2023-1169

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

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

Plaintiffs-Appellants,

v.

HIKMA PHARMACEUTICALS USA INC., HIKMA PHARMACEUTICALS PLC,

Defendants-Appellees,

HEALTH NET LLC,

Defendant

Appeal from the United States District Court for the District of Delaware
Case No. 1:20-cv-01630-RGA-JLH, Judge Richard G. Andrews

APPELLANTS' OPENING BRIEF

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March 21, 2023

Claim Language

’537 patent

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.

’861 patent

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.

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

CERTIFICATE OF INTEREST

Case Number 23-1169

Short Case Caption Amarin Pharma, Inc. v. Hikma Pharmaceuticals USA Inc.

Filing Party/Entity Amarin Pharma, Inc.; Amarin Pharmaceuticals Ireland; and Mochida Pharmaceuticals Co., Ltd.

Instructions: Complete each section of the form. In answering items 2 and 3, be specific as to which represented entities the answers apply; lack of specificity may result in non-compliance. **Please enter only one item per box; attach additional pages as needed and check the relevant box**. Counsel must immediately file an amended Certificate of Interest if information changes. Fed. Cir. R. 47.4(b).

I certify the following information and any attached sheets are accurate and complete to the best of my knowledge.

Date: 3/21/2023

Signature: /s/Nathan K. Kelley

Name: Nathan K. Kelley

1. Represented Entities. Fed. Cir. R. 47.4(a)(1).	**2. Real Party in Interest.** Fed. Cir. R. 47.4(a)(2).	**3. Parent Corporations and Stockholders.** Fed. Cir. R. 47.4(a)(3).
Provide the full names of all entities represented by undersigned counsel in this case.	Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities. ☑ None/Not Applicable	Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities. ☐ None/Not Applicable
Amarin Pharma, Inc.		Amarin Corporation plc
Amarin Pharmaceuticals Ireland Limited		Amarin Corporation plc
Mochida Pharmaceutical Co., Ltd.		N/A

☐ Additional pages attached

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

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6. Organizational Victims and Bankruptcy Cases. Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

☑ None/Not Applicable ☐ Additional pages attached

TABLE OF CONTENTS

Table of Authorities iv

Table of Abbreviations and Conventions vii

Related Cases viii

Introduction 1

Jurisdiction 2

Statement of Issues 3

Statement of the Case 4

A. Vascepa® and its demonstrated efficacy for two different treatments 4

1. Severe hypertriglyceridemia, pancreatitis, and its treatment 4

2. Amarin initially patented the use of Vascepa® to treat severe HTG 5

3. Amarin later patented the use of Vascepa® to reduce cardiovascular risk in patients with non-severe HTG or existing cardiovascular disease 6

4. Mochida's prior foundational work and patent 10

B. Hikma launched generic Vascepa®, describing it on its website, in press releases, and with a supposedly "skinny" label 12

1. Hikma submitted a Section viii statement to obtain FDA approval to sell generic Vascepa® solely to treat severe hypertriglyceridemia 12

2. Hikma's website associated its generic version of Vascepa® with a method of use beyond its approved use 14

3. Hikma issued press releases, encouraging readers to prescribe generic Vascepa® for more than treating patients with severe hypertriglyceridemia 15

4. Hikma's "skinny" label teaches the claimed limitations and omits the prior limitation of use excluding the cardiovascular risk indication 17

C. The district court proceeding....19

1. Amarin sued Hikma for inducing infringement 19

2. Hikma moved to dismiss under Rule 12(b)(6) 20

3. The magistrate judge recommended denying Hikma's motion to dismiss 21

4. The district court granted Hikma's motion 22

Summary of Argument....25

Argument....26

I. Standard of review 26

II. Amarin satisfied the pleading standard by pleading plausible infringement by Hikma 26

A. Surviving a motion to dismiss requires pleading facts sufficient to state a plausible claim for relief 27

B. Inducement requires showing direct infringement and actions taken with the intent to cause infringing conduct 29

C. Taking the allegations together, Amarin's claim against Hikma is plausible, and discovery is likely to further support Amarin's case 30

III. The district court erred by weighing the pled facts piecemeal against the plausibility pleading standard 35

IV. The district court erred by resolving the key factual dispute of what Hikma's conduct communicated to the market....39

V. The district court erred by analogizing the wrong cases....41

A. This case involves evidence showing inducement in addition to the label—it is not a "label only" case 42

B. Previous cases consistently reached a later stage than a motion to dismiss because factual issues are central to inducement 48

C. This case involves a patented use that is broader than the off-patent use—unlike in *Grunenthal* 51

Conclusion 53

Addenda

1. Memorandum Opinion, Order, and Final Judgment (Appx1-15)
2. Magistrate's Report and Recommendation (Appx1413-1430)
3. U.S. Patent No. 9,700,537 (Appx36-47)
4. U.S. Patent No. 10,568,861 (Appx77-129)

Certificate of Compliance

TABLE OF AUTHORITIES

Cases **Pages**

Amarin Pharma, Inc. v. Hikma Pharmaceuticals USA,
Case No. 20-1723 (Fed. Cir.), ECF No. 78 5

Ashcroft v. Iqbal,
556 U.S. 662 (2009).....27, 28, 35

AstraZeneca Pharms. LP v. Apotex Corp.,
669 F.3d 1370 (Fed. Cir. 2012) 50

AstraZeneca LP v. Apotex, Inc.,
633 F.3d 1042 (Fed. Cir. 2010) 29, 44, 47, 49

Ballentine v. United States,
486 F.3d 806 (3d Cir. 2007) 26

Bayer Schering Pharma AG v. Lupin, Ltd.,
676 F.3d 1316 (Fed. Cir. 2012) 49, 50

Bell Atl. Corp. v. Twombly,
550 U.S. 544 (2007).....27, 28, 35

Bill of Lading Transmission & Processing Sys. Pat. Litig., In re,
681 F.3d 1323 (Fed. Cir. 2012) 36

Burlington Coat Factory Sec. Litig., In re,
114 F.3d 1410 (3d Cir. 1997) 28

DSU Med. Corp. v. JMS Co.,
471 F.3d 1293 (Fed. Cir. 2006) 29, 30, 31

GlaxoSmithKline LLC v. Teva Pharms. USA, Inc.,
7 F.4th 1320 (Fed. Cir. 2021) 13, 24, 29, 40-43, 48, 49, 53

Grunenthal GMBH v. Alkem Labs. Ltd.,
919 F.3d 1333 (Fed. Cir. 2019) 23-24, 39, 45, 46, 49, 51, 52

HZNP Meds. LLC v. Actavis Labs. UT, Inc.,
940 F.3d 680 (Fed. Cir. 2019) 45-47, 49

Kedra v. Schroeter,
876 F.3d 424 (3d Cir. 2017) 36

MEMC Elec. Materials, Inc. v. Mitsubishi Materials Silicon Corp.,
420 F.3d 1369 (Fed. Cir. 2005) 29, 31

Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd.,
545 U.S. 913 (2005).....30, 31, 36

Scheuer v. Rhodes,
416 U.S. 232 (1974) 28

Takeda Pharms. U.S.A., Inc. v. West-Ward Pharm. Corp.,
785 F.3d 625 (Fed. Cir. 2015) 30, 47, 49

Takeda Pharms. U.S.A., Inc. v. West-Ward Pharm. Corp.,
188 F. Supp. 3d 367 (D. Del. 2016).....50

Takeda Pharms. U.S.A., Inc. v. West-Ward Pharm. Corp.,
2016 WL 723054 (D. Del. Dec. 14, 2016) 50

Tellabs, Inc. v. Makor Issues & Rts., Ltd.,
551 U.S. 308 (2007).....35, 36

Visual Memory LLC v. NVIDIA Corp.,
867 F.3d 1253 (Fed. Cir. 2017) 26

Warner-Lambert Co. v. Apotex Corp.,
316 F.3d 1348 (Fed. Cir. 2003) 30

Statutes **Pages**

15 U.S.C. § 78u–4(b)(2).....35

21 U.S.C. § 355(j)(2)(A)(vii-viii).....13

28 U.S.C. § 1295(a)(1) 3

28 U.S.C. § 1331 2

28 U.S.C. § 1338(a) 2

35 U.S.C. § 271(b) 29

35 U.S.C. § 271(e)(2)(A) 50

42 U.S.C. § 1983 36

Rules **Pages**

21 C.F.R. § 314.94(a)(12) 13

Fed. R. Civ. P. 8(a)(2) 27, 35

TABLE OF ABBREVIATIONS AND CONVENTIONS

’537 patent	U.S. Pat. No. 9,700,537
’861 patent	U.S. Pat. No. 10,568,861
Appx____	joint appendix page ____
Amarin	plaintiffs–appellants Amarin Pharma, Inc., Amarin Pharmaceuticals Ireland Ltd., and Mochida Pharmaceutical Co., Ltd., collectively
CV	cardiovascular
E-EPA	ethyl icosapentate (or icosapent ethyl)
EPA	icosapentaenoic acid
FAC	Amarin’s First Amended Complaint, Appx504-557
Hikma	defendants–appellees Hikma Pharmaceuticals USA Inc. and Hikma Pharmaceuticals PLC, collectively
HTG	hypertriglyceridemia
MTD	Hikma’s motion to dismiss first amended complaint for failure to state a claim under Fed. R. Civ. P. 12(b)(6), Appx941-968
SH	severe hypertriglyceridemia
TG	triglyceride
the asserted patents	the ’537 and ’861 patents
USPTO	United States Patent and Trademark Office
xx:*yy*-*zz*	column *xx*, lines *yy*-*zz*

RELATED CASES

No other appeals involving this civil action have been before this or any other appellate court. Appellants and their counsel are unaware of any other pending cases that will directly affect or be directly affected by the decision in this case.

