No. 2023-1169

United States Court of Appeals for the Federal Circuit

AMARIN PHARMA, INC., AMARIN PHARMACEUTICALS IRELAND LIMITED, MOCHIDA PHARMACEUTICAL CO., LTD.,
Plaintiffs-Appellants

v.

HIKMA PHARMACEUTICALS USA INC., HIKMA PHARMACEUTICALS PLC,
Defendants-Appellees

HEALTH NET LLC,
Defendant

APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE, CASE NO. 1:20-CV-01630-RGA-JLH, JUDGE RICHARD G. ANDREWS

BRIEF FOR DEFENDANTS-APPELLEES

EIMERIC REIG-PLESSIS
Winston & Strawn LLP
101 California Street
San Francisco, CA 94111
(415) 591-1000

CHARLES B. KLEIN
CLAIRE A. FUNDAKOWSKI
Winston & Strawn LLP
1901 L Street NW
Washington, DC 20036
(202) 282-5000

ALISON M. KING
Winston & Strawn LLP
35 W. Wacker Drive
Chicago, IL 60601
(312) 558-5600

Counsel for Defendants-Appellees Hikma Pharmaceuticals USA Inc. and Hikma Pharmaceuticals PLC

May 31, 2023

CLAIM LANGUAGE

U.S. Patent No. 9,700,537

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,

wherein said 3-hydroxyl-3-methylglutaryl coenzyme A reductase inhibitor is administered to the patient at least one of before, during and after administering the ethyl icosapentate; and

wherein the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor is selected from the group consisting of pravastatin, lovastatin, simvastatin, fluvastatin, atorvastatin, pitavastatin, rosuvastatin, and salts thereof, and

wherein daily dose of the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor 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.

U.S. Patent No. 10,568,861

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.

2. The method of claim 1, wherein the subject has a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL and a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL.

CERTIFICATE OF INTEREST

Counsel for Defendants-Appellees certifies the following:

1. **Represented Entities.** Fed. Cir. R. 47.4(a)(1). Provide the full names of all entities represented by undersigned counsel in this case:

Hikma Pharmaceuticals USA Inc.
Hikma Pharmaceuticals PLC

2. **Real Party in Interest.** Fed. Cir. R. 47.4(a)(2). Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities:

N/A

3. **Parent Corporations and Stockholders.** Fed. Cir. R. 47.4(a)(3). Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities:

Hikma Pharmaceuticals USA Inc. is an indirect wholly owned subsidiary of ***Hikma Pharmaceuticals, PLC***, which is a publicly held corporation. ***Hikma Pharmaceuticals, PLC*** does not have a parent corporation, and no publicly held corporation owns 10% or more of its stock.

4. **Legal Representatives.** List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

Heyman Enerio Gattuso & Hirzel LLP: Dominick T. Gattuso

5. **Related Cases.** Other than the originating case(s) for this case, are there related or prior cases that meet the criteria under Fed. Cir. R. 47.4(a)?

No

6. **Organizational Victims and Bankruptcy Cases.** Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal

cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

N/A

May 31, 2023

/s/ Charles B. Klein
CHARLES B. KLEIN
Winston & Strawn LLP
1901 L Street NW
Washington, DC 20036
(202) 282-5000
cklein@winston.com

TABLE OF CONTENTS

Page

TABLE OF CONTENTS (continued)

Page

TABLE OF AUTHORITIES

Page(s)

Cases

TABLE OF AUTHORITIES (continued)

Page(s)

TABLE OF AUTHORITIES (continued)

Page(s)

Statutes

Other Authorities

GLOSSARY OF ABBREVIATIONS

’537 patent	U.S. Patent No. 9,700,537
’861 patent	U.S. Patent No. 10,568,861
Amarin	Plaintiffs-Appellants Amarin Pharma, Inc. Amarin Pharmaceuticals Ireland Limited, and Mochida Pharmaceutical Co., Ltd., collectively
Hikma	Defendants-Appellees Hikma Pharmaceuticals USA Inc., Hikma Pharmaceuticals PLC
ANDA	abbreviated new drug application
Br.	brief (unless otherwise noted, Amarin’s opening brief, Dkt. 15)
CV	cardiovascular
EPA	eicosapentaenoic acid, also known as icosapent, icosapent ethyl, ethyl icosapentate, or EPA-E (i.e., ethyl EPA)
FAC	First Amended Complaint
FDA	U.S. Food and Drug Administration
LDL-C	low-density lipoprotein cholesterol
SH	severe hypertriglyceridemia
TG	triglyceride

STATEMENT OF RELATED CASES

No previous appeal has been taken in this action. Appellees and their counsel are not aware of any other pending cases that will directly affect or be directly affected by the decision in this case.

INTRODUCTION

This appeal involves two asserted patents limited to methods of "reducing occurrence of a cardiovascular event" or "reducing risk of cardiovascular death." Appx46 ('537 patent, cl. 1); Appx129 ('861 patent, cl. 1). Amarin alleges that Hikma "actively induces" infringement of these treatment methods under 35 U.S.C. § 271(b). But to plead infringement under this statute, Amarin had to plausibly allege that Hikma took "active steps . . . taken to encourage direct infringement." *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1305-06 (Fed. Cir. 2006) (en banc) (quoting *Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd*., 545 U.S. 913, 936 (2005)). Amarin failed to meet this legal standard.

While Amarin's own Vascepa® product is FDA-approved for reducing cardiovascular ("CV") risk in certain patients, Amarin admits that Hikma's generic product "is not FDA-approved for the CV Indication." Appx522 (FAC, ¶ 87). Amarin nonetheless pleads induced infringement based on vague, general statements—along with the ***absence*** of statements discouraging infringement—in Hikma's ANDA label and public representations. The district court thus properly found that Amarin's pleaded inducement theory is not plausible and fails as a matter of law.

At its core, Amarin's inducement allegations attempt to expand this Court's "narrow, case-specific" holding in *GlaxoSmithKline LLC v. Teva Pharm. USA, Inc.*,

7 F.4th 1320, 1326 (Fed. Cir. 2021) ("*GSK*"). In *GSK*, this Court held that substantial evidence supported the jury's finding that Teva's "so-called 'skinny label'" still actively encouraged a patented use. 7 F.4th at 1328. Amarin latches onto this holding, arguing that "*GlaxoSmithKline* is illustrative" because "[a] generic manufacturer can be liable for inducing infringement even when it has attempted to 'carve out' the patented indications with a skinny label." Br. at 29, 40. But *GSK* is limited to a case where a carved-out (or skinny) label still actively induced infringement, a materially different situation than that presented here. The Court should decline Amarin's invitation to drastically broaden the *GSK* holding, which the Solicitor General characterized as creating a "potential deterrent effect on generic-drug manufacturers' invocation of the section viii pathway." *See* Br. for United States, *Teva Pharm. USA, Inc. v. GSK LLC*, No. 22-37, at 21 (Mar. 2023).

Unlike in *GSK*, this is a true skinny label case. And, critically, there are no material issues of fact that preclude resolution at the pleadings stage. In *GSK*, there was a material dispute as to whether "Teva's partial label encouraged an infringing use" based on the scope of its labeled indication—an issue the jury resolved in the patentee's favor. *GSK*, 7 F.4th at 1327-28. But here, Amarin does not argue that Hikma's sole indication (treating severe hypertriglyceridemia) is an instruction that encourages practicing the claimed CV treatment methods. Instead, Amarin primarily argues that Hikma's label ***omits*** a statement that would discourage

infringement. *See* Appx527-528 (FAC, ¶ 108). Omissions do not actively encourage infringement, and the Patent Act does not authorize claims for passive or implied inducement. In fact, asking Hikma to do more to "make sure others avoid infringement" is a legal theory this Court has rejected as "turn[ing] the legal test on its head." *Takeda Pharm. USA, Inc. v. W.-Ward Pharm. Corp.*, 785 F.3d 625, 632 n.4 (Fed. Cir. 2015). Amarin also relies on a label statement ***warning*** about serious side effects if used in patients with CV issues. Appx534-535 (FAC, ¶ 131). But it is likewise implausible that a warning against practicing the CV treatment methods somehow encourages them. *Takeda*, 785 F.3d at 634 (agreeing with the district court that a statement that "warns patients" was "label language [that] failed to recommend or suggest to physicians that the patented . . . methods should be followed"). Unlike in *GSK*, therefore, Amarin points to no statement in Hikma's label that plausibly encourages the specifically claimed treatment methods asserted in this case.

