IN THE UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF ARKANSAS
CENTRAL DIVISION

BARBARA FRYE **PLAINTIFF**

v. **Case No. 4:21-cv-1173-KGB**

NOVARTIS PHARMACEUTICALS CORPORATION **DEFENDANT**

ORDER

Before the Court are defendant Novartis Pharmaceuticals Corporation's ("Novartis") motion to dismiss complaint (Dkt. No. 6), request for judicial notice in support of its motion to dismiss the complaint (Dkt. No. 9), and motion for hearing (Dkt. No. 10). Plaintiff Barbara Frye responded in opposition to the motion to dismiss (Dkt. No. 24). Novartis replied (Dkt. No. 27). Ms. Frye filed a notice of additional authority (Dkt. No. 29), and Novartis responded to the notice (Dkt. No. 30). For the following reasons, the Court grants the request to take judicial notice (Dkt. No. 9). The Court denies the request for hearing (Dkt. No. 10), and the Court denies the motion to dismiss (Dkt. No. 6).

I. Allegations In The Complaint

These allegations are taken from Ms. Frye's complaint (Dkt. No. 1). For purposes of resolving the pending motion to dismiss at this stage of the litigation, the Court assumes as true Ms. Frye's allegations. *See Blomker v. Jewell*, 831 F.3d 1051, 1054 (8th Cir. 2016) (internal citations omitted).

Ms. Frye maintains that "[t]his is an action for damages due to Plaintiff relating to Defendant's development, testing, manufacture, packaging, preparation, labeling, marketing, supply and/or sale of the dangerous and defective pharmaceutical product Beovu®." (Dkt. No. 1, ¶ 1). Beovu® (brolucizumab) "is a human vascular endothelial growth factor ('VEGF') inhibitor

indicated for the treatment of Neovascular (Wet) Age-Related Macular Degeneration ('AMD' or 'nAMD') in adults." (*Id.*, ¶ 18). The primary goal of treatment for wet AMD is "to maintain visual acuity, which requires drying the retina through the inhibition of new blood vessel growth and reduction of fluid leakage." (*Id.*, ¶ 19).

The Beovu molecule, formerly known as ESBA 1800 and/or RTH258, was originally developed by Switzerland-based ESABTech AG. ESABTech AG was acquired by Alcon, Inc. in September 2009, after which Alcon, Inc. and its subsidiaries, including Alcon Research, LLC f/k/a Alcon Research, Ltd., assumed ownership and all future marketing rights to Beovu (*Id.*). Novartis acquired Alcon, Inc. in April 2011, and with it, ownership and all future marketing rights to Beovu (*Id.*).

During the premarketing development process, Beovu was regulated under Investigational New Drug Application Number 112023 in the United States (*Id.*). On April 15, 2019, Novartis announced that the United States Food and Drug Administration ("FDA") accepted the Biologics License Application ("BLA") for Beovu (*Id.*, ¶ 20). At that time, Novartis noted that it had used a priority review voucher to expedite review of Beovu in the United States to make it "available as quickly as possible." (*Id.*).

Beovu received FDA approval on October 7, 2019, under BLA number 761125 (*Id.*, ¶ 21). Beovu is administered as an intravitreal injection and is intended to treat AMD by inhibiting the binding of VEGF to the VEGFR1 and VEGFR2 receptors thereby suppressing the growth of abnormal blood vessels and reducing the potential for fluid leakage into the retina. Beovu is the third VEGF inhibitor to receive FDA approval for the treatment of wet AMD (*Id.*, ¶ 23). Ms. Frye alleges that "Novartis sought to acquire and develop a new drug for the treatment of wet AMD

that they could promote as requiring less frequent injections than other VEGF inhibitors." (*Id.*, ¶ 26).

According to Ms. Frye, Novartis is the current sponsor of the BLA for Beovu and maintains primary responsibility and control over the drug and all activities and materials relating to it (*Id.*, ¶ 6). She alleges that Novartis has also been "substantively involved in the design, funding, authoring, conduct and/or publication of medical research related to Beovu." (*Id.*). Ms. Frye alleges that Novartis "was engaged in the business of developing, designing, licensing, manufacturing, distributing, selling, marketing, and or introducing into interstate commerce throughout the United States, and in the state of Arkansas, either directly or indirectly, through third-parties, subsidiaries and/or related entities, the pharmaceutical [sic] product Beovu." (*Id.*, ¶ 9).

Ms. Frye alleges that "[c]onsumers and physicians alike have been misled about Beovu's safety and efficacy, and as a result, consumers, including Plaintiff, have suffered serious and permanent eye injuries including retinal vasculitis, retinal vascular occlusion, and related sequelae." (*Id.*, ¶ 4). Ms. Frye maintains that she was prescribed and injected with Beovu on January 28, 2020, and that she thereafter developed retinal vascular occlusions and other related sequelae (*Id.*, ¶ 13). She asserts that she "began developing severe vision problems in March 2020 and was diagnosed with retinal vascular occlusion in March 2020." (*Id.*). Further, she alleges that, prior to using Beovu, she had been prescribed and used other anti-VEGF therapies without incurring any material side effects (*Id.*).

According to Ms. Frye, "[t]he instant matter involves injuries of retinal vasculitis, retinal vascular occlusion, and other acute eye injuries associated with the administration of Beovu." (*Id.*, ¶ 28). She alleges that "[r]etinal vasculitis and retinal vascular occlusions are injuries unique to

Beovu use. These injuries have been widely reported in patients taking Beovu, but are not considered to be a risk with other VEGF inhibitors." (*Id.*, ¶ 30).

