UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

TRICIA M. BARTELT, et al.,

Plaintiffs,

v.

AFFYMAX, INC., et al.,

Defendants.

Case No. 13-cv-01025-WHO

ORDER GRANTING IN PART AND DENYING IN PART MOTION TO DISMISS CONSOLIDATED AMENDED COMPLAINT

Re: Dkt. Nos. 47, 48

INTRODUCTION

On July 22, 2013, the plaintiffs filed a Consolidated Amended Complaint against defendants Affymax Inc. and four of its senior executives and directors, John A. Orwin, Herbert C. Cross, Anne-Marie, Duliege, and Jeffrey H. Knapp. Dkt. No. 45. The defendants have moved to dismiss the Consolidated Amended Complaint. Dkt. No. 47. For the reasons stated below, the motion to dismiss is GRANTED IN PART and DENIED IN PART. This order also resolves the defendants' request for judicial notice, as stated below. Dkt. No. 48

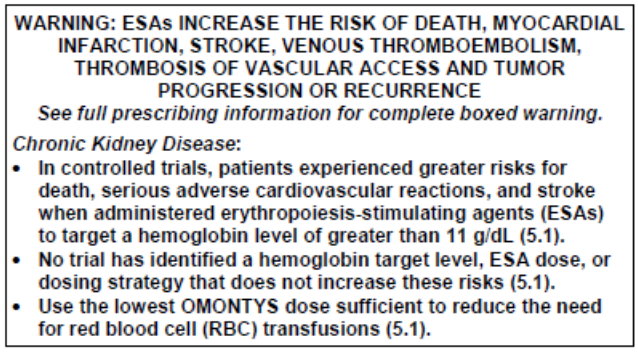
BACKGROUND[1]

Defendant Affymax is a biopharmaceutical company whose primary product is the drug Omontys. During the relevant period, defendant Orwin served as Affymax's Chief Executive Officer and a director; defendant Cross served as Chief Financial Officer; defendant Duliege

[1] The Court assumes the truth of the allegations in the Consolidated Amended Complaint.

served as Chief Medical Officer; and defendant Knapp served as Chief Commercial Officer. The plaintiffs allege that Affymax and the individual defendants violated federal securities laws by making materially false and misleading statements about Omontys, which was eventually recalled in the face of serious safety concerns, causing Affymax's stock to plummet. The plaintiffs seek to represent a class of all purchasers of Affymax common stock between August 8, 2012 and February 22, 2013 (the "class period").

Omontys is in a class of drugs known as erythropoiesis stimulating agent ("ESAs"). Like other ESAs, Omontys treats anemia by stimulating the production of red blood cells. Other ESAs for treating anemia include Epogen, sold by Amgen, and Procrit, sold by Johnson & Johnson. On March 27, 2012, the Food and Drug Administration ("FDA") approved Omontys for patients on dialysis for treatment of anemia due to chronic kidney disease. ¶ 63.[2] Because Omontys is an ESA, the FDA required it to carry a "black-box warning," the highest level of warning that the FDA can require, which warned of death and other serious risks. *See* 21 C.F.R. 201.57(c)(1.) The "black-box warning" stated:



WARNING: ESAs INCREASE THE RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, THROMBOSIS OF VASCULAR ACCESS AND TUMOR PROGRESSION OR RECURRENCE

See full prescribing information for complete boxed warning.

Chronic Kidney Disease:

- In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL (5.1).
- No trial has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase these risks (5.1).
- Use the lowest OMONTYS dose sufficient to reduce the need for red blood cell (RBC) transfusions (5.1).

Dkt. No. 49-19 (Kaban Ex. 19).[3]

On July 12, 2012, Affymax issued a press release announcing that it had entered into a

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[2] Unless otherwise noted, all paragraph citations (¶) are to the Consolidated Amended Complaint.

[3] The Court GRANTS the defendants' request to take judicial notice of the package insert approved by the FDA for Omontys (Kaban Ex. 19, Dkt. No. 49-19), including the "black-box warning." Dkt. No. 48. The plaintiffs concede that the "FDA package inserts" (Kaban Exs. 19-21) "are incorporated by reference or relied upon in the CAC." Dkt. No. 54 at 2. Plaintiffs therefore "do not object to judicial notice for these [FDA package inserts] for the limited purpose of what they state and when they were filed." *Id*. The request for judicial notice is DENIED AS MOOT to the extent that the exhibits at issue are not cited in this Order.

supply agreement with leading dialysis provider Fresenius Medical Care, ending in April 2013. ¶ 69. The press release reported that "Fresenius Medical Care North America has stated that its initial plans are to adopt the product into more than 100 dialysis centers in the U.S. over the next few weeks, and then, based on its experience, evaluate the potential to expand to additional centers." *Id.* Affymax's stock price increased 16% after the press release. ¶ 70. The plaintiffs allege that Affmyax's agreement with Fresenius accounted for the majority of Affymax's sale of Omontys during the class period. ¶ 3.

The plaintiffs allege that "in August, September, and October of 2012, some Affymax sales representatives selling Omontys to dialysis clinics in Texas, Oklahoma, Mississippi, Louisiana, and Alabama filed Adverse Event reports concerning serious reactions with Omontys." ¶ 76.

Affymax held a conference call on August 8, 2012 with investors, analysts and other market participants regarding its Q2 2012 financial results. The individual defendants participated in the conference call where "they reiterated the Company's Q2 2012 guidance and its continued success with Omontys (and in particular its long-term contracts with Fresenius) due to the product's safety and efficacy." ¶ 87. The plaintiffs allege that by this time Affymax and the individual defendants "were already aware of the adverse events caused by their most profitable drug, Omontys. They had already received reports of allergic reactions in patients associated with using the drug which had been forwarded to the FDA." ¶ 88. The plaintiffs allege that the defendants "failed to report this to the market because they knew of the serious implications this could have on their Company's ability to operate without the profits from Omontys. They also knew that any reported adverse reactions would affect their long-term relationship with Fresenius who would halt their pilot program and discontinue use of Omontys." *Id.*

In October 2012, Affymax requested a change in Omontys's label to warn "physicians and patients about the potential for allergic reactions." ¶ 78. The plaintiffs' Confidential Witness 2, a Director of Sales Training at Affymax from August 2011 to October 2012, states that Affymax's Manager of Sales Training and its Vice President of Clinical Development told Affymax employees during a conference call that the label change "was not a big deal." ¶ 78.