While Amarin also relies on written statements outside of Hikma's label, these allegations are similarly deficient under Rule 12(b)(6). Regardless of how many times Hikma stated (correctly) that its ANDA product is a "generic" or "AB" rated version of Vascepa®, this Court in *GSK* made clear that "generics could *not* be held liable . . . for merely noting (without mentioning any infringing uses) that FDA had rated a product as therapeutically equivalent to a brand-name drug." *GSK*, 7 F.4th at 1326. None of Hikma's public statements "mention[] any infringing uses," or

even mention CV risk. *See id.* Nor is it plausible that merely reporting that its products fall within the general therapeutic category of "Hypertriglyceridemia" (meaning high triglycerides)—without mentioning CV risk or CV death—encourages methods that specifically require reducing CV risk or CV death. Hikma's public statements, like its label, contain no instructions that actively encourage infringement.

In view of its reliance on vague, miscellaneous statements, Amarin repeatedly emphasizes that its inducement theory is based on the "collection" of Hikma's label and statements—not any specific instruction to infringe. *See* Br. at 39; *see also id.* at 2 (arguing "it was at least plausible that Hikma's label together with its various public statements ***collectively*** encouraged infringement") (emphasis added); *id.* at 37 (same). But without a "clear expression . . . to foster infringement," Amarin has failed to plausibly allege "affirmative steps" to encourage infringement. *DSU*, 471 F.3d at 1305-06. Combining meritless inducement theories is not enough to state a claim for relief.

Finally, allowing Amarin's inducement claims to proceed based on these scant allegations would effectively allow post-launch suits over nearly every skinny label, because brand pharmaceutical companies will almost always be able to cobble together a "collection" of allegations such as those Amarin makes here. This threat of protracted litigation alone—even if there is only a small chance of ultimately

losing—will deter ANDA filers from using section viii carve-outs, defeating Congress's intent that "one patented use will not foreclose marketing a generic drug for other unpatented ones." *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 415 (2012). The Court recognized this risk in *GSK*, clarifying that a "generic could *not* be held liable for merely marketing and selling under a 'skinny' label omitting all patented indications," as such a holding would "upset the careful balance struck with section viii carve-outs." *GSK*, 7 F.4th at 1326. The Court should decline to upset that "careful balance" here and should conclude that Amarin has failed to state a claim for relief under Rule 12(b)(6). *See id.*

For these reasons, this Court should affirm.

STATEMENT OF ISSUES

Whether the district court properly granted Hikma's motion to dismiss Amarin's First Amended Complaint for failure to state a claim for active inducement of patent infringement under 35 U.S.C. § 271(b), where neither the label for Hikma's generic drug product nor Hikma's public statements instruct using the product for "reducing occurrence of a cardiovascular event" or "reducing risk of cardiovascular death"—limitations required by Amarin's asserted patents.

STATEMENT OF THE CASE

A. Vascepa® and its approved indications

Vascepa® contains the active ingredient icosapent ethyl, which is a purified version of eicosapentaenoic acid (or EPA) found naturally in fish oil. Appx508

(FAC, ¶¶ 25, 28). FDA has approved two methods of treatment for Vascepa®. The first is "as an adjunct to diet solely to reduce triglyceride (TG) levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia" ("SH Indication"). Appx514 (FAC, ¶ 56). As Amarin acknowledges, "the primary concern with severe HTG [hypertriglyceridemia] patients is pancreatitis" due to "a patient's blood triglyceride level"—not CV risk reduction. Br. at 4. Amarin obtained the SH Indication by completing its "MARINE" study, which demonstrated that Vascepa® reduces triglyceride levels in patients with severe hypertriglyceridemia (≥ 500 mg/dL). Appx508 (FAC, ¶ 30).

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* Appx514 (FAC, ¶ 56). The two indications are undisputedly distinct. For example, as Amarin acknowledges, FDA determined "that reduced triglyceride levels were *not* correlated with reduced cardiovascular risk." Br. at 7; Appx509 (FAC, ¶ 32) (explaining FDA determined "lowered triglyceride levels . . . did not show an actual reduction in cardiovascular risk"). Amarin's clinical study to support the CV Indication, the "REDUCE-IT" trial, accordingly was

not "based on measuring the patients' triglyceride levels" and did not "focus[] on triglyceride levels" at all. Br. at 7-8; *accord* Appx509 (FAC, ¶ 33).

B. Hikma's ANDA and prior litigation

Amarin previously filed—and lost—a Hatch-Waxman patent infringement lawsuit to prevent Hikma from bringing its generic version of Vascepa® to market. In September 2016, Hikma filed an ANDA for its icosapent ethyl product with the sole indication to treat severely high triglyceride levels (≥ 500 mg/dL). Appx514 (FAC, ¶ 59); Appx525 (FAC, ¶ 99). After a bench trial, in March 2020, the U.S. District Court for the District of Nevada invalidated all patents asserted against Hikma for obviousness, and this Court affirmed the judgment. *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*, No. 2020-1723, ECF No. 90 (Fed. Cir. Nov. 4, 2020), *cert. denied*, No. 20-1119 (U.S. June 21, 2021).

Shortly before trial, in December 2019, Amarin received FDA approval for the CV Indication. Appx517 (FAC, ¶ 62). Under the Hatch-Waxman Act, Hikma was required to either amend its proposed ANDA label to match the revised Vascepa® label with the CV Indication and corresponding information or file a section viii statement with a label that carved out such information. *See* Appx526 (FAC, ¶¶ 101, 102). In January and May 2020, "Hikma submitted to FDA Section viii statements" certifying that Hikma had carved out the CV Indication and

corresponding information protected by over two dozen patents Amarin identified in the Orange Book as associated with that indication. *See* Appx526 (FAC, ¶ 104). The Orange Book is a compendium that "provides notice concerning patents covering FDA-approved drugs." Appx519 (FAC, ¶ 70). The two patents at issue in this appeal—the '537 and '861 patents—were among the patents included in Hikma's section viii statements. Appx526 (FAC, ¶ 104).

FDA approved Hikma's ANDA in May 2020, and Hikma launched its generic icosapent ethyl product in November 2020. Appx526 (FAC, ¶ 105); Appx506 (FAC, ¶¶ 11-13). Since launching its generic product, Hikma's label has remained substantively the same. *See* Appx526 (FAC ¶ 106); Appx707.

C. Amarin's allegations of actively induced infringement

Shortly after Hikma launched its icosapent ethyl product, Amarin filed this case alleging induced infringement of the '537 and '861 patents (along with a third patent that was later dismissed). Among other limitations, the '537 patent requires "[a] method of reducing occurrence of: a cardiovascular event in a hypercholesterolemia patient . . . wherein the patient has not previously had a cardiovascular event" and coadministration with a drug commonly known as a statin. Appx46 ('537 patent, cl. 1). The '861 patent similarly requires, among other limitations, "[a] method of reducing risk of cardiovascular death in a subject with established cardiovascular disease." Appx129 ('861 patent, cl. 1). At the district

court, the parties stipulated that these preambles are limiting. Appx1909-1911. Amarin's induced infringement allegations, as set forth in its First Amended Complaint, are summarized below and concern statements in (1) the FDA-approved label for Hikma's ANDA product; and (2) Hikma's public representations about its product, including on its website and in press releases.

1. Hikma's label

In relying on Hikma's label to allege induced infringement, Amarin does not allege that Hikma's sole indication covers the claimed methods of treatment. As Amarin concedes, Hikma's generic product is "not [FDA approved] for the CV Indication" and instead is "FDA approved for only the [SH] Indication." Appx521 (FAC ¶ 82); Appx522 (FAC, ¶ 87). Nor does Amarin allege that Hikma's sole indication for SH induces infringement of the CV method-of-treatment claims. The aspects of Hikma's label that Amarin relies on to support its allegations of actively induced infringement are summarized below:

Absence of limitation of use. Amarin alleges that "Hikma intentionally amended the proposed labeling for its icosapent ethyl capsules to remove the CV Limitation of Use." Appx527-528 (FAC, ¶ 108). The "CV Limitation of Use" that Amarin references is language present in the original Vascepa® label, before FDA approved the CV Indication, that stated "[t]he effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been

determined." Appx514-15 (FAC, ¶ 60). Amarin alleges that the ***absence*** of this language in Hikma's product label (as opposed to the presence of any instruction) actively induces "healthcare providers and patients [to] believe that Hikma's generic icosapent ethyl capsules could be and should be used . . . to reduce the risk of CV events" that are not mentioned anywhere in the label. Appx527-528 (FAC, ¶ 108).

Amarin's allegations make clear that Hikma never marketed its icosapent ethyl product with the CV Limitation of Use. According to Amarin, Hikma removed the CV Limitation of Use "on or about the date on which it submitted to FDA Section viii statements with respect to the Asserted Patents," i.e., before Hikma obtained FDA approval and several months before Hikma launched its product. Appx527-528 (FAC, ¶ 108); *see also* Br. at 19 ("When Hikma launched its product, its label did not include any cardiovascular Limitation of Use."). Thus, Hikma only "removed" the CV Limitation of Use from a draft label that had been submitted to FDA and was never made public nor used on any marketed product.[1] *See* Appx526-527 (FAC, ¶¶ 104-108).

