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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF ARIZONA

Iris Spedale and Daniel Spedale,

Plaintiffs,

v.

Constellation Pharmaceuticals Inc.,

Defendant.

No. CV-17-00109-PHX-JJT

ORDER

The Court now considers Defendant Constellation Pharmaceuticals, Inc.'s Motion to Exclude Expert Testimony of Dr. James P. Sutton (Doc. 55, MTE), Motion for Summary Judgment (Doc. 56, MSJ), and Objections to Portions of Dr. James P. Sutton's Declaration (*See* Doc. 68, Reply to MTE Opp'n; Doc. 69, Reply to MSJ Opp'n), as well as Plaintiffs' Motion for Leave to Respond to Defendant's Objections (Doc. 71, MFL) and Motion to Strike the Affidavit of Dr. Robert Sims (Doc. 63, MSJ Opp'n). For the reasons set forth below, the Court grants in part and denies in part Defendant's Motion to Exclude, grants in part and denies in part Defendant's Motion for Summary Judgment, and grants Plaintiffs' Motion to Strike.[1] Additionally, the Court overrules Defendant's Objections and denies Plaintiffs' Motion for Leave as moot.[2]

[1] Defendant has requested oral argument with respect to its Motion to Exclude and Motion for Summary Judgment. The Court denies Defendant's request because the issues have been fully briefed and oral argument will not aid the Court's decision. *See* Fed. R. Civ. P. 78(b) (court may decide motions without oral hearings); LRCiv. 7.2(f) (same).

[2] On January 9, 2019, Defendant filed its Reply to Plaintiffs' Opposition to Motion to Exclude and Reply to Plaintiffs' Opposition to Motion for Summary Judgment. (Reply to MTE Opp'n; Reply to MSJ Opp'n.) In both filings, Defendant objects to paragraphs 13, 15, 16–25, 36–38, 41, 43, 49, 50–52, 57, 61– 72, 75–91, 95–96, and 99–100 of Dr. Sutton's

I. FACTUAL BACKGROUND

Defendant is a Massachusetts corporation and developer and manufacturer of pharmaceuticals. (Doc. 64, Pls.' Statement of Add'l Facts & Resp. to Def.'s Statement of Facts, ("PSOAF")[3] ¶ 20.) Defendant conducts business, including sponsoring clinical trials, in Arizona, where Plaintiffs Iris Spedale and Daniel Spedale reside and the events giving rise to this suit occurred. (Doc. 59-11, Ex. K, Clinical Trial Agreement Between Constellation & Mayo Clinic Arizona ("CTA") at 2; MSJ Opp'n at 2.)

A. Ms. Spedale's Health

Ms. Spedale was first diagnosed with multiple myeloma in May 2009, at the age of sixty-six. (Doc. 64-1, Ex. 1, Spedale Medical Records I ("Spedale MR I") at 11.) Ms. Spedale sought treatment from Dr. Rafael Fonseca, M.D., at Mayo Clinic. (Doc. 57, Def.'s Statement of Facts in Supp. of MSJ ("DSOF") ¶ 3; PSOAF ¶ 5; Doc. 64, PSOAF & Resp. to DSOF ("PSOF")[4] ¶ 3.) At the time of her diagnosis, Ms. Spedale had no prior history of psychological problems; however, while using dexamethasone (a steroid) as part of her cancer treatment regimen, she experienced "steroid-induced mania syndrome." (Doc. 59-15, Ex. O, Daniel Spedale Dep. ("Mr. Spedale Dep.") at 8; PSOAF ¶ 9; Spedale MR I at 27.) In September 2009, Dr. Robert Bright, a Mayo psychiatrist, prescribed Zyprexa Zydis ("olanzapine") to Ms. Spedale to "help restore a normal sleep/wake cycle" and "provide mood stabilization." (Spedale MR I at 27.) By her October 2009 follow-up, Ms. Spedale's mood and sleep cycle had improved significantly. (*Id.* at 29.) One month later, Ms. Spedale underwent a successful stem-cell transplant, leaving her cancer in remission for three years. (*Id.* at 35; *see* Doc. 64-2, Ex. 2, Spedale Medical Records II ("Spedale MR II") at 75–76.) Ms. Spedale was treated for cancer twice more: once in 2013,

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Declaration (identical copies attached to Plaintiffs' Statement of Additional Facts and Response to Defendant's Statement of Facts (Doc. 64-17, Ex. 16, Decl. of Dr. James P. Sutton, M.D.) and Opposition to Motion to Exclude (Doc. 65-3, Ex. 3, Decl. of Dr. James P. Sutton, M.D.)). (*See* Reply to MTE Opp'n at 2–4; Reply to MSJ Opp'n at 2–3.) On January 16, 2019, Plaintiffs filed their Motion for Leave. (MFL.) Because the Court does not rely on Dr. Sutton's Declaration in deciding Defendant's summary judgment motion, the Court denies both Defendant's Objections and Plaintiff's Motion for Leave as moot.

[3] "PSOAF" refers to the first section of Doc. 64, Plaintiffs' Statement of Additional Facts.

[4] "PSOF" refers to the second section of Doc. 64, Plaintiffs' Response to Defendant's Statement of Facts.

and again in 2014, though each time with a lower dose of dexamethasone. (*See* Spedale MR II at 73 (Dr. Fonseca's "Final Report" of Aug. 19, 2013 visit, detailing treatment plan); *id.* at 59 (Dr. Fonseca's "Final Report" of Oct. 21, 2014 visit, detailing treatment plan).)

B. CPI-0610

1. Development of CPI-0610

On June 5, 2013, Defendant submitted an Investigational New Drug ("IND") Application to the FDA for its study drug, CPI-0610, a type of BET inhibitor. (DSOF ¶ 5; PSOF ¶ 5.) The International Conference on Harmonisation ("ICH") guidelines detail the types of studies required to support an IND application, as well as the sequence in which those studies should be performed. (DSOF ¶ 6; PSOF ¶ 6.) The guidelines applicable to pre-clinical safety testing for oncology drugs are known as ICH S9.[5] (Jacobson-Kram Report at 4.) Defendant's regulatory expert, Dr. Jacobson-Kram,[6] has explained the necessity of distinct guidelines with respect to oncology drugs: "[I]nitial doses in phase 1 studies with healthy volunteers generally are below a level that causes a pharmacological effect. When treating oncology patients with advanced disease, it is desirable that patients are initially dosed at levels that have pharmacological effects." (*Id.*)

a. Potential Issues with Neurotoxicity

In his report, Plaintiff's expert, neurologist Dr. James P. Sutton, suggests that Defendant failed to perform adequate preclinical safety testing for neurotoxicity on CPI-0610. (*See* Doc. 55-2, Ex. A, Dr. James P. Sutton's Expert Report ("Sutton Report") at 9–

[5] ICH S9 states: "[a]n assessment of the pharmaceutical's effect on vital organ functions (including cardiovascular, respiratory and central nervous systems) should be available before the initiation of clinical studies; such parameters could be included in general toxicology studies. Detailed clinical observations following dosing and appropriate electrocardiographic measurements in non-rodents are generally considered sufficient. Conducting stand-alone safety pharmacology studies to support studies in patients with advanced cancer is not called for. In cases where specific concerns have been identified that could put patients at significant additional risks in clinical trials, appropriate safety pharmacology studies described in ICH S7A and/or S7B should be considered. In the absence of a specific risk, such studies will not be called for to support clinical trials or for marketing." (Doc. 59-7, Ex. G, David Jacobson-Kram, Ph.D., DABT Expert Report ("Jacobson-Kram Report") at 5.)

[6] Defendant has retained Dr. Jacobson-Kram to provide an expert opinion on the regulatory submissions process for drug development, including the federal guidelines and regulations governing preclinical testing. (Jacobson-Kram Report at 3.)

10.) Dr. Jacobson-Kram disagrees. (*See generally* Jacobson-Kram Report.) Dr. Jacobson-Kram currently works as a pharmaceutical consultant specializing in non-clinical safety assessment. (*Id* at 3.) Dr. Jacobson-Kram served as head of toxicology in the FDA's Office of New Drugs for 11 years, and vice president of a contract testing laboratory for 15 years. (*Id.*)

According to Dr. Jacobson-Kram, Defendant adhered to ICH S9: "[n]o specific safety concerns were identified that would have led to additional studies described in ICH S9." (*Id.* at 5.) In both rodent and dog studies, "[n]o change in behavioral patterns were observed that might suggest neurological effects."[7] (*Id.*; *see id.* at 5–7.) Nothing in these preclinical studies indicated a risk for neurotoxicity—i.e., that CPI-0610 affected the "normal stereotypical behavior of experimental animals and no histopathology of the central nervous system was seen." (*Id.* at 8.) Dr. Jacobson-Kram opines: (1) Defendant performed all preclinical studies required by ICH S9; (2) the FDA agreed that the study was safe to proceed since they had declined to issue a clinical hold; and (3) Defendant's preclinical package is standard in the industry and consistent with regulatory guidelines. (*Id.* at 9.)

