IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

TAKEDA PHARMACEUTICALS U.S.A., INC., Plaintiff, v. PAR PHARMACEUTICAL COMPANIES, INC. and PAR PHARMACEUTICAL, INC., Defendants.	)	Civ. No. 13-1524-SLR
TAKEDA PHARMACEUTICALS U.S.A., INC., Plaintiff, v. AMNEAL PHARMACEUTICALS, LLC, Defendant.	)	Civ. No. 13-1729-SLR

MEMORANDUM ORDER

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

IT IS ORDERED that said motions for leave to find an amended complaint (Civ. No. 13-1524, D.I. 53; Civ. No. 13-1729, D.I. 36)[1] are granted, for the reasons that follow:

[1]When citing documents from both cases, the court lists the D.I. number for 13-1524 followed by the D.I. number for 13-1729.

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[2] for the prevention and treatment of gout flares. (*See* D.I. 54 at 3; D.I. 37 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").[3] (D.I. 54 at 3; D.I. 37 at 3) In conjunction 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®. (*See* D.I. 53, ex. 1 at ¶ 21; D.I. 36, ex. 1 at ¶ 17)[4] Fourteen patents – U.S. Patent Nos. 7,619,004 ("the '004 patent"); 7,601,758 ("the '758 patent"); 7,820,681 ("the '681 patent"); 7,915,269 ("the '269 patent"); 7,964,647 ("the '647 patent"); 7,981,938 ("the '938 patent"); 8,093,296 ("the '296 patent"); 8,097,655 ("the '655 patent"); 8,415,395 ("the '395 patent"); 8,415,396 ("the '396 patent"); 8,440,721 ("the '721 patent"); 8,440,722 ("the '722 patent"); 7,964,648 ("the '648 patent"); and 8,093,297 ("the '297 patent") – include claims directed to the treatment of gout (the "gout patents"). (D.I. 53, ex. 1 at ¶ 19; D.I. 36, ex. 1 at ¶ 15) Five patents – U.S. Patent Nos. 7,906,519 ("the '519 patent"); 7,935,731 ("the '731 patent"); 8,093,298 ("the '298 patent"); the '648

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

[3]"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. 55, ex. A; D.I. 38, ex. A)

[4]Takeda's Orphan Drug exclusivity for Colcrys® expires on July 29, 2016. (D.I. 53, ex. 1 at ¶ 15; D.I. 36, ex. 1 at ¶ 11)

patent, and the '297 patent – include claims directed to the treatment of FMF (the "FMF patents"). (D.I. 53, ex. 1 at ¶ 18; D.I. 36, ex. 1 at ¶ 14) The '648 and '297 patents include claims directed to the treatment of both gout and FMF.

2. **Par Pharmaceutical, Inc. ("Par").** In December 2011, Par sought approval of an Abbreviated New Drug Application ("ANDA") for a generic version of Colcrys® prior to the expiration of Takeda's patent rights. (D.I. 53, ex. 1 at ¶ 28) On February 23, 2012 and March 15, 2012, AR Holding Company, Inc. (now Takeda)[5] received Notice Letters from Par, dated February 21, 2012 and March 13, 2012 respectively, stating that it had filed an ANDA seeking approval for a generic version of Colcrys® for the treatment and prevention of gout flares. (D.I. 54 at 4 n.3; *see also* D.I. 53, ex. 1 at ¶¶ 29-30) Both Notice Letters 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 Par's proposed product. (D.I. 53, ex. 1 at ¶¶ 29-30) The letters also informed Takeda that Par was not seeking FDA approval for the treatment of the FMF indication based on a "carve out" pursuant too § 355(j)(2)(A)(viii). (*See id.*) In response, Takeda filed a complaint on April 4, 2012 alleging ten counts of infringement of certain gout patents[6] pursuant to 35 U.S.C. § 271. (*See* D.I. 53, ex. 1 at

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[5]AR Holding Company merged with Takeda on October 1, 2012 and assigned all rights and interests with respect to the patents-in-suit to Takeda. (D.I. 54 at 4 n.3)

