IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF NORTH CAROLINA

JOHNATHAN HIRTENSTEIN, Individually and on Behalf of All Others Similarly Situated,	)	
Plaintiff,	)	
v.	)	16cv1303
CEMPRA, INC., PRABHAVATHI B. FERNANDES, MARK W. HAHN, DAVID W. OLDACH,	)	
Defendants.	)	

MEMORANDUM OPINION AND ORDER

THOMAS D. SCHROEDER, Chief District Judge.

This is a putative federal securities class action on behalf of all persons[1] who owned common stock of the biopharmaceutical company, Cempra, Inc. ("Cempra"), between July 7, 2015, and November 4, 2016 (the "class period"). In their amended complaint (Doc. 46), Plaintiffs seek recovery for stock losses under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 ("Exchange Act"), as amended by the Private Securities Litigation Reform Act of 1995 ("PSLRA") and Rule 10-b5 promulgated thereunder, 17 C.F.R. § 240.10b-5. The Defendants are Cempra; Prabhavathi B. Fernandes, Ph.D., Cempra's then-chief executive officer ("CEO"), president, and member of the board of directors from the company's founding

[1] The lead Plaintiffs are Charles Craig Janies, Robert F. Colwell Jr., and Jennifer Colwell. (Doc. 40.) However, the entire putative Plaintiff class (including the lead Plaintiffs) will be referred to simply as "Plaintiffs."

in November 2005 until December 12, 2016 (Doc. 46 ¶ 22); Mark W. Hahn, Cempra's executive vice president and chief financial officer ("CFO") during the class period (Doc. 46 ¶ 25); and David W. Oldach, M.D., Cempra's chief medical officer, during the class period (together, "Defendants"). (Doc. 46 ¶ 28.) Before the court is Defendants' motion to dismiss the amended complaint for failure to state a claim pursuant to Federal Rule of Civil Procedure 12(b)(6). (Doc. 49.) Plaintiffs oppose the motion and also filed a motion to strike seven exhibits contained in the appendix to Defendants' motion (Doc. 56), which the court recently denied without opinion. (Doc. 65.)

For the reasons set forth below, Defendants' motion to dismiss will be granted. In addition, the court will address Plaintiffs' motion to strike and explain which exhibits the court considered.

I. BACKGROUND

The facts alleged in the amended complaint, which are accepted as true and viewed in the light most favorable to Plaintiffs for purposes of the present motion, and the contents of other documents which the court may consider in deciding the motion to dismiss, show the following:

Cempra is a biopharmaceutical company that develops antibiotics for the treatment of infectious diseases. (Doc. 46 ¶ 4.) Cempra's lead product, solithromycin, is being developed for the treatment of community-acquired bacterial pneumonia

("CABP"), as well as other indications. (Id.) During the class period, solithromycin was in the late stages of its clinical development for the treatment of CABP, the seventh leading cause of death and the leading cause of death due to infection in the United States, with a reported five to ten million cases per year. (Id. ¶¶ 5-6, 36.) In August 2015, the Food and Drug Administration ("FDA") granted the drug "Fast Track" designation for the short-term (five to seven day) treatment of CABP with intravenous ("IV") and oral capsules under the FDA's Fast Track program, which is designed to facilitate the development of new drugs that have the potential to address unmet medical needs and are designed to treat serious or life-threatening conditions. (Id. ¶ 6.) On May 1, 2016, Cempra completed and submitted its New Drug Applications ("NDAs") for solithromycin to the FDA for the treatment of CABP, which qualified for eight-month priority review under the Prescription User Drug Fee Act. (Id.)

Cempra generated little revenue during the class period and depended largely on raising capital through public stock offerings to sustain its business operations and complete the clinical development of solithromycin. (Id. ¶¶ 91-92.) During this period, Cempra conducted two stock offerings in order to raise capital to fund the company's operations for combined net proceeds of approximately $170 million. (Id. ¶¶ 94-95.) In January 2016, Cempra sold 4.17 million shares of common stock at a price of

$24.00 per share, resulting in net proceeds of $94 million. (Id. ¶ 94.) Between May 2016 and July 2016, Cempra sold an additional 4 million shares of common stock during an "at-the-market" offering for net proceeds of $75.1 million. (Id. ¶ 95.)

In their amended complaint, Plaintiffs allege that Defendants made false and misleading statements regarding the safety profile of the drug and failed to adequately disclose instances of drug-induced liver injury ("DILI") observed in clinical trials prior to and during the class period. (Id. ¶¶ 58-65, 67, 69-77.) According to the amended complaint, these false and misleading statements caused Cempra's common stock to trade at artificially high prices, so that when the risks were revealed by the FDA at the end of the class period, Plaintiffs suffered losses from the subsequent stock price decline. (Id. ¶¶ 12, 96-102.)

A. Solithromycin's Clinical Development Program

Solithromycin belongs to a class of antibiotics known as macrolides that are frequently prescribed to treat respiratory tract infections. (Id. ¶ 34.) Due to the serious side effects associated with another class of antibiotics known as fluoroquinolones, macrolides are the preferred first-line treatment for CABP. (Id. ¶ 35.) Solithromycin is a fourth-generation fluoroketolide macrolide-class antibiotic, which was designed to address the growing problem of antibiotic resistance among the currently-approved class of macrolides approved to treat

CABP. (Id. ¶ 5.) During the class period, analysts estimated that Cempra would earn up to $2 billion a year in sales if solithromycin were approved by the FDA. (Id. ¶ 36.)

The potential risk of DILI among this particular class of macrolides was well known to both the company and potential investors prior to the class period. In 2004, the FDA approved the drug telithromycin, known by the brand name Ketek, a third-generation macrolide and the first ketolide antibiotic. (Id. ¶ 37.) Shortly after its approval, Ketek was found to cause severe adverse effects in patients, including reversible visual disturbances, loss of consciousness, myasthenia gravis (a neurological disorder associated with improper muscle regulation), and severe liver injury that resulted in liver failure, liver transplant, and death. (Id.) These safety issues led to two congressional investigations into the FDA's approval of the drug and accusations that the FDA stifled concerns over the drug raised by its own reviewers and ignored suspicious clinical data that were later determined to be fraudulent. (Id. ¶ 37.) Ultimately, the FDA revoked Ketek's approval for treatment for all indications other than CABP and required a "black box" warning label highlighting the risk of potential liver injury. (Id.)

Cempra recognized that the approval of solithromycin depended on the company's ability to differentiate the drug from Ketek. (Id. ¶¶ 38, 69.) As a fluoroketolide, solithromycin has a nearly

identical chemical structure to Ketek, except it includes an aminophenyl group with a 1, 2, 3-triazole ring as opposed to the pyridine attached to an imidazole ring in Ketek. (Id. ¶ 38.) Cempra claimed that removing the pyridine moiety would prevent the drug from inhibiting the body's nicotinic acetylcholine receptors, which purportedly caused the severe adverse effects observed with Ketek. (Id. ¶ 38, 69.)

Prior to obtaining marketing approval, a developmental drug must undergo a series of pre-clinical and clinical trials to evaluate its safety and effectiveness for a particular treatment. (Id. ¶¶ 39-43.) Clinical trials are conducted in three distinct phases of clinical investigation in humans, identified as Phase 1, Phase 2, and Phase 3. (Id. ¶¶ 39-43); see 21 C.F.R. § 312.21. Each phase of clinical testing is designed to gather information on the safety and efficacy of the drug in human subjects. (Doc. 46 ¶ 43.) Phase 1 trials "are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness." (Id. ¶ 40 (quoting 21 C.F.R. § 312.21(a)).) Phase 2 trials are exploratory studies designed to address efficacy and to determine common short-term side effects and risks. (Doc. 46 ¶ 41); 21 C.F.R. § 312.21(b). Phase 3 trials are expanded studies to address the efficacy and safety of the drug, which generally involve hundreds of, and sometimes several

thousand, subjects. (Doc. 46 ¶ 43); 21 C.F.R. § 312.21(c). FDA rules and regulations require that a sponsor promptly report all drug-related serious adverse events ("SAEs"), including a single occurrence that is either uncommon or strongly associated with drug exposure, such as hepatic (i.e., liver) injury. (Doc. 46 ¶ 57 (citing 21 C.F.R. § 312.32(c)(1)(i)(A))); 21 C.F.R. § 312.32(c)(1)(i) (requiring sponsor to file a report within fifteen days after a determination by the sponsor that the information qualifies for reporting as a "[s]erious and unexpected suspected adverse reaction").

Cempra's development of solithromycin for treatment of CABP involved a proposed short-term course of five to seven days, depending on the mode of administration. (Doc. 51-15 at 5, 62.) Prior to the class period, Cempra completed Phase 1 and Phase 2 trials for the oral and IV dosages of solithromycin to treat CABP, which Cempra represented demonstrated a promising safety and tolerability profile for those dosages to treat CABP. (Doc. 46 ¶ 44.) Cempra disclosed in its SEC filings that the FDA placed a partial clinical hold on a Phase 1 trial for oral solithromycin and later converted it to a full clinical hold, citing concerns that the drug may have similar toxicity issues as Ketek. (Id. ¶ 45.) Cempra was eventually allowed to proceed with the trial, which it successfully completed. (Id.) The company assured investors that it had addressed the FDA's concerns but noted that

the clinical hold indicated that the FDA may subject its NDAs to heightened scrutiny in light of the Ketek experience. (Id.)

The Phase 3 clinical trial of solithromycin taken orally for the treatment of CABP ("Solitaire-Oral trial") involved 860 subjects and was conducted between December 2012 and October 2014, while the Phase 3 clinical trial for IV treatment ("Solitaire-IV trial") involved 863 subjects and was conducted between November 2013 and September 2015. (Id. ¶ 50-51.) The Phase 3 CABP clinical trials evaluated the safety and efficacy of oral and IV solithromycin compared to moxifloxacin, a fluoroquinolone considered to be the most potent drug for CABP. (Id. ¶ 50.) Both trials had the primary objective and endpoint of demonstrating statistical non-inferiority compared to moxifloxacin, while the secondary objectives included demonstrating the safety and tolerability of the drug compared to moxifloxacin. (Id.)

Cempra reported that both of the trials met their primary and secondary objectives of demonstrating solithromycin's statistical non-inferiority as compared to moxifloxacin. (Id. ¶¶ 52, 54.) Cempra disclosed that it observed in some patients elevation of the liver enzyme alanine aminotransferase ("ALT") but stated that these elevations were generally asymptomatic and reversible. (Id. ¶¶ 52, 55.) Furthermore, the company reported that no patient in either trial met the criteria of "Hy's Law," a standard used by the FDA to predict the risk of severe DILI. (Id. ¶¶ 53, 55.) To

meet Hy's Law, a patient must have an elevation of ALT or the liver enzyme aspartate aminotransferase ("AST") greater than three times the upper limit of normal ("ULN") in combination with impaired hepatic function (defined as an elevation of bilirubin (a liver byproduct) greater than two times ULN), without any evidence of an alternative cause of hepatic injury. (Id. ¶ 53; see Doc. 51-16 at 154-55 (describing Hy's Law criteria).) "A Hy's Law case predicts severe liver injury at a rate of at least 1/10 of the rate of Hy's Law cases," such that 1 case in 1,000 suggests severe injury at a rate of 1 in 10,000. (Doc. 46 ¶ 53.) However, a study of at least 3,000 patients is needed to accurately predict that no Hy's Law cases will result from a particular treatment. (Id. ¶ 53.) According to an FDA guidance document, the failure to detect a Hy's Law case does not imply that a drug with aminotransferase elevations is free from risk of severe DILI. (Id.)

In September 2015, Cempra initiated Phase 2 clinical trials to evaluate the effectiveness of solithromycin as a treatment for chronic obstructive pulmonary disease ("COPD") and non-alcoholic steatohepatitis ("NASH").[2] (Id. ¶ 48.) The company enrolled four patients in the Phase 2 COPD trial, where patients received a daily

[2] Nonalcoholic steatohepatitis is a syndrome in nonalcoholics causing liver damage that is histologically indistinguishable from alcoholic hepatitis. Merck Manual Professional: Nonalcoholic Steatohepatitis (NASH), available at https://www.merckmanuals.com/professional/hepatic-and-biliary-disorders/approach-to-the-patient-with-liver-disease/nonalcoholic-steatohepatitis-nash (last visited Oct. 24, 2018).

oral dose of 400 mg of solithromycin for twenty-eight days. (Id.; Doc. 51-11 at 15, 25, 29.) During the class period and shortly after the trial was initiated, three out of the four patients in the COPD group experienced "patterns of DILI," including ALT elevations in excess of four times ULN. (Doc. 46 ¶ 48; Doc. 51-11 at 15-17, 25-26.) After receiving twenty-three days of treatment, one patient was diagnosed with clinical cholestatic hepatitis with jaundice[3] and was discontinued from treatment. (Doc. 46 ¶ 48; Doc. 51-11 at 15-17.)[4] In that case, the patient's liver test results did not return to normal until twenty-nine days after being discontinued from treatment. (Doc. 51-11 at 16.) While the two other patients experienced asymptomatic ALT elevations (Id. at 25-26), one of these patients also continued to

[3] Cholestasis is a condition involving the reduction or stoppage of bile flow. Merck Manual Consumer: Cholestasis, available at https://www.merckmanuals.com/home/liver-and-gallbladder-disorders/manifestations-of-liver-disease/cholestasis#v758789 (last visited Oct. 24, 2018). Jaundice is a yellow discoloration of the skin caused by hyperbilirubinemia, a condition that occurs when there is too much bilirubin in the blood. Merck Manual Consumer: Jaundice in Adults, available at https://www.merckmanuals.com/home/liver-and-gallbladder-disorders/manifestations-of-liver-disease/jaundice-in-adults (last visited Oct. 24, 2018).

[4] In that case, a 69-year-old man received 400 mg of solithromycin for twenty-three days of a planned twenty-eight day course of treatment. (Doc. 51-11 at 15-17.) At Day 15, elevations of ALT and other aminotransferase enzymes were observed without any associated change in bilirubin. (Doc. 51-11 at 16.) On Day 23, further increases of ALT to 11.9 times ULN were observed, as well as a concurrent increase in bilirubin (2.2 times ULN) and the onset of eosinophilia (increase in white blood cells, indicative of infection or allergic reaction). (Doc. 51-11 at 16-17.) At this point, the patient was discontinued from treatment. (Doc. 51-11 at 16-17.)

show signs of liver injury in the form of increasing ALT elevations even after treatment was discontinued. (Doc. 46 ¶ 48; Doc. 51-11 at 25-26.) In light of these developments, Cempra reduced the dosage in the ongoing Phase 2 NASH trial to an oral dose of 200 mg of solithromycin daily for seven days, followed by 200 mg oral doses three times a week for a total course of thirteen weeks of treatment. (Doc. 46 ¶ 49; Doc. 51-12 at 3.) Cempra reported this amendment in the NASH protocol at the website ClinicalTrials.gov and to investors during the company's September 30, 2016 conference call. (Doc. 46 ¶ 49.)

