2017-1153, -2048, -2049, -2050

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

GRUNENTHAL GMBH, DEPOMED, INC.,
Plaintiffs-Cross-Appellants

v.

ALKEM LABORATORIES LIMITED, WEST-WARD PHARMACEUTICALS INTERNATIONAL LIMITED, WEST-WARD PHARMACEUTICALS CORP.,
Defendants-Appellants

ACTAVIS ELIZABETH LLC,
Defendant-Appellee

ACTAVIS LABORATORIES UT, INC.,
Defendant

Appeal from the United States District Court for the District of New Jersey in Nos. 2:13-cv-04507-CCC-MF, 2:13-cv-06929-CCC-MF, 2:13-cv-07803-CCC-MF, 2:14-cv-03941-CCC-MF, 2:14-cv-04617-CCC-MF, and 2:15-cv-06797-CCC-MF, Judge Claire C. Cecchi.

DEFENDANT-APPELLEE ACTAVIS ELIZABETH LLC'S RESPONSIVE BRIEF

Michael E. Joffre
William H. Milliken
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 New York Avenue
Washington, DC 20005
202-371-2600 (telephone)
202-371-2540 (facsimile)
mjoffre@skgf.com
wmilliken@skgf.com

Counsel for Defendant-Appellee Actavis Elizabeth LLC

Dated: January 31, 2018

CERTIFICATE OF INTEREST

Counsel for the appellee Actavis Elizabeth LLC and defendant Actavis Laboratories UT, Inc. certifies the following:

1. Full Name of Party Represented by me	2. Name of Real Party in interest (Please only include any real party in interest NOT identified in Question 3) represented by me is:	3. Parent corporations and publicly held companies that own 10% or more of stock in the party
Actavis Elizabeth LLC	Actavis Elizabeth LLC	Teva Pharmaceuticals USA, Inc.; Teva Pharmaceutical Industries Ltd.
Actavis Laboratories UT, Inc.	Actavis Laboratories UT, Inc.	Teva Pharmaceuticals USA, Inc.; Teva Pharmaceutical Industries Ltd.

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court (and who have not or will not enter an appearance in this case) are:

   Duane Morris LLC: Sheila R. Wiggins, Anthony J. Fitzpatrick, Vincent L. Capuano, Patrick C. Gallagher, Carolyn A. Alenci

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal.

   Janssen Pharmaceuticals, Inc. et al. v. Sandoz Inc. et al., Case No. 2:13-cv-06929-CCC-MF; Grünenthal GmbH et al. v. Alkem Laboratories Limited, Case No. 2:13-CV-07803-CCC-MF; Grünenthal GmbH et al. v. Roxane Laboratories, Inc., Case No. 2:14-cv-03941-CCC-MF; Grünenthal GmbH et al. v. Actavis Laboratories UT, Inc., Case No. 2:14-cv-04617-CCC-MF; and

Depomed, Inc. et al. v. Actavis Elizabeth LLC, Case No. 2:15-cv-06797-CCC-MF, all in the United States District Court for the District of New Jersey and consolidated as Grünenthal GmbH et al. v. Actavis Elizabeth LLC et al., Case No. 2:13-cv-04507.

1/31/2018
Date

/s/ *Michael E. Joffre*
Signature of Counsel

Michael E. Joffre
Printed name of counsel

Cc: Counsel of Record

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STATEMENT OF RELATED CASES

Pursuant to Federal Circuit Rule 47.5, counsel for Actavis states that no appeal in or from this civil action or proceeding was previously before this or any other appellate court.

The following cases may directly affect or be directly affected by this Court's decision in the pending appeal: *Janssen Pharmaceuticals, Inc. et al. v. Sandoz Inc. et al.*, Case No. 2:13-cv-06929-CCC-MF; *Grünenthal GmbH et al. v. Alkem Laboratories Limited*, Case No. 2:13-CV-07803-CCC-MF; *Grünenthal GmbH et al. v. Roxane Laboratories, Inc.*, Case No. 2:14-cv-03941-CCC-MF; *Grünenthal GmbH et al. v. Actavis Laboratories UT, Inc.*, Case No. 2:14-cv-04617-CCC-MF; and *Depomed, Inc. et al. v. Actavis Elizabeth LLC*, Case No. 2:15-cv-06797-CCC-MF, all in the United States District Court for the District of New Jersey and consolidated as *Grünenthal GmbH et al. v. Actavis Elizabeth LLC et al.*, Case No. 2:13-cv-04507-CCC-MF.

It is difficult to see what more Actavis could have done to avoid induced or contributory infringement in this case.

The ’130 patent claims methods of treating polyneuropathic pain with the drug tapentadol. Actavis’s generic tapentadol label specifically carves out all mention of polyneuropathic pain, including any studies concerning the treatment of neuropathic pain. Experts for both parties agree that tapentadol can be used to treat non-neuropathic pain, including pain caused by osteoarthritis and rheumatoid arthritis. And Actavis’s label makes clear that it covers such severe, long-term pain. Moreover, Plaintiffs had other patents in this case that specifically covered non-polyneuropathic pain. Actavis stipulated that its label infringed those patents.

Despite Actavis’s attempts to ensure that its label does not induce or contribute to infringement of the ’130 patent, Plaintiffs still brought suit against Actavis. Depomed asserts that—despite Actavis’s efforts to avoid the use of the term “polyneuropathic pain” in its label—doctors would still be instructed and encouraged by that label to use the generic drug to treat polyneuropathic pain. Indeed, Depomed goes so far as to suggest that there are no substantial uses of Actavis’s proposed drug *other* than to treat polyneuropathic pain, even though Plaintiffs successfully asserted patents on relieving non-polyneuropathic pain against Actavis’s proposed drug.

In the end, Depomed's cross-appeal is simply an attack on the district court's credibility determinations and factual findings. There is no reason to disturb the district court's judgment, as Depomed has not come close to showing that the district court committed clear error in finding that Actavis did not intend to induce infringement and did not contribute to infringement. Indeed, there is every reason to believe that Actavis has scrupulously avoided infringement. The district court's judgment of non-infringement should be affirmed.

COUNTERSTATEMENT OF THE ISSUES ON CROSS-APPEAL

1. Whether the district court clearly erred in finding no induced infringement of a patent on treating polyneuropathic pain where Actavis's generic label carves out all mentions of polyneuropathic pain and the district court credited expert testimony that the label would not encourage physicians to use the product to treat polyneuropathic pain.

2. Whether the district court clearly erred in finding no contributory infringement of a patent on treating polyneuropathic pain (a) where the district court credited expert testimony that Actavis's generic product would commonly be used to treat non-polyneuropathic pain, (b) Plaintiffs successfully asserted patents on treating non-polyneuropathic pain against Actavis's generic product, and (c) Plaintiffs presented no evidence that Actavis's generic product is especially adapted to infringe.

