

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 JOHN P. FRUEHAUF, M.D., Ph.D.

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1004	CV of John Bantle, MD
1005	Declaration of William J. Jusko, Ph.D.
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1007	Declaration of Paul Dalby, Ph.D.
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1009	Intentionally Left Blank
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1011	WO 2011/138421
1012	Lovshin, <i>Incretin-Based Therapies for Type 2 Diabetes Mellitus</i> , 5 NATURE REV. ENDOCRINOLOGY 262 (2009)
1013	Clinical Trial No. NCT00696657
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1015	WO 2006/097537
1016	U.S. Patent Application Pub. No. US2007/0010424
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1018	Banting, <i>The Internal Secretion of the Pancreas</i> , 7 J. LAB. CLINICAL MED. 251 (1922)
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1020	Bydureon prescribing information (Jan. 2012)
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1024	Drucker, <i>The Incretin System: Glucagon-Like Peptide-1 Receptor Agonists and Dipeptidyl Peptidase-4 Inhibitors in Type 2 Diabetes</i> , 368 LANCET 1696 (2006)
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1029	Jimenez-Solem, <i>Dulaglutide, a Long-Acting GLP-1 Analog Fused with an Fc Antibody Fragment for the Potential Treatment of Type 2 Diabetes</i> , 12 CURRENT OP. IN MOLECULAR THERAPEUTICS 790 (2010)
1030	Kim, <i>Effects of Once-Weekly Dosing of a Long-Acting Release Formulation of Exenatide on Glucose Control and Body Weight in Subjects with Type 2 Diabetes</i> , 30 DIABETES CARE 1487 (2007)
1031	Knudsen, <i>GLP-1 Derivatives as Novel Compounds for the Treatment of Type 2 Diabetes: Selection of NN2211 for Clinical Development</i> , 26 DRUGS OF THE FUTURE 677 (2001)
1032	Knudsen, <i>Glucagon-like Peptide-1: The Basis of a New Class of Treatment for Type 2 Diabetes</i> , 47 J. MED. CHEMISTRY 4128 (2004)
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1054	Landersdorfer, <i>Mechanism-Based Population Pharmacokinetic Modelling in Diabetes: Vildagliptin as a Tight Binding Inhibitor and Substrate of Dipeptidyl Peptidase IV</i> , 73 BRIT. J. CLINICAL

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1055	Landersdorfer, <i>Mechanism-Based Population Modelling of the Effects of Vildagliptin on GLP-1, Glucose and Insulin in Patients with Type 2 Diabetes</i> , 73 BRIT. J. CLINICAL PHARMACOLOGY 373 (2011) (“Landersdorfer 2011b”)
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1075	U.S. Patent No. 7,022,674
1076	<i>ClinicalTrials.gov Background</i> , CLINICALTRIALS.GOV, https://clinicaltrials.gov/ct2/about-site/background (last visited Mar. 10, 2023)
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1081	Ozempic prescribing information (Oct. 2022)
1082	Scheduling Order, <i>Novo Nordisk Inc. v. Rio Biopharmaceuticals Inc.</i> , No. 22-294 (CFC) (D. Del. June 30, 2022), ECF No. 22
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1086	“Last Update Posted” definition from ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/NCT00696657
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1095	Declaration of Dr. Maureen M. Donovan
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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 "Petitioner") to provide expert opinions concerning the administration of semaglutide for the treatment of type 2 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 oncology over the past 45 years. I am being compensated for my services as an expert at my standard consulting rate of \$750

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 am currently Professor of Clinical Medicine at the University of California, Irvine and Director of Clinical Pharmacology and Developmental Therapeutics at the University of California at Irvine's ("UC Irvine") Chao Family Comprehensive Cancer Center ("CFCCC").

5. I am involved in the direct oversight of multiple clinical trials at the CFCCC in the role of principal investigator. Several of the trials I have brought into our Cancer Center were phase I first-in-man studies, which means they were the first clinical study conducted in humans for a drug. Among other responsibilities, I work on the development and execution of clinical trials that incorporate translational endpoints, including phase I, II and III clinical trials. I also teach undergraduate students, graduate students, medical students, residents, and medical oncology fellows the principles of clinical trials in various courses.

