IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ZOGENIX, INC. and ZOGENIX INTERNATIONAL, LTD., Plaintiffs, v. APOTEX INC. and APOTEX CORP., Defendants.	)	Civil Action No. 21-1252-RGA [redacted]
ZOGENIX, INC. and ZOGENIX INTERNATIONAL LTD., Plaintiffs, v. APOTEX INC. and APOTEX CORP. et al., Defendants.	)	Civil Action No. 22-1232-RGA [redacted]

REPORT AND RECOMMENDATION[1]

Presently before the court in these Hatch-Waxman cases for patent infringement are the following motions: (1) the motion of defendants Apotex Inc. and Apotex Corp. (collectively, "Apotex") to dismiss the complaint for lack of subject matter jurisdiction and failure to state a claim under Federal Rules of Civil Procedure 12(b)(1) and 12(b)(6), respectively, (C.A. No. 22-1232-RGA, D.I. 14);[2] and (2) the motion of plaintiffs Zogenix, Inc. and Zogenix International

[1] The court's decision on the motion to dismiss in Civil Action No. 22-1232-RGA is governed by 28 U.S.C. § 636(b)(1)(B) and Fed. R. Civ. P. 72(b)(1). The court's decision on the motion to amend in Civil Action No. 21-1252-RGA is governed by 28 U.S.C. § 636(b)(1)(A) and Fed. R. Civ. P. 72(a).

[2] The briefing and filings associated with the pending motion to dismiss in Civil Action No. 22-1232-RGA are found at D.I. 15, D.I. 16, D.I. 27, and D.I. 36.

Ltd. ("Zogenix") to amend the complaint under Federal Rule of Civil Procedure 15(a); (C.A. No. 21-1252-RGA; D.I. 95).[3] For the following reasons, I recommend that the court DENY Apotex's motion to dismiss under Rule 12(b)(1) and GRANT the motion to dismiss under Rule 12(b)(6). Zogenix's motion to amend is GRANTED-IN-PART.

I. BACKGROUND[4]

Zogenix markets the drug product Fintepla®. (D.I. 1 at ¶ 3) The active pharmaceutical ingredient in Fintepla®, fenfluramine hydrochloride, is used to treat seizures associated with Dravet syndrome.[5] (*Id.* at ¶¶ 39, 43) United States Patent Nos. 10,603,290 ("the '290 patent"), 10,452,815 ("the '815 patent"), 10,947,183 ("the '183 patent"), 10,950,331 ("the '331 patent"), 10,478,441 ("the '441 patent"), and 10,478,442 ("the '442 patent") are listed in the Food and Drug Administration's ("FDA") Orange Book for Fintepla®. (C.A. No. 21-1252-RGA, D.I. 102, Ex. F) These six patents are directed to specific systems and methods of manufacturing fenfluramine and using the drug to treat seizures. United States Patent No. 11,406,606 ("the '606 patent"), which issued on August 9, 2022, is also listed in the Orange Book for Fintepla® and is directed to methods of treating patients with Dravet syndrome by administering a combination of stiripentol and reduced dosages of fenfluramine. (D.I. 1 at ¶¶ 66-68)

In June of 2021, Apotex submitted Abbreviated New Drug Application ("ANDA") No. 216108 seeking FDA approval to market a generic version of Fintepla®. Between July and October of 2021, Apotex notified Zogenix of the ANDA by filing certifications under 21 U.S.C.

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[3] The briefing and filings associated with the pending motion to amend in Civil Action No. 21-1252-RGA are found at D.I. 96, D.I. 101, D.I. 102, D.I. 105, and D.I. 109.

[4] Unless otherwise noted, citations in the Background refer to the docket in C.A. No. 22-1232-RGA.

[5] The complaint describes Dravet syndrome as "a life-threatening, rare and chronic form of childhood-onset epilepsy, often characterized by severe and unrelenting seizures despite medical treatment." (D.I. 1 at ¶ 52)

§ 355(j)(2) ("Paragraph IV certifications") for the '290, '815, '183, and '331 patents. (C.A. No. 21-1252-RGA, D.I. 95, Ex. A at ¶¶ 65-67; D.I. 102, Ex. A) [redacted][6] (C.A. No. 21-1252-RGA, D.I. 95, Ex. A at ¶ 73; Ex. E); *see* 21 U.S.C. § 355(j)(2)(A)(viii).

In response to the Paragraph IV certifications, Zogenix filed two lawsuits against Apotex for patent infringement. (C.A. No. 21-1252-RGA; C.A. No. 21-1533-RGA) Those lawsuits were subsequently consolidated for all purposes, and the parties stipulated to dismiss several of the patents from the action. (C.A. No. 21-1252-RGA, D.I. 18; D.I. 27; D.I. 69) The '606 patent was not listed among the other patents identified in the Paragraph IV certification and was not included in the patent infringement suits because it had not yet issued. (D.I. 1 at ¶¶ 71-72) Apotex has not amended its Paragraph IV certification to list the '606 patent.