COUNTERSTATEMENT OF THE CASE

A. Tapentadol Hydrochloride and the Treatment of Nociceptive and Polyneuropathic Pain

This lawsuit concerns the efforts of Actavis and other pharmaceutical companies to bring to market generic versions of Plaintiffs' opioid drug NUCYNTA® (tapentadol hydrochloride), which can be used to treat severe chronic pain.

As Depomed explains, "[t]he types of pain relevant to this appeal fall into two categories: nociceptive and neuropathic." Depomed Br. 7. Nociceptive pain is caused by actual or threatened damage to non-nerve tissue. Appx46; *see also* Depomed Br. 7. It generally manifests as a throbbing or aching sensation; examples include the feeling of hitting a thumb with a hammer or of breaking a bone. Appx46-47. Neuropathic pain, on the other hand, is caused by damage to actual nerve tissue. Appx47. "Patients generally describe neuropathic pain as a burning, electrical, shocking, or pins and needles sensation." *Id.* As Depomed asserts, "neuropathic pain is separate and distinct from nociceptive pain," and "the treatment of one is not predictive of the treatment of the other." Depomed Br. 8-9.

Neuropathic pain can be broken down into two subcategories: mononeuropathic pain and polyneuropathic pain. Mononeuropathic pain is pain arising from damage to a single nerve, while polyneuropathic pain is pain arising

from damage to multiple nerves. Appx48. Diabetic peripheral neuropathy, or DPN, is a common cause of polyneuropathic pain.

Opioids have traditionally been used "to treat purely nociceptive pain." Depomed Br. 10. It is undisputed that the use of opioids to treat neuropathic pain is controversial. *See id.* at 10, 26. "Because neuropathic pain requires 'around-the-clock' pain management, using opioids [to treat it] often leads to severe side effects, limited effectiveness, and other serious risks to a patient's quality of life." *Id.* at 10. Moreover, neuropathic pain has generally been thought to be "refractory to opioids (*i.e.*, either the opioid would be ineffective or would require very high doses to be effective)." *Id.* at 25. Accordingly, those of skill in the art do not consider opioids to be a first-line treatment for neuropathic pain. *See, e.g.*, Appx9164; Appx10700; Appx10705-10708; Appx11238.

B. The Patents-in-Suit

Plaintiffs asserted three patents in this litigation: U.S. Patent No. RE39,593 (a reissue of U.S. Patent No. 6,248,737); U.S. Patent No. 7,994,364; and U.S Patent No. 8,536,130. Appx33.

The '737 patent discloses the chemical formula for tapentadol and explains that it is "suitable for the treatment of severe pain without giving rise to the side effects which are typical of opioids." Appx375 (1:52-55). A representative claim of that patent (also contained in the '593 reissue patent and asserted against

Actavis in this litigation) recites "[a] method of treating a mammal suffering from pain, said method comprising administering to said mammal an effective analgesic amount" of tapentadol. Appx387 (26:8-10). As support for that claim, the specification discusses the results of mouse writhing pharmacological tests conducted by Grünenthal. *See* Appx385-386 (22:53-23:47); *see also* Appx63. As Depomed asserts in its brief (at 5-6), the mouse writhing test "is well-known to be a test for purely nociceptive pain," and the '593 patent discloses no other analgesic data supporting the claim directed to the treatment of pain using tapentadol. Accordingly, as Depomed argues, those of skill in the art would have understood the '593 patent's references to "pain" to refer *only* to nociceptive pain. Appx179; *see also* Depomed Br. 24 (agreeing with the district court's conclusion that "the context of the '737 patent makes clear" that the patent involves *only* the treatment of nociceptive pain because (1) the only test data it discloses is from a "purely nociceptive pain model" and (2) when physicians historically discussed the treatment of severe pain with opioids, they "th[ought] nociceptive pain only").

The '364 patent claims a particular polymorphic form, "Form A," of tapentadol. The patent also discloses methods of using tapentadol Form A to treat pain and urinary incontinence. *See* Appx388 (Abstract).

The '130 patent, the latest-issued of the patents-in-suit, relates to the use of compounds containing tapentadol to treat polyneuropathic pain. *See* Appx428-

438. As noted above, opioids have generally been thought poor candidates for the treatment of neuropathic pain, so Depomed argues that it was "unexpected and surprising" that tapentadol would be effective in patients suffering from polyneuropathic pain. Depomed Br. 11.

Plaintiffs asserted claims 1 and 2 of the '130 patent against Actavis. Claim 1 recites "[a] method of treating *polyneuropathic pain* in a subject suffering therefrom, said method comprising administering to said subject an effective polyneuropathic pain inhibiting amount of [tapentadol] or a pharmaceutically acceptable salt thereof," and claim 2 recites the method of claim 1 wherein the salt used is tapentadol hydrochloride. Appx438 (18:2-9) (emphasis added).

C. Plaintiffs' Branded Product and Actavis's Proposed Generic

Plaintiffs' branded version of tapentadol hydrochloride extended release tablets, NUCYNTA® ER, contains two indications. The label states that the drug may be used to treat

(1) "pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate"; and

(2) "neuropathic pain associated with diabetic peripheral neuropathy (DPN) in adults severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate."

Appx50299. The label describes the results of three clinical studies that support the listed indications: one study of patients with chronic low back pain ("the CLBP

study") and "two . . . studies in patients with pain related to diabetic peripheral neuropathy" ("the DPN studies"). Appx50307.

Both the FDA and Plaintiffs viewed the CLBP study as a nociceptive pain study, while the DPN studies were considered neuropathic pain studies. In characterizing the CLBP study and the first DPN study, the FDA stated that "[t]he two positive trials had different designs . . . , different populations (low back pain [LBP] and painful diabetic peripheral neuropathy [DPN]), and different types of pain (nociceptive and neuropathic)." Appx49861; *see also* Appx9174-9175 (testimony of Juergen Haussler, vice president for pain and schizophrenia development at Janssen Pharmaceuticals, which previously owned the NUCYNTA franchise). Grünenthal itself agreed with the characterization of the CLBP study as a study of nociceptive pain. *See* Appx56947.

Actavis has carved out the indication directed to "neuropathic pain associated with diabetic peripheral neuropathy" from the labeling for its proposed ANDA product. Accordingly, Actavis's label contains only the first indication listed in Plaintiffs' NUCYNTA ER label—the indication for severe chronic pain. *See* Appx52653. Actavis has also carved out from the label all references to the two DPN studies; Actavis's label mentions only the CLBP study, which, as explained above, was considered a study of nociceptive pain. *See* Appx52610-52779; *see also* Appx9207 (Weinberger); Appx9498-9500 (Brown). In fact,

Actavis's proposed label does not contain the words "neuropathic pain," "neuropathy," "polyneuropathic pain," "polyneuropathy," or any variant thereof.