B. Material Misrepresentations and Omissions

During the class period, Defendants made public statements regarding the clinical results from the Phase 3 CABP trials as well as the overall safety profile of the drug. In their amended complaint, Plaintiffs challenge several of these statements, as set forth below, as material misrepresentations and omissions.

1. July 7, 2015 Press Release

On July 7, 2015, Cempra issued a press release announcing that it had completed enrollment for the Solitaire-IV Phase 3 trial. (Doc. 46 ¶ 58.) The press release contained a quote from Fernandes, which stated in relevant part: "We remain on track to announce the top line results before year-end 2015. We believe that these results, coupled with our successful Solitaire Oral results, which we announced in January, will provide a compelling

clinical data set in our solithromycin NDA submission, expected in 2016." (Id.)[5]

2. October 16, 2015 Press Release

On October 16, 2015, Cempra issued a press release announcing positive topline results from its Solitaire-IV trial. (Id. ¶ 54.) The company reported that the trial met the primary and secondary objectives of statistical non-inferiority compared to moxifloxacin. (Id.) With regard to safety, Cempra disclosed that there were fatalities that occurred with similar frequency in both arms of the study due to pneumonia or its complications during the study period. (Id.) The company noted that more treatment-related adverse events were observed with solithromycin (34.3%) than moxifloxacin (13.1%), but stated that this difference was largely attributable to infusion site reactions of mild and moderate severity. (Id.) Cempra reported that 2.1% of IV solithromycin patients discontinued the drug due to adverse infusion-related events and noted that infusion site pain is a common side effect of intravenous macrolides but is not generally noted with fluoroquinolones such as moxifloxacin. (Id.) Cempra also reported that SAEs occurred in 6.9% of solithromycin patients and 5.4% of moxifloxacin patients, but only three SAEs were considered drug-

[5] Plaintiffs emphasize large portions of text throughout their amended complaint. Emphasis from the amended complaint is omitted throughout the remainder of this opinion unless otherwise noted.

related. (Doc. 51-5 at 7; see Doc. 46 ¶ 55.)[6] Only two of the three SAEs were associated with solithromycin; all were allergic reactions. (Doc. 51-5 at 7.) Cempra also noted that ALT elevations were observed in both treatment arms, reporting that Grade 3 ALT elevations (explained as ALT elevations of between 3 to 8 times ULN) were observed in 8.2% of solithromycin patients and 3.4% of moxifloxacin patients, and Grade 4 ALT elevations (explained as ALT elevations greater than 8 times ULN) were observed in 0.7% of solithromycin patients and 0.5% of moxifloxacin patients. (Id.) Cempra reported that "[t]reatment emergent ALT elevations were generally asymptomatic, reversible, and not associated with increased bilirubin" and "[n]o solithromycin patient met Hy's Law criteria of concurrent ALT and bilirubin elevations post-baseline." (Doc. 46 ¶ 59 (emphasis omitted).)

3. October 16, 2015 Conference Call

On October 16, 2015, Cempra held a conference call to discuss the topline results from the Solitaire Oral-IV trial. (Id. ¶ 60.) In response to a question from an analyst regarding whether any symptomatic ALT elevations were observed during the course of the clinical trial, Oldach provided the following response:

> We've gone through all of these cases and looked carefully at them. There were a few patients, for

[6] The amended complaint alleges that Cempra reported this information in an October 22, 2015 press release. (Doc. 46 ¶ 55). The same information was also included in Cempra's Form 8-K filing with the SEC. (Doc. 51-5 at 6-7.)

> instance, that had infusion pain but no symptoms relatable to right upper quadrant or liver pain. But we want to be very careful about that. So before we say categorically absolutely none, we will be going back through their cases two more times before we declare that. But generally, no symptoms, no evidence of hepatic injury that was symptomatic or with bilirubin elevation. So that was just a cautionary statement on our part just so we could be absolutely certain. But our impression is none.

(Id.) Fernandes further noted, "And remember, the [data management committee][7] has seen each of these, you know, any significant ALT elevation, during the study and did not do anything." (Id. (alteration in original).)

4. October 22, 2015 Earnings Call

On October 22, 2015, Cempra held its third quarter earnings call. (Id. ¶ 61.) During her opening remarks, Fernandes made the following statement:

> As one would expect, in both Phase 3 trials, these we saw some Grade 3 ALT elevation, and to a much lesser extent some Grade 4 ALT elevations. In almost all cases of ALT elevations among solithromycin recipients, these elevations occurred early, peaked on day four – remember, it is day one through seven – and their levels were typically declining by day seven, despite continued study drug dosing. These ALT increases were asymptomatic and resolved post treatment.
>
> No solithromycin recipient met Hy's Law criteria, defined as simultaneous ALT and bilirubin elevation – another liver factor – following dosing. There was no evidence of drug hypersensitivity reaction. For instance, one involving a combination of rash, fever, and ALT elevation, and other symptoms.

[7] This appears to be the "independent data monitoring committee," referenced in the FDA Briefing Document, that "monitor[ed] safety throughout the studies." (Doc. 51-15 at 20.)

(Id. ¶ 61.) Fernandes made additional statements during the earnings call that ALT elevations were reversible. (Id. ¶ 62 ("Now with the IV, yes, we saw a few more ALT [treat]. But again, they are all reversible." (alteration in original)); Id. ¶ 63 ("[M]ost of those ALTs came down during treatment. Many of them were down in two weeks. All of them were down in the three-week visit, the short-term follow-up visit. Okay. So there is no issue with that. So they all disappeared. That is why they are called reversible.").) David Moore, Cempra's executive vice president and chief commercial officer, also reiterated that "we have not seen hepatic dysfunction in any patient due to the study drug in our Phase 3 program." (Id. ¶ 62.)

When questioned by an analyst regarding the potential for liver toxicity, Fernandes responded as follows: "But let me again say: there is no liver toxicity. There is no hepatic toxicity. This was reversible ALT elevation and there has been no hepatic toxicity. So there is no evaluation of hepatic toxicity because we don't have any." (Id. ¶ 64.) She later emphasized that "[Ketek] ALT and our ALT have nothing to do with hepatic toxicity." (Id. ¶ 65 (alteration in original).)[8]

[8] Fernandes added, "ALT is not related to hepatic toxicity. And it is found with all drugs, including things like amoxicillin, augmentin, which we are actually giving tons of to our children today." (Id.)

5. November 19, 2015 Jefferies Global Healthcare Conference

On November 19, 2015, Cempra participated in the Jefferies Global Healthcare Conference. (Id. ¶ 67.) Fernandes spoke at the conference and made the following statements regarding the Phase 3 CABP trials in her opening remarks:

> Now when we announced some of the effects of the drug, we did mention liver enzyme increases. ALT increases. And you can see that with the intravenous, we had slightly more ALTs than in the oral, which is listed in the bottom, the Grade 3 and the Grade 4.
>
> [. . .]
>
> Now the most important things, none of them had any symptoms. They were all reversible, and there was no bilirubin increase in any of these patients. And that is a key point. If you are on this drug, if you don't measure ALTs, you won't even know because there's no symptoms at all, in these patients, and they are all reversible.
>
> [. . .]
>
> We recorded every single thing the patient said. If there was redness, if there was itching, if there was tingling, anything minor was recorded. And we are an honest company; we put out all the data.

(Id.)

6. January 7, 2016 Prospectus

On January 7, 2016, Cempra filed a prospectus with the Securities and Exchange Commission ("SEC") in connection with a stock offering. (Id. ¶ 69.) The prospectus stated in relevant part:

> Through ongoing research, we have developed multiple

> ways to differentiate solithromycin from Ketek. Our research suggests these side effects may be caused by the pyridine moiety, which forms a part of the structure of Ketek. We have demonstrated that pyridine inhibits the action of nicotinic acid acetylcholine receptors that could result in the side effects caused by Ketek.

(Id.) While the surrounding context of the prospectus is not referenced in Plaintiffs' amended complaint, this statement appeared in a section discussing several potential risks associated with the development and commercialization of solithromycin. (Doc. 51-7 at 21-24.)[9] The challenged statement in the prospectus appeared within a section entitled: "We might not successfully differentiate solithromycin from telithromycin (Ketek), a macrolide found to cause severe side effects." (Id. at 23.) Notably, the amended complaint omits the final two sentences of the paragraph, which states: "If our research is proven to be incorrect or if solithromycin demonstrates similar side effects, the FDA might not approve solithromycin, or if already approved, might withdraw approval, require us to conduct additional clinical trials or require warnings on product labeling, which would significantly harm our ability to generate revenues from solithromycin." (Id. at 24.) The prospectus goes on to caution that "[b]ecause of the Ketek experience, the macrolide class is likely to be carefully scrutinized by the FDA." (Id.)

[9] For the reasons discussed later in this opinion, the court finds that several documents, including the January 7, 2016 prospectus, may properly be considered for purposes of Cempra's motion.

In addition, the prospectus highlights several additional risks to investors. Acknowledging that the company had no products that had been approved for sale, the prospectus emphasized that "[o]ur near-term prospects are substantially dependent on our ability to develop and commercialize solithromycin . . . ." (Id. at 21.) The prospectus further noted "[w]e believe we have completed all the clinical trials necessary to support the NDA for solithromycin for CABP and have a sufficient database of both efficacy and safety. However, the FDA may disagree with our assessment and may require additional clinical data to support approval." (Id. at 22.) In addition, the prospectus also stated that "[t]he results of either of our ongoing studies of the effectiveness of solithromycin as a treatment for NASH and COPD or any other study or trial involving solithromycin, if negative, could have an adverse effect on FDA and other regulatory approval of solithromycin as a treatment for CABP as well our commercialization efforts for solithromycin and market acceptance of the same." (Id. at 24.)

7. January 14, 2016 J.P. Morgan Healthcare Conference

On January 14, 2016, Cempra participated in the J.P. Morgan Healthcare Conference. (Doc. 46 ¶ 70.) Defendant Fernandes spoke at the conference and made the following statements in her opening remarks with regard to the clinical results from the Phase 3 CABP trials:

> We would also like to show you some of the ALT results. This is the liver enzyme results. Macrolides that are excreted by the liver and are known to cause liver enzyme increases. You see the label from azithromycin, which is over there, that you see ALT increases. This does not give you the idea that this is hepatic toxic [sic]. To have hepatic toxicity, you have to have bilirubin increases, which causes — which shows damage to the liver cells. So, ALT increases plus bilirubin equals what is called [Hy's Law] and that means liver toxicity. We did not have any case in those numbers which you see there, which had both ALTs as well as bilirubin, not one in those entire two studies.
>
> So, we did not believe we had any side effects of liver toxicity in these particular patients.
>
> I will also point out that they were asymptomatic, so there was nobody who would actually — know in real life during treatment that there was even any ALT increase. What is even more important is the gra[ph] at the very bottom. Even while on study drug, the ALT levels came down. So, if it was toxic, it would not come down, obviously it would stay up. So the liver learned to handle the drug, and then it came down. So we are very pleased with the safety of this as well as the efficacy.

(Id. (alterations in original).)

8. April 13, 2016 Needham Healthcare Conference

On April 13, 2016, Fernandes spoke at the Needham Healthcare conference. (Id. ¶ 71.) While noting that the drug would be subject to review by the FDA Advisory Committee due to the prior Ketek experience, she stated that "we have very clearly differentiated solithromycin from Ketek based on its mechanism of action and the reason for its adverse event." (Id.) She further stated that "[w]e have also shown the benefit of our drug used in monotherapy up against moxifloxacin, which is not a very safe drug,

and we have a very good fully safety [sic] package for that. The benefit is obvious, that it needs to have an outpatient as well as hospital drug." (Id.)

9. May 2, 2016 Earnings Call

During a May 2, 2016 earnings call, Fernandes made the following statement during a question-and-answer session with a securities analyst regarding potential "sources of controversy" before the FDA Advisory Committee:

> So we have worked very hard, together with safety experts, people who have consulted in the past with other companies, with the FDA and so on, very aware of liver safety. We do believe that on the ketek issue, we are over that hurdle, because we have shown the mechanisms as to why ketek was toxic.
>
> However, we do have ALT. So our job is to make a comparison to the older macrolides like [erythromycin], [azithromycin], clarithromycin. All of them do have ALT increases. We have that too. But you must remember that every one of them came down, some of them even — most of them even while on study drug. So we don't believe there is a big concern.

(Doc. 46. ¶ 72.)

10. September 12, 2016 Morgan Stanley Global Healthcare Conference

On September 12, 2016, Cempra participated in the Morgan Stanley Global Healthcare conference. (Id. ¶ 73.) During a question-and-answer session at the conference, Hahn made the following statement regarding the safety profile of solithromycin: "What we see is what you expect from a macrolide: you expect ALTs to go up in the early days, and come back down. Even in continued

therapy, we saw ALT levels coming right back down." (Id. ¶ 73.)

In response to a question from an analyst about how solithromycin differs from Ketek, Hahn responded:

> We've done a lot of work characterizing what caused those issues [with Ketek]. And, mechanistically, we looked at the molecule and saw what we think the bad actor is, and we did a lot of work to identify what that bad actor caused. And it was visual disturbance; it was exacerbation of myasthenia gravis; and it was liver toxicity.
>
> All three were related to this same one bad actor called a pyridine. So if we look at solithromycin, we see that solithromycin doesn't have that bad actor on the molecule. It's a completely different structure. And in all of our trials — we have exposed over 2,000 patients and subjects over the years, and nobody has had any of those same types of issues that the folks had experienced with Ketek. So we expect the questions will come up in the [Advisory Committee meeting], but we don't — we think that we've adequately addressed those questions and we don't think there will be any issues.

(Id. ¶ 74.) When questioned during the same conference call regarding how the FDA Advisory Committee panel will view the ALT elevations observed during the clinical trials, Hahn responded:

> We think they will ask questions about those, most certainly. But we've gone through exhaustive work internally. We've hired independent consultants and advisors. We've got an advisory, or a consulting firm that brought in panels of experts and have gone through the data. What we see is what you expect from a macrolide: you expect ALTs to go up in the early days, and come back down. Even on continued therapy, we saw the ALT levels coming right back down.