2. 0610-03 Study

On June 28, 2013, the FDA approved Defendant's IND Application for CPI-0610. (Doc. 59-9, Ex. I, IND Approval at 2.) Defendant and Mayo entered into a Clinical Trial Agreement ("CTA"), agreeing that Defendant would support, and Mayo would conduct, a clinical trial entitled, "A Phase 1 Study of CPI-0610, a Small Molecule Inhibitor of BET Proteins, in Patients with Previously Treated Multiple Myeloma."[8] (CTA at 2.) The CTA defines the relationship between Defendant and Mayo, respectively, Sponsor and Institution, as that of "independent contractor." (DSOF ¶ 17; PSOF ¶ 17.) The CTA identifies Dr. P. Leif Bergsagel, M.D., as Principal Investigator,[9] "responsible for the

[7] Based on her CPI-0610 dose, Ms. Spedale's exposures were most closely mimicked at a steady state in the rat 20mg/kg dose group, which showed no significant clinical signs. (*Id.* at 6.) And Ms. Spedale's exposures were most closely mimicked at a steady state in the dog 4mg/kg dose group, which showed no significant behavioral changes. (*Id.* at 7.)

[8] The Court refers to the "Phase 1 Study of CPI-0610" as the "0610-03 Study."

[9] Under 21 C.F.R. § 312.60, an investigator "is responsible for ensuring that an

direction of the Trial in accordance with applicable [Mayo] policies and Applicable Law." (CTA at 2.)

Enrollment for the 0610-03 Study began in September 2013. (DSOF ¶¶ 1, 37; PSOF ¶¶ 1, 37.) By its conclusion, 138 patients were evaluated across three trial sites (all Phase 1 studies), at doses of 6mg to 400mg once per day and 85mg to 110mg twice per day. (DSOF ¶ 38; PSOF ¶ 38.) Of the 138 total patients, 30 patients had multiple myeloma. (DSOF ¶ 38; PSOF ¶ 38.) Ms. Spedale, the 25th patient with multiple myeloma, enrolled at the Arizona trial site (Mayo) on December 1, 2015. (DSOF ¶¶ 1, 39; PSOF ¶¶ 1, 39.) At Mayo, Ms. Spedale was the last of 5 patients with multiple myeloma evaluated at the 150mg dose. (DSOF ¶ 39; PSOF ¶ 39.) Prior to Ms. Spedale's enrollment, two trial sites reported adverse events—Massachusetts General Hospital ("MGH") and The Ohio State University Cancer Center ("OSU").[10] (DSOF ¶ 41; PSOF ¶ 41.) Ms. Spedale discussed her enrollment with Dr. Fonseca, as well as Dr. Bergsagel and Charanjit (J.R.) Singh, Mayo's clinical research coordinator. (DSOF ¶¶ 31–33, 36; PSOF ¶¶ 31–33.) Mr. Singh went over each section of the Informed Consent Document ("ICF") with Ms. Spedale before she signed it. (Doc. 59-24, Ex. X, Charanjit (J.R.) Singh Dep. ("Singh Dep.") at 54–55; PSOF ¶ 35.) Plaintiffs and Defendant disagree as to whether Ms. Spedale was fully aware of the experimental nature of the 0610-03 Study when she signed the ICF.[11] (*See* DSOF ¶ 35; PSOF ¶ 35 ("Ms. Spedale's deposition testimony is questionable, as her condition may affect her memory and responses. For this reason, her deposition was terminated early.");

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investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation." (*See* DSOF ¶ 18; PSOF ¶ 18.) The study sponsor must select qualified investigators, provide appropriate information, and ensure that the investigation is properly monitored and adheres to the IND. (DSOF ¶ 19 (citing 21 C.F.R. § 312.50); PSOF ¶ 19.)

[10] At MGH, a leukemia patient presented with "confusion," which later resolved (MGH's principal investigator deemed the patient's confusion unrelated to the study drug). (DSOF ¶ 41; PSOF ¶ 41.) At OSU, a lymphoma patient also presented with confusion, which fully resolved within forty minutes. (DSOF ¶ 41; PSOF ¶ 41.) OSU's principal investigator concluded the patient's confusion was related to the study drug, but unexpected. (DSOF ¶ 41; PSOF ¶ 41.)

[11] Dr. Sutton's Report adds color to Plaintiffs' claim that Ms. Spedale perceived CPI-0610 as a "therapeutic alternative to two approved medications with known safety and efficacy profiles." (Dr. Sutton's Report at 11.) "There is nothing in the medical record to suggest that Ms. Spedale had an alternative motivation . . . such as altruism or curiosity." (*Id.*)

see also PSOF ¶ 44 ("Mr. Singh would not have been aware of the information that [Defendant] omitted from the protocol.").)

3. ICF

Federal regulations require all clinical trials to be approved by an IRB independent of the sponsor. *See* 45 C.F.R. § 46.107 (defining the composition of an IRB); *see also* 21 C.F.R § 56.111 (defining criteria for IRB approval of research); (Doc. 59-12, Ex. L, Italo Biaggioni, M.D. Expert Report ("Biaggioni Report") at 3–4).[12] Mayo's internal IRB acted as the "IRB of record" for the 0610-03 Study and reviewed the study's protocol, including its scientific merit and associated risks. (DSOF ¶¶ 22, 47; Biaggioni Report at 4; PSOF ¶¶ 22, 47.) Mayo's IRB was tasked with ensuring the ICF accurately reflected the study's risks, contained important safety-related information, and was written in a manner comprehensible to the target population. (Biaggioni Report at 5–6.) Per the CTA, Mayo was to obtain written informed consent from each trial subject according to protocol approved by the FDA and Mayo's IRB. (CTA at 2, 5.) Dr. Bergsagel testified that he reviewed the proposed ICF and submitted it to the IRB for approval. (DSOF ¶ 25; PSOF ¶ 25.) Plaintiffs, however, claim that "the IRB and investigators were not fully informed of all the risks," resulting in an allegedly deficient ICF. (PSOF ¶ 47.)

The ICF explains:

> The main purpose of this study is to determine the highest dose of CPI-0610 that can be given without causing severe side effects. This is a Phase 1 study, which means that CPI-0610 is in very early stages of testing in humans. Future studies may then test whether or not CPI-0610 is useful against different types of cancer. CPI-0610 is experimental, which means that it is not approved by the [FDA] or other regulatory agencies around the world to treat cancer or for any other disease.

(DSOF ¶ 48; PSOF ¶ 48; Doc. 59-1, Research Participant Consent & Privacy Authorization Form ("ICF") at 4.) Next, the ICF lists five research questions:

[12] Dr. Biaggioni's Report is also attached to the Motion to Exclude. (*See* Doc. 55-1, Ex. F, Italo Biaggioni, M.D. Expert Report.)

> - What is the highest dose of CPI-0610 that can be administered to multiple myeloma patients without causing severe side effects?
> - What are the side effects of CPI-0610?
> - How much CPI-0610 is in the bloodstream at specific times after taking it, and how rapidly does the body get rid of CPI-0610?
> - What are the effects of CPI-0610 on the expression of certain genes, both in normal blood cells and multiple myeloma cells?
> - Will CPI-0610 help reduce the amount of multiple myeloma in patients' bodies?

(DSOF ¶ 49; PSOF ¶ 49.) The section addressing "possible risks or discomforts" associated with the study explains that "risks and discomforts related to CPI-0610 are not well known," and explains findings associated with CPI-0610 animal studies, as well as other potential medical issues. (DSOF ¶ 50; *see* ICF at 14–17.) The section addressing "possible benefits" of participation states:

> There may or may not be medical benefit to you. Other people may benefit from the information that is learned in this study. This is a study to help develop a new therapy for others with a similar condition.

(ICF at 17; *see* DSOF ¶ 50.)

4. Ms. Spedale's Participation in the 0610-03 Study

On November 17, 2015, Dr. Fonseca noted Ms. Spedale's cancer had reappeared in diagnostic tests, and it was time to consider "the next line of treatment in her situation." (DSOF ¶ 27; PSOF ¶ 27.) He wrote, "[t]he logical next step would be the use of carfilzomib," but "[a]nother possibility would be . . . participat[ion] in one of our clinical trials." (DSOF ¶ 27; PSOF ¶ 27.) Dr. Fonseca further stated that he had already communicated with Mayo's study coordinators and was in the process of determining Ms. Spedale's eligibility. (DSOF ¶ 27; PSOF ¶ 27.) On November 23, 2015, Mr. Singh wrote to Plaintiffs, "[Dr. Fonseca] would recommend to first try the study drug (BET inhibitor). . . . Let me know if you want to pursue the trial." (Doc. 59-17, Ex. Q, Nov. 23,

2015 email exchange between Daniel Spedale and J.R. Singh at 2; *see* DSOF ¶ 29; PSOF ¶ 29.) Mr. Spedale responded affirmatively. (*See* DSOF ¶ 30; PSOF ¶ 30.)