Because Actavis is not seeking FDA approval for an indication directed to the treatment of polyneuropathic pain, Actavis's ANDA for its generic product contains a "section viii statement" as to the '130 patent. *See* Appx77; 21 U.S.C. § 355(j)(2)(A)(viii) (if an Orange Book listed-patent for a branded drug "does not claim a use for which the applicant is seeking [FDA] approval," ANDA filer may include in its ANDA "a statement that the method of use patent does not claim such a use" in lieu of a certification under § 355(j)(2)(A)(vii)(I)-(IV)).

D. Proceedings Before the District Court

Notwithstanding the fact that Actavis carved out all references to the treatment of neuropathic pain from its proposed label, Plaintiffs sued Actavis for infringement of the '130 patent along with the '593 and '364 patents. Plaintiffs alleged that Actavis's proposed labeling would induce infringement and contribute to infringement of the '130 patent, even though Actavis's label does not contain the DPN indication, references no studies of polyneuropathic pain, and never mentions the word "polyneuropathic."

Prior to trial, Actavis stipulated to infringement of the '593 patent (which, as noted above, claims the treatment of nociceptive pain with tapentadol) and of the '364 polymorph patent. Appx38. The parties proceeded to trial on the validity of

all of the patents and on infringement of the '130 patent. As Depomed's cross-appeal concerns only infringement of the '130 patent, this brief focuses on the trial evidence relevant to that issue.

Dr. Michael Weinberger, a pain management specialist at Columbia, *see* Appx9184, testified that the severe chronic pain indication on Actavis's proposed label would not "provide any specific instruction to a physician, pharmacist or patient to use Actavis's ANDA product for the specific use to treat polyneuropathic pain." Appx9207. Dr. Weinberger explained that the label contained "no directions about using [the product] for neuropathic pain." Appx9208. Moreover, the CLBP study referenced in the label would not lead a physician to believe the product could be used for neuropathic pain because the patients in the CLBP study "were not screened to determine whether they had a neuropathic component"—meaning one could draw no conclusions from that study about whether tapentadol could be used to treat neuropathic pain. Appx9208-9210.[1] Other evidence introduced at trial indicated that CLBP is most often due to nociceptive, rather than neuropathic, causes. *See* Appx9218-9219; Appx53019.

[1] *See also* Appx9212-9213 ("Q. Dr. Weinberger, as a pain specialist, would you prescribe a product for polyneuropathic pain if it only included clinical trial information on the effectiveness for treating chronic low back pain in the general population of chronic low back pain sufferers? A. No, sir. . . . I would have no idea whether it would be effective for that condition."); Appx9223 ("Q. Dr.

Dr. Weinberger also testified that there were several non-infringing uses of tapentadol hydrochloride, including, for example, the treatment of rheumatoid arthritis and osteoarthritis (both of which cause chronic and severe nociceptive pain). *See* Appx9225; *see also* Appx 9458 (testimony of Plaintiffs' expert agreeing that osteoarthritis is a "common example" of "chronic severe nociceptive pain"). Dr. Weinberger stated that he had prescribed NUCYNTA in his own practice for these uses, and he testified that such uses were "substantial" and not "impractical, aberrant, experimental, hypothetical, far-fetched, or illusory." Appx9225-9228.

Dr. Asokumar Buvanendran, an anesthesiologist and professor of anesthesiology at Rush University Medical School, likewise testified that the severe chronic pain indication in Actavis's label did not instruct or encourage infringement of the '130 patent. *See* Appx10616-10617; Appx10676. Dr. Buvanendran also testified that there were "a substantial number of patients" to whom he had prescribed NUCYNTA ER that fell within the severe chronic pain indication but did not suffer from polyneuropathic pain. Appx10622-10623. He agreed with Dr. Weinberger that two "very common" non-infringing uses of

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Weinberger, just because an analgesic can treat low back pain does that tell a physician that it can also be effective to treat polyneuropathic pain? A. No, sir.").

tapentadol hydrochloride are the treatment of osteoarthritis and the treatment of rheumatoid arthritis. Appx10682-10683.[2]

The court also heard testimony from Plaintiffs' expert, Dr. Michelle Brown, an anesthesiologist and pain management physician. Appx9420. Dr. Brown is a member of Depomed's speakers bureau, "a group of clinicians who educate other practitioners about a particular drug that Depomed markets." Appx11851. She estimated that she is compensated approximately $50,000 per year by Depomed for her work on the speakers bureau. *See* Appx11854.

Dr. Brown testified that she would interpret the chronic severe pain indication in Actavis's label as instructing and encouraging the treatment of polyneuropathic pain because polyneuropathic pain is a type of chronic severe pain. *See* Appx9467-9468; Appx9482. However, Dr. Brown also stated that she based this belief in part on her knowledge of the DPN study that was removed from Actavis's label. *See* Appx9504-9505; Appx11886-11887.

Dr. Brown admitted that tapentadol hydrochloride can be prescribed for non-infringing uses, such as the treatment of "nociceptive pain alone." Appx9516;

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[2] Depomed's assertion in its Statement of the Case (at 21) that "[n]either Actavis's expert [Dr. Weinberg] nor West-Ward's expert [Dr. Buvanendran] testified as to the frequency of any alleged noninfringing uses of their products—and neither defendant provided any other evidence on frequency" is thus demonstrably false. The same goes for Depomed's statement (at 29) that there was "unrefuted evidence that the frequency of [non-infringing] uses [of Actavis's ANDA product] would be rare."

accord Appx9522; Appx11892. But she testified that, in her opinion, the non-infringing uses of Actavis's proposed ANDA product would not be "substantial" because polyneuropathic pain "can and often does present as pain severe enough to require daily around the clock treatment for long term [*sic*] and for which alternative treatments are ineffective." Appx9456-9457; *see also* Appx9471-9472.