In Civil Action No. 21-1252-RGA, the parties stipulated to the dismissal of the '290, '815, and '331 patents, leaving only Zogenix's cause of action for infringement of the '183 patent. (C.A. No. 21-1252-RGA, D.I. 27; D.I. 69) Zogenix sought approval from Apotex to file a proposed amended complaint adding causes of action for infringement of the '441 patent, the '442 patent, and U.S. Patent No. 10,351,510 ("the '510 patent") on July 13, 2022, and Apotex objected to the proposal as untimely. (C.A. No. 21-1252-RGA, D.I. 95, Ex. C at 3-4) Zogenix

[6] When a method-of-use patent is listed in the Orange Book, a generic applicant can seek FDA approval to label its drug only for uses not covered by the patents by submitting a "section viii statement" with the ANDA. *See* 21 U.S.C. § 355(j)(2)(A)(viii); *GlaxoSmithKline LLC v. Teva Pharms. USA, Inc.*, C.A. No. 14-878-LPS-CJB, 2016 WL 3946770, at *3 (D. Del. July 20, 2016). This "skinny label" or "section viii carveout" framework allows a generic manufacturer to sidestep the typical FDA requirement that the generic label must be identical to the brand's label. 21 U.S.C. § 355(j)(2)(A)(viii); *see Amarin Pharma, Inc. v. Hikma Pharms. USA Inc.*, 578 F. Supp. 3d 642, 644 (D. Del. 2022). To achieve a viable "skinny label," however, the generic must remove portions of the brand's label associated with the patented use. *Id.*

then filed motions for leave to amend the complaint which were later withdrawn [redacted] (C.A. No. 21-1252-RGA, D.I. 79; D.I. 86; D.I. 87; D.I. 94; C.A. No. 22-1232-RGA, D.I. 16, Exs. B-C) The pending motion to amend the complaint was filed on September 15, 2022 and seeks to add two plaintiffs and five causes of action: (1) infringement of the '441 patent under 35 U.S.C. § 271(e)(2)(A) (Count II); (2) declaratory judgment of infringement of the '441 patent under 28 U.S.C. §§ 2201 and 2202 (Count III); (3) infringement of the '442 patent under § 271(e)(2)(A) (Count IV); (4) declaratory judgment of infringement of the '442 patent under 28 U.S.C. §§ 2201 and 2202 (Count V); and (5) declaratory judgment of infringement of the '510 patent under 28 U.S.C. §§ 2201 and 2202 (Count VI). (C.A. No. 21-1252-RGA, D.I. 95, Ex. B at ¶¶ 117-97)

Zogenix filed Civil Action No. 22-1232-RGA on September 21, 2022, asserting causes of action against Apotex for infringement of the '606 patent under 35 U.S.C. § 271(e)(2)(A) (Count I) and declaratory judgment of infringement of the '606 patent (Count II). (D.I. 1) Apotex filed the pending motion to dismiss the complaint on November 14, 2022. (D.I. 14) On March 15, 2023, the parties stipulated to consolidate Civil Action No. 22-1232-RGA with Civil Action No. 21-1252-RGA and other related cases. (D.I. 58) The court heard argument on the pending motions to dismiss and amend on June 13, 2022.

II. LEGAL STANDARDS

A. Rule 12(b)(1)

Rule 12(b)(1) permits the dismissal of a claim or an action for lack of subject matter jurisdiction. Fed. R. Civ. P. 12(b)(1). Motions brought under Rule 12(b)(1) may present either a facial or factual challenge to the court's subject matter jurisdiction. *See Lincoln Benefit Life Co.*

v. AEI Life, LLC, 800 F.3d 99, 105 (3d Cir. 2015). A facial attack contests the sufficiency of the pleadings, whereas a factual attack contests the sufficiency of jurisdictional facts. *See id.* The party asserting subject matter jurisdiction bears the burden of proving that jurisdiction exists. *Mortensen v. First Fed. Sav. & Loan Ass'n*, 549 F.2d 884, 891 (3d Cir. 1977).

B. Rule 12(b)(6)

Rule 12(b)(6) permits a party to move to dismiss a complaint for failure to state a claim upon which relief can be granted. Fed. R. Civ. P. 12(b)(6). When considering a Rule 12(b)(6) motion to dismiss, the court must accept as true all factual allegations in the complaint and view them in the light most favorable to the plaintiff. *Connelly v. Lane Constr. Corp.*, 809 F.3d 780, 790-91 (3d Cir. 2016).

To state a claim upon which relief can be granted pursuant to Rule 12(b)(6), a complaint must contain a "short and plain statement of the claim showing that the pleader is entitled to relief." Fed. R. Civ. P. 8(a)(2). Although detailed factual allegations are not required, the complaint must set forth sufficient factual matter, accepted as true, to "state a claim to relief that is plausible on its face." *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 570 (2007); *see also Ashcroft v. Iqbal*, 556 U.S. 662, 663 (2009). A claim is facially plausible when the factual allegations allow the court to draw the reasonable inference that the defendant is liable for the misconduct alleged. *Iqbal*, 556 U.S. at 663; *Twombly*, 550 U.S. at 555-56.

The court's determination is not whether the non-moving party "will ultimately prevail," but whether that party is "entitled to offer evidence to support the claims." *In re Burlington Coat Factory Sec. Litig.*, 114 F.3d 1410, 1420 (3d Cir. 1997) (internal citations and quotation marks omitted). This "does not impose a probability requirement at the pleading stage," but instead "simply calls for enough facts to raise a reasonable expectation that discovery will reveal

evidence of [the necessary element]." *Phillips v. Cty. of Allegheny*, 515 F.3d 224, 234 (3d Cir. 2008) (quoting *Twombly*, 550 U.S. at 556). The court's analysis is a context-specific task requiring the court "to draw on its judicial experience and common sense." *Iqbal*, 556 U.S. at 663-64.

C. Rule 15(a)

Rule 15(a)(2) of the Federal Rules of Civil Procedure provides that after a responsive pleading has been filed, a party may amend its pleading "only with the opposing party's written consent or the court's leave," and "[t]he court should freely give leave when justice so requires." Fed. R. Civ. P. 15(a)(2). The decision to grant or deny leave to amend lies within the discretion of the court. *See Foman v. Davis*, 371 U.S. 178, 182 (1962); *In re Burlington Coat Factory Secs. Litig.*, 114 F.3d 1410, 1434 (3d Cir. 1997). The Third Circuit has adopted a liberal approach to the amendment of pleadings. *See Dole v. Arco*, 921 F.2d 484, 487 (3d Cir. 1990). In the absence of undue delay, bad faith, or dilatory motives on the part of the moving party, the amendment should be freely granted, unless it is futile or unfairly prejudicial to the non-moving party. *See Foman*, 371 U.S. at 182; *In re Burlington*, 114 F.3d at 1434.

