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NOT TO BE PUBLISHED IN THE OFFICIAL REPORTS

IN THE COURT OF APPEAL OF THE STATE OF CALIFORNIA

SECOND APPELLATE DISTRICT

DIVISION SEVEN

AIDA ROTONDO, et al., Plaintiffs and Appellants, v. AMYLIN PHARMACEUTICALS, INC., et al., Defendants and Respondents.	B275314 (Los Angeles County Super. Ct. No. JCCP4574)

APPEAL from a judgment of the Superior Court of Los Angeles County, William F. Highberger, Judge. Reversed.

Engstrom, Lipscomb & Lack, Elizabeth L. Crooke, Brian D. Depew; Law Offices of Martin N. Buchanan and Martin N. Buchanan; Girardi & Keese, Thomas V. Girardi, V. Andre Sherman; Hunter Shkolnik and Jennifer R. Liakos for Plaintiffs and Appellants.

O'Melveny & Myers, Richard B. Goetz, Amy J. Laurendeau and Houman Ehsan for Defendant and Respondent Amylin Pharmaceuticals, LLC.

Williams Connolly, Stephen D. Raber, Douglas R. Marvin, F. Lane Heard III and Kannon K. Shanmugam for Defendant and Respondent Merck Sharp & Dohme Corp.

DLA Piper, Loren H. Brown, Raymond M. Williams and Stanley J. Panikowski for Defendant and Respondent Novo Nordisk, Inc.

Pepper Hamilton, Kenneth J. King, Barry H. Boise, Aline Fairweather; Reed Smith and David E. Stanley for Defendant and Respondent Eli Lilly and Company.

Plaintiffs in this consolidated proceeding allege state-law claims asserting that pharmaceutical manufacturers failed to warn consumers that a class of diabetes medication commonly known as "incretin-based drugs" increases the risk of pancreatic cancer. The manufacturers filed a motion for summary judgment arguing that plaintiffs' claims were preempted under *Wyeth v Levine* (2009) 555 U.S. 555 (*Wyeth*) because the undisputed evidence showed the Food and Drug Administration would not have permitted a warning for pancreatic cancer. The trial court agreed and granted judgment in the manufacturers' favor.

We reverse, concluding that the trial court erroneously interpreted *Buckman Co. v. Plaintiffs' Legal Committee* (2001) 531 U.S. 341 (*Buckman*) to preclude the consideration of scientific evidence that the Food and Drug Administration had not previously evaluated.

FACTUAL BACKGROUND

A. Summary of the Plaintiffs' Claims

Plaintiffs in this consolidated proceeding are individuals, or the heirs of individuals, who developed pancreatic cancer after being prescribed one of four brand-named diabetes medications,

collectively referred to as "incretin-based drugs," that are designed to stimulate insulin secretion in pancreatic cells by increasing the level of incretin hormone. Defendants are pharmaceutical manufacturers that developed and sold the four medications at issue under the brand names "Byetta" (defendant Amylin Pharmaceuticals), "Victoza" (defendant Eli Lilly and Company), "Januvia" and "Janumet" (defendant Merck Sharp & Dohme Corporation).[1]

Plaintiffs' claims allege that defendants failed to warn consumers that incretin-based drugs increase the risk of developing pancreatic cancer. Although the Food and Drug Administration (FDA or the Administration) did not require defendants to include a pancreatic cancer warning on their product labels when the drugs were approved for market, plaintiffs contend the defendants should have amended the labels to add a warning based on subsequent research showing a causal relationship between incretin-based drugs and pancreatic cancer.

Plaintiffs filed more than 300 individual cases in Superior Court alleging failure-to-warn claims. The cases were consolidated, and the matter was assigned to Los Angeles County Superior Court Judge William Highberger. Numerous cases raising similar failure-to-warn claims involving incretin-based drugs have been filed in other state and federal jurisdictions throughout the country. In August 2013, a federal multi-district

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[1] In the scientific literature, these drugs are sometimes referred to by their active ingredient: "exenatide" (Byetta); "liraglutide" (Victoza); and "sitagliptin" (Januvia and Janumet). The parties agree that any technical differences in the drugs' chemical makeup or activation method are irrelevant to the issues presented in this appeal.

litigation was established, *In re Incretin-Mimetic Cases* (MDL # 2452), for all such claims pending in federal court. The case was assigned to Judge Anthony Battaglia in the United States District Court for the Southern District of California.[2] To minimize redundancy and inconsistent rulings, Judge Highberger and Judge Battaglia coordinated various aspects of discovery in the state and federal proceedings.

*B. **Motions for Summary Judgment***

In June 2015, defendants filed essentially identical motions for summary judgment in the state and federal proceedings arguing that plaintiffs' claims were preempted pursuant to the Supreme Court's holding in *Wyeth v Levine, supra,* 555 U.S. 555.

1. Summary of Wyeth v. Levine

The plaintiff in *Wyeth* developed gangrene after receiving a "push injection" of an anti-nausea medication. The plaintiff filed a state-law claim alleging the manufacturer had failed to warn that the drug should be administered through an IV-drip because the push injection method created an unreasonable risk of infection. The manufacturer argued that plaintiff's claim was preempted because federal regulations required it to use the exact label the FDA had approved during the application process, which did not include a warning regarding the push injection method.

