IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF UTAH, CENTRAL DIVISION

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| KENNETH CHRISTISON, Individually and as Surviving Spouse of ANNALEE CHRISTISON, Deceased, and as Personal Representative of the Estate of ANNALEE CHRISTISON, Deceased,<br><br>Plaintiff,<br><br>v.<br><br>BIOGEN IDEC INC. AND ELAN PHARMACEUTICALS, LLC,<br><br>Defendants. | **ORDER GRANTING DEFENDANTS' MOTION FOR SUMMARY JUDGMENT**<br><br>Case No. 2:11-cv-01140-DN-DBP<br><br>District Judge David Nuffer<br>Magistrate Judge Dustin B. Pead |

Defendants Biogen Idec Inc. ("Biogen") and Elan Pharmaceuticals ("Elan") (collectively "Companies") move for summary judgment on all of Mr. Christison's claims ("Motion").[1] Mr. Christison opposes summary judgment ("Opposition").[2] For the reasons set forth below, the Motion is GRANTED.

**CONTENTS**



[1] Motion for Summary Judgment and Memorandum in Support ("Motion") at 1, docket no. 166, filed Dec. 11, 2015.

[2] Plaintiff's Opposition to Defendants' Motion for Summary Judgment ("Opposition"), docket no. 175, filed Jan. 22, 2016.

## SUMMARY JUDGMENT STANDARD

Summary judgment is appropriate if "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law."[3] A factual dispute is genuine when "there is sufficient evidence on each side so that a rational trier of fact could resolve the issue either way."[4] In determining whether there is a genuine dispute as to material fact, the court should "view the factual record and draw all reasonable inferences therefrom most favorably to the nonmovant."[5]

## CAUSES OF ACTION

Mr. Christison alleges that his wife died due to Defendants' drug Tysabri. Mr. Christison's complaint includes three causes of action: (1) negligence; (2) negligent failure to

[3] Fed. R. Civ. P. 56(a).

[4] *Adler v. Wal-Mart Stores, Inc.*, 144 F.3d 664, 670 (10th Cir. 1998).

[5] *Id.*

warn; and (3) negligent misrepresentation.[6] The elements of each of these causes of action are listed below.

In overview, the facts Mr. Christison alleges to support his three claims are that the Companies had a duty to ensure that the product they provided was safe and that they had a duty to warn consumers of reasonably foreseeable dangers, but that they acted negligently in not updating the Tysabri label with sufficient information. He says the label should have included warnings about increased risk of developing a brain infection called PML if a patient had previously tested positive for JC Virus antibodies, had used immunosuppressant drugs in the past, or had taken Tysabri for an extended duration. By 2012, each of those factors was listed on the Tysabri label, but none of them were listed on the label when Mrs. Christison was taking Tysabri. Mr. Christison also alleges that the Companies should have performed research more expeditiously and commercialized the results of their anti-JCV antibody assay[7] sooner.

**Elements of Negligence**

To prevail on a negligence claim in a pharmaceutical drug case in Utah, a plaintiff must prove: "(1) that the defendant owed the plaintiff a duty, (2) that the defendant breached that duty, (3) that the breach of duty was the proximate cause of the plaintiff's injury, and (4) that the plaintiff in fact suffered injuries or damages."[8]

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[6] First Amended Complaint ¶¶ 58-71, 72-82, and 83-90, docket no. 96, filed Jan. 2, 2014.

[7] The term "anti-JCV antibody assay" is not specifically defined in the briefing, but it is defined in one of the exhibits as "a qualitative test used to detect the presence of antibodies to the JC Virus in human serum or plasma. The assay is intended for use by physicians, in conjunction with other clinical data, . . . as an aid in risk stratification for progressive multifocal encephalopathy." Record of Meeting at 3, Dept. of Health and Human Svcs., Food and Drug Administration (Nov. 18, 2010), Ex. B to Affidavit of Michael Poirier, docket no. 167-12, filed Dec. 11, 2015.

[8] *Tingey v. Radionics*, No. 04-4216, 193 F. App'x 747, 759, 2006 WL 2258872 (10th Cir. Aug. 8, 2006) (unpublished) (quoting *Webb v. Univ. of Utah*, 2005 UT 80, ¶ 9, 125 P.3d 906 (Utah 2005)).

The learned intermediary doctrine has been adopted in Utah.[9] This means that "manufacturers of prescription drugs have a duty to warn only the physician prescribing the drug, not the end user or patient."[10] The contours of this duty include making "timely and adequate warnings to the medical profession of any dangerous side effects produced by its drug of which it knows or has reason to know."[11] "The physician, after having received complete and appropriate warnings from the drug manufacturer, acts as a learned intermediary between the drug manufacturer and the patient when preparing the drug prescription."[12] This is because the physician is in the best position "to combine medical knowledge and training with an individualized understanding of the patient's needs[.]"[13] Thus, under Utah law, a drug manufacturer's duty is to give timely, adequate, complete, and appropriate warnings to the prescribing physician such that the physician can understand possible side effects and prepare a suitable prescription program for a patient.

**Elements of Negligent Failure to Warn**

In Utah, a negligent failure to warn claim consists of the following elements: (1) the defendant failed to exercise reasonable care by failing to provide an adequate warning; (2) the lack of an adequate warning made the product defective and unreasonably dangerous; and (3) the lack of an adequate warning was a cause of plaintiff's injuries.[14] As with a negligence claim, the learned intermediary doctrine applies. Therefore, a drug manufacturer's duty is to provide an adequate warning to the prescribing physician, not to the patient.

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[9] *Schaerrer v. Stewart's Plaza Pharmacy, Inc.*, 2003 UT 43, 79 P.3d 922 (Utah 2003).

[10] *Id.* ¶ 20 (citation omitted).

[11] *Id.* (citing *Barson v. E.R. Squibb & Sons*, 682 P.2d 832, 835 (Utah 1984)).

[12] *Schaerrer*, 2003 UT 43, ¶ 20 (emphasis in original).

[13] *Id.*

[14] Model Utah Jury Instructions CV1018 (2d ed. Aug. 15, 2014), http://www.utcourts.gov/resources/muji/; *See House v. Armour of America, Inc.*, 929 P.2d 340, 344 (Utah 1996).

**Elements of Negligent Misrepresentation**

"Utah long ago acknowledged the tort of negligent misrepresentation, which provides that a party injured by reasonable reliance upon a second party's careless or negligent misrepresentation of a material fact may recover damages resulting from that injury when the second party had a pecuniary interest in the transaction, was in a superior position to know the material facts, and should have reasonably foreseen that the injured party was likely to rely upon the fact."[15] "Privity of contract is not a necessary prerequisite to liability."[16]

## UNDISPUTED MATERIAL FACTS[17]

### Tysabri Background and FDA Approval

1. Biogen and Elan are drug companies that collaborated on aspects of the research, development and commercialization of Tysabri (natalizumab). Biogen manufactured Tysabri, held the FDA license, had regulatory responsibility for Tysabri in the United States, and was principally responsible for marketing Tysabri for multiple sclerosis ("MS") in the United States. Elan distributed Tysabri in the United States and also had principal responsibility for the marketing of Tysabri for Crohn's disease, another approved indication for the drug. Elan was also the license holder for Tysabri in Europe.[18]

[15] *Price-Orem Inv. Co. v. Rollins, Brown & Gunnell, Inc.*, 713 P.2d 55, 59 (Utah 1986).

[16] *Id.*

[17] These facts are drawn from the Motion, the Opposition, and Reply Brief in Support of Defendants' Joint Motion for Summary Judgment and Joint Motion in Limine to Preclude Certain Expert Testimony of Eugene O. Major, Ph.D. ("Reply"), docket no. 179, filed Feb. 16, 2016.

[18] Motion at 11, ¶ 1 (citing Antegren Development and Marketing Collaboration Agreement Between Biogen, Inc. and Elan Pharma International Limited (August 15, 2000), Ex. 44 to Motion, docket no. 168-1, filed Dec. 11, 2015; FDA Approval Letter for Tysabri (November 23, 2004 ) ("2004 Approval Letter"), Ex. 55 to Motion, docket no. 168-12, filed Dec. 11, 2015). Mr. Christison "does not dispute the content of #1." Opposition at 8-9, ¶ 1.

2. Tysabri is a recombinant, humanized, monoclonal antibody that inhibits the trafficking of inflammatory white blood cells into the central nervous system ("CNS"), and thereby protects the myelin from attack and resulting nerve cell damage.[19]

3. Data from the Tysabri clinical trials demonstrated a 67% reduction in annual MS relapses, a 42% reduction in disability progression, and an 83% reduction in new lesions (as seen on MRI) in those taking Tysabri versus those on placebo. Tysabri continues to be highly efficacious in treating MS and remains an important treatment option prescribed by specialists for thousands of patients worldwide.[20]

4. FDA first approved Tysabri in November 2004 for treatment of relapsing forms of MS.[21]

**The Companies Voluntarily Withdraw Tysabri from the Market After PML Discoveries**

5. In February 2005, Defendants received reports that two patients in ongoing clinical trials of Tysabri developed progressive multifocal leukoencephalopathy ("PML"). These

[19] Motion at 12, ¶ 2 (citing 2006 Tysabri label ("2006 Tysabri Label") at 1, Ex. 1 to Motion, docket no. 167-1, filed Dec. 11, 2015; DeWitt Expert Report ("Dewitt Expert Report") at 6, Ex. 14 to Motion, docket no. 167-14, filed Dec. 11, 2015; Rudick R, Sandrock A. Natalizumab: α4-integrin antagonist selective adhesion molecule inhibitors for MS. Expert Rev. Neurotherapeutics 2004 4(4) at 571-580, Ex. 26 to Motion, docket no. 167-26, filed Dec. 1, 2015). Undisputed by Mr. Christison. Opposition at 9, ¶ 2.

[20] Motion at 12, ¶ 3 (citing 2006 Tysabri Label at 4; 2015 Tysabri Label ("2015 Tysabri Label") at 5, Ex. 6 to Motion, docket no. 167-6, filed Dec. 11, 2015; Jones Expert Report ("Jones Expert Report") at 29, Ex. 13 to Motion, docket no. 167-13, filed Dec. 11, 2015; DeWitt Expert Report at 6; Deposition of Dr. Foley ("Foley Dep. Tr.") 148:11-149:20, Ex. 7 to Motion, docket no. 167-7, filed Dec. 11, 2015; Polman C, O'Connor P, Havrdova, E, Hutchinson, M, et al. A Randomized, Placebo-Controlled Trial of Natalizumab for Relapsing Multiple Sclerosis, N. Engl. J. Med. 2006 March 354:9: 899-910, Ex. 23 to Motion, docket no. 167-23, filed Dec. 11, 2015). Mr. Christison argues that Tysabri does not reduce relapses and nerve damage in "every patient," Opposition at 9, ¶ 3, but that is not what this fact states. Therefore, there is no genuine dispute about this fact.

[21] Motion at 12, ¶ 4 (citing 2004 Approval Letter; Jones Expert Report at 29; DeWitt Expert Report at 6). Undisputed by Mr. Christison. Opposition at 9, ¶ 4.

patients were treated with Tysabri in combination with Avonex (another MS medication) for a median of 120 weeks.[22]

6. PML had never been associated with MS, Avonex, or Tysabri prior to February 2005. PML was typically associated with AIDS and organ transplant patients.[23]

7. PML is a rare viral brain infection that is caused by the JC virus.[24]

8. The JC virus is usually harmless, ubiquitous, and is carried by the majority of adults.[25]

9. During the period in which Dr. Foley prescribed Tysabri to Mrs. Christison, some in the scientific community believed that upwards of 80% of adults had been exposed to the JC virus.[26]

10. On February 28, 2005, after learning of the two confirmed cases of PML associated with Tysabri use, Biogen voluntarily withdrew Tysabri from the market, suspended its use in clinical trials, and began a review of the data to evaluate the PML risk and research

[22] Motion at 12, ¶ 6 (citing February 28, 2005 FDA News Release ("2005 FDA News Release"), Ex. 40 to Motion, docket no. 167-39, filed Dec. 11, 2015; 2006 Tysabri Label at 7; Jones Expert Report at 31; DeWitt Expert Report at 6). Undisputed by Mr. Christison. Opposition at 9, ¶ 6.

[23] Motion at 13, ¶ 7 (citing Berger Expert Report ("Berger Expert Report") at 2, Ex. 16 to Motion, docket no. 167-16, filed Dec. 11, 2015; Jones Expert Report at 28). Undisputed by Mr. Christison. Opposition at 9, ¶ 7.

[24] Motion at 13, ¶ 8 (citing 2006 Tysabri Label at 7; Berger Expert Report at 2; DeWitt Expert Report at 6). Undisputed by Mr. Christison. Opposition at 9, ¶ 8.

[25] Motion at 13, ¶ 9 (citing Berger Expert Report at 2; Eugene O. Major, Human Polyomavirus, in Fields Virology 2175, 2176 (Knipe et al. eds., 4th ed. 2001) ("Major, Human Polyomavirus"), Ex. 21 to Motion, docket no. 167-21, filed Dec. 11, 2015; Deposition of Eugene Major, Ph.D. ("Major Dep. Tr.") 377:19- 378:6, 493:22-494:25, Ex. 9 to Motion, docket no. 167-9, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 9, ¶ 9.