The expert testimony that Plaintiffs presented on infringement of the '130 patent was in considerable tension with the evidence Plaintiffs presented to defend the patent's validity. For example, Defendants had argued that the asserted claims of the '130 patent were anticipated or rendered obvious by the '737 patent and the '593 reissue patent, which disclosed the treatment of "pain" with tapentadol hydrochloride. In opposing those arguments, Dr. Brown testified that the '737 and '593 patents did not disclose the treatment of polyneuropathic pain "[b]ecause the words 'polyneuropathic pain' [were] nowhere within" those references. Appx11160. "[B]y definition," Dr. Brown explained, "treating a population of patients who are suffering from severe pain may not include anyone suffering from polyneuropathic pain." Appx11209-11213; *see also* Appx11210 (Brown) ("[B]ecause severe [and] chronic pain . . . [is] not always polyneuropathic pain, . . . in the absence of a[n] explicit reference to or even a suggestion of polyneuropathic pain, a general disclosure of severe pain[or] chronic pain . . . does not necessarily disclose polyneuropathic pain."). Yet Dr. Brown maintained that Actavis's

proposed labeling would encourage or promote the treatment of polyneuropathic pain even though the label—just like the '737 and '593 patents—contained no "explicit reference to or even a suggestion of polyneuropathic pain," Appx11210. This tension is reflected in Depomed's brief on appeal. Depomed maintains that "it would be readily apparent to a physician . . . that the severe chronic pain indication [of Actavis's label] includes polyneuropathic pain even without the words 'polyneuropathic pain' being mentioned in the indication." Depomed Br. 31. Yet Depomed states that the '737 patent's references to "pain" and "severe pain" are inherently limited to nociceptive pain only. *Id.* at 36.

Dr. Brown also testified that the use of opioids such as tapentadol to treat neuropathic pain was and "remains controversial." Appx11169; *see also* Appx188 (noting Plaintiffs' "evidence of literature before, *and even after*, the 2007 filing date of the '130 patent suggesting that there was controversy surrounding the usefulness of opioids in treating neuropathic pain") (emphasis added); Appx9164 (Haussler) (noting that tapentadol is not a first-line option for the treatment of polyneuropathic pain); Appx10700 (Buvanendran) (same); Appx10705-10708 (Buvanendran) (same); Appx11238 (Brown) (same). Depomed reiterates this conclusion in its brief, asserting (at 10) that "before 2007, *and continuing even today*, there was widespread controversy surrounding the use and efficacy of opioids in treating neuropathic pain" (emphasis added). Yet Dr. Brown maintained

that a physician reading the label of Actavis's ANDA product—an opioid—would have understood the product to be intended for use in treating neuropathic pain, even though the label of the product does not mention that type of pain, the only study mentioned in the label is a study of nociceptive pain, and extensive evidence indicated that opioids are not a preferred treatment for polyneuropathic pain.

E. The District Court's Post-Trial Opinion

Following trial, the district court issued a lengthy and detailed opinion regarding the infringement and validity of the patents-in-suit. As relevant here, the court concluded that the '130 patent was not invalid in light of the prior art, but found that Plaintiffs had failed to show that Actavis's proposed labeling would induce or contribute to infringement of the '130 patent.

As to invalidity, the district court first held that the '130 patent was not anticipated by the '737 patent because the '737 patent does not disclose the treatment of polyneuropathic pain. Appx176. The court noted that the patent "never mentions the word 'polyneuropathic pain' or the treatment thereof"; that the only data disclosed in the '737 patent is "from the mouse writhing test, which is a purely nociceptive pain model"; and that "the state of the art prior to the filing of the '130 patent was such that when a physician discussed opioids in regard to the treatment of severe pain at that time, [s/he] did think nociceptive pain." Appx177; *see also* Appx178 (crediting testimony of Plaintiffs' expert that "in the absence of

any context to specifically indicate neuropathic pain, when the term 'pain' is used, a POSA would 'default to nociceptive pain'").

The district court also held that the asserted claims of the '130 patent were not invalid for obviousness-type double patenting over a claim of the '593 reissue patent directed to the treatment of "pain" with tapentadol, for much the same reason. "[A] POSA would have understood the term 'pain' as 'nociceptive pain,'" the district court explained, Appx183, and using an opioid to treat neuropathic pain would not have been obvious in light of the prevailing view in the art that neuropathic pain was refractory to opioids, Appx187.

With respect to induced infringement, the district court found that Actavis's label "does not encourage treatment of polyneuropathic pain," noting that "[i]n addition to carving out Indication 2 [the DPN indication] from its proposed label, Actavis has carved out all other references to neuropathic pain or neuropathy that are contained in the NUCYNTA ER label." Appx156. The court rejected Plaintiffs' argument that intent to infringe could be inferred simply "because DPN is encompassed by Indication 1" (the severe chronic pain indication), citing extensive evidence that those in the industry (including Janssen itself) did not read the severe chronic pain indication as an instruction to prescribe tapentadol to treat polyneuropathic pain. Appx157-160. The court also found that, "even assuming . . . the infringing use is on-label for Actavis's product," the "label only

instructs the user to administer the drug to treat severe chronic pain, which undisputedly includes nociceptive pain," so it "cannot reasonably be understood to be an instruction to engage in the infringing use of administering the drug to treat polyneuropathic pain." Appx164-165. "[E]ven if the label permits administration for polyneuropathic pain," the court explained, "permission is different from encouragement." Appx165.

The court also rejected Plaintiffs' argument that the inclusion of the CLBP study in the label was evidence that Actavis intended for its product to be used to treat polyneuropathic pain. The court noted that the CLBP study was "considered by the FDA, and in fact by Janssen itself, to be a study of *nociceptive* pain," Appx160 (emphasis added), and that Actavis had "presented evidence that, because the study only included information on the effectiveness for CLBP in patients in the general population without establishing whether any of them had a neuropathic component, a physician likely would not make any assessment of whether Actavis's product was useful for neuropathic pain based on the CLBP study in Actavis's label." Appx161-162.

Turning to Plaintiffs' allegations of contributory infringement, the district court found that "Defendants' experts . . . presented extensive evidence of substantial noninfringing uses for Defendants' products," including treatment of "severe chronic pain conditions that are non-neuropathic" such as "chronic non-

healing ulcers, chronic ureter and kidney or bladder obstructions, osteoarthritis, and rheumatoid arthritis." Appx174. The court rejected Plaintiffs' argument (and Dr. Brown's testimony) that these uses were insubstantial, crediting the testimony of Dr. Weinberger and Dr. Buvanendran that treating these conditions "would not be unusual, far-fetched, illusory, impractical, occasional, aberrant, or experimental uses of" tapentadol. Appx175.

SUMMARY OF ARGUMENT

1. The district court did not err—clearly or otherwise—in finding that Actavis's label will not induce infringement of the '130 patent. The evidence at trial established three critical facts that, taken together, compel the conclusion that a physician would not view Actavis's label as instructing, encouraging, or promoting the treatment of polyneuropathic pain. *First*, Actavis carved out the DPN indication from its label and removed all mention of the words "polyneuropathic pain," "neuropathic pain," or variants thereof. *Second*, the only study cited in Actavis's label is the CLBP study, which the evidence showed was a study of *nociceptive* pain. *Third*, as even Plaintiffs' experts admitted—and as Depomed reiterates in its brief—physicians do not consider opioids like tapentadol to be optimal treatments for neuropathic pain, meaning a physician reading an opioid label that does not mention neuropathic pain would not conclude that the

product should be used to treat neuropathic pain. In light of this evidence, the district court correctly concluded that Actavis is not liable for inducement.

