IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMARIN PHARMA, INC., AMARIN PHARMACEUTICALS IRELAND LIMITED, MOCHIDA PHARMACEUTICAL CO., LTD.,	:	
Plaintiffs,	:	
v.	:	C.A. No. 20-1630-RGA
HIKMA PHARMACEUTICALS USA INC., HIKMA PHARMACEUTICALS PLC, AND HEALTH NET, LLC,	:	
Defendants.	:	

HIKMA'S OPENING BRIEF IN SUPPORT OF
MOTION TO DISMISS FIRST AMENDED COMPLAINT

HEYMAN ENERIO
GATTUSO & HIRZEL LLP
Dominick T. Gattuso (#3630)
300 Delaware Avenue, Suite 200
Wilmington, DE 19801
(302) 472-7300
dgattuso@hegh.law

Attorneys for Defendants Hikma Pharmaceuticals USA Inc. and Hikma Pharmaceuticals PLC

OF COUNSEL:

Charles B. Klein
Claire A. Fundakowski
WINSTON & STRAWN LLP
1901 L Street, N.W.
Washington, DC 20036
(202) 282-5000

Eimeric Reig-Plessis
WINSTON & STRAWN LLP
101 California Street
San Francisco, CA 94111
(415) 591-6808

Alison Heydorn
WINSTON & STRAWN LLP
35 W. Wacker Drive
Chicago, Illinois 60601
(312) 558-5600

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

Other Authorities

NATURE AND STAGE OF THE PROCEEDINGS

Defendants, Hikma Pharmaceuticals USA Inc. and Hikma Pharmaceuticals PLC (together, "Hikma") are pharmaceutical companies committed to providing patients with high-quality essential medicines. Hikma manufactures oral, nasal, and sterile-injectable medicines across a diversified portfolio, including many of the medicines most needed to treat seriously ill COVID-19 patients. Over the past 10 years, Hikma has invested hundreds of millions of dollars in building and expanding its US and global manufacturing capabilities and seeks to bring more affordable generic medicines to market.

Plaintiffs (collectively, "Amarin") filed this case alleging that Hikma's launch of a generic version of Amarin's Vascepa actively induces infringement of U.S. Patent Nos. 9,700,537 ("the '537 patent"), 8,642,077 ("the '077 patent"), and 10,568,861 ("the '861 patent") (collectively, "patents-in-suit"). Hikma moved to dismiss. D.I. 11. Amarin's First Amended Complaint does not cure any defects in the original complaint. Instead, it merely adds a new defendant (Health Net, LLC), with no new material allegations against Hikma. *See* D.I. 17-1. Hikma moves under Rule 12(b)(6) to dismiss all counts against it in the First Amended Complaint, i.e., Counts I-III.

SUMMARY OF ARGUMENT

Amarin's current lawsuit is its latest attempt to stifle legitimate generic competition for its sole product, a branded fish-oil product called Vascepa (icosapent ethyl). Amarin previously filed—and lost—a Hatch-Waxman patent infringement lawsuit to prevent Hikma from bringing its generic icosapent ethyl product to market. In March 2020, the U.S. District Court for the District of Nevada found all patents asserted against Hikma's generic icosapent ethyl product (with its sole indication to treat severely high triglyceride levels) invalid as obvious, and, in September 2020, the Federal Circuit summarily affirmed. *Amarin Pharma, Inc. v. Hikma Pharm. USA*, 449

F. Supp. 3d 967 (D. Nev. 2020), *aff'd*, 819 F. App'x 932 (Fed. Cir. 2020), *reh'g denied*, 2020-1723, D.I. 90 (Fed. Cir. Nov. 4, 2020).

Hikma subsequently launched its generic product in early November 2020. Amarin then filed this second lawsuit (in a different jurisdiction), alleging that Hikma's labeling and website, as well as certain superseded press releases, supposedly induce doctors to infringe patents directed to an entirely unrelated, different, and unapproved indication—reducing the risk of certain cardiovascular events such as heart attack and stroke (the "CV Indication"). Amarin's First Amended Complaint adds Counts IV-VI against only Health Net, LLC, an insurance company.

Amarin's claims against Hikma should be dismissed under well-established precedent. In particular, Hikma never sought FDA approval for the methods of use covered by Amarin's asserted patents, and Hikma's label does not mention—and never has mentioned—this CV Indication. That is due to what is known as a "carve-out label" under "section viii" of the Hatch-Waxman Amendments. *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 415 (2012); *see also* 21 U.S.C. § 355(j)(2)(A)(viii). According to the Supreme Court, section viii "authorize[s] the FDA to approve the marketing of a generic drug for particular unpatented uses; and [it] provides the mechanism for a generic company to identify those uses, so that a product with a label matching them can quickly come to market." *Caraco*, 566 U.S. at 415. The statute thus "contemplates that one patented use will not foreclose marketing a generic drug for other unpatented ones." *Id.* Amarin apparently reads the statute differently, but its reading has been rejected.

Time and again, the Federal Circuit, this Court, and other district courts have held in rulings on pre-trial motions—including at the pleadings stage—that a generic product indicated for fewer than all FDA-approved indications for the reference product does not "***actively*** induce[]" infringement of patents covering a carved-out indication. 35 U.S.C. § 271(b) (emphasis added).