Ms. Frye maintains that, "[a]s FDA has made clear in its Guidance for Industry, even a single well-documented post-marketing adverse event report can constitute a safety signal requiring action by the manufacturer, including a potential label change, particularly if the report involves an event that is extremely rare in the absence of drug use." (*Id.*, ¶ 62). Ms. Frye alleges that "[r]etinal vasculitis and retinal vascular occlusion are adverse events that occur extremely rarely in the absence of drug use." (*Id.*, ¶ 63). Further, Ms. Frye alleges that Novartis began receiving post-marketing adverse event reports almost immediately after Beovu came on the market. Ms. Frye maintains that in November 2019 Novartis received two such reports (*Id.*, ¶¶ 65–66); that in December 2019 Novartis received two more reports (*id.* ¶ 67); that in January 2020 Novartis received 8 additional reports (*id.* ¶ 68); that in February 2020 Novartis received 39 additional reports (*id.* ¶ 69), that in March 2020, Novartis received 72 additional reports (*id.*); that in April 2020 Novartis received 33 additional reports (*id*, ¶ 70), and that in May 2020 Novartis received 18 additional reports (*id.* ¶ 71).

Ms. Frye also alleges that, "[o]n February 23, 2020, the American Society of Retina Specialists ('ASRS') issued an alert to its members in which it noted that it had received 14 reported cases of vasculitis following Beovu injections, 1 of which were designated as occlusive retinal vasculitis." (*Id.*, ¶ 31). Further, "[o]n March 30, 2020, ASRS issued an update noting the number of cases of retinal vasculitis following intravitreal injections of Beovu it had received had risen to 25, with 21 such cases involving retinal occlusion." (*Id.*, ¶ 32).

Ms. Frye maintains that, after the first ASRS communication in February 2020, "Novartis announced it was 'conducting a comprehensive review of a limited number of reported cases of

severe vision loss, inflammation and potential retinal vasculitis in patients treated with Beovu" and that it would commission an external Safety Review Committee to conduct safety evaluations for Beovu (*Id.*, ¶ 33).

Ms. Frye alleges:

> 34. Following their review and reanalysis of safety data, on April 8, 2020 Novartis confirmed the existence of a safety signal involving rare adverse events of "retinal vasculitis and/or reginal vascular occlusion that may result in severe vision loss" for Beovu.
>
> 35. Following its confirmation of a safety signal, Novartis revised the United States product labeling for Beovu on June 8, 2020 to include a new warning regarding the risk of "Retinal Vasculitis and/or Retinal Vascular Occlusion" (§ 5.2), which reads as follows:
>
> > Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of BEOVU [*see Contraindications (4.2) and Adverse Reactions (6.1)*]. Patients should be instructed to report any change in vision without delay.

Ms. Frye alleges that it is "unclear when this new warning was widely disseminated to physicians utilizing Beovu with their patients." (*Id.*, ¶ 36). She maintains that, prior to June 2020, "no warnings regarding the risk of retinal vasculitis or retinal vascular occlusion were present in the United States product labeling for Beovu (*Id.*, ¶ 37).

According to Ms. Frye, data further supporting the causal relationship between administration of Beovu and retinal vasculitis and retinal vascular occlusion injuries have been documented in the peer-reviewed medical literature since Beovu received approval in 2019 (*Id.*, ¶ 38; *see also id.*, ¶¶ 39–40 (citing and discussing certain literature)). She also alleges that case reports regarding these matters have been published in peer-reviewed medical literature (*Id.*, ¶ 42; *see also id.*, ¶¶ 43–46 (citing and discussing articles and case reports)).

Ms. Frye alleges that "[a]pproval of Beovu was based on the results of the two prospective, randomized, double-blind, multicenter Phase III studies, HAWK (NCT02307682) and HARRIER (NCT02434328), which based on the data as characterized to the FDA by Defendants, met the primary endpoint of non-inferiority to aflibercept in mean change in best-corrected visual acuity ('BCVA') from baseline to week 48." (*Id.*, ¶ 22). Ms. Frye details events surrounding a Rosenfeld & Browning editorial (*Id.*, ¶¶ 47–49), which she maintains lend support to her allegations: "Noting that the external Safety Review Committee found that incidences of retinal vasculitis and retinal vascular occlusion were higher in the HAWK and HARRIER trials than previously reported, Rosenfeld & Browning commented, '[t]hese data, and the discrepancy from the previously released results, in addition to the cases arising from the community use of brolucizumab, raise red flags.'" (*Id.*, ¶ 49).

Ms. Frye also alleges that "[r]esearchers have identified biologically plausible mechanisms through which Beovu can cause retinal vasculitis and/or retinal vascular occlusion events" and that "[v]arious theories have been proposed. . . ." (*Id.*, ¶¶ 51–52).

She asserts:

> 59. Regarding Phase III clinical trials for Beovu, the FDA also found, "Among subjects with treatment-emergent antibodies, a higher number of intraocular inflammation events were observed."
>
> 60. Novartis has also commented on anti-drug antibodies observed during clinical trials, noting "In a post-hoc unmasked assessment of the Phase III HAWK and HARRIER data, there was an observed trend toward increased incidence of [retinal vasculitis and/or retinal vascular occlusion] in patients with treatment emergent (boosted/induced) anti-drug antibodies (ADAs).

