IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BIOGEN INC. and BIOGEN MA INC., Plaintiffs, v. SANDOZ INC. and POLPHARMA BIOLOGICS S.A., Defendants.	C.A. No. 22-1190-GBW **REDACTED PUBLIC VERSION**

MEMORANDUM ORDER

Pending before the Court is Plaintiffs Biogen Inc.'s and Biogen MA Inc.'s (collectively, "Biogen") Motion for Preliminary Injunction (D.I. 74), Biogen's Motion to Strike (D.I. 162), and Defendants Sandoz Inc.'s ("Sandoz") and Polpharma Biologics S.A.'s ("Polpharma") (collectively, "Defendants") Cross-Motion to Strike (D.I. 170).[1] The Court has considered the parties' briefing (D.I. 75; D.I. 96; D.I. 138; D.I. 178; D.I. 225 (Biogen's Motion for Preliminary Injunction briefing); D.I. 163; D.I. 171; D.I. 172; D.I. 175; D.I. 193; D.I. 198 (Biogen's Motion to Strike and Defendants' Cross-Motion to Strike briefing)) and the accompanying exhibits and declarations. The Court heard oral argument on May 17, 2023 ("Tr. __"). For the reasons stated below, the Court DENIES Biogen's Motion for Preliminary Injunction, DENIES as MOOT

[1] The Court has reviewed the letter briefing related to Polpharma's Statements (D.I. 139; D.I. 227) and Biogen's response (D.I. 185). The Court will treat those statements as Polpharma joining in Sandoz's Opposition Brief to Biogen's Preliminary Injunction Motion (D.I. 138), Sandoz's Sur-Reply to Biogen's Preliminary Injunction Motion (D.I. 225), and adopting "any subsequent arguments and evidence Sandoz submits in further opposition" to Biogen's Motion for Preliminary Injunction. D.I. 139; D.I. 227.

Defendants' Cross-Motion to Strike, and DENIES-IN-PART and DENIES as MOOT-IN-PART Biogen's Motion to Strike.

I. NATURE AND STAGE OF PROCEEDINGS[2]

Biogen brought this patent infringement case against Defendants under 42 U.S.C. § 262—the Biologics Price Competition and Innovation Act ("BPCIA"). D.I. 98. Biogen developed the biologic product TYSABRI® (natalizumab) ("Tysabri"), which is "a humanized monoclonal antibody that targets the alpha-4 (or α4) integrin component of adhesion molecules found on many white blood cells." *Id.* ¶ 34. It is used to treat relapsing forms of multiple sclerosis ("MS")—a chronic, progressive, and disabling autoimmune disease of the central nervous system ("CNS"), i.e., the brain and spinal cord—and used to treat moderate to severe Crohn's Disease ("CD")—a chronic, autoimmune disease of the gastrointestinal ("GI") tract. *Id.* ¶¶ 29-33.

In February 2005, it was discovered that a small number of individuals who had received Tysabri during the clinical trials developed progressive multifocal leukoencephalopathy ("PML")—an infection of the brain. *Id.* ¶¶ 38-39. As a result, on February 28, 2005, Biogen voluntarily withdrew Tysabri from the market. *Id.* ¶ 42. Individuals may develop PML when John Cunningham polyomavirus or John Cunningham Virus ("JCV") is reactivated in the body. *Id.* ¶ 40. JCV is a virus common in adults and is usually harmless. *Id.* Individuals who have been infected with JCV can have both anti-JCV antibodies and DNA from this virus in their bodies. *Id.* ¶ 41. Biogen scientists worked on developing assays to address how to better predict whether a patient is at risk of developing PML while taking Tysabri. In January 2012, the FDA approved the "first and only clinically and analytically validated anti-JCV antibody assay, the Stratify™

[2] The Court writes for the benefit of the parties and assumes their familiarity with this action.

JCV Antibody Enzyme-Linked Immunosorbent Assay ("ELISA") Test ("Stratify" or the "Stratify assay")." *Id.* ¶ 56.

[redacted] *Id.* ¶¶ 96, 117. Tyruko is a humanized monoclonal antibody that "targets the alpha-4 integrin component of adhesion molecules found on lymphocytes, monocytes, and eosinophils." *Id.* ¶ 99. [redacted] *Id.* ¶ 122. Pursuant to the BPCIA, the parties conducted expedited discovery and preliminary injunction briefing. D.I. 26. As of the date of this Memorandum Order, the FDA's goal date for approval of Tyruko [redacted] D.I. 226, Ex. 1368 at -299; *see also* D.I. 225 at 14 (citing D.I. 226, Ex. 1368 at -299).

II. LEGAL STANDARDS

Under 42 U.S.C. § 262(l)(8)(B), "the reference product sponsor may seek a preliminary injunction prohibiting the subsection (k) applicant from engaging in the commercial manufacture or sale" of the biosimilar drug in question. Preliminary injunctive relief is an "extraordinary" remedy appropriate only in "limited circumstances." *Kos Pharms., Inc. v. Andrx Corp.*, 369 F.3d 700, 708 (3d Cir. 2004) (internal quotation marks and citation omitted); *see also Intel Corp. v. ULSI Sys. Tech., Inc.*, 995 F.2d 1566, 1568 (Fed. Cir. 1993) ("[A] preliminary injunction is a drastic and extraordinary remedy that is not to be routinely granted.") (citations omitted); *accord Cordis Corp. v. Medtronic, Inc.*, 780 F.2d 991, 996 (Fed. Cir. 1985) ("Only a viable threat of serious harm which cannot be undone authorizes exercise of a court's equitable power to enjoin before the merits are fully determined.") (internal quotation marks and citations omitted).

