No. 24-889

In the Supreme Court of the United States

HIKMA PHARMACEUTICALS USA INC. AND
HIKMA PHARMACEUTICALS PLC,
Petitioners,

v.

AMARIN PHARMA, INC., ET AL.,
Respondents

On Petition for a Writ of Certiorari to the
United States Court of Appeals for the Federal Circuit

BRIEF FOR RESPONDENTS IN OPPOSITION

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QUESTION PRESENTED

Whether the court of appeals correctly found that, on the particular constellation of facts pleaded in respondents' complaint, respondents have plausibly alleged petitioners' active inducement to infringe patented uses of respondents' innovative pharmaceutical product.

CORPORATE DISCLOSURE STATEMENT

Petitioners in this Court, the defendants-appellees below, are Hikma Pharmaceuticals USA, Inc. and Hikma Pharmaceuticals PLC.

Respondents in this Court, the plaintiffs-appellants below, are Amarin Pharma, Inc., Amarin Pharmaceuticals Ireland Limited, and Mochida Pharmaceutical Co., Ltd.

Both Amarin Pharma, Inc. and Amarin Pharmaceuticals Ireland Limited are wholly owned subsidiaries of Amarin Corporation plc, a publicly held corporation. No other publicly held corporation owns 10% or more of the stock of Amarin Pharma, Inc. or Amarin Pharmaceutical Ireland Ltd.

Mochida Pharmaceutical Co., Ltd. is a Japanese company that is publicly traded on the Tokyo Stock Exchange. No publicly held corporation owns 10% or more of the stock of Mochida Pharmaceutical Co., Ltd., and it has no parent corporation.

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STATUTORY PROVISIONS INVOLVED

The Patent Act provides at 35 U.S.C. § 271, in relevant part:

> **(b)** Whoever actively induces infringement of a patent shall be liable as an infringer.

INTRODUCTION

This case comes to the Court in its infancy: the question presented is the sufficiency of the allegations in respondents' complaint. Unsurprisingly given that posture, the petition for a writ of certiorari does not raise any significant question of law; it challenges merely the court of appeals' application of a settled legal standard to the particular combination of facts alleged. The court of appeals' intensely fact-bound decision does not warrant this Court's review.

Section 271(b) of the Patent Act creates liability for "actively induc[ing] infringement of a patent." Active inducement includes encouraging or advertising an infringing use. Respondent Amarin's drug Vascepa® has two approved uses: a first approved use that accounts for only a small fraction of the patient population, and a patented, later-approved use that accounts for the vast majority of the patient population and was hailed as a "game changer" when approved.

Petitioners, a generic drug company called Hikma Pharmaceuticals, asked the Food and Drug Administration to approve their generic drug only for Vascepa's initial (but now minority) use—even though they knew and *intended* that physicians would prescribe it most of the time for the groundbreaking, patented (and now majority) use. Despite petitioners' promise to the FDA that they would market their drug narrowly, almost as soon as the drug launched they began marketing it broadly for both the unpatented and patented uses. Across multiple press releases, websites, and their drug label, petitioners intentionally and actively encouraged physicians to prescribe Hikma's generic drug so as to infringe Amarin's patents.

Amarin pleaded all of this in a detailed, 52-page complaint. Amarin alleged, in specific terms, how Hikma's

actions and statements revealed its deliberate efforts to induce infringement. The complaint explained how Hikma conveyed the message that physicians should use Hikma's generic drug for the infringing majority use; not just for the far-less-common use for which Hikma had sought, and received, approval of its generic product.

The district court dismissed the complaint for failure to state a claim for relief, but the court of appeals correctly reversed and remanded for Amarin to have a chance to prove its claims. In doing so, the court of appeals broke no new legal ground. The court simply held that respondents have plausibly alleged active induced infringement because, taking all of the factual allegations as true at this stage, the complaint gives rise to a disputed question of fact about whether Hikma's statements communicated to healthcare providers that they should prescribe Hikma's generic drug for a patented use.

Petitioners act like they were hit with a judgment, but this case is just beginning. Infringement and any defenses to it are not yet decided, nor are any remedies. What petitioners really want is a safe-harbor from having to litigate at all—a sort of qualified immunity for generic pharmaceuticals that has no basis in statute or case law.

The petition mis-describes the reasoning of the court of appeals and elides the fact-intensive nature of the decision below. Petitioners claim a circuit split over whether induced infringement is a question of fact or law, but no such split exists and that issue affects nothing about the core dispute in this case: how physicians would understand Hikma's particular statements here. Contrary to petitioners' assertions, the court of appeals *did* require Amarin to plead "active" inducement to infringe; the court simply determined that Amarin's factual allegations, if proven, can meet that standard. Petitioners also cherry-

pick a single quotation from the opinion below to assert that the court of appeals rejected the pleading standard of *Bell Atlantic Corp.* v. *Twombly*, 550 U.S. 544 (2007). But that argument ignores the court's repeated, express application of the plausibility pleading standard. Petitioners and their amici then conclude by invoking policy considerations grounded in hypothetical facts not present in this case and, in all events, better suited for Congress.

The petition for a writ of certiorari should be denied.

STATEMENT

A. Respondents' medical innovations

This case involves petitioners' marketing of a generic version of Amarin's drug Vascepa. Vascepa treats diseases related to triglycerides in the blood.

1. Triglycerides are a necessary fat that circulates in blood, but if their levels are too high, serious problems can result. Those manifest in two relevant ways:

- "Hypertriglyceridemia" refers to having a blood triglyceride level above the acceptable level of 150 mg/dL. See C.A.App.866, 952–953. The main concern with hypertriglyceridemia is elevated cardiovascular risk. *Id.* at 866.
- "Severe hypertriglyceridemia" (or SH) refers to having a blood triglyceride level above 500 mg/dL. C.A.App.696, 866. The significantly higher triglyceride levels in an SH population result in meaningfully different medical concerns. The primary concern is not cardiovascular risk but pancreatitis. *Id.* at 866, 952.

Most patients with elevated triglycerides suffer from standard "hypertriglyceridemia," not "severe hypertriglyceridemia." See, *e.g.*, S.App.29a; C.A.App.923.[1]

2. Vascepa is a prescription drug that Amarin developed and markets in the United States. S.App.6a. Its active pharmaceutical ingredient is icosapent ethyl, also known as ethyl eicosapentaenoate, which is the ethyl ester of an omega-3 polyunsaturated fatty acid called eicosapentaenoic acid (EPA) and that is derived from fish oils. S.App.14a; C.A.App.699–700, 866. Amarin achieved FDA approval of Vascepa after investing resources into multiple significant scientific efforts.[2]

The FDA first approved Vascepa in 2012 as the only treatment for severe hypertriglyceridemia that does not raise bad cholesterol levels. Pet.App.2a–3a; S.App.6a. That was significant because the only other drug that could reduce triglyceride levels in those patients also significantly increased bad cholesterol levels. S.App.6a; C.A.App.107 (col. 1 ll. 40–45). The FDA approved Vascepa for the SH indication based on Amarin's efforts in a clinical trial focusing on patients with severe hypertriglyceridemia. S.App.6a.

After receiving that first approval for that small set of severe-hypertriglyceridemia patients, Amarin continued

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[1] "S.App." refers to the supplemental appendix accompanying this brief in opposition, which includes additional material from the record not included in the appendix to the petition.

[2] Petitioners incorrectly (Pet. 11) call the active ingredient of Vascepa "icosapent" and say it is "found naturally in fish oil." Not quite. The active pharmaceutical ingredient is not the fatty acid found in fish oil but a different molecule, assigned the nonproprietary name icosapent *ethyl*, that is *derived from* fish oil. Law Professor amici are wrong to imply (at 4) that icosapent ethyl has been known since at least the 1980s for the patented use.

to investigate other medical applications for Vascepa. Pet.App.3a. Amarin conducted an additional clinical trial to investigate whether Vascepa could be used to treat patients with elevated triglyceride levels (200-500 mg/dL) and control bad cholesterol levels. S.App.6a–7a; C.A.App. 871. That trial demonstrated that Vascepa lowered triglycerides in those patients. S.App.6a–7a; C.A.App.871–872. But the FDA was not convinced that the results proved a reduction in cardiovascular risk. *Ibid.* Amarin then conducted another five-year study (called the REDUCE-IT trial), involving more than 8,000 patients, to directly study whether Vascepa would reduce cardiovascular risk in hypertriglyceridemia patients. S.App.7a; C.A.App.832.

The REDUCE-IT trial was a massive success. It showed a 25% reduction in major cardiovascular events when coupled with statins. S.App.8a. Those results met industry-wide surprise and enthusiasm. *Ibid.* They were considered one of the most important developments in the prevention and treatment of cardiovascular disease since the discovery of statins. *Ibid.* Physicians described this use of Vascepa as "phenomenal" and a "game changer." *Ibid.*; C.A.App.852.

Based on the success of Amarin's clinical efforts, the FDA approved Vascepa for a second use: reducing cardiovascular risk in patients with hypertriglyceridemia as an adjunct to statin therapy. S.App.8a, 16a. Whereas pancreatitis is the primary concern for patients with *severe* hypertriglyceridemia, cardiovascular risk is the primary concern for hypertriglyceridemia patients. The approval was a "major milestone in cardiovascular prevention," and "healthcare providers rapidly associated" Vascepa with statins as "a method for reducing risks of cardiovascular events" in hypertriglyceridemia patients. *Id.* at 18a.

Amarin's clinical trial work was preceded by other important work by respondent Mochida. S.App.9a–10a. In the late 1990s and early 2000s, Mochida sponsored the world's first large-scale randomized controlled cardiovascular-outcomes trial (known as JELIS) of a pure drug product related to EPA. *Ibid.* JELIS showed the beneficial effect of EPA in statin-treated, hypercholesterolemic patients, as published in scientific literature in 2008. *Ibid.*

Amarin's Vascepa drug label has two approved indications that resulted from its work:

- The SH indication for patients with severe hypertriglyceridemia, as an adjunct to diet.
- The CV indication for reducing cardiovascular risk in patients with hypertriglyceridemia, as an adjunct to statin therapy.

S.App.13a–14a; Pet.App.2a–3a. The CV indication accounts for more than 90% of sales of Vascepa. C.A.App.923.

Amarin and Mochida sought to protect their research and development investment. They obtained patents covering the CV indication. See S.App.10a–13a. Amarin listed them in the FDA's Orange Book as covering Vascepa. *Id.* at 19a–20a; Pet.App.3a.[3]

B. Statutory and regulatory background

1. Drug approval

The FDA must approve all new drugs before they may be marketed in interstate commerce. 21 U.S.C. § 355(a). Federal law provides procedures for approval of new and generic drugs that differ in the burden on the applicant.

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[3] Other patents cover other innovative aspects of Vascepa, but they are not relevant here.

a. To obtain approval for a *new* drug, an applicant files a New Drug Application (NDA) that includes a proposed drug label and clinical data demonstrating the drug is safe and effective for its intended use. 21 U.S.C. § 355(b)(1)(A)(i), (vi). That requires a "long, comprehensive, and costly testing process." *FTC* v. *Actavis*, 570 U.S. 136, 142 (2013). The NDA must include "full reports of investigations" into safety and efficacy, a "full list of the articles used as components," and a "full description" of the drug's manufacturing, processing, and packaging. 21 U.S.C. § 355(b)(1); see, *e.g.*, 21 C.F.R. § 314.50(d)(1), (2), (5). The NDA must also contain the number and expiration date of any patent that claims either the drug or a method of using it. 21 U.S.C. § 355(b)(1). The FDA publishes that patent information in a database known as the Orange Book. *AstraZeneca LP* v. *Apotex, Inc.*, 633 F.3d 1042, 1045 (Fed. Cir. 2010).

b. An applicant looking to market a generic drug has a faster, cheaper path: an Abbreviated New Drug Application (ANDA). 21 U.S.C. § 355(j); see *Actavis*, 570 U.S. at 142. That allows an applicant with a "biologically equivalent" drug to "piggy-back" on existing safety and efficacy data for an approved drug, and to bypass the "costly and time-consuming studies" needed for a "pioneer drug." *Actavis*, 570 U.S. at 142 (citation omitted); see *Merck KGaA* v. *Integra Lifesciences I, Ltd.*, 545 U.S. 193, 196 n.1 (2005).

"[T]he FDA cannot authorize a generic drug that would infringe a patent." *Caraco Pharm. Labs., Ltd.* v. *Novo Nordisk A/S*, 566 U.S. 399, 405 (2012); 35 U.S.C. § 271(e)(4)(A) (requiring courts to block approval of infringing generics). An ANDA applicant must therefore affirmatively "assure the FDA" through formal certification that it "will not infringe" any patents in the Orange Book

for the reference drug. *Actavis*, 570 U.S. at 143. The generic can provide that assurance by certifying that no patent is listed; that any listed patent is already expired; or that it will not market the drug until the listed patents expire—certifications under so-called paragraphs I, II, and III, respectively. 21 U.S.C. § 355(j)(2)(A)(vii); see *Eli Lilly & Co.* v. *Medtronic, Inc.*, 496 U.S. 661, 677 (1990). Alternatively, the generic can try to market its drug sooner by certifying under paragraph IV that a listed patent "is invalid or will not be infringed by the manufacture, use, or sale" of its generic drug. 21 U.S.C. § 355(j)(2)(A)(vii)(IV). The paragraph IV pathway provides the option of Hatch-Waxman litigation, in which the brand and generic can resolve their disputes in pre-launch litigation that centers on the contents of the drug label and the ANDA. See *Actavis*, 570 U.S. at 143. The Hatch-Waxman option yields no prospect of damages, and it comes with a default 30-month automatic stay of FDA approval of the generic while litigation proceeds. See *ibid.*; *Eli Lilly*, 496 U.S. at 677–678; 21 U.S.C. § 355(j)(5)(B)(iii).[4]

A generic applicant also has another option if the reference brand drug is approved for multiple indications but only some of them are patented. Through a so-called section viii statement, a generic applicant can promise that it will market its drug *only* for methods of use not covered by Orange Book patents. See 21 U.S.C. § 355(j)(2)(A)(viii); *Caraco*, 566 U.S. at 406. If a generic pursues that option, it must propose a "skinny label" that carves out any patented methods of use. *Caraco*, 566 U.S. at 406; 21 C.F.R. § 314.94(a)(8)(iv). Choosing this option bypasses the spe-

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[4] If litigation resolves earlier than 30 months, the FDA may approve the drug if the patents are invalid or not infringed. See *Eli Lilly*, 496 U.S. at 677–678; 21 U.S.C. § 355(j)(5)(B)(iii).

cial procedural option to resolve patent issues pre-launch, and the generic is not burdened by the automatic 30-month stay of approval. And because the FDA does not independently evaluate patent infringement, the agency takes a generic at its word in asserting that the carved-out label does not infringe and promising not to market the drug for the omitted use. See, *e.g.*, 68 Fed. Reg. 36,676, 36,683 (June 18, 2003) (explaining that "reviewing patents, assessing patent challenges, and de-listing patents would involve patent law issues that are outside both our expertise and our authority"). If a generic files a section viii statement but improperly maintains infringing uses on its label or otherwise engages in infringing activity, then a patent holder like Amarin has no choice but to wait for the generic to launch.

2. Patent infringement

The Patent Act defines two kinds of infringement commonly relevant to generic drugs: inducing infringement under § 271(b) and submitting an infringing drug application under § 271(e)(2)(A). This lawsuit implicates only the former.

a. The Patent Act imposes liability on anyone that "actively induces infringement of a patent." 35 U.S.C. § 271(b). Inducement requires direct infringement by the induced third party. *Limelight Networks, Inc.* v. *Akamai Techs., Inc.*, 572 U.S. 915, 920–921 (2014). It also requires "active steps … taken to encourage direct infringement." *Metro-Goldwyn-Mayer Studios, Inc.* v. *Grokster, Ltd.*, 545 U.S. 913, 936 (2005) (citation omitted).

