

Case IPR2015-
Patent No. 8,729,094
Petition for *Inter Partes* Review
Attorney Docket No. REDDY 7.1R-010

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

DR. REDDY'S LABORATORIES, LTD. and
DR. REDDY'S LABORATORIES, INC.
Requestors

v.

HELSINN HEALTHCARE S.A. and ROCHE PALO ALTO LLC
Patent Owner

Patent No. 8,729,094
Issue Date: May 20, 2014
Title: LIQUID PHARMACEUTICAL FORMULATIONS OF PALONOSETRON

Inter Partes Review No. Unassigned

DECLARATION OF DAVID G. FRAME, PHARM.D.

(Exhibit 1023)

Dr. Reddy's Laboratories, Ltd., et al. v. Helsinn Healthcare S.A., et al.

I, DAVID G. FRAME, hereby declare as follows:

1. I am a US citizen and a resident of the state of Michigan.
2. I received a B.S. in Chemistry from St. Louis University in 1986, and a B.S. in Pharmacy and Pharm. D. in 1993 and 1994, respectively, from Wayne State University.
3. I am presently Assistant Professor of Pharmacy at the University of Michigan and Hematology/Oncology/BMT Clinical Specialist with the University of Michigan Health System. In my present positions, I teach therapeutics and pharmacology at the University of Michigan, College of Pharmacy, and, in conjunction with physicians, I treat patients who are receiving chemotherapy for hematologic malignancies and for those receiving a bone marrow transplant. In my work treating patients, I have established our antiemetic guidelines and do much of the supportive care management of these patients. I also do both clinical and translational research in the fields of oncology and infectious diseases.
4. Prior to joining the University of Michigan, I was Assistant Professor at Rush University from 1995-2006. While working at Rush University, I chaired the Chemotherapy Overview Committee at Rush Medical Center from 1995 to 2005. I was Director of Clinical Hematology/Oncology Pharmacy Services and Research at Rush University Medical Center from 1999 to 2005. In that role, I was

responsible for overseeing all clinical pharmacy oncology services and monitoring oncology patient outcomes. I was also director of the anticoagulation program for hip and knee replacement where we were responsible for supportive care issues, such as nausea and vomiting post-operatively.

5. I have taught graduate courses and have given frequent presentations on many topics in oncology, including therapies for multiple disease conditions and lectures on supportive care. I have delivered over 50 professional presentations to clinicians on the treatment of both chemotherapy induced and post-operative nausea and vomiting.

6. I have participated in designing clinical studies of 5-HT₃ receptor antagonists for treating both chemotherapy induced nausea and vomiting and post-operative nausea and vomiting. My role in the clinical studies has involved being a part of large multicenter trials, as well as designing and implementing my own randomized controlled trial for post-operative nausea and vomiting, as well as several smaller trials in the oncology setting.

7. In my years of clinical practice, I have had experience with all of the 5-HT₃ antagonists approved in the U.S., including Aloxi® (palonosetron), Zofran® (ondansetron), Kytril® (granisetron), and Anzemet® (dolasetron). I have managed nausea and vomiting using these agents in over 4000 patients.

8. Additional details of my education and experience are set forth in my curriculum vitae (Exh. 1024), which also contains a partial listing of the companies and conferences where I have been invited to speak, the lectures and short courses I have given, and the publications I have authored.

9. I was retained by litigation counsel for Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc. to serve as an expert and to testify in some of the litigations between *Helsinn Healthcare S.A. and Roche Palo Alto LLC and Dr. Reddy's Laboratories, Ltd., Dr. Reddy's Laboratories, Inc.*, identified to the Patent Trial and Appeal Board in the Notice of Related Matters in the Petition that this declaration supports.

10. I have been separately retained by Lerner, David, Littenberg, Krumholz & Mentlik, LLP ("counsel") to provide my opinions in this *Inter Partes* Review in the fields of pharmaceutical design and administration, the structure and analysis of clinical studies and their data and specifically the formulation and administering of palonosetron and other 5-HT₃ receptor antagonists recognized as having structural or functional relationships with palonosetron (sometimes collectively referred to as "setrons"). I have read and understood U.S. Patent No. 8,729,094 ("the '094 Patent") (Exh. 1001), as well as all other references discussed in this declaration. I am being compensated for my time in an amount

consistent with my customary consulting fee, and my compensation is not contingent on my opinion or the outcome of this proceeding.

I. A PERSON OF ORDINARY SKILL IN THE ART

11. I understand from counsel that patents such as the '094 Patent are neither addressed to experts nor to laymen; rather they are addressed to persons of ordinary skill in the relevant art at the time invention was made, which I have been told by counsel to assume is January 29, 2003. I also understand from counsel that factors relevant to the level of skill in the art include, without limitation: the educational level of the inventor, the types of problems encountered in the relevant area, prior art solutions to those problems, the rapidity with which innovations are made, the sophistication of the technology, and the educational level of active workers in the field.

12. As noted previously, I have attended and testified at the Trial which involved other patents related to the '094 Patent. I am not an expert in patent law but, from my recollection, none of those patents involves methods of treating CINV *per se*. That must be contrasted with claims 22-30 of the '094 Patent, which appear on their face to relate to methods of treating CINV, albeit by administering the types of formulation that are the focus of the above-identified litigations.

13. Because of my involvement in the aforementioned litigations, I know that Petitioner has taken the position that a person of ordinary skill in the art (a

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