert that AVEO had meaningful data to disclose during this period." D. 56 at 23. Defendants assert that the overall survival data was preliminary and not statistically significant. Id. at 24.

The Supreme Court has noted, however, that "statistical significance (or the lack thereof)," although not irrelevant, "is not dispositive of every case." Matrixx Initiatives, 131 S. Ct. at 1319. Here, the complaint alleges that at least some representations were made to investors about tivozanib's safety and superiority over the control drug, see, e.g., D. 49 ¶ 85, despite the fact that trial results were showing an adverse overall survival trend (and 25 percent potential increase in the risk of death) six months after treatment began. Id. ¶¶ 118-119. Given the alleged facts of this case, where the FDA had already expressed a concern with overall survival, investors could have "viewed this information as having significantly altered the total mix of information made available." Matrixx Initiatives, 131 S. Ct. at 1323 (quoting Basic Inc. v. Levinson, 485 U.S. 224, 232 (1988)) (quotations omitted).

B. Plaintiffs Have Not Sufficiently Pleaded Scienter

In a securities fraud case, plaintiffs must "'state with particularity facts giving rise to a strong inference that the defendant acted with the required state of mind.'" Greebel v. FTP Software, Inc., 194 F.3d 185, 194 (1st Cir. 1999) (quoting 15 U.S.C. § 78u–4(b)(2)). Scienter, "'embracing intent to deceive, manipulate or defraud,' may be shown where the defendants consciously intended to defraud, or that they acted with a high degree of recklessness." Aldridge v. A.T. Cross Corp., 284 F.3d 72, 82 (1st Cir. 2002) (internal citations omitted). "A complaint will survive . . . only if a reasonable person would deem the inference of scienter cogent and at least as compelling as any opposing inference one could draw from the facts alleged." Tellabs, Inc. v. Makor Issues & Rights, Ltd., 551 U.S. 308, 324 (2007). Therefore, the Court "must take into account plausible opposing inferences," id. at 323, which is a fact-specific inquiry. Aldridge v. A.T. Cross Corp., 284 F.3d 72, 82 (1st Cir. 2002). The Court must consider "whether all of the facts alleged, taken collectively, give rise to a strong inference of scienter, not whether any individual allegation, scrutinized in isolation, meets that standard." Tellabs, 551 U.S. at 323 (emphasis omitted); Aldridge, 284 F.3d at 82 (noting that a court must look at the "mix of facts" indicating fraudulent intent to show a strong inference of scienter). Ultimately, "where there are equally strong inferences for and against scienter, Tellabs now awards the draw to the plaintiff." ACA Fin. Guar. Corp., 512 F.3d at 59 (citing Tellabs, 551 U.S. at 324). To survive a motion to dismiss, the alleged facts must give rise to a *strong* inference of scienter. Greebel, 194 F.3d at 196.

Plaintiffs have failed to allege facts giving rise to a strong inference of scienter here. Although there is no checklist for such showing of scienter, little of the indicia usually relied upon to support such strong inference is alleged here. See Greebel, 194 F.3d at 196 (discussing

the "many different types of evidence as relevant to show scienter"). There is no allegation of insider trading; no divergence of internal reports and external statements on the same subject; no personal gain to the Defendants (i.e., there are no allegations of the Defendants' compensation, whether such compensation was tied to FDA approval or the capital call, discussed below) or other allegations that reflect motive other than an implicit suggestion that the Defendants acted in self-interest to preserve their positions and, presumably, their salaries.

The allegations that are made here do not amount to a strong inference of scienter. Certainly, part of Plaintiffs' showing of scienter is based upon the Defendants having made inaccurate or misleading statements. It is clear, however, that "[m]ore than mere proof that the defendants made a particular false or misleading statement is required to show scienter." Aldridge, 284 F.3d at 83. This is particularly true where the nature of the false and misleading statements, although sufficient to survive a motion to dismiss as discussed above, is at least debatable. Plaintiffs fail to make a showing beyond the nature of the statements made, particularly as to the Defendants' motive and opportunity.

As to motive, none of the Individual Defendants sold stock during the class period, undermining any scienter inference. D. 56 at 35. (In fact, one of the Individual Defendants, Ha-Ngoc, the CEO, bought 75,000 shares of common stock for over $615,000 in December 2012, D. 56 at 36 & n.16 [citing his Form 4 of which the Court may take judicial note]). Although the absence of such trading does not preclude an inference of scienter, its absence is significant, particularly when coupled with the dearth of other specific, factual allegations about motive. Plaintiffs do allege that Aveo announced a capital raise "critical to the Company's future" in January 2013 that "was facilitated by the inflation of Aveo's share price via the misrepresentations [made by Defendants]." D. 49 ¶ 103. The complaint, however, does not

provide any factual allegations regarding how the capital raise was critical to Aveo's bottom line or its future. The Court agrees with the Defendants that the capital raise, in and of itself, is less powerful evidence of motive alone, particularly in the absence of personal benefit inuring to the Defendants, D. 63 at 19-20 and cases cited.

