UNITED STATES COURT OF APPEALS

FOR THE NINTH CIRCUIT

KARIN KLEIN, Plaintiff – Appellant, v. TAP PHARMACEUTICAL PRODUCTS, INC.; ABBOTT LABORATORIES. Defendants – Appellees.	No. 11-17250 D.C. No. 2:08-cv-00681-RLH-RJJ District of Nevada, Las Vegas **Motion for Stay of Mandate Pending Petition to the Supreme Court tor Certiorari**

Appeal from the United States District Court
for the District of Nevada
Roger L. Hunt, Senior District Judge, Presiding

Submitted May 14, 2013
San Francisco, California

Decided May 17, 2013

Rehearing, and Suggestion of Rehearing en Banc, denied ~~August 30, 2013~~ **July 30, 2013**

Before: CLIFTON and BEA, Circuit Judges, and DUFFY,[1] District Judge.

[1] The Honorable Kevin Thomas Duffy, U.S. District Judge for the Southern District of New York, sitting by designation.

Plaintiff–Appellant Karin Klein hereby moves the Court to stay the mandate, up to 90 days, pending her petition to the Supreme Court for certiorari. Fed. R. App. P. 41(d)(2); 9th Cir. R. 41-1.

This appeal arises out of a failure-to-warn, pharmaceutical products liability lawsuit brought by Ms. Klein, who alleged serious injuries caused by her treatment with Lupron, beginning when she was 17 years old and resulting in total disability. The jury ruled in favor of the drug companies and the district court entered judgment accordingly. In this appeal, Ms. Klein sought a new trial. The panel affirmed. Ms. Klein rehearing and rehearing en banc, without success.

Ms. Klein contends that panel's decision was based, at least in part, on erroneous belief that the Lupron taken by Ms. Klein contained a different formulation of the drug than the Lupron referenced in the prior labels that the district court prohibited her from introducing at trial. This may not seem at first blush like an issue warranting intervention by High Court. But this is indeed a question of national importance. Lupron, in the formulation taken by Ms. Klein is popular and widely prescribed across the country. The court's erroneous label ruling will likely impact other women as they seek to hold Abbott responsible for devastating medical conditions they allege are caused by Lubron—complications that the prior labels show Abbott was previously are of but chose not to warn against.

Ms. Klein also contends that the panel's erroneously concluded that adverse incident reports (known as MedWatch reports) were properly excluded on the basis of hearsay, and because they were irrelevant on the issue of causation. The panel's decision, Ms. Klein contends, is contrary to federal regulations, which require that drug manufacturers revise their drug labeling to include a warning "as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved." *See* 21 CFR 201.80(e). A drug manufacture's required diligence includes taking into account new safety information including, among other things listed in the regulation, an *adverse event report*. *See* 21 U.S.C. § 355-1(b). The court's decision is also contrary to the Supreme Court's recent decision in *Matrixx Initiatives, Inc. v. Siracusano*, — U.S. —, 131 S.Ct. 1309 (2011) and the decisions of other circuits that have considered the issue.

This issue also involves a questions of exceptional importance—to the many women who believe they have been injured by Lupron after inadequate warning of the drug's potential adverse effects, but also, more broadly, to the many would-be plaintiffs in a wide-range of drug cases who now will be barred from use of adverse incident reports in proving their cases.

Because Ms. Klein lost her case at trial, and there is no stay of the cost award levied against her in the district court, Abbott will not be unduly burdened by a stay of the mandate.

FACTUAL BACKGROUND

This is a direct appeal from a final judgment (CR 308 [1 ER 2]) entered in favor of defendants-appellees in a pharmaceutical product liability action, following a jury trial and defense verdict (CR 302), including an award of costs taxed against appellant in the amount of $17,577.12 (CR 309 [1 ER 1]).

This appeal arises out of a failure-to-warn, pharmaceutical products liability lawsuit brought by plaintiff-appellant Karin Klein (Ms. Klein) against defendants-appellees TAP Pharmaceutical Products Inc. ("TAP") and Abbott Laboratories ("Abbott") (collectively, "TAP-Abbott"). CR 1 at 10-15 (Complaint). The pharmaceutical at issue is Lupron Depot 3.75 mg ("Lupron"). CR 1 at 10-14; CR 136 at 1-2 [2 ER 220-21]. In 1990, the federal Food and Drug Administration ("FDA") approved Lupron for the temporary management of pain in women with endometriosis. CR 136 at 2 [2 ER 221].