[26] Motion at 13, ¶ 10 (citing DeWitt Expert Report at 11; Major, Human Polyomavirus at 2175, 2176; Stolt A, Sasnauskas K, Koskela P, Lehtinen M, Dillner J. Seroepidemiology of the human polyomaviruses. J Gen Virol 2003 June; 84(Pt 6):1499-504 ("Stolt et al."), Ex. 27 to Motion, docket no. 167-27, filed Dec. 11, 2015; Rollison DE, Helzlsouer KJ, Alberg AJ, Hoffman S, Hou J, Daniel R et al. Serum antibodies to JC virus, BK virus, simian virus 40, and the risk of incident adult astrocytic brain tumors. Cancer Epidemiol Biomarkers Prev 2003 May;12(5):460-3 ("Rollison et al."), Ex. 24 to Motion, docket no. 167-24, filed Dec. 11, 2015; Stuve O, Marra CM, Cravens PD, Singh MP, Hu W, Lovett-Racke A et al. Potential risk of progressive multifocal leukoencephalopathy with natalizumab therapy: possible interventions. Arch Neurol 2007 February;64(2):169-76 ("Stuve et al."), Ex. 28 to Motion, docket no. 167-28, filed Dec. 11, 2015; Foley Dep. Tr. 201:5-202:17; Deposition of DeWitt ("DeWitt Dep. Tr.") 96:19-100:13, Ex. 8 to Motion, docket no. 167-8, filed Dec. 11, 2015; Major. Dep. Tr. 377:19-378:6, 493:22-494:25). The portions included in this fact are undisputed by Mr. Christison. Opposition at 9-10, ¶ 10.

whether there was any way to stratify the PML risk (*i.e.*, identity individual risk factors for PML that physicians could use in make prescribing decision and counseling patients).[27]

11. There are no known treatments or cures for PML.[28]

12. After Biogen's voluntary withdrawal of Tysabri, Biogen and Elan worked with experts on PML and MS to analyze the PML cases and to better understand and quantify the risk.[29]

13. In April 2005, Biogen announced its safety evaluation of Tysabri had led to the discovery of a third case of PML in a patient from a clinical trial in Belgium for the use of Tysabri in Crohn's Disease. This Crohn's disease patient was treated with Tysabri for eight months and had a history of immunosuppressant drug use. He had originally been misdiagnosed with a brain tumor.[30]

[27] Motion at 13, ¶ 11 (citing February 28, 2005 Dear Healthcare Professional Letter, Ex. 46 to Motion, docket no. 168-3, filed Dec. 11, 2015; 2005 FDA News Release; March 1, 2005 FDA Public Health Advisory, Ex. 41 to Motion, docket no. 167-40, filed Dec. 11, 2015; Jones Expert Report at 31). Undisputed by Mr. Christison. Opposition at 10, ¶ 11.

[28] Motion at 13-14, ¶ 12 (citing 2006 Tysabri Label at 7; December 11, 2009 Talking Points and FAQ on PML, Ex. 54 to Motion, docket no. 168-11, filed Dec. 11, 2015; DeWitt Expert Report at 6; DeWitt Dep. Tr. 66:11-69:6). Undisputed by Mr. Christison. Opposition at 10, ¶ 12.

[29] Motion at 14, ¶ 13 (citing Key Take-aways from March 4 PML Expert Panel Meeting ("Key Take-aways"), Ex. 45 to Motion, docket no. 168-2, filed Dec. 11, 2015; March 4, 2005 "TYSABRI Safety Update" at 217-220, Ex. 47 to Motion, docket no. 168-4, filed Dec. 11, 2015; March 7 & 8, 2006 Peripheral and Central Nervous System Drugs Advisory Committee Meeting Minutes ("March 2006 Advisory Committee Minutes"), Ex. 59 to Motion, docket no. 168-22, filed Dec. 11, 2015; Jones Expert Report at 31). Undisputed by Mr. Christison. Opposition at 10, ¶ 13.

[30] Motion at 14, ¶ 14 (citing April 2005 Dear Healthcare Professional Letter, Ex. 48 to Motion, docket no.168-5, filed Dec. 11, 2015; 2006 Tysabri Label at 7; Jones Expert Report at 31). Undisputed by Mr. Christison. Opposition at 10, ¶ 14.

**Tysabri Is Reapproved with a Black Box Warning and an FDA Mandated Risk Evaluation and Management Strategy ("REMS") Program**

14. On March 7 and 8, 2006, an FDA Advisory Panel convened to consider Biogen's proposal to permit Tysabri back on the market for treatment of relapsing forms of MS with new labeling concerning the PML risk.[31]

15. The FDA Advisory Panel recommended FDA re-approve Tysabri after the Advisory Panel reviewed the benefit and risk data, and held a public hearing at which the Advisory Panel heard testimony from MS specialists, patient advocacy groups, and patients who had been treated with Tysabri in clinical trials that Tysabri should be re-approved and returned to the market.[32]

16. On June 5, 2006, FDA reapproved Tysabri's return to the market as a monotherapy for relapsing forms of MS, subject to a number of new conditions and requirements concerning the PML risk.[33]

17. As a condition of Tysabri's re-approval, FDA required that the prescribing information include a "black box" warning informing prescribers that Tysabri use increases the risk of PML along with other warnings concerning the PML risk.[34]

18. A black box warning is a warning printed inside a black box on the first page of drug labeling.[35]

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[31] Motion at 14, ¶ 15 (citing February 16, 2006, Meeting Materials for Peripheral and Central Nervous System Drugs Advisory Committee, Ex. 57 to Motion, docket no. 168-14 to docket no. 168-20, filed Dec. 11, 2015; March 2006 Advisory Committee Minutes; Jones Expert Report at 36). Undisputed by Mr. Christison. Opposition at 10, ¶ 15.

[32] Motion at 14-15, ¶ 16 (citing March 2006 Advisory Committee Minutes; Jones Expert Report at 34-37). Undisputed by Mr. Christison. Opposition at 10, ¶ 16.

[33] Motion at 15, ¶ 17 (citing June 5, 2006 Letter from Russell Katz, M.D., of FDA to Nadine D. Cohen, Biogen ("2006 Re-approval Letter"), Ex. 62 to Motion, docket no. 168-25, filed Dec. 11, 2015; Jones Expert Report at 37). Undisputed by Mr. Christison. Opposition at 10, ¶ 17.

[34] Motion at 15, ¶ 18 (citing 2006 Tysabri Label at 1; 2006 Re-approval Letter). Undisputed by Mr. Christison. Opposition at 10, ¶ 18.

19. As stated in FDA's Guidance regarding Content and Format of Labeling:

> A boxed warning is ordinarily used to highlight for prescribers one of the following situations:
>
> • There is an adverse reaction so serious in proportion to the potential benefit from the drug (e.g., a fatal, life-threatening or permanently disabling adverse reaction) that it is essential that it be considered in assessing the risks and benefits of using the drug
>
> OR
>
> • There is a serious adverse reaction that can be prevented or reduced in frequency or severity by appropriate use of the drug (e.g., patient selection, careful monitoring, avoiding certain concomitant therapy, addition of another drug or managing patients in a specific manner, avoiding use in a specific clinical situation)
>
> OR
>
> • FDA approved the drug with restrictions to ensure safe use because FDA concluded that the drug can be safely used only if distribution or use is restricted (e.g., under 21 CFR 314.520 and 601.42 "Approval with restrictions to assure safe use" or under 505-1(f)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) "Risk Evaluation and Mitigation Strategies" Elements to assure safe use).[36]

20. The prescribing information in effect in January 2007 contained a black box warning, the strongest warning required or permitted by FDA, concerning the risk of PML.[37]

21. A "black box" warning, and numerous other warnings throughout the label concerning PML, was included in the drug's labeling throughout the time that Mrs. Christison's physician prescribed Tysabri to treat Mrs. Christison's MS.[38]

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[35] Motion at 15, ¶ 19 (citing 2006 Tysabri Label at 1; Jones Expert Report at 16, 20-21). Undisputed by Mr. Christison. Opposition at 10, ¶ 19.

[36] Motion at 15-16, ¶ 20 (citing October 2011 Guidance for Industry on Warnings and Precautions, Contraindications, and Boxed Warning Sections of Labeling for Human Prescription Drug and Biological Products – Content and Format (by US Department of Health and Human Services), Ex. 10 to Motion, docket no. 167-10, filed Dec. 11, 2015; Jones Expert Report at 16-17; Foley Dep. Tr. 174:22-176:6). Undisputed by Mr. Christison. Opposition at 10, ¶ 20.

[37] Motion at 16, ¶ 21 (citing 2006 Tysabri Label; Jones Expert Report at 16; DeWitt Expert Report at 6-7, 11- 12; 21 C.F.R. § 201.57(c)(1); 44 Fed. Reg. 37434, 37448 (FDA June 26, 1979) ("To ensure the significance of boxed warnings in drug labeling, they are permitted in labeling only when specifically required by FDA.")). Undisputed by Mr. Christison. Opposition at 10, ¶ 21.

22. At the time Mrs. Christison was first prescribed Tysabri in January 2007, the black box warning read as follows (emphasis in original):

> WARNING
>
> TYSABRI® increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. Although the cases of PML were limited to patients with recent or concomitant exposure to immunomodulators or immunosuppressants, there were too few cases to rule out the possibility that PML may occur with TYSABRI® monotherapy.
>
> • Because of the risk of PML, TYSABRI® is available only through a special restricted distribution program called the TOUCH™ Prescribing Program. Under the TOUCH™ Prescribing Program, only prescribers, infusion centers, and pharmacies associated with infusion centers registered with the program are able to prescribe, distribute, or infuse the product. In addition, TYSABRI must be administered only to patients who are enrolled in and meet all the conditions of the TOUCH™ Prescribing Program **(see WARNINGS, Progressive Multifocal Leukoencephalopathy; and WARNINGS, Prescribing, Distribution, and Administration Program for TYSABRI®).**
>
> • Healthcare professionals should monitor patients on TYSABRI® for any new sign or symptom that may be suggestive of PML. TYSABRI® dosing should be withheld immediately at the first sign or symptom suggestive of PML. For diagnosis, an evaluation that includes a gadolinium-enhanced magnetic resonance imaging (MRI) scan of the brain and, when indicated, cerebrospinal fluid analysis for JC viral DNA are recommended **(see CONTRAINDICATIONS and WARNINGS, Progressive Multifocal Leukoencephalopathy).**[39]

23. The FDA also required a "Warnings" section in the Tysabri prescribing information that stated the following regarding the PML risk:

> Progressive multifocal leukoencephalopathy, an opportunistic infection caused by the JC virus that typically occurs in patients that are immunocompromised, has occurred in 3 patients who received TYSABRI® in clinical trials (see BOXED WARNING). Two cases of PML were observed in 1869 patients with multiple sclerosis treated for a median of 120 weeks. The third case occurred among 1043 patients with Crohn's disease after the patient received 8 doses. The absolute risk

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[38] Motion at 16, ¶ 22 (citing DeWitt Expert Report at 6-7, 11-12; Christison TOUCH Forms ("Christison TOUCH Forms"), Ex. 30-31 to Motion, docket no. 167-30, docket no. 167-31, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 10, ¶ 22.

[39] Motion at 16-17, ¶ 23 (citing 2006 Tysabri Label; Jones Expert Report at 16; DeWitt Expert Report at 11-12; Foley Dep. Tr. 174:22-176:6) (bold emphasis in original). Undisputed by Mr. Christison. Opposition at 10, ¶ 23.

> for PML in patients treated with TYSABRI® cannot be precisely estimated, and factors that might increase an individual patient's risk for PML have not been identified. There are no known interventions that can reliably prevent PML or adequately treat PML if it occurs. It is not known whether early detection of PML and discontinuation of TYSABRI® will mitigate the disease. There is limited experience beyond 2 years of treatment. The relationship between the risk of PML and the duration of treatment is unknown.
>
> All three cases of PML occurred in patients who were concomitantly exposed to immunomodulators (interferon beta in the patients with multiple sclerosis) or were immunocompromised due to recent treatment with immunosuppressants (e.g., azathioprine in the patient with Crohn's disease). Ordinarily, therefore, patients receiving chronic immunosuppressant or immunomodulatory therapy or who have systemic medical conditions resulting in significantly compromised immune system function should not be treated with TYSABRI®. However, the number of cases is too few and the number of patients treated too small to reliably conclude that the risk of PML is lower in patients treated with TYSABRI® alone than in patients who are receiving other drugs that decrease immune function or who are otherwise immunocompromised.[40]

24. The prescribing information also contained the following "Indications and Usage" section:

> Because TYSABRI® increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability **(see BOXED WARNING AND WARNINGS, Progressive Multifocal Leukoencephalopathy)**, TYSABRI® is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, alternate multiple sclerosis therapies.[41]

25. As a condition of re-approval, FDA required that a Medication Guide be provided to physicians and specially trained infusion nurses. The substance of the Medication Guide is printed verbatim in the Tysabri label. Further, only TOUCH-certified prescribers could prescribe Tysabri.[42]

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[40] Motion at 17, ¶ 24 (citing 2006 Tysabri Label at 7 (emphasis in original); 2006 Re-approval Letter). Undisputed by Mr. Christison. Opposition at 10, ¶ 24.