III. APOTEX'S MOTION TO DISMISS[7]

A. Subject Matter Jurisdiction

1. Count I: Infringement of the '606 patent under 35 U.S.C. § 271(e)(2)(A)

In support of the motion to dismiss Count I of Zogenix's complaint, Apotex argues that no case or controversy exists because Apotex never filed a predicate Paragraph IV certification for the '606 patent. (D.I. 15 at 9) But Federal Circuit precedent establishes that a Paragraph IV certification specific to the '606 patent is not required before the complaint is filed to confer

[7] Citations to the record in this section refer to the docket in Civil Action No. 22-1232-RGA, unless otherwise noted.

subject matter jurisdiction. *See Vanda Pharms. Inc. v. West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1123-25 (Fed. Cir. 2018).

In *Vanda*, the Federal Circuit considered whether the district court had subject matter jurisdiction "over an action in which the asserted patent issued after the ANDA was filed and the complaint was filed before the ANDA applicant submitted a Paragraph IV certification for the asserted patent." *Id.* at 1124. There, as here, the defendant argued that a claim for infringement under § 271(e)(2) can only be based on patents that issued before the ANDA was filed, and a Paragraph IV certification for that particular patent must be submitted before an infringement suit is filed. *Id.* The Federal Circuit rejected the defendant's argument, holding that the plaintiff's "complaint alleged that [the defendant] infringed the [asserted patent] under 35 U.S.C. § 271(e)(2)(A) by filing the ANDA. Nothing more was required to establish the district court's subject matter jurisdiction pursuant to 28 U.S.C. § 1338(a)." *Id.* The Federal Circuit held "[t]he mere fact that [the defendant] had not submitted a Paragraph IV certification for the [asserted] patent until after [the plaintiff] filed suit does not establish that there was not a justiciable controversy over which the court could exercise jurisdiction." *Id.* at 1125. Because the defendant had filed an ANDA and the plaintiff subsequently sued the defendant, an actual controversy existed. *Id.*

Similarly, the court does not lack subject matter jurisdiction over Zogenix's causes of action regarding the '606 patent. "The requirements for jurisdiction in the district courts are met once a patent owner alleges that another's filing of an ANDA infringes its patent under 25 U.S.C. § 271(e)(2), and this threshold jurisdictional determination does not depend on the ultimate merits of the claims." *AstraZeneca Pharms. LP v. Apotex Corp.*, 669 F.3d 1370, 1377 (Fed. Cir. 2012). Here, Zogenix's complaint alleges that Apotex infringed the '606 patent under

§ 271(e)(2)(A) by filing the ANDA. (D.I. 1 at ¶ 81) "Nothing more [is] required to establish the district court's subject matter jurisdiction pursuant to 28 U.S.C. § 1338(a)." *Vanda*, 887 F.3d at 1124; *see also Cephalon, Inc. v. Sandoz, Inc.*, C.A. No. 11-821-SLR, 2012 WL 682045, at *5 (D. Del. Mar. 1, 2012) (concluding that an amended Paragraph IV certification is not required to confer subject matter jurisdiction over infringement claims for patents issued after the ANDA was filed).

Apotex's reliance on the court's decision in *In re Entresto (Sacubitril/Valsartan) Patent Litigation* does not require a different result. (D.I. 109) (citing C.A. No. 20-2930-RGA *et al.*, 2022 WL 4482717 (D. Del. Sept. 27, 2022)). There, the court confirmed that § 271(e)(2) and the Federal Circuit's decision in *AstraZeneca Pharms. LP v. Apotex Corp.* establish that the requirements for subject matter jurisdiction are met once the *patent owner* alleges that another's filing of an ANDA infringes its patent. *Id.* at *4 (citing *AstraZeneca*, 669 F.3d at 1377). The distinction in *Entresto* was that counterclaims alone without Paragraph IV certificatons were insufficient to invoke the court's jurisdiction. The crux of the *Entresto* court's holding was that jurisdiction under § 271(e)(2) does not extend to counterclaims brought by the ANDA filer against three patents subject to section viii statements. *Id.* at *5. That distinction is not applicable here, where the proposed causes of action for the '606 patent are brought by the patent owner.

2. Count II: Declaratory judgment of infringement of the '606 patent

Apotex argues that the court lacks subject matter jurisdiction over Zogenix's declaratory judgment claim for induced infringement of the '606 patent under 28 U.S.C. § 2201 because there is no actual case or controversy when Apotex's ANDA has not been approved and there is no suggestion that FDA approval is imminent. (D.I. 15 at 1, 18-19) Apotex maintains that

allegations of imminent FDA approval and immediate marketing of the ANDA product thereafter "are the mandatory predicate for Plaintiffs to survive a motion to dismiss." (*Id.* at 19) Apotex cites no authority supporting this position in the ANDA context. (*Id.*)

I recommend that the court deny Apotex's motion to dismiss for lack of declaratory judgment jurisdiction over Count II of Zogenix's complaint. "[T]entative approval of an ANDA is generally not a precondition to the existence of a case or controversy concerning patents listed in the Orange Book." *See Apotex, Inc. v. Daiichi Sankyo, Inc.*, 781 F.3d 1356, 1366 (Fed. Cir. 2015). Case law from this district confirms that "claims for induced infringement predicated on § 271(e)(2), filed prior to the occurrence of direct infringement, do not violate . . . the case or controversy requirement of the Declaratory Judgment Act." *Cephalon*, 629 F. Supp. 2d at 350-51 (internal quotation marks and citations omitted). The case or controversy requirement is met where, as here, Apotex has filed the ANDA and declared its intent to manufacture, market, and sell potentially infringing products if the FDA approves the ANDA. (D.I. 1 at ¶¶ 101-02) "In the context of a § 271(e)(2) infringement action, where the court is engaged in a forward-looking analysis of what defendants will do upon ANDA approval, defendants' declared intent is sufficient to make the controversy real and immediate." *Cephalon*, 629 F. Supp. 2d at 351.