This is because there can be no inducement based on a generic product label unless it "encourage[s], recommend[s], or promote[s] infringement." *HZNP Meds. LLC v. Actavis Labs. UT, Inc.*, 940 F.3d 680, 701-02 (Fed. Cir. 2019) ("*Horizon*") (citation omitted). "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." *Id.* at 702.

As Amarin concedes, Hikma's generic product is "not [FDA approved] for the CV Indication." D.I. 17 ¶¶ 82, 87. Hikma's labeling does not mention the CV Indication, much less encourage physicians to practice Amarin's related patents. In fact, Amarin never asserted any of the patents-in-suit in its first patent infringement lawsuit in Nevada against Hikma. As the Judge in Amarin's first lawsuit found, Hikma's label "do[es] not include the new [CV] indication":

> Now that Vascepa has two indications, the law "permits [Defendants] to file ANDAs directed to a subset of FDA-approved indications and even provides a mechanism for [Defendants] to affirmatively carve out" the new indication from their labels. *AstraZeneca Pharm. LP v. Apotex Corp.*, 669 F.3d 1370, 1381 (Fed. Cir. 2012). Thus, ***Defendants' current labels do not include Vascepa's new indication***….

Amarin, 449 F. Supp. 3d at 974 (emphasis added).

Now that Hikma recently launched its product, Amarin can rely on information outside of the labeling to prove inducement. But the ultimate question remains the same: "whether the [defendant's] 'instructions teach an infringing use of the device *such that* [the courts] are willing to infer from those instructions an affirmative intent to infringe the patent.'" *Takeda Pharm. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015) (emphasis in original).

Amarin's amended complaint fails to allege any instructions by Hikma—in its labeling or otherwise—that actively encourage infringement. In fact, Hikma discourages infringement. Not only does Hikma's label omit the patented CV indication, its press release announcing the launch (attached to, but not quoted in, the amended complaint) discourages that carved-out use:

> Hikma's FDA-approved Icosapent Ethyl Capsule product is indicated for the following indication: as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. ***Hikma's product is not approved for any other indication for the reference listed drug VASCEPA®.***

D.I. 17, Ex. N (emphasis added).

Amarin nonetheless alleges inducement based on three theories previously rejected by the Federal Circuit. First, according to Amarin, Hikma mentions its product's "AB" rating on its website and, thus, allegedly knows that doctors will prescribe, and pharmacies will automatically substitute, its AB-rated generic product for the CV Indication. *Id.* ¶¶ 109-111, 125-29. But the Federal Circuit rejected this precise argument—that "pharmacists and doctors will … substitute the generic for all indications"—as "unpersuasive" and "contrary to the statutory scheme." *AstraZeneca Pharm. LP v. Apotex Corp.*, 669 F.3d 1370, 1380 (Fed. Cir. 2012).

Second, Amarin alleges that Hikma should have taken even more steps to discourage infringement in its labeling and press releases. D.I. 17, ¶¶ 59-64, 107-108, 111-122. The Federal Circuit (in another case filed against Hikma) rejected this argument—finding that it "turns the legal test on its head" because the patentee "needs to show that Hikma took affirmative steps to induce, not affirmative steps to make sure others avoid infringement." *Takeda*, 785 F.3d at 632 n.4.

Third, Amarin alleges that Hikma's labeling includes vague language that does not foreclose using the generic product for non-indicated uses—including statements such as "[m]edicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet." D.I. 17, ¶¶ 130-135. The Federal Circuit's *Takeda* decision puts this argument to rest. "[V]ague 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." *Takeda*, 785 F.3d at 632 (quoting *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1364 (Fed. Cir. 2003)).

On remand in *Takeda*, Judge Robinson dismissed the complaint on similar grounds. *Takeda Pharm. U.S.A., Inc. v. W.-Ward Pharm. Corp.*, 188 F. Supp. 3d 367, 377 (D. Del. 2016), *vacated on other grounds*, 2016 WL 7230504 (D. Del. Dec. 14, 2016); *see also Takeda Pharm. U.S.A., Inc. v. W.-Ward Pharm. Corp.*, 2018 WL 6521922 (D. Del. Dec. 12, 2018) (granting summary judgment of amended complaint) (Andrews, J.). Amarin's claims should suffer the same fate.

Finally, we suspect that Amarin will rely on the Federal Circuit's recent decision in *GlaxoSmithKline LLC v. Teva Pharm. USA, Inc.*, 976 F.3d 1347 (Fed. Cir. 2020) ("*GSK*"). But that split-panel decision did not alter, and could not have altered, the controlling inducement precedent discussed above. *GSK* is distinguishable and does not apply here. So Amarin's lawsuit should be seen for what it is—a second attempted bite at the apple in a different forum to disrupt Hikma's generic launch and to block legitimate generic competition to achieve anticompetitive ends. Its lawsuit has no basis in law, and this Court should dismiss the First Amended Complaint.

CONCISE STATEMENT OF FACTS

Hikma accepts the allegations (but not characterizations of documents attached to the amended complaint) for purposes of this motion. Pertinent allegations are summarized below.