Unlike direct infringement, induced infringement requires that the defendant possessed specific intent to infringe, including "knowledge that the induced acts constitute patent infringement." *Global-Tech Appliances, Inc.* v. *SEB S.A.*, 563 U.S. 754, 761 n.2, 766 (2011); see

Commil USA, LLC v. *Cisco Sys., Inc.*, 575 U.S. 632, 639 (2015). Hikma's petition for a writ of certiorari does not raise any question about specific intent or direct infringement; petitioners do not dispute that Amarin plausibly pleaded both. The petition instead concerns only whether Amarin plausibly pleaded "active steps … taken to encourage direct infringement." *Grokster*, 545 U.S. at 936.

b. The Patent Act also independently defines as infringement submitting an application to the FDA "for a drug claimed in a patent or the use of which is claimed in a patent." 35 U.S.C. § 271(e)(2)(A). That action enables Hatch-Waxman litigation based on the ANDA itself, focusing on the drug label and ANDA specification. See, *e.g.*, *Eli Lilly*, 496 U.S. at 678. This case does not involve pre-launch Hatch-Waxman litigation.

C. The present controversy

1. Hikma pursued approval to market a generic version of Vascepa. It filed an ANDA when the FDA had approved Vascepa only for treating *severe* hypertriglyceridemia. When the FDA later approved the CV indication (and Amarin listed the patents covering the CV indication in the Orange Book), Hikma's ANDA was still pending. Hikma thus had to choose whether to respect each patent's term (through a paragraph III certification), challenge each patent pre-launch (through a paragraph IV certification), or avoid pre-launch litigation entirely through a section viii statement and promise to confine its generic to the off-patent use. Pet.App.4a.

Hikma chose the latter. S.App.26a–29a. It submitted a proposed carve-out label to the FDA, which approved it in 2020. Pet.App.4a–5a. Hikma thus received approval to market its generic product based on its promise that it was *not* seeking approval for the CV indication covered by

respondents' patents and sought approval only for the SH indication. See, *e.g.*, S.App.21a, 26a–29a.

Notwithstanding Hikma's limited approval, almost immediately it began advertising its generic for broader uses. Hikma issued several press releases related to the approval of its ANDA. Pet.App.5a–6a; S.App.30a–33a; C.A.App.613, 709, 712, 715. In them, Hikma broadcast its product as the "generic version" of Vascepa, the "generic equivalent," or "generic Vascepa." Pet.App.5a–6a; S.App. 30a–33a; C.A.App.613, 709, 712. Hikma also pointed out that Vascepa is indicated only "in part" for severe hypertriglyceridemia. Pet.App.5a–6a; S.App.30a, 32a; C.A.App. 709, 712. (Vascepa had only two approved indications.) Hikma announced it had "received FDA approval" without explaining that the approval was limited to Vascepa's far-less-common indication. Pet.App.6a; C.A.App.613. And Hikma boasted about Vascepa's value by touting that drug's *entire* domestic sales—which were overwhelmingly associated with the still-patented CV indication for which Hikma had not sought or obtained approval. Pet.App.6a–7a; S.App.30a, 32a; C.A.App.709, 712.

Hikma also marketed its generic product on its website as within the therapeutic category "Hypertriglyceridemia." That description indisputably includes *both* the SH and (patented) CV indications, even though Hikma's drug's approved indication was only for patients with SH. Pet.App.7a; S.App.33a–34a; C.A.App.820.

While Hikma's label lists only the SH indication in its "Indications and Usage" section, Pet.App.5a; C.A.App. 694, it identifies potential side effects for people having cardiovascular disease or diabetes with a risk factor for cardiovascular disease. Pet.App.5a; C.A.App.704–705. The label also refers to Amarin's REDUCE-IT trial for the CV indication. C.A.App.696. And it states that "[m]ed-

icines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet." Pet.App.5a; C.A.App.705. Hikma also amended its label to remove a statement warning that the effects of the drug "on cardiovascular mortality and morbidity" had not been determined. Pet.App.3a, 5a.

2. Based on Hikma's intentional efforts to steer sales away from Amarin's product and toward its own for a patented use, Amarin brought this suit against Hikma for inducing infringement. S.App.1a–62a; Pet.App.7a. Amarin sued under § 271(b) based on Hikma's full course of conduct, not under § 271(e)(2)(A) based on Hikma's label alone. Pet.App.7a–8a. Amarin's amended complaint alleges in detail how Hikma intentionally induced infringement through the combination of its drug label, press releases, and website. *Id.* at 9a. The amended complaint alleges that Hikma's messages and actions together communicate to healthcare providers and patients that Hikma's generic should be used for the same two indications as Vascepa—including the patented CV indication. S.App.31a–32a, 34a–38a; see also Pet.App.9a.

Hikma moved to dismiss for failure to state a claim for relief, contending that the complaint fails to allege active steps to specifically encourage infringement. Pet.App.9a. The magistrate judge recommended denying that motion, but the district judge granted it. *Id.* at 10a–11a. The district court's analysis addressed the complaint's allegations individually, not collectively. *Ibid.*

3. The court of appeals reversed, finding that Amarin's complaint plausibly alleges induced infringement and carries Amarin's burden at the pleading stage. Pet.App.15a–16a, 22a.

The court of appeals cautioned that this is not a Hatch-Waxman case under 35 U.S.C. § 271(e)(2)(A). Pet.App.

12a–13a. It also noted that this is not a "skinny label" case; the thrust of the complaint is not that Hikma's label was "not skinny enough." *Id.* at 13a. Rather, "the alleged infringement [here] is based on the generic manufacturer's skinny label *as well* as its public statement and marketing of its already-approved generic product." *Ibid.* That is, the "*totality* of the allegations." *Ibid.* The court of appeals also emphasized the "nascent" procedural stage under the plausibility standard. *Id.* at 14a.

On appeal, Hikma did not contest whether the complaint sufficiently alleges direct infringement by induced physicians or whether Hikma acted with the requisite specific intent. Pet.App.15a. The court of appeals "focus[ed] narrowly" on the question raised by Hikma of "whether Amarin's complaint plausibly plead[s]" active inducement. *Id.* at 15a–16a. The court concluded, "accepting all well-pleaded facts as true and drawing all reasonable inferences in Amarin's favor," that the complaint does. *Id.* at 16a.

The court of appeals reasoned that, although the "Indications & Usage" section of Hikma's label did not expressly instruct the patented CV use, Amarin plausibly alleges that other specific portions of the label, such as descriptions of "statin-treated patients with the same cardiovascular event history and lipid levels covered by the asserted patents," would be understood by physicians as an instruction that Hikma's product could be prescribed to treat cardiovascular risk—in violation of Amarin's patent rights. Pet.App.16a. The court also observed that Amarin alleges that Hikma improperly removed the warning against CV use, and that doing so further communicated the patented off-label use to physicians. *Ibid.*

Amarin's allegations are based on "the label *in combination* with Hikma's public statements and marketing

materials." *Id.* at 17a–18a. Reviewing those materials in detail, the court of appeals agreed that they give rise to a disputed question of fact: "what Hikma's label and public statements would communicate to patients and the marketplace." *Id.* at 18a. The court of appeals found it "at least plausible that a physician could read Hikma's press releases—touting sales figures attributable largely to an infringing use, and calling Hikma's product the 'generic version' of a drug that is indicated 'in part' for the SH indication—as an instruction or encouragement to prescribe that drug for *any* of the approved uses" of icosapent ethyl. *Id.* at 19a–20a. In other words, by broadly marketing its drug for "hypertriglyceridemia" (which includes the patented CV use), not SH, Hikma was encouraging prescribing its drug off-label for a use beyond that for which it was approved. *Ibid.* Although the court of appeals noted Hikma's use of technical "AB-rated" jargon and a disclaimer on its website, the court declined to hold that those aspects of the website categorically insulated Hikma from induced-infringement liability. *Ibid.*[5]

The court of appeals denied Hikma's petition for rehearing en banc. Pet.App.41a.

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[5] Petitioners contend (Pet. 32–33 n.8) that the court of appeals "rejected" a contention that Hikma's label contributed to inducement. That is incorrect. The decision below clarified that Amarin's theory of liability was about *all* of Hikma's conduct and was "not based *solely* on the label." Pet.App.17a (emphasis added). To be sure, Amarin disputes the adequacy of Hikma's label's carve-out. See, *e.g.*, S.App.35a–38a. But Amarin did not need to show that the label individually induced infringement to survive dismissal, because Hikma's actions *collectively* show inducement.

REASONS FOR DENYING THE PETITION

The petition for a writ of certiorari should be denied because the legal arguments raised in it are inconsequential and idiosyncratic, and because the court of appeals' decision below is correct. The Federal Circuit properly applied Section 271(b) and *Twombly*'s pleading standard to find that Amarin plausibly alleged Hikma's active induced infringement. The adequacy of the pleadings is undisputed for the other elements of induced infringement—direct infringement by induced physicians and Hikma's specific intent to see those physicians infringe. And Amarin's complaint provides detailed facts that could plausibly support a finding of active inducement.

Petitioners fail to identify any true conflict with law or precedent. Petitioners attempt to manufacture a circuit split about whether inducement is a question of fact or law, but none exists and that issue is immaterial to this case. Petitioners argue that the court of appeals discarded *Twombly*, but the court's opinion shows otherwise. And petitioners argue that the decision below failed to require active steps toward inducement, but petitioners' argument is merely a disagreement with the application of settled law to specific facts. The court of appeals *did* require active steps to induce infringement, and it (correctly) found such active steps alleged here.

Petitioners also fail to raise any important issue with broad impact. The pleading-sufficiency question is deeply fact-bound, and the court of appeals itself made clear that this is a rare case. Even if this Court wanted to review what qualifies as active induced infringement, this case would be a bad vehicle for multiple reasons.

Finally, the decision below was correct. If Hikma's press releases, website, and label communicated to physicians that they should prescribe Hikma's generic for both

approved indications—including the popular, patented one—then that is unmistakable active inducement. Amarin alleges Hikma's specific intent to communicate just that message. And the message healthcare providers would receive from Hikma's statements is a quintessential issue of fact that cannot be resolved in Hikma's favor on the pleadings.

A. The petition fails to identify any true conflict.

1. The opinion below does not conflict with any precedent of this Court or another court of appeals.

a. Petitioners contend (Pet. 24–26) there is a circuit split over whether inducement is a question of fact or law. But they identify only one case from the Ninth Circuit that purportedly breaks with the decision below, *Perfect 10, Inc.* v. *Visa International Service Association*, 494 F.3d 788 (2007), and they quote the Ninth Circuit out of context. The Ninth Circuit did not hold that inducement is a pure question of law; it dismissed the claim there for failure to plead sufficient facts. *Id.* at 801. That court properly observed that a bare assertion of "inducement," standing alone, is merely the recitation of an element of the cause of action that is not taken as true at the pleading stage. See *id.* at 802.

Petitioners also distort the decision below. The Federal Circuit did not hold that inducement *cannot* be decided on the pleadings. What it said—correctly—was: "what [message] Hikma's label and public statements would communicate to physicians and the marketplace" is a question of fact. Pet.App.18a–19a. If Hikma's statements encourage doctors to infringe the patented CV indication, then Hikma actively induced infringement. The opinion below is thus about whether Amarin's case-specific factual allegations clear the plausibility bar. In other cases, the Federal Circuit has made clear that

induced infringement *can* be decided on the pleadings if the allegations (unlike Amarin's) make the claim implausible. See, *e.g.*, *Cleveland Clinic Found.* v. *True Health Diagnostics LLC*, 859 F.3d 1352, 1364 (2017).

More generally, petitioners provide no reason to disturb the long-standing consensus that patent infringement "is a question of fact." *Markman* v. *Westview Instruments, Inc.*, 517 U.S. 370, 384 (1996) (citation omitted). Hikma did not even attempt to argue before the court of appeals that active inducement is not a question of fact.[6]

b. In any event, regardless whether the *ultimate* question of active inducement is one of law or fact, the core disputed issue in this case—how Hikma's marketing statements and labeling were understood by physicians—is plainly factual. *Cf. United States* v. *Williams*, 553 U.S. 285, 306 (2008) (calling it a "clear question[] of fact" whether the defendant "communicate[d] in a manner intended to cause another" to form a particular "belie[f]," and observing that juries "pass every day upon the reasonable import of a defendant's statements"). Amarin alleges that Hikma's statements communicate that physicians should use Hikma's generic for the well-known, overwhelmingly common, patented CV indication—one of only two approved uses for the brand drug. That factual allegation must be taken as true at this stage of the case.

Petitioners misread *Perfect 10*, which is consistent with the court of appeals' approach here. The inducement issue there was about whether processors of payments (like Visa) could be held liable for copyright infringement

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[6] Petitioners say (Pet. 26) that "commentators" have called the fact-or-law question unsettled, citing one student note. That note acknowledges that inducement "is currently a question of fact." Garrett T. Potter, Note, *Beefing Up Skinny Labels*, 97 NOTRE DAME L. REV. 1707, 1709, 1722 (2022).

by websites using their services. 494 F.3d at 792. The Ninth Circuit held (among other things) that the plaintiff had failed to allege sufficient *facts*: specifically, plaintiff alleged no "affirmative steps taken to foster infringement" and "no facts suggesting that Defendants promoted their payment system as a means to infringe." *Id.* at 800. After explaining that active steps can include "communicat[ing] an inducing message," such as "advertisement or solicitation that broadcasts a message designed to stimulate others to commit violations," the Ninth Circuit observed that the plaintiff "ha[d] not alleged that any of these standards are met or that any of these considerations [we]re present." *Id.* at 801. The plaintiff asserted merely that the defendants marketed their credit cards *generally* but provided no allegations that the defendants affirmatively promoted the infringing products. *Ibid.* The court of appeals contrasted *Grokster*, in which the operators "targeted" users of an infringing platform to draw to their own platform for infringing purposes. *Ibid.*

The outcome here is consistent with *Perfect 10*, including its contrast with *Grokster*. Like the infringers in *Grokster* who courted known users of an infringing product, Hikma is alleged to have courted prescribers of the CV indication to use their generic rather than Amarin's product. And here, the complaint *does* include specific allegations of "communicat[ing] an inducing message" like an "advertisement"—namely, Hikma's series of communications read in light of its drug label. What those messages conveyed to physicians is a fact issue of the kind that was missing in *Perfect 10*. If Hikma intended its messages to encourage infringement, and if physicians understood them that way, then that was active inducement.

2. The court of appeals did not apply the wrong pleading standard.

Petitioners accuse the Federal Circuit (Pet. 21–23) of applying an erroneous pre-*Twombly* pleading standard. Putting aside the fact that this argument seeks only fact-bound error correction, the Federal Circuit made no such error. The court quoted the pre-*Twombly* no-set-of-facts standard just once, among other cases. Pet.App.12a. But the standard actually discussed and applied throughout the opinion was indisputably correct. That is probably why Hikma's rehearing petition never suggested to the court of appeals that it had mis-applied *Twombly*.

The court of appeals relied on the *Twombly* plausibility standard time and again. See, *e.g.*, Pet.App.13a ("[W]e must consider whether the *totality* of the allegations, taken as true, plausibly plead that Hikma induced infringement."); *id.* at 14a ("[W]e are tasked with reviewing *allegations*, not findings, for plausibility, not probability."); *ibid.* ("To state a claim for induced infringement, a patent owner must plausibly allege facts[.]"); *id.* at 15a ("We therefore focus narrowly on the question whether Amarin's complaint plausibly pleads that Hikma 'actively' induced healthcare providers' direct infringement[.]"); *id.* at 18a ("Those allegations … at least plausibly state a claim[.]"); *id.* at 19a ("[W]e must accept as true Amarin's allegations and all reasonable inferences supported by those allegations. Applying this standard of review, we find it at least plausible that a physician could read Hikma's press release … as an instruction or encouragement to prescribe that drug for *any* of the approved uses[.] Further, it is at least plausible that a physician may recognize that … Hikma was encouraging prescribing the drug for an off-label use."); *id.* at 21a ("[I]t is plausible that a physician could discern an encouragement to use the generic for purposes beyond the approved SH indica-

tion."); *ibid.* (stating the court's "conclusion" as "that the totality of the allegations plausibly states a claim for induced infringement"); *ibid.* ("[W]e cannot say at this stage that those allegations are not at least plausible."); *id.* at 22a ("Amarin has plausibly pleaded that, despite its section viii carve-out, Hikma has induced infringement of the asserted patents[.]"); *ibid.* ("We hold that Amarin has plausibly pleaded that Hikma has induced infringement[.]"). The court of appeals did not ask whether there was no set of facts under which Amarin could prevail.