A movant for a preliminary injunction must establish: "(1) a reasonable likelihood of success on the merits; (2) irreparable harm if an injunction is not granted; (3) a balance of hardships tipping in its favor; and (4) the injunction's favorable impact on the public interest." *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1350 (Fed. Cir. 2001) (citation omitted). No factor is dispositive; "'rather, the district court must weigh and measure each factor against the other factors and against the form and magnitude of the relief requested.'" *Id.* (quoting *Hybritech, Inc. v. Abbott Labs.*, 849 F.2d 1446, 1451 (Fed. Cir. 1988)). However, "a movant cannot be granted a preliminary injunction unless it establishes *both* of the first two factors, *i.e.*, likelihood of success on the merits and irreparable harm." *Id.* (citations omitted). Moreover, "[w]hile granting a preliminary injunction requires analysis of all four factors, [] a trial court may . . . deny a motion based on a patentee's failure to show any one of the four factors—especially either of the first two—without analyzing the others[.]" *Jack Guttman, Inc. v. KopyKake Enters., Inc.*, 302 F.3d 1352, 1356 (Fed. Cir. 2002) (internal citations omitted); *see also Chrysler Motors Corp. v. Auto Body Panels of Ohio, Inc.*, 908 F.2d 951, 953 (Fed. Cir. 1990) ("If the injunction is denied, the absence of an adequate showing with regard to any one factor may be sufficient, given the weight or lack of it assigned the other factors, to justify the denial.").

III. DISCUSSION

a. Biogen's Motion for Preliminary Injunction

For the reasons set forth below, the Court concludes that Biogen has not met its burden of proving that it will suffer irreparable harm if an injunction is not granted and that it will likely succeed on the merits. Thus, Biogen's Motion for Preliminary Injunction is denied.

i. Irreparable Harm

"A party seeking a preliminary injunction must establish that it is likely to suffer irreparable harm if the preliminary injunction is not granted and there is a causal nexus between the alleged infringement and the alleged harm." *Metalcraft of Mayville, Inc. v. The Toro Co.*, 848 F.3d 1358, 1368 (Fed. Cir. 2017) (citation omitted). That party must make a "clear showing" that it will suffer irreparable harm and it is entitled to such relief. *Winter v. Nat. Res. Def. Council, Inc.*, 555 U.S. 7, 22 (2008). "The mere possibility or speculation of harm is insufficient." *Koninklijke Philips N.V. v. Thales DIS AIS USA LLC*, 39 F.4th 1377, 1380 (Fed. Cir. 2022) (citation omitted). The harm must also be "immediate irreparable injury" and that the harm cannot be adequately compensated through monetary damages. *Apple Inc. v. Samsung Elecs. Co., Ltd.*, 695 F.3d 1370, 1374 (Fed. Cir. 2012) ("Apple II") (internal quotation marks and citations omitted); *Celsis In Vitro, Inc. v. CellzDirect, Inc.*, 664 F.3d 922, 930 (Fed. Cir. 2012) ("[T]he irreparable harm inquiry seeks to measure harms that no damages payment, however great, could address.") (citations omitted).

Biogen argues that it will suffer irreparable harm in the form of (1) price erosion, (2) lost sales and market share, and (3) reputational harm if Tyruko is allowed to launch. D.I. 75 at 20-24. While it is true that "price erosion, loss of goodwill, damage to reputation, and loss of business opportunities are all valid grounds for finding irreparable harm," *Celsis*, 664 F.3d at 930 (citations omitted), Biogen's harms are speculative and uncertain. For example, Biogen argues that "the launch of Tyruko would permanently alter the market for Tysabri®, including by causing irreversible price erosion" and that "[t]he pricing effects on Tysabri® if Tyruko launches are difficult to predict and quantify[.]" D.I. 75 at 21. During oral argument, Biogen laid out three scenarios that may occur with the entrance of a biosimilar at a price lower than the reference product: (1) "the reference product will drop its price substantially in view of the biosimilar price

in order to continue to compete;" (2) "the reference product will just lose market share because it can't compete but it will keep its price static but it will lose market share to the new biosimilar entering;" or (3) there is some combination of scenario one and two. Tr. 45 at 3-13. Defendants, however, cite to several sources that "point away from a likely price decline" in 12 to 18 months after the biosimilar launches. D.I. 138 at 23. Accordingly, Biogen has failed to convince the Court that there will be irreparable price erosion and loss of market share before a trial is held in this case.[3]