(Id.)

11. September 30, 2016 Conference Call

During a conference call on September 30, 2016, Cempra

disclosed the interim results from the Phase 2 NASH trials. (Id. ¶¶ 49, 76.) With regard to the dosing change that occurred in the trial, Defendant Oldach stated:

> When dosing solithromycin for longer durations, we've observed ALT elevation and since one of the goals of this trial [is] to determine the optimal regimen for longer treatment period, we adjusted the dose to 200 milligrams daily for one week, followed by 200 milligrams three times a week. The lower dose is supported by the mouse model and human PK[10] data that suggest it might be efficacious. We hope to confirm this dosing regimen in the study and we are very excited with the therapeutic effects and safety profile we have seen thus far.

(Id. ¶ 76.) Cempra did disclose that one patient in the Phase 2 NASH study experienced asymptomatic ALT elevations of 4.5 times ULN after receiving an oral dose of 200 mg of solithromycin for twenty-eight days. (Doc. 51-12 at 4-5.) Cempra reported that this patient was briefly discontinued from the study, but he successfully completed the study and his ALT levels returned to normal upon receiving the reduced dosing of 200 mg of solithromycin three times per week. (Id. at 5.)

When questioned whether the dosage change was made after a patient in the NASH trial was temporarily discontinued from treatment due to ALT elevations, Fernandes responded:

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[10] Pharmacokinetics, meaning "the movement of [a] drug into, through, and out of the body — the time course of its absorption, bioavailability, distribution, metabolism, and excretion." Merck Manuals Professional: Overview of Pharmacokinetics, available at https://www.merckmanuals.com/professional/clinical-pharmacology/pharmacokinetics/overview-of-pharmacokinetics (last visited Oct. 24, 2018).

> No, we had already lowered the dose at that time. Because if you look at the modeling, the long-term dosage and our experience with it is saying that — that was more of a redundant study to show that one would be a long-term chronic dose and if you look at azithromycin, for instance with CF, in multiple doses for many weeks. It's dosed three times a week so it's not unusual for macrolides, which happen to linger intercellularly for long periods of time. That you should reduce the dose of chronic dosing.

(Doc. 46 ¶ 76.) When later questioned during the conference call regarding the amendment to the protocol, Fernandes stated that "[t]he driver [behind the decision to alter dosages] was efficacy as well as safety." (Doc. 51-12 at 9.) She also noted that "I will remind you that in our CABP trial, which we presented to you, we have seen ALT increases even during the five to seven days of treatment which comes back." (Doc. 46 ¶ 75.)

During the conference call, Fernandes made various statements touting the overall safety profile of the drug. With regard to the NASH trial, she stated:

> [W]e also wanted to show that solithromycin, of course, we believe it, is incredibly safe, even in the liver and this is the last straw which breaks the camel's back, right? So we wanted to test it in the worst case situation and tested it and we are now very comfortable with the drug.
>
> [. . .]
>
> "[A]ll of the safety data — every human exposure is submitted as part of the law. We have submitted data until at the end of August and all data comes in, every part will be exposed. And we're very pleased with the safety of the drug. And it will provide a lot of benefits to patients in many categories now and so we're

> very pleased with it. We're proud to be able to submit this data.

(Id. ¶ 76.) At no point did Cempra directly reference the Phase 2 COPD trial or disclose any additional information regarding the adverse events observed during the Phase 2 COPD trial, apart from noting that ALT elevations had been observed when dosing solithromycin for longer durations. (Id. ¶¶ 49, 76; see Doc. 51-12 at 3.))

12. October 27, 2016 Earnings Conference Call

On October 27, 2016, Cempra conducted its third quarter 2016 earnings conference call. (Doc. 46 ¶ 77.) In response to a question from a securities analyst regarding potential concerns at the FDA arising from the prior Ketek experience, Fernandes made the following statement:

> So, we started this molecule, Ketek happened, and from day one we had to differentiate it. So, we showed that the pyridine on [telithromycin] was responsible for all those bad adverse events, including the hepatotoxicity.
>
> And the visual effect was really the canary in the coalmine because they saw in all their clinical trials and the same receptor in the eye and the same receptor in the liver, which has caused those effects. And we now have to differentiate the ALT increases that have shown to occur with all macrolides and all antibiotics because of the large dose and show what that is a result of. That is not a Ketek effect. And so we have spent a lot of time doing that sort of work. And our clinical trial data really shows that this has had a great deal of efficacy and all of those ALTs were reversible and asymptomatic, as you remember.

(Id. ¶ 77 (alteration in original).)

C. Revelation of Negative Information Regarding Solithromycin

On November 2, 2016, the FDA Antimicrobial Drugs Advisory Committee released a briefing document ("FDA Briefing Document") in advance of its upcoming Advisory Committee meeting on November 4, 2016. (Id. ¶ 8.) FDA Advisory Committees provide independent and expert advice to the FDA on technical, scientific, and policy issues associated with various matters, including NDAs. (Id.) The FDA Briefing Document provided an extensive analysis of the clinical data from solithromycin's development program. (Id.) It noted, among other things, that "in general, transaminase elevations in the majority of patients appeared to be asymptomatic and generally transient." (Doc. 51-15 at 34.) It also acknowledged that "no patient in the phase 3 trials fulfilled Hy's Law criteria." (Id.) But it cautioned:

> With fewer than 1000 CABP patients exposed to solithromycin for 5-7 days, the ability to detect a Hy's Law signal was limited by both the number of patients and short duration of exposure.

(Id.) Ultimately, the FDA Briefing Document provided the following assessment:

> In the solithromycin development program to date, a range of patterns of liver injury associated with exposure to solithromycin were observed. There was a spectrum of both hepatocellular and cholestatic signatures of hepatotoxicity, in one case accompanied by eosinophilia and suggesting hypersensitivity as a mechanism for liver injury. These findings were noted among a relatively small number of patients treated with solithromycin for CABP (n=920), normal healthy

> volunteers exposed to the drug in PK studies, and a small number of patients administered solithromycin in studies of other conditions. We conclude that these findings comprise a genuine liver injury signal.

(Doc. 46 ¶ 8; Doc. 51-15 at 35.) The FDA Briefing Document further concluded that Cempra failed to adequately differentiate solithromycin from Ketek, noting:

> Despite the differences in chemical structure, the hepatic adverse effects seen with solithromycin during its development program exceed the pre-marketing hepatic signal seen with [Ketek]. Significant gaps in knowledge of the hepatic toxicity profile of solithromycin exist.

(Doc. 51-15 at 35 (emphasis omitted).)

Attached to the FDA's Briefing Document was a memorandum by FDA's Mark Avigan, M.D., an Associate Director for the Critical Path Initiatives and hepatologist for the FDA ("Avigan memorandum"). (Id. at 61.)[11] The memorandum provided an in-depth analysis of the hepatic risk associated with solithromycin. In the memorandum, Avigan detailed what he identified as thirteen potential instances of "[s]olithromycin-induced liver injury," including eight patients who participated in the Phase 3 CABP trials and five patients who suffered liver injuries during Cempra's Phase 1 or Phase 2 clinical trials that either occurred during or before the class period. (Doc. 46 ¶ 83; Doc. 51-15 at

[11] There is no allegation that the Avigan memorandum, dated September 27, 2016, was provided earlier to Cempra.

74-87.)[12] In addition to describing the eight instances of "[s]olithromycin-induced liver injury" that occurred during the Phase 3 CABP clinical trials, the Avigan memorandum stated that a "substantially higher percentage" of patients experienced ALT elevations greater than three times the ULN compared with those patients who received moxifloxacin in the Phase 3 CABP trials, including one patient who experienced ALT levels in excess of 20 times ULN. (Doc. 51-15 at 88.)

As to Cempra's effort to distinguish solithromycin from Ketek, the Avigan memorandum stated that "the impact of the elimination of the terminal pyridine-imidazole in solithromycin on risk for hepatotoxicity remains hypothetical, since the direct *in vivo* effects of this structural change on liver injury have yet to be determined." (Id. at 65.) The Avigan memorandum further noted that "[t]he sponsor has put forth a so far unproven argument that despite their pharmacological and structural similarities as ketolides, solithromycin is marked by a substantially lower potential to cause severe hepatotoxicity than [Ketek]." (Id. at 91.) The Avigan memorandum concluded:

> The presence of one case of clinically significant cholestatic hepatitis with jaundice in the relatively small exposure population of the Solithromycin

[12] Plaintiffs' amended complaint alleges that the Avigan memorandum identified six patients who suffered liver injuries during Cempra's Phase 1 or Phase 2 clinical trials that occurred during or before the class period. (Doc. 46 ¶ 83.) Plaintiffs have since acknowledged that the memorandum identifies only five patients, yet contend this error is immaterial to their claims (Doc. 55 at 17 n.6).

> Development [COPD] Program that required early discontinuation of the study drug together with the robust ALT signal seen in the CABP trials leaves an open question concerning the actual "real world" population-level risk for serious DILI associated with solithromycin, even with short duration therapeutic use.

(Id. at 92 (emphasis added).) Following the publication of the FDA Briefing Document and Avigan memorandum, Cempra's common stock price dropped from $18.65 to $7.30 per share, a decline of 61% on higher-than-average trading volume. (Doc. 46 ¶ 84.)

On November 4, 2016, the FDA Advisory Committee held its hearing, and trading in Cempra's stock was halted for the day. (Id. ¶ 85.) The Advisory Committee panel voted unanimously to approve the efficacy of solithromycin, but it concluded, by a vote of 12-1, that Cempra had not adequately characterized the risk of hepatotoxicity and liver injury. (Id.; Doc. 51-16 at 311, 322.) Notwithstanding, a slight majority of the panel (7-6) voted that the efficacy of solithromycin for the treatment of CABP outweighed the risks, including hepatotoxicity. (Doc. 51-16 at 336.)

On Monday, November 7, 2016,[13] Cempra's common stock price declined from $7.55 to $6.85 per share, a decline of 9.3% on higher than average trading. (Doc. 46 ¶ 86.) Cempra reported on December

[13] Plaintiffs' amended complaint alleges throughout that investors reacted negatively to information disclosed during the November 4, 2016 FDA Advisory Committee meeting and that Cempra's common stock dropped on November 7, 2016. (Doc. 46 ¶¶ 8, 10, 81, 83, 85, 99, 100.) However, paragraph 86 alleges that the respective dates occurred in 2014. (Id. ¶ 86.) The 2014 date appears to be a typographical error, which is confirmed by Plaintiffs' reference to the 2016 dates in their response brief. (Doc. 55 at 17, 19.)

12, 2016, that Fernandes had retired from her position effective immediately, but she would continue to be paid under contract as a consultant to the company for one year. (Id. ¶ 22.)

On December 29, 2016, Cempra announced that the FDA had issued a Complete Response Letter for solithromycin, recommending a 9,000 patient clinical trial to assess the hepatotoxicity profile of the drug prior to receiving approval. (Id. ¶ 88.) The FDA further indicated that even if the drug was approved, its label would need to disclose adequate information about hepatotoxicity risk. (Id. ¶ 11.) Cempra's stock price fell an additional 57%, declining from $6.10 to $2.60 per share on higher-than-average trading volume. (Id. ¶¶ 11, 88.)

D. Procedural History

Plaintiffs brought three securities class action lawsuits against Cempra. (Doc. 40 at 2.) After the court consolidated the cases under this first-filed action (Id. at 11-12), Plaintiffs filed an amended complaint alleging violations of Section 10(b) of the Exchange Act against all Defendants and violations of Section 20(a) of the Exchange Act against Defendants Fernandes, Hahn, and Oldach. (Doc. 46.) In their amended complaint, Plaintiffs allege Defendants made false and misleading statements regarding the safety profile of solithromycin and failed to adequately disclose instances of DILI observed in clinical trials prior to and during the class period. (Id. ¶¶ 58-65, 67, 69-77.)

Defendants move to dismiss the consolidated complaint, contending that Plaintiffs have failed to allege material false or misleading statements or allege sufficient facts to give rise to a strong inference of scienter under the PSLRA's heightened pleading standards. (Docs. 49, 50.) Plaintiffs move to strike seven exhibits in the appendix to the Defendants' motion. (Doc. 56.) On July 24, 2018, the court held a hearing on the pending motions.

II. ANALYSIS

A. Motion to Strike

Preliminary to the consideration of Defendants' motion to dismiss, Plaintiffs move to strike seven exhibits contained in the appendix that Defendants submitted in support of their motion to dismiss pursuant to Federal Rule of Civil Procedure 12(d). (Doc. 56.) As the court indicated by separate order (Doc. 65), while Plaintiffs frame their request as a motion to strike the challenged exhibits, the court has construed the motion as one to exclude the exhibits from consideration pursuant to Rule 12(d). Cf. Fed. R. Civ. P. 12(f) (permitting the court to "strike from a pleading an insufficient defense or any redundant, immaterial, impertinent, or scandalous matter"); Fed. R. Civ. P. 7(a) (defining "pleading").

The challenged exhibits are as follows:

(1) Cempra Form 8-K filed with the SEC on November 17, 2015 (Doc. 51-6);

(2) Carlos M Barrera et al., Efficacy and safety of oral solithromycin versus oral moxifloxacin for treatment of community-acquired bacterial pneumonia: a global, double-blind, multicentre, randomised, active-controlled, non-inferiority trial (SOLITAIRE-ORAL), 16 Lancet Infectious Diseases 421 (2016) (Doc. 51-9);

(3) Thomas M. File Jr. et al., SOLITAIRE-IV: A Randomized, Double-Blind, Multicenter Study Comparing the Efficacy and Safety of Intravenous-to-Oral Solithromycin to Intravenous-to-Oral Moxifloxacin for Treatment of Community-Acquired Bacterial Pneumonia, 63 Clinical Infectious Diseases 1007 (2016) (Doc. 51-13);

(4) Cempra's FDA briefing document, which was publicly filed on November 2, 2016, in advance of the FDA Advisory Committee meeting (Doc. 51-14);

(5) FDA Advisory Committee minutes from the meeting held on November 4, 2016 (Doc. 51-17);

(6) Form 4s for Oldach, which were filed with the SEC on three separate occasions during the class period (Doc. 51-18);

(7) Form 4s for Fernandes & Hahn, which were filed with the SEC on January 5, 2016. (Doc. 51-19.)