6. Since starting to work as a medical oncologist faculty member in the Division of Hematology/Oncology, Department of Internal Medicine in 1993, I have participated in weekly UC Irvine cancer clinics in the outpatient setting as a clinician and instructor for medical oncology fellows. I have also rotated on an

annual basis as the in-patient Attending Physician overseeing the cancer patient service at the UC Irvine University Hospital. I have experience treating patients with mantle-cell lymphoma (“MCL”), among other types of cancers (including lymphomas and leukemias). I also have clinical experience using the Bruton’s Tyrosine Kinase (“BTK”) inhibitor ibrutinib (brand name: Imbruvica).

7. I obtained an M.D. from Rush University in 1985 and a Ph.D. in Pharmacology from Rush University. I received my undergraduate degree in Cellular and Organismal Biology, with a minor in Chemistry, from the University of California, Santa Barbara, in 1977.

8. I completed my Internal Medicine Residency at UC Irvine in 1987. I completed my Medical Oncology Fellowship in 1990 at the National Cancer Institute in Bethesda, Maryland, which was followed by a biotechnology fellowship at the same institution, which was completed in 1992.

9. I am a member of the American Association for Cancer Research, the American Society of Clinical Oncology, the Breast and Melanoma Committees of SWOG (a National Cancer Institute supported organization that conducts clinical trials in adult cancers), and the Medical Oncology Association of Southern California (“MOASC”).

10. I have published more than 91 peer reviewed articles, book

chapters, and reviews in the field of oncology. I am an inventor on eight U.S. patents. I am also a peer reviewer for the following journal publications: Gynecologic Oncology, Breast Cancer Research and Treatment, Clinical Cancer Research, Anti-Cancer Drugs. The Cancer Journal, European Journal of Cancer, Pharmacological Research, and Cancer.

11. A current copy of my curriculum vitae is included as Ex. 1094.

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

12. In addition to my general knowledge gained as a result of my education and experience as a medical doctor and pharmaceutical scientist, 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.

13. 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.

14. I have also reviewed and considered the declaration of William J. Jusko, Ph.D. (Ex. 1005) submitted in connection with Mylan's petition for *inter*

partes review of the '462 patent, including materials and exhibits cited therein. See Ex. 1005, 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. Jusko.

15. In my opinion, International Patent Application Publication No. WO 2011/138421 ("WO421") anticipates claims 1-3 of the '462 patent.

16. In my opinion, a review article titled "Incretin-Based Therapies for Type 2 Diabetes Mellitus" ("Lovshin") authored by Julie A. Lovshin and Daniel J. Drucker, which was published in May 2009, anticipates claims 1-3 of the '462 patent.

17. In my opinion, claims 1-10 of the '462 patent would have been obvious over WO421 considering U.S. Patent Application Publication No. 2007/0010424 A1 ("'424 Publication"). It is my understanding that DRL's expert Dr. Maureen Donovan is offering an opinion that claims 4-10 would have been obvious over WO421 considering the '424 Publication, and I defer to her opinion for claims 4-10. Ex. 1095.

18. In my opinion, claims 1-10 of the '462 patent would have been obvious over International Patent Application Publication No. WO 2006/097537 A2 ("WO537") considering Lovshin. It is my understanding that Dr. Donovan is offering an opinion that claims 4-10 would have been obvious over WO537

considering Lovshin, and I defer to her opinion for claims 4-10.

19. In my opinion, claims 1-10 of the '462 patent would have been obvious over Clinical Trial No. NCT00696657 ("NCT657"), Clinical Trial No. NCT00851773 ("NCT773"), and the '424 Publication. It is my understanding that Dr. Donovan is offering an opinion that claims 4-10 would have been obvious over NCT657, NCT773, and the '424 Publication, and I defer to her opinion for claims 4-10.

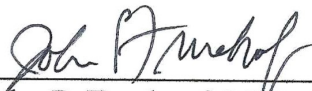
IV. CONCLUSION

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

21. 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.

22. 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 18, 2023



John P. Fruehauf, M.D., Ph.D.

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