INTRODUCTION

The generic drug approval scheme created by Congress permits a generic drug manufacturer like Hikma to copy the portion of a brand-name drug's label directed to a non-patented use of the drug so long as the generic manufacturer carves out any patented uses from its proposed label. If approved by the FDA, the generic manufacturer can market the drug, but only for the non-patented use indicated on the resulting "skinny label," which lists less than all the uses for which the brand-name drug has received approval. But even when the generic manufacturer proceeds with its skinny label, it still cannot encourage physicians to use the generic drug for the unauthorized, patented use that is not on the skinny label.

In this case, Hikma attempted to create a skinny label under this scheme. But Hikma, through multiple modes and media outside the label, encouraged prescribing physicians to replace Amarin's brand-name medication with Hikma's generic version for the patented use—the use for which Hikma's generic version was not approved. This was induced patent infringement.

The district court dismissed Amarin's complaint for failing to state a claim for induced infringement. In so doing, the district court misapplied the plausibility pleading standard by improperly considering Amarin's allegations in isolation instead of weighing them together; it made improper, implicit factual determinations

while bypassing the key factual dispute regarding what Hikma communicated to prescribing physicians; and it incorrectly analogized the case law.

Skinny-label precedent can involve difficult and close questions. The Court does not need to grapple with those questions here because this is not a true skinny-label case. Amarin's allegations are based not just on Hikma's label, but on its public statements made in press releases and on its website that encouraged physicians to prescribe Hikma's generic drug for an off-label use patented by Amarin. The district court erred when it considered each of those allegations one-by-one without considering whether it was at least plausible that Hikma's label together with its various public statements collectively encouraged infringement by prescribing physicians. And contrary to the district court's analysis, this Court's skinny-label precedent further supports inducement—especially *plausible* inducement—on the facts alleged. And the case law fully supports Amarin's view that the difficult questions and related factual disputes in this case cannot be resolved on a motion to a dismiss.

Reversal and remand is appropriate.

JURISDICTION

The district court had jurisdiction under 28 U.S.C. §§ 1331 and 1338(a), and entered partial final judgment pursuant to Fed. R. Civ. P. 54(b) on October 13, 2022.

Appx14-15; Appx507. Appellants filed a timely notice of appeal on November 9, 2022. Appx2069-2070. This Court has jurisdiction under 28 U.S.C. § 1295(a)(1).

STATEMENT OF ISSUES

1. Did the district court err by failing to consider the combined weight and effect of evidence demonstrating Hikma's repeated extra-label encouragement of using their generic version of Amarin's patented drug for *both* the approved skinny-label use of treating severe hypertriglyceridemia *and* the non-approved and infringing use of reducing cardiovascular risk in patients who do not suffer from severe hypertriglyceridemia when it dismissed Amarin's complaint for failure to state a claim?

2. Did the district court err by implicitly making a factual finding on the pleadings regarding what Hikma's conduct communicated to prescribing physicians, a key element of induced infringement?

3. Did the district court improperly analogize Amarin's allegations to *Grunenthal*, a label-only case where the asserted patent covered a use narrower than the generic label instructed, whereas Amarin alleged extra-label inducement activity by Hikma in the context of Amarin's patents, which are directed to a use broader than Hikma's approved use?

STATEMENT OF THE CASE

A. Vascepa® and its demonstrated efficacy for two different treatments

1. Severe hypertriglyceridemia, pancreatitis, and its treatment

Triglycerides, whether derived from food or made by the body, are a type of fat that circulates in human blood. While triglycerides are necessary for good health, high triglyceride levels, generally referred to as hypertriglyceridemia ("HTG"), can lead to serious conditions. Severe HTG[1] is a condition in which a patient's blood triglyceride level (measured in milligrams of triglycerides per deciliter of blood, i.e., mg/dL) exceeds 500 mg/dL. Appx696 (FAC, Ex. K ¶1). The primary concern with severe HTG patients is pancreatitis. Appx952 (MTD, 5); Appx866 (FAC, Ex. BB at ¶7).

Vascepa® is a prescription drug Amarin developed and markets in the United States. Appx508 (FAC, ¶28). Its active ingredient is ethyl icosapentate ("E-EPA") (sometimes referred to as icosapent ethyl), an ethyl ester of an omega-3 polyunsaturated fatty acid called icosapentaenoic acid ("EPA") that occurs in and is

[1] Severe hypertriglyceridemia, or severe HTG, was referred to as "SH" before the district court, and the corresponding indication was referred to as the "SH indication."

derived from fish oils. Appx1415 (R&R, 3); Appx40 ('537 patent, 3:14-40); Appx508 (FAC, ¶28).

Amarin initially studied Vascepa® in patients with severe HTG (the "Marine" trial). Appx508 (FAC, ¶30). The Marine trial demonstrated that Vascepa® lowers triglyceride levels in severe HTG patients without also raising levels of "bad" cholesterol, LDL-C. *Id*. That was a significant outcome because another drug indicated to reduce triglyceride levels—Lovaza®—can significantly increase bad cholesterol levels. Appx107 ('861 patent, 1:40-45). Following the Marine trial, the FDA approved Vascepa® as a treatment for severe HTG in 2012. Appx508 (FAC, ¶30). With that approval, Vascepa® became the first—and remains the only—medication approved for treating severe HTG that does not raise bad cholesterol levels. Appx508 (FAC, ¶30); *see* Appx107 ('861 patent, 1:40-45).

2. Amarin initially patented the use of Vascepa® to treat severe HTG

Amarin initially obtained patents covering only the use of Vascepa® to treat severe HTG ("the severe HTG patents"), but those patents are not at issue here. Amarin asserted the severe HTG patents against Hikma in 2017 after Hikma sought FDA approval to launch a generic form of Vascepa® for treating severe HTG. Appx980 (Opp., 6 n.2). In March 2020, the U.S. District Court for the District of Nevada found the severe HTG patents invalid as obvious, and, in September 2020, this Court affirmed without opinion. Appx948 (MTD, 1); *Amarin Pharma, Inc. v.*

Hikma Pharms. USA, Case No. 20-1723 (Fed. Cir. Sept. 3, 2020), ECF No. 78. Hikma's generic version of Vascepa® was then approved by the FDA for—and only for—treating severe HTG. JA521 (FAC, ¶82).

3. Amarin later patented the use of Vascepa® to reduce cardiovascular risk in patients with non-severe HTG or existing cardiovascular disease

Non-severe HTG, or simply HTG, broadly refers to the condition in which a patient's triglyceride level is above the normal acceptable level of 150 mg/dL, which is less than one-third the 500 mg/dL triglyceride level associated with severe HTG. The primary concern when it comes to HTG, as opposed to severe HTG, is not pancreatitis. *See* Appx952 (MTD, 5); Appx866 (FAC, Ex. BB at ¶7). Instead, patients with HTG, like those with hypercholesterolemia (high cholesterol) or those with an established cardiovascular disease, are at risk for adverse cardiovascular events like a heart attack, i.e., myocardial infarction. *See* Appx40 ('537 patent, 3:14-40). Thus, unlike severe HTG where pancreatitis is the primary concern, the primary concern for patients with HTG and elevated LDL cholesterol levels is cardiovascular risk reduction. Appx866 (FAC, Ex. BB at ¶7).

After completing the Marine trial and receiving FDA approval for Vascepa® to treat severe HTG, Amarin continued its clinical work and studied whether Vascepa® could alternatively be used to treat patients with elevated triglyceride levels (200 - 500 mg/dL) and controlled LDL cholesterol levels in what was known

as the "Anchor" trial. *See* Appx509 (FAC, ¶31); Appx871 (FAC, Ex. BB at ¶18).

When the Anchor trial was designed, it was generally accepted that lowering triglyceride levels correlated with reduced cardiovascular risk. Appx509 (FAC, ¶31); Appx866 (FAC, Ex. BB at ¶7). The Anchor trial was thus designed to study whether Vascepa—as an add-on to a common cholesterol-lowering therapy using drugs called "statins" would lower triglyceride levels in patients having HTG, but not severe HTG. Appx509 (FAC, ¶31) (explaining that the Anchor trial studied patients with triglycerides levels between 200 mg/dL and 500 mg/dL). While the Anchor trial demonstrated that Vascepa® lowered triglyceride levels in those patients, the FDA did not approve Vascepa® for cardiovascular risk reduction because it concluded, based on the results of other intervening studies, that reduced triglyceride levels were *not* correlated with reduced cardiovascular risk. Appx509 (FAC, ¶32) (citing Appx863-881 (FAC, Ex. BB)); Appx871-872 (FAC, Ex. BB at ¶¶19-20).

In view of the FDA's revised understanding that reduced triglyceride levels were not correlated with reduced cardiovascular risk, Amarin conducted a third clinical trial called the "REDUCE-IT" trial. Appx509 (FAC, ¶33). Rather than focusing on triglyceride levels, the REDUCE-IT trial studied whether Vascepa® could reduce cardiovascular events by following more than 8,000 patients over a median of five years. Appx509 (FAC, ¶33) (citing Appx832-843 (FAC, Ex. V)). As

in the Anchor trial, Vascepa® was evaluated in the REDUCE-IT trial as an add-on to statin therapy to determine its effect on reducing cardiovascular events in patients with elevated triglyceride levels (between 150 mg/dL and 499 mg/dL). Appx509 (FAC, ¶33); Appx832 (FAC, Ex. V at Methods). But unlike the Anchor trial, where results were based on measuring the patients' triglyceride levels, the REDUCE-IT trial directly studied whether Vascepa® reduced cardiovascular events by following patients with HTG and observing their clinical outcomes. *See* Appx509 (FAC, ¶33).

The REDUCE-IT trial was a success. The results, first announced in September 2018, showed a 25% further reduction in major cardiovascular events compared to patients on statin therapy alone. Appx509-510 (FAC ¶34) (citing Appx680-683 (FAC, Ex. H)). Those results were met with widespread enthusiasm and surprise in the field and were hailed as a "game changer." Appx510 (FAC ¶35) (citing Appx852-853 (FAC, Ex. Y); Appx855-857 (FAC, Ex. Z)).