[41] Motion at 17-18, ¶ 25 (citing 2006 Tysabri Label at 6 (emphasis in original)). Undisputed by Mr. Christison. Opposition at 10, ¶ 25.

[42] Motion at 18, ¶ 26 (citing 2006 Tysabri Label at 18-23; Jones Expert Report at 46-48; DeWitt Expert Report at 7; Christison TOUCH Forms). Undisputed by Mr. Christison. Opposition at 11, ¶ 26.

26. As part of the TOUCH program, the Tysabri Medication Guide is provided to patients prior to enrolling in the TOUCH program. When Mrs. Christison enrolled in the TOUCH program the Tysabri Medication Guide included the following:

> **What is the most important information I should know about TYSABRI®?**
>
> • **TYSABRI® increases your chance of getting a rare brain infection that usually causes death or severe disability. This infection is called progressive multifocal leukoencephalopathy (PML).** PML usually happens in people with weakened immune systems.
>
> • No one can predict who will get PML.
>
> • There is no known treatment, prevention, or cure for PML.[43]

27. FDA re-approved Tysabri in June 2006 "under the provisions of 21 CFR 601.42 (Subpart E) . . . for use as recommended in the agreed upon labeling text, required patient labeling, and the components of the TOUCH™ Risk Minimization Action Plan (RiskMAP)."[44]

28. Under § 505-1 of the FDA Amendments Act of 2007, the TOUCH RiskMAP became a Risk Evaluation and Mitigation Strategies ("REMS") program.[45]

29. FDA also mandated, as a condition of re-approval, that Tysabri only be prescribed in accordance with a mandatory "Risk Evaluation and Management Strategy," (or "REMS program"), known as the TOUCH Program ("Tysabri Outreach: Unified Commitment to Health"). In its re-approval letter, FDA ordered: "Any change to the [TOUCH] program must be discussed with FDA prior to its institution and is subject to FDA's determination that the required components are still present."[46]

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[43] Motion at 18, ¶ 27 (citing 2006 Tysabri Label at 18-23 (emphasis in original); Jones Expert Report at 48; Christison TOUCH Forms). Undisputed by Mr. Christison. Opposition at 11, ¶ 27.

[44] Motion at 18, ¶ 28 (citing 2006 Re-approval Letter). Undisputed by Mr. Christison. Opposition at 11, ¶ 28.

[45] Motion at 18, ¶ 29 (citing Jones Expert Report at 17-19; 21 U.S.C. § 355-1 (2011)). Undisputed by Mr. Christison. Opposition at 11, ¶ 29.

[46] Motion at 19, ¶ 30 (citing 2006 Re-approval Letter; Jones Expert Report at 17-19). Undisputed by Mr. Christison. Opposition at 11, ¶ 30.

30. In the June 5, 2006, re-approval letter FDA stated that the goals of the TOUCH program were: "to assess the risk of progressive multifocal leukoencephalopathy (PML) associated with Natalizumab (TYSABRI®), minimize the risk of PML, minimize death and disability due to PML, and promote informed risk-benefit decisions regarding TYSABRI® use."[47]

31. The TOUCH program requires that prior to prescribing Tysabri and enrolling the patient in the TOUCH program, physicians acknowledge in writing that they understand the PML risk and must also obtain written acknowledgement from the patient that the patient understands the PML risk.[48]

32. Before each Tysabri infusion, a specially trained infusion nurse is required to confirm that the patient has read the Medication Guide, including warnings concerning the PML risk associated with Tysabri.[49]

33. At every monthly Tysabri infusion, the specially trained infusion nurse must ask the patient a series of questions concerning their patient's understanding of the PML risk and ask about new symptoms that suggest a change in neurological condition that could potentially be an early sign of PML.[50]

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[47] Motion at 19, ¶ 31 (citing 2006 Re-approval Letter; Jones Expert Report at 17-19, 46). Undisputed by Mr. Christison. Opposition at 11, ¶ 31.

[48] Motion at 19, ¶ 32 (citing Christison TOUCH Forms; 2006 Tysabri Label at 1; 2006 Re-approval Letter). Undisputed by Mr. Christison. Opposition at 11, ¶ 32.

[49] Motion at 19, ¶ 33 (citing 2006 Tysabri Label at 7-8; Jones Expert Report at 46-47; DeWitt Expert Report at 7; Christison TOUCH Forms; Foley Dep. Tr. 246:11-249:22). Mr. Christison does not dispute that the infusion nurse "is supposed to confirm" that the patient has read the Medication Guide. Opposition at 11, ¶ 33. Therefore, there is no dispute over this fact.

[50] Motion at 20, ¶ 34 (citing 2006 Tysabri Label at 22; Christison TOUCH Forms; Foley Dep. Tr. 246:11-249:22). Mr. Christison does not dispute that the infusion nurse "must ask the patient a series of questions concerning their patient's understanding of the PML risk and ask about new symptoms that suggest a change in neurological condition that could potentially be an early sign of PML." Opposition at 11-12, ¶ 34. Therefore, there is no dispute over this fact.

34. If any such changes are reported, the infusion cannot be given without further evaluation and approval of the prescribing neurologist.[51]

35. The June 5, 2006 FDA re-approval letter to Biogen stated that "Marketing the product [Tysabri] with FPL [final printed labeling] that is not identical to approved labeling text may render the product misbranded and an unapproved new drug."[52]

36. In evaluating Tysabri prior to its return to the market in 2006, FDA requested that Biogen conduct an assessment for the presence of JCV antibody at baseline for patients entering clinical trials.[53]

37. On March 2, 2006, Biogen submitted to FDA a report on the results of antibody testing conducted at a laboratory at the National Institute of Health ("NIH")—a laboratory led by Plaintiff's expert Eugene Major, Ph.D.—of available serum samples from Tysabri-treated patients who participated in clinical trials. The report concluded "[c]urrently there is no consensus on a clinically relevant cut off for the ELISA assay or JCV antibody detection."[54]

38. Nevertheless, Biogen continued to conduct research into the potential significance of JCV antibody status in risk stratification, eventually developing an analytically and clinically

[51] Motion at 20, ¶ 35 (citing 2006 Tysabri Label; Christison TOUCH Forms; Foley Dep. Tr. 246:11-249:22). Mr. Christison does not dispute that "infusion nurses are not to administer the infusion if any such changes are reported, without further evaluation and approval of the prescribing neurologist." Opposition at 12, ¶ 35. Therefore, there is no dispute over this fact.

[52] Motion at 20, ¶ 36 (citing 2006 Re-approval Letter). The portions included in Fact No. 36 are undisputed by Mr. Christison. Opposition at 12, ¶ 36.

[53] Motion at 20, ¶ 38 (citing November 18, 2005 Letter from Russell Katz, M.D., of FDA to Nadine D. Cohen, Biogen ("Katz Letter"), Ex. 56 to Motion, docket no. 168-13, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 13, ¶ 38.

[54] Motion at 20-21, ¶ 39 (citing Mar. 2, 2006 sBLA Amendment Submission to FDA, at 54, Ex. 58 to Motion, docket no. 168-21, filed Dec. 11, 2015; Key Take-aways; Expert Report of Dr. Raphael Viscidi ("Viscidi Expert Report") at 3-5, 8-9, Ex. 15 to Motion, docket no. 167-15, filed Dec. 11, 2015; Berger Expert Report at 3; Major Dep. Tr. at 358:11 – 360:25). Undisputed by Mr. Christison. Opposition at 13, ¶ 39.

validated JCV antibody assay and supporting data that lead to FDA clearance of the assay and related Tysabri labeling changes in January 2012.[55]

**Annalee Christison's MS and Tysabri Use**

39. Annalee Christison first developed symptoms of MS in 1991, and her MS diagnosis was confirmed in 1998.[56]

40. Mrs. Christison was treated for over ten years by Dr. John Foley at the Rocky Mountain MS Clinic in Salt Lake City.[57]

41. In 1998, she was prescribed Avonex to treat her MS. In 2005, she complained of flu-like symptoms, including significant fatigue, for two days following each weekly Avonex injection.[58]

42. In 2005, while still on Avonex, Mrs. Christison was diagnosed with lesions on her spinal cord. Mrs. Christison began using a cane in this time period. By January 2006, she was suffering from increased slurred speech and increased fatigue along with occasional blurred vision. On January 18, 2006, it was Dr. Foley's medical opinion that Mrs. Christison had "remitting and relapsing multiple sclerosis now with clear-cut spinal cord involvement and progressing through Avonex . . . . At the present time she is failing Avonex therapy. . . . She

[55] Motion at 21, ¶ 40 (citing October 2006 Material Transfer Agreement ("2006 MTA"), Ex. 49 to Motion, docket no. 168-6, filed Dec. 11, 2015; December 12, 2009 Advisory Board Meeting Minutes ("December 2009 Advisory Board Minutes"), Ex. 84 to Motion, docket no. 168-47, filed Dec. 11, 2015; December 9, 2009 US Regulatory and Safety Expert Panel on PML Risk Stratification ("Dec. 9 Panel"), Ex. 53 to Motion, docket no. 168-10, filed Dec. 11, 2015; September 8, 2010, FDA Memorandum of Meeting Minutes ("Sep. 8 Minutes"), Ex. 71 to Motion, docket no. 168-34, filed Dec. 11, 2015; FDA Record of Meeting November 18, 2010 ("FDA Record Nov. 2010"), Ex. 72 to Motion, docket no. 168-35, filed Dec. 11, 2015; January 2012 Tysabri Label ("2012 Tysabri Label"), Ex. 5 to Motion, docket no. 167-5, filed Dec. 11, 2015; January 20, 2012 FDA News Release ("2012 FDA News Release"), Ex. 43 to Motion, docket no. 167-42, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 14, ¶ 40.

[56] Motion at 21, ¶ 41 (citing First Amended Complaint ¶ 49; July 16, 1998 Medical Record ("1998 Med. Rec."), Ex. 32 to Motion, docket no. 167-32, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 14, ¶ 41.

[57] Motion at 21, ¶ 42 (citing Christison Medical Records, Ex. 30-38 to Motion, docket no. 167-30 to docket no. 167-37, filed Dec. 11, 2015, Foley Dep. Tr. 18:19-20:14). Undisputed by Mr. Christison. Opposition at 14, ¶ 42.

[58] Motion at 21, ¶ 43 (citing 1998 Med. Rec.; 2004, 2005, 2006 Medical Records ("2004, 2005, 2006 Medical Records"), Ex. 33 to Motion, docket no. 167-33, filed Dec. 11, 2015; Foley Dep. Tr. 143:19-144:8). Undisputed by Mr. Christison. Opposition at 14, ¶ 43.

likely will need therapy with the new monoclonal antibody Tysabri when it is available, hopefully in April. . . . At the present time I feel that she is currently disabled."[59]

43. Prior to prescribing Tysabri, Dr. Foley concluded that Mrs. Christison had failed interferon treatment, that non-treatment was not an option for Mrs. Christison, and that the other drugs available were not appropriate options because one drug, mitoxantrone, carried a significant risk of leukemia and congestive heart failure that was greater than the small PML risk associated with Tysabri, and another, Copaxone, was weaker than Avonex and the other interferons and inappropriate for Mrs. Christison's lesions.[60]

44. Dr. Foley concluded that Mrs. Christison would be wheelchair-bound or bedridden if they could not get Mrs. Christison's MS under control. Tysabri was prescribed to mitigate her disability progression.[61]

45. Prior to prescribing Tysabri for Mrs. Christison, Dr. Foley reviewed and was familiar with the prescribing information for Tysabri that was in effect at the time, including the warnings concerning PML.[62]

46. Dr. Foley was an experienced TOUCH prescriber who was aware that Tysabri increased the risk of PML at the time he prescribed the drug to Mrs. Christison.[63]

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[59] Motion at 21-22, ¶ 45 (citing 2004, 2005, 2006 Medical Records, Foley Dep. Tr. 225:8-231:10). The portions included in this fact are undisputed by Mr. Christison. Opposition at 14, ¶ 45.

[60] Motion at 22, ¶ 46 (citing Foley Dep. Tr. 151:22-152:3, 187:10-188:25). Undisputed by Mr. Christison. Opposition at 14, ¶ 46.

[61] Motion at 22, ¶ 47 (citing Foley Dep. Tr. 230:25-231:10). Undisputed by Mr. Christison. Opposition at 14, ¶ 47.

[62] Motion at 22, ¶ 48 (citing Foley Dep. Tr. 171:9-25; Christison TOUCH Forms). Undisputed by Mr. Christison. Opposition at 14, ¶ 48.

[63] Motion at 22, ¶ 49 (citing Foley Dep. Tr. 171:9-25; Christison TOUCH Forms). Undisputed by Mr. Christison. Opposition at 15, ¶ 49.