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[2] Hereafter, we refer to the California consolidated proceeding pending before Judge Highberger as the "state proceedings," and the federal multi-district litigation pending before Judge Battaglia as the "federal proceedings."

The Supreme Court rejected this argument, explaining that although drug manufacturers are normally required to obtain FDA approval before changing a drug label, "there is . . . an FDA regulation that permits a manufacturer to make certain changes to its label before receiving the agency's approval. Among other things, this 'changes being effected' (CBE) regulation provides that if a manufacturer is changing a label to 'add or strengthen a contraindication, warning, precaution, or adverse reaction[,]' . . . it may make the labeling change upon filing its supplemental application with the FDA; it need not wait for FDA approval." (*Wyeth, supra,* 555 U.S. at p. 568 [citing 21 C.F.R. § 314.70, subd. (c)(6)(iii)(A), (C).) The Court further explained that the CBE regulation reflects a "central premise of federal drug regulation[:] that the manufacturer bears responsibility for the content of its label at all times. It is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market." (*Id.* at pp. 570-571.)

The Court clarified, however, that "the FDA retains authority to reject labeling changes made pursuant to the CBE regulation in its review of the manufacturer's supplemental application, just as it retains such authority in reviewing all supplemental applications. But absent clear evidence that the FDA would not have approved a change to [the medication's] label, we will not conclude that it was impossible for [defendant] to comply with both federal and state requirements." (*Wyeth, supra*, 555 U.S. at p. 571.)

The Court further concluded that the defendant had failed to meet that standard, explaining that there was no evidence the defendant had "ever attempted to" provide a warning about the push injection method, or that the FDA had ever prohibited the

defendant from providing such a warning. (*Wyeth, supra*, 555 U.S. at p. 571.) Instead, the record showed the defendant and the FDA "gave [only] passing attention to the issue of IV-push versus IV-drip administration." (*Ibid.*)

2. Summary of defendants' motions for summary judgment

In their motions for summary judgment, defendants argued that plaintiffs' failure-to-warn claims were preempted because there was "clear evidence" the FDA would have rejected a CBE application seeking to include a warning that incretin-based drugs increase the risk of pancreatic cancer. Defendants asserted that the CBE regulation does not permit a manufacturer to add a warning to its product label unless there is "some basis to believe there is a causal relationship" between the hazard and the drug. (See 21 C.F.R. §§ 201.57, subds. (C)(6) & (7); 314.70, subd. (c)(6)(iii)(A).) Defendants contended that several pieces of evidence established the FDA did not believe a causal relationship existed between incretin-based drugs and pancreatic cancer, and therefore would have denied any CBE application proposing such a warning.

Defendants' primary piece of evidence consisted of a four-page article published in the February 2014 issue of New England Journal of Medicine (NEJM) entitled "Pancreatic Safety of Incretin-Based Drugs — FDA and EMA Assessment." The article, co-authored by scientists from the FDA and the European Medicines Agency (EMA), explained that "within the past year, [each agency had] independently undert[aken] comprehensive evaluations of a safety signal arising from postmarketing reports of pancreatitis and pancreatic cancer in patients using incretin-based drugs."

The article described several categories of research the agencies had reviewed during their evaluation, which included (among other things): (1) a 2013 research report "revealing a possible pancreatic safety signal"; (2) more than 250 nonclinical animal studies drug manufacturers had conducted during the application and approval period; (3) several "3-month pancreatic toxicity studies in rodent model of diabetes" that manufacturers had performed at the request of the FDA; (4) tissue slides from the 3-month toxicity studies; (5) pancreatic toxicology studies the FDA had independently performed using rodents modeled to exhibit symptoms of pancreatitis and diabetes; and (6) data from more than 200 clinical trials involving incretin-based drugs.

The article stated that, based on their review of these "multiple streams of data," both agencies "agree that assertions concerning a causal association between incretin-based drugs and pancreatitis or pancreatic cancer, as expressed recently in the scientific literature and in the media, are inconsistent with the current data," and "believe that the current knowledge is adequately reflected in the production information or labeling." The article clarified, however, that neither agency had "reached a final conclusion . . . regarding such a causal relationship. Although the totality of the data that have been reviewed provides reassurance, pancreatitis will continue to be considered a risk associated with these drugs until more data are available; both agencies continue to investigate this safety signal."

The defendants' second piece of evidence was a formal rejection letter the FDA had issued in response to a citizen's petition requesting that the Administration remove Victoza from the market due to increased risks of thyroid cancer and pancreatitis. The petition further asserted that data from the

FDA's adverse event reporting system (FAERS) suggested that incretin-based drugs may increase the risk of pancreatic cancer. The FDA's rejection letter, issued in March 2014, explained that FAERS data "does not provide strong evidence of risk when the adverse event (i.e., pancreatic cancer) occurs commonly in the background untreated population and has a long latency period. Any causal association between exposure to Victoza and pancreatic cancer is indeterminate at this time."[3] The rejection letter also stated that the FDA had found "no new evidence regarding the risk of pancreatic carcinoma in association with the use of Victoza that would support any changes to current approved labeling. . . . We will continue to monitor and to review available safety information related to pancreatic cancer in patients who are receiving Victoza."

Defendants' third piece of evidence was a "Briefing Document" that an FDA advisory committee had issued in December 2014 regarding an application to market a new incretin-based drug named Saxenda. The document stated that the FDA had "explored multiple data streams to evaluate pancreatic toxicity as a potential drug safety signal, which to date, do not support pancreatic cancer as an incretin mimetic-mediated event."