Vascepa. Vascepa contains the active ingredient icosapent ethyl, which is a purified version of eicosapentaenoic acid (or EPA) found naturally in fish oil. D.I. 17, ¶¶ 25, 28. FDA has approved two methods of treatment for Vascepa. The first—and only indication on Hikma's labeling—is "as an adjunct to diet solely to reduce triglyceride (TG) levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia" ("SH Indication"). *Id.* ¶ 30 & Exs. D, K. As background, the primary concern with this patient population is a condition called pancreatitis, not cardiovascular disease. *See Amarin*, 449 F. Supp. 3d at 973.

The CV Indication, approved in late 2019, is for use "as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and

unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL)" and certain risk factors for cardiovascular disease. *See* D.I. 17, Ex. D. The two indications are distinct. For example, "the cardiovascular risk reduction was not associated with attainment of a more normal triglyceride level." *Amarin*, 449 F. Supp. 3d at 994.

Patents-in-suit. Amarin asserts induced infringement for three patents covering the CV Indication. All three patents require treating a patient with elevated cholesterol levels or cardiovascular disease (as opposed to very high triglyceride levels per the SH Indication), two of the three patents require co-administration with a statin—and, most importantly, none is directed to treating severe hypertriglyceridemia. *See* D.I. 17, ¶¶ 70-79.

The '537 patent (asserted in Count I) covers specific methods of reducing cardiovascular events in a hypercholesterolemia patient—i.e., a patient with high cholesterol—if the patient has not previously had a cardiovascular event and also takes a particular statin within a specified dose range, according to a specific dosing regimen. Representative claim 1 recites:

> 1. A method of reducing occurrence of: a cardiovascular event in a hypercholesterolemia patient consisting of identifying a patient having triglycerides (TG) of at least 150 mg/DL and HDL-C of less than 40 mg/dL in a blood sample taken from the patient as a risk factor of a cardiovascular event, wherein the patient has not previously had a cardiovascular event, and administering ethyl icosapentate in combination with a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor [i.e., a statin],
>
> wherein [the statin] is administered to the patient at least one of before, during and after administering the ethyl icosapentate; and
>
> wherein the [statin] is selected from the group consisting of pravastatin, lovastatin, simvastatin, fluvastatin, atorvastatin, pitavastatin, rosuvastatin, and salts thereof, and
>
> wherein daily dose of the [statin] are 5 to 60 mg for pravastatin, 2.5 to 60 mg for simvastatin, 10 to 180 mg for fluvastatin sodium, 5 to 120 mg for atorvastatin calcium hydrate, 0.5 to 12 mg for pitavastatin calcium, 1.25 to 60 mg for rosuvastatin calcium, 5 to 160 mg for lovastatin, and 0.075 to 0.9 mg for cerivastatin sodium.

D.I. 17, Ex. C.

The '077 patent (asserted in Count II) covers specific methods of reducing triglycerides in a subject with mixed dyslipidemia on statin therapy. Representative claim 1 recites:

> 1. A method of reducing triglycerides in a subject with mixed dyslipidemia on statin therapy comprising, administering to the subject a pharmaceutical composition comprising about 2500 mg to 5000 mg per day of ethyl eicosapentaenoate and not more than about 5%, by weight of all fatty acids, docosahexaenoic acid or its esters to effect a reduction in fasting triglyceride levels in the subject.

D.I. 17, Ex. O. Mixed dyslipidemia refers to elevated LDL cholesterol and triglyceride levels. The specification draws a distinction between "mixed dyslipidemia" and "very high triglycerides." *Id.* 16:7-10; *see also id.* 21:65-22:7.

The '861 patent (asserted in Count III) covers specific methods of reducing the risk of cardiovascular death in a patient who has cardiovascular disease. Representative claim 1 recites:

> 1. A method of reducing risk of cardiovascular death in a subject with established cardiovascular disease, the method comprising administering to said subject about 4 g of ethyl icosapentate per day for a period effective to reduce risk of cardiovascular death in the subject.

D.I. 17, Ex. P.

Hikma's labeling. Hikma carved out the CV Indication from its labeling under section viii. *Id.* ¶¶ 95, 104-106. Thus, Hikma's label is indicated solely for the SH Indication and not for any cardiovascular therapy. *See id.*, Ex. K. Nor does Hikma's label encourage co-administering its product with statins, much less according to a specific statin regimen (e.g., as required by the '537 patent). In fact, Hikma's label mentions statins only twice—in § 12.3, to report no drug-drug interactions with atorvastatin; and in § 14.2, to note that 25% of patients in the reported clinical trial happened to be taking statins. *See id.*

Amarin's inducement allegations. In its amended complaint, Amarin points to no instruction by Hikma to use its generic product for any of the specific methods covered by the

patents-in-suit. Instead, Amarin alleges the following three theories that Hikma's labeling, together with its press releases and website, supposedly encourage those specific methods:

1. Amarin's first theory is that although Hikma's product is indicated solely for the SH Indication, Hikma knows that doctors will prescribe, and pharmacies will automatically substitute, its AB-rated generic product for the CV indication as well. D.I. 17, ¶¶ 109-110, 125-129. For example, Amarin alleges: "On information and belief, Hikma is aware and intends that its generic product, which Hikma describes as AB rated to VASCEPA® for 'hypertriglyceridemia,' will be substituted for all VASCEPA® prescriptions, not just the prescriptions directed to the Severe Hypertriglyceridemia Indication." *Id.* ¶ 111. Amarin further alleges that "Hikma developed its product based on market assumptions that included the entirety of VASCEPA®'s sales, not just for sales resulting from treatment pursuant to the Severe Hypertriglyceridemia Indication." *Id.* ¶ 109.