Even though matters outside the pleadings are generally not considered on a Rule 12(b)(6) motion, see Fed. R. Civ. P. 12(d); Am. Chiropractic Ass'n v. Trigon Healthcare, Inc., 367 F.3d 212, 234 (4th Cir. 2004), "the court can consider 'documents attached to the complaint, documents incorporated by reference in the complaint, or matters of judicial notice' without converting a motion to dismiss into one for summary judgment." Plymouth Cty. Ret. Ass'n v. Primo Water Corp., 966 F. Supp. 2d 525, 536 (M.D.N.C. 2013) (quoting Sun Chem. Trading Corp. v. CBP Res., Inc., No. 1:01CV00425, 2004 WL 1777582, at *3 (M.D.N.C. July 29, 2004)).

"Courts may consider documents attached to a motion to dismiss 'so long as they are integral to the complaint and authentic.'" Id. (quoting Sec'y of State for Def. v. Trimble Navigation Ltd., 484 F.3d 700, 705 (4th Cir. 2007)); Zak v. Chelsea Therapeutics Int'l, Ltd., 780 F.3d 597, 606-08 (4th Cir. 2015); Goines v. Valley Cmty. Servs. Bd., 822 F.3d 159, 165-67 (4th Cir. 2016). "[I]n a securities fraud case, the court may consider 'public documents quoted by, relied upon, incorporated by reference or otherwise integral to the complaint.'" Plymouth, 966 F. Supp. 2d at 536-37 (quoting In re Royal Ahold N.V. Secs. & ERISA Litig., 351 F. Supp. 2d 334, 349 (D. Md. 2004)).

In addition to documents incorporated by reference or otherwise integral to the complaint, a court may consider facts and documents subject to judicial notice, provided that the court construe such facts in the light most favorable to the non-moving party. Zak, 780 F.3d at 607. Pursuant to Federal Rule of Evidence 201, a court may "'judicially notice a fact that is not subject to reasonable dispute,' provided that the fact is 'generally known within the court's territorial jurisdiction' or 'can be accurately and readily determined from sources whose accuracy cannot reasonably be questioned.'" Id. (quoting Fed. R. Evid. 201(b)). Within the context of securities fraud actions, courts routinely take judicial notice of publicly available documents that discuss the subject of the case, particularly in cases such as this where

there are allegations of fraud on the market. Plymouth, 966 F. Supp. 2d at 536–37; Johnson v. Pozen Inc., No. 1:07CV599, 2009 WL 426235, at *2 (M.D.N.C. Feb. 19, 2009) ("[I]n securities fraud cases courts routinely take judicial notice of newspaper articles, analysts reports, and press releases in order to assess what the market knew at particular points in time, even where the materials were not specifically referenced in the complaint.") (collecting cases), report and recommendation adopted, No. 1:07CV599, 2009 WL 10680297 (M.D.N.C. Sept. 29, 2009). Where the contents of documents subject to judicial notice are disputed, the court can consider the fact of their publication (if publication is not disputed), but not the truth or falsity of their contents. See United States v. Townsend, 886 F.3d 441, 444 (4th Cir. 2018) ("We may take judicial notice of facts outside the record where the fact may not be reasonably disputed and is 'relevant and critical to the matter on appeal.'" (citations omitted)); Khoja v. Orexigen Therapeutics, Inc., 899 F.3d 988, 1000 (9th Cir. 2018) ("Judicial notice under Rule 201 permits a court to notice an adjudicative fact if it is 'not subject to reasonable dispute.' A fact is 'not subject to reasonable dispute' if it is 'generally known,' or 'can be accurately and readily determined from sources whose accuracy cannot reasonably be questioned.' . . . But a court cannot take judicial notice of disputed facts contained in such public records." (quoting Fed. R. Evid. 201(b))).

At the outset, the court notes that Plaintiffs do not challenge the remaining exhibits attached to Defendants' motion. (Docs. 51-1, 51-2, 51-3, 51-4, 51-5, 51-7, 51-8, 51-10, 51-11, 51-12, 51-15, 51-16.) Each of the unchallenged exhibits is expressly referenced or otherwise relied on in the amended complaint. Accordingly, the court finds that the consideration of such exhibits is appropriate in this instance, where neither party challenges their authenticity and their content is incorporated by reference or otherwise integral to the complaint. See Plymouth, 966 F. Supp. 2d at 536–37.

The first challenged exhibit is a November 17, 2015 Form 8-K that Cempra filed with the SEC, which contains a PowerPoint Presentation that Cempra presented to investors in November of 2015 regarding its clinical development program. (Doc. 51-6.) Given that Plaintiffs do not dispute the accuracy of this public disclosure filed with the SEC, the court may take judicial notice of it. See Yates v. Mun. Mortg. & Equity, LLC, 744 F.3d 874, 881 (4th Cir. 2014) (taking judicial notice of the content of relevant SEC filings and other publicly available documents in the record).

The second and third challenged exhibits are articles that were published in peer-reviewed medical journals during the class period regarding the Phase 3 CABP clinical trials. (Doc. 51-9;

Doc. 51-13.)[14] The articles contain detailed information regarding the clinical results of the Phase 3 CABP trials. For similar reasons, the court finds that it may take judicial notice of the fact of their publication during the class period. Plymouth, 966 F. Supp. 2d at 537 ("Courts may take judicial notice of newspaper articles (particularly in cases such as this that allege fraud on the market) when they specifically discuss the subject of the case."); Garber v. Legg Mason, Inc., 537 F. Supp. 2d 597, 612 n.4 (S.D.N.Y. 2008) (taking judicial notice of several newspaper articles reflecting market knowledge of information that had allegedly been withheld), aff'd, 347 F. App'x 665 (2d Cir. 2009).

The fourth challenged exhibit is Cempra's FDA briefing document, titled "Briefing Document for the Antimicrobial Drugs Advisory Committee," which was published on the FDA's website along with the FDA's briefing document on November 2, 2016, in advance of the FDA Advisory Committee meeting. (Doc. 51-14.) In the amended complaint, Plaintiffs represent that the allegations contained in the complaint are based upon their personal knowledge and the independent investigation of their attorneys, which included a review and analysis of the FDA "Antimicrobial Drugs

[14] The article discussing the Solitaire-Oral trial was first published online on February 4, 2016, and was subsequently published in the April 2016 publication of the medical journal Lancet Infectious Diseases. (Doc. 51-9 at 2.) The article discussing the Solitaire-IV trial was published online on July 22, 2016, and was subsequently published in the October 2015 publication of the medical journal Clinical Infectious Diseases. (Doc. 51-13 at 2.)

Advisory Committee meeting materials." (Doc. 46 ¶ 2.) The amended complaint explicitly references the publication of Cempra's FDA briefing document along with the FDA's own briefing document on the FDA's website (Doc. 46 ¶ 81), and alleges that Plaintiffs suffered losses after Cempra's common stock price purportedly declined "[a]s a result of the November 2, 2016 disclosures," which included Cempra's disclosure that safety data showed "a significant signal for liver toxicity and liver injury." (Id. ¶¶ 81, 84, 98, 101.) The consideration of Cempra's FDA briefing document is highly relevant to the question of scienter, where Plaintiffs' amended complaint is premised on the purported dissonance between Cempra's public representations regarding the safety profile of solithromycin and the information ultimately disclosed in the FDA Briefing Document. See In re AstraZeneca Sec. Litig., 559 F. Supp. 2d 453, 470-71 (S.D.N.Y. 2008) (comparing the briefing documents submitted by pharmaceutical company and the FDA in advance of FDA Advisory Committee meeting for purposes of determining whether plaintiffs adequately alleged scienter with respect to claims that defendants misrepresented the safety risks associated with a developmental drug), aff'd sub nom. State Univs. Ret. Sys. of Ill. v. Astrazeneca PLC, 334 F. App'x 404 (2d Cir. 2009). Accordingly, the court will consider Cempra's FDA briefing document, as it is incorporated by reference or otherwise integral to the complaint. See Plymouth, 966 F. Supp. 2d at 536-37; In re

AstraZeneca Sec. Litig., 559 F. Supp. 2d at 470-71.

With regard to the remaining three challenged exhibits, the court concludes that it need not rely on them to resolve Defendants' motion, particularly given the comprehensive nature of the other materials that the court has determined it may consider.[15] Thus, the court will not consider those documents. Plymouth, 966 F. Supp. 2d at 537 (declining to consider challenged exhibits where unnecessary to the court's resolution of the pending motion).

B. Motion to Dismiss

Defendants move to dismiss the amended complaint for failure to state a claim upon which relief can be granted pursuant to Rule 12(b)(6). (Doc. 49.)

1. Standard of Review

Under Federal Rule of Civil Procedure 8(a)(2), a complaint must contain a "short and plain statement of the claim showing that the pleader is entitled to relief." The purpose of a motion under Rule 12(b)(6) is to "test[] the sufficiency of a complaint"

[15] While the amended complaint contains allegations regarding certain stock sales made by Oldach during the class period (Doc. 46 ¶¶ 66, 68), Plaintiffs conceded at the hearing that they did not intend to rely on stock sales made by him or any other individual to support an inference of scienter. (Doc. 64 at 60-61.) Thus, the court need not consider the Form 4 disclosures filed with the SEC regarding stock sales made by the individual Defendants. (Doc. 51-18; Doc. 51-19.) Moreover, the challenged FDA Advisory Committee Minutes exhibit (Doc. 51-17) contains a summary of minutes for the November 4, 2016 meeting of the FDA Antimicrobial Drugs Advisory Committee. Because this summary simply condenses the Committee's votes and discussion, which are contained in full in the FDA Advisory Committee Transcript (Doc. 51-16) that Plaintiffs do not challenge, the court need not consider this document.

and not to "resolve contests surrounding the facts, the merits of a claim, or the applicability of defenses." Republican Party of N.C. v. Martin, 980 F.2d 943, 952 (4th Cir. 1992). In considering a Rule 12(b)(6) motion, a court "must accept as true all of the factual allegations contained in the complaint," Erickson v. Pardus, 551 U.S. 89, 94 (2007) (per curiam), and all reasonable inferences must be drawn in the plaintiff's favor, Ibarra v. United States, 120 F.3d 472, 474 (4th Cir. 1997). To be facially plausible, a claim must "plead[] factual content that allows the court to draw the reasonable inference that the defendant is liable" and must demonstrate "more than a sheer possibility that a defendant has acted unlawfully." Ashcroft v. Iqbal, 556 U.S. 662, 678 (2009) (citing Bell Atl. Corp. v. Twombly, 550 U.S. 544, 556 (2007)).

While these standards govern the consideration of a Rule 12(b)(6) motion generally, claims of securities fraud are subject to "strict pleading standards" under Federal Rule of Civil Procedure 9(b) and the PSLRA. Singer v. Reali, 883 F.3d 425, 439 (4th Cir. 2018). In addition to the requirement that "a party must state with particularity the circumstances constituting fraud" under Rule 9(b), the PSLRA "imposes additional pleading requirements to prevent Securities Exchange Act claims from being 'employed abusively to impose substantial costs on companies and individuals whose conduct conforms to the law.'" Id. at 439

(quoting Tellabs, Inc. v. Makor Issues & Rights, Ltd., 551 U.S. 308, 313, (2007)). In particular, the PSLRA establishes heightened pleading standards with respect to allegations of falsity and scienter. Zak, 780 F.3d at 606. If a plaintiff alleges that a defendant made false or misleading statements, the PSLRA requires that the plaintiff "specify each statement alleged to have been misleading, the reason or reasons why the statement is misleading, and, if an allegation regarding the statement or omission is made on information and belief . . . state with particularity all facts on which that belief is formed." 15 U.S.C. § 78u-4(b)(1). In addition, 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). "If those exacting pleading requirements are not satisfied, the complaint must be dismissed." Singer, 883 F.3d at 439 (citing Cozzarelli v. Inspire Pharm. Inc., 549 F.3d 618, 623 (4th Cir. 2008)).

2. Section 10(b) Claims

In their amended complaint, Plaintiffs allege that Defendants made false and misleading statements about the safety profile of solithromycin and risk of liver injury by failing to adequately disclose instances of DILI that were ultimately revealed in the various FDA briefing materials. (Doc. 46 ¶¶ 58–83,112.) Plaintiffs identify challenged statements that generally fall into the following categories: (1) allegedly false and misleading

statements regarding solithromycin's overall safety profile in the Phase 3 CABP clinical trials; (2) allegedly misleading statements concerning the differentiation of solithromycin from Ketek; and (3) allegedly misleading statements regarding solithromycin's safety profile in the Phase 2 NASH study. (Doc. 46 ¶¶ 7, 79-80.) Defendants contend that the complaint fails to allege falsity or establish a strong inference of scienter as required under the PSLRA's heightened pleading standards. (Doc. 50 at 17–18, 33.) Defendants further claim that four of the challenged statements are non-actionable statements of opinion. (Id. at 31–33.)

Pursuant to Section 10(b) of the Exchange Act and Rule 10b-5, it is unlawful for a company to make a false or misleading statement or omission in connection with the sale of a security. 17 C.F.R. § 240.10b–5(b); see 15 U.S.C. § 78j(b). A plaintiff bringing a claim under Section 10(b) must establish: "(1) a material misrepresentation or omission by the defendant; (2) scienter; (3) a connection between the misrepresentation or omission and the purchase or sale of a security; (4) reliance upon the misrepresentation or omission; (5) economic loss; and (6) loss causation." Singer, 883 F.3d at 438 (quoting Stoneridge Inv. Partners, LLC v. Sci.-Atlanta, Inc., 552 U.S. 148, 157 (2008)). As noted above, claims of securities fraud are subject to heightened pleading standards with respect to falsity and scienter under Federal Rule of Civil Procedure 9(b) and the PSLRA. Id.;

Zak, 780 F.3d at 606.

To establish an actionable false or misleading statement or omission, "the challenged statement or omission must be factual i.e., one that is demonstrable as being true or false; it must be false, or the omission must render public statements misleading; and any statement or omission of fact must be material." Lerner v. Nw. Biotherapeutics, 273 F. Supp. 3d 573, 586 (D. Md. 2017) (internal quotation marks omitted); Longman v. Food Lion, Inc., 197 F.3d 675, 682 (4th Cir. 1999). "A statement or omission is material if there is a substantial likelihood that a reasonable purchaser or seller of a security (1) would consider the fact important in deciding whether to buy or sell the security or (2) would have viewed the total mix of information made available to be significantly altered by disclosure of the fact." Lerner, 273 F. Supp. 3d at 586 (internal quotation marks omitted); In re PEC Sols., Inc. Sec. Litig., 418 F.3d 379, 387 (4th Cir. 2005). "While opinion or puffery will often not be actionable, in particular contexts when it is both factual and material, it may be actionable." Lerner, 273 F. Supp. 3d at 586 (quoting Longman, 197 F.3d at 683).