Affymax disclosed the proposed label change during an investor conference call on November 8, 2012. ¶ 94. Defendant Orwin, Affymax's CEO, said:

> Since launch thousands of patients have received OMONTYS in the post-marketing setting. As anticipated, this broad experience has been helpful in further informing real-world use of the compound where infrequent, but sometimes serious, allergic reactions have been reported. To that end, we have proposed to the FDA, and have now updated our label to include, additional language regarding allergic reactions similar to that which is found in the existing labels for other ESAs. . . . allergic reactions are mentioned [on the original label], but they're not described in the same sort of wholesome way that they are in other ESAs, which is what led us, based on the experience and reported events, however infrequent, to look at that against what was in the label and decide that it made sense for us to bring the language into our label in line with what exists for the other ESAs.

Id. Similarly, defendant Duliege, Affymax's Chief Medical Officer, advised:

> Now that we have thousands of patients, literally more than 10,000 patients, we felt it was prudent to update our label with the new information that we have accumulated as part of our pharmacovigilance severance program.
>
> Specifically, the report of allergic reactions that you mentioned in the label continues to be infrequent and a result on treatment. However, some of these reactions have been more serious. Some of the most recent reaction (inaudible) have been more serious and this is what we have included as information in the label to bring, as you said, John, our label in line with the existing label of other ESAs. So, there is now a new contraindication in our label which has been added and it's OMONTYS is contraindicated in patients with serious allergic reactions to OMONTYS. And that's also reflected in the warning and precaution sections of our label.

Id. An investment analyst asked "Just like the Epogen label?" to which Duliege responded "That's right." *Id*.

The plaintiffs allege that the "Defendants misled analysts and investors by claiming that the requested label change was to keep up with competition; e.g. Epogen's label, rather than admitting to their own reports of serious allergic reactions causing hospitalizations and death." ¶ 95. Specifically, the plaintiffs allege that the defendants "did not disclose the full extent of the serious allergic reactions caused by Omontys, including death; that reports of adverse reactions were mounting; and that Affymax had made a request to the FDA for a label change primarily to warn doctors of serious allergic reactions that could occur with the injection of Omontys rather

than making its label consistent with its competitor's label. *Id*.

The FDA approved Omontys's label change on December 4, 2012. The new label warned that the use of Omontys could cause Serious Allergic Reactions. The label stated, in part:

> **Serious Allergic Reactions**
>
> Serious allergic reactions, including anaphylactic reactions, hypotension, bronchospask angioedema and generalized pruritus, may occur in patients treated with OMONTYS. Immediately and permanently discontinue OMONTYS and administer appropriate therapy if a serious allergic reaction occurs.

¶ 100. Affymax did not issue a press release to announce the label change, even though it "had received many reports of adverse reactions by patients, including anaphylactic reactions on the first use of Omontys causing death and other serious injuries requiring hospitalization" by this time. ¶¶ 102-03. As a result, according to the plaintiffs, the "label change was unknown to the market and had no significance to shareholders." ¶ 102.

On February 12, 2013, Affymax and the individual defendants conducted another conference calls with analysts where the defendants "made material representations and omissions . . . continuing to tout the product's safety and efficacy while omitting to disclose the serious problems it had with Omontys and the imminent recall that was about to occur." ¶ 106. Defendant Orwin was asked to "provide a little bit more color on the Fresenius agreement, and what kind of information they think they will need in order to make a decision to go wider with Omontys." *Id*. In response, Orwin stated

> Obviously, the safety and efficacy were established, and are typically best established in a comparative Phase 3 program. Fortunately for us, we had a very large program, and a very comprehensive evaluation of both safety and efficacy. But I think what they want to see is that they could replicate those kinds of results in their patient population, and that by treating 10,000 patients, and looking at patients as their own controls, but also looking at a matched cohort, they could learn a lot about the performance of Omontys in their patient population, before making a decision to utilize the product more broadly. . . . So, I think what they need to see is they need to see how the product performs in their population. Safety and efficacy, of course, always, but even more importantly, the dose efficiency in their population, since safety and efficacy were already fairly well-established."

Opp. at 13 (citing CAC. ¶ 106).

The next day, February 13, 2013, Fresenius announced that it would "pause further

expansion of the Omontys pilot that began in late July 2012." ¶ 108. A Form 8-K Affymax filed with the SEC the same day included a letter from Fresenius to Affymax. The letter stated, in part:

> We are writing to provide an interim update on the status of our pilot to assess the use of Omontys in the [Fresenius] dialysis facilities. . . . The assessment includes efficacy, safety and logistics related to this agent that was approved for use by the Food and Drug Administration at the end of March 2012.
>
> We will now pause expansion of the pilot that began in late July 2012. We have accumulated experience in more than 56,600 administrations in over 18,000 unique patients. . . . To date, we have seen infrequent allergic reactions in our patient population receiving their first dose of Omontys. Most of these reactions have been mild, but a small number have been serious. The rate of allergic reactions has been on the order of 1:1000 patients receiving a first dose of Omontys. The vast majority of patients who are receiving the medication on an ongoing monthly basis are tolerating it well.
>
> We are now working to analyze the full set of efficacy and safety profile information and feel that the current scale of our experience with use of the drug is adequate to complete this analysis. . . . For patients on Omontys, we recommend continued use of the agent as it has been providing effective anemia management. We plan to pause the rollout to additional facilities and patients at this time until the analyses are complete and reported to our medical staff. As many of you have become quite comfortable with the medication, physicians and facilities that have been using Omontys who wish to continue prescribing it for new patients may choose to do so.

¶ 108.