2. Amarin's second theory is that Hikma has not taken sufficient steps to discourage infringement. As incorporated into Amarin's amended complaint, however, Hikma's November 2020 press release announcing icosapent's generic launch actually does discourage its use for non-labelled indications, including the patented methods: "Hikma's product is ***not approved*** for any other indication for the reference listed drug VASCEPA®." *Id.*, Ex. N (emphasis added). According to Amarin, however, Hikma should be held liable for inducement because it has not done enough to discourage the patented methods. *See id.* ¶¶ 107-108, 111-114, 118-121, 126.

For example, Amarin alleges that Hikma's label induces infringement because it does not include an explicit "limitation of use" as to cardiovascular benefits. *See id.* ¶¶ 107-108. As Amarin alleges, from 2012 until late 2019, when FDA approved the CV Indication, the Vascepa label contained the following limitation of use: "The effect of VASCEPA on cardiovascular mortality

and morbidity in patients with severe hypertriglyceridemia has not been determined." *Id.* ¶ 60. Hikma's proposed generic label, like Vascepa's label, initially included this limitation as well. *Id.* ¶ 108. After FDA approved Vascepa's CV Indication, however, Amarin amended the Vascepa labeling to include that new indication and also to ***delete*** this limitation of use. *Id.* ¶¶ 62-65. Hikma, pursuant to FDA regulations, made conforming changes to its label by deleting this limitation of use and revised its generic labeling to omit the CV Indication under section viii. *Id.* ¶ 108. Because generic products generally need to copy the labeling of the reference drug, Hikma's revised label also omitted the limitation of use with regard to cardiovascular benefits removed from the Vascepa label. *Id.* ¶¶ 104-108, 126; *see also* 21 U.S.C. § 355(j)(2)(A)(v) (typically, generic labeling must be "the same as the labeling approved for the listed drug").

Amarin also alleges that earlier Hikma press releases from March and September 2020 (announcing the trial and appellate wins, respectively) recite the SH Indication, but do not expressly "state that Hikma's 'generic version' of VASCEPA® should not be used for the CV Indication or that the effect of icosapent ethyl on cardiovascular mortality and morbidity had not been determined." D.I. 17, ¶¶ 114, 121. According to Amarin, Hikma's failure to include such a disclaimer in these earlier press releases somehow constitutes an affirmative instruction "that Hikma's 'generic version' of VASCEPA® ***should be used for all of the same indications*** as VASCEPA®, including to reduce the risk of CV events per the CV Indication and as claimed in the" patents-in-suit. *Id.* ¶¶ 115, 122 (emphasis in original). But the actual press releases attached to the amended complaint do not say this. *Compare id.* ¶¶ 114-15, 121-22 *with id.*, Exs. L, M.

Amarin further alleges that Hikma promotes its generic product on its website as "'AB' rated in the 'Therapeutic Category: Hypertriglyceridemia.'" *Id.* ¶¶ 125-26 & Ex. T. As the exhibit attached to the amended complaint makes clear, Hikma's website did not mention—much less

actively encourage—any of the methods claimed by the patents-in-suit. *Id.*, Ex. T. On the contrary, the website said: "Hikma's generic version is indicated for fewer than all approved indications of the Reference Listed Drug." *Id.*[1] Regardless, as Amarin concedes, "FDA has explained that an AB rating reflects a decision that a generic drug is therapeutically equivalent to a branded drug ***when the generic drug is used as labeled, and it does not reflect a decision of therapeutic equivalence for off-label uses***." *Id.* ¶ 98 (emphasis added). Yet, Amarin alleges that Hikma's press releases, together with this mention of the "AB" rating on the website, "instruct, promote, and encourage" infringement even though no patented use appears in Hikma's labeling, press releases, or on its website. *Id.* ¶ 127.

3. Finally, despite the Nevada court's finding that "Defendants' current labels do not include Vascepa's new [CV] indication" (*Amarin*, 449 F. Supp. 3d at 974), Amarin points to the following snippets from Hikma's label that, when viewed collectively, allegedly encourage the non-indicated, patented methods because some patients in the reported study had elevated cholesterol levels:

- "Assess lipid levels before initiating therapy." D.I. 17, Ex. K, § 2.1.
- "Atorvastatin: In a drug-drug interaction study of 26 healthy adult subjects, icosapent ethyl 4 g/day at steady-state did not significantly change the steady-state AUCτ or Cmax of atorvastatin, 2-hydroxyatorvastatin, or 4-hydroxyatorvastatin when co-administered with atorvastatin 80 mg/day at steady state." *Id.* § 12.3.