Based on the success of the REDUCE-IT trial, the FDA approved Vascepa® for a second indication: as a treatment to reduce cardiovascular risk in patients with HTG. *See* Appx509-510 (FAC, ¶34) (citing Appx685-689 (FAC, Ex. I)); Appx517 (FAC, ¶62) (citing Appx674-678 (FAC, Ex. G)). The Vascepa® label thus includes two approved indications, the earlier "Severe Hypertriglyceridemia Indication" for treating severe HTG and the later "CV Indication" for reducing cardiovascular risk in patients with HTG. Appx514 (FAC, ¶56) (citing Appx635-648 (FAC, Ex. D)).

After the second approval, Amarin removed language from its label that indicated Vascepa® had not been approved for cardiovascular risk reduction, i.e., the "CV Limitation of Use." Appx514-517 (FAC, ¶¶60-63).

The FDA's decision to approve Vascepa® for cardiovascular risk reduction was considered a "major milestone in cardiovascular prevention." Appx518 (FAC, ¶66) (citing Appx685-689 (FAC, Ex. I)). Once Vascepa® received approval for cardiovascular risk reduction and the related limitation was removed from the Vascepa® label, "healthcare providers rapidly associated administration of [E-EPA] together with a statin as a method for reducing risk of cardiovascular events in patients with baseline triglycerides ≥ 150 mg/dL," i.e., in patients with HTG. Appx519 (FAC, ¶67).

Based on work performed in connection with the REDUCE-IT trial, Amarin obtained U.S. Patent No. 10,568,861, which is one of the two patents at issue in this appeal and, unlike the previously litigated severe HTG patents, is directed to cardiovascular risk reduction. *See* Appx107 ('861 patent, 1:49-51); Appx128 ('861 patent, 43:7-14). Claims 1 and 2 of the '861 patent cover methods for reducing the risk of cardiovascular death in patients with established cardiovascular disease by administering Vascepa:

> 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.

Appx129. On March 20, 2020, Amarin timely submitted information regarding the '861 patent to the FDA for listing in the Orange Book as covering methods of using Vascepa® to reduce cardiovascular risk. Appx520 (FAC, ¶77).

4. Mochida's prior foundational work and patent

Amarin's clinical trials related to Vascepa® were preceded by other work done by Mochida, a Japanese pharmaceutical manufacturer that later became Amarin's licensing partner, in the late 1990s and early 2000s. Appx510 (FAC, ¶36). Mochida established through its own cardiovascular outcomes trial that 1.8 grams per day of E-EPA, i.e., the same active ingredient as in Vascepa®, suppressed certain cardiovascular risk in patients with high cholesterol, i.e., hypercholesterolemic patients. Appx510-511 (FAC, ¶36); Appx616 (FAC, Ex. B at Procedures). A statistical analysis of Mochida's trial results was later conducted to assess the effect of EPA on a Japanese patient population with a particular profile of risk factors for coronary artery disease, and its results were published in a 2008 article by 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) (hereafter the "Saito article"). Appx511 (FAC, ¶¶37-40) (citing Appx615-620 (FAC, Ex. B)).

U.S. Patent No. 9,700,537, the other patent at issue in this appeal, is based on work performed in connection with the Saito article. The '537 patent describes a method of reducing the risk of a cardiovascular event by administering EPA, with the active ingredient E-EPA, in combination with a statin to a patient with high cholesterol, elevated triglycerides, and reduced HDL-C (good cholesterol). Appx1416 (R&R, 4); Appx40 ('537 patent, 3:14-40). Claim 1 states:

> 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.

Appx46. The '537 patent is assigned to Mochida, and Amarin holds the exclusive license to it. Appx512 (FAC, ¶¶42-43). On January 9, 2020, Amarin timely submitted information regarding the '537 patent to the FDA for listing in the Orange Book as covering methods of using Vascepa® to reduce cardiovascular risk. Appx519 (FAC, ¶71).[2]

The '537 and '861 patents cover the CV Indication for Vascepa®, and that CV Indication currently accounts for more than 90% of Vascepa® sales. Appx923-925 (Amarin's letter to its payer community after Hikma's generic launch); Appx540 (FAC, ¶152).

B. Hikma launched generic Vascepa®, describing it on its website, in press releases, and with a supposedly "skinny" label

1. Hikma submitted a Section viii statement to obtain FDA approval to sell generic Vascepa® solely to treat severe hypertriglyceridemia

On September 21, 2016, Hikma (through its predecessor) submitted an abbreviated new drug application for a generic version of Vascepa®. Appx525 (FAC, ¶99). While Hikma's application was pending, the '537 and '861 patents issued. *See*

[2] The record below also involved U.S. Patent No. 8,642,077, but the parties resolved their dispute regarding that patent, and it is not relevant to this appeal.

Appx36 (’537 patent); Appx77 (’861 patent); Appx613 (FAC, Ex. A). Because Amarin listed both the ’537 and ’861 patents in the Orange Book before Hikma’s generic version of Vascepa® was approved, Hikma was required to provide to the FDA either patent certifications under Section vii or a statement under Section viii. *See* 21 U.S.C. § 355(j)(2)(A)(vii-viii); 21 C.F.R. § 314.94(a)(12); Appx526 (FAC, ¶ 102). A “Section viii statement” (submitted under 21 U.S.C. § 355(j)(2)(A)(viii)), is filed when a generic applicant seeks FDA approval to label its drug only for uses *not* covered by method-of-use patents, like those at issue here. Appx524-525 (FAC, ¶ 95). Because the resulting generic’s label would include less than the full label by virtue of the excluded patented indications, it is common to refer to a generic under a Section viii statement as a “skinny label” drug. *See GlaxoSmithKline LLC v. Teva Pharms. USA, Inc.*, 7 F.4th 1320, 1328 (Fed. Cir. 2021) (per curiam) (noting that Teva’s label prepared under Section viii was “a so-called ‘skinny label.’”). In this case, Hikma submitted a Section viii statement to the FDA with respect to the ’537 and ’861 patents, seeking FDA approval for only the severe HTG indication. Appx526 (FAC, ¶ 104).

After the severe HTG patents were invalidated in the Nevada action, and based on its Section viii statement, the FDA granted final approval for Hikma’s ANDA on May 21, 2020. Appx506 (FAC, ¶ 11); Appx613 (FAC, Ex. A). Hikma

launched its generic version of Vascepa® in the United States in November 2020. Appx506 (FAC, ¶13) (citing Appx715-717 (FAC, Ex. N)).

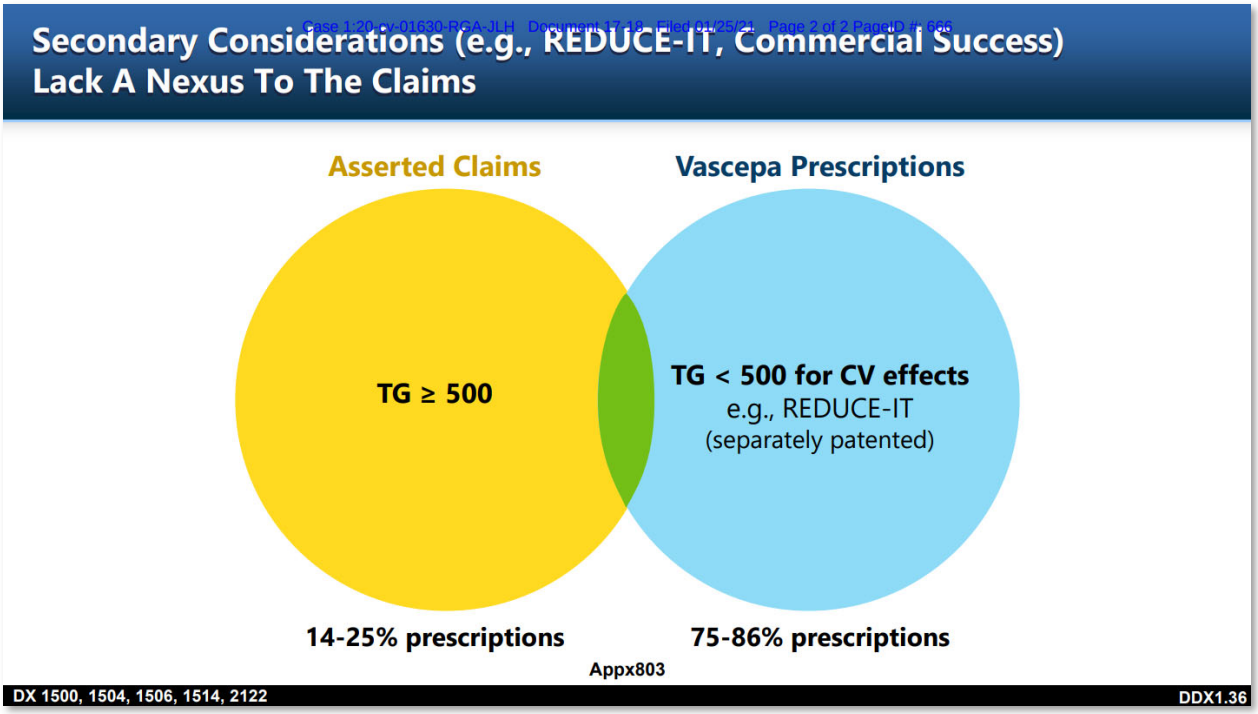
2. Hikma's website associated its generic version of Vascepa® with a method of use beyond its approved use

When Hikma launched its generic version of Vascepa®, with its approved indication limited to treating severe HTG, Hikma's website announced that its product was in the Therapeutic Category of "Hypertriglyceridemia." Appx532 (FAC ¶125) (citing Appx820 (FAC, Ex. T (Hikma's website))). Treating patients having *severe* HTG—the approved indication—means treating patients with triglyceride levels of at least 500 mg/dL. But "hypertriglyceridemia," i.e., HTG, as opposed to severe HTG, generally refers to patients having triglycerides of over 150 mg/dL who are at increased cardiovascular risk—the very patients studied in the REDUCE-IT trial for cardiovascular risk reduction. Hikma's website thus promoted its generic E-EPA capsules as therapeutically equivalent for a use beyond treating patients with severe HTG. Appx532-533 (FAC, ¶126).[3] Hikma has not explained why it declined to accurately describe the therapeutic category as Severe Hypertriglyceridemia.