These allegations are further detailed in her complaint (*Id.*, ¶¶ 105–112). Ms. Frye alleges that, "[c]onsistent with the large and growing body of evidence demonstrating a causal relationship between Beovu and retinal vasculitis and retinal vascular occlusion, and that Beovu confers a

greater risk of vision-threatening inflammatory adverse effects than alternative anti-VEGF treatments, Novartis has itself admitted to such an association." (*Id.*, ¶ 62).

For her causes of action against Novartis, Ms. Frye alleges: (1) strict liability based on failure to warn about the potential risks and complications associated with use of Beovu (Dkt. No. 1, ¶¶ 74–88); (2) negligence in connection with Novartis's testing, marketing, promotion, labeling, and distribution of Beovu (*id.* ¶¶ 89–97); and (3) fraudulent misrepresentation regarding the safety and efficacy of Beovu and Beuvo's side effects (*id.* ¶¶ 98–133). Novartis moves to dismiss Ms. Frye's complaint based on preemption and pursuant to Federal Rule of Civil Procedure 12(b)(6) asserting that Ms. Frye fails to state claims upon which relief can be granted (Dkt. No. 6).

II. Standard

A. Legal Standard For Motion To Dismiss

"To survive a motion to dismiss, a complaint must contain sufficient factual matter, accepted as true, to 'state a claim to relief that is plausible on its face.'" *Ashcraft v. Iqbal*, 556 U.S. 662, 678 (2009) (quoting *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 570 (2007)). "A claim has facial plausibility when the plaintiff pleads factual content that allows the court to draw the reasonable inference that the defendant is liable for the misconduct alleged." *Id.* (citing *Twombly*, 550 U.S. at 556). Although a complaint "does not need detailed factual allegations" to survive a Federal Rule of Civil Procedure 12(b)(6) motion to dismiss, the "[f]actual allegations must be enough to raise a right to relief above the speculative level." *Twombly*, 550 U.S. at 555. In other words, the allegations pleaded must show "more than a sheer possibility that a defendant has acted unlawfully." *Iqbal*, 556 U.S. at 678.

A court considering a motion to dismiss must accept as true all well-pleaded facts in the complaint and draw all reasonable inferences from those facts in favor of the non-moving party.

See Farm Credit Servs. of Am., FLCA v. Haun, 734 F.3d 800, 804 (8th Cir. 2013); *Coons v. Mineta*, 410 F.3d 1036, 1039 (8th Cir. 2005); *Abels v. Farmers Commodities Corp.*, 259 F.3d 910, 914 (8th Cir. 2001). However, a court need not credit conclusory allegations or "naked assertion[s] devoid of further factual enhancement." *Retro Television Network, Inc. v. Luken Commc'ns, LLC*, 696 F.3d 766, 768 (8th Cir. 2012) (alteration in original) (quoting *Iqbal*, 556 U.S. at 678)).

B. Requests To Take Judicial Notice

A court ruling on a motion to dismiss under Federal Rule of Civil Procedure 12(b)(6) may consider documents or exhibits attached to a complaint, as well as matters of public and administrative record referenced in the complaint. *See Owen v. Gen. Motors Corp.*, 533 F.3d 913, 918 (8th Cir. 2008); *Quinn v. Ocwen Fed. Bank FSB*, 470 F.3d 1240, 1244 (8th Cir. 2006). In addition, the Court may consider materials that are "necessarily embraced by the pleadings." *Nelson Auto Ctr., Inc. v. Multimedia Holdings Corp.*, 951 F.3d 952, 955 (8th Cir. 2020) (quoting *Porous Media Corp. v. Pall Corp.*, 186 F.3d 1077, 1079 (8th Cir. 1999)).

Novartis attaches several exhibits to its request for judicial notice in support of its motion to dismiss, including: (1) the October 2019 Drug Label for Beovu; (2) the June 9, 2020, approval package for Beovu; (3) the June 2020 drug label for Beovu; and (4) the June 4, 2018m FDA Questions and Answers on FDA's Adverse Event Reporting System ("FAERS") (Dkt. Nos. 9-1; 9-2; 9-3; 9-4). Ms. Frye does not address these requests in her response to the pending motion to dismiss (Dkt. No. 24).

Ms. Frye also submits for the Court's review several exhibits in her response to the motion to dismiss, including another district court's decision on a similar motion to dismiss and several of the scientific articles referenced in her complaint (Dkt. Nos. 24-1; 24-2; 24-3). Novartis did not

file an objection to the inclusion of these exhibits when it replied to the pending motion to dismiss (Dkt. No. 27).

The Court determines that the district court decision submitted by Ms. Frye is a matter of public record (Dkt. No. 24-1). The Court determines that the other materials submitted by Novartis and Ms. Frye are necessarily embraced by the pleadings and may be considered by the Court in ruling on Novartis's pending motion to dismiss (Dkt. Nos. 9-1; 9-2; 9-3; 9-4; 24-2; 24-3). However, the Court confines its examination to the face of these materials. The Court will not rely on them to make factual determinations. *See LeMay v. Mays*, 18 F.4th 283, 289 (8th Cir. 2021) (holding that while courts may consider "materials necessarily embraced by the pleadings, including exhibits attached to the complaint and matters of public record, [s]uch evidence may not. . . be viewed for the truth of the matters asserted.") (internal citations and quotation marks omitted).