Petitioners insist (Pet. 23) that the complaint "does not set forth a single fact" suggesting that Hikma actively encourages the patented use. But the court of appeals cited *many* factual allegations that together suggested precisely that. Petitioners simply disagree with the inferences drawn from those allegations. The court of appeals' conclusion was not merely that there was a "possibility" of discovery that might "support recovery." *Twombly*, 550 U.S. at 561. It was that the alleged facts collectively made Hikma's active inducement plausible. Because the case did not yet "have the benefit of fact discovery," Pet.App. 19a; *id.* at 14a, respondents' specific factual allegations are taken as true for now. That is the correct approach to evaluating a Rule 12(b)(6) motion after *Twombly*.

3. The court of appeals required active steps for induced infringement.

Petitioners also distort the decision below in asserting (Pet. 17–21) that the court of appeals did not require "active" inducement to infringe. The court of appeals *did* require active inducement, and it did not depart from this Court's precedent.

a. Petitioners argue (Pet. 17–18), citing *Global-Tech*, 563 U.S. at 760, that active inducement requires "affirmative steps to bring about the desired result." See also Pet.

17 (citing *Grokster*, 545 U.S. at 936–937, and arguing that inducement must be "shown by clear expression or other affirmative steps"). There is no dispute over that standard, which the court of appeals applied: The court stated that inducement requires "clear expression or other affirmative steps." Pet.App.15a.

The court of appeals thus framed the question before it as "whether Amarin's complaint plausibly pleads that Hikma 'actively' induced healthcare providers' direct infringement." Pet.App.15a–16a. As petitioners concede (Pet. 17), the required active steps can be advertising or instructing. And as the court of appeals observed, Hikma advertised its generic on its website for use in the broad "Hypertriglyceridemia" category and touted sales figures for the patented use. Pet.App.18a–19a. The court also relied on Hikma's press releases describing its product as the "generic version" of Vascepa and noting that Vascepa was indicated only "in part" for the off-patent SH indication. *Id.* at 18a. The *patented* use was the vastly more common of only two approved uses of Vascepa. *Id.* at 2a–3a, 18a. And the court of appeals explained why it was at least plausible that a physician would read Hikma's communications as instructing or encouraging the use of Hikma's generic for *either* of Vascepa's uses. *Id.* at 19a–20a. Petitioners merely take issue with the court's application of settled law to the facts.

b. Petitioners also assert that there is no induced infringement of a method patent unless a third party is induced to perform all the steps." Pet. 17–18 (citing *Limelight*, 572 U.S. at 921). But that is neither disputed nor contrary to the decision below.

The court of appeals did not hold that one could induce infringement *without* inducing performance of all the claimed steps. To the contrary, the decision below

explained that, when Hikma launched its generic, there were two approved uses of Vascepa: the CV indication and the off-patent SH indication. Pet.App.2a–3a. There is no dispute that the patented use was the vastly more popular one. *Id.* at 7a, 18a. Nor is there any dispute that Amarin plausibly pleaded Hikma's knowledge and intent, as well as direct infringement—in other words, that performing the CV indication infringes *all* the steps of the asserted patents. *Ibid.* The court of appeals further concluded that Amarin plausibly pleaded that Hikma encouraged the CV indication.

What petitioners really want is a *heightened* pleading standard under which a defendant cannot face discovery for induced infringement unless its communications recite all the patent claim language. That is not the law. None of this Court's cases relied on by petitioners establishes that the actively inducing advertisement or encouragement must *recite* all the claim limitations. Quite the opposite. In *Grokster*, this Court did not even require inducing statements to describe the protected work. 545 U.S. at 937–938. It was enough for a defendant to promote a device's use to infringe copyright generally, without any reference to specific copyrighted works. The "inducing message" included advertisements targeting users of the controversial music-distribution platform Napster and conveying by implication that the defendant "offered software to perform the same services" for the same directly infringing audience. *Ibid.* That was enough to constitute "active steps" to induce the direct violation of intellectual property rights. This case contains far more instruction with respect to the rights in question because the court of appeals found it plausible that the combination of Hikma's specific references to Vascepa, to Vascepa's sales, and to hypertriglyceridemia actively induced practicing the CV indication—which infringes.

c. Petitioners also contend (Pet. 19–20) that the decision below rests on a "theory of *passive* infringement." Not at all. The court of appeals required *active* steps (and found them in Amarin's complaint), as described above.

Petitioners attempt to re-characterize Amarin's complaint (Pet. 19) as if it relied on a theory that physicians would be inspired by Hikma's press releases to go and research Amarin's brand-name label. But the court of appeals never relied on that logic. It rested on the content of Hikma's press releases, Hikma's website, and Hikma's label, finding as a matter of fact that those active steps plausibly conveyed encouragement to physicians to administer Hikma's generic for *all* of Vascepa's existing approved uses—including the patented one. The infringing CV use was known before Hikma launched its product, and it was overwhelmingly more common. No prospective research by physicians was required for them to plausibly understand Hikma's communications as encouraging the known and most common use of Vascepa. Petitioners are thus plain wrong (Pet. 19–20) that the decision "*depends upon* speculation that third parties will independently research the uses of a competitor's product, based on external sources of knowledge that Hikma does not control."

d. The decision below also did not "flip the burden of proof" and impose liability for failure to discourage infringement. Contra Pet. 20–21. Petitioners invoke *Grokster* (Pet. 20) to argue that "a failure to take affirmative steps to prevent infringement" is not inducement. 545 U.S. at 939 n.12. Petitioners misread *Grokster*. That case observed that contributory copyright infringement by marketing a device cannot be based *solely* on a failure to take affirmative preventive steps. *Ibid.* It did not say that doing so is irrelevant.

In all events, the court of appeals did not find inducement adequately alleged based on Hikma's inaction. It simply explained the context of the affirmative steps that Hikma took to explain why a physician would plausibly take Hikma's statements to encourage performing the common, patented CV indication.

B. This case does not warrant this Court's review.

1. The petition does not raise any important issue with broad impact.

The petition presents no issue worthy of this Court's review. As explained above, petitioners dispute the court of appeals' application of the law to these particular factual allegations, not the law itself. Petitioners' criticisms of the decision below, moreover, do not affect the result in this case. They sound largely in policy, but those concerns are properly addressed by Congress.

Petitioners insist (Pet. 26–27) that the decision below "effectively nullifies" and "vitiates" section viii skinny-labeling carve-outs. See also AAM Amicus Br. 6–11 (similar argument). But the court of appeals nullified nothing. As the court made clear, this is not a skinny-label case. While the adequacy of Hikma's carve-out is contested, there are many more pleaded facts that together make inducement plausible. Furthermore, this case is not about liability or remedies. It is about the *pleadings*.

Petitioners also argue (Pet. 26–27) that after the decision below, it "no longer makes sense" for generics to pursue the section viii carve-out path, but they offer no evidence to back up that assertion. They suggest (Pet. 27) that it is a problem if brands "can sue anyway" when a generic adopts a carve-out label. But petitioners cite no support or law or logic for their premise that a section viii carve-out should provide a safe harbor protecting a generic that *also* markets its drug for the carved-out use.

A section viii carve-out may allow a generic to avoid pre-launch litigation under the Hatch-Waxman Act, *i.e.*, under 35 U.S.C. § 271(e)(2)(A), but it is not a shield against conventional inducement allegations under 35 U.S.C. § 271(b), especially where those allegations include extra-label marketing activity. Petitioners claim (Pet. 27) that the facts here will exist in every induced infringement case. But that assertion is belied by petitioners' admission elsewhere in the petition that there are other generics with the same label who haven't been sued. *E.g.*, Pet. 13 n.6. In other cases, the drugs, patents, indications, and conduct of the defendant will differ substantially.

Petitioners suggest (Pet. 23, 32) that the "potentially enormous expense of discovery" will deter generics from entering the market. They provide no real evidence of that, and they ignore the other side of the coin: if generics are immune from even litigating inducing acts, pharmaceutical companies will stop committing the massive resources needed to run trials for new uses after the first one. Patent trials might cost in the low millions (Pet. 32), but *clinical* trials can cost billions.[7] Often the most impactful application of a drug is not the first one (like here). In all events, the economic policy underlying the federal drug and patent laws are "for Congress, not the courts." *Georgia* v. *Public.Resource.Org, Inc.*, 590 U.S. 255, 272 (2020).

What petitioners really want is a safe harbor for generics choosing a carve-out label under section viii. But Congress knew how to draft a safe harbor. It provided one in 35 U.S.C. § 271(e)(1) for certain regulatory approval-

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[7] Joseph A. DiMasi et al., *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. HEALTH ECON. 20 (2016) ("a total pre-approval cost estimate of $2558 million (2013 dollars)" for new drugs).

related use of patents. See *Merck*, 545 U.S. at 202, 206. But Congress did not extend that protection to circumstances after approval, and it chose not to provide a safe harbor for section viii carve-outs. This Court should not create one.

2. This case is intensely fact-bound.

Certiorari is also unwarranted because this case turns on facts and any decision would have limited general applicability. The court of appeals cabined its decision as "limited to the allegations before [it] and guided by the standard of review." Pet.App.22a. And the decision reflects that this case was about the totality of a lengthy complaint—the circumstances of this drug, Hikma's active statements, and what *in fact* they communicate to physicians.

As explained above, the decision below rested on what Hikma's actions communicated *in the context of this drug*. Vascepa has two uses, each of which were noteworthy as firsts of their kinds. *Supra* at 5–7. But the earlier use is a small minority of the indications. *Supra* at 7. Vascepa has a more popular, revolutionary use that is patented. *Supra* at 6–7. The patented use is associated with the broad category of "Hypertriglyceridemia," within which Hikma marketed its generic, as opposed to the narrow category of patients who are prescribed Vascepa for its SH indication—the only approved indication for Hikma's generic. *Supra* at 11–13. And Amarin contends that Hikma's alleged carve-out was incomplete. *Supra* at 15 n.5. Finally, *what* Hikma's particular statements communicated to physicians is a factual question that cannot be resolved until discovery.

None of those facts are universal. Other generics might choose different communications strategies that do not suggest the ability to compete for market share of

non-approved uses, that do not implicate broader uses than those approved, and that do not suggest equivalency for all uses. The decision below is thus intensely connected to the particular constellation of facts in respondents' complaint. And petitioners and amici are wrong that every case will have the same facts.

Petitioners say (Pet. 29–30) that sales of a skinny-label generic will always incidentally include some sales that are off-label. But this case is not about innocent incidental profiting from off-label sales. As discussed above, respondents plausibly pleaded Hikma's *intent* to infringe. It will not always be the case that intent is undisputedly pleaded, or that the overwhelming majority of the generic's sales are for the off-label use.

3. This case is a bad vehicle to take up the issues raised by petitioners and their amici.

This case is also a poor vehicle for the issues raised by petitioners and their amici.

For one thing, the distinction between whether inducement is a question of fact or law (Pet. 24–26) has no impact here. This case is an exceptionally poor vehicle to explore that issue because there is nothing to suggest that the distinction would make any difference—in all events, the factual issue of communication remains. And at this stage, the Court does not have the benefit of findings about what Hikma's statements conveyed to physicians. This case is also therefore an extremely poor vehicle for considering whether and under what circumstances a generic's communications can establish liability.

Likewise, this case is not about a "skinny label" alone. AAM Amici contend (Br. 6–12) that the decision below will "eviscerate[]" the skinny-label statutory provision, but this case does not implicate those concerns. Not only are there additional pleaded facts here, but the adequacy of

Hikma's carve-out *is* disputed. See, *e.g.*, S.App.28a–29a, 35a–38a.[8] As the court of appeals explained, this is not a skinny-label case because Amarin pleaded "much more," and Hikma "neither 'merely' marketed its drug under a skinny label that omits all patented indications nor 'merely' noted that the FDA has rated its drug as AB-rated." Pet.App.21a.

Further, as petitioners concede (Pet. 13 n.6), Amarin has not sued any other generics having the same label as Hikma. That puts to rest any notion (Pet. 30–35) that this case imperils the viability of the skinny-label pathway and will deter generics across the board. It also belies petitioners' insistence (Pet. 27–30) that "no skinny label is safe" and the same facts fit "every generic drug with a skinny label." Petitioners also wrongly suggest (Pet. 31) that the decision "makes skinny labels *riskier* than paragraph IV certifications." But that will not be true for other generics that, unlike Hikma, do not *intend* to capitalize on and encourage patented uses their drug is not approved for, and that take care in their marketing.

Petitioners (Pet. 27–29) and amici Scholars (Br. 1–23) suggest that the decision below imperils the ability of generics and others to make equivalence statements or call their products a "generic version." But this case is a poor vehicle for that question because the decision below did not hold that saying "generic version" was sufficient for liability; indeed, the court of appeals recognized exactly the opposite, Pet.App.21a. The decision relied instead on a specific combination of facts: multiple press releases referring to generic equivalence in different ways; advertising that the equivalent drug has multiple indications; marketing the drug on the website for "Hypertriglycer-

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[8] The court of appeals did not hold otherwise. It observed that Amarin did not rely on the label *alone*. Pet.App.13a, 17a–18a.

idemia," not just SH; and touting sales figures for the more-common patented use. Petitioners also suppose (Pet. 29) that a company could face liability for a CEO estimating market size on an earnings call, but the decision below did not hold that market-size communications were sufficient.[9] Nor is this case a good vehicle to examine the significance of equivalence or compatibility statements in other industries like cellular standards (Scholars Br. 13–15), because inducement would turn heavily on facts and industry practices that may significantly differ.

Academic amici insist (Scholars Br. 9–12) that the decision will lead to "forever" patent terms. Not even close. Amici suppose that an innovator could start with a broad indication and then, after one patent's term, continually pursue more-obscure, narrower indications to patent and iteratively add to its label. But the facts alleged here are almost the opposite. Amarin's first indication was narrower, and the second was a more prevalent, broader use. The still-patented use is what the drug is most famous for and what won it praise as a "game changer." Nor does the reasoning of the decision below raise the prospect of forever-patenting—especially where token new uses are, as amici suggest, of minimal medical significance. Amici ignore that Hikma's specific intent to induce infringement was indisputably pleaded here.

Petitioners also insist (Pet. 30–35) that the decision below will "deter generics from using labeling carve-outs, which will delay market entry and raise drug prices." That is unsupported and illogical. Any deterrence is an economic consideration that depends on liability and the remedy under the facts of a particular case. This decision

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[9] Petitioners suggest (Pet. 29) that market size is "a basic consideration for any competitive product launch." Not the size of the *irrelevant* market that is under patent.

addressed neither one. Respondents will still have the burden to show entitlement to injunctive relief when they prevail, and to prove damages. And in all events, economic policy considerations are for Congress, guided by political and expert insight. They are not arguments for the courts—especially not on a motion to dismiss.

Amici insist that the decision "undermine[s] the paragraph IV process." AAM Br. 11 (capitalization normalized). But as the court of appeals made clear, this is not a paragraph IV case. Pet.App.14a–15a. There is no dispute that Hikma could have opted for paragraph IV if it wanted to resolve patentability before launch. It chose not to.

Amici also warn (AAM Br. 13) of brands "running up the meter on potential damages" before suing. But they give no example—and there is no reason to delay because damages are limited to a reasonable royalty or lost profits suffered. Brands collect more damages only if they suffer more harm. They will justifiably be motivated to timely resolve patent disputes to avoid the irreparable harm of a competitor entering the market. Amarin, for example, sued within a month. And again, that all invokes economic policy rather than law.

C. The decision below is correct.

Section 271(b) makes anyone who "actively induces infringement of a patent" liable as an infringer. The court of appeals correctly concluded that respondents plausibly pleaded a claim of induced infringement. Pet.App.22a.