[1] To address Amarin's concerns raised in its allegations—even though they do not support an inducement claim—Hikma has completely removed the March and September 2020 press releases, and omitted the "AB" rating reference, from its website. Federal Rule of Evidence 407 belies Amarin's allegation that this type of action "demonstrates Hikma's knowledge that these documents and statements "encourage[]" infringement. *Compare* D.I. 17, ¶¶ 117, 124 *with* Fed. R. Evid. 407 (evidence of subsequent remedial measures "is not admissible to prove … culpable conduct"), *and DSU Med. Corp. v. JMS Co., Ltd.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006) (inducement "requires evidence of culpable conduct").

- "Twenty-five percent of patients [in the reported clinical study] were on concomitant statin therapy." *Id.* § 14.2.

- "Heart rhythm problems which can be serious and cause hospitalization have happened *in people who take icosapent ethyl, especially in people who have* heart (cardiovascular) disease or *diabetes with a risk factor for heart (cardiovascular) disease*, or who have had heart rhythm problems in the past." *Id.* at Patient Information leaflet (emphases added).

- "Advise the patient to read the FDA-approved patient labeling before starting icosapent ethyl (Patient Information)." *Id.* § 17.

- "Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet." *Id.* at Patient Information leaflet.

LEGAL STANDARD

A complaint should be dismissed under Fed. R. Civ. P. 12(b)(6) if it does not allege "enough facts to state a claim to relief that is plausible on its face." *Phillips v. Cty. of Allegheny*, 515 F.3d 224, 234 (3d Cir. 2008) (quoting *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 570 (2007)). While a court must accept as true the allegations in the complaint, a claimant must still plead sufficient facts that, if true, satisfy the elements of the relevant cause of action. *Jang v. Boston Sci. Scimed, Inc.*, 729 F.3d 357, 367 (3d Cir. 2013). The Court is "not compelled to accept unsupported conclusions and unwarranted inferences, or a legal conclusion couched as a factual allegation." *Morrow v. Balaski*, 719 F.3d 160, 165 (3d Cir. 2013) (citation omitted).

ARGUMENT

While Congress holds direct infringers strictly liable, inducement liability under the Patent Act attaches only to one who "***actively*** induces infringement." 35 U.S.C. § 271(b) (emphasis added). The Federal Circuit, this Court, and other district courts have issued many decisions construing this simple statute in the pharmaceutical context and finding—even at the pleadings

stage—no induced infringement as a matter of law.[2] Even accepting Amarin's allegations as true, they conflict with this well-established precedent. The amended complaint should be dismissed.

I. Induced infringement requires not only knowledge of direct infringement, but also "active steps" that "specifically encourage" infringement.

It is well established that "[t]he mere existence of direct infringement by physicians, while necessary to find liability for induced infringement, is not sufficient for inducement." *Takeda*, 785 F.3d at 631. Active "inducement requires that the alleged infringer knowingly induced infringement and possessed specific intent to encourage another's infringement." *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006) (en banc) (internal quotation omitted). "[T]he intent requirement for inducement requires more than just intent to cause the acts that produce direct infringement"—"the inducer must have an affirmative intent to cause direct infringement." *Id*. It follows that proof of "inducement requires evidence of culpable ***conduct***, directed to encouraging another's infringement, not merely that the inducer had knowledge of the direct infringer's activities." *Id*. (emphasis added) (citation omitted).

In the pharmaceutical context, before launch, "the question of induced infringement turns on whether [the defendants] have the specific intent, based on the contents of their proposed labels, to encourage physicians to use their proposed ANDA products to" practice the claimed methods. *Grunenthal GMBH v. Alkem Labs., Ltd.*, 919 F.3d 1333, 1339 (Fed. Cir. 2019) (affirming no inducement because the "proposed ANDA labels do not ***specifically encourage*** use of" the drug

[2] *See, e.g.*, *Horizon*, 940 F.3d at 699-704 (Fed. Cir. 2019) (summary judgment); *Warner-Lambert*, 316 F.3d at 1366 (same); *Allergan, Inc. v. Alcon Labs., Inc.*, 324 F.3d 1322, 1334 (Fed. Cir. 2003) (same); *Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316, 1324-26 (Fed. Cir. 2012) (dismissal on pleadings); *AstraZeneca*, 669 F.3d at 1380-81 (Fed. Cir. 2012) (dismissal on pleadings); *Shire LLC v. Amneal Pharm., LLC*, 2014 WL 2861430, at *5 (D.N.J. June 23, 2014), *aff'd in part, rev'd in part on other grounds*, 802 F.3d 1301 (Fed. Cir. 2015) (summary judgment); *Allergan, Inc. v. Sandoz Inc.*, 2011 WL 3794364, at *6 (E.D. Tex. Aug. 25, 2011) (same); *ICN Pharm., Inc. v. Geneva Pharm. Tech. Corp.*, 272 F. Supp. 2d 1028, 1049 (C.D. Cal. 2003) (same); *Takeda*, 188 F. Supp. 3d at 377 (dismissal on pleadings).

product for the patented treatment) (emphasis added). After launch, the patentee still must plead "active steps" that "teach an infringing use of the device"—otherwise, there is no basis to "infer from those instructions an affirmative intent to infringe the patent." *Takeda*, 785 F.3d at 631. Importantly, where a "product has substantial noninfringing uses"—e.g., the SH Indication—"intent to induce infringement cannot be inferred." *Horizon*, 940 F.3d at 702 (quotation omitted).