III. Analysis

A. Preemption

Novartis asserts, in part, that Ms. Frye's claims are actually "fraud-on-the-FDA" claims that are pre-empted pursuant to *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341 (2001). The Court disagrees.

Buckman concerned a medical device—orthopedic bone screws—and the claim that the manufacturer had made fraudulent misrepresentations regarding the intended use of the screws in the course of obtaining approval to market its product for a use other than what had previously been approved. 531 U.S. at 343–45. In 1976, Congress passed the Medical Device Amendments ("MDA") to the Food, Drug, and Cosmetic Act, which included an express preemption provision for medical devices providing "clear evidence that Congress intended that the MDA be enforced exclusively by the federal government." *Id.* at 352. However, Congress declined to enact a similar

express preemption provision for prescription drugs. *See Wyeth v. Levine*, 555 U.S. 555, 567 (2009). As a result, if Ms. Frye's claims are subject to preemption, it would be the result of impossibility preemption—in other words, that it would be impossible for Novartis to comply with both state and federal requirements. *See id.* at 573.

Despite many amendments to the FDCA and to FDA regulations, "it has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times." *Id.* at 571. The manufacturer 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.* After FDA approval, in general, most labeling changes require advance FDA permission. *Id.* at 568; *see also* 21 C.F.R. § 314.70(b)(2)(v)(A). The regulations, however, have exceptions to the general rule, which authorize manufacturers to make certain changes to a drug label before receiving FDA approval. *See id.*

The "Changes Being Effected" ("CBE") regulation provides that the FDA may designate a "category of changes" whereby the holder of an approved application may begin distribution of its drug product upon the FDA's receipt of a supplement for a change. 21 C.F.R. § 314.70(c)(6). Two such designated changes concern product labeling to reflect "newly acquired information" (1) to "add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under [21 C.F.R.] § 201.57(c)," and (2) to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product." 21 C.F.R. § 314.70(c)(6)(iii)(A) & (C). The standard referenced regarding evidence of a casual association provides, in pertinent part, that "labeling must be revised to include a warning about clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not

have been definitely established." 21 C.F.R. § 201.57(c)(6)(i). In other words, CBE regulations contemplate not only new warnings but also strengthened warnings for risks that already appear on the initial label. 21 C.F.R. § 314.70(c)((6)(iii)(A); *see Wyeth*, 555 U.S. at 568–569.

The CBE regulation defines "newly acquired information" as:

> [D]ata, analyses, or other information not previously submitted to the Agency, which may include (but is not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events, or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA.

21 C.F.R. § 314.3(b). Newly acquired information is not limited to new data; it includes new analysis of old data. The CBE regulation reflects "the fact that risk information accumulates over time and that the same data may take on a different meaning in light of subsequent developments." *Wyeth*, 555 U.S. at 573. For example, "[i]f the sponsor submits adverse event information to FDA, and then later conducts a new analysis of data showing risks of a different type or of greater severity or frequency than did reports previously submitted to FDA, the sponsor meets the requirement for newly acquired information." *Id.* The FDA's 2008 final rule, *Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices*, adds that "information. . . previously known to the manufacturer, but not submitted to FDA" also constitutes "'newly acquired information' that may qualify for inclusion in a CBE supplement." 73 Fed. Reg. 49603.

Wyeth held that state-law claims based on drug labeling deficiencies are not preempted if the manufacturer could have relied on the CBE regulation to strengthen unilaterally the label. 555 U.S. at 573–574. Because the CBE regulation allowed the drug manufacturer to act without the FDA's prior permission, the Supreme Court explained, it was not impossible for the manufacturer to comply with both federal and state requirements. *See id.*

The FDA "retains authority to reject labeling changes made pursuant to the CBE regulation," *Wyeth*, 555 U.S. at 571, but the mere possibility of impossibility is insufficient to establish preemption. In other words, "[i]f a manufacturer can provide 'clear evidence' that the FDA would have rejected the label, then the manufacturer can show that it would have been impossible to amend the label in compliance with state law while simultaneously complying with federal law." *Gaetano v. Gilead Scis., Inc.*, 529 F. Supp. 3d 333, 339 (D.N.J. 2021) (citing *Wyeth*, 555 U.S. at 571)). In these circumstances, the drug manufacturer has demonstrated impossibility and the state law claim is preempted.

In *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668 (2019), the Supreme Court reaffirmed *Wyeth*'s holding and elaborated on its requirements. The Court reiterated that "'clear evidence' that the FDA would not have approved a change to the drug's label pre-empts a claim, grounded in state law, that a drug manufacturer failed to warn consumers of the change-related risks associated with using the drug." *Id.* at 1672. The Court also explained that "clear evidence" is evidence that shows "that the drug manufacturer fully informed the FDA of the justifications for the warning required by state law and that FDA, in turn, informed the drug manufacturer that the FDA would not approve a change to the drug's label to include that warning." *Id.*

According to Novartis, Ms. Frye fails to allege "newly acquired information" sufficient to trigger Novartis's duty to make label changes (Dkt. No. 7, at 8–17). Novartis argues that the articles and commentaries referenced in Ms. Frye's complaint regarding retinal vasculitis following a Beovu injection post-date her exposure and, as such, cannot constitute information that would trigger a label change which would have benefitted her (*Id.*, at 8).