Even though "section 10(b) and SEC Rule 10b-5 'do not create an affirmative duty to disclose any and all material information,'" the "disclosure of material information is required 'when necessary to make statements made, in the light of the

circumstances under which they were made, not misleading.'" Singer, 883 F.3d at 440 (quoting Matrixx Initiatives, Inc. v. Siracusano, 563 U.S. 27, 44 (2011)). Courts have recognized that "where the duty to disclose arises from a need to avoid false or misleading statements 'the inquiries as to duty and materiality coalesce.'" In re Sanofi-Aventis Sec. Litig., 774 F. Supp. 2d 549, 564 (S.D.N.Y. 2011) (quoting In re Time Warner Inc. Sec. Litig., 9 F.3d 259, 267 (2d Cir. 1993)). The court must consider whether the statements or omissions, when read as a whole, would have misled a reasonable investor. Lerner, 273 F. Supp. 3d at 587 (citation omitted).

"To demonstrate scienter, a plaintiff must show that the defendant acted with 'a mental state embracing intent to deceive, manipulate, or defraud.'" Zak, 780 F.3d at 606 (quoting Tellabs, 551 U.S. at 319). The Fourth Circuit has emphasized that "raising a 'strong inference' of scienter is no small burden." Cozzarelli, 549 F.3d at 624 (citing Tellabs, 551 U.S. at 321). "'[R]eckless conduct sufficient to establish a strong inference of scienter' must be 'severe,' or 'so highly unreasonable and such an extreme departure from the standard of ordinary care as to present a danger of misleading the plaintiff to the extent that the danger was either known to the defendant or so obvious that the defendant must have been aware of it.'" Lerner, 273 F. Supp. 3d at 594 (first quoting Ottmann v. Hanger Orthopedic Grp., Inc., 353 F.3d

338, 344 (4th Cir. 2003); then quoting Matrix Capital Mgmt. Fund, LP v. BearingPoint, Inc., 576 F.3d 172, 181 (4th Cir. 2009)).

Standing alone, allegations of motive and opportunity to raise capital to support ongoing business operations are generally insufficient to support a strong inference of scienter. Cozzarelli, 549 F.3d at 627 ("All investments carry risk, particularly in a field like biopharmaceuticals. If we inferred scienter from every bullish statement by a pharmaceutical company that was trying to raise funds, we would choke off the lifeblood of innovation in medicine by fueling frivolous litigation — exactly what Congress sought to avoid by enacting the PSLRA."). However, the deliberate misreporting of material information may give rise to a strong inference of scienter in certain cases. See U.S. S.E.C. v. Pirate Inv'r LLC, 580 F.3d 233, 243 (4th Cir. 2009) (holding that district court did not clearly err in finding plaintiffs established strong inference of scienter, where the court found individual defendant had actual knowledge that his statement was false at the time he made it as well as the "clear financial motive for the misrepresentations"); Medina v. Clovis Oncology, Inc., 215 F. Supp. 3d 1094, 1127 (D. Colo. 2017) (finding plaintiffs adequately alleged scienter where plaintiffs alleged that defendants had actual knowledge of the confirmed response rates of the ongoing clinical trials but continued to report the more favorable unconfirmed response rates to investors).

"In securities litigation cases premised upon a drug company's partial non-disclosure of drug trials to the investing public, the key inquiry is whether the non-disclosure at issue results in a suspiciously incomplete data set that yields a strong inference of scienter." In re Human Genome Scis. Inc. Sec. Litig., 933 F. Supp. 2d 751, 760 (D. Md. 2013) (collecting cases). As one district court noted:

> The key, of course, is the honest belief of the management in the truth of information issued to the public. If the management knows that certain facts will necessarily prevent the regulatory approval or the marketing of the drug and conceals these facts from the investing public, then there is scienter. There is also scienter if the management is reckless in dealing with such adverse facts.

In re AstraZeneca Sec. Litig., 559 F. Supp. 2d at 470.

The court must undertake a comparative analysis of the scienter allegations and any opposing inferences that may be drawn from the facts. Zak, 780 F.3d at 606. "[A] complaint will not be dismissed so long as 'the malicious inference is at least as compelling as any opposing innocent inference.'" Id. (quoting Yates, 744 F.3d at 885).

While not directly relied on by either party, the district court's decision in In re AstraZeneca Securities Litigation, 559 F. Supp. 2d 453 (S.D.N.Y. 2008), is instructive. In that case, the plaintiffs alleged that the defendants failed to disclose material information regarding the safety profile and efficacy of

a developmental drug in late-stage clinical trials, which was ultimately disclosed in the FDA briefing document that was released in advance of the FDA Advisory Committee meeting. In re AstraZeneca Sec. Litig., 559 F. Supp. 2d at 457. As in the instant case, the plaintiffs alleged, among other things, that the defendants failed to adequately disclose the risk of severe liver injury associated with the developmental drug. Id. at 457-58. In particular, the plaintiffs alleged that the defendants misrepresented the magnitude of the risk and failed to disclose that the drug contributed to or was a possible cause of or contributor to nine patient deaths from liver injury as well as a statistically significant risk of DILI. Id. at 462. With regard to scienter, the plaintiffs also alleged that the individual defendants had access to all of the relevant data that rendered the statements false or misleading.[16] Id.

The court granted the defendants' motion to dismiss, finding that the plaintiffs failed to adequately plead scienter where the case centered on a disagreement between the FDA and the company regarding the interpretation of clinical data. Id. at 471-72. The court noted:

[16] The AstraZeneca plaintiffs further alleged that the defendants met and communicated with the FDA regarding the liver toxicity problems during the class period but failed to disclose that they prepared a specific risk management program for the drug due to the concerns raised by the FDA. In re AstraZeneca Sec. Litig., 559 F. Supp. 2d at 463-64.

> As of the time when the FDA Advisory Committee met on September 10, AstraZeneca had its side of the case and the FDA staff had its side. The FDA staff view prevailed before the Advisory Committee. This does not mean that AstraZeneca was not conscientious in advocating the drug Exanta before the FDA, nor does it mean that the information issued publicly over the course of more than a year was dishonest or recklessly disseminated.

Id. at 471. In particular, the court relied on the briefing documents prepared by the defendants and the FDA staff for the FDA Advisory Committee meeting, finding that "[i]t is impossible to read the FDA document and the AstraZeneca document without concluding that both present the honest analysis and conclusions of their authors." Id. The court further noted that the plaintiffs failed to allege any "red flag" or any other indication that management believed that the drug would not be approved, noting that other facts, such as a regulatory approval of the drug in Europe, suggested otherwise. Id. at 471; see also In re Sanofi Sec. Litig., 87 F. Supp. 3d 510, 546 (S.D.N.Y. 2015) ("[T]he most plausible inference is, therefore, that defendants honestly believed their descriptions of the data and did not anticipate that the FDA would adopt a different view."), aff'd sub nom. Tongue v. Sanofi, 816 F.3d 199 (2d Cir. 2016).

a. Challenged Statements of Opinion

Defendants argue that four of the challenged statements, made by Cempra's CEO, Fernandes, are subjective statements of opinion that are not actionable as a matter of law:

(1) A July 7, 2015 press release regarding the results of the Solitaire-IV Phase 3 trial in which Fernandes stated in relevant part: "We believe that these results, coupled with our successful Solitaire Oral results, which we announced in January, will provide a compelling clinical data set in our solithromycin NDA submission." (Doc. 46 ¶ 58.)

(2) A January 14, 2016 statement regarding the Phase 3 CABP clinical trials made during her opening remarks at the J.P. Morgan Healthcare Conference in which Fernandes stated: "[W]e are very pleased with the safety of this as well as the efficacy" (Doc. 46 ¶ 70.)

(3) A May 2, 2016 statement made during a conference call to discuss the 2016 first quarter earnings regarding solithromycin's differentiation from Ketek in which she stated: "We do believe that on the [K]etek issue, we are over that hurdle, because we have shown the mechanisms as to why [K]etek was toxic." (Doc. 46 ¶ 72.)

(4) A September 30, 2016 statement made during a conference call regarding the interim Phase 2 NASH trial results, where Dr. Fernandes stated: [W]e believe [solithromycin] is incredibly safe, even in the liver . . . . And we're very pleased with the safety of the drug." (Doc. 46 ¶ 76.)

(Doc. 50 at 31-32.) Defendants contend that "Plaintiffs do not allege contrary evidence suggesting that the foregoing opinions expressed by Dr. Fernandes were not sincerely held, nor that the opinions were objectively false when made." (Id. at 32.)

With regard to Fernandes's July 7, 2015 statement that the results from the Phase 3 clinical trials will present a "compelling clinical data set," Plaintiffs allege that the complaint sufficiently alleges that Fernandes did not have a rational belief in the false statement when it was made. (Doc. 55 at 30.) Relying on the Supreme Court's decision in Omnicare, Inc. v. Laborers Dist.

Council Const. Indus. Pension Fund, 135 S. Ct. 1318 (2015), Plaintiffs further claim that "[h]aving elected to speak about solithromycin's purportedly 'compelling' clinical data, defendant Fernandes had a duty to disclose that throughout the Company's Phase 1, Phase 2, and Phase 3 clinical studies, solithromycin safety data showed a significant and genuine signal for liver toxicity and liver injury." (Id. at 29 (citing Knurr v. Orbital ATK, Inc., 276 F. Supp. 3d 527, 538 (E.D. Va. 2017) (quoting Omnicare, 135 S. Ct. at 1329)).) Plaintiffs do not address any of the other three statements in detail.

"Courts have repeatedly held 'publicly stated interpretations of the results of various clinical studies' to be 'opinions' because '[r]easonable persons may disagree over how to analyze data and interpret results, and neither lends itself to objective conclusions.'" In re Sanofi Sec. Litig., 87 F. Supp. 3d at 543 (alteration in original) (quoting In re Sanofi-Aventis Sec. Litig., 774 F. Supp. 2d at 567 & n.20 (S.D.N.Y. 2011)). Statements of opinion are generally actionable only if the plaintiff establishes that the statement was objectively false and the issuer lacked a rational belief in the veracity of the statement at the time it was made. Id. at 543–44 (citing Kleinman v. Elan Corp., PLC, 706 F.3d 145, 153 (2d Cir. 2013)).

In Omnicare, the Supreme Court addressed the standard for pleading falsity for statements of opinion in the context of a

claim brought under Section 11 of the Securities Act of 1933. 135 S. Ct. at 1331. The Court held that opinion statements may be actionable in cases where (1) the issuer makes a statement of opinion that was objectively and subjectively false when made; (2) the issuer makes a statement of opinion that contains a statement of fact that was materially misleading when made; and (3) the issuer omits facts going to the basis of the opinion, which render the opinion misleading to a reasonable investor viewing the statement fairly and in context. Id. at 1327–32. With regard to this third theory of liability arising from an omission, the Court stated:

> The investor must identify particular (and material) facts going to the basis for the issuer's opinion — facts about the inquiry the issuer did or did not conduct or the knowledge it did or did not have — whose omission makes the opinion statement at issue misleading to a reasonable person reading the statement fairly and in context.

Id. at 1332. The Court emphasized that this "is no small task for an investor," noting that the omitted fact must be material and viewed in the larger context in which it was made. Id. The Fourth Circuit has yet to address whether the standard for pleading falsity under an omissions theory of liability set forth in Omnicare applies to Section 10(b) claims. See TransEnterix Inv'r Grp. v. TransEnterix, Inc., 272 F. Supp. 3d 740, 751–52 (E.D.N.C.

2017).[17]

Here, Plaintiffs have not sufficiently alleged that Fernandes lacked a sincerely held belief in her statements when they were made or had a duty to disclose adverse events, particularly where the statements are couched as opinion and do not constitute affirmative statements that there are no safety concerns associated with the drug. See Nguyen v. New Link Genetics Corp., 297 F. Supp. 3d 472, 488–89 (S.D.N.Y. 2018) (finding statements of opinion that biopharmaceutical company was "confident" in the study design and "encouraged" by the progress of the clinical trials were "expressions of puffery and corporate optimism" that did not give rise to an actionable securities fraud claim, when couched in phrases like "suggests potential" and "we felt"). Apart from alleging that instances of DILI would have been made known to the individual defendants due to the FDA's regulatory reporting requirements, Plaintiffs provide no particularized allegations that Fernandes lacked a sincerely held belief in her optimistic statements regarding the clinical trial results. Nor do the clinical data suggest that Fernandes lacked an objective basis in fact for her opinion, where the Phase 3 CABP trials met their primary endpoint and the overall safety profile of the drug was

[17] However, at least two other circuit courts have applied Omnicare to Section 10(b) claims. City of Dearborn Heights Act 345 Police & Fire Ret. Sys. v. Align Tech., Inc., 856 F.3d 605, 616 (9th Cir. 2017); Tongue, 816 F.3d at 209-10.

subject to reasonable debate. (Doc. 46 ¶ 52, 54); see In re Sanofi Sec. Litig., 87 F. Supp. 3d at 544.

Even assuming that Omnicare's theory of liability for statements of opinion based on omission applies to Section 10(b) claims, the court concludes that the challenged statements of opinion would not be actionable, where they consist of little more than vague optimistic statements regarding the safety profile of the drug. See Tongue, 816 F.3d at 214 ("Defendants' statements were not misleading simply because the FDA disagreed with Defendants' interpretation of the data; an issuer is not liable merely because it 'knows, but fails to disclose, some fact cutting the other way.'" (quoting Omnicare, 135 S. Ct. at 1329)). With regard to Fernandes's May 2, 2016 statement regarding the Phase 2 NASH results, Plaintiffs have a stronger argument that Fernandes had a duty to disclose the adverse events in the COPD trial when discussing the overall safety profile of the drug during the conference call to discuss the preliminary results of the Phase 2 NASH trials.[18] (Doc. 46 ¶ 72.) Nevertheless, the disclosure of

[18] During the May 2, 2016 earnings call, Fernandes was questioned regarding "any potential sources of controversy" that may arise during the FDA Advisory Committee meeting, particularly in light of the prior Ketek experience. (Doc. 46 ¶ 72.) Fernandes responded as follows:

> Thank you. So we have worked very hard, together with safety experts, people who have consulted in the past with other companies, with the FDA and so on, very aware of liver safety. We do believe that on the ketek issue, we are over that

the adverse events was not required in this instance where Fernandes did not mention the COPD Phase 2 trials directly, limited her discussion to the clinical data as a whole, and made vague statements of opinion regarding the data. Cf. Tongue, 816 F.3d at 214.