II. Amarin has not alleged sufficient "active steps" by Hikma to encourage infringement.

All three causes of action should be dismissed because Amarin has failed to plead any "active steps"—i.e., express instructions—that actually "encourage, recommend, or promote infringement." *Takeda*, 785 F.3d at 630-31.

A. Alleged knowledge of direct infringement is insufficient to support an inducement claim.

"To prove inducement, a plaintiff must present evidence of active steps taken to encourage direct infringement; mere knowledge about a product's characteristics or that it may be put to infringing uses is not enough." *Horizon*, 940 F.3d at 701 (citing *Takeda*, 785 F.3d at 630-31). Ignoring this standard, Amarin alleges, "[o]n information and belief, Hikma is aware and intends that its generic product, which Hikma describes as AB rated to VASCEPA® for 'hypertriglyceridemia,' will be substituted for all VASCEPA® prescriptions, not just the prescriptions directed to the Severe Hypertriglyceridemia Indication." D.I. 17, ¶ 111.

This allegation, and similar allegations, that Hikma is aware that doctors may prescribe its generic product for the CV Indication, or that pharmacies may substitute Hikma's product for Vascepa, fall short of stating a claim for inducement. *See id.* ¶¶ 103, 109-111, 129, 135. Any such "market assumptions," *id.* ¶ 109, cannot satisfy the statutory requirement for "active[]" inducement. 35 U.S.C. § 271(b). As noted above, the Federal Circuit already found "unpersuasive" the argument "that Section viii statements and restricted generic labeling ignore

market realities because even if a generic drug is formally approved only for unpatented uses, pharmacists and doctors will nonetheless substitute the generic for all indications once it becomes available"—finding that argument "contrary to the statutory scheme." *AstraZeneca*, 669 F.3d at 1380. Amarin's theory of inducement based on mere knowledge of direct infringement is insufficient as a matter of law. *Id.* (affirming dismissal).

B. Failing to discourage infringement does not support an inducement claim.

Amarin's second theory—that Hikma needs to discourage infringement—is equally meritless. As the Federal Circuit made clear in *Takeda*, Amarin's theory that accused infringers must actively ***dis***courage the patented method "turns the legal test on its head"—after all, Amarin "needs to show that Hikma took affirmative steps to induce, not affirmative steps to make sure others avoid infringement." *Takeda*, 785 F.3d at 632 n.4. This principle belies Amarin's theory of inducement based on allegations that Hikma purportedly failed to discourage infringement.

Amarin cannot meet the pleading requirements for its inducement claims by alleging that Hikma's final label does not contain the limitation of use as to cardiovascular benefits that appeared in previously approved, outdated versions of the Vascepa labeling. D.I. 17, ¶¶ 104-108. The absence of this disclaimer does not actively encourage anybody to do anything, particularly given that Hikma's product is not approved for the CV Indication. Hikma's current label may not actively ***dis***courage the patented method. But Hikma has no legal obligation to take "affirmative steps to make sure others avoid infringement." *Takeda*, 785 F.3d at 632 n.4.

Likewise, Amarin cannot plead inducement by pointing to old press releases that—unlike Hikma's November 2020 press release—did not expressly state Hikma's product was approved only for the SH Indication. Despite the standard laid out in *Takeda*, Amarin alleges that Hikma promotes infringement merely because its older press releases did not "state that Hikma's 'generic version' of VASCEPA® should not be used for the CV Indication or that the effect of icosapent

ethyl on cardiovascular mortality and morbidity had not been determined." D.I. 17, ¶¶ 114, 121. Amarin's theory of active ***dis***couragement lacks legal basis. *Takeda*, 785 F.3d at 632 n.4.

Nor can Amarin plead inducement merely by pointing to a statement on Hikma's website that its generic icosapent ethyl product is "'AB' rated" for "Hypertriglyceridemia." D.I. 17, ¶¶ 125-26 & Ex. T. Hikma's website has never encouraged, much less "***specifically*** encourage[d]," any of the patented methods. *Grunenthal*, 919 F.3d at 1339 (emphasis added).

In short, whether "a physician, without inducement by [Hikma], prescribes a use of [icosapent] in an infringing manner . . . is legally irrelevant" to inducement liability. Amarin's pleading is deficient absent any allegation "that [Hikma] has or will promote or encourage doctors to infringe the [asserted] method patent[s.]" *Warner-Lambert*, 316 F.3d at 1364. As discussed above and in the next subsection, Amarin's amended complaint contains no such allegation.

C. Vague label language combined with speculation is insufficient to satisfy the "active steps" pleading requirement for an inducement claim.

At its heart, Amarin alleges that Hikma knows doctors are directly infringing, and it is not taking sufficient steps to discourage such infringement—allegations that, as discussed above, fail to state an inducement claim. Amarin's attempt to rely on "vague label language" in the form of miscellaneous, non-specific statements from Hikma's labelling, combined with "speculation," also falls short of pleading "active[]" inducement. *Takeda*, 785 F.3d at 632.

