IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

TAKEDA PHARMACEUTICALS U.S.A., INC.,	)	
Plaintiff,	)	
v.	)	Civ. No. 14-268-SLR
WATSON LABORATORIES, INC.,	)	
Defendant.	)	

MEMORANDUM ORDER

At Wilmington this 4th day of September, 2014, having reviewed plaintiff Takeda Pharmaceuticals' ("Takeda") motion for leave to file an amended complaint, and the papers filed in connection therewith;

IT IS ORDERED that said motion for leave to find an amended complaint (D.I. 19) is granted, for the reasons that follow:

1. **Background.** Takeda is the holder of approved New Drug Application ("NDA") Nos. 22-351 and 22-353 for the manufacture and sale of single-ingredient oral colchicine[1] for the prevention and treatment of gout flares. (*See* D.I. 20 at 3) Takeda also holds NDA No. 22-352 for the manufacture and sale of single-ingredient oral colchicine for the treatment of Familial Mediterranean Fever ("FMF").[2] In conjunction

[1]A plant extract that helps to decrease the inflammatory response associated with gout.

[2]"A rare (or orphan) disease" defined by the National Institutes of Health as one "generally considered to have a prevalence of fewer than 200,000 affected individuals in the United States." (D.I. 21, ex. A)

with the approval of its NDAs, Takeda listed seventeen patents in the publication titled "Approved Drug Products with Therapeutic Equivalence Evaluations" (known as the "Orange Book") for Colcrys®. (D.I. 19, ex. 1 at ¶ 17)[3] Fourteen patents – U.S. Patent Nos. 7,619,004; 7,601,758; 7,820,681; 7,915,269; 7,964,647; 7,981,938; 8,093,296; 8,097,655; 8,415,395; 8,415,396; 8,440,721; 8,440,722; 7,964,648 ("the '648 patent"), and 8,093,297 ("the 297 patent") – include claims directed to the treatment of gout (the "gout patents"). (*Id.* at ¶ 15) Five patents – U.S. Patent Nos. 7,906,519; 7,935,731; 8,093,298; the '648 patent; and the 297 patent – include claims directed to the treatment of FMF (the "FMF patents"). (*Id.* at ¶ 14) The '648 and '297 patents include claims directed to the treatment of both gout and FMF.

2. On or about January 31, 2014, Takeda received a Notice Letter, dated January 30, 2014, from Watson Laboratories ("Watson") informing it that Watson had filed an Abbreviated New Drug Application ("ANDA") seeking approval to market a generic version of Colcrys® for the treatment and prevention of gout flares prior to the expiration of Takeda's gout patents. (*Id.* at ¶¶ 25-26) The Notice Letter included a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("Paragraph IV Certification") certifying that the gout patents are invalid or would not be infringed by Watson's proposed product. (*See id.* at ¶ 25) In response, Takeda filed a complaint on February 27, 2014 alleging fourteen counts of infringement of the gout patents pursuant to 35 U.S.C. § 271. (*Id.* at ¶ 26; D.I. 1)

3. On May 13, 2014, Takeda received a second Notice Letter, dated May 9,

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[3]Takeda's Orphan Drug exclusivity for Colcrys® expires on July 29, 2016. (D.I. 19, ex. 1 at ¶ 11)

2014, informing it that Watson had amended its ANDA to seek approval for treatment of FMF and to "carve out[4]," or disavow, gout as a treatment indication. (*See id.* at ¶¶ 28-29) The Paragraph IV Certification included in the second Notice Letter was limited to the five FMF patents. (*Id.* at ¶ 28) The second Notice Letter "further informed Takeda that [Watson's] proposed labeling does not include dosing instructions or safety information for the treatment or prevention of gout flares." (*Id.* at ¶ 29) Takeda alleges, "[u]pon information and belief, Watson submitted a label amendment to the FDA . . . for the purpose of limiting FDA approval of its Proposed Product to the treatment of FMF and that, pursuant to § 355(j)(2)(A)(viii), Watson seeks to carve out from the FDA approved Colcrys® label . . . information regarding the treatment and prevention of gout flares . . . ." (*Id.* at ¶ 30)

4. On May 28, 2014, Takeda filed the present motion seeking to amend its complaint to add five counts (counts I-V) of infringement of the patents directed to treating FMF under § 271(b) and (e). (D.I. 19) Takeda also seeks to modify its counts with respect to the gout patents to seek a declaratory judgment that Watson's manufacture and/or sale of its proposed ANDA product will contributorily infringe the gout patents under § 271(c). (*Id.*) Specifically, Takeda seeks a declaratory judgment that Watson, upon approval of its proposed ANDA product and expiration of Takeda's Orphan Drug exclusivity, "will contribute to the infringement of the [gout patents] by

