Keywords: **enablement; written description; claim construction; anticipation**

General: **The specification does not need to describe unclaimed variants, at least with respect to methods of treating diseases.**

United Therapeutics Corp. v. Liquidia Technologies, Inc.
United States Court of Appeals for the Federal Circuit
No. 2022-2217, 2023-1021
Decided: July 24, 2023

I. Facts

Plaintiff-cross-appellant United Therapeutics Corporation ("United Therapeutics") owns U.S. Patents No. 9,593,066 ("the '066 patent") and No. 10,716,793 ("the '793 patent"), and the New Drug Application (NDA) for Tyvaso, an inhaled solution formulation of the pharmaceutical treprostinil used for treating pulmonary hypertension (PH). Experts consider that there are five subgroups of pulmonary hypertension. Groups 1, 3, 4, and 5 are caused by conditions affecting the pulmonary arteries or precapillary vessels of the lungs, while Group 2 typically develops as a result of a cardiac-based etiology.

The '066 and the '793 patents are directed to pharmaceutical compositions comprising treprostinil, used for treating pulmonary hypertension and methods of treating pulmonary hypertension via inhalation of treprostinil, respectively. Defendant-appellant Liquidia Technologies, Inc. ("Liquidia") filed an NDA for Yutrepia, a dry powder inhalation formulation of treprostinil also approved for the treatment of pulmonary hypertension. In response to Liquidia's NDA, United therapeutics sued Liquidia in the United Stated District Court for the district of Delaware alleging infringement of the '066 patent. Shortly after Liquidia filed its NDA, United Therapeutics filed another patent application that eventually issued as the '793 patent.

In parallel with United Therapeutics' suit, Liquidia filed a petition for *inter partes* review (IPR) of the '793 patent, alleging that all claims would have been unpatentable as obvious over prior art at the time of the invention. On July 19, 2022, the Board issued a Final Written Decision finding all claims of the '793 patent unpatentable as obvious. United Therapeutics filed a Request for Rehearing, challenging whether various asserted references qualified as prior art. In its Rehearing Decision, the Board found that the references were prior art, and again held the claims of the '793 patent unpatentable as obvious. United therapeutics filed a Notice of Appeal in the case on April 26, 2023. The appeal is currently pending at the Federal Circuit.

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Claim 1 of the ‘793 patent reads as follows:

> 1. A method of treating pulmonary hypertension comprising administering by inhalation to a human suffering from pulmonary hypertension a therapeutically effective single event dose of a formulation comprising treprostinil or a pharmaceutically acceptable salt thereof with an inhalation device, wherein the therapeutically effective single event doses comprises from 15 micrograms to 90 micrograms of treprostinil or a pharmaceutically acceptable salt thereof delivered in 1 to 3 breaths.

In district court, United Therapeutics argued that Liquidia’s product, when marketed, would directly infringe claims 1, 4, and 6-8 of the ‘793 patent and would also induce infringement of those claims. Liquidia responded that the asserted claims were invalid as lacking adequate enablement and written description under 35 U.S.C. § 112. The district court found that United Therapeutics showed that a single administration of treprostinil, as required by claim 1, improves a patient’s hemodynamics (the metric by which efficacy of pulmonary hypertension treatments are measured), establishing that administration of Liquidia’s Yutrepia at the claimed doses will also improve a patient’s hemodynamics. The district court concluded that United Therapeutics thus proved by a preponderance of the evidence that the administration of Yutrepia will directly infringe the claims at issue in ‘793 patent.

The district court further found that the asserted claims were not invalid for lack of enablement or written description. First, the district court construed “treating pulmonary hypertension” as encompassing all five groups of pulmonary hypertensions, nothing that the specification of the ‘793 patent expressly includes all five groups when describing “pulmonary hypertension.” Second, the district court found that a skilled artisan would not need to engage in undue experimentation to practice the full scope of the claimed treatment of pulmonary hypertension. Third, the district court found that the claims were not invalid for lack of written description.

The ‘066 Patent

In the district court, United therapeutics argued that Liquidia infringed claims 1-3, 6, 8, and 9 of the ‘066 patent. Liquidia responded that claims 1-3, 6, and 9 were invalid under 35 U.S.C. § 102 and that claims 1-3 and 6 were invalid as lacking written description support.

Liquidia appeals and United Therapeutics cross-appeals the ruling of the district court, raising several issues on appeal.