In fact, some of the sources cited by Biogen's expert himself—Dr. Amitabh Chandra—support Defendants' argument that, during the first 12 to 18 months after a biosimilar launches, the average selling price of the reference product does not materially change. For example, Dr. Chandra relies on Amgen's 2022 Biosimilar Trends Report to support several of his opinions. *See, e.g.*, D.I. 82 ¶ 83. In that same report, it shows that, for at least four reference products, the price was stable 12 to 18 months after a biosimilar entered the market. *See* D.I. 77-1, Ex. XX at -894, 889, 900, 905; D.I. 151, Ex. 1309 at 170:16-178:23. Dr. Chandra also failed to look at this specific time frame—12 to 18 months after a biosimilar launches—to determine the potential harm Biogen will suffer as a result of Tyruko entering the market. D.I. 151, Ex. 1309 85:18-22 (Q: "When you were evaluating the nature of the harm that will result from the entry of a biosimilar natalizumab, what time frame did you evaluate?" A: "It was not my assignment to evaluate -- measure harms over a particular time frame. My assignment was to discuss whether there would be harm; whether the harm was likely to be irreparable."); *see also id.* at 86:14-20 (Q: "And did you try to look at the nature of the harm that would occur specifically at 18 months after entry?" A: "I did not, sir,

[3] The Court will try its best to schedule a trial for this case before April 2025, which is 12 to 18 months after Defendants expect to launch their biosimilar.

because if I was not able to quantify the harms that happened right at entry, it's hard for me to quantify the harms that happened at 18 months.").

[redacted]. *See* D.I. 147-4, Ex. 1057 at -820; *see also id.* at Ex. 1056 at -974 [redacted]). For similar reasons, Biogen's loss of market share argument is insufficient for failing to show that the harm will be immediate and its arguments are too speculative. *Integra Lifesciences Corp. v. Hyperbranch Med. Tech., Inc.*, C.A. No. 15-819-LPS-CJB, 2016 WL 4770244, at *13 (D. Del. Aug. 12, 2016) ("[I]t is well-settled that the 'lost market share must be proven (or at least substantiated with some evidence) in order for it to support entry of a preliminary injunction, because granting preliminary injunctions on the basis of speculative loss of market share would result in granting preliminary injunctions in every patent case where the patentee practices the invention.'" (quoting *Automated Merch. Sys., Inc. v. Crane Co.*, 357 Fed. Appx. 297, 301 (Fed. Cir. 2009))). Thus, Biogen's price erosion and loss of market share arguments do not support a finding of irreparable harm. *See Takeda Pharms. U.S.A., Inc. v. Mylan Pharms. Inc.*, 967 F.3d 1339, 1349 (Fed. Cir. 2020) ("Though we [the Federal Circuit] have recognized that price erosion and loss of market share may in some cases be irreparable injuries, *see Aria Diagnostics, Inc. v. Sequenom, Inc.*, 726 F.3d 1296, 1304 (Fed. Cir. 2013), a bare assertion of irreparable harm is never sufficient to prove such harm or justify the 'extraordinary remedy' of a preliminary injunction, *see Winter*, 555 U.S. at 24.").

Further, the Court is not convinced that any purported harm could not be remedied by damages. "The availability of adequate monetary damages belies a claim of irreparable injury." *Takeda*, 967 F.3d at 1349 (quoting *Frank's GMC Truck Ctr., Inc. v. Gen. Motors Corp.*, 847 F.2d 100, 102-03 (3rd Cir. 1988)).

With respect to reputational harm, Biogen argues "[i]ntroduction of Defendants' infringing ImmunoWELL assay, [redacted] that may be difficult to communicate to the public, *could* cause confusion among physicians and patients, impugn the reliability of Stratify™, and harm Biogen's reputation as the originator of natalizumab." D.I. 75 at 23 (citations omitted) (emphasis added). Notably, Biogen itself states that its reputational harm is wholly speculative. Here too, then, Biogen's reputational harm theory falls short of a clear showing of irreparable harm.

Lastly, Biogen has not satisfied the causal nexus requirement. Causal nexus requires some connection between the alleged infringement and harm such "that the infringing feature drives consumer demand for the accused product." Apple II at 1375. "Driving demand, however, does not require a patented feature to be the only basis of consumer demand." *TEK Glob., S.R.L. v. Sealant Sys. Int'l, Inc.*, 920 F.3d 777, 792 (Fed. Cir. 2019) (citing *Apple Inc. v. Samsung Elecs. Co.*, 735 F.3d 1352, 1363 (Fed. Cir. 2013)). It is enough for the patentee "to show that a significant reason consumers bought its device was the presence of the patented features." *Id.*

There were several patents that covered the composition of and methods of treatment of Tysabri, none of which are asserted for the purposes of this preliminary injunction as they have expired. Tr. at 53:7-17. It is not disputed that the PI patents[4] do not cover the actual product—Tysabri—or its active ingredient—natalizumab. The PI patents disclose an assay for the detection of anti-JCV antibodies (the '641 patent), a method of assessing risk of PML (the '976 and '794 patents), and a method of manufacturing antibodies (the '879 patent). Accordingly, it is Biogen's

[4] Only a subset of Biogen's asserted patents is at issue for Biogen's Motion for Preliminary Injunction—U.S. Patent No. 9,316,641 ("the '641 patent"); U.S. Patent No. 10,119,976 ("the '976 patent"); U.S. Patent No. 11,280,794 ("the '794 patent"); and U.S. Patent No. 9,096,879 ("the '879 patent") (collectively, "the PI patents").

burden to show that a significant reason consumers bought its products was because of the presence of the patented features, i.e., the PI patents.