[1] Hikma did so because generic products generally need to copy the labeling of the reference drug. So when Amarin removed the limitation of use from the Vascepa® label, Hikma was likewise required to omit that language from its proposed label to obtain FDA approval. *See* 21 U.S.C. § 355(j)(2)(A)(v) (typically, generic labeling must be "the same as the labeling approved for the listed drug").

Side effects warning. Amarin points to language in the patient information leaflet at the end of the label under the heading, "What are the possible side effects of icosapent ethyl?" Appx534-535 (FAC, ¶ 131); Appx704-705. One of the "***possible side effects***" identified is "[h]eart rhythm problems which can be ***serious and cause hospitalization*** . . . ***especially in people who have heart (cardiovascular) disease or diabetes with a risk factor for heart (cardiovascular) disease***." Appx704-705 (emphasis added). This warning against using the product due to serious, possible side effects is the only instance where the label mentions cardiovascular disease. Amarin alleges—implausibly—that this warning of serious side effects for CV patients actively "encourages, promotes, and instructs treating patients" with "established cardiovascular disease," Appx534-535 (FAC, ¶ 131), and further "would encourage a healthcare provider to prescribe [Hikma's] generic product for the patented and non-approved CV Indication," Br. at 17.

General Information. Amarin also relies on language in a portion of Hikma's patient information leaflet concerning "[g]eneral information" about icosapent ethyl that states "[m]edicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet." Appx535 (FAC, ¶ 132); Appx705. Amarin contends that this language "tells readers that Hikma's product will be prescribed for reasons other than treating patients with severe HTG," without specifying what those "reasons" might be. Br. at 18; Appx535 (FAC, ¶ 132).

Clinical studies section. To support claim limitations other than the preambles, Amarin cites various other portions of Hikma's label, including the baseline characteristics of patients included in a clinical study and some patient's use of statins. *See, e.g.*, Appx534 (FAC, ¶ 130); Appx536 (FAC, ¶ 134) (citing Appx702). The only clinical study described in Hikma's ANDA label is the clinical study for "Severe Hypertriglyceridemia." Appx702. This study describes, among other things, the median baseline TG, HDL-C, and LDL-C levels for the patients included in the study. Appx702. This section also describes that "[t]wenty-five percent of patients were on concomitant statin therapy." Appx702. The clinical studies section does not mention anything about the patients' CV risk or reducing CV death.

2. Hikma's public statements

In addition to Hikma's label, Amarin relies on Hikma's press releases and other public statements to allege induced infringement.

Press releases. Amarin relies on pre-launch press releases from March and September 2020 announcing Hikma's trial and appellate wins in the Nevada litigation regarding the SH indication. *See* Appx529 (FAC, ¶ 112) (citing Appx709); Appx530 (FAC, ¶ 118) (citing Appx712). The relevant portion of the March 2020 press release is copied below:

> Vascepa® is a prescription medicine that is indicated, in part, as an adjunct to diet to reduce triglyceride levels in

> adult patients with severe (≥500 mg/dL) hypertriglyceridemia.
>
> According to IQVIA, US sales of Vascepa® were approximately $919 million in the 12 months ending February 2020.

Appx709. In the September 2020 press release, Hikma stated it "received FDA approval for the product in May 2020," followed by the below excerpt:

> Vascepa® is a prescription medicine that is indicated, in part, as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. According to IQVIA, US sales of Vascepa® were approximately $1.1 billion in the 12 months ending July 2020.

Appx712.

The only indication mentioned in the March and September 2020 press releases is the SH indication. Appx709; Appx712. Amarin nonetheless relies on these press releases to allege actively induced infringement because (1) they "do[] not state that Hikma's 'generic version' of VASCEPA® should not be used for the CV Indication" and (2) the sales data reported for Vascepa® "includes sales for ***all uses*** of Vascepa®, including the CV Indication." Appx529-530 (FAC, ¶¶ 113-114); Appx531 (FAC, ¶¶ 120-121). Based on these allegations, Amarin alleges Hikma's March and September 2020 press releases each "communicates to and instructs healthcare providers and patients that Hikma's 'generic version' of VASCEPA®

should be used for all the same indications as VASCEPA®, including to reduce the risk of CV events." Appx530 (FAC, ¶ 115); Appx531 (FAC, ¶ 122).

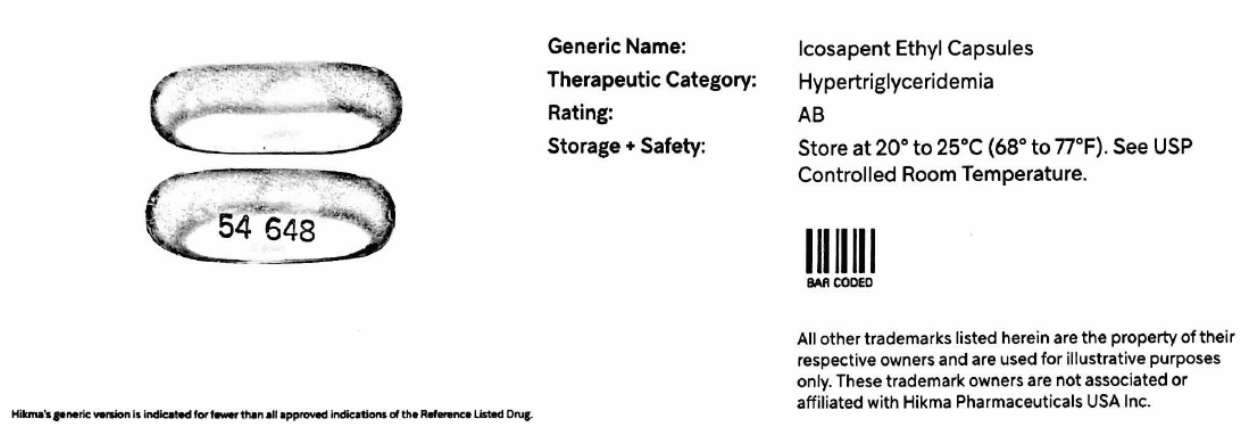
Amarin attaches to its complaint, but does not affirmatively rely on, Hikma's pre-litigation, November 2020 press release announcing its launch. *See* Appx715. Hikma's November 2020 press release is copied below (in relevant part) and expressly states that Hikma's icosapent ethyl product is indicated for the SH Indication and "not approved for any other indication for the reference listed drug VASCEPA®":

> 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®.

Appx715.

Market statements. Amarin alleges Hikma "was and is aware that over 75% of the sales of VASCEPA® since 2013 are for uses other than the Severe Hypertriglyceridemia Indication, including uses to reduce CV events," citing evidence from the parties' Nevada trial concerning the SH patents. Appx528-529 (FAC, ¶ 110) (citing, e.g., Appx803, Appx805). Amarin alleges that because it is "an AB-rated generic drug[,] . . . Hikma knew and intended that its generic product would be substituted for all VASCEPA® prescriptions, not just the prescriptions directed to the Severe Hypertriglyceridemia Indication." Appx533 (FAC, ¶ 129).

Website. Amarin relies on Hikma's website describing its icosapent ethyl product "as AB rated to VASCEPA® for 'hypertriglyceridemia.'" *See* Appx529 (FAC, ¶ 111) (citing Appx820). As shown below, however, Hikma's website also expressly states "Hikma's generic version is indicated for fewer than all approved indications of the Reference Listed Drug":



Appx820.

Amarin alleges "the 'Therapeutic Category' information . . . — 'Hypertriglyceridemia'—does not match and is broader than the Indications and Usage sections of Hikma's Label, which includes only the Severe Hypertriglyceridemia Indication." Appx532-533 (FAC, ¶ 126). Amarin does not, however, allege that reducing triglycerides encompasses reducing the risk of a cardiovascular event or cardiovascular death as required by the asserted claims. *See, e.g.*, Appx509 (FAC, ¶ 32 (alleging "lowered triglyceride levels . . . did not show an actual reduction in cardiovascular risk")).

D. The district court's dismissal of Amarin's amended complaint

Hikma moved to dismiss Amarin's amended complaint under Rule 12(b)(6) for failure to state a claim. *See* Appx948. As Hikma explained, "Amarin's amended complaint fails to allege any instructions by Hikma—in its labeling or otherwise—that actively encourage infringement." Appx950.

Magistrate Judge Hall recommended denying Hikma's motion to dismiss. *See* Appx1430. The magistrate judge recognized that "the contents of its label and public statements are undisputed," and explained that "were this an ANDA case, and were Plaintiffs' allegations based solely on the label, Plaintiffs' inducement theory might lack merit as a matter of law." Appx1426-1427. The magistrate judge nonetheless concluded that Amarin plausibly alleged that "several . . . portions of Hikma's label, taken together with Hikma's public statements, instruct physicians to use Hikma's product in a way that infringes the asserted patents." Appx1424.