There is no dispute that the complaint sufficiently alleged direct infringement—*i.e.*, that providers infringe when they prescribe Hikma's generic drug to relevant patients for the CV indication. Pet.App.15a. Respondents also undisputedly plausibly alleged specific intent—*i.e.*, that Hikma had the requisite intent and knowledge to induce infringement. *Ibid.* The only element contested on

appeal was active inducement. Under the undisputed legal standard for that element, Amarin had to plead that Hikma "encourage[d], recommend[ed], or promote[d] infringement." *Takeda Pharms. U.S.A., Inc.* v. *West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015).

As the decision below noted, Hikma's website advertised its generic for use for "Hypertriglyceridemia." Pet.App.18a. That encompasses non-severe hypertriglyceridemia, for which only the patented CV indication is relevant. *Ibid.* And Hikma touted sales figures for the patented use, thereby reinforcing its message that physicians should prescribe the generic for that purpose. *Ibid.* The court of appeals also relied on Hikma's press releases referring to its "generic version" of Vascepa (and just plain "generic Vascepa"), plus its messages to the public that Vascepa was indicated only "in part" for the Hikma-approved SH indication. *Ibid.* That obviously referred to the only *other* approved use, which was more famous and whose performance infringes. Hikma's label also included various specific statements in its clinical-studies section that referred to the patient population for the patented use. *Id.* at 16a. The court of appeals concluded that Amarin's allegations about Hikma's label together with those steps plausibly stated a claim. *Id.* at 18a–19a.

The decision below explained, correctly, that it is plausible a physician would read those communications as collectively encouraging using Hikma's product for both uses of Vascepa. Pet.App.19a. The court also explained why Hikma's marketing its drug in the therapeutic category of "Hypertriglyceridemia" encouraged off-label use. *Ibid.* The court of appeals was correct that Amarin's amended complaint plausibly pleaded active inducement.

Petitioners make much (at 18) of the idea that a defendant must actively induce another to perform "all

the steps" of the patented method. But under the undisputed facts at the current stage of the case, Amarin plausibly pleaded that administering icosapent ethyl to the target population according to the known CV indication results in all the claimed steps being performed. See, *e.g.*, Pet.App.15a. Petitioners identify no step not performed under those circumstances.

Petitioners are also wrong to suggest (Pet. 19) that the decision rested on an elaborate "passive inducement" theory in which physicians read press releases and then independently research the brand drug to learn its uses. That was not Amarin's theory of liability, and that theory is nowhere in the decision below. Liability arises, rather, from Hikma's knowledge that the relevant physicians were aware of Vascepa and from its intentional communication that physicians should prescribe Hikma's product for Vascepa's patented use. Exactly what message physicians take from Hikma's collection of communications is a question of fact that Amarin will prove at trial; the court of appeals correctly recognized that issue cannot be resolved on a motion to dismiss. Pet.App.18a–19a.

Finally, petitioners complain about the court of appeals' observation that Hikma took little care to describe its approval with any precision. But the court did not shift the burden to a defendant to discourage infringement. It simply declined petitioners' invitation to create new law and insulate a defendant from litigating. Pet.App.20a.

Conclusion

The petition for a writ of certiorari should be denied.

Respectfully submitted,

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May 15, 2025

Supplemental Appendix

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Amended Complaint (Jan. 25, 2021)
Dkt. No. 17 (D. Del.); C.A.App.504–557

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMARIN PHARMA, INC., AMARIN PHARMACEUTICALS IRELAND LIMITED, MOCHIDA PHARMACEUTICAL CO., LTD. Plaintiff, v. HIKMA PHARMACEUTICALS USA INC., HIKMA PHARMACEUTICALS PLC, AND HEALTH NET LLC, Defendant.	C.A. No.: 20-1630-RGA **JURY TRIAL DEMANDED**

FIRST AMENDED COMPLAINT FOR PATENT INFRINGEMENT AND DEMAND FOR JURY TRIAL

Plaintiffs Amarin Pharma, Inc. and Amarin Pharmaceuticals Ireland Limited ("Amarin") and Mochida Pharmaceutical Co., Ltd. ("Mochida") (collectively, "Plaintiffs"), by their attorneys, hereby allege as follows:

THE NATURE OF THE ACTION

1. This is an action for 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, the "Asserted Patents") under the Patent Laws of the United States, 35 U.S.C. § 100 et seq., including § 271(b). In violation of these laws, the Hikma Defendants are marketing their generic version of Amarin's ground-breaking VASCEPA® product to reduce the risk of cardiovascular events such as heart attack and stroke ("cardiovascular risk reduction"), and Health Net is inducing pharmacies to dispense, and patients to use it, for that purpose. VASCEPA® is the first and only innovative omega-3 acid-based product approved for cardiovascular risk reduction by the United States Food and Drug Administration.

THE PARTIES

2. Amarin Pharma, Inc. is a company organized under the laws of Delaware with its principal place of business at 440 Route 22, Suite 330, Bridgewater, NJ 08870.

3. Amarin Pharmaceuticals Ireland Limited is a company incorporated under the laws of Ireland with registered offices at 88 Harcourt Street, Dublin 2, Dublin, Ireland.

4. Mochida Pharmaceutical Co., Ltd. is a company incorporated under the laws of Japan with its principal place of business at 1-1, Ichigayahonmuracho, Shinjuku-ku, Tokyo 162-0845, Japan.

5. On information and belief, Defendant Hikma Pharmaceuticals USA Inc. is a corporation organized and existing under the laws of Delaware with its principal place

of business at 246 Industrial Way West, Eatontown, NJ 07724.

6. On information and belief, Defendant Hikma Pharmaceuticals PLC is a corporation organized and existing under the laws of the United Kingdom with its principal place of business at 1 New Burlington Place, London W1S 2HR.

7. Upon information and belief, Hikma Pharmaceuticals USA Inc. is a wholly-owned subsidiary of Hikma Pharmaceuticals PLC.

8. Upon information and belief, Hikma Pharmaceuticals USA Inc. acts at the direction, and for the benefit, of Hikma Pharmaceuticals PLC, and is controlled and/or dominated by Hikma Pharmaceuticals PLC. Hikma Pharmaceuticals USA Inc. and Hikma Pharmaceuticals PLC are hereinafter referred to together as "the Hikma Defendants" or "Hikma."

9. Upon information and belief, the Hikma Defendants collaborate with respect to the development, regulatory approval, marketing, sale, and/or distribution of pharmaceutical products. On further information and belief, the Hikma Defendants are agents of each other and/or operate in concert as integrated parts of the same business group, and enter into agreements with each other that are nearer than arm's length.

10. Upon information and belief, Hikma Pharmaceuticals USA Inc. is the current owner of ANDA No. 209457 for 1g and 0.5 g icosapent ethyl capsules purportedly bioequivalent to VASCEPA®.

11. Upon information and belief, on May 21, 2020, FDA granted final approval for the Hikma Defendants' 1g icosapent ethyl capsules under ANDA No. 209457.

12. Attached hereto as Exhibit A is a press release issued by Hikma Pharmaceuticals PLC on or about May 22, 2020 announcing that "Hikma Pharmaceuticals USA Inc. has received approval from the US Food and Drug Administration (FDA) for its Icosapent Ethyl Capsules, 1 gm, the generic equivalent to Vascepa®."

13. Attached hereto as Exhibit N is a press release issued by Hikma Pharmaceuticals PLC on or about November 5, 2020 announcing the launch of Hikma's icosapent ethyl capsules. On information and belief, on November 5, 2020, Hikma launched and began offering for sale and/or selling its generic icosapent ethyl capsules in the United States, including this jurisdiction.

14. Upon information and belief, the Hikma Defendants act collaboratively to commercially manufacture, market, distribute, offer for sale, and/or sell Hikma's icosapent ethyl capsules in the United States, including this jurisdiction.

15. On information and belief, Health Net, LLC is a limited liability company organized and existing under the laws of the State of Delaware with a principal place of business at 21281 Burbank Boulevard in Woodland Hills, California 91367. Health Net, LLC is referred to herein as "Health Net" and collectively with the Hikma Defendants as "Defendants."

16. On information and belief, Health Net, on its own and through its various subsidiaries, provides insurance coverage for patients in the United States.

JURISDICTION AND VENUE

17. This Court has subject matter jurisdiction over the action under 28 U.S.C. §§ 1331 and 1338(a).

18. This Court has personal jurisdiction over Hikma Pharmaceuticals USA Inc. because it is incorporated in Delaware and thus is present in and resides in this District, and because Hikma Pharmaceuticals USA Inc. is doing business in this District and has thus purposefully availed itself to the privileges of conducting business in Delaware.

19. Venue is proper in this District over Hikma Pharmaceuticals USA, Inc. under 28 U.S.C. § 1400(b).

20. This Court has personal jurisdiction over Hikma Pharmaceuticals PLC because, on information and belief, it manufactures, imports, offers for sale, and sells pharmaceutical drugs that are sold in the United States, including in Delaware, and derives substantial income therefrom.

21. In the alternative, this Court may exercise personal jurisdiction over Hikma Pharmaceuticals PLC pursuant to Fed. R. Civ. P. 4(k)(2) because (a) Plaintiffs' claims arise under federal law; (b) Hikma Pharmaceuticals PLC is a foreign company not subject to personal jurisdiction in the courts in any state, and (c) Hikma Pharmaceuticals PLC has sufficient contacts with the United States as a whole, including but not limited to marketing and/or selling generic pharmaceutical products that are distributed and sold throughout the United States, such that this Court's exercise of jurisdiction over Hikma Pharmaceuticals PLC satisfies due process.

22. Venue is proper in this District with respect to Hikma Pharmaceuticals PLC pursuant to 28 U.S.C. § 1391(c)(3) because it is not resident in the United States.

23. This Court has personal jurisdiction over Health Net because it is organized under the law of Delaware and thus is present in and resides in this District.

24. Venue is proper in this District over Health Net under 28 U.S.C. § 1400(b).

FACTUAL BACKGROUND

A. VASCEPA®, REDUCE-IT, JELIS and EPA's Reduction of Cardiovascular Risk

25. The three types of omega−3 fatty acids involved in human physiology are α-linolenic acid (ALA), found in plant oils, and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), both commonly found in marine (fish) oils.

26. Amarin and Mochida are recognized worldwide as the leading innovation-driven companies committed to the research and development of EPA-based drug products to treat the needs of millions of patients who are at risk of cardiovascular disease.

27. Mochida developed and markets a prescription pure EPA drug product, Epadel, in Japan.

28. Amarin developed and markets VASCEPA®, a prescription drug that contains pure EPA, in the United States.

29. Amarin conducted a series of clinical trials to support FDA approval of VASCEPA®.

30. In the MARINE trial that led to VASCEPA®'s first approval, VASCEPA® was found to lower triglycerides in patients with severe hypertriglyceridemia (≥500 mg/dL) without raising bad cholesterol, or LDL-C, levels. Upon FDA approval in 2012, VASCEPA® became the first (and still only) approved medication for treating severe hypertriglyceridemia that does not raise LDL-C.

31. After that approval to treat severe hypertriglyceridemia, Amarin continued its clinical work towards its

primary goal, approval of VASCEPA® for use in cardiovascular risk reduction. Based on an agreed protocol with the FDA, Amarin had conducted a clinical trial known as ANCHOR, in which Amarin examined VASCEPA® as an add-on to statin therapy in patients with persistent high (≥200 mg/dL and <500 mg/dL) triglycerides. As agreed with FDA, Amarin evaluated VASCEPA®'s effect on cardiovascular risk reduction based on triglyceride level lowering as a surrogate, or substitute, for cardiovascular risk reduction while awaiting the results of Amarin's REDUCE-IT trial.

32. While ANCHOR met its clinical endpoints, including the exploratory endpoint of median placebo-adjusted percent change in high-sensitivity C reactive protein (hs-CRP), *see* Ex. U (Ballantyne), FDA's view on the use of triglyceride levels as a surrogate for cardiovascular risk changed. Ex. BB. FDA identified several clinical trials where other therapies, including other omega-3 based therapies, lowered triglyceride levels in this patient population but did not show an actual reduction in cardiovascular risk. The trials failing to show a cardiovascular risk reduction included ACCORD-Lipid, AIM-HIGH, and HPS2-THRIVE.

33. Accordingly, Amarin proceeded to complete REDUCE-IT, a trial in which the effects of VASCEPA® on cardiovascular risk reduction were evaluated directly. The REDUCE-IT study was completed by Amarin at great cost. In REDUCE-IT, Amarin followed more than 8000 patients over a median of five years and evaluated the effectiveness of VASCEPA® as an add-on to statin therapy in reducing major cardiovascular events in patients with persistent elevated triglycerides. *See* Ex. V (Bhatt).

34. The results of REDUCE-IT, first announced in 2018, *see* Ex. H, were hailed as one of the most important developments in the prevention and treatment of cardiovascular disease since statins. Compared to statins alone on top of other contemporaneous medical therapy, VASCEPA® showed a 25% reduction in major cardiovascular events such as cardiovascular death, myocardial infarction, and stroke. Based on those results, in December 2019, FDA approved VASCEPA® for a second indication 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 established cardiovascular disease or diabetes mellitus and 2 or more additional risk factors for cardiovascular disease. Ex. I. Similar to the ANCHOR results, a reduction in hs-CRP was observed in REDUCE-IT which may in part explain the cardiovascular risk benefit. See Ex. V (Bhatt) at 20. This is consistent with the investigators in the ANCHOR trial, who stated that one of the potential explanations for increased cardiovascular risk might be inflammation and VASCEPA® showed a 22% reduction of hs-CRP in the mixed dyslipidemia population studied in ANCHOR. *See* Ex. U (Ballantyne); *see also* Exhibit O at col. 18, l. 11-12.

35. In a press release about this additional approval, FDA recognized that "VASCEPA is the first FDA-approved drug to reduce cardiovascular risk among patients with elevated triglyceride levels as an add-on to maximally tolerated statin therapy." Ex. J. The results of REDUCE-IT were met with widespread enthusiasm and surprise in the field and have been hailed as a "game changer" in medicine. Ex. Y; Ex. Z.

36. Amarin's work in the MARINE, ANCHOR, and REDUCE-IT clinical trials was preceded by other work done by Mochida, in Japan. In the late 1990s and early 2000s, Mochida sponsored a cardiovascular outcomes trial with Epadel in Japan, called JELIS (Japanese EPA Lipid Intervention Study). JELIS was the world's first large-scale randomized controlled cardiovascular outcomes trial of a prescription pure EPA drug product. The JELIS results reported that pure EPA suppressed coronary artery disease in Japanese hypercholesterolemic patients who routinely consume a large amount of EPA and DHA (another poly unsaturated fatty acid) from fish oil in their diet.

37. A further statistical analysis of JELIS was undertaken to assess the effect of EPA on patients with a particular profile of risk factors for coronary artery disease, and reported beneficial effects of the drug in further reducing cardiovascular events in statin-treated, hypercholesterolemic Japanese patients.

38. Those effects are published in Saito et al., titled, "Effects of EPA on coronary artery disease in hypercholesterolemic patients with multiple risk factors: Sub-analysis of primary prevention cases from the Japan EPA Lipid Intervention Study (JELIS), 200 Atherosclerosis 135-400 (2008)" [hereinafter, the "Saito Article"]. The Saito Article is attached hereto as Exhibit B.

39. The Saito Article reports on a statistical analysis of patients studied in the JELIS trial who had no history of coronary artery disease (i.e., the patients had not previously had a cardiovascular event). Ex. B (Saito) at § 2.1. The primary endpoint was major coronary events (MCE): sudden cardiac death, fatal myocardial infarction, nonfatal myocardial infarction, unstable angina pectoris including hospitalization for documented ischemic episodes, and

angioplasty/stenting or coronary artery bypass grafting. Ex. B (Saito) at § 2.3.

40. The Saito Article reports that the "EPA treatment lowered the risk for MCE for the [studied population] by 53% (HR: 0.47; 95% CI: 0.23-0.98; P = 0.43; Fig. 3)." Ex. B (Saito) at 138. By comparison, MCE risk was reduced by 18% in all primary prevention subjects treated in the JELIS clinical study. Ex. B (Saito) at 139.