47. In accordance with the TOUCH program requirements, on January 11, 2007, Mrs. Christison signed and initialed a TOUCH enrollment form which included the following statement:

> **I acknowledge that:**
>
> **…**
>
> **TYSABRI increases your chance of getting a rare brain infection that usually causes death or severe disability.**
>
> • This infection is called progressive multifocal leukoencephalopathy (PML). PML usually happens in people with weakened immune systems
>
> • No one can predict who will get PML. There is no known treatment, prevention, or cure for PML
>
> • My chance for getting PML may be higher if I am also being treated with other medicines that can weaken my immune system, including other MS treatments
>
> • Even if I use TYSABRI alone to treat my MS, it is not known if my chance for getting PML will be lower. It is also not known if treatment for a long period of time with TYSABRI can increase my chance for PML
>
> • I should call my doctor right away if I get any new or worsening symptoms that last several days especially nervous system symptoms. Some of these symptoms include a new or sudden change in my thinking, eyesight, balance, or strength, but I should also report other new or worsening symptoms[64]

48. Dr. Foley specifically communicated with his patients about the risk of PML associated with Tysabri use. Dr. Foley testified that, while he did not specifically recall his discussion with Mrs. Christison, it was his practice to sit down with each of his patients and discuss the TOUCH enrollment form and PML warnings, and ask the patient if she understood or if she had any questions concerning the PML risk. Dr. Foley's office also had an additional

[64] Motion at 23, ¶ 50 (citing Christison TOUCH Forms; Jones Expert Report at 48; Foley Dep. Tr. 167:10-171:25). Undisputed by Mr. Christison. Opposition at 15, ¶ 50.

informed consent regarding the PML risk that Mrs. Christison had to sign prior to beginning Tysabri.[65]

49. On January 11, 2007, Mrs. Christison signed an "Acknowledgment and Consent to Medical Care" that was prepared by Dr. Foley's office regarding the risk of PML associated with Tysabri use. Mr. Christison also signed the form as a witness. Mrs. Christison acknowledged:

> • "I understand that the effects of using Tysabri are not known, but may involve significant risks and complications including, but not limited to, death, PML, infection, hypersensitivity reactions including systemic reactions, and reduction in fertility. No guarantees have been made to me concerning the results of the use of Tysabri and infusion therapy, nor are there any guarantees against unfavorable results."
>
> • "I accept the risk of substantial and significant harm, including death, in hopes of obtaining treatment for MS, a serious and disabling neurologic disease."
>
> • "I understand the risks and benefits of Tysabri treatment, including that the drug increases the risk of getting PML."
>
> • "I have read and understand the Tysabri Medication Guide, which is incorporated herein, and agree that I will read it again before each Tysabri infusion."[66]

50. Mrs. Christison received her first Tysabri infusion in February 2007 and thereafter received a total of 29 monthly infusions through June 2009.[67]

51. In accordance with the TOUCH program requirements, Mrs. Christison acknowledged to a specially trained infusion nurse that she had received the Tysabri Medication

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[65] Motion at 23-24, ¶ 51 (citing Foley Dep. Tr. 161:10-166:1; January 11, 2007 Medical Records, Ex. 35 to Motion, docket no. 167-35, filed Dec. 11, 2015; Acknowledgment and Consent to Medical Care ("Consent Form"), Ex. 34 to Motion, docket no. 167-34, filed Dec. 11, 2015; Christison TOUCH Forms). Undisputed by Mr. Christison. Opposition at 15, ¶ 51.

[66] Motion at 24, ¶ 52 (citing Consent Form; Foley Dep. Tr. 162:11-167:9). Undisputed by Mr. Christison. Opposition at 15, ¶ 52.

[67] Motion at 24, ¶ 53 (citing Christison TOUCH Forms; First Amended Complaint ¶¶ 50-51). Undisputed by Mr. Christison. Opposition at 15, ¶ 53.

Guide concerning the PML risk at each of her 29 monthly Tysabri infusions through June 2009.[68]

52. In October 2008, Mrs. Christison was examined for possible PML. It was determined that Mrs. Christison did not have PML, but instead her MS had relapsed.[69]

53. In January 2009, Dr. Foley discussed the new cases of PML with Mrs. Christison and reevaluated the risk-benefit profile. Mrs. Christison wished to continue Tysabri therapy. At that time, there had been four additional confirmed cases of Tysabri associated PML in the postmarketing setting.[70]

54. Mrs. Christison had her final Tysabri infusion in June 2009. She was diagnosed with PML in July 2009 and she died on August 26, 2009.[71]

55. Mr. and Mrs. Christison discussed the risks and benefits of Tysabri before Mrs. Christison initiated Tysabri therapy.[72]

56. Mr. and Mrs. Christison made a decision together that she would transition from Avonex to Tysabri.[73]

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[68] Motion at 24, ¶ 54 (citing Christison TOUCH Forms; DeWitt Expert Report at 7; Foley Dep. Tr. 158:3-159:6). Undisputed by Mr. Christison. Opposition at 15, ¶ 54.

[69] Motion at 25, ¶ 55 (citing October 31, 2008 Medical Record, Ex. 36 to Motion, docket no. 167-36, filed Dec. 11, 2015; November 5, 2008 Medical Record, Ex. 37 to Motion, docket no. 167-37, filed Dec. 11, 2015; Foley Dep. Tr. 194:9-197:6, 217:21-226:6). The portions included in this fact are undisputed by Mr. Christison. Opposition at 16, ¶ 55.

[70] Motion at 25, ¶ 56 (citing DeWitt Expert Report at 12; PML Confirmation Date Chart through November 17, 2009 ("PML Confirmation Chart"), Ex. 51 to Motion, docket no. 168-8, filed Dec. 11, 2015; Foley Dep. Tr. 191:9-194:7). Undisputed by Mr. Christison. Opposition at 16, ¶ 56.

[71] Motion at 25, ¶ 57 (citing First Amended Complaint ¶¶ 50-54; Christison TOUCH Forms; Foley Dep. Tr. 52:16-25). Undisputed by Mr. Christison. Opposition at 16, ¶ 57.

[72] Opposition at 32, ¶ 118 (citing Deposition of Kenneth Christison ("Christison Dep. Tr.") 43:16-21, Ex. 4 to Opposition, docket no. 175-4, filed Jan. 22, 2016). Undisputed by Companies. Defendants' Response to Plaintiff's Additional Material Facts ("Response to Facts") at 2, Ex. A to Reply, docket no. 179-1, filed Feb. 16, 2016.

[73] Opposition at 32, ¶ 119 (citing Christison Dep. Tr. 123:19-24). Undisputed by Companies. Response to Facts at 2.

57. The ultimate decision about whether to stay on Tysabri belongs to the patient, not the prescriber.[74]

58. If Dr. Foley had recommended that Mrs. Christison stay on Tysabri despite its risks, but Mrs. Christison decided she wanted to discontinue, Dr. Foley would not have prescribed Tysabri to Mrs. Christison.[75]

59. Dr. Foley testified that sometimes his patients' families contribute to the ultimate decision of whether to stay on Tysabri.[76]

60. Dr. Foley understood at the time he prescribed Tysabri for Mrs. Christison that PML was caused by JCV infection.[77]

61. It is common scientific knowledge that antibodies can be evidence of prior exposure to any pathogen, including the JC virus.[78]

62. Dr. Foley knew a positive test for JCV antibodies was indicative of prior JCV exposure when he prescribed Tysabri for Mrs. Christison.[79]

63. The mere presence of antibodies does not mean that a person is currently infected with the pathogen, only that at some point in the past the person's immune system was activated by the presence of the foreign body and produced antibodies.[80]

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[74] Opposition at 32-33, ¶ 121 (citing Foley Dep. Tr. 93:5-21). Undisputed by Companies. Response to Facts at 3.

[75] Opposition at 33, ¶ 122 (citing Foley Dep. Tr. 93:5-21). Undisputed by Companies. Response to Facts at 3.

[76] Opposition at 33, ¶ 123 (citing Foley Dep. Tr. 156:15-18). Undisputed by Companies. Response to Facts at 3.

[77] Motion at 26, ¶ 60 (citing Foley Dep. Tr. 198:4-199:16, 200:11-202:3, 205:16-206:14). Undisputed by Mr. Christison. Opposition at 18, ¶ 60.

[78] Motion at 26, ¶ 61 (citing Foley Dep. Tr. 200:11-202:17; Major Dep. Tr. 493:1-12). Undisputed by Mr. Christison. Opposition at 18, ¶ 61.

[79] Motion at 26, ¶ 62 (citing Foley Dep. Tr. 200:11-202:3, 205:16-206:14). Undisputed by Mr. Christison. Opposition at 18, ¶ 62.

[80] Motion at 26, ¶ 63 (citing Foley Dep. Tr. 94:21-95:12; DeWitt Dep. Tr. 124:22-125:1, 166:21-169:13; Major Dep. Tr. 400:17-403:21). Undisputed by Mr. Christison. Opposition at 18, ¶ 63.

64. At the time of the first Tysabri-associated PML cases, it was possible that the presence of JCV antibodies would be found to be protective and thus an indicator of decreased PML risk.[81]

65. When Tysabri was reapproved in June 2006, there was no statistically significant data from which to determine whether the presence of an antibody would assist in assessing whether someone is at a higher or lower risk of getting PML.[82]

66. A person could develop PML as a result of a primary infection (i.e., first exposure to JCV) at a time when the immune system was being modulated by Tysabri treatment.[83]

67. Although a positive finding on a JCV antibody assay would indicate a necessary prerequisite to JCV infection, without data, a negative finding could not be used as evidence of decreased PML risk.[84]

68. Dr. Foley believed that Tysabri's label adequately warned him of the risk of PML at the time he prescribed the drug to Mrs. Christison and that, based on the information known at the time, it was the appropriate medical judgment to prescribe Tysabri to Mrs. Christison.[85]

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[81] Motion at 26, ¶ 64 (citing Foley Dep. Tr. 94:21-95:12, 210:6-21; DeWitt Dep. Tr. 153:1-154:22; Major Dep. Tr. 584:24-586:11). Undisputed by Mr. Christison. Opposition at 18, ¶ 64.

[82] Motion at 26, ¶ 65 (citing Viscidi Expert Report at 5-6; Berger Expert Report at 4; DeWitt Expert Report at 8; Major Dep. Tr. 411:16-416:5, 418:20-420:8, 555:11-561:12; Foley Dep. Tr. 93:22-95:25, 200:18-202:17, 205:16-210:21, 281:17-284:16; DeWitt Dep. Tr. 122:24-124:1, 166:21-169:13). The Companies initially presented this fact to state that there was "no data" from which to determine a correlation. Mr. Christison argues that it is incorrect to state there was "no data" because there were two confirmed cases of PML in 2006. Opposition at 18, ¶ 65. Mr. Christison is correct, but the citations to the record indicate that two cases did not establish a "statistically significant" number from which to draw reliable conclusions. Thus, this fact reflects that there was "no statistically significant data," which is a fact that cannot be genuinely disputed after reviewing the citations to the record.

[83] Motion at 27, ¶ 66 (citing Viscidi Expert Report at 6; Major Dep. Tr. 581:22-582:17). Undisputed by Mr. Christison. Opposition at 18, ¶ 66.

[84] Motion at 27, ¶ 67 (citing Berger Expert Report at 2; Viscidi Expert Report, at 6; DeWitt Dep. Tr. 122:24-124:1; Major Dep. Tr. 412:9-416:5, 555:25-557:2). Undisputed by Mr. Christison. Opposition at 18, ¶ 67.

[85] Motion at 27, ¶ 68 (citing Foley Dep. Tr. 196:20-198:13). Undisputed by Mr. Christison that Dr. Foley testified to this. Opposition at 18, ¶ 68.

69. Defendants' expert, Dr. Dana DeWitt, a clinical neurologist and professor of neurology at the University of Utah, opined that the Tysabri label was adequate to inform a treating neurologist of the increased PML risk associated with Tysabri use through the time Dr. Foley prescribed the drug for Mrs. Christison.[86]

**The Post-Marketing Period**

70. After Tysabri's re-approval in June 2006, there were no new confirmed cases of PML associated with Tysabri use for the remainder of 2006, 2007, and the first half of 2008.[87]

71. At the time Tysabri was returned to the market in June 2006, Defendants and FDA considered that the PML risk might be associated with duration of treatment, with the risk increasing with longer treatment duration, but there was insufficient data to support any conclusion. FDA ordered that the Tysabri label in effect when Dr. Foley first prescribed Tysabri for Mrs. Christison expressly warn that "the relationship between the risk of PML and the duration of treatment is unknown."[88]

72. As of June 2006, the two Tysabri-associated PML cases in MS patients occurred after a median of 120 weeks of treatment, while the third case in the Crohn's disease patient occurred after eight doses (32 weeks). This information was expressly stated in the Tysabri label.[89]

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[86] Motion at 27, ¶ 69 (citing DeWitt Expert Report at 2-3, 11-12). Undisputed by Mr. Christison. Opposition at 19, ¶ 69.

[87] Motion at 27, ¶ 70 (citing Safety Review Committee Meeting Minutes August 4, 2008 ("2008 Safety Minutes"), Ex. 81 to Motion, docket no. 168-44, filed Dec. 11, 2015). The portions included in this fact are undisputed by Mr. Christison. Opposition at 19, ¶ 70.

[88] Motion at 27-28, ¶ 71 (citing 2006 Tysabri Label at 7; November 18, Katz Letter; April 3, 2006 Email from Katherine Needleman, FDA to Paula Sandler, Biogen, Ex. 60 to Motion, docket no. 168-23, filed Dec. 11, 2015; April 26, 2006 Email from Katherine Needleman, FDA to Paula Sandler, Biogen, Ex. 61 to Motion, docket no. 168-24, filed Dec. 11, 2015; 2008 Safety Minutes). Undisputed by Mr. Christison. Opposition at 19, ¶ 71.