[3] Hikma knew that broader use would include the patented indication. In the Nevada trial based on Amarin's severe HTG patents, Hikma 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." Appx529 (FAC, ¶110) (citing Appx845-847 (FAC, Ex. W, ¶116)).

3. Hikma issued press releases, encouraging readers to prescribe generic Vascepa® for more than treating patients with severe hypertriglyceridemia

Beyond its website, Hikma also issued pre-launch press releases that carefully conveyed to readers that Hikma's product should be used for all uses for which Vascepa® was approved. First, the press releases indicated that Vascepa® is indicated only "in part" to treat patients with severe HTG. Appx709; Appx712. Hikma's press releases went further and identified its product as "Hikma's generic version" of Vascepa® without any qualification and in an attempt to equate Hikma's approval to the two Vascepa® indications. Appx709; Appx712. In fact, the later press release announced that Hikma had "received FDA approval of the product" without acknowledging that the approval was only for the severe HTG indication. Appx712. Taken together, Hikma made clear that Vascepa® was indicated for more than one use and then identified its own product as a generic version of Vascepa®. In describing its "generic version of Vascepa," both press releases further touted the value of *all* domestic Vascepa® sales, *id.*, even though Hikma knew more than 75% of sales were for the (patent-protected) CV Indication. Appx529 (FAC, ¶¶112-113); Appx531 (FAC, ¶¶119-120); Appx846 (¶115 (Hikma's proposed findings of fact from the Nevada trial)); Appx803 (FAC, Ex. Q). Hikma illustrated the lopsided sales in favor of the "separately patented" CV Indication during the Nevada trial in one of its demonstratives to downplay the commercial success of the SH Indication:



Appx803 (FAC, Ex. Q).

Amarin asserted those pre-launch press releases as evidence supporting its allegations that Hikma developed its product based on market assumptions that included the universe of Vascepa® sales, not just sales related to sever HTG treatment. Appx528 (FAC, ¶109). Importantly, Amarin alleged that Hikma's press releases "communicate[d] to and instruct[ed] 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 [cardiovascular] events per the CV Indication awarded to VASCEPA®, and thus promote[d] and encourage[d] that use." Appx530 (FAC, ¶115); Appx531 (FAC, ¶122). It was only after its launch that Hikma finally noted in a press release that its product had limited approval,

Appx715, but by that time Hikma had already primed the market with its earlier press releases.

4. Hikma's "skinny" label teaches the claimed limitations and omits the prior limitation of use excluding the cardiovascular risk indication

Hikma's label (Appx693-707) includes information that Amarin asserted would encourage a healthcare provider to prescribe its generic product for the patented and non-approved CV Indication. For example, the REDUCE-IT study—which was relevant solely to the CV Indication—is described in section 5.1 of Hikma's label. Appx696. Co-administering with a statin (part of the CV Indication) is discussed in sections 12.3 and 14.2. Appx701-702. And Hikma itself recognized that the patient population for the severe HTG indication overlaps in part with the patient population for the cardiovascular risk indication. Appx803 (FAC, Ex. Q). Further, Hikma's label identifies potential side effects, stating in part that people who have cardiovascular disease or diabetes with a risk factor for cardiovascular disease may experience heart rhythm problems when they take Hikma's product:

> **Heart rhythm problems (atrial fibrillation and atrial flutter).** 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.

Appx704-705 (FAC, Ex. K).

Hikma's label makes clear that: "Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet." Appx535 (FAC, ¶132); Appx705. One of Hikma's physician experts in the Nevada trial pointed to that language when explaining that "most often we use this medication for reasons other than the [severe HTG clinical trial] data, and in the patient information section it specifically tells the patients that we would potentially do that." Appx535 (FAC, ¶132) (citing Appx849-850 (FAC, Ex. X at 617)). In other words, Hikma's physician understood that the label tells readers that Hikma's product will be prescribed for reasons other than treating patients with severe HTG.

Beyond including information relevant to the CV Indication, Hikma removed a relevant Limitation of Use from its label. When Hikma submitted its ANDA (September 21, 2016), Vascepa® was approved only for the severe HTG indication, and the Vascepa® label included a statement in its Limitation of Use section, which said: "The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined." Appx514-515 (FAC, ¶60) (citing Appx650-661 (FAC, Ex. E); Appx663-672 (FAC, Ex. F)). Hikma's proposed label thus included the same Limitation of Use.

The FDA's approval of Vascepa® for the cardiovascular indication allowed *Amarin* to add a cardiovascular risk reduction indication to, and remove the cardiovascular Limitation of Use from, the Vascepa® label. However, *Hikma* also

removed the cardiovascular Limitation of Use from its proposed label and did so with knowledge of the '537 and '861 patents. Appx528 (FAC, ¶108). When Hikma launched its product, its label did not include any cardiovascular Limitation of Use. *See* Appx526 (FAC, ¶107) (citing Appx694-707 (FAC, Ex. K)). Amarin alleged that Hikma removed that Limitation of Use "so that healthcare providers and patients would believe that Hikma's generic [E-EPA] capsules could be and should be used just like VASCEPA®, including to reduce the risk of cardiovascular events per the CV Indication awarded to VASCEPA®." Appx528 (FAC, ¶108). That allegation is well founded because the market understands what the presence of the cardiovascular Limitation of Use implies because another similar well-known drug, Lovaza®, which contains EPA and lowers triglyceride levels, includes the same limitation and has not been shown to be effective for reducing cardiovascular risk. Appx516 (FAC, ¶61) (citing Appx807-818 (FAC, Ex. S)); Appx518 (FAC, ¶64).

C. The district court proceeding

1. Amarin sued Hikma for inducing infringement

On November 30, 2020, Amarin sued Hikma for inducing infringement of the '861 and '537 patents ("the asserted patents"), Appx159-166 (Compl., ¶¶120-143), and on January 25, 2021, Amarin filed its First Amended Complaint ("FAC"), Appx504-557. Amarin alleged that the combination of Hikma's label, its press releases, and its website encouraged healthcare providers to: (i) associate Hikma's

generic with the patented use of Vascepa® known to the market; and (ii) administer Hikma's generic version of Vascepa® to patients with non-severe HTG in order to reduce cardiovascular risk. Appx533 (FAC, ¶¶ 127-128).[4]

2. Hikma moved to dismiss under Rule 12(b)(6)

Hikma moved to dismiss the inducement claims under Federal Rule of Civil Procedure 12(b)(6) for failure to state a claim. Appx941-968 (MTD). Hikma did *not* dispute that Amarin sufficiently alleged that healthcare providers had directly infringed the '537 and '861 patents or that Hikma knew about the asserted patents and the direct infringement. And, Hikma admitted that the district court could consider Amarin's allegations about Hikma's website, press releases, and label. Appx950 (MTD, 3) ("Now that Hikma recently launched its product, Amarin can rely on information outside of the labeling to prove inducement."). Rather, Hikma's motion was limited to arguing that Amarin did not plausibly allege that Hikma took "active steps" to encourage that infringement, despite Amarin's allegations regarding Hikma's website and press releases in addition to its label. Appx945 (MTD, ToC); Appx1011 (Reply, 10).

[4] Amarin amended its complaint once to add allegations, mostly related to Amarin's decision to add another defendant: Health Net, LLC. Appx558. Health Net separately moved to dismiss the first amended complaint, and Health Net's motion was denied. Amarin and Health Net subsequently resolved their dispute, so Health Net is not part of or related to this appeal.

3. The magistrate judge recommended denying Hikma's motion to dismiss

The magistrate judge recommended denying Hikma's motion to dismiss. Appx503; Appx1430 (R&R, 18). Recognizing that it could not "make factual findings about what Hikma's label and advertisements communicate to physicians," Appx1414 (R&R, 2), the magistrate judge explained why Amarin's allegations could not be resolved on the pleadings. The impact of Hikma's actions on healthcare providers raised a factual dispute that could plausibly be resolved in Amarin's favor:

> Hikma urges the Court to resolve this case at the pleadings stage, pointing out that the contents of its label and public statements are undisputed. *But there is a real dispute about what those contents communicate to others*, and I do not think it is appropriate to resolve it on a motion to dismiss. Stated another way, at this stage of the case, I am not prepared to say that Hikma's label and public statements—as a matter of law—could never amount to instruction and encouragement to infringe the asserted patents.

Appx1427 (R&R, 15) (emphasis added).

The magistrate judge agreed with Hikma that it had no duty to actively discourage infringement, and further agreed that Hikma's mere knowledge of direct infringement would be insufficient on its own to state a claim. Appx1426 (R&R, 14). "But [Hikma] cannot present information in a way that encourages infringement." Appx1426 (R&R, 14). Amarin plausibly alleged that is exactly what Hikma did. The magistrate judge recognized that Amarin's various allegations

should be considered together, not individually, and viewed in a light most favorable to Amarin. *See* Appx1424-1425 (R&R, 12-13). As the magistrate judge explained, "[t]he assessment of whether a complaint plausibly alleges inducement in a pharmaceutical case is thus no different than the analysis in any other case." Appx1423 (R&R, 11).

4. The district court granted Hikma's motion

The district court overruled the magistrate judge's recommendation and granted Hikma's motion to dismiss. Appx2. Beginning with Hikma's label, the district court explained that it could find no instruction "as to CV risk reduction." Appx6. In analyzing Hikma's label, the district court focused on "CV risk reduction," and not the claimed patient population. In so doing, the "side effect" language was "hardly instruction or encouragement" to use Hikma's generic drug to reduce cardiovascular risk. Appx6. The district court opinion did not discuss whether the "side effect" language would be understood by healthcare providers as encouraging them to prescribe Hikma's generic drug to the patient population claimed in the '537 or '861 patents. And the district court found that Hikma had no duty to discourage the patented use. Appx7. Even if removing the Limitation of Use communicated to the public that Hikma's generic drug could be used to reduce cardiovascular risk, the district court reasoned that healthcare providers would

understand that as Hikma "merely describing" an infringing mode, not encouraging it. Appx7.