Karin Klein was 17 years old when she was prescribed Lupron 3.75 mg by her gynecologist, Gary Wright, M.D. 8/4/2011 AM *Trans.* at 536:25 – 537:1, CR 136 at 2 [2 ER 221]. She received six injections over a six month period, from August 2005 to January 2006. CR 136 at 2 [2 ER 221]. The Lupron injections caused Ms. Klein to suffer very serious side effects, which have left her permanently disabled. *See* 8/3/2011 AM *Trans.* at 282:22-23 [4 ER 661]; 8/3/2011 PM *Trans.* at 493:20 – 494:3 [5 ER 872-73]; 8/2/2011 PM *Trans.* at 169:20 – 171:5 [4 ER 538]; *see also* Plaintiff's Exhibits 29 (records from W. Reid

Litchfield, M.D – Desert Endocrinology), 30 (records from James Flowers, M .D. & Dr. Andrew Morovati), and 80 (disability letter – military doctor).

Ms. Klein read the Lupron Depot 3.75 mg packaging label[2] thoroughly after the first injection. 8/4/2011 AM *Trans.* at 539:6-10 [5 ER 918]. However, the label (dated January 2005) provided no warnings for many of the adverse events she has experienced, including but not limited to:

- thyroid disease;
- extreme or permanent bone-density loss;
- bone mass development inhibition;
- neck and back pain;
- long term suffering of warned adverse events.

See 8/4/2011 AM *Trans.* at 539-40 [5 ER 918-20]; *see also* Plaintiff's Exhibit 81. Moreover, had warning of these risks been adequately communicated to Ms. Klein, she would not have taken the Lupron shots; 8/4/2011 AM *Trans.* at 540:8-18 [5 ER 920]. TAP-Abbott took part in the clinical studies, the manufacture and the marketing of Lupron 3.75 mg.

[2] The January 2005 Lupron Depot 3.75 mg label was admitted at trial as Plaintiff's Exhibit 81 and Defendants' Exhibit 501. *See* CR 306 at 7; 305 at 1.

ARGUMENT

I. The Excluded Lupron Labels Contained Information Regarding the Same Formulation of Lupron, Not a Different Formulation

In the panel's Memorandum Decision, the court concluded that,

> **[t]he district court did not abuse its discretion in excluding the challenged Lupron labels because they all contained information regarding the side effects of different formulations of Lupron, rendering them insufficiently relevant, unduly prejudicial, and likely to confuse the jury.**

To the contrary, all the proffered labels contained information regarding the same formulation of Lupron, as clearly reflected in the record. Ms. Klein received Lupron 3.75 mg ("Leuprolide Acetate") with the 2005 U.S. labeling. The excluded 1995 and 1996 U.S. labels also were for Lupron 3.75 mg ("Leuprolide Acetate")—the same formulation. *See* 2 ER at 275-77 (1995 label), 280-83 (1996 label) (also attached to the Opening Brief at Addendum B-1, B2, B-3). The 2010 Danish label for Lupron 3.75 ("Leuprorelin Acetate") is also the same formulation.[3] *See* 2 ER 295-305, 308 (Danish label).

In fact, there is no evidence whatsoever in the record that the excluded prior Lupron 3.75 mg labels are for a different formulation than the Lupron 3.75 mg that Ms. Klein was administered to treat her endometriosis.

---

[3] Please refer, for example, to the label information listed for Leuprorelin Acetate on the National Institutes of Health's National Library of Medicine DailyMed service at http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=60aad237-e1da-4705-cbbb-b3ca79e89ad8 (permanent link).

The confusion here perhaps emanates from the fact that there also was an excluded prior label for a Lupron 7.50 mg formulation, which was approved prior to 1990 for the treatment of advanced prostate cancer in men (approved prior to 1990, when the label for Lupron 3.75 mg was approved with an indication for treatment of endometriosis). Prior to the panel's memorandum decision, it has never been asserted or held that the Lupron 3.75 mg approved in 1990 (the subject of the excluded prior labels) is a different formulation from the Lupron 3.75 mg that was administered to Ms. Klein. They are the exact same drug—only the label has changed.