Depomed's criticisms of the district court's reasoning are off the mark. *First*, Depomed's assertion that "noninfringing uses are *irrelevant* to the induced infringement inquiry" flatly misstates the law. *Second*, Depomed's contention that the district court incorrectly focused on DPN specifically, rather than neuropathic pain generally, mischaracterizes the district court's opinion. *Third*, Depomed's argument that the district court erred in concluding that the treatment of polyneuropathic pain was not an "intended use" of Actavis's product ignores the ample expert testimony and other evidence supporting the district court's conclusion. Simply pointing to the contrary testimony of its own experts does not enable Depomed to show clear error on the part of the district court. *Finally*, Depomed's contention that the district court incorrectly concluded that the treatment of polyneuropathic pain would be an "off-label use" of Actavis's proposed ANDA product is wrong. Actavis presented evidence showing that Janssen itself did not consider the treatment of polyneuropathic pain "on label" for the severe chronic pain indication. And in any event, the court correctly found that, even assuming *arguendo* that the infringing use *was* "on label," Actavis's label would do no more than *permit* an infringing use, which is not sufficient for inducement liability.

2. Nor did the district court err in finding that Actavis's label will not contribute to infringement of the '130 patent. Actavis cannot be liable for contributory infringement so long as its product has substantial non-infringing uses. The district court heard and credited ample testimony from Dr. Weinberger and Dr. Buvanendran that tapentadol hydrochloride is commonly used to treat pain that is not polyneuropathic—for example, pain resulting from osteoarthritis and rheumatoid arthritis. Depomed does not and cannot show that this finding was clear error. Indeed, that Depomed successfully accused Actavis of infringing a patent claim—claim 8 of the '593 patent—that is *exclusively directed to the treatment of nociceptive pain with tapentadol* (an undisputedly non-infringing use) belies any argument that Actavis's proposed ANDA product has no substantial non-infringing uses.

Depomed suggests that, in order for a non-infringing use to qualify as "substantial," there must be evidence that the non-infringing use constitutes some threshold proportion of all uses (according to Dr. Brown, 50% of all uses). That requirement has no basis in the law. A non-infringing use is "substantial" if it is not "unusual, far-fetched, illusory, impractical, occasional, aberrant, or experimental." *Vita-Mix Corp. v. Basic Holding, Inc.*, 581 F.3d 1317, 1329 n.2 (Fed. Cir. 2009). Actavis presented ample evidence that the non-infringing uses of its product would qualify as "substantial" under that definition.

Moreover, Plaintiffs failed even to address the separate requirement of a contributory infringement claim that the accused product be especially adapted for infringement of the asserted patent. This failure of proof constitutes an independent ground upon which this Court can affirm the district court's conclusion that Actavis did not contribute to infringement of the '130 patent.

The district court's judgment of non-infringement should be affirmed.

STANDARD OF REVIEW

Actavis agrees that the district court's finding of no infringement is a factual finding that this Court reviews for clear error. *See Sanofi v. Watson Labs. Inc.*, 875 F.3d 636, 645 (Fed. Cir. 2017). That standard of review "does not entitle a reviewing court to reverse the finding of the trier of fact simply because it is convinced that it would have decided the case differently." *Anderson v. City of Bessemer City, N.C.*, 470 U.S. 564, 573 (1985). Rather, reversal is permitted only when "the reviewing court on the entire evidence is left with the definite and firm conviction that a mistake has been committed." *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 395 (1948).

ARGUMENT

I. The District Court Correctly Concluded That Actavis Would Not Induce Infringement of the '130 Patent Because Actavis's Label Does Not Recommend, Encourage, or Promote the Treatment of Polyneuropathic Pain

A. Depomed Misunderstands the Legal Requirements of Induced Infringement

For a pharmaceutical company to be liable for induced infringement of a method-of-use patent based on the labeling of its drug product, "[t]he label must encourage, recommend, or promote infringement." *Takeda Pharms. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015). "The question is not just whether instructions describe the infringing mode, but whether the instructions teach an infringing use of the device *such that* we are willing to infer from those instructions an affirmative intent to infringe the patent." *Id.* (alterations, citations, and quotation marks omitted). Moreover, "vague label language cannot be combined with speculation about how physicians may act to find inducement," because that would transform "that which [this Court] ha[s] held is legally irrelevant—mere knowledge of infringing uses—into induced infringement." *Id.* (citations and quotation marks omitted). In a Hatch-Waxman case like this one, "[t]his requirement of inducing acts is particularly important . . . because the statute was designed to enable the sale of drugs for non-patented uses even though this would result in some off-label infringing uses." *Id.*

Depomed entirely mischaracterizes this legal standard. *See* Depomed Br. 63-64. Citing *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042 (Fed. Cir. 2010), Depomed instead asserts that induced infringement must be found if the proposed drug label "will cause at least some users to infringe." That is at best an incomplete statement—and at worst a mischaracterization—of *AstraZeneca*'s holding. *AstraZeneca* affirmed a finding of induced infringement (1) where the instructions of the label, if followed, would *necessarily* cause the user to infringe the asserted method claims; *and* (2) where there was extensive evidence that the accused infringer was "aware of the infringement problems presented by the proposed label" and "nonetheless proceeded with its plans to distribute its generic drug product." *See id.* at 1058, 1060-61.

Depomed's brief suggests that it is sufficient that the label describes a use such that it is *possible* that a user could follow the label instructions and infringe the patent. *See* Depomed Br. 63-64. But that is not what *AstraZeneca* held. Indeed, that reading of *AstraZeneca* was expressly rejected by this Court in *Takeda*, which reaffirmed that it is insufficient if the label merely "describ[es] the infringing mode." 785 F.3d at 631 (quoting *Toshiba Corp. v. Imation Corp.*, 681 F.3d 1358, 1365 (Fed. Cir. 2012)). "The question is not . . . whether a user following the instructions may end up using the device in an infringing way. Rather, it is whether [the] instructions teach an infringing use of the device such

that we are willing to infer from those instructions an affirmative intent to infringe the patent." *Vita-Mix Corp. v. Basic Holding, Inc.*, 581 F.3d 1317, 1329 n.2 (Fed. Cir. 2009). There is no evidence of such affirmative intent in this case. In fact, all of Actavis's actions demonstrate the opposite.

B. Actavis's Label Does Not Recommend, Encourage, or Promote the Treatment of Polyneuropathic Pain

The district court heard ample evidence that physicians would not view Actavis's label as even describing—much less encouraging or promoting—the treatment of polyneuropathic pain. The district court did not clearly err in crediting this evidence and finding that the label does not induce infringement.