The plaintiffs allege that the Fresenius pilot program was paused to "investigate the drug's safety and efficacy due to patients having serious allergic reactions." ¶ 12. Affymax stock closed down approximately 7% on February 14, 2013, following Fresenius's announcement. ¶ 109. The plaintiffs allege that "without knowing the full truth about Omontys['s] lack of safety, analysts were still positive on the stock." *Id*. Investment firm Piper Jaffray issued an analyst report on February 20, 2013 which concluded that the firm "remain[s] bullish that the companies [Affymax and Fresenius] will sign a meaningfully larger supply agreement, despite the recent pause in Fresenius's pilot program." ¶ 110.

Affymax announced a voluntary recall of Omontys on February 23, 2013. ¶ 111. Affymax issued a press release stating that it "decided to voluntarily recall all lots of Omontys . . . as a result of new postmarketing reports regarding serious hypersensitivity reactions, including

anaphylaxis, which can be life-threatening or fatal." ¶ 111. The press release also stated that:

> To date, fatal reactions have been reported in approximately 0.02% of patients following the first dose of intravenous administration. . . . The rate of overall hypersensitivity reactions reported is approximately 0.2% with approximately a third of these being serious in nature including anaphylaxis requiring prompt medical intervention and in some cases hospitalization. The companies are actively investigating these cases. In the meantime, dialysis organizations are instructed to discontinue use.

The Wall Street Journal reported on the recall on February 25, 2013, writing that "Affymax Inc. shares plunged 85% in midday trading Monday after reports of severe allergic reactions in some kidney-disease patients, including at least five deaths, prompted the company to recall its antianemia drug." ¶ 112. The Wall Street Journal also reported that "Chief Executive John A. Orwin said the company moved to pull the drug, called Omontys, after executives learned of three deaths in February tied to hypersensitivity, a sometimes fatal condition that can arise when the body's immune system reacts to drugs or other foreign intrusions, like bee stings. Those fatalities followed two earlier deaths that observers had associated more closely with cardiovascular problems rather than allergic reactions." *Id.* According to the Wall Street Journal, "the recall shocked investors who had seen encouraging signs that the antianemia drug was making inroads as a cheaper and more convenient alternative to Amgen Inc.' s blockbuster Epogen, which holds a virtual monopoly in treating anemia in patients receiving dialysis." *Id.*

The Wall Street Journal also reported that "[t]he drug's prospects looked far brighter less than two weeks ago, when [Fresenius] sent a letter suggesting that doctors comfortable with the treatment could continue administering it while Fresenius paused a pilot Omontys program to pore over its safety and effectiveness data." The Wall Street Journal also stated that Fresenius "earlier this month reported a 'small number' of allergic reactions but didn't mention any patient deaths."

According to an analyst from Robert W. Baird—the same analyst that, in November 2012, asked whether the new Omontys label was "[j]ust like the Epogen label"—the number of Omontys hypersensitivity incidents "was 100-fold greater than Amgen's Epogen and the death rate was 8.5 times higher." *Id.*

The plaintiffs allege that Affymax's and the individual defendants' rosy statements about

Omontys's outlook, without disclosing the serious adverse reactions associated with Omontys, violated Sections 10(b) of the Exchange Act and SEC Rule 10b-5 (17 C.F.R. §240.10b-5). The plaintiffs also allege that the individual defendants are liable as control persons under Section 20(a) for Affymax's violation of Section 10(b).

LEGAL STANDARD

A. Federal Rule of Civil Procedure 12(b)(6)

A motion to dismiss for failure to state a claim under Rule 12(b)(6) tests the legal sufficiency of a complaint. *Navarro v. Block*, 250 F.3d 729, 732 (9th Cir. 2001). A complaint "must contain sufficient factual matter, accepted as true, to state a claim to relief that is plausible on its face." *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009). A claim is facially plausible when it "allows the court to draw the reasonable inference that the defendant is liable for the misconduct alleged." *Id*. In considering whether the complaint is sufficient to state a claim, the court accepts as true all of the factual allegations contained in the complaint. *Id.* However, the court need not "accept as true allegations that contradict matters properly subject to judicial notice or by exhibit" or "allegations that are merely conclusory, unwarranted deductions of fact, or unreasonable inferences." *In re Gilead Scis. Sec. Litig*., 536 F.3d 1049, 1055 (9th Cir. 2008) (internal quotation marks and citations omitted).

B. Pleading Requirements in Securities Fraud Actions

Section 10(b) of the Exchange Act makes it unlawful "for any person . . . to use or employ, in connection with the purchase or sale of any security . . . any manipulative or deceptive device or contrivance in contravention of such rules and regulations as the Commission may prescribe[.]" 15 U.S.C. § 78j(b). SEC Rule 10b-5, promulgated under the authority of Section 10(b), in turn, provides that "[i]t shall be unlawful for any person . . . (a) To employ any device, scheme, or artifice to defraud, (b) To make any untrue statement of a material fact or to omit to state a material fact necessary in order to make the statements made, in light of the circumstances under which they were made, not misleading, or (c) To engage in any act, practice, or course of business which operates or would operate as a fraud or deceit upon any person, in connection with the purchase or sale of any security." 17 C.F.R. § 240.10b-5. Thus, the basic elements of a Rule 10b-

5 claim are: (1) a material misrepresentation or omission of fact, (2) scienter, (3) a connection with the purchase or sale of a security, (4) transaction and loss causation, and (5) economic loss. *In re Daou Systems, Inc.* 411 F.3d 1006, 1014 (9th Cir. 2005).

A statement or omission is misleading regarding a material fact "when there is 'a substantial likelihood that the disclosure of the omitted fact would have been viewed by the reasonable investor as having significantly altered the 'total mix' of information made available.'" *Matrixx Initiatives, Inc. v. Siracusano*, 131 S. Ct. 1309, 1318 (2011) (*citing Basic Inc. v. Levinson*, 485 U.S. 224, 231-32 (1988)). "Scienter may be established, by showing that the defendants knew their statements were false, or by showing that defendants were reckless as to the truth or falsity of their statements." *Gebhart v. S.E.C.*, 595 F.3d 1034, 1041 (9th Cir. 2010).

To establish a prove a prima facie case violation of Section 20(a), plaintiff must prove: (1) a primary violation of federal securities laws and (2) that the defendant exercised actual power or control over the primary violator (Affymax). *Howard v. Everex Sys., Inc.*, 228 F.3d 1057, 1065 (9th Cir. 2000).