II. Issues and Discussion

(1) *Did the district court err in construing the claim limitation “treating pulmonary hypertension” in claim 1 of the ‘793 patent does not include safety and efficacy?*

The district court did not err. The court held that it is improper to read in safety and efficacy requirements into the claims where they are not recited, and to do so would be to insert the FDA’s responsibilities into claims.

(2) *Did the district court err in finding the asserted claims of the '793 patent enabled and supported by the written description?*

The district court did not err. Liquidia argued that the specification of the '793 patent provides no guidance or examples of treating Group 2 pulmonary hypertension patients, and thus a skilled artisan would have to engage in undue experimentation to practice the full scope of the claimed invention.

As a preliminary matter, the court agreed with the district court that "treating pulmonary hypertension" includes treating all five groups of pulmonary hypertension patients. Further, the court held that the district court properly relied on expert testimony in finding that a skilled artisan would understand that administering treprostinil as required in claim 1 of the '793 patent would improve patient hemodynamics, even though a physician may have safety concerns in treating Group 2 pulmonary hypertension patients. The court also held that the district court did not err in finding that the claims of the '793 patent are supported by an adequate written description. The court stated that the written description requires that the specification reasonably convey to those skilled in the art that the inventor had possession of the claimed invention as of the filing date, and that the specification in the '793 patent sufficiently describes the recitations and limitations of claim 1.

(3) *Did the district court err in finding Liquidia liable for induced infringement of claims 1, 4, and 6-8 of the '793 patent?*

The district court did not err. Liquidia asserts that it cannot be held liable for induced infringement because the '793 patent was found to be unpatentable in an IPR, and an unpatentable or invalid patent cannot be infringed. United Therapeutics responds that the Board's decision on the '793 patent is not final, and a non-final Board decision does not defeat Liquidia's liability for inducing infringement of the '793 patent.

The court agreed with United Therapeutics, holding that a pending, non-final litigation does not negate an intent to infringe that is otherwise supported by evidence. Moreover, the court held that the district court did not err in its conclusion that Liquidia induced infringement. Although Liquidia did not provide hemodynamic data, it merely needs to instruct doctors and patients to administer a therapeutically effective single event dose to induce infringement.

(4) *Did the district court err in finding claims 1-3 of the '066 patent anticipated under 102, or in finding that claims 1-3 were infringed by Liquidia?*

The district court did not err. Claims 1-3 of the '066 patent are directed to a product (i.e., treprostinil) prepared by particular processes (i.e., alkylation and hydrolysis). Consequently, the court applied a standard product-by-process analysis of claims 1-3, and simply ignored the process limitations. As there was no structural or functional differences shown between the treprostinil found in the prior art and the treprostinil of claims 1-3, the court held that claims 1-3 are invalid as anticipated under 102.

As to the infringement question, the court held that it need not evaluate the parties' infringement arguments, as unpatentable or invalid claims cannot be infringed, and the district court did not clearly err in finding claims 1-3 invalid as anticipated under 102.

(5) *Did the district court err in finding that Liquidia does not infringe claims 6 and 8 of the '066 patent?*

The district court did not err. United Therapeutics argues on cross-appeal that the district court clearly erred in finding that Liquidia does not infringe claims 6 and 8 of the '066 patent, alleging that the asserted claims require that the treprostinil salt be stored at ambient temperature, and that Liquidia stores treprostinil salt at ambient temperature during production, thus infringing the claims. United Therapeutics also contends that Liquidia's promise not to make its product with batches of treprostinil salt that were stored at ambient temperature is insufficient to avoid a finding of infringement.

Liquidia asserts that it's NDA requires that the treprostinil salt be stored at a temperature of 2-8 degrees Celsius, and that the NDA storage specifications are regulatory requirements, not mere recommendations or promises. Further, Liquidia asserted that United Therapeutics mischaracterized Liquidia's production process, and that at no point is the treprostinil stored at ambient temperatures.

The court held that the district court did not err in finding non-infringement on Liquidia's behalf.

III. Conclusion

The Federal Circuit affirmed the district court on each issue raised on appeal. The Federal Circuit's decision makes clear that the specification does not need to address every possible disease subtype or non-responsive patient population to satisfy 112, as long as those limitations are not captured in the claims. Also, the decision made clear that it is improper to import safety and efficacy limitations into claims absent such recitations. The court maintained that safety and efficacy of claimed pharmaceutical products and processes is a question for the FDA.