This issue lies at the heart of Ms. Klein's appeal. Not only are the 1995-1996 Lupron Depot 3.75 mg labels for the same formulation of the drug, they *essentially admit* the allegation that Lupron 3.75 mg is associated with thyroid enlargement and extreme bone density loss—two of the adverse events suffered by Ms. Klein and omitted from the 2005 label she was given. *See id.*; *see also* CR 136 at 2-3 [2 ER 221-22] (Stipulated Facts); 1 SER 173–188 (2005 Lupron label—also attached to Ms. Klein's reply brief at Addendum B–5); *Opening Brief* at 6-8 and 18-22). Moreover, the exclusion of the prior labels was devastating to Ms. Klein's presentation of her case. In particular, it deprived her of the best means of rebutting the emphatic testimony of appellees' expert that the association she was

claiming (the association contained in the prior labels, but missing from the 2005 label) ***was biologically impossible***.[4]

The district court never found that the prior Lupron 3.75 mg labels were for different formulations, as the Memorandum Decision erroneously assumes; rather, the district court concluded that the *Lupron 7.50 mg* labels and the *foreign* labels were not admissible because they were for different formulations. *See* 7/15/2011 *Trans.* at 13:11-15:6 [1 ER 84-86]; 8/2/2011 AM *Trans.* (CR 277) at 130:24-25 [1 ER 68]. In fact, all the Lupron 3.75 mg formulations are the same. The district court nevertheless held that only the label for the 2005 Lupron 3.75 actually administered to Ms. Klein was relevant and admissible, disregarding that the prior labels for Lupron Depot 3.75 mg—the same drug Ms. Klein was administered—had essentially already admitted the association she was attempting to prove at trial. The panel makes the same error based on its incorrect assumption that the formulations are different. Rehearing should be granted.

---

[4] TAP-Abbott's expert, Dr. Richard Blackwell, testified at trial that it was "biologically impossible" for Lupron to affect the thyroid gland:

> Well, you might say, well, okay. What about the thyroid gland itself? Right? There are no receptors for GnRH. So there is no basic key on the thyroid gland for Lupron. Therefore, it is absolutely biologically impossible for Lupron to affect the thyroid gland. No textbook, no article has ever supported that contention. ***It's simply biologically impossible.***

8/5/2011 PM *Trans.* at 818:5-10 [1 ER 22] (emphasis added).

II. As a Matter of Law, MedWatch Reports Should be Admissible to Show Notice, Even if they are Insufficiently Reliable, by Themselves, to Prove Causation

The panel concludes that MedWatch reports concerning Lupron 3.75 mg were properly excluded, characterizing them as

> **hearsay reports of uncertain reliability, lacking information relevant to causation.**

Overlooked by the panel is that Ms. Klein presented other evidence on the issue of causation—The MedWatch reports were relevant to the issue of *notice*. Moreover, given that federal regulations require that adverse incident reports be monitored and reviewed by manufacturers for reasonable evidence of an association of a serious hazard with an approved drug, the admissibility of such reports to prove notice in a product liability action should be determined by this Court as a matter of law, not based on deference to the district court's findings in a particular case.

Federal regulations require that drug manufacturers, "shall revise their drug labeling to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved." 21 CFR 201.80(e). A drug manufacture's required diligence includes taking into account "new safety information," in particular "information derived from a clinical trial, an *adverse event report*, a post approval study, or *peer-reviewed biomedical literatur*e." 21 U.S.C. § 355-1(b) (emphasis added). Ms. Klein attempted to introduce both adverse even reports (MedWatch) and

medical journals and each was excluded by the district court. *See* 7/15/2011 *Trans.* at 8:20 – 10:10; and 24:9 – 25:8 [1 ER 79-81, 95-96]); 8/2/2011 AM *Trans.* at 69:3-24, 70:1-15, 76:20-82 [1 ER 43-51]; CR 281 (Ms. Klein's Trial Brief submitted as Offer of Proof Regarding Evidence of Certain Adverse Event Reports); CR 209 (Ms. Klein's objection to Defendants' MIL re Adverse Events Reports); 8/5/2011 PM *Trans.* at 868:17-870:5 [1 ER 34-36]); CR 169 Ms. Klein's Motion in *Limine* No. 10 regarding admission of similar incidents) at 1-5; CR 167 (Ms. Klein's Motion *in Limine* No. 8 regarding admission of MedWatch reports and adverse events) and CR 169; *Opening Brief* at 8-10. This was error.