C. Federal Rule of Civil Procedure 9(b) and the PSLRA

Under the Private Securities Litigation Reform Act ("PSLRA"), securities fraud claims must satisfy the heightened pleading standards set forth in Rule 9(b) of the Federal Rules of Civil Procedure and the PSLRA itself. *Zucco Partners, LLC v. Digimarc Corp*., 552 F.3d 981, 990 (9th Cir. 2009). Rule 9(b) requires a plaintiff alleging fraud or mistake to "state with particularity the circumstances constituting fraud or mistake." Fed. R. Civ. P. 9(b). The PSLRA requires a plaintiff alleging securities fraud to "plead with particularity both falsity and scienter." *Zucco Partners*, 552 F.3d at 990-91; *accord Tellabs, Inc. v. Makor Issues & Rights, Ltd*., 551 U.S. 308, 314 (2007). With respect to falsity, the complaint must "specify each statement alleged to have been misleading, [and] the reason or reasons why the statement is misleading." 15 U.S.C. § 78u–4(b)(1). With respect to scienter, the complaint must "state with particularity facts giving rise to a strong inference that the defendant acted with the required state of mind." 15 U.S.C. § 78u–4(b)(2).

To satisfy the requisite state of mind element, "a complaint must allege that the defendant[

] made false or misleading statements either intentionally or with deliberate recklessness." *Zucco*, 552 F.3d at 991 (citation omitted). Facts showing mere recklessness, or a motive to commit fraud and opportunity to do so, provide some reasonable inference of intent, but are not sufficient to establish a strong inference of deliberate recklessness. *In re VeriFone Holdings, Inc. Sec. Litig*., 704 F.3d 694, 701 (9th Cir. 2012) (citation omitted). As such, the Court "must consider plausible nonculpable explanations for the defendant's conduct, as well as inferences favoring the plaintiff." *Tellabs*, 551 U.S. at 323–24. In evaluating whether a complaint satisfies the "strong inference" requirement, courts must consider the allegations and other relevant material holistically, not "scrutinized in isolation." *VeriFone*, 704 F.3d at 701.

DISCUSSION

The plaintiffs allege three categories of misleading statements: statements regarding i) Fresenius expanding use of Omontys; ii) the safety and efficacy of Omontys; and iii) the reasons for the change to the label of Omontys. The allegedly misleading statements identified by the plaintiffs occurred on August 8, 2012 (¶ 87), November 8, 2012 (¶ 94) and February 12, 2013 (¶ 106). *See also* Dkt. No. 53 ("Opp.") at 11-13 (plaintiffs' opposition brief identifying the misleading statements). All three categories rely on the allegation that Affymax and the individual defendants "knew that there were serious adverse reactions to Omontys which negated the Company's statements about the drug's safety and efficacy" but nonetheless "continued to disseminate materially false and misleading statements regarding Omontys, causing their financial statements and projections to be materially false and misleading, in violation of the Exchange Act." ¶ 10; *see also id*. ("Defendants knew, or recklessly disregarded the fact, that as early as August 2012, the use of Omontys was linked to allergic reactions and respiratory distress."). The substance and materiality of the defendants' knowledge of adverse reactions associated with Omontys at the time of the statements identified by the plaintiffs is therefore central to the plaintiffs' claims.

A. August 8, 2012 statements

The plaintiffs allege that the defendants' August 8, 2012 statements mislead the market about the safety and efficacy of Omontys and about Fresenius's supposed continuing and

expanding adoption of Omontys. ¶¶ 87, 106; Opp. ("Opp.") at 13. The plaintiffs allege that defendant Duliege's statement that "we haven't heard anything of concern back. It continues to progress as planned, so no nothing specific that way," falsely represented that Omontys did not present any safety concerns, even though "Defendants were well aware that the injection of Omontys caused patients severe allergic reactions, resulting in hospitalization and death." Opp. at 13 (citing ¶ 87). The plaintiffs likewise allege that defendant Cross mislead investors when he stated "I think the increase in Q2 was very consistent with our expectations and so, I don't--we don't have any reason to update our guidance at this point." *Id*. In addition, according to the plaintiffs, at this time the defendants already knew that Fresenius's patients would likely convert back to Epogen based on the adverse reactions associated with Omontys and, consequently, the defendants mislead the market by describing Fresenius as "converting" to Omontys, rather than merely considering Omontys on a pilot program basis. ¶¶ 87, 106; Opp. at 11-13.

In response, the defendants argue that the first adverse event was reported to the FDA on August 14, 2012—a week after the statements at issue—and, consequently, the plaintiffs do not adequately allege that these statements were false when made or that the defendants had the requisite scienter. Dkt. No. 58 at 4.

The Court agrees that the timing of the first reported adverse events precludes plaintiffs' claims based on the August 8, 2012 statements. Exhibit 1 to the plaintiffs' opposition brief lists the adverse events associated with Omontys reported to the FDA. Dkt. No. 53-1 (the "adverse events report").[4] Consistent with the adverse events report (page 4), the parties agree that the first

[4] Per 21 C.F.R. Section 314.80(a), after a drug has gone to market, the drug manufacturer is required to report adverse events experienced by patients using the drug to the FDA. Adverse events that are life-threatening or result in death or hospitalization must be reported within 15 calendar days (expedited). 21 C.F.R. § 314.80(c). Less serious events must be reported periodically (non-expedited). *Id*. Adverse events must be reported when the adverse events are "associated with the use of a drug in humans, whether or not considered drug related." 21 C.F.R. § 314.80(a). Accordingly, a reported adverse event does not necessarily signify that the drug caused the adverse event. *See also* 21 C.F.R. § 314.80 (a reported adverse event "does not necessarily reflect a conclusion by the applicant or FDA that the report or information constitutes an admission that the drug caused or contributed to an adverse effect.").