Similarly, Novartis argues that the allegations regarding physician-reported adverse events received by Novartis prior to Ms. Frye's Beovu injection also cannot constitute newly acquired

information because the adverse event reports do not represent new evidence of a "different type or greater severity or frequency than previously included" in Novartis's submission to the FDA (*Id.*, at 13) (citing 21 C.F.R. § 601.12(f)(6)). Further, according to Novartis, adverse reports are merely anecdotal descriptions of something that happened to a person and do not purport to reach a causal association (*Id.*, at 14).

The Court is not persuaded by Novartis's assertions and arguments at this stage of the litigation. First, notwithstanding the inapplicability of *Buckman*, and the fact that Beovu is not a medical device, Ms. Frye's complaint cannot fairly be characterized as seeking recovery for fraud perpetrated on the FDA in connection with Beovu's approval. Instead, Ms. Frye's allegations concern Novartis's purported failure to update its labeling as required by the CBE regulations and Novartis's responsibility regarding the content of Beovu's label. *Wyeth*, 555 U.S. at 570–71.

The Court acknowledges that Ms. Frye does allege that Novartis knew that it failed to present accurate data in its submission to the FDA concerning adverse events in its Phase III clinical trials (Dkt. No. 24, at 6–7). However, taken in context, these allegations illustrate Novartis's state of mind—what Novartis knew and when Novartis knew it—more so than any claim of fraud on the FDA. Further, Ms. Frye specifically pled in her fraudulent misrepresentation claims that Novartis's misrepresentations at issue were communicated directly to Ms. Frye, as well as to her healthcare providers—not the FDA (Dkt. No. 1, ¶¶ 36–37, 76, 91, 101). Ms. Frye's claims are based on Novartis's duty to warn consumers and physicians, not Novartis's duty to submit accurate data to the FDA.[1]

[1] To the extent Novartis or Ms. Frye intended for this Court to evaluate pre-approval and post-approval claims, *see generally Stube v. Pfizer, Inc.*, 446 F.Supp.3d 424 (W.D. Ark. 2020), the Court did not understand the parties to structure their briefing in that manner. As a result, the Court has not structured its Order in that manner.

Novartis, at all times, was responsible for the content of its labeling – in crafting the label and ensuring the warnings remain adequate as long Beovu was on the market. *See Wyeth*, 555 U.S. at 570–71. The CBE regulations allowed Novartis to change labeling to reflect "newly acquired information" to add or strengthen warnings, or advise of adverse reaction for which there is evidence of a causal association. *See id.* at 568; 21 C.F.R. § 314.70(c)(6)(iii)(A). The regulations required Novartis to include a warning "as soon as there [wa]s reasonable evidence of an association of a serious hazard" with Beovu. *See Wyeth*, 555 U.S. at 571; 21 C.F.R. § 201.57(c)(6)(i). Further, the Court rejects Novartis's efforts at this stage of the litigation to suggest that "newly acquired information" has a narrow meaning.

Under the law, "newly acquired information" may include, but is not limited to, "new clinical studies, reports of adverse events, or new analyses of previously submitted data, if the studies, events or analysis reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA." 21 C.F.R. § 601.12(f)(6). Here, Ms. Frye alleges that Novartis received adverse event reports prior to her initial Beovu injections (Dkt. No. 24, at 8). Ms. Frye also alleges that Novartis funded and authored a review and reanalysis of its clinical trials data that was published online prior to Ms. Frye's Beovu injections (*Id.*, at 7). This review concluded that there was a causal connection between Beovu injections and retinal vasculitis (*Id.*). The Court in *Wyeth* made clear that "newly acquired information" is not limited only to new data but includes the analysis of data previously submitted. 555 U.S. at 569.

Contrary to Novartis's arguments, this Court is unable to conclude that, as a matter of law, the physician-reported adverse event reports, as well as the review and reanalysis of Novartis's Phase III clinical trial data, does not constitute newly acquired information of events or analyses revealing risks different in type or of greater severity than previously reported to the FDA. At this

stage of the litigation and on the record before it, the Court is also unable to conclude that, as a matter of law, even if the physician-reported adverse events and review and reanalysis of the Phase III clinical trial data were newly acquired information, it was information that failed to trigger Novartis's obligation to warn adequately of the risks and adverse events associated with Beovu injections.

Finally, Novartis asks the Court to conclude that the physician-reported adverse events do not constitute newly acquired information because the reports of retinal occlusions in Beovu patients were explicitly included in Novartis's initial FDA-approved label for Beovu (Dkt. No. 7, at 3, 17–18). According to Novartis, the October 2019 label for Beovu included a contraindication for active intraocular inflammation and various other warnings concerning potential vision injuries (*Id.*, at 2–3). Even if the Court accepts the label that Novartis submits as authentic, the Court still would have to determine, as a matter of law, whether the information in the label accurately and unambiguously conveyed the scope and nature of the risk to prescribing physicians to rule in Novartis's favor on this issue. Ms. Frye alleges facts that dispute whether the warning was sufficiently explicit and detailed (Dkt No. 24, at 18–20). Further, to make the determination Novartis requests at this stage of the litigation, the Court would have to rule on this dispute without any testimony or evidence from qualified experts, something which the Court is unwilling, and ill-equipped, to do. *See Vallejo v. Amgen, Inc.*, Case No. 8:14-cv-50, 2014 WL 4922901, at *3 (D. Neb. 2014).

