

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

STEADYMED LTD.,

Petitioner,

v.

UNITED THERAPEUTICS CORPORATION,

Patent Owner.

Case IPR2016-00006
Patent 8,497,393

**DECLARATION OF ROBERT M. WILLIAMS, Ph.D., IN SUPPORT OF
PATENT OWNER RESPONSE TO PETITION**

TABLE OF CONTENTS

I.	QUALIFICATIONS AND BACKGROUND.....	3
A.	Education and Experience.....	3
B.	Materials Considered.....	12
II.	LEGAL STANDARDS PROVIDED BY COUNSEL	12
A.	THE PERSON OF ORDINARY SKILL IN THE ART	12
B.	ANTICIPATION	14
C.	OBVIOUSNESS.....	14
III.	SUMMARY OF OPINIONS.....	16
IV.	THE '393 PATENT	16
V.	CLAIM CONSTRUCTION.....	18
VI.	PHARES DOES NOT ANTICIPATE CLAIMS 1-5, 7-9, 11-14, OR 16-20 OF THE '393 PATENT	21
A.	THE PRODUCT DISCLOSED IN PHARES IS PHYSICALLY DIFFERENT THAN THE PRODUCTS DISCLOSED IN THE '393 PATENT CLAIMS	22
B.	PHARES DOES NOT DISCLOSE SEVERAL OTHER CLAIM LIMITATIONS.....	25
VII.	NONE OF THE CLAIMS OF THE '393 PATENT ARE RENDERED OBVIOUS BY THE PRIOR ART.....	27
A.	THE PRODUCT OF THE '393 PATENT IS STRUCTURALLY DIFFERENT THAN THE PRODUCT OF THE PRIOR ART.....	28
B.	CLAIMS 1-5, 7-9, 11-14, AND 16-20 ARE NOT RENDERED OBVIOUS BY THE COMBINATION OF MORIARTY AND PHARES	34
C.	CLAIMS 6, 10, 15, 21, AND 22 ARE NOT RENDERED OBVIOUS BY THE COMBINATION OF MORIARTY, PHARES, KAWAKAMI, AND EGE.....	36
	APPENDIX A.....	42
	APPENDIX B.....	47

I have been retained by the law firm of Wilson Sonsini Goodrich & Rosati (“WSGR”) as an expert consultant to United Therapeutics Corporation (“UTC”) in connection with the above-identified matter to provide expert testimony concerning U.S. Patent No. 8,497,393 (“the ‘393 Patent”, Ex. 1001) by Batra *et al.*, entitled “Process to prepare Treprostinil, the active ingredient in Remodulin,” issued on July 30, 2013. At the request of Counsel for UTC, I hereby submit this expert declaration.

I. Qualifications and Background

A. Education and Experience

1. I am a tenured University Distinguished Professor of Chemistry at Colorado State University (CSU). I currently serve as the Director for the Colorado Center for Drug Discovery. I also served as co-Director (Experimental Therapeutics) for the Infectious Diseases Supercluster Initiative and also served as co-Director for the Cancer Supercluster Initiative at CSU. My *curriculum vitae* is attached hereto as Exhibit A (Ex. 2021).

2. I received a B.A. in Chemistry from Syracuse University in 1975, and did laboratory research in the field of synthetic organic chemistry under the guidance of the recent Nobel Laureate Professor Ei-ichi Negishi. In 1979, I received both a Master’s degree and Ph.D. degree in Organic Chemistry from the Massachusetts Institute of Technology (MIT) under the direction of Professor William H. Rastetter. Upon graduating from MIT, I spent one year (1979-80) as a postdoctoral fellow at Harvard University in the laboratories of the Nobel Laureate, the late Professor Robert B. Woodward, whose laboratory was subsequently managed by Professor Yoshito Kishi.

3. Subsequent to my fellowship at Harvard, I served as an Assistant Professor at Colorado State University from 1980–84. I was tenured and promoted early, to the rank of

IPR2016-00006
patent 8,497,393

Associate Professor in 1985, and in 1988, I was promoted to the rank of Full Professor. In 2002, I was named a University Distinguished Professor, which is my current position. University Distinguished Professor is the highest academic rank at Colorado State University, and there are a maximum of twelve University Distinguished Professors at any given time out of a faculty of 1,200. This is a lifetime appointment until retirement, whereupon Emeritus status is granted. In addition to my positions at Colorado State University, I was a Visiting Professor of Chemistry at Harvard University from 1994–95, at which time I was sponsored by Professor Stuart L. Schreiber and taught a sophomore organic chemistry course for pre-medical students, Chem 17. I was also a Visiting Professor of Chemistry at the University of California at Berkeley in 1990 and worked in the laboratory of Professor Peter G. Schultz.

4. I have extensive experience in the field of synthetic organic chemistry and medicinal chemistry with an emphasis on biologically active compounds including anti-tumor agents, heterocycles, antibiotics, anti-fungal agents, anti-viral agents, immunomodulators, amino acids, peptides and alkaloids, among many other classes of biologically active organic substances. My organic chemistry research interests include the total synthesis of novel natural and synthetic products, heterocyclic chemistry, asymmetric synthesis, synthetic methodology, process chemistry, and reaction mechanisms. I have extensive experience in the synthesis, chemistry, conformational analysis, biochemical activity, and biological activity of a range of organic compounds.

5. My research laboratory at Colorado State University has worked extensively on the chemistry and biology of numerous drugs over my career, including Quinocarcin (Quinocarmycin citrate), Tetrazomine, Bioxalomycin, Ecteinascidin 743 (Yondelis[®] or trabectedin), Renieramycin, Cribrostatin-4, Jorumycin, the Mitomycins, FR900482, FK973,

IPR2016-00006
patent 8,497,393

FK317, FK228 (Romidepsin), Largazole, Stephacidins A and B, Avrainvillamide, Spirotryprostatins, TMC-95A/B, Rottlerin, and Antimycin, amongst many others.

6. I have been the Principal Investigator on numerous research grants from Federal agencies, such as the National Institutes of Health (NIH) and the National Science Foundation (NSF) as well as from various Foundations, and corporations to synthesize biologically active compounds on both small laboratory scale as well as larger industrial scales.

7. I held a funded research collaboration with the Infectious Diseases Research Institute (IDRI), in Seattle, Washington, to develop several novel adjuvants for the treatment and prevention of autoimmune diseases, infectious diseases and cancer (2010).

8. From 1991-1993, I held a research grant from Symphony Pharmaceuticals, located in Philadelphia, Pennsylvania, to prepare anti-HIV drugs based on inhibition of the HIV protease. I supervised a graduate student who prepared several very potent peptide isosteres that exhibited in vitro activity against HIV.

9. I have taught undergraduate and graduate courses in organic chemistry, organic synthesis, biosynthesis, biological chemistry, drug design, and the synthesis of natural products. I have also lectured at numerous professional conferences, universities, and in corporate R&D laboratories in those areas.

10. I am a Scientific Founder, Acting President, and Chair of the Scientific Advisory Board of Cetya Therapeutics, a company that is developing several drugs, including drugs for the treatment of various cancers, multiple myeloma, autoimmune diseases, and hemoglobinopathies. I also direct all of the process scale synthesis optimization and drug formulation studies being conducted on Cetya's HDAC inhibitors. This includes injectable formulations as well as oral formulations. Specifically, I directed and supervised post-doctoral researchers in my laboratory

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