On de novo review, Judge Andrews overruled the magistrate judge's recommendation and granted Hikma's motion to dismiss. Appx2. The district court noted that, "[t]wo days after the Report issued, the Court of Appeals issued the most recent authoritative opinion concerning skinny labels" in the Court's decision after the panel rehearing in *GSK*. Appx4 (citing *GSK*, 7 F.4th 1320). Under this new precedent, the district court rejected Amarin's argument that "Hikma's label is 'not-skinny-enough,'" Appx4, concluding "the label does not instruct CV risk reduction,"

Appx7. The district court concluded that the absence of the CV Limitation of Use in Hikma's label "does not plausibly teach CV risk reduction," citing Federal Circuit precedent that rejected the argument that "generic labels must contain a 'clear statement' discouraging use of the patented indication." Appx7. The district court also concluded that "the warning as to side effects" in Hikma's label "is hardly an instruction or encouragement." Appx6. With respect to Hikma's public statements, the district court concluded that Hikma's press releases did not include "an inducing act," Appx7-8, and that the category "hypertriglyceridemia" on Hikma's website did "not rise to the level of encouraging, recommending, or promoting taking Hikma's generic for the reduction of CV risk," Appx8. Concluding "that Amarin's complaint has failed to plead inducement based on Hikma's label or public statements," the district court granted Hikma's motion to dismiss. Appx9.

SUMMARY OF ARGUMENT

I. "Whoever ***actively induces*** infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b) (emphasis added). Precedent makes clear that, to state a claim for actively induced infringement, Amarin was required to plausibly allege Hikma took "active steps . . . taken to encourage direct infringement." *DSU*, 471 F.3d at 1305 (quoting *Grokster*, 545 U.S. at 936). To "actively induce[] infringement," the accused inducer must "lead on" or "influence" another to infringe and "the inducement must involve the taking of affirmative steps to bring about the

desired result." *Global-Tech Appliances, Inc. v. SEB S.A.*, 563 U.S. 754, 760 (2011). As this Court in *GSK* confirmed, "[w]hen a plaintiff relies on a drug's label accompanying the marketing of a drug to prove intent, '[t]he label must encourage, recommend, or promote infringement.'" *GSK*, 7 F.4th at 1327 (citing *Takeda*, 785 F.3d at 631). The *GSK* panel thus agreed that "generics could not be held liable for merely marketing and selling under a 'skinny' label omitting all patented indications, or for merely noting (without mentioning any infringing uses) that FDA had rated a product as therapeutically equivalent to a brand-name drug." *Id.* at 1326.

IIA. This Court has previously rejected each of Amarin's label-based inducement theories. Amarin's allegations do not include any "***active*** steps" by Hikma in the form of "***instructions*** [that] teach an infringing use[.]" *Takeda*, 785 F.3d at 630-31. This case is thus far weaker than other cases holding, as a matter of law, that vague label instructions do not actively encourage infringement of specific treatment methods. *See, e.g.*, *HZNP Meds. LLC v. Actavis Labs. UT, Inc.*, 940 F.3d 680, 702 (Fed. Cir. 2019) (granting summary judgment of no inducement because "describing the infringing use" is insufficient to find "specific intent and action to induce infringement"). And Amarin's reliance on Hikma's alleged knowledge of direct infringement ignores this Court's precedent that "mere knowledge about a product's characteristics or that it may be put to infringing uses is not enough." *Id.* at 701.

This case is markedly different from Amarin's lead case, *GSK*, where this Court affirmed a jury verdict—in a "narrow, case-specific" decision—finding that the carved-out product "label contained information encouraging each claimed step and the preamble" of the asserted patent claims. *GSK*, 7 F.4th at 1326, 1330. In *GSK*, unlike here, "[a]ll of the claim limitations were contained in the Indication section . . . , the Clinical Study section . . . , and the Dosage and Administration section. . . ." *Id.* at 1329.

IIB-C. Amarin also relies on vague promotional statements by Hikma, but none even describes, much less plausibly encourages, each element of a specifically claimed treatment method. In *GSK*, the extra-label evidence of infringement cited by the patentee was relevant only to the extent it "would point physicians to [Teva's] partial label, which, for the reasons above, the jury was free to credit as evidence of induced infringement." *GSK*, 7 F.4th at 1335 n.7. In contrast, Amarin points to no instructions in Hikma's label that plausibly induces infringement. Nor does it point to instructions encouraging infringement in Hikma's promotional statements. Thus, while Amarin urges the Court to consider its inducement evidence "collectively," Br. at 2, doing so does not change the undeniable fact that neither Hikma's product label nor any of its promotional statements (individually or collectively) actively leads on or influences a third party to practice each and every limitation of an

asserted patent claim. Judge Andrews properly so held, and that holding should be affirmed.

III. In the absence of any plausible allegations that Hikma took active steps to encourage infringement, the proper remedy here is dismissal under Rule 12(b)(6) based on the pleadings. Amarin alleges there is a "key factual dispute" that precludes resolution on the pleadings, Br. at 39-40, but no such factual dispute exists. Unlike other inducement cases cited by Amarin, the key issue here is the absence of any instruction—not the disputed scope of an instruction. The undisputed statements at issue do not plausibly induce infringement under the legal standard and, thus, the Court can decide this case as a matter of law based on the pleadings.

IV. Allowing Amarin's facially deficient inducement claims to proceed past the pleadings stage in this post-launch lawsuit would encourage meritless post-launch lawsuits in similar skinny label cases—effectively eviscerating section viii of the Hatch-Waxman Act. Rather than radically expand its "narrow" decision in *GSK*, this Court should continue to avoid "upset[ting] the careful balance struck with section viii carve-outs" and affirm the district court's decision below. *GSK*, 7 F.4th at 1326.

STANDARD OF REVIEW

This Court reviews a motion to dismiss for failure to state a claim under the law of the regional circuit, which in the Third Circuit is de novo. *Visual Memory*

LLC v. NVDIA Corp., 867 F.3d 1253, 1257 (Fed. Cir. 2017); *Ballentine v. United States*, 486 F.3d 806, 808 (3d Cir. 2007). A complaint should be dismissed under Rule 12(b)(6) of the Federal Rules of Civil Procedure 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)). The standard for plausibility is satisfied when the complaint's factual content "allows the court to draw the reasonable inference that the defendant is liable for the misconduct alleged." *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009). "Where a complaint pleads facts that are merely consistent with a defendant's liability, it stops short of the line between possibility and plausibility of entitlement to relief." *Id.* (quotation marks omitted).

While the 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). Moreover, "[w]here 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." *ALA, Inc. v. CCAIR, Inc.*, 29 F.3d 855, 859 n.8 (3d Cir. 1994).

ARGUMENT

I. To plausibly allege induced infringement, Amarin must allege Hikma took active steps to encourage all limitations of an asserted patent claim.

To survive the pleadings stage, Amarin's complaint must plausibly allege each element of induced infringement, including that Hikma took active steps to encourage infringement of all limitations in at least one claim. By statute, "[w]hoever ***actively*** induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b) (emphasis added). "[I]nduced infringement under § 271(b) requires knowledge that the induced acts constitute patent infringement." *Global-Tech*, 563 U.S. at 766. Additionally, to "actively induce[] infringement[,]" the accused inducer must "lead on" or "influence" another to infringe and "the inducement must involve the taking of affirmative steps to bring about the desired result." *Id.* at 760. Under this standard, to plausibly allege induced infringement, "the inducer must have an affirmative intent to cause direct infringement" with "***evidence of culpable conduct***, directed to encouraging another's infringement." *DSU*, 471 F.3d at 1306 (emphasis added) (citation omitted).

This same legal principle has been applied consistently across inducement cases. Whether the case is rooted in an ANDA label, post-launch communications, or a different field altogether, inducement cannot be found absent (1) "active steps" that (2) "specifically encourage" infringement. *Grunenthal GMBH v. Alkem Labs. Ltd.*, 919 F.3d 1333, 1339–40 (Fed. Cir. 2019); *GSK*, 7 F.4th at 1334 (induced

infringement requires "[e]vidence of active steps taken to encourage direct infringement") (quoting *Grokster*, 545 U.S. at 936); *HZNP*, 940 F.3d at 702 ("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."); *accord Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365 (Fed. Cir. 2003) (explaining in a label-based case that "the substantive determination whether actual infringement or inducement will take place is determined by traditional patent infringement analysis, just the same as it is in other infringement suits, including those in a non-ANDA context").

The required "active steps" to induce infringement include "advertising an infringing use or instructing how to engage in an infringing use," as such steps "show an affirmative intent that the product be used to infringe, and . . . that infringement was encouraged." *Grokster*, 545 U.S. at 936 (citation and alterations omitted); *Takeda*, 785 F.3d at 630–31 (explaining "instructions teach[ing] an infringing use" qualify as "active steps").