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[4]"Where the Orange Book lists a method of use patent that 'does not claim a use for which the applicant is seeking approval,' an applicant may instead submit a statement under 21 U.S.C. § 355(j)(2)(A)(viii) averring that the ANDA excludes all uses claimed in the patent ('Section viii statement')." *AstraZeneca Pharms. LP v. Apotex Corp.*, 669 F.3d 1370, 1374 (Fed. Cir. 2012) (citing *Warner–Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1360–61 (Fed. Cir. 2003)).

others, by offering to sell, selling, or distributing within the United States or importing into the United States generic Colcrys® for the treatment and prevention of gout flares" in violation of § 271(c). (*Id.*, ex. 1 at counts IV-XVIII)

5. In support of its motion to amend, Takeda alleges that physicians will prescribe a drug for "off-label" uses of colchicine "whether or not that indication appears on the generic label" (*Id.* at ¶ 21), and that pharmacists will substitute Watson's generic colchicine for Takeda's branded drug "irrespective of whether the generic drug is FDA-approved for the indication for which the brand drug was prescribed." (*Id.* at ¶ 22) Takeda has provided the following allegation relating to the percentage of the prevalence of use of colchicine to treat FMF:

> According to national prescription data from Encuity Research, for the ten-year period between June 2004 and June 2013, approximately only 15,000 colchicine prescriptions were written for FMF patients in the United States over the past ten years. According to this national prescription data, less than one percent (0.16%) (or 1 in 625) of patients prescribed colchicine were being treated for FMF. And among prescriptions written for FDA-approved uses for colchicine—gout and FMF—approximately 0.18% (or 1 in 555) of the prescriptions were for FMF, while approximately 99.82% of the prescriptions were for gout.

(*Id.* at ¶ 19)[5]

6. The court has not entered a scheduling order and discovery has not begun. A Rule 16 Conference was held on June 2, 2014.

7. **Standard.** Rule 15(a) of the Federal Rules of Civil Procedure provides that

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[5]Takeda has submitted data that on average, about 0.16% of approximately 9.2 million total colchicine prescriptions (for FMF, gout, and unapproved uses) written in the United States between 2004 and 2013 has been for the treatment of FMF. (D.I. 21, ¶¶ 4-7, exs. B-E)

the court "should freely give leave [to amend the pleadings] when justice so requires." Fed. R. Civ. P. 15(a)(2). The factors to consider in weighing a motion for leave to amend are well-settled: (1) whether the amendment has been unduly delayed; (2) whether the amendment would unfairly prejudice the non-moving party; (3) whether the amendment is brought for some improper purpose; and (4) whether the amendment is futile. *See Foman v. Davis*, 371 U.S. 178, 182 (1962). Courts "ha[ve] discretion to deny a motion to amend for reasons of 'undue delay, bad faith or dilatory motive on the part of the movant, repeated failure to cure deficiencies by amendments previously allowed, undue prejudice to the opposing party by virtue of allowance of the amendment, futility of amendment, etc.'" *Merck & Co., Inc. v. Apotex, Inc.*, 287 Fed. App'x 884, 888 (Fed. Cir. 2008) (quoting *Foman*, 371 U.S. at 182).

8. **Analysis.** As Watson does not oppose Takeda's proposed amendment to counts I-III, and opposes new counts IV and V only to the extent that they seek a declaratory judgment of contributory infringement under § 271(c) based on the gout patents[6] (D.I. 29 at 8 n.4), Takeda's motion is granted with respect to the addition of claims directed to infringement of the FMF patents under § 271(b) and (e). With respect to the remaining counts directed to the gout patents, Watson argues that the court should deny Takeda's motion as futile because: (1) the court lacks subject matter jurisdiction over the new declaratory judgement allegations; and (2) Takeda has failed to state a claim for contributory infringement for which relief can be granted. (D.I. 29 at 9) There is no dispute that Takeda does not have a viable claim under § 271(e)(2) as

[6]Counts IV and V refer to the '648 and '297 patents – those directed to the treatment of both FMF and gout.

Watson only seeks regulatory approval directed to the treatment of FMF, and "a patented method of using a drug can only be infringed under § 271(e)(2) by filing an ANDA that seeks approval to market the drug for that use." *AstraZeneca Pharms. LP v. Apotex Corp.*, 669 F.3d 1370, 1379 (Fed. Cir. 2012) (citing *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1358-59 (Fed. Cir. 2003)). The question before the court, therefore, is whether Takeda may properly add claims for a declaratory judgment that Watson's proposed ANDA product will infringe the gout patents under § 271(c).