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[3] The NEJM article included similar language, explaining that "although the disproportionate spontaneous reporting of adverse events is commonly interpreted as a safety signal, there are inherent limitations to the ability to establish causal relationships, including the evaluation of events with high background rates, long latency periods, or a possible contribution by the disease itself."

Finally, defendants noted that after the FDA had published the NEJM article, it approved four new incretin-based drugs in 2014, and did not require any warning for pancreatic cancer.

Defendants argued that considered together, the above evidence demonstrated the FDA had conducted a thorough scientific investigation regarding the potential risk of pancreatic cancer, and concluded that no warning was warranted.

3. Plaintiffs' opposition

Plaintiffs, however, argued that the FDA had repeatedly clarified that it had not yet made a final determination whether incretin-based drugs increase the risk of pancreatic cancer. In support, plaintiffs submitted evidence showing that in March 2013, the FDA issued a formal announcement that it was evaluating new findings suggesting that incretin-based drugs increased the risk of pancreatic "pre-cancerous cellular changes." The announcement emphasized that the FDA had "not reached any new conclusions about safety risks with incretin[] drugs," and would "communicate its final conclusions and recommendations when its review is complete." Plaintiffs argued that since issuing that communication in 2013, the FDA had not made any subsequent, formal communication reporting its final conclusions on the issue.

Plaintiffs noted that the NEJM article included similar language, clarifying that the FDA had not reached a "final conclusion at this time regarding such a causal relationship." Moreover, during the Saxenda application process, the FDA had reported that it "continued [to see] accrual of disproportionate number of [Victoza] associated . . . pancreatic cancers relative to all other drugs in the [FAERS]."

Plaintiffs also argued that they had identified several categories of "'new safety information'" that the FDA had not "considered . . . in any of its reviews." First, plaintiffs cited a 100-page report from Health Canada (the FDA's Canadian counterpart) finding that sitagliptin (the active ingredient in Januvia and Janumet) may increase the risk of pancreatic cancer. Second, plaintiffs contended that evidence obtained during discovery showed that the "pooled data analysis" defendants had submitted to the FDA omitted "a number of studies that reported cancer," resulting in a statistical imbalance that was unknown to the FDA. Third, plaintiffs asserted that their expert witnesses had reviewed tissue slides from some of the defendants' nonclinical studies, and found evidence of pre-cancerous lesions that defendants had not identified or reported to the FDA. Fourth, plaintiffs cited a nonclinical study that a UCLA research team had performed using the "Kras mouse," a rodent engineered to have susceptibilities to pancreatic cancer common in aging persons with diabetes. The study concluded that incretin-based drugs "advance[d] the rate" of formation of precancerous lesions in pancreas cells. Finally, plaintiffs cited a "pooled analysis" that David Madigan, a statistics professor at Columbia University, had performed on data from numerous clinical trials. Madigan's analysis showed that the rate of pancreatic cancer among diabetics who had been treated with incretin-based drugs greatly exceeded the background rate of pancreatic cancer among diabetics.

Plaintiffs asserted that the FDA's repeated statements that it was still evaluating the pancreatic cancer risk of incretin-based drugs, combined with the new safety information plaintiffs had identified, demonstrated that it was not clear that the FDA

would have rejected a CBE application seeking to add a warning for pancreatic cancer.

4. Defendants' reply brief

In their reply brief, defendants argued that the new safety information plaintiffs had identified in their opposition was "not relevant to a preemption analysis." In support, defendants cited *Buckman, supra,* 531 U.S. 341, which held that federal law preempted a state-law claim alleging the defendant had improperly obtained approval of a medical device by fraudulently withholding information from the FDA during the application process. The Court concluded that the "state-law fraud-on-the FDA claims" was "impliedly preempted" because it conflicted with the "FDA's responsibility to police fraud consistently with the Administration's judgment and objectives." (*Id*. at pp. 348, 350.)

Defendants contended that although *Buckman* did not involve a state-law failure-to-warn claim, the policy rationale underlying the decision nonetheless precluded the court from considering what evidence the FDA had evaluated when making its determination that incretin-based drugs did not present a risk of pancreatic cancer. Alternatively, defendants asserted that *Buckman* precluded consideration of any evidence the FDA had not previously reviewed when evaluating the risk of pancreatic cancer.

C. ***Argument and Decision***

1. Oral argument

By agreement of the parties, Judge Highberger and Judge Battaglia held a joint hearing on the defendants' federal and

state summary judgment motions. Defendants argued that the NEJM article and the FDA's subsequent statements regarding incretin-based drugs satisfied *Wyeth's* "clear evidence" standard because they showed the Administration had "focused on the [specific] safety issue" plaintiffs had raised, and declared that the current labeling was adequate. Defendants also argued that plaintiffs' assertion that they had discovered new evidence of causation that was not previously submitted to the FDA amounted to a "fraud on the FDA" claim precluded under *Buckman*: "It doesn't matter whether you believe that [additional] evidence is strong or not. The FDA is competent to police its own docket. That is what the *Buckman* case says."