First, and most importantly, Actavis affirmatively carved out from its proposed label the DPN indication found in the NUCYNTA label, as well as *all references to neuropathic pain*. The "Indications and Usage" section of Actavis's label thus states only that its product may be used to treat "pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate." Appx52653; Appx54655. Actavis's affirmative decision to carve out all references to polyneuropathic pain from its proposed labeling strongly evidences an intent not to infringe the '130 patent. *See Otsuka Pharm. Co. v. Torrent Pharms. Ltd.*, 99 F. Supp. 3d 461, 485 (D.N.J. 2015) (defendant's decision to carve out the patented indication "would seem to negate any reasonable inference of an active intent to induce infringement").

Second, the "Clinical Studies" section of Actavis's label discusses only the CLBP study. Appx52673. That study, as explained above, was viewed by those in the industry (including the FDA and Grünenthal itself) as a study of nociceptive, not neuropathic, pain, meaning a physician reading the label would not understand that the product had been shown to be effective in treating neuropathic pain. *See* Appx161-162; *see also* Appx9208-9210 (Weinberger). Indeed, even Plaintiffs' expert Dr. Brown admitted that she "wouldn't assume just because something can manage chronic severe low back pain that it would also be effective to treat polyneuropathic pain." Appx9510; *accord* Appx11884; Depomed Br. 9 (admitting that "[j]ust as nociceptive pain and neuropathic pain are separate and distinct, *the treatment of one is not predictive of the other*") (emphasis added); Depomed Br. 36 (same). On the contrary, a physician would likely assume the exact opposite, given that "[o]pioids have been known to treat *purely nociceptive pain*," and "continuing even today, there [is] widespread controversy surrounding the use and efficacy of opioids in treating neuropathic pain." Depomed Br. 10 (emphasis added).

Third, the district court heard ample evidence—including testimony from Plaintiffs' own experts—indicating that skilled artisans do not consider opioids like tapentadol to be first-line treatments for neuropathic pain. Again, Depomed admits as much, stating that that "even today" the use of opioids to treat

polyneuropathic pain is "controvers[ial]." Depomed Br. 10 (emphasis added); *see also* Depomed Br. 26 (noting the district court's agreement with this proposition). That strongly suggests that a physician faced with an opioid label that contains no indication for the treatment of neuropathic pain, no studies involving neuropathic pain, and no mention even of the words "neuropathic pain" would *not* conclude that the opioid could or should be used to treat neuropathic pain. Dr. Ossipov, who testified for Plaintiffs regarding the validity of the '130 patent, agreed with this proposition. He explicitly stated that, in order to for him to conclude that an opioid compound would be useful in treating neuropathic pain, he "would need to see information in a document that would show empirically that it treats polyneuropathic pain"—in other words, he would need to see a *study of neuropathic pain*. Appx11362-11363. These statements directly contradict Depomed's assertion (at 21) that—based on Actavis's proposed labeling, which contains no reference to neuropathic pain and mentions only the CLBP study—"it would be readily apparent to physicians and other prescribers (like the experts) that polyneuropathic pain is an 'intended use' approved by FDA."

Depomed cannot have it both ways. It cannot credibly argue both (1) that a skilled artisan would view prior art references like the '737 and '593 patents, which disclose the use of an opioid to treat "severe pain" generally, as referring *only* to the treatment of nociceptive pain because historically—and "even today"—

opioids are not favored for the treatment of neuropathic pain; and (2) that a skilled artisan would nonetheless view an opioid label stating that the opioid can be used to treat "pain" as an instruction and encouragement to use the drug to treat neuropathic pain. Depomed's first argument is the correct one: as the district court correctly found, a skilled artisan faced with a reference to treating severe pain with an opioid would "think nociceptive pain only." Depomed Br. 24; *see also id.* at 37, 42. It necessarily follows that a skilled artisan reading Actavis's proposed label—which, like the '737 and '593 patents, contains *no reference* to neuropathic pain—would understand the label as an instruction *only* to treat nociceptive pain.

At most, Plaintiffs presented evidence indicating that, because polyneuropathic pain is a type of severe chronic pain, Actavis's label *permits* infringement. But it is not sufficient that the label merely "describ[es] . . . an infringing mode," *Takeda*, 785 F.3d at 831; as the district court correctly stated, "permission is different from encouragement." Appx165; *see also Shire LLC v. Amneal Pharms.*, 2014 WL 2861430, at *4-5 (D.N.J. June 23, 2014) (label stating that drug could be taken "with or without food" did not induce infringement of patent claiming administration of the drug with food because the label was "indifferent to which option is selected" and at most "permit[ted] an infringing use"), *rev'd in part on other grounds*, 802 F.3d 1301 (Fed. Cir. 2015). Nor does it matter that some physicians might find Janssen's DPN studies in their own

research and thus conclude that Actavis's product could be used to treat neuropathic pain. "[V]ague label language cannot be combined with speculation about how physicians may act to find inducement." *Takeda*, 785 F.3d at 632; *see also United Therapeutics Corp. v. Sandoz, Inc.*, 2014 WL 4259153, at *19 (D.N.J. Aug. 29, 2014) (rejecting "the theory that a scholarly scavenger hunt—which may be incited by a reference in [the] proposed label, which may be undertaken by some physicians, and may ultimately result in a discovery which leads some physicians to prescribe [the product for an infringing use], despite Defendant's carve out—may constitute evidence of . . . intent to induce physicians to engage in infringing conduct").[3]

What Depomed is apparently asking for is an instruction on Actavis's label to "prescribe this for everything but polyneuropathic pain." Appx11889 (Brown); *see also* Appx11937 (Brown) ("Q. What would the label look like if somebody wanted to avoid infringement of the '130 patent, in your opinion? A. I would put under limitations of use to prescribe this for everything but polyneuropathic pain."). But that "turns the legal test on its head." *Takeda*, 785 F.3d at 632 n.4.

[3] Depomed's bald assertion (at 66) that Actavis was "aware from [its] own experts that the label presented . . . infringement problems" is flatly wrong. Depomed cites to no evidence supporting this contention, and in fact all of the evidence is to the contrary: Both Dr. Weinberger and Dr. Buvanendran testified that Actavis's label would *not* recommend, encourage, or promote the use of Actavis's tapentadol product to treat polyneuropathic pain.

Depomed "needs to show that [Actavis] took affirmative steps to induce, not affirmative steps to make sure others avoid infringement." *Id.* Depomed failed to make the required showing.

C. Depomed's Attacks on the District Court's Reasoning Lack Merit

Depomed criticizes the district court's reasoning on several grounds, but each of Depomed's arguments is premised on either a misunderstanding of the law or a simple disagreement with the district court's factual findings. Depomed has not come close to showing that the district court incorrectly applied the law or clearly erred in finding the facts.