Critically, such active steps must include a "clear expression . . . to foster infringement." *DSU*, 471 F.3d at 1305-06. Advertising with "vague" language "cannot be combined with speculation about how [others] may act to find inducement." *Takeda*, 785 F.3d at 632. And "[m]erely describing an infringing mode is not the same as recommending, encouraging, or promoting an infringing

use." *Id*. at 631 (citations, alterations omitted). Particularly where "a product has substantial noninfringing uses, intent to induce infringement cannot be inferred even when the [alleged inducer] has actual knowledge that some users of its product may be infringing the patent." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1059 (Fed. Cir. 2010) (citation omitted).

II. Under this Court's precedent, Amarin failed to plausibly allege induced infringement.

Applying this Court's precedent, Amarin failed to plausibly allege active steps to encourage infringement. To plausibly allege induced infringement, Amarin was required to plead "***active*** steps" that actually "***instruct[]*** . . . an infringing use[.]" *Takeda*, 785 F.3d at 630-631. None of Amarin's inducement evidence plausibly satisfies this requirement, and combining Amarin's meritless theories cannot state a claim for relief. The district court properly dismissed Amarin's complaint for failure to state a claim, and this Court should affirm the district court's judgment.

A. Amarin's allegations that Hikma's label induces infringement are contrary to law, illogical, and otherwise implausible.

Amarin vaguely alleges Hikma's label instructs physicians to practice the claimed CV methods-of-treatment, but it fails to identify any such actual instruction. Amarin primarily argues that the ***absence*** of language discouraging infringement in Hikma's label actively induces infringement—advocating for a new standard of passive or implied, instead of actively induced, infringement. Secondarily, Amarin

points to a ***warning*** against using Hikma's product in patients with CV disease, the opposite of encouragement. *See* Br. at 33-34. On their face, these are plainly not instructions "recommending, encouraging, or promoting an infringing use." *Takeda*, 785 F.3d at 631. Amarin's inducement allegations are far weaker than those presented in *HZNP*, *Grunenthal*, and others where this Court found no instructions encouraging infringement. And as discussed further below, this case is nothing like the facts at issue in *GSK*, where (unlike here), the ANDA filer "failed to carve out all patented indications." *GSK*, 7 F.4th at 1326.

As noted above, Amarin's lead argument for label-based inducement is the ***absence*** of information. Amarin alleges that Hikma's label induces infringement because it does not include an explicit "limitation of use" against using Hikma's product to achieve CV benefits. Appx526-528 (FAC, ¶¶ 107-108). As Amarin alleges, Hikma's draft label—before its product was ever marketed—included the same statement as the original Vascepa® label that "[t]he effect of [icosapent ethyl] on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined." *See* Appx650-661; Appx663-672. To be sure, Hikma removed that draft statement before marketing its product (because that statement was omitted from the Vascepa® label, which Hikma had to copy). But Hikma's ***silence*** as to its product's effects on "cardiovascular mortality and morbidity" in its marketed label cannot plausibly instruct infringement. *See id.*

Hikma has no legal obligation to take "affirmative steps to make sure others avoid infringement." *Takeda*, 785 F.3d at 632 n.4. The mere ***absence*** of additional discouraging language cannot induce infringement as a matter of law. In fact, Amarin's argument "turns the legal test on its head." *Id.*

Amarin also relies on a warning—the opposite of an encouraging instruction. Amarin points to the heading "What are the possible ***side effects*** of icosapent ethyl," where Hikma's label warns about "[h]eart rhythm problems which can be ***serious*** and ***cause hospitalization*** . . . especially ***in people who have heart (cardiovascular) disease*** or diabetes with ***a risk factor for heart (cardiovascular) disease***." Appx704-705 (emphases added). Amarin illogically alleges that this stern ***warning*** against administering Hikma's product to patients with CV disease—the label's sole reference to CV patients—somehow instructs physicians to administer Hikma's product to these same patients for the specific purpose of reducing the "occurrence of a cardiovascular event" and "risk of cardiovascular death." Appx46 ('537 patent, cl. 1); Appx129 ('861 patent, cl. 1). This allegation is not just implausible, it is borderline frivolous. *See, e.g.*, *Takeda*, 785 F.3d at 634 (agreeing with the district court that a statement that "warns patients" was "label language [that] failed to recommend or suggest to physicians that the patented . . . methods should be followed"); *see also Takeda Pharm. USA, Inc. v. W.-Ward Pharm. Corp.*, 72 F. Supp. 3d 539, 547 (D. Del. 2014) (the district court below explaining "there is a

rather significant difference between a warning and an instruction") (citation omitted).

Amarin's remaining allegations are far too vague to meet the standard for active inducement. Amarin relies on vague label language that "[m]edicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet." Appx535 (FAC, ¶ 132) (citing Appx705). As this Court has recognized, however, "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." *Takeda*, 785 F.3d at 632 (quoting *Warner-Lambert*, 316 F.3d at 1364).

Amarin also relies on various portions of Hikma's clinical studies section, including "descriptions of statin-treated patients with the same . . . lipid levels covered by the patented methods."[2] Br. at 33. These allegations do not concern "reducing occurrence of a cardiovascular event" or "reducing risk of cardiovascular death." Appx46 ('537 patent, cl. 1); Appx129 ('861 patent, cl. 1). Instead, they

[2] Amarin also contends its "REDUCE-IT trial related to cardiovascular risk reduction was described on the [Hikma] label too." Br. at 33-34 (citing Appx696, § 5.1). But Section 5.1 of Hikma's label does not "describe" the REDUCE-IT trial; it merely reports a safety warning about the "incidence of atrial fibrillation." Appx696, § 5.1.

concern Amarin's allegations that different limitations are satisfied, such as "concomitantly receiving statin therapy" or the patients' baseline characteristics. *See* Appx534 (FAC, ¶ 130); Appx536 (FAC, ¶ 134). As Amarin acknowledges, these statements are also merely "descriptions," Br. at 33, and "[m]erely describing an infringing mode is not the same as recommending, encouraging, or promoting an infringing use." *Takeda*, 785 F.3d at 631; *see also HZNP*, 940 F.3d at 701–02 (affirming that "permission does not amount to encouragement"; "[m]erely describing the infringing use . . . will not suffice").

Against this backdrop, Amarin summarily argues "this is not a true skinny label case" and attempts to analogize this case to *GSK*—"[t]he leading precedent from this Court." Br. at 2, 49. But *GSK* was a "narrow, case-specific review of substantial evidence" that was decided under materially different circumstances. *GSK*, 7 F.4th at 1326. Most notably, in *GSK* the ANDA filer "failed to carve out all patented indications." *Id.*; *see also id.* at 1334 (explaining the label "instructed physicians to use [the product] in an infringing manner"). As the Court explained, in *GSK* the carved-out product "label contained information encouraging ***each claimed step*** and the preamble" of the asserted patent claims. *Id.* at 1330 (emphasis added); *see also id.* at 1329 (explaining "[a]ll of the claim limitations were contained in the Indication section . . . , the Clinical Study section . . . , and the Dosage and Administration section. . . ."). This Court concluded that "Teva's partial label did

not effectively carve out the patented use, and thus, Teva was selling its generic with a label which infringed the method claim." *Id.* at 1338.

The same is true in Amarin's other lead case with "extra-label evidence," Br. at 42, *AstraZeneca*, where there were "***instructions*** in [the ANDA filer's] proposed label that will cause at least some users to infringe the asserted method claims." *AstraZeneca*, 633 F.3d at 1060 (emphasis added). In *AstraZeneca*, this Court emphasized that the district court "found that, despite being aware of the infringement problem ***presented by the proposed label***, Apotex nonetheless proceeded with its plans to distribute its generic drug product." *Id.* (emphasis added). This Court has previously distinguished *AstraZeneca* on this very basis. *See, e.g.*, *Grunenthal*, 919 F.3d at 1340 (distinguishing *AstraZeneca* because "the defendant proceeded with a plan to distribute the generic drug knowing that its label posed infringement problems").

Here, unlike in *GSK* or *AstraZeneca*, none of the evidence Amarin cites in support of its inducement allegations amounts to a labeled instruction that encourages all limitations of any asserted patent claim. This is a true skinny label case, which alone leaves it starkly distinguishable from *GSK* and *AstraZeneca*.

B. Amarin's allegations that Hikma's public statements outside its label induce infringement are implausible.

Apart from Hikma's label, Amarin primarily relies on statements it contends are analogous to those at issue in *GSK*. Br. at 42-43. But the non-label statements

at issue in *GSK* supported the inducement finding there under "limited circumstances, when substantial evidence supports the jury's presumed determination regarding ***the label's*** contents." *GSK*, 7 F.4th at 1335 (emphasis added). None of the public statements Amarin cites amount to instructions at all, let alone instructions to practice the specific CV methods-of-treatment recited by the asserted patents.

1. Amarin does not plausibly allege that Hikma's mere reference to "Hypertriglyceridemia" is an active step encouraging infringement of reducing CV risk or death.