Apotex cites *TSMC Technology, Inc. v. Zond, LLC*, a patent infringement dispute regarding circuit devices which did not involve an ANDA filing or FDA approval. (D.I. 15 at 19) (citing *TSMC*, C.A. No. 14-721-LPS-CJB, 2014 WL 7498398, at *3-4 (D. Del. Jan. 8, 2014); *see also Pieczenik v. Bayer Corp.*, 2010 WL 11537536 (D.N.J. June 25, 2010) (dismissing a *pro se* plaintiff's patent infringement complaint for failure to satisfy the Rule 8 pleading standard, with no discussion of FDA approval or an ANDA filing)). Apotex also cites *In re Entresto*, which held that the court lacked declaratory judgment jurisdiction over the defendants'

counterclaims after they submitted section viii statements affirming that the ANDA product labels would omit infringing uses. *In re Entresto*, 2022 WL 4482717, at *1, 4-5. The court distinguished its analysis of the defendants' counterclaims from the jurisdictional requirements of a patent owner's infringement claims under § 271(e)(2). *Id.* at *4-5. The court did not consider how the imminence of FDA approval for an ANDA product factors into an analysis of declaratory judgment jurisdiction over a patent owner's claims.

Apotex also maintains that the court lacks declaratory judgment jurisdiction over Count II of the complaint because Zogenix's induced infringement allegations are factually deficient for the same reasons its § 271(e)(2) claim cannot survive. (D.I. 15 at 19) Specifically, Apotex challenges the merits of the complaint's allegations that Apotex's ANDA label teaches, encourages, or recommends the use of fenfluramine in combination with stiripentol. (D.I. 36 at 8-10) These arguments are appropriately addressed at § III.B, *infra*, in the context of Apotex's motion to dismiss under Rule 12(b)(6).

B. Sufficiency of the Pleaded Infringement Allegations

Although the court has subject matter jurisdiction over Zogenix's claims for the reasons set forth at § III.A, *supra*, I recommend that the court grant Apotex's motion to dismiss Zogenix's induced infringement claims under Rule 12(b)(6) for failure to state a claim upon which relief can be granted.[8] "Whoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b). To prevail on a claim of induced infringement, the plaintiff

[8] In its opening brief, Apotex alleges that Zogenix has no cause of action for direct infringement under § 271(a) because "there is no dispute that Apotex does not treat patients directly[.]" (D.I. 15 at 19) Apotex further notes that "Plaintiffs do not assert contributory infringement under § 271(c) but use[] the term 'contributing' in their Prayer for Relief." (*Id.* at 19 n.8) Zogenix confirms that its argument is limited to induced infringement under § 271(b), and the complaint's discussion of direct infringement is limited to its applicability as a requisite element of a cause of action for induced infringement. (D.I. 27 at 11 n.2) (citing *Limelight Networks, Inc. v. Akamai Techs., Inc.*, 572 U.S. 915, 920-21 (2014)).

must show that: (1) there is an underlying act of direct infringement, (2) the alleged infringer knowingly induced the direct infringement, and (3) the alleged infringer possessed specific intent to encourage the acts of direct infringement. *See Enplas Display Device Corp. v. Seoul Semiconductor Co.*, 909 F.3d 398, 407 (Fed. Cir. 2018). "[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*, 669 F.3d at 1379.

The asserted claims of the '606 patent and the associated use code listed in the Orange Book require the use of fenfluramine in combination with stiripentol. Asserted claim 15 of the '606 patent recites a method of reducing or controlling seizures in a patient by "reducing a dosage of fenfluramine . . . by 30% to 60% based on the patient being treated with a therapeutically effective amount of stiripentol, whereby the dosage of fenfluramine . . . is reduced as compared to an amount of fenfluramine . . . without stiripentol." (D.I. 1, Ex. 2 at 20:16-27) Consistent with the claim language, the Orange Book lists the '606 patent under use code U-3406, which is defined as "use of fenfluramine at reduced amounts with stiripentol for the treatment of seizures associated with Dravet syndrome." (D.I. 16, Ex. A) To plausibly state a claim for induced infringement of the '606 patent, the complaint must allege that Apotex's ANDA label encourages, recommends, or promotes an infringing use of fenfluramine with stiripentol. (D.I. 27 at 11); *see Sanofi v. Watson Labs. Inc.*, 875 F.3d 636, 644 (Fed. Cir. 2017) ("When proof of intent to encourage depends on the label . . . the label must encourage, recommend, or promote infringement.") (citations and quotations omitted).

Here, the complaint does not plausibly allege that Apotex's ANDA label encourages or instructs an infringing use because Apotex's label carves out references to fenfluramine administered concomitantly with stiripentol. (*See, e.g.*, D.I. 16, Ex. C at § 2.2) Zogenix focuses

on three aspects of the ANDA label to support its position that the label nonetheless encourages an infringing use: (1) the warnings and side effects of fenfluramine described at § 12.1 of the label; (2) the dosing instructions at §§ 2.3, 2.4, 7.1, and 8.6 of the label; and (3) the clinical study data at § 14.1 of the label. (D.I. 27 at 15-18) For the following reasons, these portions of the ANDA label do not plausibly show that Apotex took affirmative steps to induce infringement. *See Amarin Pharma, Inc. v. Hikma Pharms. USA Inc.*, 578 F. Supp. 3d 642, 646 (D. Del. 2022).