1. Depomed's argument (at 67) that "noninfringing uses are *irrelevant* to the induced infringement inquiry" is wrong. This Court has stated precisely the opposite, noting that, "*[e]specially where a product has substantial noninfringing uses*, intent to induce infringement cannot be inferred even when the defendant has actual knowledge that some users of its product may be infringing the patent." *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365 (Fed. Cir. 2003) (emphasis added); *see also Takeda*, 785 F.3d at 633 (finding no inducement in part because accused product was "rarely use[d]" for an infringing purpose and "frequently" used for a non-infringing purpose). *Sanofi*, the case that Depomed cites for the proposition that non-infringing uses are irrelevant to the inducement question, says nothing of the sort. Rather, *Sanofi* states that the presence of

substantial non-infringing uses does not *preclude* a finding of inducement. *See Sanofi*, 875 F.3d at 646 (rejecting the argument that, because the accused product had "substantial non-infringing uses not forbidden by the proposed labels, the district court *could not permissibly find intent to encourage an infringing use*") (emphasis added). But the presence of such uses is still highly *relevant* to the inducement inquiry. *See Warner-Lambert*, 316 F.3d at 1365.

Here, the district court credited the testimony of Dr. Weinberger and Dr. Buvanendran that "doctors can and likely will follow the instructions on Actavis's label to prescribe Actavis's product for noninfringing purposes, such as treating nociceptive and neuropathic pain." Appx166. Indeed, Plaintiffs have alleged—successfully—that Actavis's product will infringe claim 8 of the '593 patent, which, by Depomed's own admission, describes *only* the treatment of nociceptive pain with tapentadol (a use that indisputably does not infringe the '130 patent). Accordingly, even accepting Depomed's contention that some doctors will prescribe the product for polyneuropathic pain (and even assuming that Actavis knows that they will do so), "intent to induce infringement cannot be inferred." *Warner-Lambert*, 316 F.3d at 1365.

2. Depomed next contends (at 68-69) that the district court incorrectly focused on DPN rather than polyneuropathic pain generally. That is wrong. Plaintiffs argued to the district court that a physician prescribing tapentadol would

"know[] that FDA requires two pivotal studies for approval of an indication" and thus, upon reading a label "with only one study," would "search[] for the remaining studies that support the indication before prescribing a drug." Appx17873 (¶ 226). Plaintiffs' theory was that a physician conducting such a search would find the DPN study and conclude that the generic tapentadol product could be used to treat DPN (which is a form of polyneuropathic pain). *See, e.g.*, *id.* The portions of the district court's opinion addressing DPN specifically were responsive to this argument. *See* Appx158-160; Appx 170-171 (rejecting the contention that induced infringement could be found because a physician might find the DPN study through a "scholarly scavenger hunt"). Elsewhere in its opinion, the district court focused on polyneuropathic pain generally. *See, e.g.*, Appx156-158; Appx160-169.

3. Depomed also protests (at 69-70) that the district court erred in concluding that Actavis's label does not provide evidence of Actavis's intent that its product be used to treat polyneuropathic pain. This is simply a misguided attempt to reargue the facts on appeal. As explained in detail above, the district court heard extensive expert testimony that a physician reading Actavis's label would not view the label as an instruction to prescribe the product to treat neuropathic pain because (1) the label does not mention polyneuropathic pain; (2) the only study cited in the label was a study of nociceptive pain; and (3) physicians

do not consider opioids like tapentadol to be first-line treatments for neuropathic pain. The district court did not clearly err in crediting that testimony.

Nor did the court clearly err in rejecting Dr. Brown's contrary testimony. As the court explained, Dr. Brown's opinions as to induced infringement impermissibly "relied on her knowledge of the exact information that Actavis carved out (*i.e.*, the presence of the DPN indication and the summary of DPN studies in the NUCYNTA ER label)." Appx158; *see also* Appx9504-9505 (Brown); Appx11886-11887 (Brown). The district court also noted that Dr. Brown had significant "professional connections with Depomed and Janssen" and that part of her work for those entities involved "educat[ing] other practitioners about Depomed's NUCYNTA products." Appx157-158; *see also* Appx11854 (Brown's admission that she is compensated approximately $50,000 per year for her work on Depomed's speakers bureau). The district court's subsequent decision not to accord significant weight to Dr. Brown's testimony regarding how an ordinary physician would interpret Actavis's label was thus entirely reasonable. Indeed, those are precisely the sorts of credibility determinations that district courts are well positioned to make.

4. Finally, Depomed criticizes (at 70-72) the district court's conclusion that the treatment of polyneuropathic pain would be an "off-label" use of Actavis's proposed ANDA product. This contention is flawed for two reasons.

First, Actavis presented ample evidence that a physician *would* consider the treatment of polyneuropathic pain with Actavis's product to be an off-label use. Indeed, *Janssen itself* considered the treatment of polyneuropathic pain to be an off-label use of NUCYNTA when the branded product contained only the severe chronic pain indication. An internal Janssen document that pre-dates the addition of the DPN indication to the NUCYNTA label notes that, "[w]hile some [providers] are using tapentadol to treat chronic low back pain, *many more are treating conditions off-label*. *Conditions include DPN . . . [and] postherpetic neuralgia . . . .*" Appx53069 (emphasis added); *see also* Appx9502-9504 (Brown). The district court did not clearly err in crediting this evidence. And even Depomed admits that a plaintiff faces a "difficult hurdle" in showing that a defendant intends its product to be used for off-label uses, "given that off-label uses are not approved uses by FDA." Depomed Br. 71. For the reasons stated above, Plaintiffs did not clear that hurdle here.

Second, the district court also found in the alternative that, even assuming "the infringing use is on-label for Actavis's product," Actavis's label would, at most, "*permit*[] administration for polyneuropathic pain." Appx164-165 (emphasis added). And, as the district court correctly stated, that is not sufficient for inducement liability. Appx165; *see also Takeda*, 785 F.3d at 631; *Shire*, 2014 WL 2861430, at *5 ("[P]ermission is different from encouragement.").

The district court's judgment of no induced infringement should be affirmed.

II. The District Court Correctly Concluded That Actavis Would Not Contributorily Infringe the '130 Patent Because Actavis's Proposed ANDA Product Has Substantial Non-Infringing Uses and Is Not Especially Made or Adapted to Infringe the '130 Patent

A. Depomed Ignores the Legal Standard For Contributory Infringement

A defendant can be liable for contributory infringement only if the accused product is not "suitable for substantial non-infringing use." *Vita-Mix,* 581 F.3d at 1327 (quoting 35 U.S.C. § 271(c)). "[N]on-infringing uses are substantial when they are not unusual, far-fetched, illusory, impractical, occasional, aberrant, or experimental." *Id.* The plaintiff has the burden to "prove the lack of substantial non-infringing uses." *Toshiba Corp.*, 681 F.3d at 1363. The plaintiff must also prove that the product is "especially made or especially adapted for use in an infringement of [the] patent." *Lucent Techs., Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1320 (Fed. Cir. 2009).