Impossibility preemption is an affirmative defense. The "burden for demonstrating impossibility rests with the party asserting preemption." *Holley v. Gilead Scis., Inc.*, 379 F. Supp. 3d 809, 819 (N.D. Cal 2019) (citing *Wyeth*, 555 U.S. at 573)). If preemption is to be the basis for a Rule 12(b)(6) dismissal, a defendant "must show that the defense is apparent on the face of the

complaint and documents relied on in the complaint," *Lupian v. Joseph Cory Holdings LLC*, 905 F.3d 127, 130 (3d Cir. 2018) (internal quotation marks omitted). *See also ABF Freight Sys., Inc. v. Int'l Bhd. of Teamsters*, 728 F.3d 853, 861 (8th Cir. 2013) (finding the basis for dismissal must be "apparent on the face of the complaint"). Moreover, "the factual allegations relevant to preemption must be viewed in the light most favorable to the plaintiff." *Galper v. JP Morgan Chase Bank, N.A.*, 802 F.3d 437, 444 (2d Cir. 2015); s*ee also Ideus v. Teva Pharms. USA, Inc.*, 2017 WL 6389630, at *2 (D. Neb. Dec. 12, 2017) (quoting *Galper* and stating the same). Here, the CBE regulations, viewed in Ms. Frye's favor based on the allegations in her complaint, would permit Novartis to strengthen unilaterally Beovu's warning to comport with Arkansas law regarding Novartis's duty to warn adequately physicians about risks associated with Beovu.

For these reasons, the Court cannot conclude at this stage of the litigation, as a matter of law, that it would be impossible for Novartis to comply with both state law and the pertinent federal requirements.

B. Failure To Warn

Novartis also moves to dismiss Ms. Frye's failure to warn claims under Federal Rule of Civil Procedure 12(b)(6). Arkansas law requires defendants to provide an adequate warning regarding the dangers associated with use of their product. *See Boehm v. Eli Lilly & Co.*, 747 F.3d 501, 505 (8th Cir. 2014). Ms. Frye alleges a breach of this duty under both a strict liability theory (Count I) and a negligence theory (Count II).

Generally, product liability law requires the manufacturer to warn the ultimate user of the risks of its product. *See Thomas v. Borg-Warner Morse TEC LLC*, 362 F. Supp. 3d 610, 615 (E.D. Ark. 2018). This duty exists under either a strict liability theory or a negligence theory. *West v. Searle & Co.*, 806 S.W.2d 608, 613 (Ark. 1991). Under Arkansas law, a drug warning is adequate

so long as it puts a reasonably prudent physician on notice of a particular risk that the manufacturer has actual or constructive knowledge of at the time of distribution. *In re Prempro Prods. Liab. Litig.*, 514 F.3d 825, 830 (8th Cir. 2008).

In the context of prescription drugs, Arkansas recognizes that physicians play a critical mediating role between drug manufacturer and patient. *See Wilichowski v. Bos. Sci. Corp.*, Case No. 5:21-cv-5024, 2021 WL 798869, at *3 (W.D. Ark. Mar. 2, 2021). Accordingly, Arkansas has adopted the "learned intermediary rule," which "assumes that it is reasonable for a manufacturer to rely on the prescribing physician to forward to the patient, who is the ultimate user of the drug products, any warnings regarding their possible side effects." *Hill v. Searle Lab'ys, a Div. of Searle Pharms., Inc.*, 884 F.2d 1064, 1070 (8th Cir. 1989). As adopted in Arkansas, the learned intermediary doctrine "provides an exception to the general rule that a manufacturer has a duty to warn the ultimate user of the risks of its products." *Kowalski v. Rose Drugs of Dardanelle, Inc.*, 378 S.W.3d 109, 120 (Ark. 2011). "'[A] drug manufacturer may rely on the prescribing physician to warn the ultimate consumer of the risks of a prescription drug. The physician acts as the 'learned intermediary' between the manufacturer and the ultimate consumer.'" *Id.* (quoting *West*, 806 S.W.2d at 613). In applying the doctrine to prescription drugs, the Arkansas Supreme Court explained: (1) the patient relies on her physician's independent medical judgment that the drug is appropriate—not on the manufacturer, (2) "it is virtually impossible in many cases for a manufacturer to directly warn each patient," and (3) imposing "a duty to warn the user directly would interfere with the relationship between the doctor and the patient." *Id.*; *see also Bell v. Pfizer, Inc.*, 716 F.3d 1087, 1097 (8th Cir. 2013).

As a result, Novartis is "legally obligated to provide 'meaningful and complete' warnings" to Ms. Frye's healthcare provider, but not to Ms. Frye directly. *Sharp v. Ethicon, Inc.*, Case No.

2:20-cv-2028, 2020 WL 1434566, at *3 (W.D. Ark. Mar. 24, 2020); *see also Kirsch v. Picker Int'l, Inc.*, 753 F.2d 670, 671 (8th Cir. 1985) ("[A] warning to the physician is deemed a warning to the patient; the manufacturer need not communicate directly with all ultimate users of" pharmaceutical products).