Plaintiffs, however, argued that the defendants were merely speculating "about what the FDA would have done if [the manufacturers] had ever actually submitted a CBE concerning pancreatic cancer." Plaintiffs further asserted that they had identified "lots of significant evidence of a causal relationship between the incretin drugs and pancreatic cancer that the FDA does not appear to have been aware of or considered in its review that led to publication of the [NEJM] article." Plaintiffs clarified that they were not asserting that "defendants [had] failed to properly disclose this information to the FDA," but rather were asserting that the FDA did not "consider any of this new information in [any of the materials] that the defendants [had] point[ed] to as clear evidence. But defendants could have included such information in a CBE application to add a warning or an adverse reaction."

During oral argument, Judge Highberger requested that the parties address whether the court or a jury should determine if there was clear evidence that the FDA would have rejected a

warning for pancreatic cancer. Defendants argued that federal preemption is generally a question of law for the court to decide, and that there was no reason to depart from that rule in this case. Plaintiffs disagreed, asserting that a jury should determine whether there was clear evidence that the FDA would have rejected a pancreatic cancer warning. Following the hearing, Judge Highberger requested supplemental briefing to address the issue, which the parties filed in both the state and federal proceedings.

2. Rulings on the motions for summary judgment

a. Judge Battaglia's order granting summary judgment in the federal proceedings

On November 9, 2015, Judge Battaglia issued an order granting defendants' motion for summary judgment in the federal proceedings. Judge Battaglia initially concluded that the issue of "preemption presents purely a question of law appropriate for resolution by summary judgment." (*In re Incretin-Based Therapies Products Liability Litigation* (S.D. Cal. 2015) 142 F.Supp.3d 1108, 1114 (*Incretin-Based Therapies Litigation*), vacated (9th Cir. 2017) 721 Fed.Appx. 580.)

Judge Battaglia further held that the NEJM article and defendant's other materials conclusively established the FDA would not have approved any warning asserting that incretin-based drugs may increase the risk of pancreatic cancer. According to the court, defendants' evidence established "the FDA ha[d] considered pancreatic cancer risk," and "concluded that a causal association between the drugs and pancreatic cancer is indeterminate. This falls below the science-based regulatory standards that govern what must be included in

product labeling. [Citation.]" (*Incretin-Based Therapies Litigation, supra,* 142 F.Supp.3d at p. 1123.)

Judge Battaglia also rejected what he described as the "central theory" of plaintiffs' opposition: that "new safety information exist[ed] that could support a labeling change." (*Incretin-Based Therapies Litigation, supra,* 142 F.Supp.3d at pp. 1128-1129.) Judge Battaglia concluded he was precluded from considering this "new safety information" based on the "policy rationale underlying [*Buckman*, *supra*, 531 U.S. 341]." Judge Battaglia explained that, as in *Buckman*, evaluating what additional evidence the defendants could have or should have submitted to the FDA would "'inevitably conflict with the FDA's responsibility to police fraud.'"

Judge Battaglia further noted that it was "unclear whether the FDA considered this [new] information, and if it did not, whether this data would have altered the FDA's conclusion. The parties' experts dispute whether the information was material to the FDA's analysis and offer little clarity on this point. . . . A reevaluation of scientific data or a judicial challenge to the accuracy of the FDA's conclusions would disrupt the 'delicate balance of statutory objectives' the *Buckman* Court sought to preserve. [Citation.]" (*Incretin-Based Therapies Litigation, supra,* 142 F.Supp.3d at pp. 1130-1131.)

b. Judge Highberger's order granting summary judgment in the state proceedings

A week after Judge Battaglia issued his order in the federal proceedings, Judge Highberger filed an order granting summary judgment in the state proceedings that "incorporated" Judge

Battaglia's decision.[4] Judge Highberger agreed that the determination whether defendants had produced sufficient evidence to establish preemption under *Wyeth* "should be resolved exclusively by the judge, even if there are preliminary disputed facts which have to be resolved before the ultimate 'question of law' can be fully and finally resolved."

Judge Highberger also "fully agree[d] with Judge Battaglia's analysis that there was 'clear evidence' that the FDA would not have approved plaintiffs' desired label change." Judge Highberger emphasized the importance of the NEJM article, explaining that the parties had not identified any other case in which "the FDA ha[d] gone to these lengths to publicly convey its views. These were obviously not random or happenstance comments now taken out of context. An article by FDA employees does not get published in a peer-reviewed medical journal without substantial conscious thought and effort."

Finally, Judge Highberger agreed that *Buckman* precluded consideration of any evidence the FDA had not considered when evaluating the risk of pancreatic cancer: "The Court gives no weight . . . to proffered items which were not in the public domain or not shown to be information submitted to the FDA some time prior to the February 2014 issuance of the NEJM article based on [*Buckman*.]" Judge Highberger explained that "the holding in *Buckman* prevents the Court and parties from second guessing what the FDA relied on, creating a de facto privilege prohibiting the 'should have submitted' line of inquiry and argument."

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[4] In a footnote, Judge Highberger clarified that the only portion of Judge Battaglia's decision he was not incorporating into his opinion consisted of a subsection addressing the federal standards applicable to motions for summary judgment.

According to Judge Highberger, the court could "only extrapolate the FDA's likely behavior based on how they acted on the information known to them at all relevant times. For this reason and consistent with [*Buckman*], this Court must disregard this portion of plaintiffs' factual showing as preempted by [*Buckman*]."