Again, Hikma's label is not indicated for any cardiovascular therapy, much less the specific cardiovascular methods-of-treatment covered by the patents-in-suit. To support its inducement claims, Amarin alleges that the clinical trial reported in Hikma's labeling included patients with elevated lipid levels, 25% of the patients in that study happened to be taking a statin, some patients taking icosapent have cardiovascular disease, and "[m]edicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet." D.I. 17, ¶¶ 130-134.

But critically, Hikma's product label—attached to the amended complaint—never encourages doctors or patients to use the drug: (1) with a statin to reduce cardiovascular events in a hypercholesterolemia patient who had not previously experienced such an event, (2) to reduce triglycerides in a subject with mixed dyslipidemia, or (3) with a statin to reduce risk of cardiovascular death in a subject with established cardiovascular disease. *See ALA, Inc. v. CCAIR, Inc.*, 29 F.3d 855, 859 n.8 (3d Cir. 1994) ("Where there is a disparity between a written instrument annexed to a pleading and an allegation in the pleading based thereon, the written instrument will control."). The label thus does not actively induce infringement as a matter of law.

Amarin's inducement theory misses the critical distinction between pleading direct infringement, where strict liability is imposed, and pleading induced infringement—which requires allegations of both specific intent and affirmative steps to induce infringement. "If some physicians nonetheless choose to prescribe" Hikma's product off label for a patented method, "they will do so based on their own independent belief that [this] provides a benefit for their patients. [The] label does not instruct them to do so. It is not enough that a user following the instructions may end up practicing the patented method." *United Therapeutics Corp. v. Sandoz, Inc.*, 2014 WL 4259153, at *19, *21 (D.N.J. Aug. 29, 2014) (rejecting theory of inducement based on "a scholarly scavenger hunt" that "*may* be incited by a reference in the [generic] label"). Again, Hikma's press release announcing the product launch clarifies that the generic product is approved only for the SH Indication, consistent with the product label itself—the opposite of inducement.

Indeed, the Federal Circuit has held that drug labels do not induce infringement even though the patented methods undisputedly fell within the scope of FDA approval. In *Grunenthal*, the drug was indicated to treat "severe chronic pain," which included the patented use to treat "polyneuropathic pain." 919 F.3d at 1339. The patentee argued that the indication would

inevitably lead at least some doctors to infringe. But the Federal Circuit rejected that theory, holding that "even if severe chronic pain includes polyneuropathic pain, it also includes [other kinds of severe chronic] pain. Therefore, the proposed ANDA labels do not ***specifically encourage*** use of [the drug] for treatment of polyneuropathic pain." *Id*. (emphasis added).

Similarly, the patented method in *Horizon* requires a user to "(1) apply the inventive formulation, (2) wait for the area to dry, and (3) apply sunscreen, insect repellant, or a second topical medication." 940 F.3d at 702. The label describes each of these steps, instructing users to "wait until the treated area is dry before applying a second topical agent." *Id*. at 686 (quotation and alteration omitted). Yet the Federal Circuit found no inducement: While "[t]he patented method here requires three distinct steps," the label "only require[s] the first step of this method." *Id*. at 702. Because "the label does not ***require*** subsequent application" of another drug, as required by the asserted claims, the label "does not encourage infringement." *Id*. (emphasis added). Put simply: "Merely describing the infringing use . . . will not suffice; specific intent and action to induce infringement must be shown." *Id.*

Here, Hikma's label never describes any method covered by the patents-in-suit, much less requires or otherwise specifically encourages such a method. This case is indistinguishable from *Takeda*, where Hikma's label was indicated solely for ***preventing*** gout flares, but Takeda alleged infringement of patents covering methods of ***treating*** acute gout flares because Hikma's label said: "If you have a gout flare while taking [the product], tell your healthcare provider"—a statement Takeda alleged would inevitably lead to doctors advising patients to use Hikma's generic product to treat the flare. *Takeda*, 785 F.3d at 632. The Federal Circuit disagreed, holding 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.* (quoting *Warner-Lambert*, 316 F.3d at 1364); *cf. Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 845 F.3d 1357, 1369 (Fed. Cir. 2017) (confirming "'vague' instructions that require one to 'look outside the label to understand the alleged implicit encouragement' do not, without more, induce infringement"; finding liability because "[t]he instructions are unambiguous on their face and encourage or recommend infringement") (quoting *Takeda*, 785 F.3d at 632, 634).

On remand, relying on the Federal Circuit's *Takeda* decision, Judge Robinson dismissed Takeda's amended complaint under Rule 12(b)(6) because Hikma's label in that case is "not a sufficient catalyst to constitute 'active steps taken to encourage direct infringement.'" *Takeda*, 188 F. Supp. 3d at 377 (quoting *Takeda*, 785 F.3d at 630). This case is no different. Amarin cannot rely on vague statements in Hikma's labeling, such as "[m]edicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet." D.I. 17, ¶¶ 130-134. Hikma's label never encourages using the product to treat patients with elevated cholesterol levels, or to reduce cardiovascular events—much less to reduce the risk of cardiovascular death.