On December 10, 2015, Ms. Spedale began the 0610-03 Study's fourteen-day regimen. (DSOF ¶ 2; PSOF ¶ 2.) On December 29, 2015, Ms. Spedale exhibited mild forms of grade 1 mania, which rapidly worsened to grade 3. (DSOF ¶ 3; PSOF ¶ 3.) Ms. Spedale continued to experience manic symptoms into 2017, attributing them to CPI-0610.[13] (DSOF ¶ 4; PSOF ¶ 4.)

II. PROCEDURAL BACKGROUND

Plaintiffs filed this case on January 13, 2017. (Doc. 1, Compl.) Plaintiffs allege that prior to the 0610-03 Study, Ms. Spedale was "rational," "able to perform her usual duties and provide comfort, society and support to her family." (*Id.* ¶ 41.) In October 2016, after attempting a complex care plan that included live-in aides and regular fly-in visits from her son and sister, Ms. Spedale "was placed in an assisted living facility, out of concerns for her own safety and security as a result of her mental state." (*Id.* ¶¶ 44, 47.) Estranged from his wife,[14] Mr. Spedale suffered nerve damage and subsequently underwent back surgery and received multiple spine injections. (*Id.* ¶¶ 48, 50.) Currently, Mr. Spedale resides in an elder-care facility to receive "assistance with his ongoing physical needs." (*Id.* ¶ 51.)

Plaintiffs make four claims. The first three are based on the theory that Defendant knew or should have known of certain neurological risks associated with CPI-0610. First, Plaintiffs allege Defendant negligently drafted the ICF, failing to adequately disclose CPI-0610's risks. (*Id.* ¶¶ 58–73.) Second, Plaintiffs allege Defendant intentionally, recklessly, and/or negligently enrolled Ms. Spedale in the 0610-03 Study without obtaining her full informed consent. (*Id.* ¶¶ 74–81.) Third, Plaintiffs allege Defendant is strictly liable for failing to provide adequate warnings with respect to CPI-0610, designing an unreasonably

[13] Plaintiffs dispute Defendant's claim that Ms. Spedale has "returned to her normal self." (DSOF ¶ 4; PSOF ¶ 4.) "On the contrary, Ms. Spedale's mental condition has never recovered to her pre-clinical trial status." (PSOF ¶ 4; *see* PSOAF ¶¶ 75–81.)

[14] As her paranoia worsened, Ms. Spedale obtained a protective order against Mr. Spedale, requiring him to leave their residence and move into a third-story walk-up apartment. Frequently climbing up and down stairs allegedly caused his nerve damage. (Compl. ¶¶ 35, 48.)

dangerous product, and inadequately testing the product. (*Id.* ¶¶ 82–88.) Fourth, Plaintiffs allege Defendant caused Mr. Spedale to suffer the loss of his wife's companionship, services, and society. (*Id.* ¶¶ 89–90.) Plaintiffs also seek punitive damages. (*Id.* ¶ 91.) Defendant now seeks summary judgment on all causes of action.

III. MOTION TO STRIKE

Plaintiffs move to strike the Affidavit of Dr. Robert Sims because "it fails to state that it is made under penalty of perjury" as required by 28 U.S.C. § 1746. (MSJ Opp'n at 4; *see* Doc. 55-3, Ex. G, Aff. of Dr. Robert Sims ("Aff. I"); Doc. 59-8, Ex. H, Aff. of Dr. Sims ("Aff. II") (identical filing).) The Court agrees. Although the Affidavit is signed, it fails to substantially comply with § 1746, which requires that any affidavit state "under penalty of perjury that the foregoing is true and correct." § 1746; *see Schroeder v. McDonald*, 55 F.3d 454, 460 n.10 (9th Cir. 1995) (stating pleading substantially complied with § 1746 when plaintiff stated under penalty of perjury that contents were true and correct); *Kersting v. United States*, 865 F. Supp. 669, 676 (D. Haw. 1994) ("As long as an unsworn declaration contains the phrase 'under penalty of perjury' and states that the document is true, the verification requirements of 28 U.S.C. § 1746 are satisfied."). Here, the Affidavit states: "The foregoing statements made by me are true and correct to the best of my knowledge. I am aware that if the foregoing are willfully false, I am subject to punishment." (Aff. I at 4; Aff. II at 5.) Because the Affidavit makes only one of the two required assertions, the Court grants Plaintiffs' Motion to Strike.

IV. MOTION TO EXCLUDE

A. Legal Standard

Rule 702 provides:

> A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:
>
> **(a)** the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;
>
> **(b)** the testimony is based on sufficient facts or data;

> **(c)** the testimony is the product of reliable principles and methods; and
>
> **(d)** the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702. Under Rule 702, the trial court acts as "gatekeeper," ensuring proffered scientific testimony meets certain standards of relevance and reliability before admission. *Daubert v. Merrell Dow Pharm., Inc.* ("*Daubert I*"), 509 U.S. 579, 590–95 (1993).

1. Reliability

An expert opinion is reliable if based on proper methods and procedures rather than "subjective belief or unsupported speculation." *Id.* at 590. The test for reliability "'is not the correctness of the expert's conclusions but the soundness of his methodology.'" *Stilwell v. Smith & Nephew, Inc.*, 482 F.3d 1187, 1192 (9th Cir. 2007) (quoting *Daubert v. Merrell Dow Pharm., Inc.* ("*Daubert II*"), 43 F.3d 1311, 1318 (9th Cir. 1995)). Alternative or opposing opinions or tests do not "preclude the admission of the expert's testimony—they go to the *weight*, not the admissibility." *Kennedy v. Collagen Corp.*, 161 F.3d 1226, 1231 (9th Cir. 1998). The same is true of "[d]isputes as to the strength of [an expert's] credentials, faults in his use of [a particular] methodology, or lack of textual authority for his opinion . . . ." *Id.* (quotation omitted).

The proffering party must demonstrate expert testimony's admissibility by a preponderance of the evidence. *Daubert I*, 509 U.S. at 592 n.10. The district court considers four factors to determine whether the testimony will assist the trier of fact: "(i) whether the expert is qualified; (ii) whether the subject matter of the testimony is proper for the jury's consideration; (iii) whether the testimony conforms to a generally accepted explanatory theory; and (iv) whether the probative value of the testimony outweighs its prejudicial effect." *Scott v. Ross*, 140 F.3d 1275, 1285–86 (9th Cir. 1998) (citations omitted). Whether an expert seeks to "testify about matters growing naturally and directly out of research they have conducted independent of the litigation, or whether they have developed their opinions expressly for the purpose of testifying" is highly significant. *Daubert II*, 43 F.3d at 1317. If the proposed testimony is not based on independent research, the court may rely

on "other objective, verifiable evidence that the testimony is based on 'scientifically valid principles.'" *Id.* at 1317–18. Ultimately, "judges are entitled to broad discretion when discharging their gatekeeping function." *United States v. Hankey*, 203 F.3d 1160, 1168 (9th Cir. 2000) (citing *Kumho Tire Co. v. Carmichael*, 562 U.S. 137, 149–153 (1999)).

2. Relevance

The district court must exclude proffered scientific evidence unless it is "convinced that it speaks clearly and directly to an issue in dispute in the case, and that it will not mislead the jury." *Cloud v. Pfizer Inc.*, 198 F. Supp. 2d 1118, 1130 (D. Ariz. 2001) (citing *Daubert II*, 43 F.3d at 1321). The district court "assessing a professor of expert scientific testimony . . . should also be mindful of other applicable rules," including Federal Rule of Evidence 403, which allows "exclusion of relevant evidence 'if its probative value is substantially outweighed by the danger of unfair prejudice, confusion of issues, or misleading the jury. . . .'" *Daubert I*, 509 U.S. at 595 (citing Fed. R. Evid. 403).

B. Dr. Sutton's Opinions

Dr. Sutton offers ten opinions: (1) Defendant negligently advanced CPI-0610 from animal studies to human clinical trials;[15] (2) Ms. Spedale "suffered severe and irreversible brain injury as the direct result of exposure to a toxic dose of CPI-0610";[16] (3) Ms. Spedale suffered mania and psychosis as a result of this toxic exposure;[17] (4) Defendant "relied on flawed reasoning in suggesting that the continuation of [Ms. Spedale]'s symptoms after discontinuation of CPI-0610 suggests a lack of causality"; (5) Mayo never obtained Ms. Spedale's full informed consent because: (a) she may have perceived CPI-0610 to be a therapeutic alternative to cancer medication; and (b) the ICF did not adequately reflect the

[15] Dr. Sutton opines that Defendant "failed to adequately test for potential neurotoxicity in violation of basic guidelines for preclinical safety testing of an investigational new drug." (Sutton Report at 9.) Dr. Sutton further opines that Defendant did not see a need to conduct further safety testing "because they chose not to look for any." (*Id.* at 10.)