[6]The ten patents included the '004, '758, '681, '269, '647, '648, '938, '296, '297, and '655 patents. (Civ. No. 12-419, D.I. 1) The '395 and '396 patents were added by amendment on June 13, 2013. (*See id.* at D.I. 74) The '721 and '722 patents were not included because "Takeda had not yet received notice of Paragraph IV Certifications from Par with respect to these two later-issued patents." (Civ. No. 13-1524, D.I. 54 at 4 n. 4)

¶ 31; Civ. No. 12-419, D.I. 1)

3. On or about July 22, 2013, Takeda received a third Notice Letter from Par informing it that Par had amended its ANDA to seek approval for the treatment of FMF and to "carve out,"[7] or disavow, gout as a treatment indication. (*See* Civ. No. 13-1524, D.I. 53, ex. 1 at ¶¶ 33-35) The Paragraph IV Certification included in the third Notice Letter was limited to the five FMF patents. (*See id.* at ¶ 33) The third Notice Letter "further informed Takeda that [Par's] proposed labeling does not include dosing instructions or safety information for the treatment or prevention of gout flares." (*Id.* at ¶ 34) "Par recently 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), Par seeks to carve out from the FDA approved Colcrys® label . . . information regarding the treatment and prevention of gout flares . . . ." (*Id.* at ¶ 35) In response to Par's notice, Takeda filed the present action alleging infringement of the FMF patents under § 271 on August 30, 2013. (D.I. 1)

4. **Amneal Pharmaceuticals, LLC ("Amneal").** In September 2012, Amneal sought approval of an ANDA for a generic version of Colcrys® prior to the expiration of Takeda's patent rights. (*See* Civ. No. 13-1729, D.I. 36, ex. 1 at ¶ 24) On or about February 21, 2013, Takeda received a Notice Letter from Amneal, dated February 20, 2013, stating that it had filed an ANDA seeking approval for a generic version of

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[7]"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)).

Colcrys® for the treatment and prevention of gout flares. (*Id.* at ¶ 25) The Notice Letter included a Paragraph IV Certification certifying that the gout patents are invalid or would not be infringed by Amneal's proposed product. (*Id.*) The letter also informed Takeda that Amneal was not seeking FDA approval for the treatment of the FMF indication based on a "carve out" pursuant too § 355(j)(2)(A)(viii). (See *id.*) In response, Takeda filed a complaint on March 28, 2013 alleging ten counts of infringement of certain gout patents[8] pursuant to 35 U.S.C. § 271. (*See id.* at ¶ 26; Civ. No. 13-493, D.I. 1)

5. On August 28, 2013, during fact discovery in Civ. No. 13-493, Amneal notified Takeda that it had voluntarily decided to withdraw its request for FDA approval with respect to the treatment and prevention of gout flares. (Civ. No. 13-1729, D.I. 36, ex. 1 at ¶ 27) On or about September 10, 2013, Takeda received a second Notice Letter from Amneal, which included a Paragraph IV Certification limited to the five FMF patents. (*See id.* at ¶ 28) The second Notice Letter "further informed Takeda that [Amneal's] proposed labeling does not include dosing instructions or safety information for the treatment or prevention of gout flares." (*Id.* at ¶ 29) Takeda alleges that, "[u]pon information and belief, on or about September 6, 2013, Amneal 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), Amneal seeks to carve out from the FDA approved Colcrys® label . . . information regarding the

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[8]Takeda asserted the same gout patents it had against Par in 12-419, enumerated *supra* n.6. The '395 and '396 patents were similarly added by amendment on June 7, 2013. (Civ. No. 13-493, D.I. 30) The '721 and '722 patents were added by amendment on July 16, 2013. (*Id.* at D.I. 45) The complaint was amended a third time on August 21, 2013 "to make certain revisions to its Second Amended Complaint consistent with the facts in the instant action." (*Id.* at D.I. 59 at 3, ¶ 8; D.I. 60)

treatment and prevention of gout flares . . . ." (*Id.* at ¶ 30) In response to Amneal's notice, Takeda filed the present lawsuit alleging infringement of the FMF patents under § 271 on October 21, 2013. (D.I. 1)