Plaintiffs attach a 99-page FDA Adverse Event Report as Exhibit 1 to their Opposition, purportedly obtained by the plaintiffs through a FOIA request. The report lists adverse events associated with Omontys reported by the manufacturer (Affymax) or health care professionals, patients or others not associated with Affymax. The defendants argue that "[t]he Court should

death associated with Omontys was reported by Affymax to the FDA on August 14, 2012. *See* Opp. at 20 (plaintiffs asserting that "The first death was reported August 14, 2012"); Dkt. No. 58 at 4 (defendants stating: "as Exhibit 1 to the Opposition demonstrates, that [death reported on August 14, 2012] was the first [serious adverse event] of any type reported"). As the defendants point out, the death reported on August 14, 2012 is the first report of any adverse event in the report. A second adverse event was also reported that day of an anaphylactic reaction[5] and chest discomfort. The event was deemed life-threatening and required hospitalization. Dkt. No. 53-1 at 5. The Court will not presume, absent specific factual allegations, that the defendants were aware of the adverse events before they were reported to the FDA.[6] The plaintiffs have accordingly failed to allege either falsity or scienter regarding the August 8, 2012 statements.

B. November 8, 2012 statements

The plaintiffs allege that the following statements by defendants Orwin and Knapp on

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reject any arguments by Plaintiffs based on this exhibit as it is not part of the relevant pleadings." Dkt. No. 58 at 4 n.3. The defendants themselves, however, make arguments based on the exhibit, conceding its authenticity, accuracy and relevance. *See id*. ("as Exhibit 1 to the Opposition demonstrates, that [death reported on August 14, 2012] was the first [serious adverse event] of any type reported"); *id*. at 6 n.5 ("Exhibit 1 cited by the Plaintiffs is consistent with this assessment.").

Moreover, the report is referenced extensively in the CAC. *See, e.g.*, ¶ 18 ("Close to 100 'adverse events' tied to the drug were reported to the FDA beginning in August 2012, including 14 deaths by February 22, 2013, the day before the recall."), ¶ 19 ("There can be no doubt that Defendant Orwin knew of these adverse event reports as early as August since, by definition, many of them had to come directly from the manufacturer on an expedited basis."), ¶ 21 ("The first adverse event report due to anaphylaxis was received at the FDA in August 2012."), ¶ 76 ("In August, September, and October of 2012, some Affymax sales representatives selling Omontys to dialysis clinics in Texas, Oklahoma, Mississippi, Louisiana, and Alabama filed Adverse Event reports concerning serious reactions with Omontys."), ¶¶ 88, 96, 116. As the foregoing demonstrates, the Adverse Event Report attached as Exhibit 1 to the Opposition is essential to the CAC and no party questions its authenticity. The Court therefore may properly consider Exhibit 1 in connection with this motion to dismiss. *See, e.g., Sanders v. Brown*, 504 F.3d 903, 910 (9th Cir. 2007) ("Review [on a motion to dismiss] is generally limited to the contents of the complaint, but a court can consider a document on which the complaint relies if the document is central to the plaintiff's claim, and no party questions the authenticity of the document.").

[5] Plaintiffs define anaphylaxis as "an acute allergic reaction in which the airways constrict and patients struggle to breathe, blood pressure plummets and the heart may beat erratically and be unable to pump enough blood." ¶ 19. The defendants assert that the Mayo Clinic defines anaphylaxis as "a severe potentially life-threatening allergic reaction." Dkt. No. 47 at 5 n.3 (citing www.mayoclinic.com/health/anaphylaxis/DS00009).

[6] At oral argument, counsel for the plaintiffs referred to documentation purportedly showing that Affymax was aware of adverse events before August 8, 2012. However, these allegations were not included in the Consolidated Amended Complaint and were not properly before the Court. The plaintiffs may state these allegations in an amended complaint and the Court will review their materiality upon a renewed motion to dismiss.

November 8, 2012 "concealed the true economic prospects for Omontys by touting the future success of their relationship [with Fresenius] despite their knowledge that this relationship was in jeopardy":

> - [Defendant Orwin] "Fresenius is well underway in gaining clinical and operational experience with converting centers to Omontys and we believe that they are pleased with their overall experience so far. We look forward to potentially expanding our relationship with Fresenius for the longer term, broader contract in the future."
>
> (…)
>
> "Yes. And as to what they're particularly pleased about, I would say that they've remarked that they're pleased with the overall levels experienced,…. I will say that I'm very pleased with the customers that we've signed so far and with the potential that exists with them for significant uptake of Omontys."
>
> - [Defendant Knapp] "Fresenius to date is treating approximately 10,000 patients in this program. It is our expectation that they will continue to treat these patients under our existing supply agreement until this agreement ends or we execute a new agreement. . . . While there is no guarantee of expanded business, we continue to be very encouraged by the ongoing high level of interest and the overall rate of adoption. Over the coming months we expect to see many of the organizations that decided to pilot Omontys begin making their decision to move forward with full or close to full-scale conversions. . . . And I'm -- I feel very confident with what we've seen today that there won't be surprises at the end of this."
>
> (…)
>
> "Yes, this is Jeff. The -- it's a difficult question to answer, in part because it really varies from customer to customer and kind of their confidence in the drug, their just overall level and readiness to try new things. . . .As you might well know, some of these MDOs that we announced during our previous quarterly call have now been using it for a few months and I think are much more closer to making a decision and I think we'll see the benefits of that begin hopefully in this current quarter and certainly well into 2013." *Id.*

Opp. at 12 (citing ¶ 94).

The plaintiffs argue that, contrary to these statements, by November 8, 2012, the defendants knew based on the adverse event reports that Affymax's relationship with Fresenius

was in jeopardy that Fresnius's patients would likely not continue using Omontys. The plaintiffs also assert that the defendants misrepresented that Fresenius's customers had "converted" to Omontys while Fresenius was in fact assessing Omontys under a pilot program. The plaintiffs argue that the defendants' statements therefore "concealed the true economic prospects for Omontys." Opp. at 13.