[16] According to Dr. Sutton, "there was no event between 2011 and 2016 other than her exposure to CPI-0610 . . . that would provide an alternative explanation" for Ms. Spedale's mania and psychosis. (Sutton Report at 10.)

[17] Dr. Sutton explains that "[f]rontal lobe white matter abnormalities of the type described in Ms. Spedale's MRI scan are known to be linked to mania," and "[h]istone modification of the type caused by BET inhibitors such as CPI-0610 is known to play a major role in psychiatric illnesses including mania and psychosis." (Sutton Report at 10.)

risks associated with CPI-0610; (6) Defendant "is culpable in the failure to obtain informed consent";[18] (7) "[Defendant]'s protocol . . . failed to ensure human subject protection"; (8) Defendant "was negligent in its choice of Michael Cooper as its [Chief Medical Officer]"; (9) Defendant "was negligent in not keeping abreast of BET inhibitor research in a manner that would allow for . . . immediate action to ensure human subject safety";[19] and (10) Ms. Spedale "has suffered permanent and irreparable psychological injury." (Sutton Report at 9–14.) Defendant moves to exclude Dr. Sutton's Report and proposed testimony as his opinions are insufficiently reliable under Rule 702 and *Daubert I*. (MTE at 2.)

C. Admissibility of Dr. Sutton's Expert Opinions

1. Reliability

a. Dr. Sutton's Qualifications

Dr. Sutton is a board-certified neurologist in California. (Doc. 55-2, Ex. B, James P. Sutton, M.D. Dep. ("Sutton Dep.") at 35; Sutton Report at 18.) He has been practicing medicine since 1984 and currently serves as medical director of Pacific Neuroscience Medical Group. (Sutton Dep. at 34; Sutton Report at 17.) The bulk of his "clinical practice consists of patients with complex neuropsychiatric issues due to neurodegenerative disease, many of whom have organic psychoses."[20] (Sutton Report at 2.) Dr. Sutton has served as principal investigator in over one hundred trials and in that capacity, has "reviewed an equal number of clinical protocols and investigative brochures, as well as SUSAR[21] safety reports numbering in the thousands." (*Id.*; *see id.* at 18–26 (detailing trials (beginning in 1992) in which Dr. Sutton has participated).) Dr. Sutton does not typically

[18] He suggests that as the study's sponsor, Defendant was responsible for monitoring the trial site's activities and documents, including the process of obtaining a participant's informed consent. (Sutton Report at 12.) Because Defendant did not "review, discover, and request a change" in the ICF, Defendant failed to obtain full informed consent from Ms. Spedale. (*Id.*)

[19] Specifically, Defendant failed to consider the nexus between BET inhibitors and neurotoxicity. (Sutton Report at 14; *see also id.* ("Dr. Allis's report was not the type that a drug company studying BET inhibitors would be expected to miss. It was published in Nature Neuroscience and it appears that a press release may have gone out.").)

[20] Alongside his clinical practice, Dr. Sutton has studied "preclinical safety data for well over fifty investigational new drugs," and "authored a chapter on the genetics of rare and unusual movement disorders, reviewing the relationship between genetics, cellular biology, and phenotype for each disorder." (Sutton Report at 2.)

[21] Suspected Unexpected Serious Adverse Reaction ("SUSAR"). (MTE Opp'n at 3.)

conduct Phase 1 trials, in part, "because the type of phase one studies that would be of or in neurology often require hospitalization," and it is "simpler . . . to focus on phase two and three." (Sutton Dep. at 45.)

Dr. Sutton states that "[t]hrough [] education, training, experience, review of the medical literature and other professional activities," he is "familiar with the scientific, medical, ethical, regulatory, and legal foundations for the conduct of human subject medical research." (Sutton Report at 2.) Importantly, Dr. Sutton testified about the protocol he utilizes when enrolling a candidate in a clinical trial:

> I would set up a visit for them to come in, go over the consent document page by page, item by item, and I highlight, basically, each area, explain what it means, what the significance is. I will take time to go over the safety information, explain to them that I want them to understand what it means, what it doesn't mean, so they don't . . . gloss over it, because it is, often, I don't want to say 'hidden,' but in the middle of a document that could be 25 pages. I make sure they understand, see if they have questions, and then after they do that, I give them the informed consent to take home, look at, discuss with whomever they may wish, and then let us know if they want to participate.

(Sutton Dep. at 41–42.)

Defendant argues that although Dr. Sutton is a clinical neurologist, he is unqualified to offer opinions in the three general areas: (1) standard of care; (2) informed consent; and (3) causation. (*See* MTE at 2–3.) Defendant contends that Dr. Sutton lacks "expertise in clinical trial studies, BET inhibitors, oncology drugs, and the guidelines and requirements . . . [of] the FDA submission process." (*Id.* at 5; *see id.* ("Dr. Sutton has no specific knowledge about other BET inhibitor trials and whether these trials conducted additional neurotoxicity in the pre-clinical phase.") Defendant also emphasizes Dr. Sutton's lack of experience with Phase 1 clinical trials, particularly trials involving oncology drugs or BET inhibitors. (*Id.* at 6 (citing Sutton Dep. at 45, 47–48).) Finally, Defendant suggests that Dr. Sutton is insufficiently familiar with federal regulations governing pre-clinical phases of cancer study drugs.[22] (MTE at 7.)

[22] Defendant argues that this case mirrors *Cloud*, where a psychiatrist with over thirty-three years of experience was precluded from testifying because the court found his opinions

Plaintiffs maintain that this case does not hinge on questions involving the approval process for oncological study drugs, but on whether CPI-0610 "caused neurological damage, and whether [Defendant] knew or should have known that someone," who has "a history of drug-induced mania, should be in a Phase 1 trial of [CPI-0610]." (MTE Opp'n at 2.) The Court agrees with Plaintiffs.

First, while Defendant is correct that Ms. Spedale's participation in a Phase 1 clinical trial for an oncological drug triggered this lawsuit, Ms. Spedale's neurological damage is the injury at issue. (MTE at 5.) Consequently, Dr. Sutton's lack of training in oncology is not fatal to his proposed report and testimony. Indeed, Dr. Sutton has significant experience in clinical trials of drugs specifically related to neurological disorders, in addition to his extensive experience in reviewing clinical trial protocols, investigative brochures, and SUSAR safety reports. (*See* Sutton Dep. at 36–37; Sutton Report at 2, 18–26.)

Second, Defendant improperly minimizes Dr. Sutton's familiarity with federal regulations governing pre-clinical phases of cancer study drugs. Dr. Sutton testified that he reviewed relevant regulations in connection with his work in this case, and included them in his Report as he saw fit. (*See* Sutton Dep. at 57–59.) That Dr. Sutton does not explain the regulations in his Report does not mean that he is unfamiliar with them. (*See id.* at 58; MTE Opp'n at 12.)

b. Dr. Sutton's Methodology

Defendant does not individually engage each of Dr. Sutton's opinions, but divides its Motion to Exclude into three parts: (1) "Additional Neurotoxicity Testing Should have been Performed in the Preclinical Phase"; (2) "[E]xclusion criteria was inadequately drafted"; and (3) "The informed consent was inaccurate." (MTE at 10, 15, 17.)

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were developed for the purpose of testifying. (MTE at 8 (citing *Cloud*, 198 F. Supp. 2d at 1130, 1135).) The Court disagrees. The psychiatrist offered as an expert in *Cloud* had little experience conducting clinical trials and, most notably, did not even consider himself an expert in the relevant fields of suicidology and psychopharmacology. *See id.* at 1130–31. Here, in addition to other relevant knowledge and training, Dr. Sutton is a practicing neurologist with decades of experience serving as a principal investigator in clinical trials.

(1) Additional Testing in the Preclinical Phase

In reaching opinions related to the need for more preclinical safety testing, Defendant argues that Dr. Sutton does "not rely on any published data of specific BET inhibitors that were linked to psychiatric disorders." (*Id.* at 11.) Instead, Dr. Sutton applies broad research principles to arrive at a very general hypothesis: "since a BET inhibitor is known to affect DNA transcription, [CPI-0610] can be linked to very general and broad research on epigenetic modification." (*Id.*) Defendant, however, does not cite a specific part of Dr. Sutton's Report or deposition testimony promulgating such a hypothesis. (*See generally* MTE.) Where he does opine that Ms. Spedale "suffered disabling mania and psychosis" as the result of a toxic dose of CPI-0610, Dr. Sutton explains that "[h]istone modification of the type caused by BET inhibitors such as CPI-0610 is known to play a role in psychiatric illnesses including mania and psychosis." (Sutton Report at 10.) Further, he states that while BET inhibitors interfere with mRNA transcription, valproic acid, "one of the most effective pharmacological therapies for mania," actually increases mRNA transcription in a manner opposite to BET inhibitors such as CPI-0610. (*Id.* at 11.)