Even if they are insufficiently reliable by themselves to prove causation, adverse incident reports, such as MedWatch reports, clearly are admissible to prove other facts in issue, such as notice. *See, e.g.*, *Weyth v. Levine*, 555 U.S. 555, 129 S. Ct. 1187 (2009) and *Delaware v. Rowatt*, 244 P.3d 765 (Nev. 2010) (adverse event reports admitted at the trial). In *Benedi v. McNeil–P.P.C., Inc.*, 66 F.3d 1378 (4th Cir. 1995), the Fourth Circuit ruled that the district court properly admitted case reports known as Drug Experience Reports ("DERs") to show that the defendant had notice that its product could cause the type of injury sustained by the plaintiff. The court noted that adverse reaction reports offered to show the defendant's knowledge of the potential hazard are not hearsay because they are not

offered to prove the truth of the matter asserted but rather to show the defendant's state of mind.[5] Id., 66 F.3d at 1385.

21 CFR 201.80(e) requires that drug manufacturers such as TAP-Abbott craft adequate labels and ensure that the warnings remain adequate. *Wyeth v. Levine*, 555 U.S. 555 (2009). The Supreme Court recently undertook an in-depth analysis of the importance of attention to adverse event reporting data—and their relevance to questions of notice—in *Matrixx Initiatives, Inc. v. Siracusano*, — U.S. —, 131 S.Ct. 1309 (2011), a shareholder securities fraud action based on a pharmaceutical company's concealment of adverse event data. The Court considered a great deal of evidence and argument from both the medical and scientific research community about the importance of adverse event data in formulating an opinion about causation and its relevance to placing everyone on notice of potential serious hazards associated with pharmaceutical drugs. *Id.* at 1319-1320 (citing briefing from a group of preeminent medical researchers who routinely rely on adverse event data). The Supreme Court held that even though

[5] The court also rejected the defendant's contention that the reports were unduly prejudicial and should have been excluded under Fed. R. Evid. Rule 403. The court concluded that the dissimilarities between the plaintiff's situation and those described in the DERs "do not affect the admissibility of the evidence, but rather go to the weight the jury gives to the evidence." *Id.* at 1386. Accord *Smith v. Wyeth-Ayerst Labs.*, 278 F. Supp. 684, 704 (W.D. N.C. 2003) (because the evidence was offered to prove notice and was accompanied by a limiting instruction, "the Court cannot find that the probative value is substantially outweighed by the danger of unfair prejudice to Defendant.").

adverse event reports may not be statistically significant of causation in and of themselves, a lack of statistical significance does not itself render them unreliable. *Id*. at 1320-1321. To the contrary, the Supreme Court deemed adverse event reports material to any consideration of whether a pharmaceutical company had notice of certain dangers associated with its drug and the possibility–even if not statistically significant—of a causative link. *See id.* at 1322-1323. The panel's conclusion that the MedWatch reports in this case were nevertheless inadmissible hearsay, and unreliable, misunderstands purpose for which the evidence was offered—proof of notice—and its probative value and admissibility for this purpose.

III. This Case Involves Questions Of Exceptional National Importance

The questions presented here are questions of national health, and women's health in particular. Abbott has plead guilty to criminal conduct in connection with its marketing of Lupron, and paid hundreds of millions of dollars in civil penalties and criminal fines in this regard. Essentially, Plaintiff alleges that Abbott purposefully removed the thyroid disease and bone density loss warnings, which existed in prior Lupron 3.75 mg labels, for the indication of endometriosis, in order to bolster its sales of the drug she was administered. Had she and her doctor been given the prior warnings for thyroid disease and extreme bone density loss, she never would have taken the drug, and it is safe to assume that other women across

the nation are in the same position now that Ms. Klein was in during the 2005 period, when she was administered the drug.

CONCLUSION

For the reasons set forth above, it is respectfully requested that this Court stay the mandate, up to 90 days, pending her petition to the Supreme Court for certiorari.

DATED: August 7, 2013.

STERLING LAW, LLC

/s/ Beau Sterling

BEAU STERLING
Counsel for Appellant

CERTIFICATE OF SERVICE

I hereby certify that on this date, August 7, 2013, I electronically filed the foregoing **Motion for Stay of Mandate Pending Petition to the Supreme Court tor Certiorari** with the Clerk of the Court for the United States Court of Appeals for the Ninth Circuit by using the appellate CM/ECF system. Participants in the case who are registered CM/ECF users will be served by the appellate CM/ECF system. All parties in this matter are registered users.

/s/ Beau Sterling

BEAU STERLING