Here, Biogen argues that "Defendants' own documents and statements to the FDA, the [redacted] D.I. 178 at 15 (quoting D.I. 179-1, Ex. P5 at -640). Defendants argue that Biogen has failed to show that the claimed features of the preliminary injunction patents "are a cause of demand for its now-unpatented natalizumab product" and that "Biogen wrongly conflates demand for JCV testing *generally* (involving a test that uses unpatented technology found in the prior art) with demand for the *patented* features of STRATIFY (a confirmatory step that Biogen concedes is used [redacted] or a .9 threshold that is not in the label and rarely used by neurologists)." D.I. 225 at 12 (emphasis in original). Based on the current record, the Court agrees with Defendants that Biogen has not shown that a significant reason consumers buy its products is because of the presence of the PI patents features.

The Court has reviewed Dr. Chandra's declaration and agrees with Defendants that he had not "evaluated whether the patented features drive demand for the assay or Tysabri" and "he did not analyze whether the launch of the assay (as compared to other factors) increased sales of Tysabri." D.I. 225 at 13 (citing D.I. 226, Ex. 1367 at 11:18-21, 15:21-18:1. 20:12-22:3; D.I. 151, Ex. 1309 at 147:20-148:1). Curiously, from 2015 to 2021, Biogen never identified any of the PI patents as protecting the Tysabri drug in its Form 10-K. D.I. 151, Ex. 1293 at -700, Ex. 1304 at -929, Ex. 1305 at -110, Ex. 1306 at -319, Ex. 1307 at -514, Ex. 1308 at -715; D.I. 151-3, Ex. 1320

[5] Defendants are developing an anti-JCV antibody assay known as "ImmunoWELL JCV IgG Test" ("ImmunoWELL"). D.I. 98 ¶ 79.

at -930. It was not until February 15, 2023—26 days after Biogen filed its motion for preliminary injunction—that Biogen listed three of the four PI patents in its 2022 Form 10-K. D.I. 151-1, Ex. 1314 at -834.

Biogen also appears to misstate the significance of the 0.9 index value in the industry. [redacted]

[redacted]. D.I. 144 (Dr. Pleasure Decl.) ¶¶ 34-37, 57. Biogen's corporate representative, Dr. Robin L. Avila-Carey, confirmed this fact. D.I. 148-1, Ex. 1225 at 100:21-101:1. Furthermore, there is evidence in the record that casts doubt on Biogen's assertion that the index value 0.9 is the standard of care. D.I. 144 (Dr. Pleasure Decl.) ¶¶ 44-49, 70-75, 100. Thus, Biogen's causal nexus arguments are at best attenuated.

For the reasons stated above, Biogen has not made a clear showing that it will suffer irreparable harm. Biogen's alleged harms are not immediate, substantial, or irreparable and Biogen has failed to demonstrate a causal nexus.

ii. Likelihood of Success on the Merits

"Because granting a preliminary injunction requires finding that the moving party has demonstrated a likelihood of success on the merits and that irreparable harm is likely in the absence of an injunction, a trial court may deny a motion based on a patentee's failure to show irreparable harm without analyzing the other factors." *Vertigo Media, Inc. v. Earbuds Inc.*, C.A. No. 21-120-MN, 2021 WL 4806410, at *5 (D. Del. Oct. 14, 2021) (citing *Jack Guttman*, 302 F.3d at 1356; *Chestnut Hill Sound Inc v. Apple Inc.*, C.A. No. 15-261-RGA, 2015 WL 6870037, at *2 (D. Del. Nov. 6, 2015)); *see also Ill. Tool Works, Inc. v. Grip-Pak Inc.*, 906 F.2d 679, 682 n.3 (Fed. Cir. 1990) ("absence of irreparable harm ... ma[kes] unnecessary a consideration of ... [the] likelihood of success in proving infringement."). That said, the parties spent most of their oral argument time

arguing about this factor—the likelihood of success on the merits. Thus, the Court will briefly address some of those arguments below.

"To establish a likelihood of success on the merits, a patentee must show that it will likely prove infringement of the asserted claims and that its infringement claim will likely withstand the alleged infringer's challenges to patent validity and enforceability. A preliminary injunction should not issue if the accused infringer 'raises a substantial question concerning either infringement or validity.'" *Metalcraft*, 848 F.3d at 1364 (citations omitted). In other words, the Court should not issue a preliminary injunction if Defendants "assert[] an infringement or invalidity defense that the patentee cannot prove 'lacks substantial merit.'" *Amazon.com, Inc.*, 239 F.3d at 1350-51 (quoting *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1364 (Fed. Cir. 1997)).

1. The '641 Patent

The core dispute between the parties is whether Defendants' ImmunoWELL Assay will infringe claims 1 and 2 of the '641 patent under the Doctrine of Equivalents ("DOE"). Tr. 12:16-21.