D. ***Intervening Legal Developments***

1. Reversal of Judge Battaglia's order granting summary judgment

While this appeal was pending, the United States Court of Appeal for the Ninth Circuit issued a unanimous decision reversing Judge Battaglia's grant of summary judgment. In their briefing to the Ninth Circuit, the plaintiffs argued that Judge Battaglia had erred in concluding that: (1) defendants' evidence was sufficient to satisfy *Wyeth's* "clear evidence" standard; and (2) *Buckman* precluded consideration of any evidence that was not reviewed or addressed by the FDA.

The Ninth Circuit reversed on the second issue, and elected not to address the first: "We do not decide whether the defendants met their burden under [*Wyeth's*] 'clear evidence' test because we hold the district court misapplied [*Buckman*] . . . to deem the plaintiffs' newly discovered evidence 'irrelevant' to the court's preemption analysis at the summary judgment stage. . . . [This] error[] . . . independently warrant[s] reversal." (*Incretin-Based Therapies Products Liability Litigation* (9th Cir. 2017) 721 Fed.Appx. 580, 581-582 (*Incretin-Based Therapies Litigation II).*)[5]

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[5] The Ninth Circuit also held that the district court had "misapplied . . . *Buckman* to impermissibly circumscribe discovery," which the court described as an additional,

The Ninth Circuit explained that *Buckman* included language clarifying that the state-law "fraud-on-the-FDA claims" at issue in that case existed "solely by virtue of the [federal] disclosure requirements," which the Court had distinguished from state-law failure-to-warn claims predicated on traditional principles of tort law. The Ninth Circuit further explained that in *Stengel v. Medtronic Inc.* (9th Cir. 2013) 704 F.3d 1224 (*Stengel*), an en banc panel of the court held that *Buckman* did not preempt a state-law failure-to-warn claim asserting that a medical device manufacturer had breached its duty of care by withholding information from the FDA "because the plaintiffs' claim 'rest[ed] on a state-law duty that parallel[ed] a federal-law duty' and was 'independent of the FDA's pre-market approval process that was at issue in *Buckman*. . . .' [Citation.]" (*Incretin-Based Therapies Litigation II, supra,* 721 Fed.Appx. at p. 582.)

Applying the reasoning of *Stengel*, the Ninth Circuit held Judge Battaglia had erred in "characteriz[ing] . . . plaintiffs' state-law claims as 'fraud-on-the-FDA type allegations.' The plaintiffs asserted common-law failure-to-warn claims arising from a state-law duty that paralleled a [federally]-imposed duty, as was the case in *Stengel* . . ., where we found the state-law claims not to be preempted." (*Incretin-Based Therapies Litigation II, supra,* 721 Fed.Appx. at p. 582.) The court further concluded that Judge Battaglia had erred in finding that "*Buckman* . . . preclude[d] its consideration of 'new safety information' the plaintiffs uncovered . . . including a signal assessment completed by Health Canada and evidence from

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independent basis for reversal. (*Incretin-Based Therapies Litigation II, supra,* 721 Fed.Appx. at p. 582.) That issue has not been raised in this appeal.

animal studies and clinical trials." (*Incretin-Based Therapies Litigation II, supra,* 721 Fed.Appx. at p. 583.)

Finally, the Ninth Circuit noted that Judge Battaglia's order found that it was unclear from the parties' evidence whether the FDA had considered plaintiffs' new safety information, or whether the new evidence would have altered the FDA's conclusion. According to the Ninth Circuit, this "[u]ncertainty about whether the FDA considered the 'new safety information' and whether it would have altered the FDA's conclusion establishes that a disputed issue of material fact should have prevented entry of summary judgment on the defendants' preemption claim." (*Incretin-Based Therapies Litigation II, supra,* 721 Fed.Appx. at p. 584.)

2. Supreme Court's Grant of Review in Merck Sharp & Dohme Corp. v. Albrecht, No. 17-290

After the parties completed their briefing in this matter, the Supreme Court granted review in *In re Fosamax (Alendronate Sodium) Products Liability Litigation* (3d Cir. 2017) 852 F.3d 268 (*Fosamax*), cert. granted *Merck Sharp & Dohme Corp. v. Albrecht,* June 28, 2018, __ U.S. __ [138 S. Ct. 2705].)

The Third Circuit's decision in *Fosamax* addressed three issues related to *Wyeth* preemption. First, the court analyzed what *Wyeth* meant by "clear evidence," noting that the Supreme Court had never "define[d] the 'clear evidence' standard or explain[ed] how courts should apply it." (*Fosamax*, *supra*, 852 F.3d at p. 284.) The Third Circuit concluded that the term "clear evidence" was not meant to "refer . . . to the type of facts that a manufacturer must show, or to the circumstances in which preemption will be appropriate," but rather was intended to announce a "clear and convincing" standard of proof: "The

manufacturer must prove that the FDA would have rejected a warning not simply by a preponderance of the evidence, as in most civil cases, but by 'clear evidence.'" (*Id*. at p. 285.)

Second, *Fosamax* considered whether *Wyeth's* "'clear evidence' test poses a legal or factual question." (*Fosamax*, *supra*, 852 F.3d at p. 284.) The court observed that most decisions conducting a *Wyeth* analysis had treated the issue as a question of law, but provided no explanation for that determination. The Third Circuit disagreed with that conclusion, holding that the "question of whether the FDA would have rejected a proposed label change is a question of fact that must be answered by a jury." (*Id*. at p. 286.") Thus, the court explained, to prevail on summary judgment, the defendant must produce evidence showing that "no reasonable jury applying the clear-evidence standard of proof could conclude that the FDA would have approved a label change." (*Id*. at p. 282.)