Defendant next suggests that Dr. Sutton relies exclusively on an article co-written by one of Defendant's co-founders, C. David Allis ("Allis Article"), to demonstrate correlation between BET inhibitors and psychiatric disorders.[23] (*See* MTE at 13; *see also id.* at 12 ("Dr. Sutton seeks . . . refuge for his hypothesis by relying on the Allis Article's findings.").) Defendant argues that, like the expert in *Cloud*, Dr. Sutton improperly relies on "the Allis Article as the sole basis for why [Defendant] should have conducted additional testing, revised its protocol and its exclusion criteria." (MTE at 13 (citing *Cloud*, 198 F. Supp. 2d at 1132).) The Court disagrees. Dr. Sutton's Report and proposed testimony are based on thirty-four medical and scientific references, as well as his knowledge and experience as a clinical neurologist. (*See* MTE Opp'n at 12; *see also* Dr. Sutton Report at 15–16 (listing references).) And, significantly, he does not opine about

[23] Erica Korb, Maro Herre, Ilana Zucker-Scharff, Robert B. Darnell & C. David Allis, *BET protein Brd4 activates transcription in neurons and BET inhibitor Jq1 blocks memory in mice*, 18 Nature Neuroscience 1464 (2015).

the IND submission process, but testified that had Defendant conducted additional preclinical testing for neurotoxicity, such testing would have enabled a more careful drafting process for both the study protocol and ICF. (Sutton Dep. at 67; *see id.* at 64–68.) Furthermore, *Cloud* is distinguishable because, in that case, the proposed expert testified that he did not consider one of the key articles *he* cited in support of his ultimate conclusion to be "reliable scientific evidence." *See Cloud*, 198 F. Supp. 2d at 1133. Here, Dr. Sutton is not an out-of-field practitioner relying on a single article to substantiate his opinions.

Finally, Defendant posits that Dr. Sutton's lack of awareness as to other BET inhibitor studies reporting manic or psychotic episodes "undermines his own opinion and reliability as an expert." (MTE at 13.) Dr. Sutton testified that regardless of whether other BET inhibitor studies reflected such findings, his opinion about the connection between CPI-0610 and Ms. Spedale's neurological issues would remain unmoved, in part, due to myriad unknown variables in such studies. (Sutton Dep. at 63–65.) And while Defendant appears to take issue with Dr. Sutton's unwillingness to state that he could have predicted a particular outcome for Ms. Spedale, according to Dr. Sutton, the issue is not "[p]redicting a bad outcome," but rather, "not insuring the safety of the research participants who then had a bad outcome." (*Id.* at 66.) The Court finds this distinction apt—Plaintiffs do not rely upon Dr. Sutton to predict specific outcomes with respect to clinical trials involving BET inhibitors.

(2) Inadequate Exclusion Criteria

Defendant takes issue with two of Dr. Sutton's critiques of the clinical trial protocol. First, the lack of exclusion criteria for subjects who had other treatment options, and second, the lack of exclusion criteria for patients with prior or active central nervous system neurological or psychiatric illnesses. (MTE at 15; Sutton Report at 12.) In support, Defendant cites Section Four of the protocol:

> The patients enrolled in this study will be adults (aged ≥ 18 years) with a histologically or cytologically confirmed diagnosis of multiple myeloma that has progressed following standard treatment, and for whom further effective standard treatment is not available.

Doc. 55-1, Ex. E, Clinical Trial Protocol at 40.) Dr. Sutton's opinion hinges on safety; he testified that although the protocol states that this study is for patients "for whom further effective standard treatment is not available," that statement is not included in the relevant subsection titled, "Exclusion [C]riteria," essentially removing that information from the patient's mind.[24] (Sutton Dep. at 99; Sutton Report at 11–12.) Defendant counters that Dr. Sutton's opinion is "anecdotal and personal." (MTE at 16.) That may be, but Dr. Sutton's reliance on his extensive clinical background and experience in this context does not justify exclusion. Among other qualifications, Dr. Sutton has been practicing for over thirty years and has been involved in more than 150 clinical trials. *See Primiano v. Cook*, 598 F.3d 558, 567 (9th Cir. 2010) (admitting expert's testimony with "sufficient basis in education and experience").

Second, Defendant argues that Dr. Sutton solely and improperly relies on the Allis Article to opine that Defendant failed to ensure human subject protection by failing to include exclusion criteria or precautionary provisions for patients with prior or active central nervous system neurological or psychiatric illness. (MTE at 16.) Plaintiff does not disagree with Defendant—Dr. Sutton relies on the Allis Article to reach his opinion, but sufficiently explains his criteria for doing so.[25] The jury may reject Dr. Sutton's opinions; it may conclude that Defendant adequately drafted the exclusion criteria. *See Primiano*, 598 F.3d at 568. But the Court cannot close the door to these "relevant opinion[s] offered

[24] Dr. Sutton testified that "if the information is presented in a manner that [] disappears, then the question is, first of all, why, and then second of all, who then becomes responsible?" (Sutton Dep. at 99.)

[25] Dr. Sutton offers numerous statements in support of this opinion:

(1) "The information should have been known by the drug company, given that the article is based on research . . . and published by one of its founders . . . . They should have thought about the possibility that there could be injury to the central nervous system. They should have made sure there was an exclusion for psychiatric disorders, they should have changed the protocol." (Sutton Dep. at 71.)

(2) "I would expect any drug company doing research on bromodomain inhibitors and epigenetics would be keeping abreast of the field." (*Id.* at 75.)

(3) Dr. Sutton testified that Ms. Spedale had a predisposition to psychosis from steroids, and, as such, any reasonable protocol would have excluded her from the trial. (*Id.* at 76.)

(4) Explaining the difference between "prior" and "concurrent" in terms of the protocol's drafting, Dr. Sutton explains that as currently written, "you would absolutely enroll someone with a past history of mania on that exclusion or inclusion criteria." (Sutton Dep. at 78.)

with sufficient foundation by one qualified to give it." *Id.*; *see also Murray v. S. Route Maritime SA*, 870 F.3d 915, 925 (9th Cir. 2017) ("[T]he appropriate way to discredit [an expert]'s theory [is] through competing evidence and incisive cross-examination.").

(3) Inadequately Drafted ICF

Defendant argues that Dr. Sutton lacks the necessary experience to opine about drafting informed consent and/or protocols, and that where he opines that the ICF fails to specify certain risks associated with CPI-0610, he does so without support. (MTE at 17.) Defendant argues that its IRB expert, Dr. Biaggioni, confirmed that the ICF "complied with all applicable guidelines and regulations," and that Dr. Sutton has not claimed otherwise. (*Id.*; Biaggioni Report at 8–9.) Yet Dr. Sutton's opinion that Ms. Spedale's *full* informed consent was never obtained is not based on his understanding of the duty and/or role of the IRB; it is based on his belief that Ms. Spedale should have been given certain information prior to enrollment—information Defendant neglected to account for in their study design. (Sutton Report at 11–12.) While Mayo's IRB was "responsible for reviewing, amending and finalizing the ICF," Defendant was ultimately responsible for providing the underlying information. (MTE at 17; Sutton Report at 11–12.) As discussed above, Dr. Sutton is qualified to render these opinions.

2. Relevance

a. Proposed Opinion 5

While Dr. Sutton's opinions concerning the adequacy of the ICF speak "clearly and directly to an issue in dispute in the case," his opinion that Ms. Spedale never fully consented to participate in the 0610-03 Study because she may have perceived CPI-0610 to be a therapeutic treatment does not. *Cloud*, 198 F. Supp. 2d at 1130; (*see* Sutton Report at 11 (Opinions 5(a)–(d))). The ICF sufficiently discloses the study's experimental nature. It unambiguously states that the "main purpose of the study is to determine the highest dose of CPI-0610 that can be given without causing severe side effects," and explains that because the 0610-03 Study is a Phase 1 study, "CPI-0610 is in very early stages" of human testing. (ICF at 4.) Additionally, the five research questions posed by the 0610-03 Study

all reflect the experimental nature of the trial. (*See id.*) Whatever its other issues may be, the ICF does not portray CPI-0610 as a "therapeutic alternative" to cancer-treating medications. (*See* ICF at 17 ("There may or may not be medical benefit to you . . . . This study may help to develop a new therapy for others with a similar condition.").) And where Dr. Sutton opines that nothing in the medical record indicates other options were discussed with Ms. Spedale, even if that were true, such a discussion does not fall within the scope of Defendant's role as drug manufacturer and sponsor. (Sutton Report at 12 (Opinion 5(d)).) Consequently, the Court excludes proposed opinions 5(a)–(d), and 5(g).[26]