The '641 patent, titled "Assay for JC Virus Antibodies," discloses methods for testing the presence of JCV in samples. For the purposes of the preliminary injunction, Biogen asserts claims 1 and 2 of the '641 patent, which recite:

> 1. A method of evaluating a subject for presence of JC virus antibodies, said method comprising:
>
> a. contacting a biological sample obtained from a subject with highly purified VP1 particles (HPVLPs) in solution under conditions suitable for binding of a JC Virus (JCV) antibody in the sample to an HPVLP, thereby providing a pre-incubated sample;

b. contacting the pre-incubated sample with HPVLPs immobilized on a solid substrate under conditions suitable for binding of a JCV antibody in the sample to an HPVLP;

c. detecting the level of JCV antibody in the pre-incubated sample binding to the immobilized HPVLPs; and

d. comparing the detected level of JCV antibody in the pre-incubated sample binding to the immobilized HPVLPs to a reference value, which corresponds to a detected level of JCV antibody in a pre-incubated control sample, wherein the pre-incubated control sample was pre-incubated in the absence of HPVLPs in solution, thereby providing a pre-incubated control sample, and wherein the pre-incubated control sample was contacted with HPVLPs immobilized on a solid substrate under conditions suitable for binding of a JCV antibody in the sample to an HPVLP

thereby evaluating the subject for presence of JC virus antibodies.

2. The method of claim 1, wherein the biological sample obtained from the subject is classified as positive for JCV antibody when the level of JCV antibody in the pre-incubated biological sample binding to the immobilized HPVLPs is lower than the reference value by more than a predetermined amount; and wherein the biological sample obtained from the subject is classified as negative for JCV antibody when the level of JCV antibody in the pre-incubated biological sample binding to the immobilized HPVLPs is lower than the reference value by less than a predetermined amount.

'641 patent, claims 1 and 2.

There is no dispute that Biogen's anti-JCV antibody assay Stratify practices the '641 patent. D.I. 75; D.I. 138. Stratify has two parts: (1) a detection assay, which determined whether a patient had JCV antibodies; and (2) a confirmation assay, which assessed whether a patient which initially had indeterminate results had JCV antibodies. The question is whether under DOE, Defendants' ImmuoWELL performs substantially the same function in substantially the same way with substantially the same result as Biogen's Stratify. *See Intendis v. Glenmark Pharms.*, 822 F.3d 1355, 1360-61 (Fed. Cir. 2016). Defendants argue that ImmunoWELL does not use

"HPVLPs in solution" to make a "pre-incubated sample" and instead uses chicken IgY antibodies without pre-incubation. D.I. 138 at 8. According to Defendants, these differences make their ImmunoWELL substantially different from what the claims require. Biogen disagrees and argues:

> [chicken] IgY antibodies and HPVLPs perform substantially the same function (to compete for binding with the immobilized HPVLPs to confirm the presence of anti-JCV antibodies in the sample); operate in substantially the same way (via a competition assay that involves preparing a solution containing a patient sample and a competitive binding agent under conditions that will permit binding to HPVLPs, then contacting that solution to immobilized HPVLPs); and achieve substantially the same result (where the comparison of the results of the competition assay to a control determines presence of JCV antibodies).

D.I. 75 at 11-12.

Here, on the current record, the Court concludes that Defendants' ImmuoWELL does not perform substantially the same function in substantially the same way with substantially the same result as Biogen's Stratify. Defendants' ImmunoWELL uses a different competitive binding agent than Stratify. ImmunoWELL uses a chicken IgY antibody while Stratify uses HPVLPs in solution. The Court is not convinced that chicken IgY antibodies perform substantially the same function in substantially the same way, with substantially the same results as the claimed HPVLPs. Chicken IgY antibodies are not equivalent biological molecules to HPVLPs. One is an antibody, while the other is an antigen.[6]

The chicken IgY antibodies and the HPVLPs in solution also do not perform the same function in the same way. The HPVLPs used in Stratify bind to JCV antibodies during a pre-

[6] During oral argument, Defendants' counsel provided a brief explanation regarding the difference between an antibody and an antigen: "An antibody is not the same thing an as antigen. An antibody actually binds to an antigen. That is the thing that's the target of the antibody, they are opposite sides of the coin not the same side of the coin." Tr. 67 at 19-22. Biogen's expert—Dr. Raphael Viscidi—also agreed that antibodies and antigens are not "equivalent biological molecules." D.I. 226, Ex. 1366 at 305:17-306:3.

incubation step, while the chicken IgY antibodies in ImmunoWELL do not. For Stratify, after the patient sample makes contact with the HPVLPs in a solution, the JCV antibodies found in the patients' sample must bind to the HPVLP "under conditions suitable for binding." '641 patent, claim 1. In contrast, the ImmunoWELL does not have this pre-incubation step. The patient sample and the chicken IgY antibodies are mixed together at the same time and there are no HPVLPs in solution. Tr. at 63:23-64:14.

Furthermore, preliminary injunctions based on infringement by DOE are not common because the "highly factual inquiry rarely comes clear on a premature record." *Jeneric/Pentron, Inc. v. Dillon Co., Inc.*, 205 F.3d 1377, 1384 (Fed. Cir. 2000). For the reasons stated above, the Court cannot conclude, at this stage of the litigation for purposes of a preliminary injunction, that Defendants' ImmunoWELL is substantially equivalent to Biogen's Stratify. Thus, Defendants have raised a substantial question concerning infringement.

3. The '976 and '794 Patents

Biogen argues that Defendants will induce infringement of at least claims 9, 11, 21, and 26 of the '976 patent and claim 1 of the '794 patent. According to Biogen, Defendants will induce infringement of these patents "by directing physicians to treat MS patients with Tyruko" through its Tyruko's materials, like its label, REMS material, ImmunoWELL JCV assay label, and publications. D.I. 75 at 14-18.