6. **Motions to amend.** On May 30, 2014, Takeda filed the present motions seeking to amend its complaints to seek a declaratory judgment that Par's and Amneal's (collectively, "defendants") manufacture and/or sale of their proposed ANDA products will contributorily infringe the gout patents under § 271(c). (D.I. 53; D.I. 36)[9] Specifically, Takeda seeks to modify counts IV and V to seek a declaratory judgment that defendants, upon approval of their proposed ANDA products and expiration of Takeda's Orphan Drug exclusivity, "will contribute to the infringement of the '648 and '297 patents by others,[10] 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). (*See* D.I. 53, ex. 1 at counts IV-V; D.I. 36, ex. 1 at counts IV-V) Takeda also seeks to add twelve claims (counts VI-XVII) seeking declaratory judgments that defendants' proposed ANDA products will contribute to the infringement of the remaining gout patents under § 271(c). (D.I. 53, ex. 1 at counts VI-XVII; D.I. 36, ex. 1 at counts VI-XVII)

7. In support of its motions to amend, Takeda alleges that physicians will prescribe a drug for "off-label" uses of colchicine "whether or not that indication appears

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[9]Takeda had previously filed a motion to amend its complaint on May 13, 2014 (D.I. 46; D.I. 31), but filed a notice to withdraw the motion on May 30, 2014. (D.I. 52; D.I. 35) It subsequently filed the present motions in the above-captioned cases.

[10]Directed to the treatment of both gout and FMF.

on the generic label" (D.I. 53, ex. 1 at ¶ 25; D.I. 36, ex. 1 at ¶ 21), and that pharmacists will substitute defendants' 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." (D.I. 53, ex. 1 at ¶ 26; D.I. 36, ex. 1 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.

(D.I. 53, ex. 1 at ¶ 23; D.I. 36, ex. 1 at ¶ 19)[11]

8. The court's scheduling order requires that all motions to amend the pleadings be filed by August 1, 2014. (D.I. 18; D.I. 14) The parties have stipulated to extend fact discovery to be completed by October 31, 2014. (D.I. 88; D.I. 63) Trial is scheduled for August 3, 2015. (D.I. 18; D.I. 14) Civ. Nos. 12-419 and 13-493, related to the gout patents, were stayed on September 17, 2013. (Civ. No. 12-419, D.I. 98; Civ. No. 13-493, D.I. 66)

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

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[11]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. (*See* Civ. No. 13-1524, D.I. 55, ¶¶ 9-12, exs. G-J)

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).

10. **Analysis.** Defendants argue that the court should deny Takeda's motions 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. There is no dispute that Takeda does not have a viable claim under § 271(e)(2), as defendants only seek 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 defendants' proposed ANDA products will infringe the gout patents under § 271(c).

11. 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).

12. "[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)).

13. 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 defendants' Notice Letters, the parties undeniably had a substantial controversy amenable to adjudication. The issue at bar is whether the court is bound by defendants' representations to the FDA that they will not market colchicine for the prevention and treatment of gout flares, even when all the realities of the market indicate otherwise.

14. 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.

15. Looking at the circumstances of record, it is at least plausible, if not predictable, that defendants' generic products will be sold off-label. As noted, this litigation commenced with defendants filing Notice Letters stating that they were seeking approval for a generic version of Colcrys® for the treatment and prevention of

gout flares, meaningful preparation towards infringing activity.[12] For defendants 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.

16. Under these unique circumstances, the court finds that Takeda has demonstrated, by a preponderance of the evidence, that the off-label sale of defendants' generic versions 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.

17. **Conclusion.** For the foregoing reasons, Takeda's motions to amend are granted. (D.I. 53; D.I. 36)

United States District Judge

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