For these reasons, the court finds that these four challenged statements constitute opinion and are not actionable as a matter of law.

b. Statements Challenged as False or Misleading

i. Allegedly False and Misleading Statements Regarding Solithromycin's Safety Profile in the Phase 3 CABP Trials

Plaintiffs challenge several statements made by Defendants regarding the safety profile of the drug during the Phase 3 CABP clinical trials. (Doc. 46 ¶¶ 58–64, 67, 70, 72, 75.) The individual Defendants made various optimistic public statements regarding the Phase 3 clinical trials, repeatedly assuring investors that the ALT elevations were "reversible and asymptomatic" and that none of the patients in the clinical trial

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> hurdle, because we have shown the mechanisms as to why ketek was toxic.
>
> However, we do have ALT. So our job is to make a comparison to the older macrolides like [erythromycin], [azithromycin], clarithromycin. All of them do have ALT increases. We have that too. But you must remember that every one of them came down, some of them even – most of them even while on study drug. So we don't believe there is a big concern.

(Id. (emphasis added) (alteration in original).)

met Hy's Law, a criteria developed to predict instances of severe DILI. (See, e.g., id. ¶¶ 53 (noting that Hy's law is "an indicator that a drug could cause serious liver injury"), 59–63, 67, 70, 72, 75.) In addition, Defendants made statements denying that the clinical results demonstrated any liver toxicity. (See, e.g., id. ¶ 64.) Plaintiffs claim that these allegations represent a "textbook case" for the violations of securities laws, where Defendants were made aware of eight patients who experienced DILI during the Phase 3 trials and failed to disclose them. (Doc. 55 at 22-23.)

First, Plaintiffs allege that three of the challenged statements denying any indication of liver toxicity in the Phase 3 studies were "objectively false" when made. (Id. at 22 (citing Doc. 46 ¶¶ 60, 64–65).) Plaintiffs dispute Defendants' characterization that the public statements are consistent with the clinical data reported by the FDA, noting that "Defendants' 'consistency' argument fails to direct this Court to a single example where they disclosed, either prior to or during the Class Period, the instances of DILI suffered by patients taking solithromycin." (Id. at 23.)

Second, Plaintiffs allege that Defendants made several misleading statements regarding ALT elevations observed during the Phase 3 clinical trials by failing to disclose the eight patients that experienced symptoms of DILI, who were subsequently

identified in the Avigan memorandum. (Id. at 24.) Plaintiffs contend that "Defendants were actively, yet misleadingly, assuring investors that solithromycin was not associated with any liver-safety problems beyond elevated ALT." (Id. at 25.) They claim that the complaint alleges "numerous statements made by Defendants where they spoke about liver-safety signals in the Phase 3 studies, but remained silent concerning the known instances of liver toxicity and DILI that had already occurred." (Id. at 24 (citing ¶¶ 59, 61, 67, 70, 73-75).)

Defendants contend that Plaintiffs do not "allege a single contemporaneous fact supporting an inference that any statement was false or misleading when made." (Doc. 59 at 5.) Defendants maintain that the Avigan memorandum and FDA Briefing Document merely confirm the publicly reported clinical data regarding the Phase 3 CABP clinical trials, even if the authors ultimately interpreted the data differently. (Id. at 9-11.) Defendants claim that Plaintiffs "erroneously equate ALT elevation with DILI" (id. at 4) and contend they had no legal duty to report "the eight alleged instances of DILI" because "ALT elevations — which Defendants disclosed — are not synonymous with liver injury." (Id. at 11.)

Most of the challenged statements appear to closely track the reported clinical data. See, e.g., (Doc. 46 ¶ 59 ("Treatment emergent ALT elevations were generally asymptomatic, reversible,

and not associated with increased bilirubin. No solithromycin patient met Hy's Law criteria of concurrent ALT and bilirubin elevations post-baseline."); id. ¶ 61 ("These ALT increases were asymptomatic and resolved post treatment. No solithromycin recipient met Hy's Law criteria, defined as simultaneous ALT and bilirubin elevation – another liver factor — following dosing. There was no evidence of drug hypersensitivity reaction. For instance, one involving a combination of rash, fever, and ALT elevation, and other symptoms.").) Nothing in the FDA Briefing materials indicates that any of these statements is false.

It is also not the case that Defendants denied any evidence or "signal" of liver injury of any kind. Rather, Defendants' statements acknowledged that solithromycin, like many other antibiotics, had the potential for some form of liver injury (see, e.g., id. ¶ 65 (noting that common antibiotics for children cause increases in liver enzymes); id. ¶ 60 (stating, in response to an analyst question about the ALT elevations disclosed in Cempra's October 16, 2015 press release and whether there were symptomatic patients in the Phase 3 Solitaire-IV trial, that there were "generally, no symptoms, no evidence of hepatic injury that was symptomatic or with bilirubin elevation," and that "the [data management committee] has seen each of these, you know, any significant ALT elevation, during the study and did not do anything.")), but reflected the belief that there was no evidence

of severe liver injury, as determined by Hy's Law.

As to the assessments of the eight patients in the Phase 3 CABP clinical trials within the Avigan memorandum, Defendants argue they "merely confirm Defendants' repeated public statements concerning ALT elevations observed during the CABP studies." (Doc. 50 at 28.) This is not entirely accurate. The challenged statements deny any actual cases of liver toxicity. (Doc. 46 ¶ 64 ("But let me again say: there is no liver toxicity. There is no hepatic toxicity. This was reversible ALT elevation and there has been no hepatic toxicity. So there is no evaluation of hepatic toxicity because we don't have any."); id. ¶ 77 ("And our clinical trial data really shows that this has had a great deal of efficacy and all of those ALTs were reversible and asymptomatic, as you remember." (emphasis added))). To this extent, Defendants are correct.[19]

[19] During the hearing, Plaintiffs appeared to concede that these statements were not necessarily false, but misleading. (Doc. 64 at 35–36, 47–48.) Nevertheless, neither the Avigan memorandum nor the FDA Briefing Document confirmed that all of the patients in the Phase 3 CABP trials experienced asymptomatic ALT elevations, but rather stated that the observed ALT elevations were generally asymptomatic. (See, e.g., Doc. 51-15 at 34; Doc. 51-11 at 3.) While the FDA briefing documents confirmed that patients within the Phase 3 trials were generally asymptomatic, at least one patient in the Phase 3 Oral CABP trials experienced a symptom of liver injury that was attributed by the site investigator to the drug in conjunction with elevated ALT and AST levels. (Doc. 51-11 at 28.) In the Phase 3 Oral CABP trial, a 61-year-old female experienced symptomatic ALT elevations in the form of right hypochondium pain, which the site investigator considered to be drug-related. (Id.) While the patient's ALT elevations returned to normal after day 15, the patient experienced alkaline phosphatase ("ALP") elevations that did not return to normal until day 29 of the study. (Id.) In his memorandum,

However, the FDA Briefing Document went further and concluded that while no actual cases of liver toxicity resulted, the clinical trial results demonstrated the *potential* for liver toxicity. (See, e.g., Doc. 51-15 at 80 ("These values in a Severity Level I injury point to a predominantly hepatocellular pattern of toxicity.").) When considered within the "total mix" of information available to investors, however, it is doubtful that Defendants' statements would constitute material misrepresentations, where the clinical results were subject to interpretation and elevated liver enzyme and other data were otherwise available to the public in the form of the published articles and SEC filings. (E.g., Doc. 51-1; Doc. 51-5; Doc. 51-6; Doc. 51-9 at 9-10; Doc. 51-13 at 10); see In re Sanofi Sec. Litig., 87 F. Supp. 3d at 547 (holding that plaintiffs failed to adequately plead falsity regarding allegedly false and misleading statements regarding safety of a drug in clinical development, where the adverse effects of the drug had been reported in two separate medical journals prior to the class period); Lerner, 273 F. Supp. 3d at 587-88 (holding that plaintiffs failed to adequately plead falsity with regard to the defendants' statements regarding the initial and ongoing clinical trials, finding the plaintiffs failed to demonstrate that the defendants

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Avigan stated "this case of acute mild cholestatic liver injury is 'Probable' in its causal association with solithromycin." (Id.)

falsely or inaccurately reported their conclusions, but rather disagreed with their methodology).

Ultimately, the court need not resolve the issue of falsity, because even assuming Plaintiffs have adequately alleged falsity with respect to some of the challenged statements, they fail to allege sufficient facts to establish a strong inference of scienter.

As a general matter, Plaintiffs point to the fact that Defendants had the motive and opportunity to mislead investors in advance of the stock sales as supporting a strong inference of scienter. (Doc. 55 at 36–38.) Plaintiffs claim that solithromycin represented the "lynchpin" product for this biopharmaceutical company that had yet to bring a drug successfully to market. (Id. at 35.) They note that Cempra was a developmental drug company that was operating at a loss and "heavily reliant on additional capital during the Class Period." (Id. at 37.) Defendants argue that Plaintiffs' "[b]are allegations of 'motive and opportunity'" are insufficient to support a strong inference of scienter. (Doc. 50 at 34–35.)

To be sure, Plaintiffs need not identify irrefutable evidence "of the 'smoking-gun' genre" in order to establish a strong inference of scienter. Tellabs, 551 U.S. at 324. But their amended complaint fails to support a strong inference of scienter in this regard. For example, there is no allegation that the

individual Defendants acted with a pecuniary motive for personal financial gain. See id. at 325 (noting that allegations of "personal financial gain may weigh heavily in favor of a scienter inference," but are not dispositive).[20] Every for-profit company is motivated by financial gain in our free enterprise system. Without more, Plaintiffs' allegations of motive and opportunity based on the company's need to raise capital are insufficient to establish a strong inference of scienter. See Cozzarelli, 549 F.3d at 627.

Plaintiffs also argue that the fact that Fernandes was "terminated" soon after the class period supports an inference of scienter. (Doc. 55 at 36.) Defendants note that the complaint alleges only that Fernandes "retired" in December of 2016 and contains no specific allegations that she was terminated as a result of the FDA disclosures. (Doc. 59 at 20 (citing Doc. 46 ¶ 22).) Without additional relevant factual allegations, "[s]ubsequent resignations by executives are insufficient to support a strong inference of scienter." In re Swisher Hygine, Inc., No. 3:12-MD-2384, 2015 WL 4132157, at *12 (W.D.N.C. July 8, 2015) (alteration in original) (quoting Iron Workers Local 16

[20] The amended complaint does reference certain stock sales made by Oldach. (See Doc. 46 ¶¶ 66, 68.) During the hearing on the present motions, Plaintiffs conceded that they did not intend to rely on Oldach's stock sales to meet their burden of alleging a strong inference of scienter. (Doc. 64 at 60–61; see Doc. 55 at 37 n.10.)

Pension Fund v. Hilb Rogal & Hobbs Co., 432 F. Supp. 2d 571, 593-94 (E.D. Va. 2006)); Schueneman v. Arena Pharm., Inc., 840 F.3d 698, 709 n.8 (9th Cir. 2016) ("We have cautioned securities plaintiffs that, absent some truly compelling allegations, we will not consider routine business behavior (like firing people or raising capital) to serve as the basis for scienter." (citation omitted)).

Plaintiffs allege that Defendants had actual knowledge of the misrepresentations and omissions of material facts, or acted with reckless disregard for the truth by failing to ascertain and disclose facts regarding the adverse events observed during the clinical trials. (Doc. 46 ¶¶ 117-18.) Plaintiffs argue that "the requisite strong inference of scienter is established by the Defendants' own admissions of knowledge regarding the full safety profile of solithromycin." (Doc. 55 at 31 (citing Doc. 46 ¶¶ 60, 67).) Plaintiffs contend that the case is not, as Defendants contend, a matter of two differing interpretations of the same clinical data, but instead revolves around the failure to disclose that documented instances of DILI occurred. (Doc. 55 at 35-36.) Plaintiffs allege that Cempra would have been aware of each adverse event "virtually immediately" due to the FDA's reporting requirements. (Doc. 55 at 33 (citing Doc. 46 ¶¶ 57, 83).) They note that each of the Defendants spoke about the clinical trial results and concerns with liver safety in detail. (Id. at 34-35.)

They also rely on statements made by Defendants during the class period admitting that they had access to and knowledge of all of the clinical data. (Id. at 32-34.)

Defendants contend that Plaintiffs' argument "rests on the faulty premise that ALT elevations themselves constitute DILI." (Doc. 59 at 19.) They further contend that the complaint is devoid of "any allegations of contemporaneous fact that the Defendants 'knew of the undisclosed instances of DILI'" at the time such statements were made. (Id.) Defendants contend that the most plausible inference is they did not anticipate that the FDA would adopt a different view of the data. (Doc. 50 at 38.)

Here, the key inquiry is whether Defendants were sufficiently reckless with adverse information to give rise to a strong inference of scienter. See Cozzarelli, 549 F.3d at 623 ("To prove the necessary mental state of scienter, negligence is not enough. A plaintiff must show either 'intentional misconduct' or such 'severe recklessness' that the danger of misleading investors was 'either known to the defendant or so obvious that the defendant must have been aware of it.'" (quoting Ottman, 353 F.3d at 343-44)).

Whether Plaintiffs have alleged facts giving rise to a strong inference of scienter depends on whether "the facts as a whole more plausibly suggest that the defendant acted innocently — or even negligently — rather than with intent or severe recklessness."

Id. at 624. Plaintiffs argue that Defendants' intent to deceive is shown by Defendants' various statements assuring investors that they had carefully reviewed the relevant clinical data. (Doc. 55 at 32-33 (citing Doc. 46 ¶¶ 60, 67).) Plaintiffs contend that these statements lead to the strong inference that "Defendants were both aware of, and had access to, the Phase 3 DILI events at the time they made their alleged false and misleading statements." (Id. at 33.) Citing the FDA's requirement to "promptly report instances of SAEs," Plaintiffs allege that Defendants "became aware virtually immediately of any instances of DILI that occurred during the studies." (Doc. 46 ¶ 57 (emphasis in original) (citing 21 C.F.R. § 312.32(c)(1)(i)(A)).)

Defendants respond by arguing that the most plausible inference to draw from the facts is that "Cempra endeavored to describe its solithromycin development efforts and to provide meaningful updates on trial data, and 'that defendants honestly believed their descriptions of the data and did not anticipate that the FDA would adopt a different view.'" (Doc. 50 at 38 (quoting In re Sanofi Sec. Litig., 87 F. Supp. 3d at 546).)