Finally, the court considered whether the defendant's evidence, which showed the FDA had previously rejected a warning that was similar to the plaintiffs' proposed warning, was sufficient to establish preemption under *Wyeth*. The court concluded that based on ambiguous language in the FDA's prior rejection letter, a reasonable jury could find the FDA might have approved the wording of the plaintiffs' proposed warning.

The defendant's petition for writ of certiorari to the United State Supreme Court argued that the Third Circuit (and several other lower courts) had interpreted and applied *Wyeth's* "clear evidence" standard in a manner that rendered the preemption defense "meaningless." The petition asserted that the Court should grant review to provide "guidance illustrating the kinds of facts that prove preemption under [*Wyeth*]," and "fashion an

administrable rule of law that protects the Supremacy Clause." The petition also argued the Third Circuit had erred in holding that *Wyeth* imposed a "clear and convincing" standard of proof, and that a jury, rather than the court, should decide the issue of preemption.

The United States filed an amicus brief recommending that the Court grant review. The United States agreed that the Third Circuit had erred in concluding that preemption was a factual question for the jury to decide, and had further erred in finding that defendants' evidence was insufficient to satisfy *Wyeth's* clear evidence standard. The United States asserted that review was appropriate to provide clarity regarding "the proper method . . . [and] analytical framework for resolving FDA preemption issues [under] *Wyeth*." On June 28, 2018, the Supreme Court granted the petition.[6]

DISCUSSION

Plaintiffs raise the same two arguments the federal plaintiffs asserted in their appeal to the Ninth Circuit, contending: (1) the defendants failed to present clear evidence that the FDA would have rejected a CBE application seeking to add a warning for pancreatic cancer; and (2) *Buckman* does not preclude consideration of the plaintiffs' "new safety evidence." Plaintiffs also raise a third argument that was not presented in the federal appeal, asserting that the determination whether the

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6 After the Supreme Court granted the petition for writ of certiorari, we sent a letter requesting that the parties meet and confer regarding whether this appeal should be held in abeyance pending the Court's resolution in the *Fosamax* case. The parties were unable to come to an agreement regarding that issue.

FDA would have rejected a warning for pancreatic cancer is a question of fact that must be answered by a jury.

As discussed in more detail below, we agree with the Ninth Circuit's conclusion that *Buckman* does not preclude consideration of the plaintiffs' new safety evidence. We likewise conclude that the trial court's refusal to consider this evidence independently requires reversal of the judgment, and therefore do not address whether the defendants satisfied their evidentiary burden under *Wyeth*, or whether the determination of *Wyeth* preemption presents a question of fact to which the right to jury trial attaches.[7]

A. Summary of Relevant Case Law

1. Buckman Co. v. Plaintiffs' Legal Committee

The plaintiffs in *Buckman*, *supra*, 531 U.S. 341, alleged state-law claims asserting "that [defendants] made fraudulent representations to the FDA as to the intended use of [orthopedic bone screws], and that, as a result, the devices were improperly [approved] and were subsequently used to the plaintiffs' detriment." (*Id*. at p. 347.) Defendants argued the claims were preempted under the Federal Food, Drug, and Cosmetic Act (FDCA), as amended by the Medical Device Amendments of 1976 (MDA).

In its analysis, the Supreme Court initially explained that the presumption against preemption which exists when Congress has legislated in a field traditionally occupied by the states did

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[7] As discussed in our factual summary, it appears the United States Supreme Court intends to provide guidance regarding these two issues in *Merck Sharp & Dohme Corp. v. Albrecht*, S. Ct. Docket No. 17-290.

not apply to plaintiffs' fraud claims: "Policing fraud against federal agencies is hardly 'a field which the States have traditionally occupied,' [citation], ... To the contrary, the relationship between a federal agency and the entity it regulates is inherently federal in character because the relationship originates from, is governed by, and terminates according to federal law. [Citation.] . . . . Accordingly — and in contrast to situations implicating 'federalism concerns and the historic primacy of state regulation of matters of health and safety,' [citation] – no presumption against pre-emption obtains in this case." (*Buckman*, *supra*, 531 U.S. at pp. 347-348.)

Having dispensed with the presumption, the Court concluded that plaintiffs' "state-law fraud-on-the-FDA claims conflict with, and are therefore impliedly pre-empted by, federal law. The conflict stems from the fact that the federal statutory scheme amply empowers the FDA to punish and deter fraud against the Administration, and that this authority is used by the Administration to achieve a somewhat delicate balance of statutory objectives. The balance sought by the Administration can be skewed by allowing fraud-on-the-FDA claims under state tort law." (*Buckman*, *supra*, 531 U.S. at p. 348.)

In support of its holding, the Court noted that the governing statutory and regulatory scheme contained "various provisions aimed at detecting, deterring, and punishing false statements made during [the] . . . approval process[]. The FDA is empowered to investigate suspected fraud, [citation], and citizens may report wrongdoing and petition the agency to take action. . . . The FDA thus has at its disposal a variety of enforcement options that allow it to make a measured response to suspected fraud upon the Agency." (*Buckman*, *supra*, 531 U.S. at p. 349 [internal

footnotes omitted].) According to the Court, "State-law fraud-on-the-FDA claims inevitably conflict with the FDA's responsibility to police fraud consistently with the Agency's judgment and objectives." (*Id.* at p. 350.)