[89] Motion at 28, ¶ 72 (citing 2006 Tysabri Label at 7). Undisputed by Mr. Christison. Opposition at 19, ¶ 72.

73. In July 2008, the first two Tysabri-associated PML cases after the reintroduction of Tysabri were confirmed.[90]

74. After evaluating the two additional Tysabri-associated PML cases in July 2008, Biogen requested that FDA update the label to reflect the treatment duration in those cases. In August 2008, FDA approved a Tysabri labeling change stating that Tysabri-associated PML can occur in cases of Tysabri monotherapy and further updated the label to state: "There is limited experience beyond two years of treatment. The relationship between the risk of PML and the duration of treatment is unknown, but most cases of PML were in patients who received more than one year of treatment."[91]

75. By the end of 2008, two additional cases of Tysabri-associated PML were confirmed following the two Tysabri-associated PML cases reported in July 2008 (total of four confirmed Tysabri-associated PML cases in 2008).[92]

76. Mrs. Christison's final Tysabri infusion was in June 2009.[93]

77. On July 24, 2009, Mrs. Christison became the eleventh confirmed case of Tysabri-associated PML in the post-marketing setting.[94]

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[90] Motion at 28, ¶ 73 (citing 2008 Safety Minutes; August 1, 2008 Agency Telephone Contact Report ("2008 Teleconference Minutes"); Ex. 63 to Motion, docket no. 168-26, filed Dec. 11, 2015; August 2008 FDA Information for Healthcare Professionals – Natalizumab Injection for Intravenous Use, *available at* http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm126592.htm (last visited November 18, 2015), Ex. 86 to Motion, docket no. 168-49, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 19, ¶ 73.

[91] Motion at 28, ¶ 74 (citing August 2008 Tysabri label ("2008 Tysabri Label"), Ex. 2 to Motion, docket no. 167-2, filed Dec. 11, 2015; 2008 Teleconference Minutes; August 25, 2008 FDA Approval Letter, Ex. 64 to Motion, docket no. 168-27, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 19, ¶ 74.

[92] Motion at 29, ¶ 75 (citing Safety Minutes April 24, 2009, Ex. 82 to Motion, docket no. 168-45, filed Dec. 11, 2015; PML Confirmation Chart). Undisputed by Mr. Christison. Opposition at 19, ¶ 75.

[93] Motion at 29, ¶ 76 (citing Christison TOUCH Forms; DeWitt Expert Report at 2-3, 8-9, 11). Undisputed by Mr. Christison. Opposition at 19, ¶ 76.

[94] Motion at 29, ¶ 77 (citing DeWitt Expert Report at 8; August 5, 2009 Letter from Nadine D. Cohen, Biogen to Russell Katz, M.D., FDA, Ex. 65 to Motion, docket no. 168-28, filed Dec. 11, 2015; PML Confirmation Chart; June 2009 Tysabri Update, Ex. 50 to Motion, docket no. 168-7, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 19, ¶ 77.

78. In October 2009, Biogen had eight pre-PML blood samples from Tysabri patients who later developed PML available for testing and research, including testing for JCV antibodies.[95]

79. In November 2009, FDA approved an update to the Tysabri label to read: "In patients treated with Tysabri, the risk of PML increases with longer treatment duration, and for patients treated for 24 to 36 months is generally similar to the rates seen in clinical trials. There is limited experience beyond 3 years of treatment."[96]

80. In July 2010 FDA approved an update to the Tysabri label stating: "The risk of PML is also increased in patients who have been treated with an immunosuppressant prior to receiving Tysabri. This increased risk appears to be independent of Tysabri treatment duration."[97]

81. From 2005 through 2009 there was no published literature correlating the risk of PML with the presence or absence of JCV antibodies circulating in the bloodstream.[98]

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[95] Motion at 29, ¶ 78 (citing November 24, 2009 email chain regarding PML patient samples, Ex. 52 to Motion, docket no. 168-9, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 19, ¶ 78.

[96] Motion at 29, ¶ 79 (citing November 2009 Tysabri label at p. 4, Ex. 3 to Motion, docket no. 167-3, filed Dec. 11, 2015; September 17, 2009 Press Release, Ex. 42 to Motion, docket no. 167-41, filed Dec. 11, 2015; Safety Minutes September 21, 2009, Ex. 83 to Motion, docket no. 168-46, filed Dec. 11, 2015; September 21, 2009 Email from Tammy Phinney, Biogen to James Reese, FDA, Ex. 66 to Motion, docket no. 168-29, filed Dec. 11, 2015; September 27, 2009 Email from Tammy Phinney, Biogen to James Reese, FDA, Ex. 67 to Motion, docket no. 168-30, filed Dec. 11, 2015; October 16, 2009 Email from Tammy Phinney, Biogen to James Reese, FDA, Ex. 68 to Motion, docket no. 168-31, filed Dec. 11, 2015; November 6, 2009 Letter from Nadine Cohen, Biogen to Russell Katz, M.D., FDA, Ex. 69 to Motion, docket no. 168-32, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 19, ¶ 79.

[97] Motion at 29, ¶ 80 (citing July 2010 Tysabri label at p. 4, Ex. 4 to Motion, docket no. 167-4, filed Dec. 11, 2015; Safety Minutes May 14, 2010, Ex. 85 to Motion, docket no. 168-48, filed Dec. 11, 2015; July 12, 2010 Letter from Nadine Cohen, Biogen to Russell Katz, M.D., FDA, Ex. 70 to Motion, docket no. 168-33, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 19, ¶ 80.

[98] Motion at 30, ¶ 81 (citing Berger Expert Report at 3; DeWitt Expert Report at 9-10; Viscidi Expert Report at 6-7; Major Dep. Tr. 411:16-415:18, 418:20-420:8; Gorelik, L. et al. (2010), Anti-JC Virus Antibodies: Implications for PML Risk Stratification. Ann Neurol., 68: 295–303 ("Gorelik, L. et al."), Ex. 22 to Motion, docket no. 167-22, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 19, ¶ 81.

**Additional Material Facts Regarding the JCV Antibody Assay**

82. After Tysabri was removed from the market in 2005 and throughout the time Mrs. Christison was prescribed Tysabri, Defendants' scientists and others in the field pursued what they thought to be the most likely risk stratification tool by devoting research efforts to finding JC virus DNA in the blood and periphery through Polymerase Chain Reaction (PCR) assay testing. PCR testing was thought to be the most likely risk stratification tool due to the fact that in order to develop PML a person must be infected with the JC virus, and because the virus must move through the body to get to the CNS and mutate into a form that can replicate in CNS tissue.[99]

83. In 2010, PCR testing in Tysabri patients was found to be "unlikely to be useful" as a PML risk stratification tool in data published in the Annals of Neurology.[100]

84. In late 2009, Biogen scientists developed an "analytically validated" assay that could reliably detect JCV antibodies in the blood. Using the "analytically validated" assay, Biogen scientists determined that 53.6% of Tysabri-treated MS patients tested positive for JCV antibodies. The assay had not, however, been "clinically validated."[101]

85. "Analytically validated" means "accurately measuring the expression level of a protein of interest."[102]

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[99] Motion at 30, 82 (citing Viscidi Expert Report at 6-8; Berger Expert Report at 3; Rudick RA, et al. Assessment of JC virus DNA in blood and urine from natalizumab-treated patients. Ann. Neurol. 2010; 68(3):304-310 ("Rudick RA, et al."), Ex. 25 to Motion, docket no. 167-25, filed Dec. 11, 2015; Key Take-aways; Major Dep. Tr. 397:4-398:12, 444:21-445:24). The portions included in this fact are undisputed by Mr. Christison. Opposition at 19-20, ¶ 82.

[100] Motion at 30, ¶ 83 (citing Rudick RA, et al.). Undisputed by Mr. Christison. Opposition at 20, ¶ 83.

[101] Motion at 30-31, ¶ 84 (citing Gorelik, L., et al.; Viscidi Expert Report at 15; December 2009 Advisory Board Minutes). The portions included in this fact are undisputed by Mr. Christison. Opposition at 20, ¶ 84.

[102] Motion at 31, ¶ 85 (citing August 6, 2014 Guidance for Industry and Food and Drug Administration Staff on In Vitro Companion Diagnostic Devices (by US Department of Health and Human Services) ("August 6, 2014 Guidance") at 6, Ex. 11 to Motion, docket no. 167-11, filed Dec. 11, 2015; Jones Expert Report at 22; DeWitt Dep. Tr. 166:21-169:13). The portions included in this fact are undisputed by Mr. Christison. Opposition at 20, ¶ 85.

86. "Clinically validated" means "identifying those patients at increased risk for a serious adverse effect." Clinical validation is an FDA requirement for any labeling claim or the marketing of any drug or device for use in the diagnosis or treatment of a disease.[103]

87. In late 2009, Biogen convened Advisory Boards of MS experts and regulatory experts to discuss the data Biogen scientists had developed regarding JCV antibodies using the assay that Biogen had developed.[104]

88. At the December 12, 2009 Advisory Board, most, but not all, of the medical experts agreed that the idea of using JCV antibody testing in risk stratification could have merit and that Biogen's research in the area should be pursued.[105]

89. At an Advisory Board meeting with US regulatory experts on December 9, 2009, the observation that 11 of 11 patients with pre-PML samples had positive JCV antibodies (using an assay with a seroprevalence rate of 54% in the MS population) was discussed and the general consensus from the regulatory experts was the "data on the assay was too preliminary to be of predictive value" regarding PML at that time.[106]

90. On September 8, 2010 and November 18, 2010 representatives of Biogen and Elan met with FDA to discuss Biogen's JCV antibody assay and related proposed labeling changes based on the data that was available as of that time. True, complete, and accurate copies of FDA's official meting minutes are attached to the affidavit of Michael Poirier, Vice President

[103] Motion at 31, ¶ 86 (citing August 6, 2014 Guidance at 6; Jones Expert Report at 22; Viscidi Expert Report at 4-5; DeWitt Dep. Tr. 166:25-169:13; Sep. 8 Minutes). The portions included in this fact are undisputed by Mr. Christison. Opposition at 20-21, ¶ 86.

[104] Motion at 31, ¶ 87 (citing December 2009 Advisory Board Minutes; Dec. 9 Panel; Viscidi Expert Report at 10). Undisputed by Mr. Christison. Opposition at 21, ¶ 87.

[105] Motion at 31, ¶ 88 (citing December 2009 Advisory Board Minutes; Viscidi Expert Report at 10). The portions included in this fact are undisputed by Mr. Christison. Opposition at 21, ¶ 88.

[106] Motion at 31-32, ¶ 89 (citing December 2009 Advisory Board Minutes; Viscidi Expert Report at 15). Undisputed by Mr. Christison. Opposition at 21-22, ¶ 89.

of Asset Management at Biogen. Mr. Poirier attended the meetings with FDA and attests that the official meeting minutes accurately reflect the substance of those meetings.[107]

91. On September 8, 2010, Defendants met with FDA's Center for Drug Evaluation and Research ("CDER") to discuss a potential labeling change based on Biogen's ongoing research regarding JCV antibodies.[108]

92. As detailed in FDA's official meeting minutes on September 8, 2010, FDA rejected Biogen's proposal to add information to the Tysabri label regarding the significance of JCV antibody status due to the insufficiency of available data:

> **Sponsor Question 5:** Does the Agency agree that the proposed labeling concepts reflect the information that should be provided in the prescribing information for TYSABRI?
>
> **The proposed labeling concepts are as follows:**
>
> • Individual anti-JCV antibody status is one consideration in determining the benefit/risk of TYSABRI
>
> • Screening for serum anti-JCV antibody should be performed prior to initiating therapy and annually thereafter
>
> • Patients who are anti-JCV negative have a lower risk of developing PML than those who are anti-JCV antibody positive
>
> • There is an increased risk for PML in anti-JCV antibody positive patients
>
> **FDA Pre-Meeting Comments:** As discussed in the answers above, ***the Division does not believe that there is currently sufficient information to support the clinical utility of the anti-JCV antibody assay in determining the risk for PML*** and the benefit/risk of TYSABRI. The Division does, however, agree that the test may be promising and that it should [be] studied carefully to address the concerns identified in our responses.[109]

[107] Motion at 32, ¶ 90 (citing Affidavit of Michael Poirier, docket no. 167-12, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 22, ¶ 90.

[108] Motion at 33, ¶ 91 (citing Sep. 8 Minutes). Undisputed by Mr. Christison. Opposition at 22, ¶ 91.

[109] Motion at 32-33, ¶ 92 (citing Sep. 8 Minutes at 5). Undisputed by Mr. Christison. Opposition at 22-23, ¶ 92.