B. The Asserted Patents

41. On July 11, 2017, the United States Patent and Trademark Office ("USPTO") duly and legally issued the '537 patent, titled "Composition for Preventing the Occurrence of Cardiovascular Event in Multiple Risk Patient," and naming Mitsuhiro Yokoyama, Hideki Origasa, Masunori Matsuzaki, Yuji Matsuzawa and Yasushi Saito as inventors. A true and correct copy of the '537 patent is attached to this complaint as Exhibit C.

42. The '537 patent is assigned to Mochida Pharmaceutical Co., Ltd.

43. Amarin Pharma, Inc. holds an exclusive license to the '537 patent.

44. The '537 patent reflects and claims the analysis and outcome published in the Saito Article. *See, e.g.*, Ex. C at Example 1 (col. 13, ll. 1 to col. 15, ll. 61 (including the referenced tables and figures)).

45. Claim 1 of the '537 patent recites as follows:

> 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.

46. On February 4, 2014, the USPTO duly and legally issued the '077, titled "Stable Pharmaceutical Composition and Methods of Using Same," and naming Mehar Manku, Ian Osterloh, Pierre Wicker, Rene Braeckman, and Paresh Soni as inventors. A true and correct copy of the '077 patent is attached to this complaint as Exhibit O.

47. The '077 patent is assigned to Amarin Pharmaceuticals Ireland Limited.

48. Amarin Pharma, Inc. holds an exclusive license to the '077 patent.

49. Claims 1 and 8 of the '077 patent recites as follows:

> 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.
>
> 8. The method of claim 1 wherein the subject exhibits a reduction in hs-CRP compared to placebo control.

50. On February 25, 2020, the USPTO duly and legally issued the '861 patent, titled "Methods of reducing the risk of a cardiovascular event in a subject at risk for cardiovascular disease," and naming Paresh Soni as the inventor. A true and correct copy of the '861 patent is attached to this complaint as Exhibit P.

51. The '861 patent is assigned to Amarin Pharmaceuticals Ireland Limited.

52. Amarin Pharma, Inc. holds an exclusive license to the '861 patent.

53. Claims 1 and 2 of the '861 patent recite as follows:

> 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.

C. Amarin's VASCEPA® Receives FDA Approval for Reducing the Risk of Certain Cardiovascular Events in Patients with High Triglycerides and Low HDL-C Levels Concurrently on Statin Therapy

54. Amarin Pharmaceuticals Ireland Limited is the current holder of NDA No. 202057 for 1 g and 0.5 g icosapent ethyl capsules. Amarin Pharma, Inc. is Amarin Pharmaceuticals Ireland Limited's agent in the United States for purposes of communicating with the FDA regarding NDA No. 202057. Amarin Pharmaceuticals Ireland Limited and Amarin Pharma, Inc. market both strengths of the approved drug product under the tradename VASCEPA®.

55. A true, correct, and complete copy of the current FDA-approved Prescribing Information for VASCEPA®, covering both the 1 g and 0.5 g strengths, is attached as Exhibit D.

56. VASCEPA® is indicated as (1) an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia (the "Severe Hypertriglyceridemia Indication"), and (2) 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 established cardiovascular disease or diabetes mellitus and 2 or more additional risk factors for cardiovascular disease (the "CV Indication"). Ex. D, § 1.

57. FDA first approved 1 g strength icosapent ethyl capsules, sold under the trade name VASCEPA®, pursuant to NDA No. 202057 on July 26, 2012.

58. A supplement to NDA No. 202057 for the 0.5 g strength of icosapent ethyl capsules was approved on February 16, 2017.

59. From July 26, 2012 through December 12, 2019, the sole indication for which VASCEPA® had received FDA approval was the Severe Hypertriglyceridemia Indication. FDA approval was based, in part, on the MARINE clinical trial and information from that trial is included on the VASCEPA® label. *See* Ex. E (VASCEPA® July 2012 label); Ex. F (VASCEPA® Feb. 2017 label).

60. From 2012 through December 12, 2019, the label for VASCEPA® contained the following limitation of use: "The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined" (the "CV Limitation of Use"). *See* Ex. E (VASCEPA® July 2012 label); Ex. F (VASCEPA® Feb. 2017 label). The CV Limitation of Use appeared in three places on the VASCEPA® label during that time period. *See* Ex. E at Highlights of Prescribing Information and Sections 1 and 14; Ex. F (same). The CV Limitation of Use as it appears in the VASCEPA® Label approved by FDA in February 2017 is reproduced below with annotations in red:

HIGHLIGHTS OF PRESCRIBING INFORMATION

VASCEPA® (icosapent ethyl) Capsules, for oral use
Initial U.S. Approval: 2012

These highlights do not include all the information needed to us VASCEPA® safely and effectively. See full prescribing information fo VASCEPA.

----------INDICATIONS AND USAGE----------

VASCEPA is an ethyl ester of eicosapentaenoic acid (EPA) indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. (1)

Limitations of Use:
•The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined. (1)

•The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined. (1)

Ex. F at Highlights of Prescribing Information.

1 INDICATIONS AND USAGE

VASCEPA® (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.

Usage Considerations: Patients should be placed on an appropriate lipid-lowering diet and exercise regimen before receiving VASCEPA and should continue this diet and exercise regimen with VASCEPA.

Attempts should be made to control any medical problems such as diabetes mellitus, hypothyroidism, and alcohol intake that may contribute to lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (such as beta blockers, thiazides, estrogens) should be discontinued or changed, if possible, prior to consideration of TG-lowering drug therapy.

Limitations of Use:

The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined.

Id. § 1.

VASCEPA 4 grams per day reduced median TG, VLDL-C, and Apo B levels from baseline relative to placebo. The reduction in TG observed with VASCEPA was not associated with elevations in LDL-C levels relative to placebo.

The effect of VASCEPA on the risk of pancreatitis in patients with severe hypertriglyceridemia has not been determined.

The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined.

Id. § 14.

61. The CV Limitation of use appearing on the VASCEPA® label from 2012 through December 12, 2019 was consistent with other products in the therapeutic category, such as LOVAZA®, a combination of ethyl esters of omega 3 fatty acids including EPA. To illustrate, the version of the LOVAZA® label approved by FDA on April 3, 2019 also contained the CV Limitation of Use, as shown below with an annotation in red:

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LOVAZA safely and effectively. See full prescribing information for LOVAZA.

LOVAZA (omega-3-acid ethyl esters capsules), for oral use
Initial U.S. Approval: 2004

INDICATIONS AND USAGE

LOVAZA is a combination of ethyl esters of omega 3 fatty acids, principally eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia (HTG). (1)

Limitations of Use:

- The effect of LOVAZA on the risk for pancreatitis has not been determined. (1)
- The effect of LOVAZA on cardiovascular mortality and morbidity has not been determined. (1)

Ex. S at Highlights of Prescribing Information.

62. On December 13, 2019, FDA approved VASCEPA® for the CV Indication, based on the results of the REDUCE-IT clinical trial. *See* Ex. G.

63. In conjunction with VASCEPA®'s approval for the CV Indication, the VASCEPA® label was modified to remove the CV Limitation of Use and add the CV Indication, among other changes. *Compare* Ex. D, *with* Exs. E and F.

64. To illustrate, the Highlights of Prescribing Information of the VASCEPA® label as approved by FDA in December 2019 lacks the CV Limitation of Use:

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VASCEPA® safely and effectively. See full prescribing information for VASCEPA.

VASCEPA® (icosapent ethyl) capsules, for oral use
Initial U.S. Approval: 2012

----------RECENT MAJOR CHANGES----------

Indications and Usage (1)	12/2019
Warnings and Precautions, Atrial Fibrillation/Flutter (5.1)	12/2019
Warnings and Precautions, Bleeding (5.3)	12/2019

----------INDICATIONS AND USAGE----------

VASCEPA is an ethyl ester of eicosapentaenoic acid (EPA) indicated:

- 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
  - established cardiovascular disease or
  - diabetes mellitus and 2 or more additional risk factors for cardiovascular disease. (1)
- as an adjunct to diet to reduce TG levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia. (1)

Limitations of Use:

- The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined. (1)

----------DOSAGE AND ADMINISTRATION----------

See Ex. D. This is in contrast with the 2019 LOVAZA® label which still contains the CV Limitation of Use. *See* Ex. S.

65. The current VASCEPA® label instructs, recommends, and encourages administering icosapent ethyl in combination with a statin to patients with baseline triglycerides ≥ 150 mg/dL to reduce the risk of a cardiovascular event in a daily dose of 4 grams per day. *See* Ex. D. Notably, FDA did not include an upper limit on the triglyceride range for the CV Indication.

66. FDA's December 13, 2019 approval of VASCEPA® for the CV Indication was hailed as "a major milestone in cardiovascular prevention." Ex. I. As the lead investigator for the REDUCE-IT study explained, "Nothing this significant has happened in the world of cardiovascular prevention since the introduction of statins nearly three decades ago. Many patients stand to benefit from this historic advance in care." *Id.*

67. On information and belief, following VASCEPA®'s approval for the CV Indication and the concurrent removal of the CV Limitation of Use from the VASCEPA® label, healthcare providers rapidly associated administration of icosapent ethyl together with a statin as a method for reducing risk of cardiovascular events in patients with baseline triglycerides ≥ 150 mg/dL.

68. On information and belief, the Hikma Defendants learned that FDA approved VASCEPA® for the CV Indication on or around December 13, 2019 because, on information and belief, the Hikma Defendants regularly monitor the approval status of brand-name drugs serving as the RLD for its generic drug candidates, and thus learned of VASCEPA® additional approval either from the FDA's press release announcing the same (Ex. J), Amarin's press release announcing the same (Ex. I), or in some other form.

69. On information and belief, Health Net, which is a health insurance provider, learned that FDA approved VASCEPA® for the CV Indication on or around December 13, 2019 because, on information and belief, Health Net regularly monitors the approved indications for drugs that it covers for its health insurance plans and on its formulary lists and for which it directs or provides payment.

D. Amarin Listed the Asserted Patents Patent in the FDA's Orange Book as Covering VASCEPA®

70. In conjunction with NDA No. 202057, Amarin submitted patent information relating to VASCEPA® to FDA for listing in the "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly referred to the "Orange Book," which provides notice concerning patents covering FDA-approved drugs.

71. On January 9, 2020, Amarin timely submitted patent information regarding the '537 patent to FDA for listing in the Orange Book as covering methods of using VASCEPA® pursuant to 21 U.S.C. § 355(c)(2) and 21 C.F.R. § 314.53(d)(3).

72. The '537 patent was listed in the Orange Book on or about January 10, 2020 with patent use code U-2707, "Use of VASCEPA as an adjunct to statin therapy to reduce the occurrence of a cardiovascular event in an adult patient with hypercholesterolemia."

73. Methods of using VASCEPA® (icosapent ethyl) capsules, 1 g and 0.5 g, for treating patients as provided in the VASCEPA® label are covered by at least one claim of the '537 patent.

74. On January 6, 2020, Amarin timely submitted patent information regarding the '077 patent to FDA for listing in the Orange Book as covering methods of using VASCEPA® pursuant to 21 U.S.C. § 355(c)(2) and 21 C.F.R. § 314.53(d)(3).

75. The '077 patent was listed in the Orange Book on or about January 6, 2020 with patent use code U-2693, "Use of VASCEPA to reduce triglycerides in a mixed dyslipidemia adult patient with elevated triglyceride (TG) levels (>= 150 mg/dL) and on statin therapy."

76. Methods of using VASCEPA® (icosapent ethyl) capsules, 1 g and 0.5 g, for treating patients as provided in the VASCEPA® label are covered by at least one claim of the '077 patent.

77. On March 20, 2020, Amarin timely submitted patent information regarding the '861 patent to FDA for listing in the Orange Book as covering methods of using VASCEPA® pursuant to 21 U.S.C. § 355(c)(2) and 21 C.F.R. § 314.53(d)(3).

78. The '861 patent was listed in the Orange Book on or about March 20, 2020 with patent use code U-2756, "Use of VASCEPA as an adjunct to statin therapy to reduce the risk of cardiovascular death in an adult patient with established cardiovascular disease."

79. Methods of using VASCEPA® (icosapent ethyl) capsules, 1 g and 0.5 g, for treating patients as provided in the VASCEPA® label are covered by at least one claim of the '861 patent.

80. On information and belief, the Hikma Defendants learned that Amarin listed the '537, '077, and '861 patents in the Orange Book as covering VASCEPA® at or around their time of listing in the Orange Book because, on information and belief, the Hikma Defendants regularly

monitor the Orange Book for updated patent listings made for brand-name drugs serving as the RLD for their generic drug candidates.

81. On information and belief, Health Net monitors FDA approval of generic versions of drugs that are listed on its formularies, on which VASCEPA® was and still is listed. Exs. CC, DD, and EE. As such, Health Net would have been aware of the FDA-approved indication for the Hikma Defendants' generic version of VASCEPA®.

82. The Hikma Defendants' generic version of VASCEPA® was FDA approved for only the Severe Hypertriglyceridemia Indication, and not for the CV Indication.

83. It is known in the field, and Health Net would have been aware, that when a generic product is approved for fewer than all the indications than its corresponding branded drug, it is often because there are patents that cover the indications for which the generic is not approved.

84. It is known in the field, and Health Net would have been aware, that any patents covering a branded drug, such as VASCEPA®, are listed in the Orange Book. Thus, on information and belief, once the Hikma Defendants' generic version of VASCEPA® was approved with only the Severe Hypertriglyceridemia Indication, Health Net knew, or should have known, that the CV Indication was covered by patents, including the patents-in-suit, listed in the Orange Book.

85. Alternatively, on information and belief, Health Net was aware that the '537, '077, and '861 patents are listed in the Orange Book as covering VASCEPA® on or around the date that Plaintiffs filed the original Complaint

in this matter asserting that the Hikma Defendants' generic version of VASCEPA® infringed those patents.

86. On November 30, 2020, Amarin issued a press release about the filing of the original Complaint. Ex. FF. The press release states that "Hikma has induced the infringement of U.S. Patent Nos. 9,700,537 (Composition for preventing the occurrence of cardiovascular event in multiple risk patient), 8,642,077 (Stable pharmaceutical composition and methods of using same), and 10,568,861 (Methods of reducing the risk of a cardiovascular event in a subject at risk for cardiovascular disease) by making, selling, offering to sell and importing generic icosapent ethyl capsules in or into the United States." It further states that Amarin is seeking:

> a permanent injunction against Hikma's unlawful inducement of infringing uses of its generic product to reduce cardiovascular risk and monetary damages in an amount sufficient to compensate Amarin for such infringement. Amarin is considering its legal options against similarly situated parties acting in concert with Hikma by making or selling any drug product or component thereof covered by the subject patents, or inducing others to do the same.

87. On December 11, 2020, Amarin sent a letter to the payer community, including Envolve, the Pharmacy Benefit Manager ("PBM") that Health Net, on information and belief, uses to manage its pharmacy benefits, concerning the launch of the Hikma Defendants' generic version of VASCEPA®. Ex. GG. In the letter, sent via electronic mail to Mr. Mike Flynn at Envolve Pharmacy Solutions, Inc. ("Envolve"), who Amarin uses as its point of contact for Health Net, Amarin explained that the Hikma

Defendants' generic version of VASCEPA® is not FDA-approved for the CV Indication:

> Furthermore, Hikma's generic icosapent ethyl product is indicated as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. Severe (≥500 mg/dL) hypertriglyceridemia represents <10% of the overall utilization of VASCEPA. It is important to note that, unlike the Hikma generic, VASCEPA is also indicated for cardiovascular (CV) risk reduction on top of statin therapy. ***The Hikma generic does not have an FDA-approved indication for CV risk reduction***.

Ex. GG (emphasis added).

88. In the letter, Amarin also informed the recipients that it had "sued Hikma for patent infringement for encouraging use of its generic product in the CV risk reduction indication. Amarin maintains patent exclusivity for CV risk reduction, and the Hikma generic should not be dispensed for this indication." Ex. GG.

89. Thus, Health Net was or should have been aware that actions that encourage the sale or use of Hikma's generic version of VASCEPA® for the CV Indication would induce infringement of the patents-in-suit.