B. The District Court Correctly Found That Actavis's Proposed ANDA Product Has Substantial Non-Infringing Uses: Treating Nociceptive Pain and Mononeuropathic Pain

The district court heard extensive testimony from Drs. Weinberger and Buvanendran that tapentadol hydrochloride is commonly used to treat types of non-polyneuropathic (*i.e.*, nociceptive and mononeuropathic) pain—for example, rheumatoid arthritis and osteoarthritis. *See, e.g.*, Appx9225 (Weinberger); Appx10622-10623 (Buvanendran); Appx10682-10683 (Buvanendran). Moreover,

even Plaintiffs' expert Dr. Brown admitted that the majority of her patients suffering from severe pain have no polyneuropathic component to that pain. *See* Appx11181-11182 (Brown) (admitting that only "40 to 50 percent" of severe pain sufferers have "some component of their pain due to polyneuropathic pain"). This testimony provides ample basis for the district court's conclusion that the potential non-infringing uses of Actavis's proposed ANDA product are "substantial" and not "impractical, aberrant, experimental, hypothetical, far-fetched, or illusory," Appx9225-9228 (Weinberger); *see also Vita-Mix*, 581 F.3d at 1327.

Depomed's statement (at 74) that it presented "unrefuted evidence that the 'frequency' of [non-infringing] uses would be *rare*" is thus simply a mischaracterization of the record. Depomed's evidence was not "unrefuted" at all. Drs. Weinberger and Buvanendran testified that the non-infringing uses would be "common," Appx10682-10683, and Depomed's expert Dr. Brown testified the opposite. The district court credited Drs. Weinberger and Buvanendran and did not credit Dr. Brown. *See, e.g.*, Appx174-175. Depomed does not and cannot show that the district court clearly erred in so doing. *Cf. Anderson*, 470 U.S. at 575 (finding of fact that is based on a trial judge's "decision to credit the testimony of one of two or more witnesses, each of whom has told a coherent and facially plausible story that is not contradicted by extrinsic evidence . . . can virtually never be clear error").

Indeed, Depomed's contention that Actavis's tapentadol product has no substantial non-infringing uses is fundamentally irreconcilable with Plaintiffs' (successful) allegations of infringement of the '593 patent. The '593 patent, by Depomed's own admission, "is limited to the treatment of nociceptive pain, which is *separate, distinct, and not predictive of polyneuropathic pain treatment*." Depomed Br. 41 (emphasis added). The *only way* Actavis's product can infringe the '593 patent, then, is by treating nociceptive pain—but the treatment of nociceptive pain is a use *that does not infringe* the '130 patent.

Depomed's brief appears to suggest (at 73-74) that, in order to be deemed "substantial" in the contributory infringement context, non-infringing uses must meet some numerical threshold. This argument echoes the testimony of Dr. Brown, who stated that, in her view, "substantial" would mean "greater than 50 percent." Appx9521; *see also* Appx9522 ("Substantial to me means more likely than not."). But Depomed cites to no case imposing such a numerical threshold, and for good reason—this requirement has no basis in the law. *See, e.g.*, *Sanofi v. Glenmark Pharms. Inc., USA*, 204 F. Supp. 3d 665, 684 (D. Del. 2016) (concluding that non-infringing uses were "substantial" where approximately 20% of patients who took the accused drug product were not taking it in an infringing manner).

The only relevant question, as this Court's precedents make clear, is whether the non-infringing uses are "substantial"—that is, whether they are "not unusual, far-fetched, illusory, impractical, occasional, aberrant, or experimental." *Vita-Mix*, 581 F.3d at 1327; *see also In re Bill of Lading Transmission & Processing Sys. Patent Litig.*, 681 F.3d 1323, 1337 (Fed. Cir. 2012) (same). As Drs. Weinberger and Buvanendran testified, and as the district court correctly found, the non-infringing uses here meet that standard. Indeed, Dr. Buvanendran testified that using tapentadol to treat osteoarthritis and rheumatoid arthritis—two undisputedly non-infringing uses, *see* Appx9474 (Brown)—would be "very common." Appx10683. And again, Depomed should not be heard to argue that the treatment of nociceptive pain with tapentadol is an "insubstantial use" after suing Actavis for infringing a patent claim directed to that very indication.

C. Plaintiffs Offered No Evidence That Actavis's ANDA Product Is Especially Made or Adapted to Infringe the '130 Patent

Because the district court found that Actavis's ANDA product has substantial non-infringing uses, it never reached the issue of whether the ANDA product is "especially made or especially adapted" for an infringing use—an independent requirement for a claim of contributory infringement. 35 U.S.C. § 271(c). Plaintiffs failed to present *any* evidence on—or even to address—this element of their contributory infringement claim. Plaintiffs' expert at trial could not give an opinion as to whether Actavis's product is especially made for treating

polyneuropathic pain, *see* Appx9517, and Plaintiffs' post-trial briefing did not address this aspect of the contributory infringement inquiry. *See* Appx17711-17714. That failure is unsurprising. For the reasons stated throughout this brief, Actavis's ANDA product is *not* especially made or adapted to treat polyneuropathic pain. Plaintiffs' failure of proof on this element provides an independent ground upon which this Court can affirm the judgment below. *See, e.g.*, *Schaefer Fan Co., Inc. v. J & D Mfg.*, 265 F.3d 1282, 1290-91 (Fed. Cir. 2001) (appellate court will not "supplement a record or take additional evidence to correct a failure of proof" in the district court).

CONCLUSION

For these reasons, Actavis respectfully requests that the Court affirm the district court's judgment of non-infringement of the '130 patent as to Actavis.

Dated: January 31, 2018

Respectfully submitted,

/s/ *Michael E. Joffre*

Michael E. Joffre
William H. Milliken
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 New York Avenue
Washington, DC 20005
202-371-2600 (telephone)
202-371-2540 (facsimile)
mjoffre@skgf.com
wmilliken@skgf.com

Counsel for Defendant-Appellee
Actavis Elizabeth LLC

FORM 30. Certificate of Service

Form 30
Rev. 03/16

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

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Michael E. Joffre	/s/ Michael E. Joffre
Name of Counsel	Signature of Counsel

Law Firm	Sterne, Kessler, Goldstein & Fox P.L.L.C.
Address	1100 New York Avenue, NW
City, State, Zip	Washington, DC 20005
Telephone Number	202-772-8856
Fax Number	202-371-2540
E-Mail Address	mjoffre@skgf.com

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/s/ Michael E. Joffre

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Michael E. Joffre

(Name of Attorney)

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