The district court then set the label aside to separately analyze the non-label allegations: "Since I find that the label does not instruct CV risk reduction, the question is whether Hikma's public statements, including press releases and Hikma's website, induce infringement." *Id.*

As to Hikma's pre-launch press releases, the district court concluded that advertising its product as the "generic equivalent" of Vascepa® did not expose Hikma to liability under *GlaxoSmithKline* and citing sales figures for infringing uses goes to Hikma's "intent to induce" but does not count as an inducing act. Appx8.

Turning to Hikma's website that advertised Hikma's product in the "hypertriglyceridemia" therapeutic category, the district court acknowledged that "Amarin has pled that the category 'hypertriglyceridemia' includes infringing uses." Appx8. Again, isolating the analysis, the district court reasoned "[t]he question is whether this is enough, without a label or other public statements instructing as to infringing use, to induce infringement," and decided the answer was "no." Appx8.

To justify its conclusion, the district court compared the facts here to the facts in *GlaxoSmithKline* (finding infringement) and *Grunenthal GMBH v. Alkem Labs. Ltd.*, 919 F.3d 1333 (Fed. Cir. 2019) (finding no infringement), and concluded this case was more like *Grunenthal* than *GlaxoSmithKline*. Appx8-9. The district court

attempted to distinguish Teva's press releases in *GlaxoSmithKline*, which described the Teva product as a generic "cardiovascular agent," a category that included infringing and non-infringing uses, from Hikma's website. Appx9. The district court found Hikma's website was less like the press releases in *GlaxoSmithKline* and more like the label at issue in *Grunenthal*, where the label included a broader, non-patented category, which by definition covered a narrower, patented use. Appx9. In *Grunenthal*, this Court found that listing the non-patented, broader category on the label was not a specific encouragement to use the drug for the narrower, patented purpose. *Grunenthal*, 919 F.3d at 1339; *see* Appx9. The district court did not comment on the distinction between *Grunenthal* and this case, namely, that the relationship between the non-patented use and patented use is reversed: the non-patented use here (i.e., the severe HTG indication) is *narrower* than the patented use (i.e., the cardiovascular risk reduction indication for general HTG). Hikma's website did not list a non-patented use that included a narrower patented use like the *Grunenthal* label; instead, Hikma listed a broader general HTG therapeutic category where the majority of prescriptions would be for the patented use to reduce cardiovascular risk. *See* Appx820 (FAC, Ex. T); Appx529 (FAC, ¶¶112-113); Appx531 (FAC, ¶¶119-120).

The district court concluded that Amarin "failed to plead inducement based on Hikma's label or public statements" and granted Hikma's motion to dismiss the first amended complaint. Appx9.

SUMMARY OF ARGUMENT

This case involves Hikma's so called skinny-label generic version of Amarin's breakthrough Vascepa® medication, but the evidence in this case goes beyond the label, skinny or not. This is a pleadings standard case. Yes, Amarin alleged that Hikma's skinny label was not skinny enough, i.e., that it covered patented methods of treatment. But Amarin alleged more than that.

Amarin alleged that Hikma, knowing that the "vast majority" of Vascepa® prescriptions were for the patented breakthrough cardiovascular risk reduction treatment, undertook a series of communications with the market with the intent that its generic be used to replace Vascepa® for the patented use. Hikma broadcast a broader therapeutic category (hypertriglyceridemia) than it had approval for (severe hypertriglyceridemia) and then emphasized the generic equivalency of its product with Vascepa®—most often used for cardiovascular risk reduction—through Hikma's website, multiple press releases, and the language of Hikma's label. It is more than plausible that Hikma intended these active steps to influence prescribing physicians to replace Vascepa® with its generic for the patented use. That was

enough to satisfy the pleading requirements and survive the motion to dismiss. Holding otherwise resulted in multiple errors.

The district court erred by: (1) weighing Amarin's allegations separately and in isolation against the plausibility pleading standard rather than considering whether, as Amarin pled, Hikma's conduct as a whole induced infringement; (2) making implicit factual findings on the key question of what Hikma's conduct communicated to prescribing physicians; and (3) misapplying skinny-label precedent. Those errors effectively and improperly elevated the pleading standard to deprive Amarin of its right to pursue a more than plausible claim for induced infringement. Reversal and remand is appropriate.

ARGUMENT

I. Standard of review

This Court reviews motions to dismiss for failure to state a claim under the law of the regional circuit. *Visual Memory LLC v. NVIDIA Corp.*, 867 F.3d 1253, 1257 (Fed. Cir. 2017). The Third Circuit reviews the district court's grant of such a motion de novo. *Ballentine v. United States*, 486 F.3d 806, 808 (3d Cir. 2007).

II. Amarin satisfied the pleading standard by pleading plausible infringement by Hikma

The requirement to state a plausible claim for relief at the pleading stage is not demanding. The specific claim here, induced infringement, requires encouragement or promotion of an infringing use. Amarin pled multiple facts that

together demonstrated how Hikma encouraged or promoted prescribing physicians to replace Amarin's Vascepa® with Hikma's generic for the patented use of reducing cardiovascular risk in patients with elevated triglyceride levels.

A. Surviving a motion to dismiss requires pleading facts sufficient to state a plausible claim for relief

"To survive a motion to dismiss, a complaint must contain sufficient factual matter, accepted as true, to 'state a claim to relief that is plausible on its face.'" *Ashcroft v. Iqbal,* 556 U.S. 662, 678 (2009) (quoting *Bell Atl. Corp. v. Twombly,* 550 U.S. 544, 570 (2007)). Only "a short and plain statement of the claim showing that the pleader is entitled to relief" is required. Fed. R. Civ. P. 8(a)(2). Factual allegations are reviewed "on the assumption that all the allegations in the complaint are true (even if doubtful in fact)." *Twombly,* 550 U.S. at 555. The allegations do not need to be detailed. *Id.* Instead, "[f]actual allegations must be enough to raise a right to relief above the speculative level," as opposed to allegations that provide a "formulaic recitation" of the claim elements. *Id*.

This was not a case where Amarin merely speculated about what doctors might do. Instead, Amarin set forth allegations of how Hikma used multiple communications on its website, press releases, and label together to encourage using its generic as a replacement for Vascepa® for the patented use. Those allegations easily exceeded mere speculation.

A claim is plausible when the complaint contains "factual content that allows the court to draw the reasonable inference that the defendant is liable for the misconduct alleged." *Iqbal,* 556 U.S. at 678 (citing *Twombly*, 550 U.S. at 556). The plausibility requirement is not a "probability requirement." *Twombly,* 550 U.S. at 556. "[I]t simply calls for enough fact to raise a reasonable expectation that discovery will reveal evidence" showing the alleged misconduct. *Id.* "[A] well-pleaded complaint may proceed even if it strikes a savvy judge that actual proof of those facts is improbable, and 'that a recovery is very remote and unlikely.'" *Id.* (quoting *Scheuer v. Rhodes*, 416 U.S. 232, 236 (1974)). "The issue is not whether a plaintiff will ultimately prevail but whether the claimant is entitled to offer evidence to support the claims." *In re Burlington Coat Factory Sec. Litig.*, 114 F.3d 1410, 1420 (3d Cir. 1997).

Amarin alleged facts showing how Hikma's multiple communications plausibly encouraged infringement. Those allegations highlighted a key factual dispute over how prescribing physicians would understand Hikma's multiple communications—a dispute that would be informed by discovery and expert testimony. But even without that discovery and testimony—prematurely cutoff by the district court—Amarin's alleged facts were enough to create a "reasonable inference," *Iqbal,* 556 U.S. at 678, that Hikma's multiple communications encouraged physicians to use Hikma's generic for the patented use.

B. Inducement requires showing direct infringement and actions taken with the intent to cause infringing conduct

Section 271(b) of Title 35 provides that "[w]hoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b). To state a claim of induced infringement under § 271(b), the complaint must plausibly allege that: (1) there has been direct infringement; (2) the defendant knowingly induced infringement; and (3) the defendant possessed the intent to encourage another's infringement. *MEMC Elec. Materials, Inc. v. Mitsubishi Materials Silicon Corp.*, 420 F.3d 1369, 1378 (Fed. Cir. 2005).

A generic manufacturer can be liable for inducing infringement even when it has attempted to "carve out" the patented indications with a skinny label. *GlaxoSmithKline*, 7 F.4th at 1338; *see AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1056-61 (Fed. Cir. 2010) (affirming grant of preliminary injunction against generic manufacturer for inducing infringement of the patented use even though generic product was approved for the non-patented use). Thus, in considering a motion to dismiss in a pharmaceutical case like this, the court must still determine whether the complaint plausibly alleges inducement.

The inducement inquiry considers whether the complaint plausibly alleges that the generic manufacturer "offer[ed] a product with the object of promoting its use to infringe, as shown by clear expression or other affirmative steps taken to foster infringement." *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1305-06 (Fed. Cir.

2006) (en banc in relevant part). And the Supreme Court has held that advertising or instructing an infringing use is evidence of active steps that both encourage infringement and demonstrate the affirmative intent to induce infringement. *Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd.*, 545 U.S. 913, 936 (2005); *see Takeda Pharms. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 630-31 (Fed. Cir. 2015) ("Inducement can be found where there is '[e]vidence of active steps taken to encourage direct infringement,' which can in turn be found in 'advertising an infringing use or instructing how to engage in an infringing use.'") (quoting *Grokster*, 545 U.S. at 936). Rather than alleging a defendant's "mere knowledge" that its product could be used to infringe, *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1364 (Fed. Cir. 2003), allegations should plausibly suggest "culpable conduct, directed to encouraging another's infringement." *DSU Med.*, 471 F.3d at 1306.

C. Taking the allegations together, Amarin's claim against Hikma is plausible, and discovery is likely to further support Amarin's case

Under the plausibility pleading standard, Amarin was not required to prove its inducement claim to survive the motion to dismiss. Amarin was only required to plead a plausible claim for relief. Amarin did so.