Both the '976 and '794 patents, titled "Method of Assessing Risk of PML," are directed to "methods of assessing a patient's risk of developing [PML]." '976 patent at 1:15-17. The '794

patent is a continuation of the '976 patent. For the purposes of the preliminary injunction, Biogen asserts claims 9[7], 11, 21, and 26[8] of the '976 patent, which recite:

> 1. A method of evaluating a patient's risk of developing Progressive Multifocal Leukoencephalopathy (PML), the method comprising:
>
> determining a JC virus (JCV) antibody titer in a biological sample from the patient, wherein the patient has a negative prior immunosuppressant exposure classification; wherein
>
> if the titer is determined to be above a pre-determined level, the patient is determined to be at a higher risk of developing PML, and wherein
>
> if the titer is determined to be at or below an index level of 0.9, the patient is determined to be at a lower risk of developing PML.
>
> 7. The method of claim 1, wherein if the patient is determined to be at lower risk of developing PML, then the patient is classified as being suitable for treatment with an anti-VLA-4 therapy.
>
> 9. The method of claim 7, wherein the anti-VLA-4 therapy is a natalizumab therapy.
>
> 11. The method of claim 1, further comprising determining a second or further JCV antibody titer in a second or further biological sample from the patient, wherein the second or further biological sample is obtained from the patient at a period of time after the first biological sample, and wherein:
>
> if the titer is determined to be above zero, but at or below a pre-determined level in the two or more samples, the patient is determined to be at a lower risk of developing PML, and
>
> if the titer is determined to be above a pre-determined level in the two or more samples, the patient is determined to be at a higher risk of developing PML

[7] Asserted claim 9 of the '976 patent depends from claim 7, which depends from claim 1.

[8] Asserted claim 26 depends from claim 25.

> 21. The method of claim 11, wherein the patient as has received an anti-VLA-4 therapy during the period of time
>
> 25. A method of treating an MS patient, comprising:
>
> > administering an anti-VLA4 antibody responsive to a determination of a JC virus (JCV) antibody titer at or below an index level of 0.9 in a patient having a negative prior immunosuppressant exposure classification, thereby treating the patient.
>
> 26. The method of claim 25, wherein the anti-VLA4 antibody is natalizumab.

'976 patent, claims 1, 7, 9, 11, 21, 25, and 26.

For the purposes of the preliminary injunction, Biogen asserts claim 1 of the '794 patent, which recites:

> 1. A method of treating a subject in need thereof with natalizumab therapy, the method comprising:
>
> > a) determining an anti-JC virus (JCV) antibody titer in two or more biological samples obtained from the subject over a period of time, wherein the titer is determined to be at or below an index value of 0.9 in the two or more samples; and
> >
> > b) administering natalizumab to the subject, thereby treating the subject with the natalizumab therapy, wherein the subject suffers from multiple sclerosis or a relapsing form of multiple sclerosis.

'794 patent, claim 1.

To support its induced infringement argument, Biogen relies on the proposed Tyruko label and REMS materials, which "(i) direct physicians to administer Tyruko to suitable MS patients who are determined to be at a lower risk of developing PML; where (ii) the patient is determined to be at lower risk of PML if the patient's JCV antibody titer is determined to be at or below an index level of 0.9, when the patient has no prior immunosuppressant exposure." D.I. 75 at 17.

Both Tysabri's label and REMS materials, however, do not recite the 0.9 index value claim limitation. *See* D.I. 144 (Dr. Pleasure Decl.) ¶¶ 34-38, 57, 84-86; D.I. 148-1, Ex. 1225 at 100:21-101:1, 124:23-125:4, 161:8-17; D.I. 148-3, Ex. 1235 at 58:22-25. Because the labels and REM materials for Tysabri and Tyruko will be similar, Tyruko's label and REMs materials also do not recite the 0.9 index value. D.I. 76-1, Ex. HH (proposed Tyruko label); *id.*, Ex. W (Tyruko REMS material).

Under 35 U.S.C. § 271(b), "[w]hoever actively induces infringement of a patent shall be liable as an infringer." Direct infringement is a predicate for induced infringement. *See Vanda Pharms. Inc. v. West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1129 (Fed. Cir. 2018); *Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 845 F.3d 1357, 1364-65 (Fed. Cir. 2017). "It also 'must be established that the defendant possessed specific intent to encourage another's infringement and not merely that the defendant had knowledge of the acts alleged to constitute inducement.'" *Vanda*, 887 F.3d at 1129 (quoting *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006) (en banc in relevant part) (internal quotation omitted)). When undertaking this inquiry, the Court must consider the product's label as a whole. *Lundbeck v. Lupin Ltd.*, C.A. No. 18-88-LPS, 2021 WL 4944963, at *105 (D. Del. Sept. 30, 2021). "When 'the label, taken in its entirety, fails to recommend or suggest to a physician that [the drug] is safe and effective for inducing the claimed combination of effects in patients,' intent to induce infringement is lacking." *Id.* (quoting *Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316, 1324 (Fed. Cir. 2012)). "Therefore, the inducement analysis is guided by whether the proposed generic labeling, taken in its entirety, encourages, recommends, or promotes an infringing use." *Id.* (citing *Takeda Pharms. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015)).