1. Strict Liability

Under Arkansas law and the Arkansas product liability statute, the "supplier of a product is strictly liable for an injury caused by the product if a plaintiff proves both: (1) that the product was in a defective condition when it left the defendant's control such that it was unreasonably dangerous and (2) that the defective condition was a proximate cause of the plaintiff's injury. Ark. Code Ann. § 4–86–102(a); *Harrell v. Madison Cnty. Miss. Mote Co.*, 370 F.3d 760, 762 (8th Cir. 2004) (quoting *Boerner v. Brown & Williamson Tobacco Co.*, 260 F.3d 837, 842 (8th Cir. 2001)); *Chandler v. Wal-Mart Stores Inc.*, 498 S.W.3d 766, 770 (Ark. Ct. App. 2016); *Madden v. Mercedez-Benz USA, Inc.*, 481 S.W.3d 455 (Ark. Ct. App. 2016). A "defective condition" is one that renders a product unsafe for reasonably foreseeable use and consumption. Ark. Code Ann. § 16–116–102(2). There are three general varieties of product defects: manufacturing defects, design defects, and inadequate warnings. *West v. Searle & Co.*, 806 S.W.2d 608 (Ark. 1991).

To find a "defective condition" with respect to an allegedly inadequate warning label unreasonably dangerous, the defect "must pose an actual danger to person or property, which exceeds 'that contemplated by the ordinary and reasonable buyer, taking into account any special knowledge of the buyer concerning the characteristics, propensities, risks, dangers, and proper and improper uses of the product.'" *J&B Tankers, Inc. v. Navistar Int'l Corp.*, 539 F. Supp. 3d 955, 959 (E.D. Ark. 2021) (quoting *Purina Mills, Inc. v. Askins*, 317 Ark. 58, 66 (1994)). Having

reviewed the allegations in Ms. Frye's complaint, the Court concludes Ms. Frye alleges sufficient facts to state a claim on this point.

Proximate cause requires that "the defective aspect of the product cause the injury." *Sharp v. Ethicon, Inc.*, Case No. 2:20-cv-2028, 2020 WL 1434566, at *3 (W.D. Ark. Mar. 24, 2020) (quoting *Brinkley v. Pfizer, Inc.*, 772 F.3d 1133, 1138 (8th Cir. 2014)). Having reviewed the allegations in Ms. Frye's complaint, the Court concludes Ms. Frye alleges sufficient facts to state a claim on this point.

Under the learned intermediary rule, "[a] manufacturer's inadequate warning is not a proximate cause of a plaintiff's harm [if] the prescribing physician had independent knowledge of the risk that the inadequate warning should have communicated." *Fullington v. Pfizer, Inc.*, 720 F.3d 739, 747 (8th Cir. 2013). Ms. Frye's complaint expressly alleges the label failed to warn adequately her healthcare providers of the dangers associated with Beovu. There is no indication that her healthcare providers possessed independent knowledge regarding the degree of risk Beovu posed to Ms. Frye.

For these reasons, the Court denies Novartis's motion to dismiss Ms. Frye's strict liability claim.

2. Negligence

Novartis, in seeking dismissal of Ms. Frye's complaint, does not raise an argument as to negligence that is separate or distinct from Novartis's arguments for dismissal of Ms. Frye's strict liability and fraudulent misrepresentation claims. In Count II, Ms. Frye alleges that Novartis was negligent in testing, marketing, promotion, labeling, and distribution of its prescription medication Beovu; she sustained damages; and such negligence was the proximate cause of her damages.

An inadequate warning may provide "evidence of negligence on the part of the manufacturer," *Hill v. Searle Lab'ys, a Div. of Searle Pharms., Inc.*, 884 F.2d 1064, 1070 (8th Cir. 1989), and Ms. Frye alleges sufficient facts to state a claim that the inadequate warning caused her injuries. Because Novartis confines its motion to dismiss to the failure to warn allegations in Ms. Frye's complaint, the Court confines its analysis of the motion in the same way. The allegations in Ms. Frye's complaint are sufficient to state a claim for relief regarding Novartis's alleged negligent failure to warn. Those allegations, identified in detail in this Order, include the physician-reported adverse events, Novartis's failure to present accurate adverse event data to the FDA, and Novartis's reevaluation of its Phase III clinical trial data showing a causal connection between Beovu injections and retinal vasculitis. The Court cannot determine at this early stage of the proceedings, as a matter of law, that Novartis's failure to update its label was reasonable in the light of these risks.

For these reasons, the Court concludes that Ms. Frye adequately pleads negligence theories, and the Court denies Novartis's motion to dismiss Ms. Frye's negligence claim.

C. Fraudulent Misrepresentation

Novartis also moves to dismiss Ms. Frye's fraudulent misrepresentation claim pursuant to Federal Rules of Civil Procedure 9 and 12(b)(6). Arkansas recognizes, as relevant here, two variations of liability premised on fraud: (1) fraudulent misrepresentation, and (2) fraudulent omission or concealment. "In alleging fraud or mistake, a party must state with particularity the circumstances constituting fraud or mistake." Fed. R. Civ. P. 9. Under the heightened pleading requirements of Rule 9(b), "the complaint must identify the 'who, what, where, when, and how' of the alleged fraud." *Johnson v. Gilead Scis., Inc.*, 563 F. Supp. 3d 981, 990 (E.D. Mo. 2021) (citing *U.S. ex rel. Joshi v. St. Luke's Hosp., Inc.*, 441 F.3d 552, 556 (8th Cir. 2006)). However,

pleading the particular circumstances constituting fraud is interpreted "in harmony with the principles of notice pleading." *Drobnak v. Andersen Corp.*, 561 F.3d 778, 783 (8th Cir. 2009) (citing *Schaller Tel. Co. v. Golden Sky Sys., Inc.*, 298 F.3d 736, 746 (8th Cir. 2002)). The heightened pleading standard for complaints of fraud or misrepresentation is intended to allow a specific and quick response to potentially damaging allegations. *See id.* However, Rule 9(b) provides that knowledge, intent, and other conditions of a defendant's mind may be generally alleged. Further, facts constituting the misrepresentation that are peculiarly within the defendant's knowledge maybe pled on information and belief. *Id.*