In support of its position that the ANDA label induces infringement, Zogenix relies on warning language in the ANDA label explaining that [redacted] (D.I. 16, Ex. C at § 12.1) According to Zogenix, this language would encourage a physician to prescribe a reduced amount of fenfluramine in conjunction with stiripentol to minimize the health risks associated with fenfluramine. (D.I. 27 at 17-18; 6/12/2023 Tr.) But this warning about side effects from using fenfluramine does not amount to an instruction to use a reduced amount of fenfluramine in combination with stiripentol. *See Amarin*, 578 F. Supp. 3d at 646 ("[A] warning is just that—a warning. It is not an instruction[.]") (internal quotations and citations omitted). Even if a physician reading the ANDA label's description of side effects from treatment with fenfluramine were to decide to reduce the dosage of fenfluramine and prescribe a concomitant anti-epileptic drug ("AED"), nothing in the ANDA label endorses this treatment method as an effective way to reduce the identified side effects.

The Federal Circuit has considered and rejected a similar argument about the impact of warnings in an ANDA label. In *HZNP Medicines LLC v. Actavis Laboratories UT, Inc.*, the Federal Circuit considered an ANDA label which instructed patients to apply the drug to the

knees and cautioned them to avoid exposure to natural or artificial sunlight on the treated knees. 940 F.3d 680, 701 (Fed. Cir. 2019). The plaintiff argued that this warning showed the application of sunscreen was medically necessary and resulted in induced infringement of the asserted patents, which included a limitation requiring the application of sunscreen. *Id.* The Federal Circuit disagreed, holding that the ANDA label permitted, but did not require, the application of sunscreen. *Id.* at 702. Similarly, the warning in Apotex's ANDA label regarding the side effects of fenfluramine do not amount to a requirement to administer a reduced amount of fenfluramine or to combine fenfluramine with stiripentol.

A review of the dosing instructions in the ANDA label further supports Apotex's position that the label does not instruct users to coadminister fenfluramine and stiripentol. (D.I. 15 at 14-18; D.I. 16, Ex. C at §§ 2.3, 2.4, 7.1, 8.6) The complaint alleges that the titration schedule in Apotex's ANDA label encourages or promotes infringement of the '606 patent because the ANDA label indicates a 30% to 60% reduction in the amount of fenfluramine administered to a patient taking concomitant stiripentol. (D.I. 1 at ¶¶ 88-89) But Apotex's ANDA label includes a titration table setting forth an initial and maintenance dosing schedule for patients taking fenfluramine "without concomitant stiripentol," as well as modifications to the dosing schedule which also specify that the patients are not taking concomitant stiripentol. (D.I. 16, Ex. C at §§ 2.2, 2.3, 2.4) These dosing instructions cannot plausibly be construed to encourage a physician to prescribe fenfluramine in conjunction with stiripentol. *See Amarin*, 578 F. Supp. 3d at 646 (finding an ANDA label warning that icosapent ethyl could cause serious side effects in people who have cardiovascular disease was "hardly instruction or encouragement" to use icosapent ethyl to reduce cardiovascular risk).

Zogenix argues that the ANDA label induces infringement of the '606 patent because it contemplates a reduction in the dosage of fenfluramine for patients taking concomitant stiripentol. (D.I. 27 at 15) The ANDA label contemplates a reduced maximum daily dosage of 17 mg for patients taking another AED and a strong CYP1A2 or CYP2D6 inhibitor, or patients taking another AED who suffer from a renal impairment. (D.I. 16, Ex. C at §§ 7.1, 8.6) But the ANDA label does not suggest that "another AED" necessarily refers to stiripentol, and the parties acknowledge the existence of other AEDs such as valproate and clobazam. (6/13/2023 Tr.) In fact, the ANDA label [redacted] (*Id.*, Ex. C at § 14.1) These allegations do not support an inference that the ANDA label "would inevitably lead some consumers to practice the claimed method." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010).

Finally, the two clinical studies described in Apotex's ANDA label do not encourage or instruct a reduction in the dose of fenfluramine administered to a patient receiving stiripentol. (D.I. 16, Ex. C at § 14.1) Perhaps because Study 1 evaluated the administration of fenfluramine in patients who were not receiving stiripentol, Zogenix's pleading does not allege that Study 1 supports its claim for induced infringement. (*Id.*; D.I. 1 at ¶¶ 57-59) Instead, Zogenix focuses on [redacted] (D.I. 16, Ex. C at § 14.1) Apotex's ANDA label does not identify the other AED used in Study 2 as stiripentol. (*Id.*)

The complaint alleges that the description of Study 2 in Apotex's ANDA label teaches the use of stiripentol in combination with fenfluramine because the Fintepla® label identifies stiripentol as the concomitant AED in Study 2, and the clinical trial data is publicly available.

(D.I. 1 at ¶¶ 58-59) But Zogenix cannot rely on the Fintepla® label to establish that Apotex's ANDA label encourages, recommends, or promotes an infringing use. *See Eli Lilly & Co. v. Teva Parenteral Meds. Inc.*, 845 F.3d 1357, 1369 (Fed. Cir. 2017) (explaining that " 'vague' instructions that require one to 'look outside the label to understand the alleged implicit encouragement' do not, without more, induce infringement."); *Takeda Pharms. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 634 (Fed. Cir. 2015) (rejecting the plaintiff's reliance on information outside the ANDA label "to understand the alleged implicit encouragement in the [ANDA] label."). The description of Study 2 in the ANDA label omits the clinical trial identifier and specifies that 100% of patients in Study 2 were receiving "between 2 and 4 concomitant AEDs." (D.I. 16, Ex. C at § 14.1) Even if the reference to AEDs in Study 2 is read to encompass a potentially infringing use of fenfluramine in combination with stiripentol, the label's inclusion of both infringing and non-infringing uses is not sufficient to "specifically encourage" the use of the generic for the patented indication. *Amarin*, 578 F. Supp. 3d at 647 (citing *Grunenthal GmbH v. Alkem Lab'ys Ltd.*, 919 F.3d 1333, 1339 (Fed. Cir. 2019)).