The Federal Circuit's *GlaxoSmithKline LLC v. Teva Pharms. USA, Inc.*, 7 F.4th 1320 (Fed. Cir. 2021) also re-affirmed that, if a party alleges that the drug label induces infringement by physicians, *the label* "'must encourage, recommend, or promote infringement.'" *Id.* at 1327 (quoting *Takeda*, 785 F.3d at 631). Biogen improperly attempts to recast *GlaxoSmithKline* "as supporting that the label need not recite the claim elements." D.I. 225 at 7 (citing D.I. 178 at 10).[9] In *GlaxoSmithKline*, the Court credited the expert's testimony when he "marched through Teva's label explaining how it met the limitations of claim 1" and "provided testimony that Teva's partial label instructed the claimed treatment and use." *GlaxoSmithKline*, 7 F.4th at 1329. In other words, the expert provided element-by-element testimony that Teva's partial label explicitly instructed the claimed elements. *Id.*[10]

Because Tyruko's proposed label fails to recite each and every claim limitation, specifically the 0.9 index value, Tyruko's label does not induce infringement because it does not encourage, recommend, or promote an infringing use.

4. The '879 Patent

Biogen argues that Defendants infringe the '879 patent because Defendants supplement the Tyruko cell culture with glutamine to reduce serine misincorporation during manufacturing. D.I. 75 at 19-20. Defendants disagree and argue that they do not add asparagine or a metabolic precursor of asparagine in a feed medium, and "even if glutamine is considered a metabolic

[9] The Federal Circuit has also held that "'vague' instructions that require one to 'look outside the label to understand the alleged implicit encouragement' do not, without more, induce infringement." *Eli Lilly*, 845 F.3d at 1369 (quoting *Takeda*, 785 F.3d at 632, 634).

[10] The Federal Circuit in *GlaxoSmithKline* held that its opinion is a "narrow, case-specific review." *GlaxoSmithKline*, 7 F.4th at 1326.

precursor of asparagine, as Biogen argues, Biogen has not shown that the glutamine in Sandoz's process, in fact, *reduces* serine misincorporation." D.I. 138 at 18.

The '879 patent, titled "Method of Supplementing Culture Media to Prevent Undesirable Amino Acid Substitutions," discloses "a method to minimize substitutions of amino acids during translation of a protein/polypeptide of interest." '879 patent at 5:33-37. More specifically, "the invention provides a method of minimizing the substitution of asparagine residues by serine residues by altering the concentration of asparagine, glutamine, and/or serine in the culture media." *Id.* at 5:37-40. Asserted claim 13 depends from claim 12, which depends from claim 1. As such, all three claims are recited below:

> 1. A method for preventing misincorporation of serine in place of asparagine during translation of a polypeptide of interest in a mammalian cell, comprising:
>
> (a) providing a culture comprising the cell in growth media, wherein the culture has a volume of at least 500 liters;
>
> (b) supplementing the culture with a feed medium comprising asparagine, or a metabolic precursor thereof, in an amount sufficient to reduce serine misincorporation; and
>
> (c) maintaining the supplemented culture under conditions appropriate for expression of the polypeptide of interest, wherein the polypeptide of interest expressed by the cell comprises less than about 3% serine misincorporated in place of asparagine.
>
> 12. The method of claim 1, wherein the feed medium comprises glutamine in an amount sufficient to reduce serine misincorporation.
>
> 13. The method of claim 12, wherein the supplemented culture comprises between about 1 mM to about 10 mM glutamine.

'879 patent, claims 1, 12, and 13.

The parties do not dispute that Defendants use [redacted] of glutamine during the manufacturing process of Tyruko. D.I. 75 at 20; D.I. 225 at 11. Claim 1, which claim 12 depends from, states that, during the claimed method, the manufacturer must "supplement[] the culture with a feed medium comprising asparagine, or a metabolic precursor thereof, in an amount sufficient to reduce serine misincorporation." '879 patent, claims 1, 12. The Court finds that there is no evidence on the current record that Defendants use glutamine to *reduce* serine misincorporation.[11] According to Dr. Michael Butler, "[g]lutamine was not added to growth or batch medium during the biosimilar natalizumab manufacturing process with serine misincorporation in mind, but rather to [redacted] D.I. 142 ¶ 72; *see also* D.I. 140 (Dr. Derlacz Decl.) ¶ 8 ("Glutamine is only added to the [redacted] and the reason it is added is to promote [redacted] Confusingly, during oral argument, Biogen argued that Defendants are improperly contending that the preamble is limiting, and because the preamble is not limiting, there is no supplementation requirement of the purposes of reducing misincorporation. Tr. at 39-40. Biogen, however, ignores the fact that the supplementation to reduce serine misincorporation is a limitation present in the body of the claims. '879 patent, claim 1. Thus, with respect to the '879 patent, Biogen has not persuaded the Court that it is likely to succeed in proving infringement.

For the reasons stated above, Biogen has failed to carry its burden of demonstrating a likelihood of success on the merits with respect to all of the PI patents.