Because Hikma did not dispute either that its generic form of Vascepa® was being used to reduce cardiovascular risk or that such use directly infringed the asserted patents, the issue before the district court was whether Amarin had pled

facts plausibly showing Hikma acted to induce that infringement. *MEMC Elec. Materials*, 420 F.3d at 1378. Amarin pled multiple facts that plausibly demonstrated how Hikma's cumulative actions were taken with the intent to encourage and promote infringement. *Grokster*, 545 U.S. at 936; *DSU Med.*, 471 F.3d at 1305-06.

First, on its website, Hikma described its generic as being therapeutically equivalent to Vascepa® in a broad indication category of "hypertriglyceridemia," i.e., HTG generally. Appx532 (FAC ¶125) (citing Appx820 (FAC, Ex. T (Hikma's website))). That broad category exceeds Hikma's authorized use to treat *severe* HTG in patients with triglyceride levels above 500 mg/dL because it includes the unauthorized, patented use to reduce cardiovascular risk in patients with triglyceride levels above 150 mg/dL, i.e., patients who suffer from HTG (where the primary concern is cardiovascular risk reduction) but not *severe* HTG (where the primary concern is pancreatitis). Appx532-533 (FAC, ¶¶125, 126). Thus, Hikma communicated to the market that its generic was equivalent to Vascepa® for the patented use.

Second, Hikma's marketing campaign included press releases that communicated to the market that Hikma's generic was equivalent to Vascepa® without limitation on use. At the close of the Nevada trial over the severe HTG patents, Hikma announced that it was seeking approval for "its generic version of Vascepa®." Appx709-710. That press release did not divulge that Hikma was

seeking approval only for a particular use of Vascepa®. To the contrary, Hikma identified that particular use as only among the indications for which Vascepa® was approved. *Id.* (describing Vascepa® as "a prescription medicine that is indicated, in part, … to reduce triglyceride levels in adult patients with severe … hypertriglyceridemia."). When Hikma received approval, it announced that the FDA had approved "its [E-EPA] Capsules, 1 gm, *the generic equivalent to Vascepa*." Appx613 (emphasis added). There is no equivocation in that press release, which speaks in terms of the approval of a drug, not a use, and fails to acknowledge that the FDA had approved its generic only for a single indication. And then when Hikma won on appeal following the Nevada trial, it again announced it had received approval for its generic version of Vascepa® without mentioning that approval was limited to the less common indication. Appx712-713. Beyond its silence about the nature of its limited approval, Hikma added that "US sales of Vascepa were approximately $1.1 billion in the 12 months ending in July 2020." *Id.* That figure was extraordinarily misleading in context because, as discussed below, Hikma was aware that those sales were almost all for the use of Vascepa® to treat cardiovascular risk in patients with HTG, a use for which Hikma could not legally compete.

Third, in making these associations, Hikma was aware that the vast majority of prescriptions for Vascepa® were for reducing cardiovascular risk and not for treating severe HTG—the only indication for which its generic is approved. In the

earlier Nevada trial involving the severe HTG patents, Hikma made such an admission even before the FDA had given Amarin approval to market Vascepa® for that use. *See, e.g.*, Appx846 ¶115 (Hikma's proposed finding of fact that "the vast majority of Vascepa prescriptions—over 75%—have been for . . . treating patients with triglycerides below 500 mg/dL."); Appx847 ¶440 (Hikma's proposed finding of fact that "the 'vast majority' of Vascepa® prescriptions are off-label, to patients with triglyceride levels lower than 500 mg/dl"); Appx528-529, Appx535 (FAC, ¶¶110, 132). Following FDA approval of treating cardiovascular risk, that second indication accounted for more than 90% of uses of Vascepa®. Appx923-925 (Amarin's letter to its payer community after Hikma's generic launch); Appx540 (FAC, ¶152). And Hikma knew that doctors had "rapidly associated" Vascepa® with treatment of patients with HTG to reduce cardiovascular risk. Appx519 (FAC, ¶67). Thus, Hikma's communications, which failed to mention that limited nature of the FDA's approval, relied on that association between Vascepa® and the patented use for which Hikma's generic equivalent was not authorized.

Fourth, while Hikma removed some instructions for the unauthorized use from its supposedly skinny label, it maintained in the clinical studies section descriptions of statin-treated patients with the same cardiovascular event history and lipid levels covered by the patented methods. Appx534-536 (FAC, ¶¶130-131, 134); Appx702 (FAC, Ex. K §14.2). And the well-known REDUCE-IT trial related to

cardiovascular risk reduction was described on the label too. Appx696 (FAC, Ex. K § 5.1).

Fifth, Hikma omitted the CV Limitation of Use from its label, a limitation that appears on the only other medication on the market that contains E-EPA and is indicated for lowering triglyceride levels, Lovaza®. Appx514-517 (FAC, ¶¶ 60-61); Appx527-528 (FAC, ¶108). The absence of this limitation, present on the Lovaza® label and understood by physicians, was another way the label communicated to the market that Hikma's generic could be used for the unauthorized, patented cardiovascular risk reduction indication. Appx535-536 (FAC, ¶ 133).

Sixth, Hikma's label identifies a patient population with triglyceride levels above 150 mg/dL that overlaps with patients being treated for cardiovascular risk. Appx696 (FAC, Ex. K § 1).

Far from a purely speculative or formulaic recitation of claim elements, Amarin's complaint presents a clear theory of how Hikma's communications plausibly encouraged or promoted the patented and unapproved use of Hikma's generic version of Vascepa® to reduce cardiovascular risk in patients with elevated triglyceride levels. As the magistrate judge recognized, those factually supported allegations cleared the low pleading bar and prevented dismissal. But rather than reviewing the pled facts and actions together against the low bar of plausibility, the district court considered each fact in isolation. Even if no pled fact by itself could

support the reasonable inference that Hikma has induced infringement, that is irrelevant. Amarin pled that Hikma's multiple communications together encouraged and promoted doctors' use of Hikma's generic for the patented and unapproved use. Those multiple pled facts cleared the low bar for plausibility.

III. The district court erred by weighing the pled facts piecemeal against the plausibility pleading standard

By considering each factual allegation in isolation, the district court transformed the inquiry from one requiring "a short and plain statement of the claim showing that the pleader is entitled to relief," Fed. R. Civ. P. 8(a)(2), into an exacting inquiry requiring a single act to sustain the plausibility of Amarin's case. That was error.

The plausibility pleading standard simply requires sufficient factual material to show the claim for relief is plausible on its face, *Iqbal,* 556 U.S. at 678, to "raise a right to relief above the speculative level," *Twombly,* 550 U.S. at 555, and to allow "the court to draw the reasonable inference that the defendant is liable for the misconduct alleged," *Iqbal,* 556 U.S. at 678. It does not require pleading a single fact that by itself establishes the plausibility of a claim because "courts must consider the complaint in its entirety." *Tellabs, Inc. v. Makor Issues & Rts., Ltd.*, 551 U.S. 308, 322 (2007). In the context of the pleading requirement for scienter under the Private Securities Litigation Reform Act, 15 U.S.C. § 78u–4(b)(2), the Supreme Court explained, "The inquiry . . . is whether all of the facts alleged, taken

collectively, give rise to a strong inference of scienter, not whether any individual allegation, scrutinized in isolation, meets that standard." *Id.* at 322-23.

The Third Circuit applied the Supreme Court's rule in the context of a civil rights complaint under 42 U.S.C. § 1983 when it reversed the district court's grant of a motion to dismiss for failure to state a claim. *Kedra v. Schroeter*, 876 F.3d 424, 432 (3d Cir. 2017). In reversing, the court explained that the district court had "done the inverse of what we are required to do at the pleading stage," i.e., "[i]nstead of considering the complaint as a whole, [the district court] consider[ed] 'whether any individual allegation, scrutinized in isolation, meets that standard.'" *Id.* at 444 (quoting *Tellabs*, 551 U.S. at 322-23). Inducement is similarly not limited to a single act. It considers whether the defendant took "active steps . . . to encourage direct infringement." *Grokster*, 545 U.S. at 936. *Cf. In re Bill of Lading Transmission & Processing Sys. Pat. Litig.*, 681 F.3d 1323, 1343 (Fed. Cir. 2012) (finding induced infringement plausible and that the district court erred by concluding otherwise where "the district court analyzed the individual facts in the [] Amended Complaint in isolation and without reference to the background of the invention"). Thus, establishing a plausible inducement claim does not require a single act.

But that is effectively what the district court required here. It decoupled Hikma's actions to determine whether one portion of Hikma's conduct in *isolation* encouraged infringement instead of considering—as Amarin pled—whether

Hikma's *cumulative* conduct encouraged infringement. *See* Appx5 ("These allegations fall into two categories . . . ."); Appx6 ("The bulk of the briefing and oral argument was directed to Hikma's label, and I will address those arguments first."); Appx9 ("Amarin's complaint has failed to plead inducement based on Hikma's label or public statements . . . ."). To be clear, Amarin maintains that Hikma's press releases, its website, and even its label are enough to clear the pleading standard even if considered in isolation. But even if each piece were not enough in isolation, the district court further erred by not considering them collectively.

This error effectively raised the pleading requirement by weighing the allegations separately. The district court isolated the allegations of inducement based on the label from the allegations based on the other public statements. *See* Appx7 ("Since I find that the label does not instruct CV risk reduction, the question is whether Hikma's public statements, including press releases and Hikma's website, induce infringement."). But the district court went even further and isolated the allegations of inducement for portions of Hikma's public statements from other portions. *See* Appx8 ("Amarin has pled that the category 'hypertriglyceridemia' includes infringing uses. The question is whether this is enough, *without a label or other public statements* instructing as to infringing use, to induce infringement.") (emphasis added).