D. Amarin's claims viewed as a whole fail to state an inducement claim.

Amarin cannot support its inducement claim with speculation that healthcare providers "will inevitably practice" patented methods not covered by Hikma's indication or approved labeling. *Id.*, ¶¶ 133, 135. As the Federal Circuit explained in *Grunenthal*, induced infringement requires an ***instruction*** by the accused infringer that "would inevitably lead some consumers to practice the claimed method." 919 F.3d at 1340. Here, in contrast, Amarin alleges no instruction that even mentions, much less specifically encourages, any of the methods claimed by the patents-in-suit. Amarin's flawed amended complaint is little more than a last-ditch effort by a company that previously tried and was unsuccessful in staving off generic competition on its sole product.

III. Amarin cannot rely on the recent *GSK* case to survive this motion to dismiss.

Although not mentioned in its amended complaint, Amarin may rely on the recent Federal Circuit decision in *GSK*, which upheld a jury verdict that Teva's generic product induces infringement even though the product initially launched with a carved-out label. Amarin can find no solace in that highly fact-specific (and split) decision.

Importantly, the *GSK* majority did not (and could not) overrule the precedent discussed above—including the decisions in *Takeda*, *Grunenthal*, *Horizon*, *AstraZeneca*, *Bayer*, and *Warner-Lambert*. After all, the Federal Circuit "respects the principle of stare decisis and follows its own precedential decisions unless the decisions are 'overruled by the court en banc, or by other controlling authority such as an intervening ... Supreme Court decision.'" *Teva Pharm. USA, Inc. v. Novartis Pharm. Corp.*, 482 F.3d 1330, 1338 (Fed. Cir. 2007) (citation omitted); *accord Johnston v. IVAC Corp.,* 885 F.2d 1574, 1579 (Fed. Cir. 1989). Indeed, the majority did not cite, much less distinguish, any of these precedential decisions—all of which continue to control the analysis here. *See generally GSK*, 976 F.3d at 1348-57 (Fed. Cir. 2020).

The majority's decision in *GSK* is subject to a pending petition for rehearing, and thus may be amended or reversed. Regardless of its ultimate fate, however, the *GSK* decision is factually distinguishable on several grounds. First, in *GSK*, Teva initially launched its product with a carved-out label, but later reversed course and included the patented method in its labeling. *GSK*, 976 F.3d at 1350 ("Teva amended its label to include the [patented] indication…."). This unique fact pattern was presented to a jury, and the decision thus focused on jury deference. *See id.* at 1351-52 (applying strict JMOL standard), 1355-56 (finding "substantial evidence to support the jury's findings"). By contrast, Hikma launched with a standard section viii carved-out label that has remained unchanged. Unlike in *GSK*, there is no basis under the controlling precedent discussed above for the allegations here to proceed to a jury.

Second, the *GSK* jury was presented not only with a label that eventually included the patented methods, but also with Teva press releases silent on the scope of generic approval. *Id.* at 1353-54. Even putting aside the pending dispute in that case as to whether those press releases were sufficient to support a jury verdict given the unique circumstances of that case, this case involves materially different facts. As discussed, Hikma's press release announcing its generic launch expressly says, "Hikma's product is not approved for any other indication for the reference listed drug VASCEPA®"—removing any doubt as to the limited scope of Hikma's labeling. D.I. 17, Ex. N. There was no such disclaimer in *GSK*. And no reasonable jury could conclude from Hikma's press release that it is telling doctors its generic product is approved for the CV Indication.

Third, the *GSK* jury was presented with Teva's "product catalogs" listing "AB ratings and … compar[ing] Teva's [generic product] with [the branded product.]" *GSK*, 976 F.3d at 1354. The majority relied on this comparison and expert testimony, stating "that the FDA's 'general position is that if you compare one product to another by name, you are implying the use of the product.'" *Id.* Although Hikma's website initially listed its product as AB rated, its website did not and does not even mention Vascepa, much less compare the products, and says that the generic product "is indicated for fewer than all approved indications…." *See* D.I. 17, ¶ 125, Ex. T.

In sum, regardless of how the Federal Circuit—or Supreme Court—resolves the *GSK* case, it does not apply here. The principles of inducement law have been made clear time and again in multiple Federal Circuit decisions. Following that precedent leads to only one conclusion: Amarin's allegations are insufficient to state a viable claim for induced infringement.

CONCLUSION

Hikma respectfully requests that the Court dismiss Counts I-III of the First Amended Complaint with prejudice.

HEYMAN ENERIO
GATTUSO & HIRZEL LLP

/s/ Dominick T. Gattuso
Dominick T. Gattuso (#3630)
300 Delaware Avenue, Suite 200
Wilmington, DE 19801
(302) 472-7300
dgattuso@hegh.law

Attorneys for Defendants Hikma Pharmaceuticals USA Inc. and Hikma Pharmaceuticals PLC

OF COUNSEL:

Charles B. Klein
Claire A. Fundakowski
WINSTON & STRAWN LLP
1901 L Street, N.W.
Washington, DC 20036
(202) 282-5000

Eimeric Reig-Plessis
WINSTON & STRAWN LLP
101 California Street
San Francisco, CA 94111
(415) 591-6808

Alison Heydorn
WINSTON & STRAWN LLP
35 W. Wacker Drive
Chicago, Illinois 60601
(312) 558-5600

Dated: January 27, 2021