[11] For the purposes of this motion, the Court will assume glutamine is considered a metabolic precursor of asparagine. This Memorandum Order, however, does not prevent Defendants from pursuing this argument later during the litigation.

iii. Remaining Factors

While the Court need not address the third factor—the balance of hardships—and fourth factor—whether an injunction is in the public interest, *Polymer Techs., Inc. v. Bridwell*, 103 F.3d 970, 973-74 (Fed. Cir. 1996), the Court will briefly address why the fourth factor also weighs in favor of denying the motion for preliminary injunction. "[A]lthough there exists a public interest in protecting rights secured by valid patents, the focus of the district court's public interest analysis should be whether there exists some critical public interest that would be injured by the grant of preliminary relief." *Hybritech*, 849 F.2d at 1458. "For pharmaceutical drugs that prolong and save lives, there is a critical public interest in affordable access to those drugs." *Genentech, Inc. v. Immunex Rhode Island Corp.*, 395 F. Supp. 3d 357, 366 (D. Del. 2019), *aff'd*, 964 F.3d 1109 (Fed. Cir. 2020). For that reason, the fourth factor also weighs in favor of denying the motion for preliminary injunction.

b. Biogen's Motion to Strike and Defendants' Cross-Motion to Strike

Biogen seeks to strike the following: (1) paragraphs 17-19 and 21-41 of the Declaration of Alex Brill (the "Brill Declaration") (D.I. 141); (2) paragraphs 108-153 and 166-174 of the Declaration of Samuel J. Pleasure, M.D., Ph.D. (the "Pleasure Declaration") (D.I 144); and (3) the Declaration of Rafal Derlacz (the "Derlacz Declaration") in its entirety (D.I. 140). D.I. 162. The Court did not rely on paragraphs 17-19 and 21-41 of the Brill Declaration or paragraphs 108-153 and 166-174 of the Pleasure Declaration. Thus, the Court need not address the merits of Biogen's Motion to Strike as they relate to these Declarations and the Court will deny them as moot.

With respect to the Derlacz Declaration, Biogen argues that this declaration should be stricken in its entirety "in view of Polpharma's improper one-sided discovery approach in this case." D.I. 163 at 2. This Court disagrees. The facts do not suggest that Polpharma has been

"dodging discovery" or concealing Dr. Derlacz. D.I. 172 at 1-2. For example, several documents produced by Sandoz named Dr. Derlacz. *See, e.g.*, *id.* at Ex. C. On December 9, 2022, Sandoz's 30(b)(6) witness testified during her deposition that she had spoken to Dr. Derlacz regarding the development and manufacturing process for Tyruko. *Id,* at Ex. D at 18:9-14, 19:4-21:6. Thus, Biogen's motion to strike the Derlacz Declaration in its entirety is denied.

With respect to Defendants' Cross-Motion to Strike, because the Court denies Biogen's Motion for Preliminary Injunction, this motion is denied as moot.

IV. CONCLUSION[12]

For the foregoing reasons, the Court denies Biogen's motion for preliminary injunction and denies as moot Defendants' cross-motion to strike, and denies-in-part and denies as moot-in-part Biogen's motion to strike.

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[12] A week after this Court heard oral argument on Biogen's Motion for Preliminary Injunction, Biogen filed a revised proposed order "to add reference to Stratify™" because the original proposed order (D.I. 74-1) "inadvertently omitted enjoining use of Biogen's Stratify™ assay." D.I. 257. Defendants argue that this revised proposed order "is improper." D.I. 258. Biogen's revised proposed order does not change this Court's analysis for denying the preliminary injunction as discussed above.

WHEREFORE, at Wilmington this 20th day of June, 2023, **IT IS HEREBY ORDERED** that:

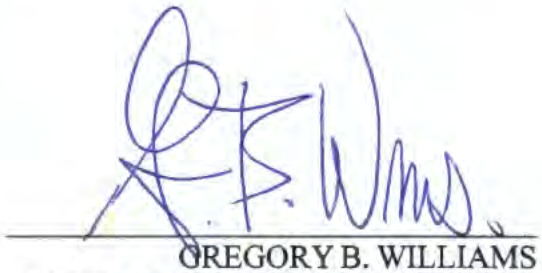
1. Biogen's Motion for Preliminary Injunction (D.I. 74) is **DENIED**.

2. Biogen's Motion to Strike (D.I. 162) with respect to the Brill and Pleasure Declaration is **DENIED** as **MOOT** and **DENIED** with respect to the Derlacz Declaration.

3. Defendants' Cross-Motion to Strike (D.I. 170) is **DENIED** as **MOOT**.

4. Because this Memorandum Order is filed under seal, the parties shall meet and confer and submit a joint proposed redacted version no later than seven (7) days after the date of this Memorandum Order. In the absence of a timely request compliant with applicable standards, the Court will unseal the entire Memorandum Order.

5. Not later than thirty (30) days from the date of this Memorandum Order, the parties shall meet and confer and file a joint proposed Scheduling Order in this action consistent with the applicable form Scheduling Order of Judge Williams, which is posted at http://www.ded.uscourts.gov (*See* Chambers, Judge Williams, Forms), along with a cover letter requesting the Court to enter the joint proposed Scheduling Order (if there are no disputes or other issues concerning scheduling that the Court needs to address) or to schedule the Scheduling Conference. If there are disputes or other issues the Court needs to address in the joint proposed Scheduling Order, in the cover letter, the parties shall direct the Court to the paragraph numbers in the joint proposed Scheduling Order which those appear.



GREGORY B. WILLIAMS
UNITED STATES DISTRICT JUDGE