Amarin's primary argument concerns Hikma's website, where Hikma reported that its icosapent ethyl product was "AB" rated and that the "Therapeutic Category" is "Hypertriglyceridemia." *See* Br. at 31 (citing Appx 532 (FAC, ¶ 125) (citing Appx820)). Amarin alleges that the category "Hypertriglyceridemia"—meaning high triglycerides—"does not match and is broader than the Indications and Usage section of Hikma's label, which includes only the Severe Hypertriglyceridemia Indication." Appx532-33 (FAC, ¶ 126). In its brief, Amarin argues this "Therapeutic Category" encourages infringement "because it includes the unauthorized, patented use to reduce cardiovascular risk in patients with triglyceride levels above 150 mg/dL." Br. at 31.

For multiple and distinct reasons, Hikma's website statements do not amount to active steps encouraging infringement. In particular, (1) Amarin does not plausibly allege that the therapeutic category "Hypertriglyceridemia" encompasses the specific CV method-of-treatment claims, which are unrelated to reducing triglycerides; (2) Hikma's reference to this therapeutic category is not an "instruction" as opposed to a mere vague description of the therapeutic category that includes Hikma's indicated use; and (3) the broad category of "Hypertriglyceridemia" does not specifically encourage and require the CV methods-of-treatment, as opposed to Hikma's FDA-approved indication for severe hypertriglyceridemia.

First, Amarin does not plausibly allege that Hikma's characterization of the therapeutic category as "Hypertriglyceridemia" encompasses CV method-of-treatment claims. The asserted patents are not directed to reducing any sort of hypertriglyceridemia, i.e., high triglycerides. Instead, they are directed to methods of "reducing occurrence of a cardiovascular event" or "reducing risk of cardiovascular death," among other limitations. Appx46 ('537 patent, cl. 1); Appx129 ('861 patent, cl. 1). Amarin's own allegations confirm that reducing triglycerides is different from the claimed CV methods-of-treatment. According to Amarin's pleadings, "lowered triglyceride levels . . . did ***not*** show an actual reduction in cardiovascular risk." Appx509 (FAC, ¶ 32) (emphasis added); Br. at 7-8 (explaining Amarin obtained the

CV Indication through a clinical study that was not "based on measuring the patients' triglyceride levels" and did not "focus[] on triglyceride levels" at all); *accord* Appx509 (FAC, ¶ 33).

Notably, despite its refrain that this Court should consider Hikma's various "statements collectively," Br. at 2, Amarin ignores that just below Hikma's "Hypertriglyceridemia" statement, Hikma expressly states that "Hikma's generic version is indicated for fewer than all approved indications of the Reference Listed Drug." Appx820. Particularly when viewed in context, it is implausible to interpret Hikma's statement of the therapeutic category "Hypertriglyceridemia" as referring to the CV method-of-treatment claims.

Second, even had Amarin plausibly alleged that the therapeutic category of "Hypertriglyceridemia" encompassed CV methods-of-treatment (it did not), Amarin does not plausibly allege that merely mentioning the therapeutic category "Hypertriglyceridemia" constitutes an instruction. Amarin alleges only that this category is "broader" than the specific hypertriglyceridemia indication covered by Hikma's label, severe hypertriglyceridemia. *See* Appx532-33 (FAC, ¶ 126). The mere reporting of the therapeutic category "Hypertriglyceridemia" cannot amount to an active step encouraging a physician to perform the specific methods of "reducing occurrence of a cardiovascular event" or "reducing risk of cardiovascular death." Such an interpretation would be at odds with this Court's precedent that even "describing

the infringing use" is insufficient to find "specific intent and action to induce infringement." *HZNP*, 940 F.3d at 702; *see also Takeda*, 785 F.3d at 632 ("vague label language cannot be combined with speculation about how physicians may act to find inducement").

Third, even if "Hypertriglyceridemia" plausibly could be viewed as an instruction (it cannot), this Court has previously rejected inducement arguments where the statements in question did not include any instruction ***requiring*** the claimed methods. For example, in *HZNP*, the Court explained that even viewing the patentee's evidence "in the light most favorable," there were no "material issues of fact that prevent summary judgment" because the statement in question did not "***require***" practicing a claimed step and thus "intent to induce infringement cannot be inferred." *HZNP*, 940 F.3d at 702.

The Court's decision in *GSK* does not hold otherwise. In *GSK*, there was a material issue of fact whether the labeled instruction "to reduce cardiovascular mortality" in patients who "have a left ventricular ejection fraction of ≤ 40% (with or without symptomatic heart failure) . . . satisfied the 'decreasing mortality caused by congestive heart failure in a patient' limitation." *GSK*, 7 F.4th at 1327-28. The Court concluded that the trial evidence showed the labeled indication encompassed an instruction requiring the claimed method. As the Court explained, Teva's expert conceded that all patients with "a left ventricular ejection fraction of less than or

equal to 40% with symptomatic heart failure (as recited on Teva's partial label) would be diagnosed as suffering from congestive heart failure," the disputed method-of-treatment. *Id.* at 1328. In the presence of what the Court held was an express instruction encouraging infringement, the Court reasoned Teva could not escape liability simply because its label also included instructions where there would be no infringement. *Id.* at 1329-30 (disagreeing that "encourag[ing] both infringing and noninfringing uses . . . somehow obviates infringement").

Consistent with this case law, the district court concluded that Hikma's reference to "Hypertriglyceridemia" with an "AB" rating did not "rise to the level of encouraging, recommending, or promoting taking Hikma's generic for the reduction of CV risk." Appx8. Citing *GSK* and *Grunenthal*, the district court reasoned both that (1) the "broader category" of "hypertriglyceridemia" did not "specifically encourage" an infringing use; and (2) the website's reference to an "AB rating" points to Hikma's label, which "had no infringing indications." Appx9 (citing *Grunenthal*, 919 F.3d at 1339; *GSK*, 7 F.4th at 1335 n.7).

Amarin argues *Grunenthal* is distinguishable because "the 'broader category' in *Grunenthal* was the off-patent treatment," while here, "this case involves a broader patented use that covers a larger patient population." Br. at 51-52. But the district court's reference to the "broader category" concerned the category of "Hypertriglyceridemia"—not either the patented use or the off-patent use. *See* Appx8-

9. The district court did not indicate that the relative amounts of patients in the patented or off-patented categories affected its analysis, and neither did the Court in *Grunenthal*. In any event, the district court's decision focused on the absence of language that "rise[d] to the level of encouraging, recommending" infringement, coupled with the "'AB rating' [that] points to the label," which only includes non-infringing indications. Appx8-9.

For any or all of the above reasons, Hikma's website does not include any active steps encouraging infringement.

2. Amarin's remaining allegations do not pertain to the requirement of "active steps" to encourage infringement.

The remainder of Amarin's inducement allegations concern either Hikma's supposed knowledge of direct infringement, or its allegations that Hikma should have done more to discourage infringement. But time and again, this Court has rejected each of these inducement theories, leaving Amarin's allegations implausible as a matter of law.

For example, Amarin alleges Hikma should have done more to deter infringement in its pre-launch press releases, criticizing them because they "do[] not state that Hikma's 'generic version' of VASCEPA® should not be used for the CV Indication." Appx530 (FAC, ¶ 114); Appx531 (FAC, ¶ 121). Yet, on their face, both press releases reference ***only*** the SH Indication with no mention of the CV Indication. Appx709; Appx712. Without any instruction to practice the CV method-

of-treatment claims, Hikma was under no obligation to affirmatively discourage infringement. As this Court explained, accepting such an allegation as evidence of inducement would "turn[] 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. Amarin's argument also ignores that the only press release it cites that issued ***after*** Hikma's launch (but before any litigation) expressly stated that Hikma's product is "not approved for any other indication for the reference listed drug VASCEPA®" other than the SH Indication. Appx715.

Amarin also alleges that Hikma "identifies and describes its generic version of VASCEPA® as 'AB' rated," which according to Amarin, means Hikma "knew and intended that its generic product be substituted for all VASCEPA® prescriptions," not just those for SH. Appx533 (FAC, ¶¶ 127-129). The Court in *GSK* made clear that, while Teva's "AB rated representations" supported the infringement finding, the panel did "not hold that an AB rating in a true section viii carve-out (one in which a label was produced that had no infringing indications) would be evidence of inducement." *GSK*, 7 F.4th at 1335, n.7; *id.* at 1335 (explaining the AB-rating was relevant solely "under these limited circumstances, when substantial evidence supports the jury's presumed determination regarding the label's contents"). This is because it would be "contrary to the statutory scheme" to

find inducement under the theory that "pharmacists and doctors will … substitute the generic for all indications." *AstraZeneca Pharm. LP v. Apotex Corp.*, 669 F.3d 1370, 1380 (Fed. Cir. 2012).