93. FDA's official meeting minutes from the meeting with Biogen on September 8, 2010, reflect FDA's concerns regarding the data presented by Biogen, stating among other concerns:

> • "It is too early in the analysis of this methodology to determine the value of this marker as a PML risk stratification tool";
>
> • "The results are based on only a small population (only 17 patients had pre-PML antibody status tested)";
>
> • "[W]e do not believe that there is sufficient supporting information at this time to describe the clinical utility of the assay in the approved prescribing information for TYSABRI";
>
> • "It appears that the results you describe are based on testing that was done after patients had already been exposed to Tysabri. It would be more useful, in determining the value of the test, if there were results of serial anti-JCV antibody tests for patients beginning before exposure to Tysabri and then at fixed times following administration of Tysabri (e.g. to identify whether rising antibody titers are predictive of PML)";
>
> • "It is not clear how these results would guide therapy in antibody positive patients";
>
> • "Based on [changes in assay results over time] we are concerned about the stability of the determination, and the utility in using it to predict development of PML";
>
> • "Based on the information you have presented, antibody-negative patients would have a lower risk of developing PML. It is not clear how this information would help guide therapy, particularly given the uncertainty related to the stability of the result in a given individual over time."[110]

94. On November 18, 2010, Defendants again met with FDA regulators, this time at FDA's Center for Devices and Radiological Health ("CDRH"), to discuss a Biogen proposal to make Biogen's JCV antibody assay available to Tysabri prescribers as a "laboratory developed test" ("LDT") kit prior to FDA clearance of the Biogen assay and related labeling changes.[111]

[110] Motion at 33, ¶ 93 (citing Sep. 8 Minutes at 2-3). Undisputed by Mr. Christison. Opposition at 23-24, ¶ 93.

[111] Motion at 34, ¶ 94 (citing FDA Record Nov. 2010). Undisputed by Mr. Christison. Opposition at 24, ¶ 94.

95. On November 18, 2010, FDA again rejected Biogen's proposal concerning the JCV antibody assay and reiterated in the official meeting minutes FDA's conclusion that "[t]he usefulness of this test in treatment with Tysabri has not been established."[112]

96. As reflected in FDA's official meeting minutes from the meeting with Biogen on November 18, 2010, FDA stated that Biogen's JCV antibody assay could not be made available for use with Tysabri until the antibody assay was cleared by FDA for use in the clinical setting as a medical device and a labeling change for Tysabri was approved after the submission of clinical data. FDA's official meeting minutes document FDA's concerns regarding the sufficiency of Biogen's JCV antibody assay data, stating among other comments:

> • "If the drug labeling specifies this device as critical in order to determine therapy, the sponsor/test must comply with FDA regulations for in vitro diagnostic devices";
>
> • "The information provided does not allow us to determine the clinical utility for the intended use claims";
>
> • "Regarding the analytical accuracy studies performed, you have evaluated the analytical accuracy versus urine shed viral DNA. This is not a valid comparator as the antibodies demonstrate prior exposure to the virus and are not comparable to urine shed viral DNA which may or may not occur in association with a JCV infection and latency in the kidneys or elsewhere in the urinary tract";
>
> • "Your proposal to assess the agreement between your commercial kit and your LDT test (which is essentially the same device) is not acceptable as a means to evaluate your device performance. As stated above, we recommend that you assess the clinical performance of your device in the context of the drug trial";
>
> • "The risk and hence the classification of the device cannot be determined until its use is established via the drug label";
>
> • "CDRH expressed concerns about the stability of the antibody response based on the data submitted to the agency in the briefing document";
>
> • "This specific assay does not have any intended use other than to be used with the drug. Therefore, an LDT could not be cleared/approved before the assay is mentioned in the drug label";

[112] Motion at 35, ¶ 95 (citing FDA Record Nov. 2010). Undisputed by Mr. Christison. Opposition at 24-25, ¶ 95.

> • "It was noted that the anti-JCV antibody assay has limited positive predictive value as an independent risk factor, but it may have potential benefits within an algorithm which considers other risk factors. CDER will evaluate these issues during review of the sBLA submission, which will include additional analyses related to anti-JCV antibody testing results and their clinical utility";
>
> • "The final decision regarding the utility and drug label modification will be determined by CDER subsequent to the evaluation of the sBLA";
>
> • "The Agency confirmed that an LDT clearance for the proposed indications could only take place after the clinical division had approved the label change that described the clinical utility of the assay."[113]

97. In light of FDA's rejection of a labeling change in September 2010, and rejection of making Biogen's assay available to physicians based on the insufficiency of the available scientific evidence concerning its clinical utility in November 2010, over the course of the next year Biogen continued to sponsor the STRATIFY clinical trials (which began in March 2010), and worked with FDA to demonstrate the usefulness of the assay in the clinical setting.[114]

98. Biogen sponsored two clinical trials related to JCV antibodies and Tysabri use, collecting blood samples from Tysabri patients for research purposes: STRATIFY-1 and STRATIFY-2. Both clinical trials enrolled their first patients in March 2010. The purpose of STRATIFY-1 was "to define the prevalence of anti-JC virus (JCV) antibodies in multiple sclerosis (MS) patients and to evaluate the analytical false-negative rate of a 2-step anti-JC virus antibody assay." The purpose of STRATIFY-2 was to "demonstrate that the incidence of

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[113] Motion at 34-35, ¶ 96 (citing FDA Record Nov. 2010). Mr. Christison does not dispute that this is what the FDA meeting minutes stated. Opposition at 26, ¶ 96.

[114] Motion at 35, ¶ 97 (citing Letter from Nadine D. Cohen, Biogen to Russell Katz, M.D., FDA (December 21, 2010), Ex. 73 to Motion, docket no. 168-36, filed Dec. 11, 2015; April 15, 2011 Letter from Nadine D. Cohen, Biogen to Russell Katz, M.D., FDA, Ex. 74 to Motion, docket no. 168-37, filed Dec. 11, 2015; April 29, 2011 Letter from Nadine D. Cohen, Biogen to Russell Katz, M.D., FDA, Ex. 75 to Motion, docket no. 168-38, filed Dec. 11, 2015; November 4, 2011 Letter from Nadine D. Cohen, Biogen to Russell Katz, M.D., FDA, Ex. 79 to Motion, docket no. 168-42, filed Dec. 11, 2015; May 13, 2011 Letter from Nadine D. Cohen, Biogen to Russell Katz, M.D., FDA, Ex. 76 to Motion, docket no. 168-39, filed Dec. 11, 2015; May 27, 2011 Letter from Nadine D. Cohen, Biogen to Russell Katz, M.D., FDA, Ex. 77 to Motion, docket no. 168-40, filed Dec. 11, 2015; December 9, 2011 Letter from Nadine D. Cohen, Biogen to Russell Katz, M.D., FDA, Ex. 80 to Motion, docket no. 168-43, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 27, ¶ 97.

progressive multifocal leukoencephalopathy (PML) in natalizumab-treated participants who do not have detectable antibodies to John Cunningham virus (JCV) (antibody negative) is lower than in participants who have detectable antibodies to JCV (antibody positive)."[115]

99. In October 2011, Biogen again requested FDA allow the Tysabri label to be amended to include information concerning the significance of JCV antibodies based on data from ongoing research and clinical trial data.[116]

100. The October 2011 submission from Biogen to FDA proposing a Tysabri label change regarding the significance of JCV antibodies included data showing that 37 of 37 pre-PML blood samples were positive for JCV antibodies using an assay that determined the background "seropositivity" rate in the MS population was 54%.[117]

101. On January 20, 2012, FDA announced it had cleared the STRATIFY JCV antibody assay and approved an associated Tysabri labeling change regarding the significance of JCV antibodies. FDA issued a press release announcing that this antibody test was the "first test for risk of rare brain infection in some people treated with Tysabri."[118]

102. The May 2015 Tysabri label—the current label in effect—states "the reported rate of seroconversion in patients with MS (changing from anti-JCV antibody negative to positive and remaining positive in subsequent testing) is 3 to 8 percent annually."[119]

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[115] Motion at 35-36, ¶ 98 (citing Bozic, C., Anti-John Cunningham Virus Antibody Prevalence in MS Patients: Baseline Results of STRATIFY-1, August 10, 2011, BIIBELAN (IND 006895) 107908), Ex. 19 to Motion, docket no. 167-19, filed Dec. 11, 2015; ClinicalTrials.gov Description of STRATIFY-2, Ex. 20 to Motion, docket no. 167-20, filed Dec. 11, 2015; Jones Expert Report at 52-53). Undisputed by Mr. Christison. Opposition at 27, ¶ 98.

[116] Motion at 36, ¶ 99 (citing October 5, 2011 Letter from Nadine D. Cohen, Biogen to Russell Katz, M.D., FDA ("October 5, 2011 Cohen Letter"), Ex. 78 to Motion, docket no. 168-41, filed Dec. 11, 2015). Undisputed by Mr. Christison. Opposition at 27, ¶ 99.

[117] Motion at 36, ¶ 100 (citing October 5, 2011 Cohen Letter; Jones Expert Report at 53-54). Undisputed by Mr. Christison. Opposition at 27, ¶ 100.

[118] Motion at 36, ¶ 101 (citing 2012 FDA News Release; 2012 Tysabri Label; Jones Expert Report at 54). Undisputed by Mr. Christison. Opposition at 27, ¶ 101.

[119] Motion at 37, ¶ 102 (citing 2015 Tysabri Label at 5). Undisputed by Mr. Christison. Opposition at 27, ¶ 102.

**Mr. Christison's Expert Testimony**

103. Plaintiff's only retained expert in this case is Eugene Major, Ph.D.[120]

104. Dr. Major is not a medical doctor or neurologist.[121]

105. Dr. Major is not a regulatory expert.[122]

106. Dr. Major did not review the Tysabri regulatory file in preparing his expert report.[123]

107. Dr. Major offers no opinions related to the duration warning or prior immunosuppressant warning.[124]

108. Dr. Major states in his report that Biogen could have developed a "commercially available" JCV antibody assay by 2007 and "[u]nder the circumstances it would have been reasonable for Biogen to communicate to patients through the TOUCH program, whose purpose is to educate physicians and patients on the risk of PML, that JC Virus causes PML and therefore prior exposure as measured by the presence of antibody was a factor in the assessment of the risk."[125]

[120] Motion at 37, ¶ 103 (citing January 30, 2015, Plaintiff's Expert Disclosure, Ex. 18 to Motion, docket no. 167-18, filed Dec. 11, 2015; Expert Report of Eugene Major ("Major Expert Report"), Ex. 17 to Motion, docket no. 167-17, filed Dec. 11, 2015). The portions included in this fact are undisputed by Mr. Christison. Opposition at 27, ¶ 103.

[121] Motion at 37, ¶ 104 (citing Major Dep. Tr. 144:14-21, 141:18-25, 142:14-17, 142:20-21, 143:24-144:3; Major Expert Report). Undisputed by Mr. Christison. Opposition at 27, ¶ 104.

[122] Motion at 37, ¶ 107 (citing Major Dep. Tr. 147:6-150:8, 183:6-8 ("I am not a regulatory expert.")). Undisputed by Mr. Christison. Opposition at 29, ¶ 107.

[123] Motion at 37, ¶ 109 (citing Major Dep. Tr. 121:4-21). Undisputed by Mr. Christison. Opposition at 29, ¶ 109.

[124] Motion at 37, ¶ 111 (citing Major Expert Report at 10-11). Undisputed by Mr. Christison. Opposition at 31, ¶ 111.

[125] Motion at 38, ¶ 113 (citing Major Expert Report at 10-11). Undisputed by Mr. Christison. Opposition at 31, ¶ 113.

109. Dr. Major's report states: "It would therefore have been prudent for Biogen to communicate to physicians, healthcare providers and patients that the JC Virus Antibody test might be useful in helping to assess a higher risk of PML."[126]

**NIH Licensed Assay to Biogen**

110. NIH licensed a serologic assay for the detection and differentiation of antibodies directed against JC or BK Viruses. In the License Agreement, Biogen represented that it "has the facilities, personnel, and expertise to use the Materials or the Licensed Products for commercial purposes and agrees to expend reasonable efforts and resources to develop the Materials or the Licensed Products for commercial use or commercial research."[127]

111. The JCV antibody assay NIH licensed to Biogen was developed by Dr. Major.[128]

112. The NIH JC Virus Antibody Assay, developed by Dr. Major, is not FDA approved, but could be used in practice by a Tysabri-prescribing neurologist such as Dr. Foley.[129]

**DISCUSSION**

The Companies argue that they are entitled to summary judgment on several grounds. First, they argue that they are entitled to summary judgment because Mr. Christison has "failed to adduce expert testimony regarding any alleged inadequacies in Tysabri's PML warnings."[130] Second, they argue that they are entitled to summary judgment because "the warnings

[126] Motion at 38, ¶ 114 (citing Major Expert Report at 9). Undisputed by Mr. Christison. Opposition at 31, ¶ 114.

[127] Opposition at 32, ¶ 116 (citing 2006 MTA). Undisputed by Companies. Response to Facts at 2.

[128] Opposition at 32, ¶ 117 (citing 2006 MTA). Undisputed by Companies. Response to Facts at 2.

[129] Opposition at 33, ¶ 125 (citing Major Dep. Tr. 100:8-22). Companies do not dispute that a physician could use the NIH JC Virus Antibody Assay according to the physician's independent medical judgment, but the Companies dispute that they could officially warn physicians about the risks of PML and JCV antibodies prior to obtaining FDA approval. Response to Facts at 4.