The Court excludes proposed opinions 5(h) and 5(i) for similar reasons. The 0610-03 Study was a dose-escalation study, which means that patients in the first group received a certain dose of CPI-0610, and if no one in the group presented a dose-limiting toxicity ("DLT"), each subsequent group would receive a higher dose until at least two patients presented at least one DLT. (Sutton Report at 5.) The 0610-03 Study defined DLT as a "Grade III or 'Severe Adverse Event,'" or, "[s]omething medically significant but not life-threatening." (*Id.*) Dr. Sutton opines that the ICF does not sufficiently explain the risks associated with a dose-escalation study (such as death and DLTs). (Sutton Report at 12 (Opinion 5(i)).) The ICF itself states otherwise. The ICF explicitly states: "[t]he dose of CPI-0610 will continue to be increased until unacceptable side effects occur in patients." (ICF at 5–6.) And, whether Ms. Spedale properly read that the study involved "the risk of death" is not at issue.

b. Proposed Opinions 4, 8, and 9

Defendant specifically attacks the relevance of Dr. Sutton's opinions concerning Defendant's liability, proposed opinions 4, 8, and 9. (MTE at 18.) Without explaining *why* Plaintiffs cannot establish liability, Defendant argues that Dr. Sutton's opinions are irrelevant because he has not spoken with any of Defendant's employees involved with the 0610-03 Study. (*Id.*) Defendant does not cite any supporting authority indicating that such

[26] Opinion 5(g) pertains to Ms. Spedale's medical record: "In the notes the day of signing informed consent, there is no record of what transpired." (Sutton Report at 12.) This statement is irrelevant, particularly with respect to Defendant's liability, since Defendant does not oversee the physician-patient relationship between Dr. Fonseca and Ms. Spedale.

discussions are a precondition of relevance. (*See generally id.*) The Court, therefore, is unmoved. Proposed opinions 4 and 9 speak "clearly and directly" to the extent of Defendant's duty to participants in the 0610-03 Study, and whether Defendant's omissions were responsible for harm suffered by Plaintiffs. *Cloud*, 198 F. Supp. 2d at 1130.

However, the Court finds that proposed opinion 8, which states that Defendant "was negligent in the choice of Dr. Michael Cooper as their CMO" has little to no bearing on the ultimate issues in this case. (Sutton Report at 12.) In fact, admitting this scientific-adjacent opinion could potentially mislead the jury to decide that if Defendant negligently selected Dr. Cooper as CMO, Defendant is liable for inadequately drafting the ICF. *See Daubert II*, 43 F.3d at 1321; *see also Daubert I*, 509 U.S. at 595 (explaining that scientific expert testimony "can be both powerful and quite misleading" because it is difficult to evaluate). The Court accordingly excludes proposed opinion 8.

D. Conclusion

Although Defendant may disagree with Dr. Sutton's conclusions, Defendant will have the opportunity to offer the testimony of its own rebuttal expert and to cross-examine Dr. Sutton to explore the limitations of his analysis and conclusions. Any such limitations will go to the weight, not the admissibility, of Dr. Sutton's testimony. With the exception of proposed opinions 5(a)–(d), 5(g)–(i), and 8, Dr. Sutton's opinions are admissible. The Court grants in part and denies in part Defendant's Motion to Exclude.

V. DEFENDANT'S MOTION FOR SUMMARY JUDGMENT

A. Legal Standard

Summary judgment is properly granted when: (1) no genuine issues of material fact remain; and (2) after viewing the evidence most favorably to the non-moving party, the movant is clearly entitled to prevail as a matter of law. Fed. R. Civ. P. 56(a); *Celotex Corp. v. Catrett*, 477 U.S. 317, 322–23 (1986); *Eisenberg v. Ins. Co. of N. Am.*, 815 F.2d 1285, 1288–89 (9th Cir. 1987). A fact is "material" when, under the governing substantive law, it could affect the outcome of the case. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248

(1986). A "genuine issue" of material fact arises if "the evidence is such that a reasonable jury could return a verdict for the nonmoving party." *Id.*

The moving party bears the initial burden of identifying the portions of the record, including pleadings, depositions, answers to interrogatories, admissions, and affidavits, that it believes demonstrate the absence of a genuine issue of material fact. *Celotex Corp.*, 477 U.S. at 323. If the moving party meets its initial burden, the opposing party must establish the existence of a genuine dispute as to any material fact. *See Matsushita Elec. Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 585–86 (1986). There is no issue for trial unless there is sufficient evidence favoring the non-moving party. *See Anderson*, 477 U.S. at 249. "If the evidence is merely colorable or is not significantly probative, summary judgment may be granted." *Id.* at 249–50 (citations omitted). A plaintiff cannot create a genuine issue for trial based solely upon subjective belief. *Bradley v. Harcourt, Brace & Co.*, 104 F.3d 267, 270 (9th Cir. 1996). However, "[t]he evidence of the non-movant is to be believed, and all justifiable inferences are to be drawn in his favor." *Anderson*, 477 U.S. at 255 (citation omitted).

B. Analysis

1. Count One: Negligence

Plaintiffs argue that Defendant failed to provide Mayo with adequate information about CPI-0610's risks and benefits, thereby preventing Mayo from obtaining full informed consent from study participants.[27] (*See* PSOAF ¶¶ 31, 34–35, 47–48; Compl. ¶¶ 58–73.) Plaintiffs argue that Defendant knew or should have known of the risks of certain adverse effects, including neurotoxicity, associated with CPI-0610 beforehand. (*See* PSOAF ¶ 35; Compl. ¶ 59.) "'To establish a claim for negligence, a plaintiff must

[27] Plaintiffs also argue that Defendant "misrepresented, in the [ICF] and otherwise, that [CPI-0610] was a 'treatment' for multiple myeloma." (Opp'n to MSJ at 15; *see* PSOAF ¶¶ 44–45; PSOF ¶¶ 49–50; Compl. ¶ 65.) Defendant denies this depiction, and emphasizes that the ICF "educated the enrollee that there may not be a medical benefit of taking the study drug and there [were] potential risks associated with the study drug." (DSOF ¶ 50.) The Court agrees with Defendant. As discussed above, with respect to Dr. Sutton's proposed opinions 5(a)–(d), the ICF does not present CPI-0610 (or the 0610-03 Study) as a treatment for multiple myeloma. *See supra* Section IV.C.2.a. The Court grants summary judgment with respect to Plaintiffs' negligent misrepresentation claim.

prove . . . : (1) a duty requiring the defendant to conform to a certain standard of care; (2) a breach by the defendant of that standard; (3) a causal connection between the defendant's conduct and the resulting injury; and (4) actual damages.'" *Diaz v. Phx. Lubrication Serv., Inc.*, 230 P.3d 718, 721 (Ariz. Ct. App. 2010) (quoting *Gipson v. Kasey*, 150 P.3d 228, 230 (Ariz. 2007)). "Ordinarily, summary judgment is not appropriate in negligence actions because breach of the duty of reasonable care and proximate cause are fact questions for the jury." *Matthews v. Greyhound Lines, Inc.*, 882 F. Supp. 146, 148 (D. Ariz. 1995) (citation omitted)). "Nevertheless, summary judgment is appropriate where all reasonable people must draw the same conclusion." *Id.* (citation omitted).

a. Duty

In a clinical trial setting, Defendant argues, the sponsor's duty does not run to the participants, but to the investigators. (MSJ at 17–18.) Therefore, as the 0610-03 Study's sponsor, Defendant denies any duty to Ms. Spedale. (*Id.* at 18.) Plaintiffs respond that Defendant acted negligently by failing to adhere to federal regulations governing clinical trials. (MSJ Opp'n at 12 (citing 21 C.F.R. §§ 312.3(b), 312.50, 312.60; 45 C.F.R. § 46.116).) According to Plaintiffs, federal regulations enacted for the safety of trial subjects impose duties upon sponsors that flow to trial subjects. (MSJ Opp'n at 12.) Plaintiffs most persuasively cite to § 312.50, which states in part:

> Sponsors are responsible for selecting qualified investigators, providing them with the information they need to conduct an investigation properly, ensuring proper monitoring of the investigation(s), ensuring that the investigation(s) is conducted in accordance with the general investigational plan and protocols contained in the IND, maintaining an effective IND with respect to the investigations, and ensuring that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug.

(*Id.*) Plaintiffs argue that Defendant's responsibility accordingly included disclosing significant risks associated with CPI-0610. (*See id.* at 12–13); *see also* 21 C.F.R. § 312.55 (imposing duties on sponsors, distinct from those imposed on investigators, to provide information required to draft proper ICFs); *Butler v. Juno Therapeutics, Inc.*, No. H-18-898, 2019 WL 2568477, at *22–23 (S.D. Tex. June 21, 2019) (explaining how 21 C.F.R.

