Petitioner

v.

UNITED THERAPEUTICS CORPORATION
Patent Owner

Patent No. 10,716,793 B2
Issue Date: July 21, 2020
Title: TREPROSTINIL ADMINISTRATION BY INHALATION

Inter Partes Review No. IPR2021-00406

DECLARATION OF DR. WERNER SEEGER

2. I am a paid consultant for United Therapeutics, which I understand is the assignee of the '793 patent, in connection with IPR2021-00406. My compensation does not depend on the content of this declaration, the substance of any other testimony that I may offer in connection with this proceeding or the disposition of this proceeding.

Ghofrani Review Article

3. I am a co-author of the German language article: Hossein Ardeschi Ghofrani *et al*. "Neue Therapieoptionen in der Behandlung der pulmonalarteriellen Hypertonie,"[1] *Herz*, 30, 4 (June 2005): 296-302 ("the Ghofrani article"). I understand that Liquidia Technologies, Inc. ("Liquidia") submitted this publication along with an English language translation of the article in this proceeding as Exhibit 1010, which I have reviewed.

[1] The title is translated as "Pulmonary hypertension – new aspects of therapy" in Exhibit 1010.

5. Dr. Hossein A. Ghofrani—the first listed author—has experience in the use of phosphodiesterase inhibitors for treatment of pulmonary hypertension. He drafted the section of the Ghofrani article relating to phosphodiesterase inhibitors. I know Dr. Ghofrani drafted this section of the Ghofrani article because I asked him to draft this section and communicated with him about it. In Exhibit 1010, this section in English begins at the bottom of page 11 and continues through page 13. Dr. Ghofrani was listed as a co-author on the Ghofrani article because he drafted this portion of the article and the other portions noted below.

6. Drs. Frank Reichenberger and Friedrich Grimminger both have experience in the use of selective endothelin A receptor agonists for treating pulmonary hypertension. I know Drs. Reichenberger and Grimminger drafted this section of the Ghofrani article because I asked them to draft this section and communicated with them about it. Together they drafted the section of the Ghofrani article relating to selective endothelin A receptor agonists. In Exhibit 1010, this section is in English on page 11. Drs. Reichenberger and Grimminger

and inhaled treprostinil. In Exhibit 1010, this section is in English and begins on page 10 and continues through page 11. (Ex. 1010, p. 11). Although the information in this excerpt for the article was compiled and composed by Dr. Voswinckel and myself, the individuals who designed the underlying clinical studies with inhaled treprostinil are the same as the ones listed as inventors on the patents, as explained in more detail below. We of course performed the studies discussed in the Ghofrani article, wrote the excerpt quoted above, and submitted it for publication before it was published in June 2005 based upon our work together designing the clinical study.

8. The co-inventors designed the underlying clinical studies with inhaled treprostinil described in the following 2 sentences quoted above from the Ghofrani article: "Initial trials in Giessen have shown proof of efficacy of inhaled treprostinil for the effective reduction of the pulmonary vascular resistance (PVR) [6]. In this first study, 17 patients with severe pre-capillary pulmonary hypertension were administered inhaled treprostinil (15 mcg/inhalation)." The

received an inhaled dosage of 15 mcg.

9. Regarding dosage of inhaled treprostinil, the Ghofrani review article notes that patients were "administered inhaled treprostinil (15 mcg/inhalation)." The word "inhalation" in that sentence (in both German and English) does not mean "breath," but rather, refers to the overall inhalation event stretching over minutes. This is clear under our typical use of that terminology.

10. With respect to the 29-patient study citing the reference of endnote "[6]" (Voswinckel 2004 ESC Abstract) for support, which used an inhalation period of six minutes (reference [6] of Ex. 1010 is Ex. 1007, and p. 5 of Ex. 1007 states that "6 min" was used), this indicates that a continuous nebulizer was being used where dose per breath is not measured (without pulsing or an opto-acoustical trigger), as in the first two studies using an unmodified OptiNeb® device discussed below (paragraph 24).

11. Although the Ghofrani review article states that treprostinil showed a strong pulmonary selectivity "so that it is possible to increase the dosage to up to

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.