UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

WATSON LABORATORIES, INC.
Petitioner

v.

UNITED THERAPEUTICS, INC.
Patent Owner

Patent No. 9,358,240
Issue Date: June 7, 2016
Title: TREPROSTINIL ADMINISTRATION BY INHALATION

Inter Partes Review No. 2017-01621

DECLARATION OF DR. FRIEDRICH GRIMMINGER

4812-7351-8670

I, Dr. Friedrich Grimminger, hereby declare as follows:

1. I am a member of University of Giessen and Marburg Lung Center ("UGMLC"), a research center at the University Hospital Giessen studying pulmonary hypertension.

2. I am not a paid consultant for United Therapeutics Corporation, which I understand is the assignee of U.S. Patent No. 9,358,240, in connection with IPR2017-01621.

3. I am a co-author of the German language article: Hossein Ardeschir 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 Watson Laboratories, Inc. ("Watson") submitted an English language translation of this article in this proceeding as Exhibit 1005, which I have reviewed.

4. Dr. Frank Reichenberger and I both have experience in the use of selective endothelin A receptor agonists for treatment pulmonary hypertension. Therefore, we were asked by Dr. Werner Seeger to draft and, indeed, drafted the section of the Ghofrani article relating to selective endothelin A receptor agonists. In Exhibit 1005, this section is on page 3. In line with the normal practice in the

[1] The title is translated as "New therapies in the treatment of pulmonary hypertension" in Exhibit 1005.

UGMLC research center, both Dr. Reichenberger and I were listed as authors on the Ghofrani article for this contribution.

5. I did not make material contributions to any other section of the Ghofrani article, and I specifically did not contribute to the following excerpt:

> 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). This led to a major reduction in pulmonary selective pressure and resistance with an overall duration of action of > 180 min. In direct comparison with inhaled iloprost, inhaled treprostinil showed a stronger pulmonary selectivity, so that it is possible to increase the dosage to up to 90 mcg (absolute inhaled dose per inhalation exercise) without adverse effects occurring [6]. Due to these unique properties (pronounced pulmonary selectivity and long duration of action after an individual inhalation), it is possible to reduce the number inhalations necessary to up to four per day; the inhalation period can be reduced to < 1 min. by selecting a suitable device. Additionally, the initial data shows that it is technically feasible for there to be only one to two breaths in an application.

The information in this excerpt was compiled and composed by Dr. Robert Voswinckel and Dr. Werner Seeger, and the idea to perform the underlying work originated with them.

6. Dr. Hossein A. Ghofrani – the first listed author –drafted the section of the Ghofrani article relating to phosphodiesterase inhibitors, and the remaining sections on vasoactive therapy, inhaled iloprost, combination therapies, and treatment of early forms of treatment of pulmonary hypertension, as well as the introduction were drafted by Dr. Hossein A. Ghofrani and Dr. Werner Seeger.

[*The remainder of this page is intentionally left blank*]

7. I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code.

Date: October 11, 2017

Dr. Friedrich Grimminger