90. Further, on November 16, 2020, even before filing this lawsuit against Hikma, Amarin held a clinical review meeting with Envolve, which, on information and belief, provides PBM services to Health Net. This meeting was attended by several people from Health Net's PBM Envolve, including Mr. Mike Flynn, who served as Amarin's contact for Health Net. At that meeting, Amarin

discussed the clinical data to support VASCEPA®'s CV Indication, as well as detailed how the approved indications on the labels for VASCEPA® and Hikma's generic version of VASCEPA® differed.

91. In the alternative, Health Net is at least aware as of the service of this Amended Complaint that its actions encourage the sale or use of Hikma's generic version of VASCEPA® for the CV indication, and that those actions would induce infringement of the patents-in-suit.

ACTS GIVING RISE TO THIS ACTION FOR THE HIKMA DEFENDANTS' INFRINGEMENT OF THE PATENTS IN-SUIT

92. The Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the "Hatch-Waxman Act," amended the Federal Food, Drug, and Cosmetic Act ("FDCA") and governs approvals of generic drugs. Under Section 505(j) of the amended FDCA, codified at 21 U.S.C. § 355(j), companies wishing to bring a generic version of a branded prescription drug to market can submit an Abbreviated New Drug Application ("ANDA") to the FDA.

93. The ANDA process allows the generic drug company to avoid the expensive clinical trials required of an NDA holder to demonstrate a drug's safety and effectiveness by relying on the original NDA submission for that purpose. This process results in an enormous cost and time savings to the generic drug company. Reliance on the innovator company's data and the ability to "free ride" on the innovator company's development saves the generic drug company millions of dollars and years in development and clinical research costs.

94. The Hatch-Waxman Act also contains provisions meant to balance the competing interests of innovator and

generic drug companies. When seeking ANDA approval, the generic applicant must consult the Orange Book and make certain certifications with respect to each patent listed for the branded drug. The generic applicant can certify that no patent information appears in the Orange Book ("Paragraph I certification"); that the listed patent has already expired ("Paragraph II certification"); that the applicant will not market the generic version before the date on which the patent will expire ("Paragraph III certification"); or that the patent is invalid or will not be infringed by the manufacture, use, or sale of the drug for which the ANDA is submitted ("Paragraph IV certification"). 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV). When a Paragraph IV certification is made, the generic applicant must also provide notice of the certification to the innovator company, who can choose to enforce its patents in federal court.

95. When the listed patent is a method-of-use patent, like the Asserted Patents, the generic applicant can attempt to seek FDA approval to label its drug only for uses not covered by the patent, in which case a statement is submitted under 21 U.S.C. § 355(j)(2)(A)(viii), commonly known as a "Section viii statement" or "Section viii carve-out," in place of a patent certification. The generic applicant is not obligated to provide notice of a Section viii statement to the innovator company.

96. For an Orange Book-listed method-of-use patent that has not expired, whether to make a Paragraph III or Paragraph IV certification or a Section viii statement is a calculated business decision the generic applicant makes after evaluating the associated commercial risks.

97. It is the generic applicant's responsibility to ensure that the marketing and sale of its ANDA product (including the associated labeling, not limited to the

Indications and Usage section) pursuant to a Section viii statement does not infringe the patents referenced in the Section viii statement. Indeed, FDA describes its role with respect to patents as "ministerial," has observed that it "lack[s] expertise in patent matters," and does not make patent infringement determinations when reviewing the labeling associated with a Section viii statement. 68 Fed. Reg. 36,683. Courts have found generic manufacturer's labels, approved subject to a Section viii statement, to nonetheless be evidence of patent infringement.

98. The Orange Book also contains therapeutic equivalence ratings for multisource prescription drug products. The agency developed these ratings in the 1970s in response to states that requested guidance as they implemented laws to encourage generic substitution. 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.

99. On information and belief, on or about September 21, 2016, Hikma (through its predecessor) submitted ANDA No. 209457 for generic copies of VASCEPA® (icosapent ethyl) 1 mg under Section 505(j) of the FDCA.

100. On information and belief, Hikma Pharmaceuticals USA, Inc. is the current owner of ANDA No. 209457.

101. As an ANDA filer, Hikma was required to provide to FDA patent certifications or Section viii statements addressing each of the patents timely listed in the Orange Book for VASCEPA® before FDA finally approved ANDA No. 209457. 21 C.F.R. § 314.94(a)(12).

102. At the time the Asserted Patents were listed in the Orange Book, FDA had not yet finally approved

ANDA No. 209457. Thus, before FDA's final approval of ANDA No. 209457 in May 2020, Hikma was required to provide to FDA either patent certifications or Section viii statements as to the Asserted Patents. 21 C.F.R. § 314.94(a)(12).

103. On information and belief, Hikma knew, at least because of the Asserted Patents' listing in the Orange Book as covering VASCEPA®, that use of icosapent ethyl just like VASCEPA® would constitute direct infringement of the Asserted Patents.

104. On information and belief, Hikma submitted to FDA Section viii statements with respect to the Asserted Patents after January 9, 2020 and before May 21, 2020.

105. On information and belief, on or about May 21, 2020, the FDA granted final approval for Hikma's ANDA No. 209457 with Section viii statements for the Asserted Patents, including labeling prepared by Hikma with full knowledge of the Asserted Patents.

106. On information and belief, a true and correct copy of Hikma's labeling that is provided with its icosapent ethyl capsules, and reflecting its Section viii statement strategy for the Asserted Patents, is attached hereto as Exhibit K ("Hikma's Label").

107. Like the current VASCEPA® label, Hikma's Label does not include the CV Limitation of Use. *Compare* Ex. D *with* Ex. K at Highlights of Prescribing Information and Sections 1 and 14. As shown below, the relevant sections of Hikma's Label lack the CV Limitation of Use:

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ICOSAPENT ETHYL CAPSULES safely and effectively. See full prescribing information for ICOSAPENT ETHYL CAPSULES.

ICOSAPENT ETHYL capsules, for oral use
Initial U.S. Approval: 2012

-- **RECENT MAJOR CHANGES** --

Warnings and Precautions, Atrial Fibrillation/Flutter (5.1)	12/2019
Warnings and Precautions, Bleeding (5.3)	12/2019

-- **INDICATIONS AND USAGE** --

Icosapent ethyl capsules are an ethyl ester of eicosapentaenoic acid (EPA) indicated:

- as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia. (1)

Limitations of Use:

- The effect of icosapent ethyl on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined. (1)

-------------------------------------- **DOSAGE AND ADMINISTRATION** --------------------------------------

Ex. K at Highlights of Prescribing Information.

1 INDICATIONS AND USAGE

Icosapent ethyl is indicated:

- as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.

Limitations of Use

The effect of icosapent ethyl on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

Ex. K at § 1.

Icosapent ethyl 4 grams per day reduced median TG, VLDL-C, and Apo B levels from baseline relative to placebo. The reduction in TG observed with icosapent ethyl was not associated with elevations in LDL-C levels relative to placebo.

Ex. K at § 14.

108. On information and belief, from the time Hikma submitted ANDA No. 209457 to FDA in September 2016 and until Hikma submitted to FDA Section viii statements with respect to the Asserted Patents, the proposed label for Hikma's icosapent ethyl capsules prepared by Hikma contained the CV Limitation of Use. On information and belief, on or about the date on which it submitted to FDA Section viii statements with respect to the Asserted Patents, Hikma intentionally amended the proposed labeling for its icosapent ethyl capsules to remove

the CV Limitation of Use. On information and belief, with knowledge of the Asserted Patents, Hikma removed the CV Limitation of Use from the Hikma Label so that healthcare providers and patients would believe that Hikma's generic icosapent ethyl capsules could be and should be used just like VASCEPA®, including to reduce the risk of CV events per the CV Indication awarded to VASCEPA®. Hikma's removal of the CV Limitation of Use from the Hikma Label demonstrates Hikma's specific intent to induce infringement of the Asserted Patents.

109. On information and belief, Hikma has always intended for its icosapent ethyl capsules to be used in the place of VASCEPA® for all of VASCEPA®'s uses. On information and belief, 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.

110. On information and belief, 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. Ex. W (Nevada Case, D.I. 373) ¶ 115. At the trial concerning Hikma's infringement of the patents related to the Severe Hypertriglyceridemia Indication,[1] Hikma, through its counsel, repeatedly argued that the "vast majority" of prescriptions for VASCEPA® are for uses other than for the Severe Hypertriglyceridemia Indication. Ex. W (Nevada Case, D.I. 377) ¶ 440; Ex. AA (Nevada Case Trial Tr.) at 1252-1253 (Hoffman); *see also* Ex. Q (Nevada Case

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[1] Amarin Pharma, Inc. et al. v. Hikma Pharmaceuticals USA, Inc. et al., Case No. 1:16-cv-02525-MMD-NJK (D. Nev.) [hereinafter the "Nevada Case"].

DDX 1-36); Ex. R (Nevada Case DDX 8.13). At trial in the Nevada Case, Hikma, through its counsel, acknowledged that there are "several reasons why a physician might prescribe Vascepa (or the Hikma Defendants' ANDA Products) … other than to treat severe hypertriglyceridemia," including to reduce cardiovascular risk. Ex. W (Nevada Case, D.I. 377) ¶ 116.

111. 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. *See* Ex. T ("Hikma's Website"). Hikma Pharmaceuticals PLC issued a press release on March 31, 2020 referencing "Hikma's generic version of Amarin Corporation's Vascepa® (icosapent ethyl) 1 gm capsules." A true and correct copy of this press release, obtained from Hikma's website is attached hereto as Exhibit L ("Hikma's March 2020 Press Release").

112. In Hikma's March 2020 Press Release, Hikma stated that "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." Ex. L (emphasis added).

113. The $919 million in Vascepa® sales referenced in Hikma's March 2020 Press Release includes sales for ***all uses*** of Vascepa®, including the CV Indication (which Hikma knew made up more than 75% of VASCEPA®'s sales).

114. Hikma's March 2020 Press Release does 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. *See* Ex. L.

115. Hikma's March 2020 Press Release 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 per the CV Indication awarded to VASCEPA®, and thus promotes and encourages that use.

116. Hikma's March 2020 Press Release demonstrates Hikma's specific intent to encourage infringement of the Asserted Patents.

117. On information and belief, in mid-October 2020, Hikma purported to remove the March 2020 Press Release from the "Newsroom" page of its website. On information and belief, that action demonstrates Hikma's knowledge that the March 2020 Press Release encourages healthcare providers and patients to use Hikma's "generic version" of VASCEPA® for all the same indications as VASCEPA®, including to reduce the risk of CV events per the CV Indication awarded to VASCEPA® and as claimed in the Asserted Patents. However, Hikma's March 2020 Press Release is still accessible as of November 30, 2020 on Hikma's website at the following URL: https://www.hikma.com/media/2766/vascepa-press-release-positive-march-30-20200-720pmet-final.pdf.

118. Hikma Pharmaceuticals PLC issued a press release on September 3, 2020 referencing "Hikma's generic version of Vascepa® (icosapent ethyl) 1 gm [capsules]." A true and correct copy of this press release is attached hereto as Exhibit M ("Hikma's September 2020 Press Release").

119. In Hikma's September 2020 Press Release, Hikma stated that "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." Ex. M (emphasis added).

120. The $1.1 billion in Vascepa® sales referenced in Hikma's September 2020 Press Release includes sales for all uses of Vascepa®, including the CV Indication (which Hikma knew made up more than 75% of sales).

121. Hikma's September 2020 Press Release does 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. *See* Ex. M.

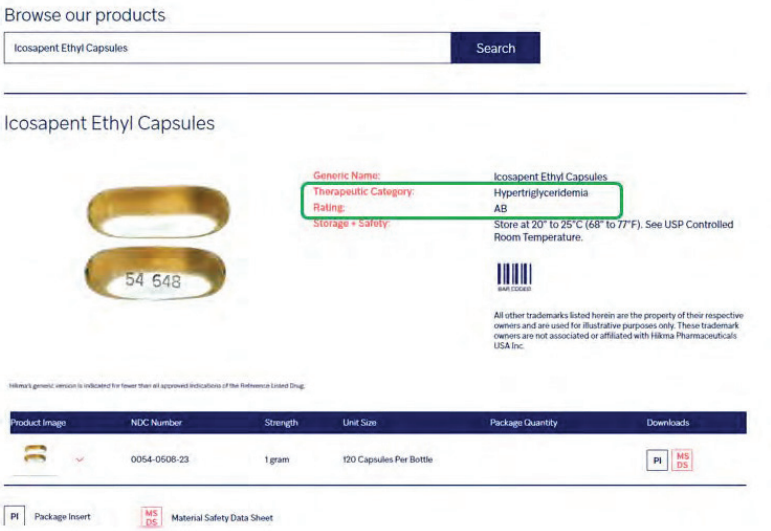
122. Hikma's September 2020 Press Release communicates to and instructs healthcare providers and patients that Hikma's "generic version" of VASCEPA® ***should be used for all the same indications*** as VASCEPA®, including to reduce the risk of CV events per the CV Indication awarded to VASCEPA® and as claimed in the Asserted Patents, and thus promotes and encourages that use.

123. Hikma's September 2020 Press Release demonstrates Hikma's specific intent to encourage infringement of the Asserted Patents.

124. On information and belief, in mid-October 2020, Hikma purported to remove the September 2020 Press Release from the "Newsroom" page of its website. On information and belief, that action demonstrates Hikma's knowledge that the September 2020 Press Release encourages healthcare providers and patients to use

Hikma's "generic version" of VASCEPA® for all the same indications as VASCEPA®, including to reduce the risk of CV events per the CV Indication awarded to VASCEPA®. However, Hikma's September 2020 Press Release is still accessible as of November 30, 2020 on Hikma's website at the following URL: https://www.hikma.com/media/2836/vascepa-statement-september-2020-vfinal.pdf.

125. Further, Hikma has launched its generic version of VASCEPA® and promoted to the market, including on its website, that it is "AB" rated in the "Therapeutic Category: Hypertriglyceridemia." A copy of the product information for Hikma's Icosapent Ethyl Capsules communicated on Hikma's Website is reproduced below with a green annotation.



See Ex. T.

126. Notably, the "Therapeutic Category" information for Hikma's Icosapent Ethyl Capsules communicated on Hikma's Website—"Hypertriglyceridemia"—

does not match and is broader than the Indications and Usage sections of Hikma's Label, which includes only the Severe Hypertriglyceridemia Indication (i.e., triglycerides ≥ 500 mg/dL). Moreover, Hikma's Label does not include the CV Limitation of Use included on the original VASCEPA® label. *Compare* Ex. K, *with* Ex. E.

127. Hikma's March and September 2020 Press Releases, together with Hikma's Website that identifies and describes its generic version of VASCEPA® as "AB" rated in the therapeutic category "Hypertriglyceridemia," and the Hikma Label, instruct, promote, and encourage healthcare providers and patients to administer Hikma's generic icosapent ethyl capsules to hypercholesterolemia patients with triglycerides of at least about 150 mg/dL and HDL-C of less than about 40 mg/dL and who are taking a statin, to reduce the risk of occurrence of a cardiovascular event, as covered by claims of the Asserted Patent.

128. As described above, the totality of Hikma's March 2020 Press Release and September 2020 Press Release, the Hikma Label, and the Hikma Website, instruct, promote, and encourage healthcare providers and patients to administer Hikma's icosapent ethyl capsules just like VASCEPA® including to reduce the risk of CV events per the CV Indication awarded to VASCEPA®.

129. On information and belief, Hikma knew that when an AB-rated generic drug is available, many pharmacies and/or third party payers of prescription drugs (e.g., health insurance plans, Medicare and Medicaid programs) have adopted policies that encourage or require the substitution of the AB-rated generic drugs for the branded drugs, regardless of whether the generic drug label includes all the indications in the branded drug labeling. Some (but not all) states have similar policies. As a

result, on information and belief, 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.