Ms. Frye styles her claim as one for fraudulent misrepresentation, but she asserts "fraudulent, intentional and material misrepresentations and omissions regarding the safety and efficacy of Beovu and of Beovu's side effects, including that concerning an increased risk for retinal vasculitis, retinal vascular occlusion, and related sequelae" were communicated to Ms. Frye and her healthcare providers "directly through promotional materials, advertising, product inserts, and the product monograph. . ." (Dkt. No. 1, ¶ 99). As a result, the Court examines fraudulent misrepresentation and fraudulent omission or concealment.

1. Fraudulent Misrepresentation

Under Arkansas law, fraudulent misrepresentation consists of the following five elements: (1) that the defendant made a false representation of material fact; (2) that the defendant knew that the representation was false or that there was insufficient evidence upon which to make the representation; (3) that the defendant intended to induce action or inaction by the plaintiff in reliance upon the representation; (4) that the plaintiff justifiably relied on the representation; and (5) that the plaintiff suffered damage as a result of the false representation. *See KBX, Inc. v. Zero Grade Farms*, 639 S.W.3d 352 (Ark. 2022).

According to the Arkansas Supreme Court, "[m]isrepresentation, also commonly referred to as deceit or fraud, has [long] been an intentional tort in Arkansas." *S. Cnty., Inc. v. First W. Loan Co.*, 871 S.W.2d 325, 326 (Ark. 1994). Ms. Frye's allegations satisfy the intent requirements for this claim. Ms. Frye alleges that Novartis "knew that the material misrepresentations they were making regarding the safety, efficacy, and side effects of Beovu were false" and further alleges that Novartis "fraudulently and intentionally made misrepresentations and/or actively concealed, suppressed, or omitted this material information with the intention and specific desire to induce consumers and the medical community, including Plaintiff and Plaintiff's healthcare providers, to use, prescribe, and purchase Beovu." (Dkt. No. 1, ¶¶ 100–101).

Novartis argues that Ms. Frye has only alleged conclusory allegations of fraud and has failed to plead facts showing her injuries resulted from reliance on any of Novartis's alleged false statements (Dkt. No. 7, at 21–24). The Court disagrees. The fraud that Ms. Frye complains of is set forth with sufficient factual allegations to support her claim at this stage of the litigation (Dkt. No. 1, ¶¶ 103–130). Further, Novartis's assertion that Ms. Frye failed to plead facts showing reliance on a misrepresentation ignores that Ms. Frye alleges that she, as well as her healthcare providers, all relied on Novartis's alleged misrepresentations and omissions to the detriment of Ms. Frye (Dkt. No. 7, at 23). Ms. Frye alleges that Novartis intended to induce reliance by Ms. Frye and/or her healthcare providers on these material misrepresentations and/or omissions (*Id.*, ¶ 102). Further, she alleges that she and her healthcare providers justifiably and reasonably relied on these material misrepresentations and/or omissions (Dkt. No. 1, ¶¶ 131–132). In addition, Ms. Frye specifically alleges that she was harmed and how she was harmed as a result (*Id.*, ¶ 133).

2. Fraudulent Omission Or Concealment

"Fraud also extends to concealment of material information and nondisclosure of certain pertinent information." *Curtis Lumber Co. v. Louisiana Pacific Corp.*, 618 F.3d 762, 772 (8th Cir. 2010). However, "[t]he law distinguishes between. . . mere silence and the suppression or concealment of a fact." *Farm Bureau Pol'y Holders & Members v. Farm Bureau Mut. Ins. Co. of Ark.*, 984 S.W.2d 6, 14 (Ark. 1998) (quoting 37 Am. Jur. 2d Fraud and Deceit § 145). Not every situation comes with a duty to speak. As a result, many courts hold that silence, to be actionable, "must relate to a material matter known to the party and which it is his legal duty to communicate," because "[w]here there is no obligation to speak, silence cannot be termed 'suppression,' and therefore is not a fraud." *Id.*

Fraud also requires some affirmative act done with intent to deceive, and liability for fraudulent omission is no different. *Farm Bureau*, 984 S.W. 2d at 14. "To prevail in a case of fraudulent nondisclosure, the plaintiff must prove that the defendant concealed a material fact known to it." *Hobson v. Entergy Arkansas, Inc.*, 432 S.W.3d 117, 125 (Ark. Ct. App. 2014) (citing *Downum v. Downum*, 274 S.W.3d 349 (Ark. Ct. App. 2008)).

Taken together, Ms. Frye's allegations suffice to allege this claim and withstand Novartis's motion to dismiss (Dkt. No. 1, ¶¶ 104, 110–125).

IV. Conclusion

For the foregoing reasons, the Court grants the request to take judicial notice (Dkt. No. 9). The Court denies the request for hearing (Dkt. No. 10), and the Court denies the motion to dismiss (Dkt. No. 6).

It is so ordered this 19th day of September, 2022.

Kristine G. Baker
United States District Judge