Viewing these provisions of the ANDA label in the light most favorable to Zogenix, it is plausible to infer that some users might infringe. But this is not enough to adequately plead that the ANDA label actively induces or instructs users to perform the patented method. *See HZNP*, 940 F.3d at 701-02 ("Merely describing the infringing use, or knowing of the possibility of infringement, will not suffice; specific intent and action to induce infringement must be shown."). Because Apotex's ANDA label does not instruct users on the patented indications, and because users would have to go beyond the ANDA label to arrive at infringing uses, Zogenix's induced infringement claim cannot survive. *See Amarin*, 578 F. Supp. 3d at 646-47

(granting motion to dismiss complaint that failed to plead inducement based on the contents of the ANDA label).

In making this recommendation, the court acknowledges that circumstances may exist in other cases where an ANDA label's carveout is not "skinny" enough, and the ANDA label may induce infringement despite the attempt at a carveout. These cases may give rise to disputed issues of fact requiring discovery and/or expert testimony. *See, e.g.*, *GlaxoSmithKline LLC v. Teva Pharms. USA, Inc.*, 7 F.4th 1320, 1330 (Fed. Cir. 2021) (finding that the district court erred by treating the fact question of whether the skinny label instructed a physician to prescribe the generic for a claimed use as a legal question). Generally, however, "generics [can] *not* be held liable for merely marketing and selling under a 'skinny' label omitting all patented indications." *Id.* at 1326; *see also id.* at 1350 (Prost, J., dissenting) ("[I]nferring intentional encouragement to infringe a method—from a label that has intentionally omitted everything that the brand said covers the method—is a lot to ask of a reasonable factfinder.").

The narrow scope of the Federal Circuit's holding in *GlaxoSmithKline* was reiterated in *Amarin*, which held that dismissal of an induced infringement claim at the pleadings stage was warranted because the generic label did not encourage, promote, or instruct an infringing use to reduce cardiovascular risk. 578 F. Supp. 3d at 645. There, as here, the court concluded that a notice regarding side effects in the ANDA label did not constitute an instruction to use the ANDA product in an infringing manner. *Id.* at 646. The court also explained that the removal of an infringing limitation from the ANDA label was sufficient, and the defendant had no duty to affirmatively discourage the infringing use. *Id.* The ANDA label in the instant case likewise confirms that Apotex removed all references to the administration of fenfluramine "with stiripentol," and several sections of the ANDA label specify that the dosage instructions apply to

patients taking fenfluramine "without concomitant stiripentol." (D.I. 16, Ex. C at §§ 2.2, 2.3, 2.4)

The reasoning in *Amarin* is supported by two Federal Circuit cases. In *Takeda Pharmaceuticals U.S.A., Inc. v. West-Ward Pharmaceutical Corp.*, the Federal Circuit rejected the argument that ANDA labels must include a "clear statement" discouraging the infringing use. 785 F.3d 625, 632 n.4 (Fed. Cir. 2015). The Federal Circuit in *Takeda* clarified that a generic defendant has no obligation to take "affirmative steps to make sure others avoid infringement." *Id.* Instead, a plaintiff challenging the sufficiency of a section viii carveout must plausibly plead that the defendant took affirmative steps to induce infringement. *Id.* Critically, the Federal Circuit explained that "vague label language cannot be combined with speculation about how physicians may act to find inducement. This would seem to too easily transform that which we have held is 'legally irrelevant'—mere knowledge of infringing uses—into induced infringement." *Id.* at 632 (citations omitted).

In *Grunenthal GmbH v. Alkem Laboratories, Ltd.*, the Federal Circuit addressed an ANDA label indicated for the treatment of severe chronic pain. 919 F.3d 1333, 1339 (Fed. Cir. 2019). The ANDA label cited studies addressing nociceptive pain, whereas the patented use was to treat polyneuropathic pain. *Id.* The evidence showed that "severe chronic pain" would include both polyneuropathic pain and nociceptive pain. *Id.* Because the proposed ANDA label did not specifically encourage the use of the generic drug for treatment of polyneuropathic pain, the plaintiff could not prevail on its induced infringement claim even though some users might use the ANDA product to treat polyneuropathic pain. *Id.* at 1339-40. The Federal Circuit emphasized that the relevant inquiry turned on the contents of the proposed ANDA label, and the ANDA label itself must encourage, recommend, or promote infringement. *Id.* at 1339. Because

Apotex's ANDA label does not instruct or encourage users to treat Dravet syndrome with a reduced dosage of fenfluramine in combination with stiripentol, the complaint fails to state a claim for induced infringement. *See Grunenthal GmbH v. Alkem Labs. Ltd.*, 919 F.3d 1333, 1339 (Fed. Cir. 2019).