130. Like the VASCEPA® label, Hikma's Label encourages, promotes, and instructs treating patients who present with, as determined by blood draw (*see, e.g.*, Ex. K, § 2 ("Assess lipid levels before initiating therapy.")), **(a)** a baseline total cholesterol level of ≥ 220 mg/dL, which a skilled artisan would recognize as signifying hypercholesterolemia (*see, e.g.*, *id.* § 14.2, tbl 2 (for treatment group, "baseline" "TG (mg/dL)" is 254)); **(b)** a baseline triglyceride level ≥ 150 mg/dL (*see, e.g.*, *id.* (for treatment group, "baseline" "TG (mg/dL)" is 680); *id.* § 6.1 ("Hypertriglyceridemia Trials: In two randomized . . . trials in patients with triglyceride levels between 200 and 2000 mg/dL treated for 12 weeks [with icosapent ethyl]")); **(c)** a baseline HDL-C level less than 40 mg/dL (*see*, *e.g.*, *id.* § 14.2, tbl 2 (for treatment group, "baseline" "HDL-C (mg/dL)" is 27)); and who are **(d)** concomitantly receiving statin therapy, including for example 10-80 mg of atorvastatin (*see*, *e.g.*, *id.* § 14.2 ("Twenty-five percent of patients were on concomitant statin therapy"); *id.* § 12.3 ("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 AUC_{τ} or C_{max} of atorvastatin, 2-hydroxyatorvastatin, or 4-hydroxyatorvastatin when co-administered with atorvastatin 80 mg/day at steady state.")), and **(e)** have not had a previous cardiovascular event (*see*, *e.g.*, *id.* at Patient Information leaflet ("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.") (emphases added); *id.* § 17 ("Advise the patient to read the FDA-approved patient labeling before starting icosapent ethyl (Patient Information).")).

131. Like the VASCEPA® label, Hikma's Label encourages, promotes, and instructs treating patients who present with **(a)** established cardiovascular disease (*see, e.g.*, Ex. K at Patient Information leaflet ("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.") (emphasis added); *id.* § 17 ("Advise the patient to read the FDA-approved patient labeling before starting icosapent ethyl (Patient Information)."), **(b)** a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL (*see, e.g.*, *id.* § 14.2 ("Patients whose baseline TG levels were between 500 and 2,000 mg/dL were enrolled in this study"); *id.* § 6.1 ("Hypertriglyceridemia Trials: In two randomized trials in patients with triglyceride levels between 200 and 2000 mg/dL treated for 12 weeks [with icosapent ethyl]")), and **(c)** a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL (*see, e.g.*, *id.* § 14.2, tbl 2 (for treatment group, "baseline" "LDL-C (mg/dL)" is 91)), **(d)** with about 4 g of icosapent ethyl (ethyl icosapentate) per day (*see id.* § 2.2)).

132. In addition, Hikma's 2020 Label states in its Patient Information leaflet: "Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet." See Ex. K. At trial, one of Hikma's physician experts pointed to this sentence during trial that "most often we use this medication for reasons other than the MARINE data, and in the patient information

section it specifically tells the patients that we would potentially do that." Ex. X (Nevada Case, Trial Tr.) at 617.

133. Thus, a healthcare provider with knowledge of the significance of FDA approving VASCEPA® for the CV Indication, and the consequential removal of the CV Limitation of Use from the VASCEPA® label in conjunction with that approval, the contents of Hikma's March and September 2020 Press Releases, Hikma's Website, and Hikma's Label, will inevitably practice at least the methods the '537 and '861 patents by administering icosapent ethyl to at least some patients with the characteristics required by those claims and at a dose of 4g per day, including for a period effective to reduce risk of cardiovascular death.

134. Like the VASCEPA® label, Hikma's Label encourages, promotes and instructs treating patients who present with **(a)** mixed dyslipidemia (*see, e.g.*, Ex. K, § 14.2 ("Patients whose baseline TG levels were between 500 and 2,000 mg/dL were enrolled in this study"); *id.* § 6.1 ("Hypertriglyceridemia Trials: In two randomized trials in patients with triglyceride levels between 200 and 2000 mg/dL treated for 12 weeks [with icosapent ethyl]. . . ."); *id.* § 14.2, tbl 2 (for treatment group, "baseline" "LDL-C (mg/dL)" is 91)); id. § 14.2, tbl 2 (for treatment group, "baseline" "HDL-C (mg/dL)" is 27), and **(b)** who are on statin therapy (*see, e.g.*, *id.* § 14.2 ("Twenty-five percent of patients were on concomitant statin therapy"), with **(c)** a pharmaceutical composition comprising about 4 g of icosapent ethyl (ethyl eicosapentaenoate) per day and not more than about 5%, by weight of all fatty acids, docosahexaenoic acid or its esters (*see, e.g.*, *id.* § 2.2; Nevada Case, D.I. 381 (Bench Order) at 8 ("The 'pharmaceutical composition' in Hikma's ANDA Product, if approved, will comprise 'at least about 96% by

weight of all fatty acids present, ethyl eicosapentaenoate[,] and substantially no docosahexaenoic acid or its esters'"), to **(d)** effect a reduction in fasting triglyceride levels in the subject (see, e.g., Ex. K at § 1 ("Icosapent ethyl is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.")); and **(e)** wherein the patients exhibit a reduction in hs-CRP compared to placebo control (*see, e.g.*, Ex. U (Ballantyne) at abstract, Fig. 3, 5.).

135. For all the reasons set forth above, Hikma knows of and specifically intends for healthcare providers to administer its icosapent ethyl capsules in the place of VASCEPA® and to practice the methods of the Asserted Patents by administering icosapent ethyl to at least some patients with the characteristics required by those claims in the dose and for the duration required by those claims, and for the purposes recited in those claims, and its labeling and marketing materials promote, encourage, and instruct healthcare providers to practice the methods of the Asserted Patents.

ACTS GIVING RISE TO THIS ACTION FOR HEALTH NET'S INFRINGEMENT OF THE PATENTS-IN-SUIT

136. Amarin incorporates paragraphs 1 to 135 as if fully set forth herein.

137. On information and belief, Health Net offers a variety of different health insurance plans and /or prescription drug benefit plans, on its own or through its subsidiaries, throughout the United States. On information and belief, Health Net contracts with Envolve to provide pharmacy benefit management ("PBM") services for many of Health Net's plans. On information and belief,

Health Net sets the benefits and chooses which drugs it will cover and pay for on its formularies.

138. Before the launch of the Hikma Defendants' generic version of VASCEPA®, VASCEPA® was the only pure EPA product approved by FDA.

139. VASCEPA® was covered by Health Net health insurance plans and appeared on formularies used by Health Net as a covered drug before the approval and launch of the Hikma Defendants' generic version of VASCEPA®. At that time, it was the only pure EPA (icosapent ethyl) product covered by or on formularies used by Health Net.

140. After the launch of the Hikma Defendants' generic version of VASCEPA®, Health Net added the generic product to formularies, meaning that it would provide insurance coverage and/or payment for Hikma's generic version of VASCEPA®.

141. For example, the Health Net 2021 Classic Formulary and the Health Net 2021 Prime Formulary, which, on information and belief, are both formularies for Health Net's Medicare business, include Hikma's generic version of VASCEPA®, referred to as "icosapent ethyl caps." Exs. CC and DD. In addition, Hikma's generic version of VASCEPA® is included in Health Net's 2021 Essential Rx Drug List formulary. Ex. EE.

142. Indeed, the Health Net 2021 Classic Formulary and the Health Net 2021 Prime Formulary encourage the prescription and use of Hikma's generic version of VASCEPA®.

143. VASCEPA® is on these formularies as a tier 3 drug. Ex. CC at 25; Ex. DD at 23. By contrast, Hikma's generic version of VASCEPA®, referred to as "icosapent ethyl caps" (in lower case italics), is on the Health Net

2021 Classic Formulary and the Health Net 2021 Prime Formulary as a tier 1 drug. *Id.*

144. Health Net makes no distinction on its formulary listing for Hikma's generic version of VASCEPA® with respect to the CV Indication versus the Severe Hypertriglyceridemia Indication, even though Hikma's generic version of VASCEPA® is not approved for the former. Thus, Hikma's generic version of VASCEPA® is on tier 1 for all potential uses of the drug, and not merely for its approved Severe Hypertriglyceridemia Indication. By so doing, Health Net has intentionally disregarded the patent rights associated with the CV Indication asserted in this action.

145. On information and belief, the placement of a drug on a lower tier leads to a lower patient copayment than placement of a drug on a higher tier. Thus, on information and belief, as a tier 1 drug, Hikma's generic version of VASCEPA® has a lower patient copayment than VASCEPA®.

146. Health Net's inclusion of the Hikma Defendants' generic version of VASCEPA® at tier 1 on the Health Net 2021 Classic Formulary and the Health Net 2021 Prime Formulary encourages pharmacists to dispense it and patients to use it instead of VASCEPA® given VASCEPA®'s placement on tier 3, for both the Severe Hypertriglyceridemia Indication and the patented CV Indication, even though Hikma's generic version of VASCEPA® is not approved by the FDA for the patented CV Indication.

147. The Health Net 2021 Classic Formulary and the Health Net 2021 Prime Formulary also promote and encourage the use of Hikma's generic version of VASCEPA® in other ways. Both formularies state that

"[o]ur plan covers both brand name and generic drugs. A generic drug is approved by FDA as having the same active ingredient as the brand name drug. Generally, generic drugs cost less than brand name drugs." Exs. CC and DD at iii.

148. Both formularies also state that "We may immediately remove a brand name drug on our Drug List if we are replacing it with a new generic drug that will appear on the same or lower cost sharing tier and with the same or fewer restrictions. ***Also, when adding the new generic drug, we may decide to keep the brand name drug on our Drug List, but immediately move it to a different cost-sharing tier or add new restrictions***. If you are currently taking that brand name drug, we may not tell you in advance before we make that change, but we will later provide you with information about the specific change(s) we have made." Exs. CC and DD at i.

149. In addition, on information and belief, with the Health Net 2021 Classic Formulary and the Health Net 2021 Prime Formulary, Health Net covers and directs payment for Hikma's generic version of VASCEPA® for both the Severe Hypertriglyceridemia Indication, for which it is FDA approved, and the CV Indication, for which Hikma did not seek or receive FDA approval.

150. Because Health Net covers and directs payment for the Hikma Defendants' generic version of VASCEPA® for prescriptions for both the Severe Hypertriglyceridemia Indication and the CV Indication, Health Net knows and intends that it is covering and directing payment for prescriptions of Hikma's generic version of VASCEPA® for the CV Indication.

151. On information and belief, Health Net knows that when an AB-rated generic drug is available, many pharmacies have adopted policies that encourage or require the substitution of the AB-rated generic drugs for the branded drugs, regardless of whether the generic drug label includes all the indications in the branded drug labeling. Some (but not all) states have similar policies. As a result, on information and belief, Health Net knew and intended that its generic product would be substituted for all VASCEPA® prescriptions, not just the prescriptions directed to the Severe Hypertriglyceridemia Indication.

152. Indeed, available market data indicates that less than 10% of the prescriptions of VASCEPA® are currently in the Severe Hypertriglyceridemia population and thus could be covered under the Severe Hypertriglyceridemia Indication. And Amarin stated in its December 11, 2020 letter to payers that "[s]evere (≥500 mg/dL) hypertriglyceridemia represents <10% of the overall utilization of VASCEPA." Ex. GG. On information and belief, Health Net would have been aware of this or similar data and would have known and understood that the vast majority of prescriptions for VASCEPA® are for the CV Indication, for which Hikma's generic version of VASCEPA® does not have FDA approval. Thus, Health Net would have known, understood, and intended that, in covering and directing payment for Hikma's generic version of VASCEPA® for any indication it may be prescribed for, it was covering and directing payment for Hikma's generic version of VASCEPA® for the CV Indication.

153. In addition, before the approval of Hikma's generic version of VASCEPA®, VASCEPA® was on Health Net's Essential Rx Drug List, which, on information and

belief, relates to Health Net's commercial business, as a covered drug, but it was only covered if it was being prescribed for a condition that was listed on Health Net's Prior Authorization ("PA") form for VASCEPA®. Ex. HH.

154. Health Net's PA for VASCEPA® lists both of the FDA-approved indications for VASCEPA®—the Severe Hypertriglyceridemia Indication and the CV Indication. Ex. HH. It then details the criteria that must be met before VASCEPA® can be covered. For "Initial Approval Criteria," the PA includes two options: (1) "Hypertriglyceridemia without ASCVD," where the patient has "[f]asting triglycerides ≥ 500 mg/dL," and (2) "Reduction of Cardiovascular Disease Risk" with "[d]ocumentation (labs must be within 90 days) of fasting triglycerides between 150-499 mg/dL" and, "[f]or members on statin therapy," "Vascepa is prescribed in conjunction with a statin at the maximally tolerated dose." Ex. HH.

155. The VASCEPA® PA, and the information that it requires be collected, demonstrates that Health Net is aware that VASCEPA® is prescribed for two indications—the Severe Hypertriglyceridemia Indication and the CV Indication.

156. After the launch of the Hikma Defendants' generic version of VASCEPA®, Health Net added that generic version to its Health Net Essential Drug list. (Ex EE (formulary from website) at 37.) Health Net characterizes this list as including "a list of drugs covered by Health Net" that "is selected by Health Net, along with a team of health care providers." Ex. II.

157. The Health Net Essential Rx Drug List currently includes Hikma's generic version of VASCEPA®, referred to as "icoaspent ethyl caps." Ex. EE at 28. As

with the Health Net 2021 Classic Formulary and the Health Net 2021 Prime Formulary, the Health Net Essential Rx Drug list includes VASCEPA® as a tier 3 drug and Hikma's generic version of VASCEPA® (icosapent ethyl caps) as a tier 1 drug. (*Id.*)

158. When an insurance provider covers a medication, and particularly when it covers it at a lower tier, it employs the economic incentive of lower patient copayments to encourage pharmacists to fill prescriptions with that medication, and encourages patients to use that medication. Health Net's coverage of the Hikma Defendants' generic version of VASCEPA® as a tier 1 drug on the Essential Rx Drug List encourages pharmacists to dispense it and patients to use it, particularly as compared to VASCEPA®, which is on tier 3.

159. In addition, like it does for VASCEPA®, the Health Net Essential Rx Drug List requires a PA for the Hikma Defendants' generic version of VASCEPA® that details the criteria that must be met before it can be covered. Ex. EE at 28. On information and belief, the PA used for the Hikma Defendants' generic version of VASCEPA® collects the same information as the PA for VASCEPA®. Thus, it collects information as to whether the drug is being prescribed for the Severe Hypertriglyceridemia Indication or the CV Indication. Health Net's use of this PA for the Hikma Defendants' generic version of VASCEPA® demonstrates that Health Net knows what indication the product is being prescribed for, and chooses to cover it for both indications.

160. On information and belief, Health Net, for the Health Net Essential Rx Drug List, covers the Hikma Defendants' generic version of VASCEPA® if it meets any of the conditions on the PA. In other words, on information and belief, Health Net covers the Hikma

Defendants' generic version of VASCEPA® for prescriptions for both the Severe Hypertriglyceridemia Indication and the CV Indication. And based on the PA, Health Net knows and intends that it is covering prescriptions of Hikma's generic version of VASCEPA® for the CV Indication.

161. Because Health Net, on its the Health Net Essential Rx Drug List, covers and directs payment for the Hikma Defendants' generic version of VASCEPA®, for prescriptions for patients meeting either the Severe Hypertriglyceridemia Indication or the CV Indication, it is aware and intends and causes some pharmacies to dispense, and some patients to use, the product for the CV Indication.

162. On information and belief, based on Health Net's actions, pharmacies are dispensing, and patients are using, Hikma's generic version of VASCEPA® for the CV indication. Indeed, current data shows that Hikma's generic version of VASCEPA® has over 20% of the total volume of VASCEPA® for Health Net's business.

COUNT I

(Infringement of the '537 Patent Under 35 U.S.C. § 271(b) by the Hikma Defendants)

163. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

164. On information and belief the Hikma Defendants have been and are inducing others to infringe the '537 patent in this District and elsewhere in the United States by making, offering to sell, selling, importing, and otherwise promoting and distributing highly pure icosapent ethyl capsules to reduce the occurrence of a cardiovascular event, including a fatal cardiovascular event, in

hypercholesterolemia patients with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event, and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering highly pure EPA in combination with the statin.

