

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

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

v.

NOVO NORDISK A/S,
Patent Owner

U.S. Patent No. 10,335,462 to Jensen
Issue Date: July 2, 2019
Title: Use Of Long-Acting Glp-1 Peptides

Inter Partes Review No. IPR2024-00009

DECLARATION OF RANDALL M. ZUSMAN, M.D.

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1011	WO 2011/138421
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1097	<i>Mylan Pharmaceuticals Inc., v. Novo Nordisk A/S</i> , IPR2023-00724, Paper 10 (PTAB Oct. 4, 2023)

I. INTRODUCTION

1. I have been retained by the law firm Winston & Strawn LLP on behalf of Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc., (hereinafter, collectively, "DRL" or "Petitioners") to provide expert opinions concerning the administration of semaglutide for the treatment of diabetes.

2. I have been asked to provide my opinions related to U.S. Patent No. 10,335,462 ("the '462 patent") (Ex. 1001) and the scientific and technical knowledge regarding the subject matter of the '462 patent. I understand that Mylan Pharmaceuticals Inc. ("Mylan") filed an *inter partes* review petition ("Mylan's petition") against claims 1-10 of the '462 patent, and the Patent Trial and Appeal Board instituted Mylan's petition on October 4, 2023. *See* Ex. 1097, *Mylan Pharmaceuticals Inc., v. Novo Nordisk A/S*, IPR2023-00724, Paper 10 ("Mylan IPR"). I understand that DRL petitions for *inter partes* review of the same claims of the '462 patent as the Mylan IPR on the same grounds, and DRL requests to join the Mylan IPR. I submit this declaration in support of DRL's petition for *inter partes* review.

3. My opinions in this declaration are based on the documents I cite along with my professional training, experience and knowledge that I have acquired working in the field of cardiology. I am being compensated for my services as an expert at my standard consulting rate of \$1,050 per hour. My

compensation is in no way contingent on the substance of my opinions or the outcome of this case.

II. BACKGROUND AND QUALIFICATIONS

4. I obtained a Bachelor of Science degree in Chemistry with Highest Honors from the University of Michigan in 1969.

5. I obtained an M.D. from Yale University School of Medicine in 1973.

6. Since June 2009, I have been a physician at Massachusetts General Hospital (“MGH”) in Boston, Massachusetts. Also at MGH, I was an assistant physician from January 1985 to December 1988 and an associate physician from January 1989 to December 2008. Throughout my time at MGH, my practice has focused on cardiology.

7. Since 1982, I have been the Director of the Hypertension Section, Cardiology Division, Medical Services at MGH.

8. I have been board-certified in Internal Medicine by the American Board of Internal Medicine since 1976. I have also been board-certified in Cardiovascular Diseases by the American Board of Internal Medicine since 1983.

9. Peer-reviewed journals have published more than 45 original reports, more than 80 clinical communications, and more than 30 review articles

that I authored or co-authored. I am also the author or co-author of numerous book chapters relating to cardiology, cardiovascular disease, and hypertension.

10. I am an active member of several professional societies, including: the American Society of Nephrology (member since 1976); the American Heart Association (member since 1978); the American Society of Hypertension (member since 1988, clinical specialist in hypertension since 1999, and member of the association of hypertension specialists since 2009); and the American College of Cardiology (fellow since 1990).

11. Since 1981, I have served on the editorial boards of numerous journals, including the Journal of Clinical Hypertension, Journal of Hypertension, Reviews in Contemporary Pharmacotherapy, and Cardiology and Therapy. I have also served as an ad hoc reviewer for journals such as the New England Journal of Medicine, Circulation, the Journal of Clinical Investigation, Hypertension, the American Journal of Hypertension, the Journal of the American College of Cardiology, the American Journal of Cardiology, the Journal of the American Society of Hypertension, Circulation Research, and the American Journal of Medicine.

12. From January 2001 to June 2016, I served as a cardiology consultant for the Medical Department of the Massachusetts Institute of Technology in Cambridge, Massachusetts.

13. Since June 1994, I have been an associate professor of medicine at Harvard Medical School (“HMS”) in Boston, Massachusetts. Prior to that, I served at HMS as an instructor from January 1978 to June 1980, and as an assistant professor from July 1980 to December 1993.

14. My current professional activities are divided into clinical service, teaching, and administrative responsibilities, focusing primarily on the care of patients with hypertension, hyperlipidemia (hypercholesterolemia and/or hypertriglyceridemia), cardiovascular risk factors, and vascular disease. As a cardiologist specializing in the reduction of the cardiovascular risk of my patients, I am routinely involved in the treatment of hypertension, hyperlipidemia, diabetes mellitus, and obesity. The practice of cardiology has now branched into the use of drugs, previously traditionally prescribed by endocrinologists/diabetologists. In particular, I now regularly prescribe the GLP-1 agonists (for example, semaglutide), as well as the full range of other drugs that impact the body’s metabolic pathways, to facilitate the control of my patient’s HgBA1c (blood sugar), lipid profile and weight, and in so doing reduce their cardiovascular risk. My very active outpatient practice includes many patients who were intolerant of previously prescribed anti-hypertensive medications and referred to me for the development of an effective anti-hypertensive regimen, while others have marked lipid disorders which have been resistant to standard therapies and/or have been

intolerant of those therapies (used to reduce their cardiovascular risk profile). I estimate that about 40% of my patients present with type 2 diabetes mellitus; of those, about 20% also present with some form of kidney disease.