According to the adverse event report, by November 8, 2012, the adverse events associated with Omontys and reported to the FDA included four deaths, three life-threatening events, and six other events requiring hospitalization. However, there is no factual allegation in the Consolidated Amended Complaint from which the Court can conclude that this degree of adverse events concerned Fresenius or otherwise jeopardized the Affymax-Fresenius relationship. On the contrary, three months later (February 13, 2013), when Fresenius announced that it would "pause expansion" of the Omontys pilot program, it acknowledged that it had "seen infrequent allergic reactions" to Omontys, including a "small number [that] have been serious." ¶ 108. Nonetheless, Fresenius recommended continued use of Omontys "as it has been providing effective anemia management." *Id*. The letter concluded by noting that "[a]s many of you have become quite comfortable with the medication, physicians and facilities that have been using Omontys who wish to continue prescribing it for new patients may choose to do so." *Id.*

The plaintiffs also argue that the defendants' proffered reason for seeking to change Omontys's label in October 2012—" to bring the language into our label in line with what exists for the other ESAs"—misled the market because the change was in fact sought in response to the serious adverse events reported in connection with Omontys.[7] Opp. at 14 (citing ¶ 94). In their opposition to the motion to dismiss, the plaintiffs identify the following two statements that allegedly misrepresented the reasons for the label change:

> - [Defendant Orwin] "Since launch thousands of patients have received Omontys in the post-marketing setting. As anticipated, this broad experience has been helpful in further informing real-

[7] The plaintiffs allege that the defendants' proffered reasoning for the label change was misleading; they do not allege that the new label was not, in fact, "in line with what exists for other ESAs."

> world use of the compound where infrequent, but sometimes serious, allergic reactions have been reported. To that end, we have proposed to the FDA, and have now updated our label to include, additional language regarding allergic reactions similar to that which is found in the existing labels for other ESAs. . . . And you're right; allergic reactions are mentioned, but they're not described in the same sort of wholesome way that they are in other ESAs, which is what led us, based on the experience and reported events, however infrequent, to look at that against what was in the label and decide that it made sense for us to bring the language into our label in line with what exists for the other ESAs. But, I'll let Anne-Marie speak specifically to that language."
>
> - [Defendant Duliege] "Now that we have thousands of patients, literally more than 10,000 patients, we felt it was prudent to update our label with the new information that we have accumulated as part of our pharmacovigilance severance program. Specifically, the report of allergic reactions that you mentioned in the label continues to be infrequent and a result on treatment. However, some of these reactions have been more serious. Some of the most recent reaction (inaudible) have been more serious and this is what we have included as information in the label to bring, as you said, John, our label in line with the existing label of other ESA. . . ."

Opp. at 14 (citing ¶ 94).

The defendants respond that the plaintiffs do not adequately allege that the statements were false because the defendants expressly stated that the label change was "prompted" by adverse events associated with Omontys. Dkt. No. 58 at 8. Specifically, defendant Orwin stated that the change was proposed after "infrequent, but sometimes serious, allergic reactions have been reported" and that Affymax was "led" to seek the change "based on the experience and reported events." Similarly, defendant Duliege stated that Affymax "felt it was prudent to update our label with new information that we have accumulated as part of our pharmacovigilance [surveillance] program" and that "[s]ome of the most recent reaction (inaudible) have been more serious." Affymax's Form 10-Q filed the same day likewise stated that "in November 2012, we revised the Omontys label to reflect adverse events from post-marketing spontaneous reports related to serious allergic reactions." Dkt. No. 49-9 at 34 (Kaban Decl., Ex. 9).

In light of the defendants' express disclosures that the label change was sought in response

to adverse events associated with Omontys, the Court agrees that the plaintiffs have not adequately alleged that the defendants falsely represented that the label change was sought to make the label consistent with other ESAs.

C. February 12, 2013 statements

The plaintiffs allege that the following February 12, 2013 statements by defendant Orwin during a conference call with investors misrepresented the safety and efficacy of Omontys:

> And the question was -- to provide a little bit more color on the Fresenius agreement, and what kind of information they think they will need in order to make a decision to go wider with Omontys. . . . Obviously, the safety and efficacy were established, and are typically best established in a comparative Phase 3 program. Fortunately for us, we had a very large program, and a very comprehensive evaluation of both safety and efficacy. But I think what they want to see is that they could replicate those kinds of results in their patient population, and that by treating 10,000 patients, and looking at patients as their own controls, but also looking at a matched cohort, they could learn a lot about the performance of Omontys in their patient population, before making a decision to utilize the product more broadly. . . . So, I think what they need to see is they need to see how the product performs in their population. Safety and efficacy, of course, always, but even more importantly, the dose efficiency in their population, since safety and efficacy were already fairly well-established.

Opp. at 13 (citing ¶ 106)[8]. The plaintiffs allege that these statements were false "because Defendants gave the market the impression that the real issue [with Fresenius's pilot assessment of Omontys] was dose efficacy and *not* safety and efficacy, when, by this point in time, Defendants were well aware that the injection of Omontys caused patients severe allergic reactions, resulting in hospitalization and death. Opp. at 13 (citing ¶ 106). The plaintiffs allege that "[o]ver 100 'adverse events' tied to the drug were reported to the FDA beginning in August 2012, including 7 deaths prior to this conference call." *Id.*

In response, the defendants argue that "Plaintiffs fail to establish that Affymax or any

[8] The plaintiffs' opposition brief erroneously identifies the February 12, 2013 statement in paragraph 106 of the Consolidated Amended Complaint as occurring on August 8, 2012. *See* Opp. at 13.

Defendant had a duty to disclose this information at the time of the statement."[9] Dkt. No. 58 at 5. Citing *Matrixx Initiatives, Inc. v. Siracusano,* 131 S. Ct. 1309, 1321 (2011), the defendants argue that the plaintiffs have failed to established "the 'something more' that is required before a drug manufacturer has an affirmative duty to disclose post-marketing SAEs." In support, the defendants argue that four "important, publicly disclosed facts" establish that the adverse events reported do not "var[y] materially (in frequency, severity or some other way) from what would have been expected based on the publicly disclosed information:"

- The "black box" warning for Omontys, reproduced above, states that "ESAs increase the risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access and tumor progression and recurrence;"
- The Omontys label "also made clear that, during the Phase 3 clinical trials, 22.8% of the patients receiving OMONTYS either died or suffered heart attacks or other serious adverse cardiovascular events;"
- In November 2012, Affymax publicly disclosed that it had modified the Omontys label as a result of serious post-marketing allergic reactions; and
- "the patient population for Omontys is an extremely sick one, suffering from Chronic Kidney Disease and related anemia and requiring dialysis" and the "average life span of all dialysis patients is sadly less than three years."