§§ 312.50, 312.55 may impose duties on drug manufacturers that flow to clinical trial participants). Plaintiffs cite to *Zeman v. Williams*, where the court determined that while "the investigator has a major, if not the major, role in obtaining a properly informed consent[,]" other persons, "particularly the trial's sponsor, might also have a responsibility to help assure that the investigator actually gets a properly informed consent." No. 11-10204-GAO, 2014 WL 3058298, at *3 (D. Mass July 7, 2014). "If the investigator fails to inform a subject about some substantial risk because the sponsor has failed to adequately inform the investigator about the risk, the sponsor may be liable in tort." *Id.* The Court agrees with the general principle espoused by *Zeman*: if the sponsor does not fulfill its duty to the investigator, then, by extension, it does not fulfill its duty to the participant. *See Butler*, 2019 WL 2568477, at *23.

b. Breach

The issue, then, is whether Defendant fulfilled its duty to Mayo's IRB by (1) conducting appropriate preclinical safety testing on CPI-0610 and (2) accurately conveying necessary information to Mayo's IRB so that the investigators could secure full informed consent from participants. Dr. Sutton opines that Defendant did not fulfill its duty to Ms. Spedale because it failed to "monitor the site's activities and documents, including the [informed consent] process and the ICF." (Sutton Report at 12.) Dr. Jacobson-Kram does not directly address Dr. Sutton's opinion, only opining that Defendant "performed due diligence in its preclinical safety assessment," in part, because "[t]he preclinical package that [he] reviewed is standard in the industry and consistent with the regulatory guidelines." (Jacobson-Kram Report at 9.) Based on the difference in the opinions offered by Plaintiffs' and Defendant's respective experts on the proper standard of care, the Court finds that there is a genuine dispute of material fact as to whether Defendant breached its duty of care to Ms. Spedale.

c. Proximate Cause

At this juncture, the Court concludes that Plaintiffs have demonstrated that, at the very least, there is a genuine dispute as to whether Defendant's negligence caused

Plaintiffs' injuries. Dr. Sutton opines that: (1) abnormalities indicated in Ms. Spedale's MRI are known to be linked to mania; (2) Ms. Spedale's mania was temporally linked to exposure to CPI-0610; and (3) BET inhibitors such as CPI-0610 cause a kind of histone modification that plays a "major role" in psychiatric illnesses. (Sutton Report at 10.) While Defendant argues that Plaintiffs cannot demonstrate a reasonable connection between Defendant's act or omission and Plaintiffs' injuries, this argument is mostly premised on its assertion that it owed no duty to Ms. Spedale. (*See* MSJ at 18 ("If there is no duty, there can be no breach and it would be impossible for [Defendant]'s conduct to be the proximate cause of [P]laintiffs' injuries.").) Because the Court finds that a duty flowed from Defendant to Ms. Spedale, Defendant's argument is moot.

Defendant engages the issue of causation more thoroughly in its arguments against Plaintiffs' strict liability claim. (*See* MSJ at 14–15.) Defendant cites its own neuropsychiatric expert [Dr. Maurice Preter]'s opinion that Ms. Spedale's "year and a half of grossly disturbed sleep patterns preceding her mania, combined with anxiety, and multiple courses of chemotherapy all could have caused or contributed to Ms. Spedale's mania." (*Id.* at 14.) Defendant also emphasizes that Ms. Spedale was taking several medications while participating in the 0610-03 Study, and one of those medications, Prednisone, "is known for aggravating pre-existing psychiatric conditions." (*Id.* at 15.) Defendant argues that "[t]his is not a case of strict liability. This case comes down to whether or not there is negligence." (*Id.*) The Court agrees. Whether Defendant acted negligently—namely, the issues of breach and causation—are fact questions for the jury. *See Matthews*, 882 F. Supp. at 148.

That Defendant identifies potential culprits such as chemotherapy and Prednisone does not mean Dr. Sutton's opinions pertaining to proximate cause amount to "sheer speculation." (MSJ at 15.) Proximate cause may be found even where the defendant's act or omission is not the singular cause of injury. *Wisener v. State*, 598 P.2d 511, 513 (Ariz. 1979). Because Plaintiffs have raised triable issues of fact regarding breach and causation, the Court denies summary judgment with respect to Plaintiffs' negligent drafting claim.

2. Count Two: Informed Consent

"Plaintiffs alleging lack of informed consent must show two types of causation: (1) the plaintiff would have declined the treatment with adequate disclosure; and (2) the treatment proximately caused injury to the plaintiff." *Rice v. Brakel*, 310 P.3d 16, 22 (Ariz. Ct. App. 2013) (citation omitted). While expert testimony is required to demonstrate the second type of causation, it is not required to demonstrate the first. *Gorney v. Meaney*, 150 P.3d 799, 804 (Ariz. Ct. App. 2007). Plaintiffs can testify themselves as to whether they would have declined the treatment with adequate disclosure, and such information falls within the experiential scope of the average juror. *See id.*; *see also Adams v. Amore*, 895 P.2d 1016, 1018 (Ariz. Ct. App. 1994) (explaining that expert testimony derives from the need for "specialized knowledge"). And Dr. Sutton's opinions concerning proximate causation, discussed with respect to Plaintiff's negligent drafting claim, apply in this context as well.

Plaintiffs' informed consent claim operates on the same set of facts as their negligent drafting claim. (*See* PSOAF ¶¶ 31, 34–35, 47–48; Compl. ¶¶ 74–81.) They introduce evidence that had she been fully aware of its risks, Ms. Spedale would not have participated in the study. (PSOAF ¶¶ 53, 57, 58; Compl. ¶¶ 78–80.) Defendant argues that the informed consent claim lacks merit for three reasons: (1) Plaintiffs concede that Ms. Spedale did not read the ICF and Mayo did not inform her of its contents; (2) Defendant is not responsible for Mayo's failure to obtain informed consent because Defendant and Mayo explicitly agreed that Mayo was an independent contractor; and (3) the ICF contained sufficient information regarding known and unknown risks. (*See* MSJ at 7–10.)

Apart from its third reason, Defendant's arguments primarily underscore that the ICF's sufficiency, both in its form and implementation, fell under Mayo's purview.[28] (*See,*

[28] Defendant also argues that under the learned intermediary doctrine ("LID"), "a manufacturer satisfies its duty to warn end users by giving appropriate warnings to the specialized class of persons who may prescribe or administer the product." (MSJ at 9.) But, in Arizona, the LID is "less a rule of causation and more a standard for determining when a drug manufacturer has satisfied its duty to warn." *Watts v. Medicis Pharm. Corp.*, 365 P.3d 944, 949 (Ariz. 2016) (quotation omitted). As discussed above, there is a genuine dispute as to whether Defendant satisfied its duty to warn Ms. Spedale. Thus, Defendant's LID argument does not supplement its defense against Plaintiffs' informed consent claim.

e.g., *id.* at 7 ("[Defendant] can have no liability since obtaining the informed consent was the responsibility . . . of the . . . trial site.").) However, if Defendant breached its duty of care to Ms. Spedale by failing to perform due diligence in the preclinical testing phase, the ICF could also be deemed deficient for lack of material information. Because the fate of Plaintiffs' informed consent claim rises and falls with their negligent drafting claim, the Court denies summary judgment with respect to Plaintiffs' informed consent claim.

3. Count Three: Strict Products Liability

Arizona has adopted the doctrine of strict products liability as set forth in Restatement (Second) of Torts § 402A. *Gaston v. Hunter*, 588 P.2d 326, 338 (Ariz. Ct. App. 1978) . A party may be held strictly liable for selling a product in a defective condition that is unreasonably dangerous to a user or consumer. *Scheller v. Wilson Certified Foods, Inc.*, 559 P.2d 1074, 1076 (Ariz. Ct. App. 1976). To establish a prima facie case of strict liability, a plaintiff must show: (1) the product was in a defective condition when it left the defendant's control; (2) the defective condition made the product unreasonably dangerous; and (3) the defect caused plaintiff's injuries.[29] *Jimenez v. Sears, Roebuck & Co.*, 904 P.2d 861, 864 (Ariz. 1995). There are three defective conditions theories: (1) manufacturing defects, (2) design defects, and (3) informational defects. *Brown v. Sears, Roebuck & Co.*, 667 P.2d 750, 756 (Ariz. Ct. App. 1983). Plaintiffs allege strict liability under all three. (*See* MSJ Opp'n at 16–18; Compl. ¶¶ 82–88.)

a. Manufacturing Defect

Section 402A's definition of "defective condition" works best in the context of a manufacturing defect: a manufacturing or assembling abnormality that yields an unintended and unexpected product. Restatement (Second) of Torts § 402A cmt. g (Am. Law Inst. 1975); *see Brady v. Melody Homes Mfr.*, 589 P.2d 896, 899 (Ariz. Ct. App. 1978), *disapproved of on other grounds by Dart v. Wiebe Mfg., Inc.*, 709 P.2d 876 (Ariz.

[29] Defendant argues that since there was no "sale" within the meaning of § 402A, it cannot be held strictly liable. (*See* MSJ at 10–11.) This is not so. Arizona courts do not construe the term "seller" so strictly: "[T]he policies which justify the application of strict products liability principles to those who manufacture and [s]ell products also apply to those who manufacture and [s]upply products to consumers on an investigational basis . . . ." *Gaston*, 588 P.2d at 339.