As to Ha-Ngoc, the CEO, in particular, the allegations of scienter are no greater. Plaintiffs ask the Court to ascribe scienter, at least in part, to the nature of his role in the Company. D. 60 at 32. It is well-settled, however, that "[g]eneral inferences that the defendants, by virtue of their position within the company, must have known about the company's problems when they undertook allegedly fraudulent actions" are not adequate to allege scienter. Coyne v. Metabolix, Inc., 943 F. Supp. 2d 259, 272 (D. Mass. 2013) (citing Lirette v. Shiva Corp., 27 F. Supp. 2d 268, 283 (D. Mass. 1998)); see Maldonado v. Dominguez, 137 F.3d 1, 9-10 (1st Cir. 1998) (noting that "the pleading of scienter may not rest on a bare inference that a defendant must have had knowledge of the facts"). That is, Plaintiffs' allegation that "it is expected that, at a minimum, Defendants Hag-Ngoc" attended certain meetings because "the participation of the Chief Executive Officer . . . in crucial meetings with the FDA would be standard practice for a company of AVEO's size, especially when it involved the company's flagship drug candidate," D. 49 ¶ 79, does not alone carry the day on this issue. Even declining to infer scienter under the "core operations theory," D. 63 at 12-13 and case cited, certainly, the role of the defendant in the company and the importance of the product at issue (here self-identified as Aveo's "lead product candidate," D. 49 ¶¶ 70, 89) to the company's bottom line are not immaterial to whether a strong inference of scienter has been shown. See South Ferry LP, No. 2 v. Killinger, 542 F.3d 776, 784 (9th Cir. 2008) (concluding that, post-Tellabs, "[a]llegations that rely on the core-operations inference are among the allegations that may be considered in the complete PSLRA analysis").

Such inference about the CEO's role cannot here, however, in the absence of other relevant evidence, give rise to a strong inference of scienter as to this defendant. Similarly, there are some instances in which a "scienter gap" can be filled the nature of the statements made by a defendant, see Reese v. Malone, 747 F.3d 557, 572 (9th Cir. 2014) (concluding that the defendant had bridged the scienter gap with her own statements and citing the timing of statement and her motive to mischaracterize information in finding that a strong inference of scienter has been show), but such is not the case here given the nature of the defendant's statements and the absence of other evidence reflecting scienter.

At most, the showing of scienter here amounts to the allegedly knowingly false or misleading statements made by Ha-Ngoc, Slichenmyer and Johnston, the suspect timing of at least the statements made on the heels of the May 2012 meeting with the FDA, and generalized implications about the Defendants' self-interest in making such statements to maintain their positions and salaries at the Company. Such allegations do not give rise to a strong inference, as they must at the motion to dismiss stage, Greebel, 194 F.3d at 197, in this case.

C. Section 20(a) Count

Finally, Defendants argue that Plaintiffs' § 20(a) claim must be dismissed because Plaintiffs have not adequately pled a primary violation of § 10(b) and Rule 10b–5. D. 56 at 37. Since the Court has now held that the Plaintiffs have failed to state a claim under § 10(b) and Rule 10b–5, the Court will dismiss Plaintiffs' claim on this ground.

Defendants further argue that, with respect to DePinho, Plaintiffs have failed to allege any facts that he "engaged in any control" of Aveo at all. Id. "To meet the control element, the alleged controlling person must not only have the general power to control the company, but must also actually exercise control over the company." Aldridge, 284 F.3d at 85. "[D]irector

status alone does not constitute control." In re Lernout & Hauspie Sec. Litig., 286 B.R. 33, 39 (D. Mass. 2002) (citation omitted) (alteration in original). Here, Plaintiffs have not sufficiently alleged that DePinho "actively participat[ed] in the decisionmaking processes of the corporation." Aldridge, 284 F.3d at 85. Plaintiffs have alleged generally that all of "the Individual Defendants participated in the operation and management of AVEO, and/or directed and oversaw the operation and management of AVEO's business and regulatory affairs and investor communications." D. 49 ¶ 163. With respect to DePinho specifically, however, Plaintiffs allege only that "DePinho had co-founded AVEO," id. ¶ 15, had previously served on Aveo's scientific advisory board, id. ¶ 36, and "remained a director and major shareholder," id. ¶ 15. These allegations are insufficient to demonstrate that DePinho continued to exercise a substantial degree of control over Aveo. Accordingly, the Court will dismiss the § 20 (a) claim against DePinho on these grounds as well.

V. Conclusion

For the above reasons, the Court ALLOWS Defendants' motion to dismiss, D. 55. Such dismissal shall be without prejudice.

So Ordered.

/s/ Denise J. Casper
United States District Judge