In contrast, the magistrate judge's report and recommendation fairly considered the cumulative allegations as Amarin pled. The magistrate judge noted how Amarin alleged that "portions of Hikma's label, *taken together* with Hikma's public statements, instruct physicians to use Hikma's product in a way that infringes the asserted patents." Appx1424 (R&R, 12) (emphasis added). And rejecting Hikma's arguments about label-only ANDA case law, the magistrate judge explained, "were this an ANDA case, and were [Amarin's] allegations based solely on the label, [Amarin's] inducement theory might lack merit as a matter of law. But this is not an ANDA case, and *[Amarin's] allegations are not based solely on the label*." Appx1426 (R&R, 14) (emphasis added). Thus, the magistrate judge concluded that, when "*taken together* and viewed in the light most favorable to [Amarin]," Amarin's allegations "plausibly suggest . . . that Hikma's *label and public statements* could instruct and/or encourage third parties to use its product for the CV indication, which [Amarin] allege[s] is covered by the asserted patents; and [] that Hikma both knew and intended that third parties would use its product for that purpose." Appx1425 (R&R, 13) (emphasis added).

The report and recommendation properly applied the pleading standard based on what Amarin pled, but the district court did not. This Court should reverse.

IV. The district court erred by resolving the key factual dispute of what Hikma's conduct communicated to the market

Although "the contents of [Hikma's] label and public statements are undisputed," "there is a real dispute about what those contents communicate to others, and I do not think it is appropriate to resolve it on a motion to dismiss." Appx1427 (R&R, 15). With this explanation, the magistrate judge foreshadowed another error by the district court.

Infringement is a fact question. *Grunenthal GMBH v. Alkem Labs. Ltd.*, 919 F.3d 1333, 1339 (Fed. Cir. 2019). In evaluating Amarin's allegations of induced infringement, the key issue is whether Hikma acted to encourage or promote infringement with the intent to cause such infringement. And as the magistrate judge explained, Amarin alleged that "several . . . portions of Hikma's label, taken together with Hikma's public statements, *instruct physicians* to use Hikma's product in a way that infringes the asserted patents." Appx1424 (R&R, 12) (emphasis added). Thus, the key factual dispute was what Hikma's conduct as described in Amarin's factual allegations communicated to prescribing physicians. Although the magistrate judge recognized this key disputed issue—which should have precluded dismissal—the district court ignored it.

Instead of turning to discovery and expert testimony to illuminate how physicians would have understood Hikma's collection of communications through its website, press releases, and label, the district court short-circuited the process and

implicitly decided the key factual dispute on a motion to dismiss. Appx536-537 (FAC, ¶135) ("For all the reasons set forth above, Hikma knows of and specifically intends for healthcare providers to administer its [E-EPA] capsules in the place of VASCEPA® . . . and its labeling and marketing materials promote, encourage, and instruct healthcare providers to practice the methods of the Asserted Patents"). The district court made that inappropriate finding without addressing the question of what was communicated to physicians. *See* Appx6 (determining that Hikma's specific warning about side effects was not "instruction or encouragement"); Appx7 (determining that "the lack of a [cardiovascular] limitation on Hikma's label does not plausibly teach [cardiovascular] risk reduction"); Appx8 (determining that Hikma's broad category listing on its website "does not rise to the level of encouraging, recommending, or promoting taking Hikma's generic for the reduction of [cardiovascular] risk").

GlaxoSmithKline is illustrative. There, the factfinder reviewed exactly what the district court in this case prevented Amarin from presenting—discovery and expert testimony addressing what Hikma's promotional activities and label communicated to prescribing physicians. This Court extensively discussed the expert testimony. *GlaxoSmithKline*, 7 F.4th at 1328-38. In doing so, the Court noted how "GSK's cardiology expert, Dr. McCullough, explained that doctors, the alleged direct infringers, receive information about generic drug products from a variety of

sources, including the drug labels," and "then walked through each element of claim 1 of the [asserted] patent and compared it to Teva's partial label." *Id.* at 1328.

The fact that *GlaxoSmithKline* proceeded through discovery to trial highlights the evidence-depriving error that dismissal in the face of disputed key factual questions caused in this case. And *GlaxoSmithKline* even addressed a parallel error: "Critically, the district court erred by treating this fact question—whether [a certain] indication instructs a physician to prescribe carvedilol for a claimed use—as though it were a legal one for it to decide *de novo*." *Id.* at 1330. Although that case went to trial, the district court usurped the jury's factfinding role on JMOL and "decided the [relevant indication] portion of Teva's label was insufficient to find that the label instructed an infringing use." *Id.* As explained above, the district court in this case made multiple similar *factual* determinations, assessing the weight of the evidence without explicitly considering the key factual question of what that evidence communicated to prescribing physicians.

For "a quintessential fact question," *id.* at 1328, involving "a real dispute about what [Hikma's label and public statements] communicate to others," it was "not . . . appropriate to resolve [] on a motion to dismiss," Appx1427 (R&R, 15). The district court erred when it did so.

V. The district court erred by analogizing the wrong cases

The district court also erred in its misapplication of skinny-label precedent.

A. This case involves evidence showing inducement in addition to the label—it is not a "label only" case

This case is like *GlaxoSmithKline* and *AstraZeneca* in that those cases also included extra-label evidence to show inducement. In *GlaxoSmithKline*, this Court vacated a grant of JMOL for non-infringement and reinstated a jury's verdict finding induced infringement. 7 F.4th at 1323. As discussed above, the Court relied on detailed expert testimony from Dr. McCullough, including the assertion that doctors obtain information about generic medications from drug labels and other sources. *Id.* at 1328-38. The Court found evidence showing that "Teva intended its label to affect physician's prescribing practices," but that was "not the only evidence" because "GSK also presented extensive expert testimony along with Teva's marketing efforts, catalogs, press releases, and testimony from Teva's own witnesses, showing that Teva encouraged carvedilol sales for [congestive heart failure] despite its attempted carve-out." *Id.* at 1335.

Similar to Hikma's website, Appx820, Teva's first press release described its medication as "the AB rated generic equivalent of [GSK]'s Coreg® Tablets" and as "indicated for *treatment of heart failure* and hypertension." *Id.* at 1335-36 (internal quotations omitted) (emphasis in original). The Court noted how Teva's press release used the term "heart failure" in a way that did "not parse between congestive heart failure," i.e., the patented use, and the specific "post-MI LVD" indication that was not patented. *Id.* at 1336. "This [was] not an errant reference to 'heart failure';

it [was] Teva in a press release telling the world that its generic is a substitute for GSK's Coreg® tablets to treat congestive heart failure in the same manner as Coreg® (which is a method that infringed the '000 patent)." *Id.* And the Court noted Dr. McCullough's additional testimony that this press release "indicate[d] physicians should prescribe generic carvedilol for heart failure." *Id.* Teva's second press release "stated that it had received final approval to market its Generic version of [GSK]'s cardiovascular agent Coreg® (Carvedilol) Tablets." *Id.* (internal quotations omitted). Again, Dr. McCullough testified what this communicated to doctors by explaining how Teva's "use of 'cardiovascular agent' indicated to doctors they could use Teva's carvedilol 'for all indications,' including heart failure." *Id.* (internal quotations omitted).

Like the communications in *GlaxoSmithKline* of therapeutic equivalence in a general category of "heart failure" and as a general "cardiovascular agent" that encompassed the patented use to treat congestive heart failure, *id.* at 1335–36, Hikma communicated that its generic medication was equivalent for a general therapeutic category of "hypertriglyceridemia" and listed sales for the whole Vascepa® market to encompass the patented use to reduce cardiovascular risk in patients with HTG. *See* Appx529-533 (FAC, ¶¶111-116, 118-123, 125, 126); Appx612-613 (Hikma's press release on May 22, 2020); Appx708-710 (Hikma's press release on March 31, 2020); Appx711-713 (Hikma's press release on

September 3, 2020). Thus, this case is like *GlaxoSmithKline* in that inducement is shown by more than the label—except the district court erred here by preventing Amarin from developing the case and addressing the key factual dispute.

AstraZeneca is another case with parallels to the dispute here. This Court affirmed the district court's grant of a preliminary injunction that prohibited Apotex's launch of a generic version of AstraZeneca's budesonide medication. 633 F.3d at 1045. The label instructed patients that it was "desirable to downward-titrate to the lowest effective dose once asthma stability is achieved." *Id.* at 1057. AstraZeneca argued this "proposed label would induce consumers to infringe the asserted method claims because the label implicitly instructed users to administer the generic drug once daily," which was covered by the patented method. *Id.* The district court agreed, but it also relied on a letter from the FDA discussing once-daily dosing that demonstrated how Apotex was both communicating about and aware of the infringement problem. *Id.* at 1057, 1059-60. Apotex's awareness of the infringement problem and decision to distribute the generic with the problematic language in the label "formed the basis of the district court's specific intent finding," and the "district court correctly concluded" this was evidence of active steps to encourage infringement. *Id.* at 1059-60. Thus, *AstraZeneca* was another case where inducement, and specifically the necessary intent to induce, was supported by the label plus more. Like in *AstraZeneca*, Amarin alleged that the label itself

demonstrated Hikma's intent to encourage physicians to treat patients with HTG while supporting those label allegations with additional allegations about Hikma's conduct beyond its generic label.

Instead of those cases, the district court here relied on *Grunenthal*, while Hikma cited *HZNP Medicines LLC v. Actavis Laboratories UT, Inc.*, 940 F.3d 680 (Fed. Cir. 2019), and *Takeda*, which relied on *only* the label for inducement. As the magistrate judge explained, "unlike the allegations in this case, the evidence in those cases related solely to the effects of the generic labels." Appx1427.