[130] Motion at 38.

concerning the risk of PML with Tysabri treatment were adequate as a matter of law."[131] Third, they argue they are entitled to summary judgment because Mr. Christison "cannot establish proximate cause."[132] Fourth, they argue they are entitled to summary judgment because they "had no legal duty to develop and commercialize a JCV antibody assay."[133] Fifth, they argue they are entitled to summary judgment on the pendent claims of negligence and negligent misrepresentation because the PML warnings were adequate.[134] Finally, the Companies argue they are entitled to summary judgment because the claims brought by Mr. Christison are preempted by federal law.[135] Mr. Christison opposes each of these arguments.

**The Companies Are Entitled to Summary Judgment Because Mr. Christison Does Not Have Expert Testimony Regarding Any Alleged Inadequacies in Tysabri's Warning Label**

First, the Companies argue they are entitled to summary judgment because Mr. Christison has "failed to adduce expert testimony regarding any alleged inadequacies in Tysabri's PML warnings."[136] The Companies argue that "only a physician or someone with specialized knowledge would be qualified to determine whether the warning was adequate."[137] They argue that a "lay jury could not possibly evaluate and reach a judgment as to the adequacy of the Tysabri warnings" because of the "complexity of the medical issues in this case" and because "the labeling at issue contains extensive PML warnings[.]"[138] The Companies point to a federal district court decision in Massachusetts stating that "expert testimony is particularly appropriate

[131] *Id.* at 46.

[132] *Id.* at 54.

[133] *Id.* at 58.

[134] *Id.* at 60.

[135] *Id.* at 62.

[136] *Id.* at 38.

[137] *Id.* at 39-40.

[138] *Id.* at 40.

when the manufacturer does provide some warning, in order to determine the adequacy of that warning."[139]

Mr. Christison disagrees, arguing that he does not need expert testimony because "[a] jury is more than qualified to call on their own life experiences, as well as listen to witness testimony regarding the adequacy of Tysabri's warnings considering the information known, or reasonably available to Defendants before Mrs. Christison's death, and determine whether a different label would have changed the outcome."[140]

Mr. Christison is incorrect. A lay jury is not able to call on "their own life experiences" to determine the adequacy of a drug label. "Where the injury involves obscure medical factors which are beyond an ordinary lay person's knowledge, necessitating speculation in making a finding, there must be expert testimony that the [defendant's conduct] probably caused the injury."[141] The injuries alleged in this case[142] involve obscure medical factors which are beyond an ordinary lay person's knowledge. They stem from Mrs. Christison becoming infected with PML, a "rare viral brain infection that is caused by the JC Virus."[143] There are no known treatments or cures for PML.[144] The connection between PML, the JC Virus, and Tysabri has been extensively researched by medical professionals for many years.[145] A lay jury would not be able to determine by calling upon "their own life experiences" and would be speculating in making findings about the adequacy of the Tysabri warning label, which warned extensively

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[139] *Id.* at 40.

[140] Opposition at 39.

[141] *Lundgren*, 2013 WL 3087726 at *1 (alteration in original).

[142] *See* First Amended Complaint ¶¶ 71, 82.

[143] Undisputed Fact No. 7.

[144] Undisputed Fact No. 11.

[145] Undisputed Fact Nos. 5-38.

about PML. Therefore, "there must be expert testimony that the [defendant's conduct] probably caused the injury."[146]

Mr. Christison contends, however, that he does not need an expert to establish causation because "there is no question that Tysabri caused Mrs. Christison's PML."[147] Therefore, according to Mr. Christison, "[t]he only causation question is whether Mrs. Christison would have continued Tysabri therapy with a more adequate label based on Dr. Foley [sic] recommendation or Mrs. Christison's final decision."[148] But Mr. Christison is incorrect on this point as well because Mr. Christison does not have a qualified expert to testify on what "a more adequate label" would contain.[149]

A trial court may make a legal ruling on causation if "(1) there is no evidence to establish a causal connection, thus leaving causation to jury speculation, or (2) where reasonable persons could not differ on the inferences to be derived from the evidence on proximate causation."[150] Here, "there is no evidence to establish a causal connection" because Mr. Christison has failed to provide an expert to testify about "a more adequate label." Therefore, Mr. Christison is unable to establish causation and, because each claim requires Mr. Christison to establish causation,[151] his claims fail.

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[146] *Lundgren*, 2013 WL 3087726 at *1 (alteration in original).

[147] Opposition at 39.

[148] *Id.*

[149] *See* Order Granting in Part and Denying in Part Defendants' Joint Motion in Limine at 4-8, docket no. 195, filed Aug. 5, 2016 (excluding Dr. Major's testimony regarding adequacy of the warning).

[150] *Ladd*, 264 P.3d at 756 (internal quotation marks omitted).

[151] *See Tingey*, 193 F. App'x at 759 (quoting *Webb*, 2005 UT 80, ¶ 9, 125 P.3d 906) (listing causation as necessary element of negligence claim); *House*, 929 P.2d at 344 (listing causation as necessary element of failure to warn claim); *Price-Orem*, 713 P.2d at 59 (including causation as necessary element of negligent misrepresentation claim by stating that "a party injured by reasonable reliance upon a second party's careless or negligent misrepresentation of a material fact may recover damages resulting from that injury"); *see also Lundgren*, 2013 WL 3087726 at *1 (citing authorities discussing causation in claims for negligence, failure to warn, and misrepresentation).

As noted by other courts, "expert testimony is particularly appropriate when the manufacturer does provide some warning, in order to determine the adequacy of that warning."[152] Here, it is undisputed that Tysabri included a warning.[153] Thus, an expert is required to determine the adequacy of the warning. Specifically, it requires an expert who is familiar with drug labeling and the process by which a drug is prescribed to a patient. Without testimony from such an expert, the jury is left to speculate as to whether the label adequately warned about the dangers of Tysabri and its possible link to PML. A lay jury is not able to determine the adequacy of a label because they are not medical professionals, do not prescribe drugs, and are not familiar with the complex medical issues raised by PML, the JC Virus, and Tysabri. Other courts have noted that "warnings directed at doctors require expert testimony because they are 'so distinctively related to some science, profession, business, or occupation as to be beyond the ken of the average layman.'"[154] Accordingly, summary judgment is GRANTED in favor of the Companies on each cause of action due to Mr. Christison's failure to provide expert testimony regarding causation and the adequacy of the Tysabri label.

**The Companies Are Entitled to Summary Judgment Because the Tysabri Label Was Adequate Regarding PML**

"Wholly apart from Plaintiff's failure to adduce expert testimony . . . [,]"[155] the Companies argue they are entitled to summary judgment because "the warnings concerning the risk of PML with Tysabri treatment were adequate as a matter of law."[156] They argue that their

[152] *Laspesa v. Arrow Int'l, Inc.*, No. 07cv12370-NG, 2009 WL 5217030, *6 (D. Mass. Dec. 23, 2009) (citing *Wyeth Laboratories, Inc. v. Fortenberry*, 530 So.2d 688, 691 (Miss. 1988); *see also Mulhall v. Hannafin*, 841 N.Y.S. 2d 292, 286-87 (N.Y.A.D. 2007).

[153] Undisputed Fact Nos. 22, 23.

[154] *Laspesa*, 2009 WL 5217030 at *6 (quoting *Wyeth Laboratories*, 530 So.2d at 692 (quoting *Dion v. Graduate Hosp. of the Univ. of Pennsylvania*, 360 Pa.Super. 416, 425 (Pa.Super.Ct. 1987))).

[155] Motion at 47

[156] *Id.* at 46.

duty was to properly warn Dr. Foley, who was Mrs. Christison's prescribing physician, and that they fulfilled that duty by providing a clear warning about the risks of Tysabri and PML.[157] The Companies argue that the three-part *House* test[158] normally applies for determining adequacy of a drug label, but that the Model Utah Jury Instructions state that the *House* framework "may not be appropriate if a regulatory body, such as the [FDA], directs that a specific warning must be given for a product."[159] One of the ways to determine if the *House* framework is met, according to the Companies, is to determine whether the warning is "accurate, clear, and unambiguous."[160] The Companies state that a warning is "clear" if it is "direct, unequivocal and sufficiently forceful to convey the risk."[161] One way to do that, the Companies argue, is to look at whether "information regarding the 'precise malady incurred' was communicated in prescribing information."[162]

Mr. Christison, on the other hand, argues that the proper standard asks whether "reasonable minds could reach *only one result* taking all disputed facts and inferences in a light most favorable to the non-moving party."[163] Mr. Christison argues that summary judgment is not appropriate on the adequacy of the warning because "there is an important fact question for the jury to answer regarding whether Tysabri's label was adequate based on the scientific information and knowledge available at the time."[164] Mr. Christison argues that in the thirty

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[157] *Id.* at 47-48.

[158] *House*, 886 P.2d at 551 (stating a warning should "(1) be designed so it can reasonably be expected to catch the attention of the consumer; (2) be comprehensible and give a fair indication of the specific risks involved with the product; and (3) be of an intensity justified by the magnitude of the risk.").

[159] Motion at 48 (citing MUJI 2d, CV 1009).

[160] Motion at 49 (citing *McDowell v. Eli Lilly and Co.*, 58 F.Supp.3d 391, 403-406 (S.D.N.Y. 2014)).

[161] Motion at 49 (citing *Martin v. Hacker*, 83 N.Y.2d 1, 11 (N.Y. 1993)).

[162] Motion at 49 (citing *Alston v. Caraco Pharm., Inc.*, 670 F.Supp.2d 279, 284 (S.D.N.Y. 2009)).

[163] Opposition at 44-45 (quoting *House*, 886 P.2d at 551) (emphasis added by Mr. Christison).

[164] Opposition at 46.

months following Mrs. Christison's PML diagnosis, the Companies uncovered additional risk factors that should have been included at the time Mrs. Christison was taking Tysabri.[165] Mr. Christison argues that:

> the "general warning 'Tysabri may increase [your] risk of developing PML' was unclear, ambiguous, and inadequate because it mistakenly treated all Tysabri patients as equals. Step two of the *House* test is that the warning must be comprehensible and give a fair indication of the specific risks involved with the product. Mrs. Christison was led to believe her risk of developing PML was the same as every other patient in Dr. Foley's office, and every other MS patient on Tysabri. It is unquestionable that this was inaccurate, but unfortunately Dr. Foley and Mrs. Christison did not have full information.[166]

In Utah, the learned intermediary doctrine applies, which means that "manufacturers of prescription drugs have a duty to warn *only the physician prescribing the drug*, not the end user or patient."[167] Thus, the duty is does not run to the patient; it runs to "the medical profession." If a manufacturer fails to fulfill that duty, and causes damage or injury to a plaintiff, the "manufacturer will be held directly liable to the patient for breach of the duty to make timely and adequate warnings to the medical profession of any dangerous side effects produced by its drug of which it knows or has reason to know."[168]

The Companies are correct that the labeling is adequate as a matter of law. If the Model Utah Jury Instructions test is applied, the Companies provided an adequate warning because the FDA controlled what warnings could be given with respect to Tysabri.[169] If the *House* test is used, the Companies provided an adequate warning because the Tysabri warning (1) was designed so it could reasonably be expected to catch the attention of the consumer; (2) was

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[165] *Id.*

[166] *Id.* at 45-46 (alteration in original).

[167] *Schaerrer*, 79 P.3d at 928, ¶ 20 (emphasis added).

[168] *Id.*

[169] *See* Undisputed Fact Nos. 4, 16-29, 35, 74, 79, 80, 92-96, 101 (describing FDA's involvement in the wording of the Tysabri warnings).

comprehensible and gave a fair indication of the specific risks involved with Tysabri; and (3) was of an intensity justified by the magnitude of the risk.

First, it is undisputed that as a condition of Tysabri's re-approval in 2006 the FDA required that the prescribing information contain a "black box" warning about PML,[170] which is the strongest warning required or permitted by FDA.[171] The black box warning, as the most serious warning available, can be reasonably expected to catch the attention of the consumer. Second, it is also undisputed that the Tysabri prescribing information included specific warnings about Tysabri increasing the risk of becoming infected with PML.[172] The Warnings section specifically identified JC Virus, noting that PML is caused by the JC Virus, but that "the absolute risk for PML in patients treated with Tysabri cannot be precisely estimated, and factors that might increase an individual patient's risk for PML have not been identified."[173] This was a fair and comprehensible indication of the specific risks associated with Tysabri. Finally, the intensity of the warning matched the magnitude of the risk. The black box warning indicated that Tysabri "increases the risk of" PML, and explained that PML "usually leads to death or severe disability."[174] Appropriately, this warning was not qualified or minimized in any way because the magnitude of the risk—death or severe disability—was of the highest possible degree. Thus, the *House* factors are satisfied.

Moreover, Dr. Foley, the prescribing physician, testified that the warning was adequate. While he does not have the expertise to opine on the specialized area of labeling, his view as the prescriber and intended audience for the warning is probative. When asked whether he believed

[170] Undisputed Fact No. 17, 18.

[171] Undisputed Fact No. 20.

[172] Undisputed Fact Nos. 22-24.

[173] Undisputed Fact No. 23.