The Court distinguished *Medtronic, Inc. v. Lohr* (1996) 518 U.S. 470 (*Medtronic*), which held that the FDCA and MDA did not preempt a state-law negligence claim alleging that the manufacturer of a pacemaker had failed to warn consumers that the product had a tendency to fail. The Court explained that the claims in *Medtronic* "arose from the manufacturer's alleged failure to use reasonable care in the production of the product, not solely from the violation of FDCA requirements. [Citation.] In the present case, however, the fraud claims exist solely by virtue of the FDCA disclosure requirements. . . . [¶] In sum, were plaintiffs to maintain their fraud-on-the-agency claims here, they would not be relying on traditional state tort law which had predated the federal enactments in questions. On the contrary, the existence of these federal enactments is a critical element in their case." (*Buckman*, *supra*, 531 U.S. at pp. 352-353.)

2. Cases applying Buckman

In *Stengel v. Medtronic Inc.*, *supra*, 704 F.3d 1224, an en banc panel of the Ninth Circuit held that *Buckman* did not preempt a state-law claim alleging that a medical device manufacturer had breached its duty of care under Arizona law by failing to report known risks of the device to the FDA. The Ninth Circuit explained that unlike the "fraud-on-the-FDA claims" at issue in *Buckman*, plaintiffs' claims did not rely solely on the existence of FDCA disclosure law, but rather were based on "settled Arizona law . . . that protects the safety and health of Arizona citizens by imposing a . . . duty of reasonable care on

product manufacturers" that requires them to "produce products with appropriate warning[s]," and "warn of dangers . . . the manufacturer discovers after sale." (*Id*. at p. 1233.) In the court's view, *Buckman* was limited to state-law claims that depend entirely on the existence of the FDCA and MDA's disclosure requirements, and did not extend to "state-law claim[s] in which the state-law duty of care 'parallels' a federal-law duty imposed by [the FDCA or MDA]." (*Id*. at p. 1226; see also *McClellan v. I-Flow Corp*. (9th Cir. 2015) 776 F.3d 1035, 1040 [*Buckman* inapplicable to state-law failure-to-warn claim for violations of duty that was "'parallel to federal requirements"]; *Hughes v. Boston Scientific Corp*. (5th Cir. 2011) 631 F.3d 762, 765 [state-law failure-to-warn claim premised on violation of FDA regulations not preempted under *Buckman*]; *Bausch v. Stryker Corp*. (7th Cir. 2010) 630 F.3d 546, 549.)

In *Coleman v. Medtronic, Inc*. (2014) 223 Cal.App.4th 413, Division Five of this District agreed with *Stengel's* analysis in holding that *Buckman* did not apply to a state-law product liability claim that was predicated on the defendant's failure to inform the FDA of adverse events involving a previously-approved medical device. The court explained that under *Buckman*, a "state law cause of action for violation of the FDCA is [preempted] . . . if it is cognizable only by virtue of the provisions of the FDCA itself, rather than traditional state tort law. . . . [Preemption does not apply when the state law claim] is based . . . [on] the type of conduct that would traditionally give rise to liability under state law." (*Id*. at pp. 425-426.) The court agreed with *Stengel*'s conclusion that "state law causes of action that refer to federal statutes and regulations as providing the

basis for state law liability are not impliedly preempted because they remain based in traditional state tort law." (*Id*. at p. 426.)

Applying that analytical framework, *Coleman* concluded that, as in *Stengel*, the plaintiff's state-law claim sought to impose a state-law duty that was parallel to federal disclosure requirements. Specifically, California tort law requires manufacturers to adequately warn consumers of known or knowable risks associated with its products, while federal law requires that manufacturers of medical devices notify the FDA "whenever the device may have caused or contributed to death or serious injury." (*Id*. at p. 428.)

B. Buckman Does Not Preclude Consideration of Plaintiffs' "New Safety Evidence"

Plaintiffs argue the trial court misapplied *Buckman* in finding that plaintiffs' "new safety evidence"— evidence the FDA had not previously evaluated in assessing whether incretin-based drugs pose a risk of pancreatic cancer – was "irrelevant" to the preemption analysis under *Wyeth*.

Defendants concede *Buckman's* preemption rationale does not apply to state-law claims alleging that a pharmaceutical manufacturer failed to warn about the risk associated with its product. As discussed above, *Wyeth* makes clear that such a claim is subject to preemption only when there is clear evidence that the FDA would have rejected an application seeking to provide the proposed warning. Indeed, *Wyeth* specifically distinguished the "state law fraud-on-the agency claims" at issue in *Buckman* from state-law failure to warn claims that are based on "state regulation of health and safety." (*Wyeth*, *supra*, 555 U.S. at p. 565, fn. 3.)

Acknowledging that *Buckman* does not preclude the type of claim at issue in this case, defendants nonetheless contend that *Buckman* limits the type of evidence that may be considered when evaluating *Wyeth's* "clear evidence" standard. Defendants contend *Buckman* bars consideration of any evidence that manufacturers are alleged to have misreported or intentionally withheld from the FDA. We reject this argument.