In *Grunenthal*, this Court affirmed a finding of no induced infringement following a bench trial. 919 F.3d at 1336. There, the brand medication had two indications, the off-patent treatment of "moderate to severe chronic pain in adults," and the patented treatment of "neuropathic pain associated with diabetic peripheral neuropathy (DPN)," which was "a type of [polyneuropathic] pain." *Id.* at 1338. Hikma and another generic manufacturer carved out treatment of DPN. *Id.* at 1339. The inducement inquiry turned on whether Hikma and the other generic had "the specific intent, based on the contents of their proposed labels, to encourage physicians to use their proposed ANDA products to treat polyneuropathic pain." *Id.* The brand owners argued that severe chronic pain, which remained on the generic labels, was broad enough to include the specific patented treatment of polyneuropathic pain. *Id.* This Court disagreed because the off-patent treatment of

severe chronic pain more broadly included other categories: "[E]ven if severe chronic pain includes polyneuropathic pain, it also includes mononeuropathic pain and nociceptive pain." *Id.*

Critically, the brand owners in *Grunenthal* "point[ed] only to the indications of the proposed labels as grounds for inducement." *Id.* at 1340. And the label had effectively carved out the patented indication, which included removing reference to clinical studies for the patented indication: "[I]t is undisputed that neither of the accused ANDA labels list an indication for the management of pain associated with DPN. Nor do they mention any DPN clinical studies, which served as the basis for FDA approval of [the brand medication's] indication for the treatment of neuropathic pain." *Id.* at 1339-40. Thus, *Grunenthal* was a case where inducement was argued based on the label alone, and the generic labels had fully excised the patented indication. In contrast, this case involves allegations of actions beyond the label, as well as allegations that the label was not skinny enough.

In *HZNP*, this Court affirmed a grant of summary judgment finding no induced infringement for patents related to treating osteoarthritis. 940 F.3d at 683. The patented method in *HZNP* required three steps: "(1) apply the inventive formulation, (2) wait for the area to dry, and (3) apply sunscreen, insect repellant, or a second topical medication." *Id.* at 702. But the generic label's instructions only required the first application step with a warning that the area should be allowed to

dry before application of a sunscreen, etc. *Id.* That warning was not enough to show encouragement to infringe because the "evidence, viewed in the light most favorable to [the plaintiff], establishe[d] that some users *might* infringe." *Id.* (emphasis added). The evidence did "not establish that 'the proposed label instruct[ed] users to perform the patented method.'" *Id.* (quoting *AstraZeneca*, 633 F.3d at 1060). *HZNP* like *Grunenthal*, was thus a case that relied on the label alone.

In *Takeda*, Hikma sought approval for a generic medication for the prophylactic treatment of gout but not for the patented "treatment of acute gout flares." 785 F.3d at 630. Hikma's label stated the generic was "indicated for prophylaxis," included a limitation of use that the "safety and effectiveness of [the generic] for acute treatment of gout flares during prophylaxis has not been studied," and included a warning that "[i]f you have a gout flare while taking [the generic], tell your healthcare provider." *Id.* (internal quotations omitted). Takeda argued that the warning would induce infringement because, for a patient using the generic for prophylaxis, "the physician would likely tell the patient to use the [generic] product to treat the acute flare." *Id.* Although Takeda attempted to use evidence beyond the label to demonstrate that the warning would lead physicians to prescribe the generic for the infringing use of treating acute gout flares, the Court found none of the evidence supported inducement. *Id.* at 632.

"[E]ven if we do look outside the label, there is no evidence that the label would necessarily lead doctors who are consulted by patients taking [the generic] to prescribe an off-label use of it to treat acute gout flares." *Id.* The additional evidence did not show additional encouragement or promotion. Instead, the evidence was meant to show how the warning would "inevitably" lead doctors to prescribe the generic for off-label infringing uses, but the evidence failed to show even that. *Id.* *Takeda* was a case that relied on the label alone to show encouragement, and at that, it relied on a warning to see a doctor as the only encouragement to induce infringement. Unlike *Takeda*, this case relies on communications beyond the label.

Like *GlaxoSmithKline* and *AstraZeneca*, this is a case where a label plus more demonstrates inducement. It is not a case like *Grunenthal*, *HZNP*, or *Takeda*, where the generic label alone was used to show an action intended to induce. The district court erred when it relied on *Grunenthal* and distinguished *GlaxoSmithKline*.

B. Previous cases consistently reached a later stage than a motion to dismiss because factual issues are central to inducement

Every leading skinny-label case discussed here and at the district court reached a more advanced posture than a motion to dismiss. *See* Appx1427 (R&R, 15) (magistrate judge noting how "none of those cases [relied upon by Hikma] was resolved at the motion to dismiss stage."). That makes sense. Infringement is a "quintessential fact question," *GlaxoSmithKline*, 7 F.4th at 1328, and induced infringement hinges on factual determinations.

The leading precedent from this Court highlights that the motion to dismiss was an improper vehicle for resolving the key issues in this case—none of the significant cases were appealed from a dismissal on the pleadings. *See GlaxoSmithKline*, 7 F.4th at 1323 (reversing judgment as a matter of law after a jury trial finding infringement); *AstraZeneca*, 633 F.3d at 1045 (affirming grant of preliminary injunction finding likelihood of showing induced infringement); *Grunenthal*, 919 F.3d at 1338 (affirming bench trial finding no infringement); *HZNP*, 940 F.3d at 682, 686 (affirming grant of summary judgment for non-infringement); *Takeda*, 785 F.3d at 627 (affirming denial of preliminary injunction finding no likelihood of showing induced infringement).

To be sure, cases at the preliminary injunction stage are early-stage cases. But a preliminary injunction is a discretionary grant that requires likelihood of success on the merits, *see, e.g.*, *AstraZeneca*, 633 F.3d at 1049, whereas the grant of a motion to dismiss requires the absence of even a plausible claim for relief.

Before the district court, Hikma asserted that there were "many decisions" "even at the pleadings stage" where there was no induced infringement as a matter of law. Appx481-482 n.2 (Hikma's brief in support of its motion to dismiss). Of the ten cases Hikma cited in support, it only described three as involving a dismissal on the pleadings. *Id.* Each of those cases is distinguishable. *Bayer Schering Pharma AG v. Lupin, Ltd.*, was not a skinny-label case—the generic and brand labels were

identical—nor did it involve inducement of an FDA approved use. 676 F.3d 1316, 1321 (Fed. Cir. 2012). *AstraZeneca Pharmaceuticals LP v. Apotex Corp.*, turned on the question of whether infringement under 35 U.S.C. § 271(e)(2)(A) could be based on an ANDA seeking to market a drug that was not patented and for a use that was not patented. 669 F.3d 1370, 1378-79 (Fed. Cir. 2012). And while *Takeda Pharmaceuticals U.S.A., Inc. v. West-Ward Pharmaceutical Corp.*, did involve a dismissal on the pleadings of an inducement claim, that was based on the district court's conclusion that Takeda's allegations were "too conclusory to pass muster." 188 F. Supp. 3d 367, 377 (D. Del. 2016). Significantly, the *Takeda* district court vacated that very dismissal in light of the low pleading standard after Takeda amended its complaint with allegations about specific communications that Takeda argued amounted to active encouragement. *Takeda Pharms. U.S.C., Inv. v. West-Ward Pharm. Corp.*, 2016 WL 723054 at *2 (D. Del. Dec. 14, 2016). Amarin's specific allegations regarding Hikma's website and press releases position this case squarely within the analysis of that later vacatur of the *Takeda* dismissal.

The fact that all the leading skinny-label cases were more advanced than a motion to dismiss confirms that the district erred when it granted the motion to dismiss.

C. This case involves a patented use that is broader than the off-patent use—unlike in *Grunenthal*

Amarin's patented use to reduce cardiovascular risk in patients with HTG covers a broader set of patients than the off-patent use to treat patients with severe HTG. In other words, more patients suffer from elevated triglyceride levels above 150 mg/dL, i.e., patients with HTG, than the subset with levels above 500 mg/dL, i.e., patients with *severe* HTG. The district court analogized to *Grunenthal* and got this point exactly backwards. Vascepa®'s additional patented indication is not simply a subset of its original indication—it is a different use of the drug to treat a broader patient population for which there was a different clinical concern.

Describing the distinct situation in *Grunenthal*, the district court here explained how "a label indicated for '[m]oderate to severe chronic pain,' which included both infringing and non-infringing uses, did 'not specifically encourage use' of the generic for the patented treatment." Appx9 (quoting *Grunenthal,* 919 F.3d at 1339) (modification in original). And the district court concluded, "[t]his case is more like *Grunenthal,* where the broader category simply includes both infringing and non-infringing uses, without 'specifically encourage[ing]' the use of the generic for the non-infringing uses." Appx9 (quoting *Grunenthal,* 919 F.3d at 1339) (modification in original). But the "broader category" in *Grunenthal* was the off-patent treatment of "moderate to severe chronic pain in adults." *Grunenthal*, 919 F.3d at 1338. That method was directed to a broader group of patients than those

with "neuropathic pain associated with diabetic peripheral neuropathy (DPN)," which was "a type of polyneuropathic pain." *Id*. This Court rejected the argument that the generic label for the broader, off-patent use induced the specific, patented use because the off-patented treatment of severe chronic pain more broadly included other categories: "[E]ven if severe chronic pain includes polyneuropathic pain, it also includes mononeuropathic pain and nociceptive pain." *Id.* In sum, *Grunenthal* was a case where encouraging treatment of patients with moderate to severe pain was not enough to induce the specific and patented treatment of polyneuropathic pain.

In contrast, this case involves a broader patented use that covers a larger patient population with HTG generally (triglycerides above 150 mg/dL) and an off-patent use that covers a narrower patient population with *severe* HTG (triglycerides above 500 mg/dL). Both *Grunenthal* and this case involve generic labels that pointed at a broader category of patients. The difference is that, in *Grunenthal*, that broader category of patients, i.e., those suffering from severe chronic pain, was tied to the off-patent indication. *Id*. Whereas here, the broader category of patients that Hikma's press releases and website identify, i.e., those with HTG generally, is associated with the patented use.

That distinction, misapplied by the district court, changes the factual question of what Hikma's conduct would have communicated to prescribing physicians. This

case is more like *GlaxoSmithKline*, where communications that the generic medication was therapeutically equivalent for a broad category of "heart failure" and as a general "cardiovascular agent" associated the generic with the broader patented use to treat congestive heart failure. 7 F.4th at 1335-36.

CONCLUSION

Amarin stated a claim for relief that was at least plausible. The order dismissing Amarin's first amended complaint should be reversed, and the case should be remanded for further proceedings.

Respectfully submitted,

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