Dkt. No. 58 at 7.

a. Material falsity

The Court finds that the plaintiffs have adequately pleaded that defendant Orwin's statements on February 12, 2013 were misleading and misrepresented the safety of Omontys. Specifically, Orwin represented that the safety of Omontys was already "established," and therefore not a concern, when he stated that "[o]bviously, the safety and efficacy were established, and are typically best established in a comparative Phase 3 program. Fortunately for us, we had a very large program, and a very comprehensive evaluation of both safety and efficacy." ¶ 106.

[9] The Court rejects the defendants' assertion that this statement is not actionable because it "has little to do with the safety of Omontys; rather, it relates to the type of analysis of Omontys Affymax expected Fresenius, a major chain of dialysis centers, to undertake prior to expanding its use of the drug in additional centers." Dkt. No. 58 at 5. Even if the statement related to the type of analysis Affymax expected Fresenius to undertake, the question remains whether the statement misled the market about the safety of Omontys.

Orwin reinforced this impression when he stated that "I think what they [Fresenius] need to see is they need to see how the product performs in their population. Safety and efficacy, of course, always, *but even more importantly, the dose efficiency in their population, since safety and efficacy were already fairly well-established*." *Id*. (emphasis added). Given the serious adverse events reported to the FDA by this time, including, by the Court's count, nine deaths, four life-threatening events, and sixteen other events requiring hospitalization (Dkt. No. 53-1), the plaintiffs have adequately pleaded that these statements were false.

The Court further finds that the misrepresentation was material. In *Matrixx*, the Supreme Court held that "the materiality of adverse event reports cannot be reduced to a bright-line rule and a pharmaceutical manufacturer does not necessarily need to disclose all reports of adverse events. *Matrixx*, 131 S. Ct. at 1313-14, 1321. As the Court explained, "[a]dverse event reports are daily events in the pharmaceutical industry; in 2009, the FDA entered nearly 500,000 such reports into its reporting system" and "[t]he fact that a user of a drug has suffered an adverse event, standing alone, does not mean that the drug caused that event." *Id*. Rather than a bright-line rule, *Matrixx* instructs that the "question remains whether a *reasonable* investor would have viewed the nondisclosed information as having *significantly* altered the 'total mix' of information made available." *Id*. (emphasis in original and internal punctuation omitted) (citing *Basic*, 485 U.S. at 232). Accordingly, "the mere existence of reports of adverse events—which says nothing in and of itself about whether the drug is causing the adverse events—will not satisfy this [total mix of information] standard." *Id*. Rather, "something more is needed" to make the existence of reports of adverse events something which a reasonable investor would view as significantly altering the 'total mix' of information made available. *Id*. "[T]hat something more is not limited to statistical significance and can come from the source, content, and context of the [adverse event] reports. *Id*. (internal punctuation and citation omitted).

Notably, the *Matrixx* Court concluded that such a "contextual inquiry may reveal in some cases that reasonable investors would have viewed reports of adverse events as material even though the reports did not provide statistically significant evidence of a causal link. *Id*. In fact, the *Matrixx* Court concluded that it was substantially likely that a reasonable investor would have

viewed adverse event reports "about more than 10 patients who had lost their sense of smell after using Zicam" as having significantly altered the total mix of information made available. *Id*. at 1322-23.

Here, given that Omontys is Affymax's primary product, the Court further finds it substantially likely that a reasonable investor would have viewed over two dozen fatal, life-threatening and other adverse reactions to Omontys requiring hospitalization as significantly altering the "total mix" of information made available. *See, e.g.*, *id* at 1323 ("Assuming the complaint's allegations to be true, however, Matrixx had information indicating a significant risk to its leading revenue-generating product."). The Court accordingly finds the misrepresentations material, notwithstanding the four "important, publicly disclosed facts" identified by the defendants.

First, as the defendants recognized when they proposed a label change, the original "black box" warning did not warn of the serious allergic reactions seen in "real-world use" of Omontys. ¶ 94. It is one thing to note generally that a class of drugs, to which Omontys belongs, "increase[] the risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access and tumor progression and recurrence." It is a wholly different matter to disclose to the market that this particular drug has been linked to over two dozen deaths, life-threatening conditions and other adverse reactions requiring hospitalization.

Second, the defendants' reliance on the label's package insert is misguided.[10] As an initial matter, the package insert referenced the clinical trials in the context of demonstrating the *safety* of Omontys, not the dangers. *See* Dkt. No. 49-19 (Kaban Decl., Exs. 19 at § 14 ("The efficacy and safety of Omontys in patients with CKD on dialysis were demonstrated in two randomized, active-controlled, open-label, multi-center clinical studies . . . ."). Moreover, the defendants themselves

[10] The 14-page package insert states, in the portion cited by the defendants, "Studies 1 and 2 had a pre-specified, prospective, pooled analysis of a composite cardiovascular safety endpoint consisting of death, myocardial infarction, stroke, or serious adverse events of congestive heart failure, unstable angina or arrhythmia. In patients receiving Omontys, 22.8% experienced one of these events compared to 24.4% receiving epoetin (hazard ratio 0.95, 95% CI 0.77, 1.17)." Dkt. No. 49-19 (Kaban Decl., Exs. 19 at § 14).

note that "the average life span of all dialysis patients is sadly less than three years." Nothing in the package insert indicates that 22.8% of patients suffered "serious adverse cardiovascular events" as a result of the Omontys rather than as a result of their medical conditions. Indeed, if Omontys caused serious adverse reactions in over a quarter of its users it presumably would never have been approved by the FDA.

