United States Court of Appeals for the Federal Circuit

UNITED THERAPEUTICS CORPORATION,
Plaintiff-Cross-Appellant

v.

LIQUIDIA TECHNOLOGIES, INC.,
Defendant-Appellant

2022-2217, 2023-1021

Appeals from the United States District Court for the District of Delaware in No. 1:20-cv-00755-RGA-JLH, Judge Richard G. Andrews.

Decided: July 24, 2023

SANYA SUKDUANG, Cooley LLP, Washington, DC, argued for defendant-appellant. Also represented by JONATHAN DAVIES; DEEPA KANNAPPAN, Palo Alto, CA; ERIK BENTON MILCH, Reston, VA.

WILLIAM M. JAY, Goodwin Procter LLP, Washington, DC, argued for plaintiff-cross-appellant. Also represented by WILLIAM COVINGTON JACKSON, JAIME SANTOS, ROHINIYURIE TASHIMA, JENNY J. ZHANG; GERARD JUSTIN CEDRONE, Boston, MA; ADAM WILLIAM BURROWBRIDGE. McDermott Will & Emery, LLP, Washington, DC; DOUGLAS H. CARSTEN, ARTHUR PAUL DYKHUIS, Irvine, CA;

SHAUN R. SNADER, United Therapeutics Corporation, Washington, DC.

Before LOURIE, DYK, and STOLL, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Liquidia Technologies, Inc. ("Liquidia") appeals from a decision of the United States District Court for the District of Delaware holding that (1) claims 1, 4, and 6–8 of U.S. Patent 10,716,793 ("the '793 patent") are not invalid and are infringed by Liquidia and (2) claims 1–3 of U.S. Patent 9,593,066 ("the '066 patent") are invalid as anticipated, but are otherwise infringed by Liquidia. United Therapeutics Corporation ("United Therapeutics") cross-appeals from the court's decision holding that (1) claims 1–3, 6, and 9 of the '066 patent are invalid as anticipated and (2) claims 6, 8, and 9 of the '066 patent are not infringed by Liquidia. *See United Therapeutics Corp. v. Liquidia Techs., Inc.*, 624 F. Supp. 3d 436 (D. Del. 2022) ("*Decision*"). For the reasons provided below, we affirm.

BACKGROUND

United Therapeutics holds New Drug Application ("NDA") No. 022387 for Tyvaso®, an inhaled solution formulation of treprostinil approved for the treatment of pulmonary hypertension ("PH"). Pulmonary hypertension is a potentially life-threatening condition characterized generally by abnormally high blood pressure in the lungs. For many patients, treprostinil is used in treating pulmonary hypertension because it is a vasodilator that reduces vasoconstriction in the pulmonary vasculature, thereby decreasing blood pressure.

Experts consider that there are five subgroups of pulmonary hypertension: Group 1, pulmonary arterial hypertension ("PAH"); Group 2, pulmonary venous hypertension, *i.e.*, pulmonary hypertension related to left-heart disease;

Group 3, pulmonary hypertension associated with disorders damaging the lungs; Group 4, pulmonary hypertension caused by chronic thrombotic or embolic disease, including chronic blood clots in the lungs; and Group 5, a miscellaneous category for conditions that do not fit well into the other four subgroups. Groups 1, 3, 4, and 5 are caused by conditions affecting the pulmonary arteries or precapillary vessels of the lungs ("precapillary PH"), while Group 2 typically develops as a result of a cardiac-based etiology ("postcapillary PH"). Due to differing etiologies, each group may require group-specific treatment.

United Therapeutics owns the '793 and '066 patents, which are generally directed to methods of treating pulmonary hypertension and to pharmaceutical compositions comprising treprostinil. The '793 and '066 patents are listed in the FDA's Orange Book for Tyvaso.

Liquidia filed NDA No. 213005 for Yutrepia™ under § 505(b)(2) of the Food, Drug, and Cosmetic Act (codified at 21 U.S.C. § 355(b)(2)). [1] Yutrepia is a dry powder

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[1] Under the Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman amendments to the Food, Drug, and Cosmetic Act), an NDA filed under § 505(b)(2) contains full reports of investigations of safety and effectiveness, where at least some of the information used for approval comes from studies that were not conducted for or by the applicant. Such an NDA is one of two abbreviated approval pathways introduced by the Hatch-Waxman amendments, the other being an abbreviated new drug application ("ANDA") filed under § 505(j) (codified at 21 U.S.C. § 355(j)). 35 U.S.C. § 271(e)(2), the statutory provision delineating acts of infringement, covers both types of applications: "It shall be an act of infringement to submit . . . an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in

inhalation formulation of treprostinil but is not a generic version of any currently marketed drug. Pursuant to § 505(c)(3)(C) (codified at 21 U.S.C. § 355(c)(3)(C)), United Therapeutics sued Liquidia within 45 days of receipt of notice of Liquidia's NDA in the United States District Court for the District of Delaware alleging infringement of the '066 patent. J.A. 171, 190. In addition, after Liquidia filed its NDA, United Therapeutics filed another patent application that eventually issued as the '793 patent, which was subsequently added to the district court litigation. J.A. 208.

In parallel, 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. *Liquidia Techs., Inc. v. United Therapeutics Corp.*, No. IPR2021-00406, 2022 WL 2820717 (P.T.A.B. July 19, 2022). United Therapeutics filed a Request for Rehearing, challenging whether various asserted references qualified as prior art. J.A. 36648. In its Rehearing Decision, the Board found that the references were prior art, again holding the claims of the '793 patent unpatentable as obvious. United Therapeutics filed a Notice of Appeal in that case on April 26, 2023. Liquidia filed a motion for expedited appeal, which has been denied. The appeal is currently pending in this court.

I. The '793 Patent

The '793 patent is directed to a method of treating pulmonary hypertension comprising inhalation of treprostinil. Asserted claim 1 of the '793 patent is the only independent claim and reads as follows:

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section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent[.]"

> 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 dose comprises from 15 micrograms to 90 micrograms of treprostinil or a pharmaceutically acceptable salt thereof delivered in 1 to 3 breaths.

'793 patent at col. 18 ll. 23–31.

The additional asserted dependent claims include limitations directed to dry powder inhalers (claim 4), powder formulations (claim 6), powder formulations comprising particles less than 5 micrometers in diameter (claim 7), and formulations containing no metacresol (claim 8). *See id.* col. 18 ll. 36–37, 40–45.

In the district court, United Therapeutics argued that, although Liquidia's proposed product had not yet been marketed, when marketed, it (1) would directly infringe claims 1, 4, and 6–8 of the '793 patent and (2) 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, establishing that administration of Liquidia's Yutrepia, comprising treprostinil, at the claimed doses will also improve a patient's hemodynamics. The court concluded that United Therapeutics thus proved by a preponderance of the evidence that the administration of Yutrepia will directly infringe claims 1, 4, and 6–8 of the '793 patent.

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