Here, the court finds that the facts as a whole more plausibly suggest that Defendants were acting innocently or negligently rather than deliberately misreporting material information or recklessly disregarding the truth. Under the PSLRA pleading standard for scienter, given two plausible inferences of intent

motivating the alleged false or misleading statements, one nefarious and one innocent, the court "must weigh those competing inferences and determine whether plaintiff's inference of scienter is 'cogent and at least as compelling' as defendants' inference." Cozzarelli, 549 F.3d at 626 (quoting Tellabs, 551 U.S. at 324); see also Yates, 744 F.3d at 885. Defendants' review and knowledge of the clinical results does not preclude them from reaching a different interpretation of the data. See In re AstraZeneca Sec. Litig, 559 F. Supp. 2d at 470 ("[P]articularly in the testing and development stage, the possible beneficial effects of a drug may be accompanied by adverse side effects, and there may be uncertainty as to how the risk-benefit balance ultimately turns out, and how it will be viewed by regulators.").

To the extent Plaintiffs' case rests on a challenge to Cempra's reliance on Hy's Law as a predictor of severe liver injury, it is insufficient to support a strong inference of intent. FDA presenter Dr. Gopinath explained in the FDA Advisory Committee's meeting that "[t]he single most specific predictor for the potential of severe hepatotoxicity is encapsulated in Hy's Law." (Doc. 51-16 at 152-53.) The FDA Briefing Document appendix also includes a "Disease Severity Scale" developed by the National Institutes of Health's Drug-Induced Liver Injury Network (DILIN) Study Group. (Doc. 51-15 at 95.) This "Disease Severity Scale" defines "severe" liver injury as the presence of "[e]levated ALT

and/or Alk P and serum bilirubin ≥2.5 mg/dl" and the presence of either "[h]epatic failure (INR ≥1.5, ascites or encephalopathy" or "[o]ther organ failure renal/pulmonary) [due to] dili." (Id.) It is logical that Defendants' explanations of the clinical trial results would therefore be made in the context of Hy's Law.

Apart from two SAEs that were attributable to allergic reactions to solithromycin in the Solitaire-IV trial, Plaintiffs have not identified any other drug-related SAE in the Phase 3 CABP trials which would have been subject to the FDA's reporting requirements and relevant to the allegedly misleading statements. (Doc. 46 ¶¶ 52 (noting that Cempra reported "no SAEs were considered study drug related" in the Solitaire-Oral trial), 55 (noting Cempra reported that only two SAEs associated with solithromycin in the Solitaire-IV trial were considered drug-related, both of which were allergic reactions).) Indeed, the FDA Briefing Document noted that apart from one liver-related SAE associated with moxifloxacin, "no other liver-related SAEs were noted in either arm [of the study]" in the pooled clinical results from the Phase 3 CABP trials. (Doc. 51-15 at 30.) In fact, the FDA Advisory Committee voted, albeit narrowly, in favor of approving solithromycin for use. (Doc. 51-16 at 336.) Under such circumstances, it is difficult to say that any Defendant actually knew or should have known that the FDA would ultimately reach a different interpretation of the data. See In re AstraZeneca Sec.

Litig., 559 F. Supp. 2d at 471.

Even assuming that Defendants may have been negligent in the manner in which they reported some of the clinical results, their conduct did not amount to "an extreme departure from the standard of ordinary care." Lerner, 273 F. Supp. 3d at 594. "The Fourth Circuit makes clear that the '[r]eckless conduct sufficient to establish a strong inference of scienter' must be 'severe.'" Id. Plaintiffs fail to plausibly allege that Defendants knew that certain facts would prevent the regulatory approval or marketing of solithromycin and concealed those facts from the investing public. In re AstraZeneca Sec. Litig., 559 F. Supp. 2d at 470. Indeed, Cempra made important parts of the allegedly problematic trial results publicly available prior to the end of the class period through two scientific articles published in peer-reviewed medical journals. (Doc. 51-9 (publishing the results of the Phase 3 Solitaire Oral trial online on February 4, 2016, and noting Grade 3 and 4 ALT and AST findings); Doc. 51-13 (publishing the results of the Phase 3 Solitaire-IV trial online on July 22, 2016, and noting SAEs, ALT and results at > 5 ULN)).)

Additionally, Cempra's October 16, 2015 press release and Form 8-K filed with the SEC disclosed the elevated ALT in patients treated with solithromycin during the Phase 3 CABP trials, describing the ALT elevations as "generally asymptomatic, reversible, and not associated with increased bilirubin," and

adding that "[n]o solithromycin patient met Hy's Law criteria of concurrent ALT and bilirubin elevations post-baseline." (Doc. 46 ¶ 59.) These public documents described the results in the Avigan memorandum that Plaintiffs allege Cempra failed to disclose. (Id. ¶ 83.)

The FDA confirmed these findings. During the FDA Advisory Committee meeting, Dr. Avigan stated that during the Phase 3 trials: "we never saw a severe or serious liver injury." (Doc. 51-16 at 255-56.) Yet, the Avigan memorandum acknowledged that the results for the eight patients in the Phase 3 CABP trial were "solithromycin-induced liver injury" and concluded there was an "open question concerning the actual 'real-world' population-level risk for serious DILI associated with solithromycin." (Doc. 51-15 at 92 (emphasis added).) This was reiterated during the FDA Advisory Committee meeting, when Dr. Avigan stated that the issue was whether the trials "tested enough people to feel comfortable with where the risk may lie to say that we haven't seen an event." (Doc. 51-16 at 257, 258.)[21] Based on this record, even if Cempra was negligent to describe the trial results without noting that failure to meet Hy's Law criteria "does not imply that a drug with aminotransferase elevations is free from risk of severe DILI,"

[21] As noted earlier, the FDA Advisory Committee meeting transcript was one of the exhibits Plaintiffs do not challenge in their motion to strike.

Cempra did not recklessly claim that there was no risk of severe DILI in future trials. (Id. at 156; Doc. 46 ¶ 53); cf. In re Medimmune, Inc. Sec. Litig., 873 F. Supp. 953, 967 (D. Md. 1995) (finding challenged statement that "[t]here's absolutely no question about efficacy" to be actionable). Rather, the company simply reported its Phase 3 CABP trial results based on the data, and the Avigan memorandum agreed that no serious liver injury was observed. Accordingly, the record fails to suggest that Cempra was acting intentionally or recklessly when describing its Phase 3 CABP results, as opposed to simply stating its interpretation of them. See In re Sanofi Sec. Litig., 87 F. Supp. 3d at 543.

Moreover, the FDA never concluded that Cempra's trials showed a risk of severe DILI. Rather, the FDA's Complete Response Letter only required additional safety information to characterize solithromycin's hepatotoxicity. (Doc. 46 ¶¶ 11, 88.) The FDA recommended a comparative study with 9,000 CABP patients exposed to solithromycin and indicated that if solithromycin were approved, the drug's label would need to include "adequate information about the potential for hepatotoxicity." (Id. ¶ 11.) Thus, the FDA did not conclude that Cempra's statements were factually inaccurate but simply determined that more data should be obtained before drawing those same positive interpretations. Therefore, the most compelling inference is that any disparity between the challenged statements and the information disclosed by

the FDA appears to reflect a difference of opinion regarding the interpretation of the clinical results, rather than a concerted effort to deceive the investing public. See In re AstraZeneca Sec. Litig., 559 F. Supp. 2d at 471.

ii. Allegedly Misleading Statements Concerning the Differentiation of Solithromycin from Ketek

Plaintiffs allege that Defendants made six misleading statements during the class period concerning the differentiation of solithromycin from Ketek. (Doc. 46 ¶¶ 65, 69, 71, 72, 74, 77.)[22] Within many of these statements, Defendants expressed confidence regarding Cempra's ability to differentiate the drug due to differences in its chemical structure. (See, e.g., id. ¶¶ 69 ("Through ongoing research, we have developed multiple ways to differentiate solithromycin from Ketek. Our research suggests these [Ketek] side effects may be caused by the pyridine moiety, which forms a part of the structure of Ketek. . . . Solithromycin . . . [does] not have a pyridine component."), 71 ("[W]e have very clearly differentiated solithromycin from Ketek based on its mechanism of action and the reason for its adverse event.").) In addition, three of the challenged statements seek to differentiate the drugs on the basis

[22] For the reasons previously discussed, the challenged statement by Fernandes during the May 2, 2016 earnings conference call (Doc. 46 ¶ 72) constitutes a non-actionable opinion.

of the results of the clinical trial. (Id. ¶¶ 65, 74, 77.)

Plaintiffs claim that these statements were misleading because "Defendants knew that patients in the clinical development of solithromycin had, in fact, suffered DILI just like they had with Ketek." (Doc. 55 at 27.) Plaintiffs allege that the FDA Briefing Document "stated that Cempra presented no evidence to support any claim that solithromycin had a substantially lower potential to cause liver toxicity versus Ketek." (Doc. 46 ¶ 82.) Plaintiffs also note that the FDA Briefing Document disclosed that "hepatic adverse effects seen with solithromycin during its clinical trials exceed the pre-marketing hepatic signal seen with [Ketek]." (Doc. 51-15 at 35; Doc. 55 at 28.)

Defendants dispute Plaintiffs' claim regarding the FDA Briefing Document, arguing that "[a]t most, the FDA Advisory Committee and Dr. Avigan expressed uncertainty about whether solithromycin's differing chemical structure would prevent the side-effects seen with Ketek post-approval." (Doc. 59 at 12.) Defendants further contend that Plaintiffs offer no support for their assertion that patients suffered DILI "just like" Ketek, noting that patients in the Phase 3 CABP trials did not exhibit any of the symptoms associated with Ketek. (Id. at 13.)[23] Finally,

[23] Defendants note that no patient exhibited other common symptoms of Ketek, including myasthenia gravis, a condition causing a form of muscle weakness. (Doc. 59 at 13.) During the FDA Advisory Committee meeting, however, FDA presenter Dr. Gopinath noted that patients with existing

Defendants contend that the FDA Briefing Document's observation that the pre-marketing hepatic signal of solithromycin exceeded that of Ketek has limited relevance given that any connection between Ketek and idiosyncratic DILI was only observed during the post-marketing period. (Id. at 13-14.)

The court concludes that the challenged statements regarding Cempra's ability to differentiate solithromycin from Ketek on the basis of its chemical structure are not actionable in this case. (Doc. 46 ¶¶ 69, 71.) Plaintiffs' allegation that Cempra presented "no evidence" to differentiate solithromycin from Ketek is contradicted by Cempra's clinical trials. As noted in Cempra's FDA briefing document, Cempra conducted a detailed analysis of its clinical results, with particular attention to the adverse events observed with Ketek. (Doc. 51-14 at 130.) In addition, Cempra relied on a complex computational model of DILI, performed by an independent service, to assess the risk of Hy's Law cases or incidents of severe idiosyncratic liver injury from use of the drug. (Id. at 122-23; Doc. 51-15 at 90.) The Avigan memorandum noted that Cempra's modeling predicted that the "main driver of hepatocyte loss causing the range of ALT and ALP abnormalities

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diagnoses of myasthenia gravis were excluded from the clinical trials and found that the clinical trials did not provide "any information about what potential impact solithromycin would have on this group of patients." (Doc. 51-16 at 151.) Dr. Gopinath confirmed that visual disorders were not observed but found that there "was a very significant signal" of hepatotoxicity. (Id. at 152.)

that were observed in the clinical study program" were likely to be "most strongly connected to drug-induced mitochondrial toxicity," which was different from that thought to be associated with erythromycin. (Doc. 51-15 at 90.) The Avigan memorandum concluded that the Cempra modeling "may become more valuable in the long-term as more information accrues," but that "with the limited power of study subject liver test data that has been used, a firm conclusion that solithromycin is not associated with a risk for clinically serious idiosyncratic hepatotoxicity cannot be drawn." (Id. at 90-91 (emphasis added).) The Avigan memorandum recommended more studies, using telithromycin (Ketek) as a positive control, and concluded that Cempra's argument that solithromycin "is marked by a substantially lower potential to cause severe hepatotoxicity than telithromycin [Ketek]" was "so far unproven." (Id.) So, even though the FDA ultimately found Cempra's arguments to be unpersuasive, it is untrue that Defendants presented no evidence to support their claim.

Indeed, the cautionary language contained in Cempra's January 7, 2016 prospectus undermines any claim that the challenged statements regarding Cempra's ability to differentiate solithromycin from Ketek based on its chemical composition were in fact misleading. (Doc. 46 ¶ 69; Doc. 51-7 at 22-23.) The prospectus alerted investors that Cempra "might not successfully differentiate solithromycin from telithromycin (Ketek), a

macrolide found to cause severe side effects," noting that "[b]ecause of the Ketek experience, the macrolide class is likely to be carefully scrutinized by the FDA." (Doc. 51-7 at 23-24.) The prospectus further noted that "[t]he results of either of our ongoing studies of the effectiveness of solithromycin as a treatment for NASH and COPD or any other study or trial involving solithromycin, if negative, could have an adverse effect on FDA and other regulatory approval of solithromycin as a treatment for CABP as well as our commercialization efforts for solithromycin and market acceptance of the same." (Id. at 24.)[24] Through this

[24] The complete statement of the prospectus provided:

> **We might not successfully differentiate solithromycin from telithromycin (Ketek®), a macrolide found to cause severe side effects.**
>
> Ketek is a macrolide antibiotic that the FDA approved in 2004 for the treatment of multi-drug resistant pneumococci and other CABP bacteria. Soon after release, however, Ketek was found to cause reversible visual disturbances, exacerbate myasthenia gravis (a neurological disorder characterized by improper muscle regulation) and cause liver failure. These effects led the FDA to require the drug label for Ketek to include a strengthened warning section regarding specific drug-related adverse events and contributed to Ketek being withdrawn in 2007 for the treatment of all infections other than CABP. Our research suggests these side effects may be caused by the pyridine moiety, which forms a part of the structure of Ketek. We have demonstrated that pyridine inhibits the action of nicotinic acid acetylcholine receptors that could result in the side effects caused by Ketek. Solithromycin and older generation macrolides, including azithromycin and clarithromycin, that have been widely marketed do not have a pyridine component. If our research is proven to be incorrect or if solithromycin demonstrates similar side effects, the FDA might not approve solithromycin, or, if already approved, might withdraw approval, require us to conduct additional clinical trials or

cautionary language, therefore, investors were clearly advised of the risks surrounding Cempra's ability to successfully differentiate solithromycin from Ketek. When read in light of the prospectus, the challenged statements did not present an obvious danger of misleading a reasonable investor. Lerner, 273 F. Supp. 3d at 594. Consequently, there is no reckless conduct sufficient to establish a strong inference of scienter.