Amarin's allegation that "Hikma was aware that the vast majority of prescriptions for Vascepa® were for reducing cardiovascular risk and not for treating severe HTG" does not convert Hikma's benign statements into active steps to encourage infringement. *See* Br. at 32; *see also* Appx528 (FAC, ¶ 110) (citing, e.g., Appx803, Appx805). This Court has repeatedly made clear that it is not enough "that the inducer had knowledge of the direct infringer's activities"; "inducement requires evidence of culpable conduct, directed to encouraging another's infringement." *DSU*, 471 F.3d at 1306; *HZNP*, 940 F.3d at 701 ("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."). Amarin's failure to plausibly allege any active steps to encourage direct infringement leaves Hikma's knowledge of the Vascepa® market legally irrelevant.

Relatedly, Amarin cannot plausibly allege active steps to encourage infringement based on Hikma's report of Vascepa®'s sales in its press releases. *See* Br. at 32. Amarin alleges that the figures Hikma reported "include[] sales for ***all uses*** of Vascepa®, including the CV Indication." Appx529 (FAC, ¶ 113); Appx531

(FAC, ¶ 120). This is a factual statement about the Vascepa® market—Hikma's reporting of a sales figure does not encourage a physician to do anything. As this Court explained in *Takeda*, "vague [] 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*, 316 F.3d at 1364).

In sum, as with its label, Hikma's public statements do not involve "advertising an infringing use or instructing how to engage in an infringing use." *See Groskter*, 545 U.S. at 936. Amarin has not plausibly alleged that Hikma took "active steps" to encourage infringement. *See id.*

C. Combining Hikma's label and public statements does not transform these vague statements into active steps to encourage infringement.

In the absence of any active steps or instructions encouraging infringement, Amarin urges the Court to hold that it plausibly alleged induced infringement based on "Hikma's label together with its various public statements ***collectively***." Br. at 2 (emphasis added). In effect, Amarin asks the Court to hold that the collection of Hikma's vague, miscellaneous statements transform Hikma's communications into active steps to encourage infringement. Amarin cites no support for its expansive

interpretation of inducement law. Whether Amarin's allegations are considered individually or collectively, Amarin failed to plausibly allege induced infringement.

Contrary to Amarin's argument, this Court has repeatedly required an ***instruction***, i.e. an active step, to find inducement of a claimed method. In *GSK*—Amarin's lead case—the jury's verdict was supported by evidence that the label "instructed physicians to use [the product] in an infringing manner." *GSK*, 7 F.4th at 1334. Amarin characterizes *AstraZeneca* as "another case with parallels to the dispute here," Br. at 44, yet that case likewise involved "instructions in [the ANDA filer's] proposed label that will cause at least some users to infringe the asserted method claims." *AstraZeneca*, 633 F.3d at 1060. Indeed, inducement cases frequently involve multiple, distinct statements—but without a single active step encouraging infringement, there can be no induced infringement. *See, e.g.*, *HZNP*, 940 F.3d at 700-02, n.11 (combination of separate statements to "[w]ait until the treated area is dry before applying sunscreen" and "avoid exposure to natural or artificial sunlight" resulted in "no material dispute that the instructions do not reflect specific intent to induce"); *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).

Both in view of the case law and the facts alleged, Amarin's argument that the district court erroneously "weigh[ed] the pled facts piecemeal" lacks merit. *See* Br. at 35. The district court thoroughly considered Amarin's inducement allegations and concluded "Hikma's label does not plausibly teach CV risk reduction" and Amarin's remaining evidence did "not rise to the level of encouraging, recommending, or promoting taking Hikma's Generic for the reduction of CV risk." Appx7-8. While the district court considered Hikma's label first, this is the same process this Court followed in *GSK*, beginning its analysis with whether "Teva's partial ***label*** instructed the method of use claimed" before reaching any non-label evidence. *See GSK*, 7 F.4th at 1328 (emphasis added). The district court did not err in reaching its judgment, and in any event, this Court can reach the same conclusion on de novo review.

In sum, the Court should reject Amarin's request to combine its flawed inducement theories to find it stated a claim for relief. The Court should affirm the district court's dismissal of Amarin's complaint for failure to state a claim.

III. Dismissal on the pleadings is appropriate in view of the inducement allegations here.

In view of Amarin's deficient inducement allegations, the proper remedy here is dismissal of Amarin's complaint. Amarin argues "the difficult questions and

related factual disputes in this case cannot be resolved on a motion to dismiss," Br. at 2, but there are no material issues of fact that preclude this Court from deciding this case as a matter of law.

The statements from Hikma's label, website, and press releases that allegedly induce infringement are addressed in the pleadings and are undisputed. *See* Br. at 39. As Amarin recognizes, the question before the Court is thus whether Amarin's allegations based on these undisputed, written statements "plausibly show[] Hikma ***acted*** to induce . . . infringement." Br. at 31 (emphasis added). That is, the question is whether Hikma's label and public statements amount to "***active steps*** taken to encourage direct infringement" based on "***instructions*** [that] teach an infringing use of the [accused product]." *Takeda*, 785 F.3d at 630–31 (emphases added; quotations omitted). As discussed above, Amarin's inducement allegations do not rely on any instructions, much less instructions that specifically encourage the claimed CV methods-of-treatment. Where, as here, the patentee failed to plausibly allege any active steps to encourage infringement, non-infringement is decided as a matter of law. *See* Fed. R. Civ. P. 12(b)(6); *see also* cases cited *infra*.

Amarin relies on the Court's decision in *GSK* to argue its inducement allegations cannot be decided on the pleadings, but again, *GSK* concerned an inducement theory materially distinct from the theory at issue here. *See* Br. at 40-41. Amarin argues "*GlaxoSmithKline* is illustrative," pointing out that there, the

Court held "the district court erred by treating this fact question—whether [a certain] indication instructs a physician to prescribe carvedilol for a claimed use—as though it were a legal one for it to decide *de novo*." *Id.* at 41 (quoting *GSK*, 7 F.4th at 1330). Critically, in *GSK*, the patentee relied on an ***instruction*** to support its inducement case, and it was a question of fact whether that instruction concerned an infringing use. In particular, in *GSK* there was a material issue of fact whether "Teva's partial label encouraged an infringing use" based on its inclusion of an indication "to reduce cardiovascular mortality" in patients who "have a left ventricular ejection fraction of ≤ 40% (with or without symptomatic heart failure)." *GSK*, 7 F.4th at 1327-28. It was a question of fact whether this instruction "satisfied the 'decreasing mortality caused by congestive heart failure in a patient' limitation," which the jury resolved in the patentee's favor. *Id.* at 1328.

Here, Amarin does not point to an instruction to support its inducement allegations. Unlike the patentee in *GSK*, Amarin does not allege that Hikma's sole indication satisfies the disputed CV method-of-use limitations, and instead, it broadly relies on a "collection" of vague communications to allege inducement. *See* Br. at 39-40. This is not a case raising an issue of fact about the ***scope*** of an instruction; it is the dearth of any relevant instruction that renders Amarin's amended complaint deficient. Absent any plausible allegations that Hikma's statements gave rise to an instruction, Amarin failed to state a claim for induced infringement. *See,*

e.g., *AstraZeneca*, 633 F.3d at 1060 ("The pertinent question is whether the proposed label ***instructs*** users to perform the patented method."); *Eli Lilly*, 845 F.3d at 1369 (finding "inevitabl[e]" inducement only where the "***instructions*** are unambiguous on their face and encourage or recommend infringement") (emphases added).

That this case is at the pleadings stage does not otherwise justify allowing Amarin's deficient inducement claim to proceed. Contrary to Amarin's broad assertion that "induced infringement hinges on factual determinations," Br. at 48, courts have repeatedly resolved induced infringement claims before trial and even at the pleadings stage where, as here, the patentee failed to raise a material issue of fact that the defendant engaged in active steps to induce infringement. *See, e.g.*, *Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316, 1324 (Fed. Cir. 2012) (affirming dismissal on the pleadings where, as a matter of law, the "label cannot instruct (and the ANDA proposed label cannot induce infringement of) the method of use claimed"); *AstraZeneca*, 669 F.3d at 1377, 1380 (holding the patentee "failed to state a viable claim for relief" where the patentee's inducement allegations hinged on the theory that despite "restricted generic labeling . . . pharmacists and doctors will nonetheless substitute the generic for all indications"); *HZNP*, 940 F.3d at 702 (rejecting argument that "there are material issues of fact that prevent summary judgment" and agreeing with the district court that "there can be no material dispute that the [labeled] instructions do not reflect specific intent to induce"); *Ca. Beach*

Co., LLC v. Exqline, Inc., No. 20-01994-WHA, 2020 WL 6544457, at *3 (N.D. Cal. Nov. 7, 2020) (granting motion to dismiss where the "amended complaint alleges no more than [defendant's] ordinary course of business" absent any "*affirmative* action to recommend, encourage, promote, or suggest infringement") (emphasis in original); *Ferring Pharm. Inc. v. Lupin Inc.*, No. 1:19-cv-913-RGA, 2020 WL 3414750, at *4 (D. Del. June 22, 2020) (granting motion for judgment on the pleadings and rejecting argument that "discovery is necessary to determine whether Defendants' proposed ANDA label encourages, recommends, or promotes an infringing use").