Third, while Affymax referred to "serious allergic reactions" when it discussed the proposed label change in November 2012, it emphasized that the reactions were "infrequent" and suggested that the reactions were in line with reactions to other ESAs. Whether or not that was true in November 2012, by February 12, 2013, the deaths, life-threatening reactions and other reactions requiring hospitalization had more than doubled. As stated above, the Court finds that a reasonable investor would have found that the adverse events reported by February 12, 2013 significantly altered the total mix of information available. By February 12, 2013, nine deaths, four life-threatening events, and sixteen other events requiring hospitalization had already been reported to the FDA. In the eleven days between February 12 and February 23, when Affymax announced a total recall of Omontys, five additional deaths, one life-threatening reaction and one other reaction requiring hospitalization had been reported to the FDA. If Affymax believed that these additional adverse events warranted a total recall of Omontys, it stands to reason that a reasonable investor would have found that the adverse events reported by February 12, 2013 significantly altered the total mix of available information.

Fourth, the assertion that the "average life span of all dialysis patients is sadly less than three years" has nothing to do with information linking use of Omontys to deaths and other serious reactions.

b. Scienter

The Court also finds that the plaintiffs have adequately alleged that Orwin acted with the requisite scienter when he made the misrepresentations discussed above. "[W]hen determining whether the pleaded facts give rise to a 'strong' inference of scienter [a required under the PSLRA], the court must take into account plausible opposing inferences." *Zucco Partners, LLC v. Digimarc Corp.*, 552 F.3d 981, 991 (9th Cir. 2009) (citation and internal punctuation omitted). "A

court must compare the malicious and innocent inferences cognizable from the facts pled in the complaint, and only allow the complaint to survive a motion to dismiss if the malicious inference is at least as compelling as any opposing innocent inference." *Id.* "Scienter may be established, by showing that the defendants knew their statements were false, or by showing that defendants were reckless as to the truth or falsity of their statements." *Gebhart v. S.E.C.*, 595 F.3d 1034, 1041 (9th Cir. 2010).

Here, as nearly all of the adverse events were reported to the FDA by Affymax there is no dispute that Affymax was aware of the adverse events. Plaintiffs have therefore adequately alleged that Orwin, Affymax's CEO, knew that his statements that the safety of Omontys had already been "established" were false, or that he was reckless regarding the truth or falsity of those statements. The interference that Orwin acted with the requisite knowledge or recklessness is more compelling than the interference that he did not. Scienter is therefore established.

c. Safe harbor for forward-looking statements

The PSLRA includes "safe harbor" provisions for forward-looking statements. "The provisions provide that a person shall not be liable for any 'forward-looking statement' that is 'identified' as such, and is accompanied 'by meaningful cautionary statements identifying important factors that could cause actual results to differ materially from those in the forward-looking statement.'" *No. 84 Employer-Teamster Joint Council Pension Trust Fund v. Am. W. Holding Corp.*, 320 F.3d 920, 936 (9th Cir. 2003) (citing 15 U.S.C. § 78u-5(c)(1)(A)(i)). A "forward-looking statement" is any statement regarding (1) financial projections, (2) plans and objectives of management for future operations, (3) future economic performance, or (4) the assumptions "underlying or related to" any of these issues. *Id.*

Orwin's February 12, 2013 statements are not forward looking because they relate to the "established" safety of Omontys, not projections, plans, objectives, future performance, or the assumptions underlying those issues. The safe harbor provisions therefore do not apply to these statements. *Cf. id.* at 397 ("the statements by America West do not constitute 'forward-looking' statements. Each is a disclosure of the fine imposed by the settlement agreement for past violations of FAA regulations and a description of the present effects of their imposition on the

company").

d. Loss causation

To state a Rule 10b–5 claim, "the plaintiff shall have the burden of proving that the act or omission of the defendant alleged to violate this chapter caused the loss for which the plaintiff seeks to recover damages." *In re Daou Sys.,* 411 F.3d at 1014 (citing 15 U.S.C. § 78u–4(b)(4)). "To establish loss causation plaintiffs must show that the stock price dropped after the truth was 'revealed.'" *In re LeapFrog Enterprises, Inc. Sec. Litig.*, 527 F. Supp. 2d 1033, 1040-41 (N.D. Cal. 2007). There is no dispute that the stock price of Affymax dropped after the adverse reactions associated with Omontys were revealed when Affymax announced the recall. The plaintiffs have therefore adequately pleaded loss causation regarding the February 12, 2013 statements.

D. Violation of Section 20(a)

To establish a prove a prima facie case violation of Section 20(a), plaintiff must prove: (1) a primary violation of federal securities laws and (2) that the defendant exercised actual power or control over the primary violator (Affymax). *Howard v. Everex Sys., Inc.*, 228 F.3d 1057, 1065 (9th Cir. 2000).

The defendants argue that the section 20(a) claim fails because the Consolidated Amended Complaint "offers only boilerplate allegations of control based on 'executive status.'" Dkt. No. 47 at 25 (citing ¶¶ 130-31). The Court agrees. The plaintiffs have not pleaded any factual allegations from which the Court can conclude that the individual defendants "exercised actual power or control over the primary violator," notwithstanding their executive status. *See, e.g.,Paracor Fin., Inc. v. Gen. Elec. Capital Corp.,* 96 F.3d 1151, 1163 (9th Cir.1996) ("The fact that a person is a CEO or other high-ranking officer within a company does not create a presumption that he or she is a 'controlling person.'").

CONCLUSION

The defendants' motion to dismiss is GRANTED IN PART and DENIED IN PART. The defendants' motion is GRANTED regarding Count I (violations of Section 10(b) and SEC Rule 10b–5) against individual defendants Cross, Duliege, and Knapp. The motion is GRANTED

regarding Count I (violations of Section 10(b) and SEC Rule 10b–5) against Affymax and individual defendant Orwin based on the August 2012 and November 2012 statements. The motion is GRANTED regarding Count II (violation of Section 20(a)) against all defendants. The Consolidated Amended Complaint is DISMISSED WITHOUT PREJUDICE with regard to the claims identified above. Any amended complaint shall be filed within 30 days of this Order.

The motion is DENIED regarding Count I (violations of Section 10(b) and SEC Rule 10b–5) against Affymax and individual defendant Orwin based only on the February 12, 2013 statements regarding the safety of Omontys.

IT IS SO ORDERED.

Dated: January 21, 2014

WILLIAM H. ORRICK
United States District Judge

United States District Court
Northern District of California