Plaintiffs' arguments as to the challenged statements differentiating the drug from Ketek on the basis of the clinical results present a closer question, given Cempra's failure to disclose the adverse events observed in the Phase 2 COPD trials. (See Doc. 46 ¶¶ 65, 74, 77.) In particular, Plaintiffs point to Hahn's statements at the Morgan Stanley Global Healthcare Conference on September 12, 2016. (Id. ¶¶ 73-74.) In response to a question from an analyst regarding "what happened with Ketek and how solithromycin differs," Hahn responded: "in all of our trials – we have exposed over 2,000 patients and subjects over the years, and nobody has had any of those same types of issues that the folks

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> require warnings on product labeling, which would significantly harm our ability to generate revenues from solithromycin. Even if the FDA approves solithromycin, physicians may not be convinced that solithromycin is a safe and effective treatment for CABP and other infections. If physicians believe solithromycin demonstrates characteristics similar to Ketek, they might not prescribe solithromycin, which would negatively affect our revenues.

(Doc. 51-2 at 6.)

had experienced with Ketek." (Id. ¶ 74.) But this statement was not made in the abstract. In that same response, Hahn had identified the issues caused by Ketek as "visual disturbance," "exacerbation of myasthenia gravis," and "liver toxicity."[25] (Id.) In this context, therefore, the statement does not appear to be false, but its accuracy is subject to criticism insofar as the FDA noted that persons with a diagnosis of myasthenia gravis were excluded from the study and some participants, while not experiencing liver toxicity as measured by Hy's Law, had "a very significant signal" of liver toxicity. See note 23 supra.

Plaintiffs also point to Hahn's response to a question during the same conference regarding how the FDA Advisory Committee panel will address the ALT elevations observed during the clinical trials. Hahn responded: "What we see is what you expect from a macrolide: you expect ALTs to go up in the early days, and come back down. Even on continued therapy, we saw the ALT levels coming right back down." (Id. (emphasis added).) While Hahn's statements were broad in scope, purporting to cover "all" of Cempra's trials,

[25] In discussing toxicity for Ketek, the FDA Briefing Document notes that some participants in the Ketek clinical trials developed "reversible hepatitis with or without jaundice," and "a comprehensive assessment of 42 published and spontaneously reported post-marketing cases of clinically significant telithromycin-associated liver injury" performed by an FDA expert panel found that four of those cases involved the severe outcome of death, one required a liver transplant, and a total of 26 were judged to be "highly likely" or "probable" in their causal association with telithromycin. (Doc. 51-15 at 64-65; see also id. at 89-90 (Avigan memorandum noting same).)

he failed to disclose the adverse events in the Phase 2 COPD trials, where at least one participant exhibited clear symptoms of liver injury and his liver test results did not return to normal until twenty-nine days after being discontinued from treatment. (See Doc. 51-11 at 15-17.)

At least with regard to Cempra's Phase 3 CABP clinical trials, Defendants correctly note that there is limited evidence of serious idiosyncratic liver toxicity or other notable symptoms that were associated with Ketek, even if the FDA ultimately found that the clinical data demonstrated a "signal" for hepatic injury. (Doc. 59 at 12–13.) The clinical data supported Cempra's interpretation of the clinical results. The fact that the FDA ultimately gave the data different weight does not necessarily render the challenged statements misleading. It cannot be said that Cempra's statements are "such an extreme departure from the standard of ordinary care" that the Defendants "must have been aware" of such an obvious danger of misleading the plaintiffs. Lerner, 273 F. Supp. 3d at 594 (internal quotation marks omitted).

Nevertheless, the adverse events observed during the Phase 2 COPD trial did provide a much more concerning indicator of idiosyncratic liver injury similar to what had been observed with Ketek. Indeed, Cempra's January 7, 2016 prospectus acknowledged generally that the company's ongoing studies involving solithromycin, including the COPD study, "if negative, could have

an adverse effect on FDA and other regulatory approval of solithromycin as a treatment for CABP as well as our commercialization efforts for solithromycin and market acceptance of the same." (Doc. 51-7 at 24.)

In particular, one patient in the Phase 2 COPD study developed cholestatic hepatitis, and his liver test results did not return to normal until twenty-nine days after treatment of solithromycin was discontinued. (Doc. 51-11 at 15-16.) During the FDA Advisory Committee hearing, Oldach acknowledged this was a case of DILI. (Doc. 51-16 at 111 ("[W]e agree that the COPD patient with cholestatic hepatitis had a drug-induced liver entry [sic]. There's no question. But we think this is due to dose and duration, something which we were actively exploring in our trials.").) Notably, however, the patient was ultimately determined not to meet Hy's Law criteria. (Id. at 89.)[26] Even though these adverse events occurred in the Phase 2 trial for a different treatment, Cempra and its executive officers were well aware that all clinical data would be considered by FDA in the approval process. Fernandes publicly acknowledged as much in an investor call. (Doc. 46 ¶ 76

[26] The Avigan memorandum characterized this case as follows: "The case represents a clinically significant episode of solithromycin-induced hepatotoxicity (Severity Level 2) marked by jaundice and pruritis, in which a causal association with the study drug in my view is 'Highly Likely'." (Doc. 51-11 at 16.) While concurrent elevations of bilirubin were observed in the patient, the hepatic safety advisory board determined that the patient did not meet Hy's Law criteria. (Doc. 51-16 at 89; Doc. 51-11 at 15-17; Doc. 51-14 at 167.)

("So all of the safety data — every human exposure is submitted as part of the law. We have submitted data until at the end of August and all data comes in, every part will be exposed. And we're very pleased with the safety of the drug. . . . We're proud to be able to submit this data.").)

However, even assuming that Plaintiffs plausibly pleaded that Hahn's challenged statements were false or misleading because Hahn failed to disclose the results of the Phase 2 COPD trials (id. ¶ 74), this failure, given the context of the statements made, does not provide a strong inference of scienter. The question is not whether a reasonable person could infer that scienter existed, but whether the inference of scienter is "strong — and compelling, and powerful — when it is weighed against the opposing inferences that may be drawn from the facts in their entirety." Cozzarelli, 549 F.3d at 624. As Defendants note, the COPD clinical trial concerned a much longer term of treatment with solithromycin — 28 days. The facts, when viewed in the light most favorable to Plaintiffs, are more consistent with the Defendants having acted on the belief that the COPD adverse events were distinguishable from the five to seven day treatment plan for which Cempra was seeking regulatory approval for the CABP application. (Doc. 51-15 at 62.) This conclusion is supported by the Avigan memorandum's notation that solithromycin may have a "steep dose-liver injury response curve." (Doc. 51-15 at 78.)

A comparison of the extensive briefing materials prepared by the FDA staff and Cempra reveals that each side had its own interpretation of the data. See In re AstraZeneca Sec. Litig., 559 F. Supp. 2d at 471. When evaluating the facts alleged in the amended complaint holistically, the more compelling inference is that Defendants had a good faith belief in their interpretation of the clinical data, and any failure to disclose the adverse events in the COPD trials did not result from any dishonest or reckless behavior. See Yates, 744 F.3d at 893 (holding that plaintiffs failed to meet their burden of pleading scienter under the PSLRA, where the facts indicated that the "more compelling . . . inference [was] that the [defendants] were, at most, negligent"); In re AstraZeneca Sec. Litig., 559 F. Supp. 2d at 471-72 (finding that the plaintiffs had "not alleged an inference of scienter as compelling as the opposing inference" where there were two possible analyses and conclusions based on the data); In re Human Genome Scis. Inc. Sec. Litig., 933 F. Supp. 2d at 761 (finding Defendants' failure to disclose adverse event within ongoing clinical trial insufficient to support strong inference of scienter where the Defendants never mentioned the study by name or gave any concrete details regarding the study); cf. Schueneman, 840 F.3d at 708 (holding that plaintiffs adequately alleged scienter where defendants affirmatively represented that "all the animal studies that [had] been completed" supported the

company's case for approval of developmental drug, but failed to disclose adverse results in an animal study about which the FDA had expressed particular interest).

iii. Allegedly Misleading Statements Regarding Solithromycin's Safety Profile in the Phase 2 NASH Study

Finally, Plaintiffs allege that Cempra amended the protocol for the Phase 2 NASH clinical trial to reduce the dosage amounts of solithromycin because of the adverse effects observed in the Phase 2 COPD trial, but failed to adequately disclose this point to investors. (Doc. 46 ¶¶ 75-76; Doc. 55 at 28.) On September 30, 2016, Cempra held a conference call for analysts and investors to discuss the preliminary results of the Phase 2 NASH clinical trial. (Doc. 46 ¶ 76; Doc. 51-12.) During the question-and-answer session, Oldach acknowledged that the dosing regimen was changed to address ALT elevations observed when treating patients with solithromycin for longer durations, but he did not disclose the full extent of the adverse events observed during the COPD clinical trials. (Doc. 46 ¶ 76; Doc. 51-12.)[27] Fernandes also

[27] During the September 30, 2016 conference call, Oldach stated:

> When dosing solithromycin for longer durations, we've observed ALT elevation and since one of the goals of this trial [was] to determine the optimal regimen for longer treatment period, we adjusted the dose to 200 milligrams daily for one week, followed by 200 milligrams three times a week. The lower dose is supported by the mouse model and human PK data that suggest it might be efficacious. We hope to confirm this dosing regimen in the study and we are very excited with

stated that the company had submitted all of the clinical data to the FDA as part of the approval process and reiterated that "we're very pleased with the safety of the drug." (Doc. 46 ¶ 76; Doc. 51-12 at 13.) When later questioned regarding the amendment to the protocol during the conference call, Fernandes said that "[t]he driver [behind the decision to alter dosages] was efficacy as well as safety." (Doc. 51-12 at 9.)

Plaintiffs allege that Oldach's statement regarding the amendment of the protocol of the Phase 2 NASH trial was false and misleading because he failed to disclose that the amendment occurred due to "patterns of DILI observed in the Phase 2 COPD trial," citing the FDA Briefing Document. (Doc. 46 ¶ 82; Doc. 55 at 28.)[28] Defendants contend the FDA Briefing Document does not contain any such statement (Doc. 50 at 29 n.13), and the court can find no such statement. FDA Presenter Dr. Gopinath did state during the FDA Advisory Committee meeting that "after considering some of the safety information that came out of the COPD trial, the protocol for the NASH trial was amended." (Doc. 51-16 at 171.) Defendants contend that Oldach's statement regarding the Phase 2

> the therapeutic effects and safety profile we have seen thus far.

(Doc. 46 ¶ 76.)

[28] The complaint alleges "the FDA's briefing document disclosed that the Company had amended the Phase 2 NASH study protocol . . . because of patterns of DILI observed in the Phase 2 COPD trial." (Doc. 46 ¶ 82.)

trials is "not at all inconsistent with Plaintiffs' allegation that Cempra adjusted the dose due to observations from the Phase 2 COPD trial." (Doc. 50 at 30.)

While Section 10(b) and Rule 10b-5 "do not create an affirmative duty to disclose any and all material information," Singer, 883 F.3d at 440 (citation omitted), it is a closer question whether Oldach had a duty to disclose the complete rationale for the dosing change when he referenced ALT elevations observed "[w]hen dosing solithromycin for longer durations," even if he did not refer to the clinical study by name. (Doc. 46 ¶ 76.) Defendants' argument — that Oldach's reference to just ALT elevations is consistent with the Phase 2 COPD trial results — conflicts with the distinction Defendants draw between ALT elevation and DILI in defending against the other challenged statements. At least one patient during the COPD Phase 2 trials demonstrated clear symptoms of DILI. (See Doc. 46 ¶ 82; see also Doc. 51-11 at 15-17; Doc. 51-16 at 111.) In these circumstances, where Cempra was noting the increased ALT elevations in other phases of its solithromycin trials where DILI was not identified, Oldach's reference to just ALT elevations and not DILI in the Phase 2 NASH trial plausibly "would have misled a reasonable investor." Lerner, 273 F. Supp. 3d at 586.

Nevertheless, Plaintiffs again fail to adequately allege a strong inference of scienter with respect to these challenged

statements relating exclusively to the Phase 2 NASH trials. During the same conference call, Fernandes clarified that the dosage change was made for "efficacy as well as safety." (Doc. 51-12 at 9.) This mirrors the explanation given by FDA presenter, Dr. Gopinath, that changes were made to the NASH trial protocol "after considering some of the safety information that came out of the COPD trial." (Doc. 50 at 29-30 n.13 (quoting 51-16 at 171).) In light of the conflicting interpretations of DILI, and for reasons similar to those previously discussed, the court finds that the allegations with respect to these challenged statements do not support a finding of a strong inference of scienter. See In re Human Genome Scis. Inc. Sec. Litig., 933 F. Supp. 2d at 761.

3. Section 20(a) Claims

Plaintiffs also allege the individual Defendants violated § 20(a) of the Exchange Act. (Doc. 46 ¶¶ 121-24.) Section 20(a) imposes liability on any person who "directly or indirectly, controls any person liable" for violations of the Exchange Act, "unless the controlling person acted in good faith and did not directly or indirectly induce the act or acts constituting the violation or cause of action." 15 U.S.C. § 78t(a). Plaintiffs have alleged that each of the individual Defendants had authority over the content and dissemination of the challenged statements and qualifies as a control person within the meaning of Section 20(a) of the Exchange Act. (Doc. 46 ¶¶ 24, 27, 30.) Because the

court finds that Plaintiffs fail to state a claim regarding the predicate violation of Section 10(b), Plaintiffs' Section 20(a) claims cannot proceed. BearingPoint, 576 F.3d at 192 ("Because the complaint fails to withstand a Rule 12(b)(6) motion with respect to the predicate violation of § 10(b), it also fails with respect to the § 20(a) claims.")

III. CONCLUSION

Having reviewed all alleged misrepresentations and all other alleged bases for scienter, individually and collectively, the court finds that they are insufficient to raise a strong inference that any Defendant intended to mislead any investor, or acted recklessly. For the reasons stated, the court finds that Plaintiffs have failed to state a claim for relief upon which relief can be granted under Section 10(b) or Section 20(a) of the Exchange Act, or Rule 10b-5.

IT IS THEREFORE ORDERED that the Defendants' motion to dismiss (Doc. 49) be GRANTED and the Plaintiffs' amended complaint (Doc. 46) be DISMISSED.

/s/ Thomas D. Schroeder
United States District Judge

October 26, 2018