165. On information and belief, healthcare providers administering and/or patients using the Hikma Defendants' generic version of Vascepa® capsules within the United States do so in combination with a statin to, among other reasons, reduce the occurrence of a cardiovascular event in the patient population recited in claim 1 of the '537 patent, and thus directly infringe at least one claim of the '537 patent.

166. On information and belief, the Hikma Defendants possessed the specific intent to encourage direct infringement of the '537 patent. On information and belief, the Hikma Defendants knew about the '537 patent at least as of when it was listed in the Orange Book and before performing the activities referenced in paragraph 121.

167. Alternatively, the Hikma Defendants subjectively believed that there was a high probability that the use of icosapent ethyl capsules for reducing the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patients with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event, and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering highly pure EPA in combination with the statin, was protected by a valid patent, and that the activities referenced in paragraph 121 would actively induce

infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded themselves to the infringing nature of their sales of a generic version of VASCEPA®.

168. On information and belief, the Hikma Defendants knew that the administration or use of their generic version of VASCEPA® would be for reducing the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patients with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering highly pure EPA in combination with the statin, and so would be an act of direct infringement of the '537 patent, and that the activities referenced in paragraph 121 would actively induce direct infringement of the '537 patent. On information and belief, despite such knowledge, the Hikma Defendants have been and are actively inducing the infringement of the '537 patent by others, and are doing do willfully and deliberately.

169. On information and belief, the Hikma Defendants will continue to induce infringement of the '537 patent unless and until enjoined by the Court.

170. As a result of the Hikma Defendants' inducement of infringement of the '537 patent, Plaintiffs have suffered damages, including lost profits.

COUNT II

(Infringement of the '077 Patent Under 35 U.S.C. § 271(b) by the Hikma Defendants)

171. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

172. On information and belief the Hikma Defendants have been and are inducing others to infringe the '077 patent in this District and elsewhere in the United States by making, offering to sell, selling, importing, and otherwise promoting and distributing highly pure icosapent ethyl capsules to reduce triglycerides in a subject with mixed dyslipidemia by administering about 4 g of ethyl eicosapentaenoate per day.

173. On information and belief, healthcare providers administering and/or patients using 4 g per day of the Hikma Defendants' generic version of Vascepa® capsules within the United States do so, among other reasons, to reduce fasting triglyceride and hs-CRP levels in patients with mixed dyslipidemia, and thus directly infringe at least claim 8 of the '077 patent.

174. On information and belief, the Hikma Defendants possessed the specific intent to encourage direct infringement of the '077 patent. On information and belief, the Hikma Defendants knew about the '077 patent at least as of when it was listed in the Orange Book and before performing the activities referenced in paragraph 129.

175. Alternatively, the Hikma Defendants subjectively believed that there was a high probability that the administration and use of 4 g per day of highly pure icosapent ethyl capsules for reducing fasting triglyceride and hs-CRP levels in subjects with mixed dyslipidemia was protected by a valid patent, and that the activities

referenced in paragraph 129 would actively induce infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded themselves to the infringing nature of their sales of a generic version of VASCEPA®.

176. On information and belief, the Hikma Defendants knew that the administration or use of their generic version of VASCEPA® would be for daily administration of a 4 g/day dose to reduce fasting triglyceride and hs-CRP levels in subjects with mixed dyslipidemia, and so would be an act of direct infringement of the '077 patent, and that the activities referenced in paragraph 129 would actively induce direct infringement of the '077 patent. On information and belief, despite such knowledge, the Hikma Defendants have been and are actively inducing the infringement of the '077 patent by others, and are doing do willfully and deliberately.

177. On information and belief, the Hikma Defendants will continue to induce infringement of the '077 patent unless and until enjoined by the Court.

178. As a result of the Hikma Defendants' inducement of infringement of the '077 patent, Plaintiffs have suffered damages, including lost profits.

COUNT III

(Infringement of the '861 Patent Under 35 U.S.C. § 271(b) by the Hikma Defendants)

179. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

180. On information and belief the Hikma Defendants have been and are inducing others to infringe the '861 patent in this District and elsewhere in the United States by making, offering to sell, selling, importing, and otherwise

promoting and distributing highly pure icosapent ethyl capsules to reduce the risk of a cardiovascular death in a subject with established cardiovascular disease, including subjects with 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, by administering about 4 g of ethyl icosapentate per day for a period effective to reduce risk of cardiovascular death.

181. On information and belief, healthcare providers administering and/or patients using 4 g per day of the Hikma Defendants' generic version of Vascepa® capsules within the United States do so, among other reasons, to reduce the risk of cardiovascular death in patients with established cardiovascular disease, including the patient population recited in claims 1 and 2, and thus directly infringe at least claim 1 and 2 of the '861 patent.

182. On information and belief, the Hikma Defendants possessed the specific intent to encourage direct infringement of the '861 patent. On information and belief, the Hikma Defendants knew about the '861 patent at least as of when it was listed in the Orange Book and before performing the activities referenced in paragraph 137.

183. Alternatively, the Hikma Defendants subjectively believed that there was a high probability that the administration and use of 4 g per day of icosapent ethyl capsules for reducing risk of cardiovascular death in a subject with established cardiovascular disease, including subjects with 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, for a period effective to reduce risk of cardiovascular death, was protected by a valid patent, and that the activities referenced in paragraph 137 would actively induce infringement of the patent, but took deliberate steps to avoid

confirming those facts, and therefore willfully blinded themselves to the infringing nature of their sales of a generic version of VASCEPA®.

184. On information and belief, the Hikma Defendants knew that the administration or use of their generic version of VASCEPA® would be for daily administration of a 4 g/day dose to reduce risk of cardiovascular death in a subject with established cardiovascular disease, including subjects with 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, for a period effective to reduce risk of cardiovascular death, and so would be an act of direct infringement of the '861 patent, and that the activities referenced in paragraph 137 would actively induce direct infringement of the '861 patent. On information and belief, despite such knowledge, the Hikma Defendants have been and are actively inducing the infringement of the '861 patent by others, and are doing do willfully and deliberately.

185. On information and belief, the Hikma Defendants will continue to induce infringement of the '861 patent unless and until enjoined by the Court.

186. As a result of the Hikma Defendants' inducement of infringement of the '861 patent, Plaintiffs have suffered damages, including lost profits.

COUNT IV

(Infringement of the '537 Patent Under 35 U.S.C. § 271(b) by Health Net)

187. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

188. On information and belief, by covering and/or directing or providing payment for others' use of the Hikma

Defendants' generic version of VASCEPA® for the CV Indication, Health Net has been and is inducing others to use, offer to sell, sell, or otherwise promote or distribute the Hikma Defendants' generic version of VASCEPA® to reduce the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patients with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event, and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering the Hikma Defendants' generic version of VASCEPA® in combination with the statin, thereby infringing the '537 patent.

189. On information and belief, healthcare providers administering and/or patients using the Hikma Defendants' generic version of VASECPA® capsules within the United States do so in combination with a statin to, among other reasons, reduce the occurrence of a cardiovascular event in the patient population recited in claim 1 of the '537 patent, and thus directly infringe at least one claim of the '537 patent.

190. On information and belief, Health Net possessed the specific intent to encourage direct infringement of the '537 patent. On information and belief, Health Net knew about the '537 patent at least as of when the Hikma Defendants' generic version of VASCEPA® was launched with a label listing only the Severe Hypertriglyceridemia Indication; and/or when Amarin announced the filing of this lawsuit against the Hikma Defendants; and/or when Amarin sent a letter to payers, including Health Net's contracted Pharmacy Benefit Manufacturer Envolve, informing them of the filing of the patent exclusivity for the CV Indication and about this lawsuit against the Hikma

Defendants, and before performing the activities referenced in paragraph 188. In the alternative, Health Net knows about the '537 patent at least as of the filing of this Amended Complaint and continues the activities referenced in paragraph 188.

191. Alternatively, Health Net subjectively believed that there was a high probability that the use of the Hikma Defendants' generic version of VASCEPA® for reducing the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patients with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event, and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering highly pure EPA in combination with the statin, was protected by a valid patent, and that the activities referenced in paragraph 188 would actively induce infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded itself to the infringing nature of the use and sale of the Hikma Defendants' generic version of VASCEPA®.

192. On information and belief, Health Net knew that the administration or use of the Hikma Defendants' generic version of VASCEPA® would include the use for reducing the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patients with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering highly pure EPA in combination

with the statin, and so would be an act of direct infringement of the '537 patent, and that the activities referenced in paragraph 188 would actively induce direct infringement of the '537 patent. On information and belief, despite such knowledge, Health Net has been and is actively inducing the infringement of the '537 patent by others, and is doing do willfully and deliberately.

193. On information and belief, Health Net will continue to induce infringement of the '537 patent unless and until enjoined by the Court.

194. As a result of Health Net's inducement of infringement of the '537 patent, Plaintiffs have suffered damages.

COUNT V

(Infringement of the '077 Patent Under 35 U.S.C. § 271(b) by Health Net)

195. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

196. On information and belief, by covering and/or directing or providing payment for others' use of the Hikma Defendants' generic version of VASCEPA® for the CV Indication, Health Net has been and is inducing others to use, offer to sell, sell, or otherwise promote and distribute the Hikma Defendants' generic version of VASCEPA® to reduce triglycerides in a subject with mixed dyslipidemia by administering about 4 g of ethyl eicosapentaenoate per day, thereby infringing the '077 patent.

197. On information and belief, healthcare providers administering and/or patients using 4 g per day of the Hikma Defendants' generic version of VASCEPA® capsules within the United States do so, among other reasons, to reduce fasting triglyceride and hs-CRP levels in

patients with mixed dyslipidemia, and thus directly infringe at least claim 8 of the '077 patent.

198. On information and belief, Health Net possessed the specific intent to encourage direct infringement of the '077 patent. On information and belief, Health Net knew about the '077 patent at least as of when the Hikma Defendants' generic version of VASCEPA® was launched with a label listing only the Severe Hypertriglyceridemia Indication; and/or when Amarin announced the filing of this lawsuit against the Hikma Defendants; and/or when Amarin sent a letter to payers, including Health Net's contracted Pharmacy Benefit Manufacturer Envolve, informing them of the filing of the patent exclusivity for the CV Indication and about this lawsuit against the Hikma Defendants, and before performing the activities referenced in paragraph 196. In the alternative, Health Net knows about the '077 patent at least as of the filing of this Amended Complaint and continues the activities referenced in paragraph 196.

199. Alternatively, Health Net subjectively believed that there was a high probability that the administration and use of 4 g per day of the Hikma Defendants' generic version of VASCEPA® for reducing fasting triglyceride and hs-CRP levels in subjects with mixed dyslipidemia was protected by a valid patent, and that the activities referenced in paragraph 196 would actively induce infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded itself to the infringing nature of the use and sale of the Hikma Defendants' generic version of VASCEPA®.

200. On information and belief, Health Net knew that the administration or use of the Hikma Defendants' generic version of VASCEPA® would include for daily administration of a 4 g/day dose to reduce fasting

triglyceride and hs-CRP levels in subjects with mixed dyslipidemia, and so would be an act of direct infringement of the '077 patent, and that the activities referenced in paragraph 196 would actively induce direct infringement of the '077 patent. On information and belief, despite such knowledge, Health Net has been and is actively inducing the infringement of the '077 patent by others, and is doing do willfully and deliberately.

201. On information and belief, Health Net will continue to induce infringement of the '077 patent unless and until enjoined by the Court.

202. As a result of Health Net's inducement of infringement of the '077 patent, Plaintiffs have suffered damages.

COUNT VI

(Infringement of the '861 Patent Under 35 U.S.C. § 271(b) by Health Net)

203. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

204. On information and belief, by covering and/or directing or providing payment for others' use of the Hikma Defendants' generic version of VASCEPA® for the CV Indication, Health Net has been and is inducing others to use, offer to sell, sell, or otherwise promote and distribute the Hikma Defendants' generic version of VASCEPA® to reduce the risk of a cardiovascular death in a subject with established cardiovascular disease, including subjects with 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, by administering about 4 g of ethyl icosapentate per day for a period

effective to reduce risk of cardiovascular death, thereby infringing the '861 patent.

205. On information and belief, healthcare providers administering and/or patients using 4 g per day of the Hikma Defendants' generic version of VASCEPA® capsules within the United States do so, among other reasons, to reduce the risk of cardiovascular death in patients with established cardiovascular disease, including the patient population recited in claims 1 and 2, and thus directly infringe at least claim 1 and 2 of the '861 patent.

206. On information and belief, Health Net possessed the specific intent to encourage direct infringement of the '861 patent. On information and belief, Health Net knew about the '861 patent at least as of when the Hikma Defendants' generic version of VASCEPA® was launched with a label listing only the Severe Hypertriglyceridemia Indication; and/or when Amarin announced the filing of this lawsuit against the Hikma Defendants; and/or when Amarin sent a letter to payers, including Health Net's contracted Pharmacy Benefit Manufacturer Envolve, informing them of the filing of the patent exclusivity for the CV Indication and about this lawsuit against the Hikma Defendants, and before performing the activities referenced in paragraph 204. In the alternative, Health Net knows about the '861 patent at least as of the filing of this Amended Complaint and continues the activities referenced in paragraph 204.

207. Alternatively, Health Net subjectively believed that there was a high probability that the administration and use of 4 g per day of icosapent ethyl capsules for reducing risk of cardiovascular death in a subject with established cardiovascular disease, including subjects with 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, for a period effective to reduce risk of cardiovascular death, was protected by a valid patent, and that the activities referenced in paragraph 204 would actively induce infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded itself to the infringing nature of the use and sale of the Hikma Defendants' generic version of VASCEPA®.

208. On information and belief, Health Net knew that the administration or use of the Hikma Defendants' generic version of VASCEPA® would include daily administration of a 4 g/day dose to reduce risk of cardiovascular death in a subject with established cardiovascular disease, including subjects with 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, for a period effective to reduce risk of cardiovascular death, and so would be an act of direct infringement of the '861 patent, and that the activities referenced in paragraph 204 would actively induce direct infringement of the '861 patent. On information and belief, despite such knowledge, Health Net has been and is actively inducing the infringement of the '861 patent by others, and is doing do willfully and deliberately.

209. On information and belief, Health Net will continue to induce infringement of the '861 patent unless and until enjoined by the Court.

210. As a result of Health Net's inducement of infringement of the '861 patent, Plaintiffs have suffered damages.

JURY TRIAL DEMAND

211. Pursuant to Federal Rule of Civil Procedure 38(b), Plaintiffs hereby demand a trial by jury of all issues so triable.

PRAYER FOR RELIEF

Plaintiffs respectfully pray for the following relief:

a) Enter judgment that the Hikma Defendants have induced the infringement of the '537, '077, and '861 patents by making, selling, offering to sell and importing generic icosapent ethyl capsules in or into the United States;

b) Enter judgment that Health Net has induced the infringement of the '537, '077, and '861 patents by covering and/or providing payment for others' use, offer to sell, or sale of the Hikma Defendants' generic version of VASCEPA® in the United States;

c) Enter judgment that Defendants' infringement of the '537, '077, and '861 patents has been and is willful;

d) Issue an injunction under 35 U.S.C. § 283 permanently enjoining all Defendants, their officers, agents, servants, employees, licensees, representatives, and attorneys, and all other persons acting or attempting to act in active concert or participation with them or acting on their behalf, from, directly or indirectly, making, selling, offering to sell, and importing into the United States any drug product for a use that is covered by the '537, '077, and '861 patents;

e) Award Plaintiffs damages in an amount sufficient to compensate them for Defendants' infringement of the '537, '077, and '861 patents, together with prejudgment and post-judgment interests and costs under 35 U.S.C. § 284;

f) Declare this to be exceptional case under 35 U.S.C. § 285 and award Plaintiffs their reasonable attorneys' fees, expenses, and costs incurred in this action;

g) Perform an accounting of Defendants' infringing activities through trial and judgment; and

h) Award Plaintiffs such other and further relief as this Court deems just and proper.

Dated: January 25, 2021

FISH & RICHARDSON P.C.

By: */s/ Jeremy D. Anderson*

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