First, only a portion of plaintiffs' "new safety evidence" consists of information that defendants allegedly had in their possession, but failed to disclose, or otherwise misreported, to the FDA. Plaintiffs have not alleged, for example, that defendants played any role in withholding the Health Canada report,[8] the UCLA research involving the Kras mouse or the analysis that the plaintiffs' experts performed. Instead, plaintiffs assert that if a drug manufacturer included this new information in a CBE application, it might affect the FDA's views regarding the risks of pancreatic cancer. Defendants provide no argument explaining why *Buckman* precludes the use of information that is not alleged to have been intentionally withheld from, or misreported to, the

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[8] At oral argument, defendants' counsel asserted that plaintiffs were no longer relying on the Health Canada report to show that disputed questions of fact exist as to whether the FDA would have approved a pancreatic cancer warning for incretin-based drugs. The plaintiffs, however, cited and discussed the Health Canada report at length in their oppositions to the state and federal motions for summary judgment, and also discussed the report in their appellate briefing to the Ninth Circuit. Although their appellate brief in this case does not specifically reference the Health Canada report, nothing in the record indicates plaintiffs have abandoned reliance on that document.

FDA, but rather is simply information the Administration has not had the opportunity to review.

The second problem with defendants' application of *Buckman* is that the California Court of Appeal and numerous federal circuit courts have concluded that *Buckman*'s preemption principles do not apply to product liability claims alleging the defendant breached its state-law duty of care by withholding information from the FDA. Given that *Buckman* has been found not to apply to failure-to-warn claims that are predicated on defendant's withholding of information from the FDA, we fail to see why it would preclude consideration of evidence that defendants allegedly failed to report to the FDA in this case. Because *Buckman's* rationale does not apply to the type of claim at issue here, we find no basis to conclude that it limits the type of evidence that plaintiffs may use to prove their claim.

Defendants have not cited any decision that has applied *Buckman* to categorically prohibit the use of newly-discovered evidence when assessing preemption under *Wyeth*. Defendants correctly note that some district courts have held that *Buckman* precludes the use of evidence in pharmaceutical failure-to-warn cases that "is offered only to show that the FDA was misled, or that information was intentionally concealed from the FDA." (*Bouchard v. American Home Products Corp*. (N.D. Ohio 2002) 213 F.Supp.2d 802, 812; *In re Baycol Products Litigation* (D. Minn. 2007) 532 F.Supp.2d 1029, 1053 ["to the extent [the expert's] testimony is offered only to show that the FDA was misled, or that information was intentionally concealed from the FDA, the testimony must be excluded [under *Buckman*]"].) However, even if we assume those decisions were correctly decided, in this case the plaintiffs' "new safety evidence" was not

offered "only to show" that defendants misled or intentionally withheld information from the FDA. Instead, plaintiffs offered the evidence to show there was scientific information the FDA had not yet considered that might impact its views on the propriety of a pancreatic cancer warning. Stated differently, even if we assume *Buckman* would preclude plaintiffs from arguing that the evidence shows the defendants intentionally withheld information from (or intentionally misled) the FDA, we find nothing in *Buckman* that precludes plaintiffs from relying on previously undisclosed evidence to show that the FDA might have approved a pancreatic cancer warning.

We also agree with the Ninth Circuit's conclusion that the trial court's refusal to consider plaintiffs' new safety evidence requires reversal of the judgment. Judge Highberger's decision incorporated Judge Battaglia's findings that the parties' evidence did not show whether the FDA had actually considered plaintiffs' new evidence, or whether "this data would have altered the FDA's conclusion." The court additionally found that the parties' experts had presented conflicting opinions whether the new information was material to the FDA's analysis. As explained by the Ninth Circuit, this uncertainty regarding what effect (if any) the plaintiffs' new evidence might have had on the FDA's conclusions demonstrates the existence of a disputed issue of material fact that "should have prevented entry of summary judgment."[9] (*Incretin-Based Therapies Litigation II*, *supra*, 721

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[9] At the summary judgment stage of the proceedings, the existence of a disputed issue of material fact prevents entry of judgment regardless of whether *Wyeth* preemption presents a question of law that the court must decide, or a question of fact to which the right to jury attaches. The key inquiry at summary

Fed.Appx. at p. 584; see *Teselle v. McLoughlin* (2009) 173 Cal.App.4th 156, 163, fn. 7 ["'A defendant is entitled to summary judgment [only] if the record establishes as matter of law that . . . plaintiff's asserted causes of action [cannot succeed]'"].)

DISPOSITION

The trial court's judgment is reversed and the matter is remanded for further proceedings. Each party shall bear its own costs on appeal.

ZELON, J.

We concur:

PERLUSS, P. J.

FEUER, J.

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judgment is whether a triable issue of material fact exists, meaning "evidence that would allow a reasonable trier of fact to find the underlying fact in favor of the party opposing the motion. . . ." (*Aguilar v. Atlantic Richfield Co.* (2001) 25 Cal.4th 826, 850.) For purposes of this standard, it is immaterial whether the trier of fact will be the court or a jury. Because the trial court found there was conflicting evidence regarding what effect the excluded data might have had on the FDA's conclusions about the propriety of a pancreatic cancer warning, the motion must be denied even if that factual question will ultimately be resolved through a bench trial, rather than a jury trial.