Zogenix relies on the Federal Circuit's decision in *AstraZeneca LP v. Apotex, Inc.* to support its position that specific intent can be inferred because Apotex's ANDA label would encourage "at least some users" to infringe the asserted method claims. (D.I. 27 at 18-19); *AstraZeneca*, 633 F.3d at 1059-60. The *Grunenthal* court distinguished *AstraZeneca* on its facts, noting that the defendant in *AstraZeneca* distributed its generic drug despite knowing its label presented infringement problems because the dosing instructions encouraged users to administer the lowest effective dose on an infringing, once-daily basis. *Grunenthal*, 919 F.3d at 1340. In contrast, the *Grunenthal* court confirmed that an ANDA label which does not implicitly or explicitly encourage or instruct users to take an infringing action cannot support a claim for induced infringement. *Id.*

In this case, the factual allegations in the complaint and the content of Apotex's ANDA label do not plausibly support a finding that the ANDA label encourages, promotes, or instructs an infringing use, even when viewed in the light most favorable to Zogenix. Consequently, dismissal under Rule 12(b)(6) is appropriate.

C. Zogenix's Request for Leave to Amend

Zogenix requests leave to amend if the court is inclined to grant Apotex's motion to dismiss, noting that its complaint in this matter was filed before Apotex's most recent amendment to its ANDA label. (D.I. 27 at 20) To determine whether Apotex's label could plausibly induce infringement of the asserted method claim of the '606 patent, the court

considers the ANDA label in relation to the asserted claim. *See HZNP*, 940 F.3d at 699 ("We review Actavis's ANDA label in relation to the asserted claims of the methods-of-use patents to evaluate if the district court erred in concluding that Actavis's label does not induce infringement of those particular claims."). The court has completed this inquiry in the instant decision, analyzing claim 15 of the '606 patent in conjunction with Apotex's updated ANDA label. (D.I. 16, Ex. C) Under these circumstances, Zogenix has failed to establish how an amended pleading would not be futile. Zogenix's alternative request for leave to amend is therefore denied.

IV. ZOGENIX'S MOTION TO AMEND[9]

Apotex opposes Zogenix's motion to amend, arguing that the proposed cause of action for infringement of the '510 patent is untimely, and the proposed causes of action for infringement of the '441 and '442 patents are futile. (D.I. 101 at 12-19) For the following reasons, Zogenix's motion to amend is GRANTED with respect to the claims for infringement of the '510 patent and DENIED with respect to the claims for infringement of the '441 and '442 patents.

A. Undue Delay, Bad Faith, and Prejudice

There is no dispute that Zogenix moved to amend the complaint on September 15, 2022, well within the February 3, 2023 deadline for amended pleadings set forth in the operative scheduling order. (D.I. 43 at ¶ 3) Nonetheless, Apotex objects to Zogenix's proposed amended pleading as untimely and rejects Zogenix's assertion that discovery was needed before Zogenix could assert a claim for infringement of the '510 patent, which is nearly identical to the '183 patent asserted in Zogenix's original complaint. (D.I. 101 at 19) Zogenix maintains that discovery on the '510 patent was necessary because, unlike the '183 patent, the '510 patent was

[9] Citations to the record in this section refer to the docket in Civil Action No. 21-1252-RGA, unless otherwise noted.

not listed in the Orange Book and Apotex was therefore not required to provide notice of the patent. (D.I. 105 at 7-8)

Under the Rule 15(a) framework, the court finds that there is no undue delay, bad faith, or dilatory motive by Zogenix. Zogenix timely sought leave to amend on September 15, 2022, nearly five months before the deadline for amended pleadings expired. (D.I. 117; D.I. 31 at ¶ 2) A motion for leave to amend filed on or before the deadline for amended pleadings generally precludes a finding of undue delay. *See Vitaworks IP, LLC v. Glanbia Nutritionals (NA), Inc.*, C.A. No. 19-2259-CFC, 2021 WL 5061707, at *1 (D. Del. Oct. 26, 2021) (finding no undue delay where plaintiff sought leave to amend two months before the deadline for amended pleadings); *Invensas Corp. v. Renesas Elecs. Corp.*, C.A. No. 11-448-GMS-CJB, 2013 WL 1776112, at *3 (D. Del. Apr. 24, 2013) (finding no undue delay where plaintiff filed motion for leave to amend on deadline for amended pleadings). Apotex cites no case authority from this district and no binding authority from the Third Circuit finding undue delay when the proposed amended pleading was made within the deadline for amended pleadings in the operative scheduling order. (D.I. 101 at 19)

The similarities between the '183 patent and the '510 patent do not support a finding of undue delay or bad faith. It was not unreasonable for Zogenix to obtain discovery before pursuing a cause of action for infringement of the '510 patent because, unlike the '183 patent, the '510 patent was not listed in the Orange Book and Apotex was not required to provide notice of the patent. (D.I. 102, Ex. F) Moreover, the asserted claims of the '183 patent are directed to compositions of fenfluramine, whereas the claims of the '510 patent recite methods of making fenfluramine. (D.I. 95, Ex. A at Exs. 2, 5) The four-month period between Apotex's production of its ANDA in discovery and Zogenix's proposal to add a claim for infringement of the '510

patent is not undue. (D.I. 46; D.I. 95, Ex. C at 4); *see Vitaworks*, 2021 WL 5061707, at *1 (finding five-month delay between resolution of IPR proceedings and service of plaintiff's claim charts was not undue in the context of a motion to amend).

Nor is Zogenix's proposed addition of the '510 patent prejudicial to Apotex. The only prejudice identified by Apotex is "the prospect of defending against the '510 patent, which should have been asserted long ago (if at all)[.]" (D.I. 101 at 20) Apotex has not "show[n] that it was unfairly disadvantaged or deprived of the opportunity to present facts or evidence which it would have offered had the . . . amendments been timely." *Bechtel v. Robinson*, 886 F.2d 644, 652 (3d Cir. 1989) (quoting *Heyl & Patterson Int'l, Inc. v. F.D. Rich Housing of Virgin Islands, Inc.*, 663 F.2d 419, 426 (3d Cir. 1981)).