9. The Declaratory Judgment Act requires an actual controversy between the parties before a federal court may exercise jurisdiction. 28 U.S.C. § 2201(a). A plaintiff bringing an action for declaratory judgment must prove, by a preponderance of the evidence, that an actual controversy exists. *See Shell Oil Co. v. Amoco Corp.*, 970 F.2d 885, 887 (Fed. Cir. 1992). An actual controversy exists where "the facts alleged, under all the circumstances, show that there is a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." *MedImmune, Inc. v. Genentech, Inc.*, 549 U.S. 118, 127 (2007) (quoting *Maryland Cas. Co. v. Pac. Coal & Oil Co.*, 312 U.S. 270, 273, (1941)). This is not a bright-line test. *See, e.g., Maryland Cas.*, 312 U.S. at 273; *Sony Elecs., Inc. v. Guardian Media Techs., Ltd.*, 497 F.3d 1271, 1283 (Fed. Cir. 2007).

10. "[T]he phrase 'case of actual controversy' in the [Declaratory Judgment] Act refers to the type of 'Cases' and 'Controversies' that are justiciable under Article III." *MedImmune*, 549 U.S. at 127 (citing *Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227 (1937)). Consequently, the analysis of whether "a case of actual controversy" exists is

essentially an analysis of whether Article III standing exists. *See generally id.*; *see also, e.g.*, *Sandisk Corp. v. STMicroelectronics, Inc.*, 480 F.3d 1372, 1381 (Fed. Cir. 2007); *Micron Tech., Inc. v. Mosaid Techs., Inc.*, 518 F.3d 897, 901 (Fed. Cir. 2008). For Article III standing to exist, a plaintiff must show "injury in fact, connection between the challenged conduct and the injury, and redressability of the injury by the requested remedy." *Allergan, Inc. v. Alcon Labs., Inc.*, 324 F.3d 1322, 1331 (Fed. Cir. 2003) (citing *Steel Co. v. Citizens for a Better Env't*, 523 U.S. 83, 103-04 (1998)).

11. As noted above, the ultimate question that must be addressed "is whether the facts alleged, under all the circumstances, show that there is a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." *MedImmune*, 549 U.S. at 127 (quoting *Maryland Cas.*, 312 U.S. at 273). Certainly the parties to this litigation have adverse legal interests. And, at the commencement of these ANDA proceedings initiated by Watson's Notice Letter, the parties undeniably had a substantial controversy amenable to adjudication. The issue at bar is whether the court is bound by Watson's representations to the FDA that it will not market colchicine for the prevention and treatment of gout flares, even when all the realities of the market indicate otherwise.

12. In this regard, there can be no dispute that "off-label prescribing - the prescription of a medication in a manner different from that approved by the FDA - is legal and common." Randall S. Stafford, *Regulating Off-Label Drug Use - Rethinking the Role of the FDA*, 358 NEW ENG. J. MED. 1427, 1427 (2008) ("Stafford"). *See generally Buckman Co. v. Plaintiffs' Legal Committee*, 531 U.S. 341, 350-51 and n.5

(2001). Indeed, it has been suggested that the FDA itself has a "permissive attitude toward the promotion of off-label uses of drugs." *See* Stafford at 1428.

13. Looking at the circumstances of record, it is at least plausible, if not predictable, that Watson's generic products will be sold off-label. As noted, this litigation commenced with Watson filing a Notice Letter stating that it was seeking approval for a generic version of Colcrys® for the treatment and prevention of gout flares, meaningful preparation towards infringing activity.[7] For Watson to forego the more lucrative gout market and settle only for the nominal FMF market is not a credible scenario, especially where the "off-label" use for gout has been found by the FDA to be safe and effective, i.e., health risks are of minimal concern to prescribing physicians.

14. Under these unique circumstances, the court finds that Takeda has demonstrated, by a preponderance of the evidence, that the off-label sale of Watson's generic version of Colcrys® for the treatment and prevention of gout flares is likely. To put the point more bluntly, where a party is suspected of gaming the statutory regime in order to gain an economic advantage not contemplated by Congress, it is appropriate to recognize that an actual controversy exists of sufficient immediacy and reality to warrant the issuance of a declaratory judgment.

15. **Conclusion.** For the foregoing reasons, Takeda's motion to amend is granted. (D.I. 19)

United States District Judge

[7] *See Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1571 (Fed. Cir. 1997).