15. As a clinician scientist, I have participated in many landmark clinical trials that have established standard of care principles in the treatment of patients with cardiovascular disease. These contributions include the use of pharmacologic therapy as well as non-drug based strategies for the treatment of patients post-myocardial infarction with asymptomatic LV dysfunction, survivors of myocardial infarction with moderate elevations of LDL cholesterol, patients with elevated hs-CRP concentrations to reduce cardiovascular risk, cardiac arrhythmias, and newly diagnosed patients with diabetes mellitus. My most recent clinical research focused on the determination of the mechanism by which the relaxation response produces a reduction in blood pressure in hypertensive patients.

16. My teaching responsibilities include formal contributions as an attending physician (Cardiology Consultation Service and Step-Down Unit Visit), classroom lectures in the HST program, and participation in multiple post-graduate CME courses at HMS, as well as a visiting professor at many hospitals and medical schools around the country. One of my most important teaching roles is as a “curbside consultant” to the medical staff, interns, residents and

fellows of MGH who seek my advice on a regular basis regarding the reduction of the cardiovascular risk profile of the patients for whom they are responsible.

17. I have also focused on activities that promote patient and community education. Through my many appearances on the local and national news, and the publication of the Harvard Medical School Special Health Report on Hypertension, I have contributed to the public's understanding of this disease and helped them to make changes in their lifestyle and understand the use of their medications to reduce their cardiovascular risk. My career has involved clinical research relating to cardiovascular risk reduction (hypertension, hyperlipidemia, LV dysfunction, diabetes mellitus, atrial fibrillation), including the study of conventional approaches to blood pressure control (pharmacologic therapy) as well as complementary or alternative medical strategies (acupuncture, relaxation response). I have been involved in technological developments, study design, and, basic scientific and laboratory research that has led to a greater understanding of renal physiology and blood pressure control. The long term consequences of this effort have been a better understanding of hypertension, hyperlipidemia, and cardiovascular disease, and an improved treatment algorithm for the reduction of cardiovascular mortality and morbidity worldwide.

18. Additional information regarding my background, qualifications, publications, and presentations is provided in my *curriculum vitae*, which is included as Ex. 1092.

III. INFORMATION RELIED UPON AND OPINIONS REGARDING THE '462 PATENT

19. In addition to my general knowledge gained as a result of my education and experience as a medical doctor, I have reviewed and considered, among other things, the '462 patent, the prosecution history of the '462 patent, and the prior art of record discussed herein.

20. I also reviewed the Institution Decision issued by the Board in IPR2023-00724 instituting *inter partes* review of the same challenged claims of the '462 patent with respect to all grounds in Mylan's petition. *See* Ex. 1097, IPR2023-00724, Institution Decision, Paper 10. I agree with the Board's reasoning in its Institution Decision, which concerns the same claims of the same patent challenged here.

21. I have also reviewed and considered the declaration of John Bantle, M.D. (Ex. 1003) submitted in connection with Mylan's petition for *inter partes* review of the '462 patent, including materials and exhibits cited therein. *See* Ex. 1003, IPR2023-00724, Mylan's Petition, Paper 1. I agree with, and hereby adopt and incorporate by reference, all of the opinions set forth in the

declaration of Dr. Bantle.

22. Based on my view of the prior art, it is my opinion that claims 1-10 of the '462 patent are anticipated and/or would have been obvious over the following prior art references, alone or in combination:

a) Ground 1: International Patent App. Pub. No. WO 2011/128421 (“WO421”) (Ex. 1011) anticipated claims 1-3 of the '462 patent;

b) Ground 2: Lovshin, *Incretin-Based Therapies for Type 2 Diabetes Mellitus*, 5 NATURE REV. ENDOCRINOLOGY 262 (2009) (“Lovshin”) (Ex. 1012) anticipated claims 1-3 of the '462 patent;

c) Ground 3: Claims 1–10 of the '462 patent would have been obvious over WO421 in view of U.S. Patent Application Pub. No. US2007/0010424 (the “'424 publication”) (Ex. 1016);

d) Ground 4: Claims 1–10 of the '462 patent would have been obvious over International Patent App. Pub. No. WO 2006/097537 (“WO537”) (Ex. 1015) in view of Lovshin; and

e) Ground 5: Claims 1–10 of the '462 patent would have been obvious over Clinical Trial No. NCT00696657 (“NCT657”) (Ex. 1013) in view of Clinical Trial No. NCT00851773 (“NCT773”) (Ex. 1014) and further in view of the '424 publication.

IV. CONCLUSION

23. This declaration is based on my present assessment of material and information currently available to me.

24. I understand that this declaration will be filed as evidence in a contested case before the Patent Trial and Appeal Board of the United States Patent and Trademark Office. I also understand that I may be subject to cross-examination concerning this declaration, and I will appear for cross-examination, if required of me, during the time allotted for cross-examination.

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

Date: October 19, 2023

/Randall M. Zusman, MD/

Randall M. Zusman, M.D.