For the foregoing reasons, Zogenix's motion to amend the complaint to add a cause of action for infringement of the '510 patent is GRANTED.

B. Futility

1. Jurisdiction

Apotex alleges that Zogenix lacks subject matter jurisdiction to bring its proposed causes of action for infringement of the '441 and '442 patents under 35 U.S.C. § 271(e)(2) because Apotex did not file a Paragraph IV certification for either patent. (D.I. 101 at 12-13) Zogenix responds that a Paragraph IV certification is not required for jurisdiction under § 271(e)(2) because the "jurisdictional trigger was properly pulled by the filing of an ANDA and the initial Paragraph IV certification," thus conferring jurisdiction over the '441 and '442 patents without a Paragraph IV certification. (D.I. 105 at 1-2) (quoting *Cephalon, Inc. v. Sandoz, Inc.*, C.A. No. 11-821-SLR, 2012 WL 682045, at *5 (D. Del. Mar. 1, 2012)). For the reasons set forth at §

III.A, *supra*, the court does not lack subject matter or declaratory judgment jurisdiction over Zogenix's causes of action regarding the '441 and '442 patents.

2. Contents of Apotex's label

Although the court has jurisdiction over the claims in Zogenix's proposed amended complaint, the amended pleading does not plausibly state a claim for induced infringement of the '441 and '442 patents based on Apotex's ANDA label for many of the reasons discussed at § III.B, *supra*.[10] As with the '606 patent, the use code and asserted claims of the '441 and '442 patents require the use of fenfluramine in combination with stiripentol, whereas Apotex's ANDA label describes the use of fenfluramine only without stiripentol. (D.I. 95, Ex. A at Exs. 3-4, 6) A review of the ANDA label's side effect warnings, dosing instructions, and clinical trial information further supports Apotex's position that the label adequately carves out the infringing use of fenfluramine in combination with stiripentol for the same reasons set forth at § III.B, *supra*. (*Id.*, Ex. A at Ex. 6)

V. CONCLUSION

For the foregoing reasons, I recommend that the court DENY Apotex's motion to dismiss under Rule 12(b)(1) and GRANT Apotex's motion to dismiss under Rule 12(b)(6). (D.I. 14) Zogenix's motion to amend is GRANTED-IN-PART. (D.I. 95) Specifically, the motion to

[10] In its answering brief, Apotex alleges that Zogenix has no cause of action for direct infringement under § 271(a) because "there is no dispute that Apotex does not treat patients directly[.]" (D.I. 101 at 18) Apotex further notes that "[w]hether Section 271(c) is alleged is unclear, as that appears only in the Prayer for Relief and not in the substantive allegations." (*Id.* at 18 n.9) Zogenix's reply brief does not discuss independent claims for direct infringement under § 271(a) or claims for contributory infringement under § 271(c). Instead, Zogenix's argument is limited to its claims of induced infringement under § 271(b). (D.I. 105) The court does not read the proposed amended pleading to assert claims for contributory infringement. Moreover, the proposed amended complaint's discussion of direct infringement is limited to its applicability as a requisite element of a cause of action for induced infringement. *See Toshiba Corp. v. Imation Corp.*, 681 F.3d 1358, 1363 (Fed. Cir. 2012) (explaining that a patentee "must show direct infringement" to prove a cause of action for induced infringement).

amend is GRANTED with respect to claims pertaining to the '510 patent, and it is DENIED with respect to claims pertaining to the '441 and '442 patents. An Order consistent with the court's ruling on the motion to amend shall issue.

Given that the court has relied upon material that technically remains under seal, the court is releasing this Report and Recommendation under seal, pending review by the parties. In the unlikely event that the parties believe that certain material in this Report and Recommendation should be redacted, the parties shall jointly submit a proposed redacted version by no later than **June 23, 2023**, for review by the court, along with a motion supported by a declaration that includes a clear, factually detailed explanation as to why disclosure of any proposed redacted material would "work a clearly defined and serious injury to the party seeking closure." *See In re Avandia Mktg., Sales Practices & Prods. Liab. Litig.*, 924 F.3d 662, 672 (3d Cir. 2019) (quoting *Miller v. Ind. Hosp.*, 16 F.3d 549, 551 (3d Cir. 1994) (internal quotation marks omitted)). If the parties do not file a proposed redacted version and corresponding motion, or if the court determines the motion lacks a meritorious basis, the documents will be unsealed within fourteen (14) days of the date the Report and Recommendation issued.

The Report and Recommendation on Apotex's motion to dismiss is filed pursuant to 28 U.S.C. § 636(b)(1)(B), Fed. R. Civ. P. 72(b)(1), and D. Del. LR 72.1(a)(3). The court's decision on Zogenix's motion to amend is filed pursuant to 28 U.S.C. § 636(b)(1)(A), Fed. R. Civ. P. 72(a), and D. Del. LR 72.1(a)(2). The parties may serve and file specific written objections within fourteen (14) days after being served with a copy of this Report and Recommendation. Fed. R. Civ. P. 72(b)(2). The objections and responses to the objections are limited to ten (10) pages each. The failure of a party to object to legal conclusions may result in the loss of the right to de novo review in the District Court. *See Sincavage v. Barnhart*, 171 F. App'x 924, 925 n.1

(3d Cir. 2006); *Henderson v. Carlson*, 812 F.2d 874, 878-79 (3d Cir. 1987).

The parties are directed to the court's Standing Order For Objections Filed Under Fed. R. Civ. P. 72, dated March 7, 2022, a copy of which is available on the court's website, http://www.ded.uscourts.gov.

Dated: June 16, 2023

Sherry R. Fallon
UNITED STATES MAGISTRATE JUDGE