1985). This test, sometimes called the consumer expectation test, permits strict liability where a product does not perform as safely as a reasonable consumer would expect when used in its reasonably intended manner. *See Dart*, 709 P.2d at 878–89. A plaintiff should compare the injury-inducing product with other non-defective products in the same line. *Brady*, P.2d at 899.

Plaintiffs argue that a jury could readily conclude that CPI-0610's distribution was not justified, either to the general population or to an individual with Ms. Spedale's medical history. (MSJ Opp'n at 18.) Precisely what sort of manufacturing defect would persuade a jury to come to such a conclusion, Plaintiffs do not say. While Plaintiffs have offered sufficient evidence to survive summary judgment with respect to their negligent drafting and informed consent claims, both of those claims spotlight Defendant's conduct—namely, Defendant's alleged omission of material information from the ICF. Because a strict liability manufacturing defect claim necessarily concerns the product itself, Plaintiffs have not met their burden to show evidence on which a reasonable jury could reasonably find for them. *Anderson*, 477 U.S. at 252. The Court grants summary judgment with respect to Plaintiffs' manufacturing defect claim.

b. Design Defect

Arizona courts have adopted two alternate tests to establish the existence of an unreasonably dangerous design defect: (1) the consumer expectation test, and (2) the risk/benefit analysis. *Dart*, 709 P.2d at 879. The consumer expectation test applies where an ordinary consumer has experience with the product and thus has a reasonable expectation of how safely it should perform. *See id.* at 878–79. The risk/benefit analysis applies where an ordinary consumer lacks experience with the product, and thus lacks a reasonable expectation as to its "safe" performance. *See id.* Because experimental drugs are beyond the ordinary consumer's knowledge and experience, the risk/benefit analysis applies. Here, the fact-finder must decide whether the benefits of the challenged design outweigh any dangers inherent in the design. *Dart*, 709 P.2d at 879; *see also Byrns v.*

Riddell, 550 P.2d 1065, 1068 (Ariz. 1976) (explaining the *Byrns* factors used by Arizona courts in the risk/benefit analysis).

Plaintiffs' design defect claim is nearly indistinguishable from its manufacturing defect claim. (*See* MSJ Opp'n at 18.) As a result, it fails for many of the same reasons. Plaintiffs do not offer evidence supporting the existence of a reasonable alternative design to CPI-0610 and are likely unable to do so because of the experimental stage at which Ms. Spedale encountered the study drug. Alleged issues with the 0610-03 Study do not pertain to CPI-0610's design, but to the study's design. (*See, e.g.*, Sutton Report at 12 (Defendant's "protocol 0610-03 failed to ensure human subject protection.").) Such arguments overlook the core of a design defect claim: whether the study drug itself is unreasonably dangerous. *See Dart*, 709 P.2d at 878–80. The Court grants summary judgment with respect to Plaintiffs' design defect claim.

c. Informational Defect (Failure to Warn)

Under Arizona law, a manufacturer has a duty to warn of dangers inherent in the intended use or reasonably foreseeable use of a product. *Kavanaugh v. Kavanaugh*, 641 P.2d 258, 262 (Ariz. Ct. App. 1981). To succeed in an informational defect claim, a plaintiff must prove "that the defendant did not adequately warn of a particular risk that was known or knowable in light of the generally recognized and prevailing best scientific and medical knowledge available at the time of manufacture and distribution." *Powers v. Taser Int'l, Inc.*, 174 P.3d 777, 783 (Ariz. Ct. App. 2007) (quotation omitted). A seller is charged "'with knowledge of what reasonable testing would reveal.'" *Id.* at 784 (quoting Restatement (Third) of Torts: Products Liability § 2 cmt. m (Am. Law Inst. 1997)). But where the danger is obvious or known to the user, liability will not lie. *Raschke v. Carrier Corp.*, 703 P.2d 556, 559 (Ariz. Ct. App. 1985).

Unlike manufacturing or design defect claims, an informational defect claim "relates to a failure extraneous to the product itself." *Powers*, 174 P.3d at 783. An informational defect claim is thus "rooted in negligence to a greater extent than manufacturing or design defect theories," because it concerns the manufacturer's conduct

in a way that the other two theories do not. *Id.* (quotation omitted). The same issues that prevent the Court from granting summary judgment with respect to Plaintiffs' negligent drafting and informed consent claims prevent the court from doing so here. If Defendant did not conduct "reasonable testing" in the preclinical testing phase, it would still be "charged with knowledge of what reasonable testing would [have] reveal[ed]." *Id.* at 784 (quotation omitted). And if that knowledge would have removed someone with Ms. Spedale's medical history from the participant population, Defendant is liable for the resulting informational defect. The Court denies summary judgment with respect to Plaintiffs' informational defect claim.

4. Count Four: Loss of Consortium & Punitive Damages

a. Loss of Consortium

Loss of consortium is "a loss of capacity to exchange love, affection, society, companionship, comfort, care and moral support." *Pierce v. Casas Adobes Baptist Church*, 782 P.2d 1162, 1165 (Ariz. 1989). Because loss of consortium is a derivative claim, "all elements of the underlying cause must be proven before the claim can exist." *Barnes v. Outlaw*, 964 P.2d 484, 487 (Ariz. 1998). Plaintiffs argue that Mr. Spedale has suffered the loss of his wife's companionship, services, and society due to Defendant's negligence, failure to obtain informed consent, and other improper conduct. (Compl. ¶ 89.) Defendant does not address Mr. Spedale's loss of consortium claim in its summary judgment motion, so the Court denies summary judgment with respect to this claim.[30]

b. Punitive Damages

To recover punitive damages under Arizona law, "something more is required over and above the mere commission of a tort." *Linthicum v. Nationwide Life Ins. Co.*, 723 P.2d 675, 679 (Ariz. 1986) (quotation omitted). A plaintiff must prove by clear and convincing evidence that the defendant engaged in aggravated and outrageous conduct with an evil mind. *Linthicum*, 723 P.2d 680–81. This is so because punitive damages "primarily further

[30] Regardless, Defendant is not entitled to summary judgment here because Plaintiffs have established a genuine dispute concerning three of the underlying tort claims: negligent drafting, informed consent, and strict liability informational defect.

the same objectives underlying criminal law: punishing the defendant and deterring the defendant and others from future misconduct." *Gurule v. Ill. Mut. Life & Cas. Co.*, 734 P.2d 85, 86 (Ariz. 1987). The chief question, then, is motive. *Volz v. Coleman Co., Inc.*, 748 P.2d 1191, 1194 (Ariz. 1987). Because defendants rarely admit to an "evil mind," improper motive is often inferred from sufficiently oppressive, outrageous, or intolerable conduct. *Id.*; *see Linthicum*, 723 P.2d at 680. And Plaintiffs do not offer any evidence of such conduct. (*See generally* PSOF; MSJ Opp'n.) The Court grants summary judgment with respect to Plaintiffs' punitive damages claim.

VI. CONCLUSION

The Court grants in part and denies in part Defendant's Motion to Exclude. (Doc. 55.) Specifically, the Court excludes proposed opinions 5(a)–(d), 5(g)–(i), and 8. The Court grants in part and denies in part Defendant's Motion for Summary Judgment. (Doc. 56.) The Court grants summary judgment on Plaintiffs' negligent misrepresentation claim, but denies summary judgment on Plaintiffs' negligent drafting and informed consent claims. The Court additionally grants summary judgment on Plaintiffs' manufacturing and design defect claims, but denies summary judgment on Plaintiffs' informational defect claim. Finally, the Court denies summary judgment on Mr. Spedale's loss of consortium claim, and grants summary judgment on Plaintiffs' punitive damages claim.

IT IS ORDERED granting in part and denying in part Defendant's Motion to Exclude Expert Testimony of Dr. James P. Sutton (Doc. 55).

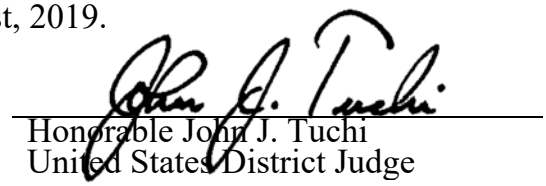
IT IS FURTHER ORDERED granting in part and denying in part Defendant's Motion for Summary Judgment (Doc. 56).

IT IS FURTHER ORDERED denying Defendant's Objections to Dr. James P. Sutton's Declaration as moot (Doc. 68; Doc. 69).

IT IS FURTHER ORDERED denying Plaintiffs' Motion for Leave to Respond to Defendant's Objections to Dr. James P. Sutton's Declaration as moot (Doc. 71).

IT IS FURTHER ORDERED granting Plaintiffs' Motion to Strike the Affidavit of Dr. Robert Sims (Doc. 63).

Dated this 16th day of August, 2019.



Honorable John J. Tuchi
United States District Judge