Finally, dismissal on the pleadings is not improper due to a purported need for further fact discovery. Amarin attempts to analogize this case to the *Takeda* district court, where Amarin argues the district court vacated its prior dismissal on the pleadings "after Takeda amended its complaint with allegations about specific communications that Takeda argued amounted to active encouragement." Br. at 50 (citing *Takeda Pharm U.S.A., Inc. v. West-Ward Pharm. Corp.*, No. 14-1268-SLR, 2016 WL 7230504, at *2 (D. Del. Dec. 14, 2016)). Contrary to Amarin's arguments, this case is not "squarely within the analysis . . . of the *Takeda* dismissal." *Id.* The *Takeda* district court allowed "a reasonable opportunity [for] further investigation or discovery" solely because the amended complaint alleged active steps to induce infringement based on "sales representatives' [alleged oral] statements telling

healthcare providers to prescribe Mitigare for the unapproved indications covered by Takeda's patents." *Takeda*, 2016 WL 7230504, at *2 (citation omitted). There, discovery was necessary to determine the scope of the alleged—and hotly disputed—***oral statements***, and whether such statements encouraged infringement.[3] No similar allegations exist here. In fact, Amarin's entire theory of active steps to induce infringement is cabined to the written statements it attached to its complaint, the contents of which are "undisputed." *See* Br. at 39 ("[T]he contents of [Hikma's] label and public statements are undisputed.") (quoting Appx1427). The scope of Amarin's inducement evidence—based solely on written statements—is conceptually no different from label-based cases where the Court has agreed the contents can be reviewed as a matter of law. *See, e.g.*, *HZNP*, 940 F.3d at 701 (agreeing that where the "only evidence of inducement depends upon Actavis's label, . . . there [we]re no material issues of fact" to preclude resolution on summary judgment).

In sum, where, as here, the factual allegations fail to "raise a right to relief above the speculative level" and cross "the line from conceivable to plausible," it is appropriate to dismiss the complaint for failure to state a claim. *Twombly*, 550 U.S.

[3] This is the only case cited by Amarin allowing a case filed after a generic-product launch to proceed past a motion to dismiss when the carved-out (or skinny) label does not induce infringement.

at 555, 570. As explained further below, "[i]n the absence of any evidence that [Hikma] has or will promote or encourage doctors to infringe the [CV] method patent, there has been raised no genuine issue of material fact." *Warner-Lambert*, 316 F.3d at 1364.

IV. Allowing Amarin's case to proceed past the pleadings stage would eviscerate the careful balance struck with section viii carve-outs.

This is not an ordinary inducement case—it is a test case to determine whether section viii carve-outs remain a viable strategy to expedite less expensive generic drugs. Amarin transparently hopes to broaden the Court's narrow decision in *GSK* to effectively eviscerate such section viii carve-outs. In view of the significant implications that would result from allowing Amarin's inducement claims to proceed past the pleadings stage, as the district court observed, there was "even an amicus brief" filed in support of Hikma's motion to dismiss. Appx2; *see also* Appx1498 ("The claims in this case threaten to make a dead letter out of the 'skinny label' regime . . . ."). The Court should reject Amarin's invitation to depart from its precedent and should affirm the district court's dismissal of Amarin's inducement claims.

This Court has repeatedly recognized the danger in permitting patentees to allege induced infringement over ANDA products that are approved solely for unpatented uses. In *GSK*, the Court revised its previous opinion to avoid "upset[ting] the careful balance struck with section viii carve-outs" and to ensure that "generics

could *not* be held liable for merely marketing and selling under a 'skinny' label omitting all patented indications." *GSK*, 7 F.4th at 1326 (citation omitted). In doing so, it made clear that *GSK* concerned only a "narrow, case-specific review of substantial evidence" over a label that "***failed*** to carve out all patented indications." *Id.* (emphasis added). In *Warner-Lambert*, this Court similarly cautioned against allowing patentees to assert induced infringement over "any competitor's ANDA seeking approval to market an off-patent drug for an approved use not covered by the patent," as doing so would "effectively . . . bar[] [generic companies] altogether from entering the market." *Warner–Lambert*, 316 F.3d at 1359. This Court emphasized the same concern in *AstraZeneca*, explaining that allowing inducement allegations based on "speculative arguments would allow a pioneer drug manufacturer to maintain de facto indefinite exclusivity over a pharmaceutical compound"—an outcome that would be "contrary to the statutory scheme." *AstraZeneca*, 669 F.3d at 1380.

Yet this is the relief Amarin seeks here. Without plausibly alleging that Hikma's label failed to carve out the specific CV methods-of-treatment recited by the asserted patents, Amarin nonetheless attempts to restrain Hikma's market competition by pointing to various vague, public statements. In fact, both the magistrate judge and district court agreed that Amarin's label-based inducement allegations were implausible. *See* Appx1426 ("[W]ere Plaintiffs' allegations based

solely on the label, Plaintiffs' inducement theory might lack merit as a matter of law."); Appx7 ("[T]he label does not instruct CV risk reduction.").

Reversing the district court's judgment under these circumstances would open the floodgates to meritless post-launch suits in every skinny label case, contravening congressional intent and effectively nullifying section viii. As the Supreme Court recognized, section viii expressly "authorize[s] the FDA to approve the marketing of a generic drug for particular unpatented uses . . . so that a product with a label matching them can quickly come to market." *Caraco*, 566 U.S. at 415. The statute itself accordingly "contemplates that one patented use will not foreclose marketing a generic drug for other unpatented ones." *Id.* "[B]ecause the statute was designed to enable the sale of drugs for non-patented uses even though this would result in some off-label infringing uses," this Court has observed that the "requirement of inducing acts is particularly important in the Hatch–Waxman Act context." *Takeda*, 785 F.3d at 631.

But under Amarin's inducement theory, virtually any complaint brought after a generic-drug launch could survive the pleadings stage based on vague allegations of inducement—in light of which "[n]o generic manufacture could sensibly undertake the risk of bringing a skinny labelled generic to market." Appx1498-1499. If Amarin's view were accepted, branded drugmakers could simply wait until the generic launches to bring a lawsuit that would otherwise "lack merit as a matter of

law" in "an ANDA case" filed before launch. Appx1426. Congress did not enact the carve-out process so that generics would be liable for exactly the same conduct after launch that they are not liable for before launch. Allowing this case to proceed past the pleadings stage would leave generics with no reason to use section viii—defeating Congress's goal to "speed the introduction of low-cost generic drugs to the market." *Caraco*, 566 U.S. at 405. As the Solicitor General explained, the Court's decision in *GSK* produced a "potential deterrent effect on generic-drug manufacturers' invocation of the section viii pathway." Br. for United States, *Teva Pharm. USA, Inc. v. GSK LLC*, No. 22-37, at 21 (Mar. 2023). This Court should reject Amarin's request to expand *GSK*'s holding further, which would eviscerate section viii as a path to expedite generic-drug competition.

CONCLUSION

The judgment should be affirmed.

Respectfully submitted,

/s/ Charles B. Klein

CHARLES B. KLEIN
CLAIRE A. FUNDAKOWSKI
Winston & Strawn LLP
1901 L Street NW
Washington, DC 20036
(202) 282-5000
cklein@winston.com
cfundakowski@winston.com

EIMERIC REIG-PLESSIS
Winston & Strawn LLP
101 California Street
San Francisco, CA 94111
(415) 591-1000
ereigplessis@winston.com

ALISON M. KING
Winston & Strawn LLP
35 W. Wacker Drive
Chicago, IL 60601
(312) 558-5600
aheydorn@winston.com

Counsel for Defendants-Appellees Hikma Pharmaceuticals USA Inc. and Hikma Pharmaceuticals PLC

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CERTIFICATE OF SERVICE

I certify that true and correct copies of the foregoing *Brief for Defendants-Appellees* were caused to be served on May 31, 2023, on all counsel of record by the CM/ECF system.

May 31, 2023

/s/ Charles B. Klein

CHARLES B. KLEIN
Winston & Strawn LLP
1901 L Street NW
Washington, DC 20036
(202) 282-5000
cklein@winston.com

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1. This brief complies with the type-volume limitation of Federal Rule of Appellate Procedure 32(a)(7)(B) because it contains 11,139 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(a)(7)(B)(iii) and Federal Circuit Rule 32(b).

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May 31, 2023

/s/ Charles B. Klein

CHARLES B. KLEIN
Winston & Strawn LLP
1901 L Street NW
Washington, DC 20036
(202) 282-5000
cklein@winston.com