[174] Undisputed Fact No. 22.

the drug labeling on Tysabri was adequate, he testified "[o]f course. Otherwise, I wouldn't . . . have prescribed it at that time."[175] Defendants' expert, Dr. Dana DeWitt, a clinical neurologist and professor of neurology at the University of Utah, also testified that the Tysabri label was adequate to inform a treating neurologist of the increased PML risk associated with Tysabri use through the time Dr. Foley prescribed the drug for Mrs. Christison.[176] This shows that the label adequately warned the medical profession of the dangerous side effects of Tysabri, specifically PML.

The Tysabri warning label was also adequate because it warned of the "precise malady incurred."[177] Throughout the label, the risk of PML is highlighted. For example, the black box warning explains that Tysabri increases the risk of PML, which "usually leads to death or severe disability."[178] The label does not qualify or minimize the risk of PML and explains the limitations under which Tysabri may be taken.[179] The Tenth Circuit has upheld summary judgment on a failure to warn claim where "the warnings provided by [defendant] *reasonably cautioned against each of the specific risks* alleged by [plaintiff]."[180] Here, the Tysabri label reasonably cautioned against the specific risks of PML. Mr. Christison cites to no authority that would require the Companies to include a warning more intensive than what was included in 2006.

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[175] Foley Dep. Tr. at 197:1-2.

[176] Undisputed Fact No. 69.

[177] *Alston*, 670 F.Supp.2d at 284.

[178] Undisputed Fact No. 22.

[179] Undisputed Fact No. 22.

[180] *Ralston v. Smith & Nephew Richards, Inc.*, 275 F.3d 965, 976 (10th Cir. 2001) (emphasis added).

Mr. Christison emphasizes that the warning must be "adequate based on the scientific information and knowledge available at the time."[181] He argues that "Mrs. Christison was led to believe her risk of developing PML was the same as every other patient in Dr. Foley's office" when in fact it was not because she had tested positive for JC Virus antibodies.[182] Mr. Christison argues the label should have reflected that there was a higher risk of developing PML if a patient had tested positive for JC Virus antibodies. But Mr. Christison's position is inconsistent with the undisputed facts, which show that a reliable relationship between JC Virus antibodies and PML was not established until *after* Mrs. Christison's passing. Thus, the Tysabri label was based on the scientific information *available at the time.*

Mrs. Christison was diagnosed with PML in July 2009, and died in August 2009.[183] In December 2009, about 4 months *after* her death, the relationship between JC Virus and PML was discussed at a meeting with US regulatory experts and the minutes reflect that "data on the assay was *too preliminary to be of predictive value*" regarding PML at that time.[184] The following year, in September 2010, representatives of the Companies met with FDA to discuss Biogen's JCV antibody assay and related proposed labeling changes based on the data that was available as of that time, and the FDA rejected Biogen's proposal to add information to the Tysabri label concerning the significance of JCV antibody status.[185] In November 2010, the FDA again rejected Biogen's proposal to make changes to the Tysabri label concerning the JCV antibody assay, stating that "the usefulness of this test in treatment with Tysabri has not been

[181] Opposition at 46.

[182] *Id.* at 45-46.

[183] Undisputed Fact Nos. 54, 77.

[184] Undisputed Fact No. 89 (emphasis added).

[185] *See* Undisputed Fact Nos. 90-93.

established."[186] If the scientific information and knowledge *a year after* Mrs. Christison's passing was insufficient to include a warning about JCV antibodies, it cannot be said that the scientific information and knowledge available *before* her passing was sufficient to support a labeling change. Thus, the Tysabri label reflected scientific knowledge available at the time Mrs. Christison took Tysabri. Mr. Christison's demands for an updated warning label are not required by law nor supported by the scientific knowledge available when Mrs. Christison was taking Tysabri.

As one recent court has noted, a warning on a prescription drug should be "evaluated as a whole and not through the nitpicking prism of an interested legal advocate after the fact."[187] "[A]ny resulting vagueness can be overcome if, when read as a whole, the warning conveys a meaning as to the consequences that is unmistakable."[188] Here, the Tysabri label clearly conveys a warning that taking Tysabri would increase the risk of PML, and that due to the preliminary nature of the research in 2006, there was no reliable correlation between length of treatment, use with other immunosuppressant drugs, or a positive indication of JC Virus antibodies. Mr. Christison's request that that information be placed on the label is aided by hindsight rather than the scientific information *available at the time*. For these reasons, summary judgment is GRANTED in favor of the Companies on each of the causes of action. This is an independent ground for summary judgment.

[186] Undisputed Fact Nos. 94-96.

[187] *McDowell*, 58 F.Supp.3d at 403.

[188] *Id*.

**The Companies Are Not Entitled to Summary Judgment on the Grounds that They Had No Legal Duty to Develop an Assay**

The Companies argue that they are entitled to summary judgment because they "had no legal duty to develop and commercialize a JCV antibody assay."[189] The Companies are incorrect. This is not grounds for summary judgment. The question regarding duty is not whether the Companies had an obligation to engage in a *specific act*, such as developing an assay. The question is whether the Companies engaged in "reasonable conduct in light of the apparent risk."[190] "Reasonable conduct" is informed by "[e]xpert testimony and relevant statutory authority."[191] Mr. Christison's expert, Dr. Major is allowed to testify about the state of technology and research regarding JC Virus, PML, and Tysabri, which jurors could use to determine whether the Companies engaged in "reasonable conduct." Thus, summary judgment is not warranted on the grounds that the Companies believe they had no legal duty to develop an assay.

However, there are independent grounds for summary judgment. Mr. Christison does not have an expert to testify as to regulatory matters or matters involving a treating physician's decisions, which is fatal to Mr. Christison's case. Mr. Christison is also unable to establish inadequacy of the Tysabri warning, which is fatal to his case. Mr. Christison also is unable to establish causation, which is required to be established under each of the causes of action alleged in Mr. Christison's complaint.[192] Thus, the ruling in this section does not negate summary judgment in favor of the Companies.

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[189] Motion at 58.

[190] *Downing v. Hyland Pharmacy*, 2008 UT 65, ¶¶ 11-12, 194 P.3d 944 (Utah 2008).

[191] *Id.*

[192] *See Tingey*, 193 F. App'x at 759 (quoting *Webb*, 2005 UT 80, ¶ 9, 125 P.3d 906) (listing causation as necessary element of negligence claim); *House*, 929 P.2d at 344 (listing causation as necessary element of failure to warn claim); *Price-Orem*, 713 P.2d at 59 (including causation as necessary element of negligent misrepresentation claim

**The Companies Are Entitled to Summary Judgment on the State Law Claims Because the PML Warnings Were Adequate**

Next, the Companies argue they are entitled to summary judgment on the "remaining 'tag-along' claims of negligence and negligent misrepresentation" because the PML warnings were adequate.[193] It has already been established that the PML warnings on the Tysabri label were adequate as a matter of law and that Mr. Christison lacks expert testimony as to essential elements of his claims. Thus, it is clear that Mr. Christison's negligent failure to warn claim should be dismissed, along with all of Mr. Christison's other claims.[194]

**Mr. Christison's Claims Are Preempted under Federal Law Because There Is "Clear Evidence" that the FDA Would Not Have Approved a Change to the Label Prior to 2012**

Finally, the Companies argue they are entitled to summary judgment because the state law claims brought by Mr. Christison are preempted by federal law.[195] The Companies are correct because the FDA must approve changes to a drug's label and there is "clear evidence" that the FDA would not have approved a change to the Tysabri label regarding JCV antibodies before 2012.

"Generally speaking, a manufacturer may only change a drug label after the FDA approves a supplemental application."[196] However, there is "an FDA regulation that permits a manufacturer to make certain changes to its label before receiving the agency's approval."[197]

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by stating that "a party injured by reasonable reliance upon a second party's careless or negligent misrepresentation of a material fact may recover damages resulting from that injury"); *see also Lundgren*, 2013 WL 3087726 at *1 (citing authorities discussing causation in claims for negligence, failure to warn, and misrepresentation).

[193] Motion at 60.

[194] *See McDowell*, 58 F.Supp.3d at 410-411 (dismissing claims for negligence and negligent misrepresentation after finding that failure to warn claim was inadequate as a matter of law) (citing *Ames v. Apothecon, Inc.*, 431 F.Supp.2d 566, 567-68 (D.Md. 2006) (granting summary judgment based on proximate cause and stating other claims including negligence claims can be "reduce[d] down" to failure to warn claims)).

[195] *Id.* at 62.

[196] *Wyeth v. Levine*, 555 U.S. 555, 568 (2009).

[197] *Id.*

That regulation is known as the "changes being effected" ("CBE") regulation, and it "provides that if a manufacturer is changing a label to 'add or strengthen a contraindication, warning, precaution, or adverse reaction' . . . it may make the labeling change upon filing its supplemental application with the FDA; it need not wait for FDA approval."[198] But if there is "clear evidence that the FDA would not have approved a change" to the label, the manufacturer is under no obligation to make any change to the label.[199]

Here, there is clear evidence that the FDA would not have approved a change to the Tysabri label before 2012 to include a warning regarding JCV antibodies. As noted by the Companies:

> In September 2010, Biogen met with regulators at FDA to discuss a potential labeling change regarding JCV antibodies based on Biogen's analysis of 17 blood samples that Biogen had obtained from Tysabri-treated patients who later developed PML. In November 2010, Biogen met with the FDA regulators responsible for approving laboratory tests and medical devices to discuss whether the assay could be made available to physicians pending the results of further clinical research to support a labeling change concerning antibodies. On both occasions FDA rejected the proposed labeling change concerning antibody testing and the use of the assay with Tysabri, concluding that there was insufficient data to support a labeling change concerning the significance of JCV antibodies in relation to PML risk. FDA stated that "[W]e do not believe that there is sufficient supporting information at this time to describe the clinical utility of the assay in the approved prescribing information for TYSABRI.[200]

The same conclusion was reached in 2009 with even fewer confirmed results.[201]

This case is very similar to *In re Depakote*,[202] where the court found "clear evidence" that the FDA would not have approved a change to the drug label even though the manufacturer "tried, on various occasions, to secure approval of [the] warning, and its requests were twice

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[198] *Id.*

[199] *Id.* at 571.

[200] Motion at 69.

[201] Undisputed Fact Nos. 87-89.

[202] *In re Depakote*, 87 F.Supp.3d 916 (S.D. Ill. 2015).

denied by the FDA."[203] The court found it significant that the FDA rejected the proposed warning because the available scientific evidence at the time was not sufficient, and therefore it was "highly unlikely that the available scientific evidence, *seven years prior* to that date in 1999, would have supported the addition of such a warning."[204]

This case is also similar to *Rheinfrank v. Abbott Laboratories*,[205] where the court held that preemption was appropriate because there was clear evidence that the FDA would not have approved the proposed labeling change.[206]

The FDA was aware of the potential link between JCV antibodies and PML as early as 2006,[207] but the FDA did not approve changes to the Tysabri label regarding JCV antibodies until 2012.[208] The Companies are correct that "[i]f 17 Tysabri-association pre-PML samples were insufficient to persuade FDA in 2010 of the predictive value of antibody testing in connection with PML risk stratification, there clearly would not have been sufficient data more than two years earlier . . . ."[209] Accordingly, there is "clear evidence" that the FDA would not have approved a change to the Tysabri label prior to Mrs. Christison's death, and the causes of action that Mr. Christison raises in this matter—negligence; negligent failure to warn; and negligent misrepresentation—which are based in state law, are preempted by federal requirements mandating FDA approval of changes to a drug's warning label. Summary judgment

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[203] *Id.* at 922.

[204] *Id.* (emphasis in original).

[205] *Rheinfrank v. Abbott Labs.*, 119 F.Supp.3d 749 (S.D. Ohio 2015).

[206] *Id.* at 766 (citing cases); *see also In re Celexa and Lexapro Marketing and Sales Practices Litigation*, 779 F.3d 34 (1st Cir. 2015) (holding that federal law preempted the state law claims because the Federal Food, Drug, and Cosmetic Act ("FDCA") prohibited unilateral changes to FDA-approved labels, and therefore prohibited the drug manufacturer from changing its label in light of state law requirements).

[207] Undisputed Fact No. 36.

[208] Undisputed Fact No. 101.

[209] Motion at 71.

is GRANTED in favor of the Companies on the independent grounds of preemption, in addition to the other reasons for summary judgment stated in this memorandum decision and order.

## CONCLUSION

Summary judgment in favor of the Companies is warranted on three independent grounds: (1) Mr. Christison's state law claims are preempted since there is "clear evidence" that the FDA would not have approved a change to the Tysabri label prior to Mrs. Christison's death and, therefore, the CBE regulation does not apply; (2) the Tysabri label was adequate as a matter of law because the FDA exercised significant control over the labeling, the Tysabri label clearly and specifically warned about the risk of PML according to the scientific information available at the time; and (3) Mr. Christison has failed to provide expert testimony to support any argument regarding an alleged inadequacy in the Tysabri warning label. Accordingly, summary judgment is GRANTED in favor of the Companies.

## ORDER

IT IS HEREBY ORDERED that the Motion[210] is GRANTED.

Dated August 5, 2016.

BY THE COURT:

David Nuffer
United States District Judge

[210] Motion for Summary Judgment and Memorandum in Support ("Motion"), docket no. 166, filed Dec. 11, 2015.