**CONTAINS PROTECTIVE ORDER MATERIAL** Paper _____

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
U.S. Patent 8,497,393

---

**DECLARATION OF ROBERT R. RUFFOLO, Jr., Ph.D. IN SUPPORT OF PATENT OWNER RESPONSE TO PETITION**

**TABLE OF CONTENTS**

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 the retired (as of 2008) President of Research and Development for Wyeth Pharmaceuticals (now Pfizer Inc.) and Corporate Senior Vice President of Wyeth (now Pfizer Inc.). I am currently Managing Director of Ruffolo Consulting, LLC, a consulting company serving the pharmaceutical and biotechnology industries**.**

2. I have studied, researched, taught (in medical and pharmacy schools), worked and managed all aspects of the pharmaceutical drug discovery and development fields for over 35 years. I received my Bachelor of Science (B.S.) degree in Pharmacy (*summa cum laude*, and *With Distinction*) in 1973 from The Ohio State University, and was licensed to practice Pharmacy in 1973. I received my Doctor of Philosophy (Ph.D.) degree in Pharmacology in the fields of autonomic and cardiovascular pharmacology in 1976 also from The Ohio State University. My doctoral research included the areas of drug-receptor interactions, autonomic pharmacology, cardiovascular pharmacology, adrenergic drugs, stereochemistry and the study of the stereochemical aspects of adrenergic drugs and their receptors. During the period of my undergraduate and graduate education, I authored or co-authored a number of peer-reviewed research articles describing that work.

3. Upon earning my Ph.D. degree, I remained at The Ohio State University as a Postdoctoral Fellow for six months, and extended my research on drug-receptor interactions and drug-receptor theory. From 1977-1978, I worked as a Staff Fellow and Postdoctoral Fellow [Pharmacology Research Associate Training (PRAT) Fellow] at the National Heart Lung and Blood Institute of the National Institutes of Health (NIH) in the laboratory of Dr. Marshall Nierenberg (Nobel Laureate for breaking the genetic code), where my research focused on neurobiology, and in particular on synapse formation in brain, spinal cord and skeletal muscle.

4. In 1978, I began my independent career in the pharmaceutical industry at Eli Lilly & Company as Senior Pharmacologist in the Department of Cell Biology. I subsequently became Senior Pharmacologist in the Department of Cardiovascular Pharmacology in 1981, and was promoted to Research Scientist in 1982. I then became Chairman of the Cardiovascular Research Committee in 1983, where I continued my research in cardiovascular pharmacology, adrenergic drugs, drug-receptor theory, stereochemistry and the stereochemical basis of drug action. My work also expanded into the area of structure-activity relationships and drug design. Shortly after joining Eli Lilly & Company, I was also assigned to supervise a medicinal chemistry laboratory that was dedicated to my work in stereochemistry and structure-activity relationships, and which I personally directed. While working at Eli Lilly & Company, I was credited with discovering the complex mechanism of action of the newly marketed drug for the treatment of acute congestive heart failure, dobutamine (Dobutrex®), which involved the complex interplay of the different pharmacological activities of both enantiomers of the drug, each acting on multiple adrenergic receptors and their subtypes..

5. In 1984, I joined SmithKline Beckman Pharmaceuticals (now GlaxoSmithKline PLC) as Director of Cardiovascular Pharmacology, where I continued my work in cardiovascular

pharmacology, adrenergic drugs, drug-receptor theory, stereochemistry, the stereochemical basis of drug action, structure-activity relationships and drug design. As Director of the Department of Cardiovascular Pharmacology, I supervised a staff of approximately 40 researchers and scientists in the field of cardiovascular drug discovery and development. Throughout my tenure at SmithKline Beckman Pharmaceuticals (and its subsequent corporate identities that changed through mergers and acquisitions), I also maintained my own laboratory and conducted studies on the pharmacology of cardiovascular drugs, drug-receptor interactions, adrenergic pharmacology, stereochemistry, the steric aspects of drug action, and structure-activity relationships related to new drug discovery.

6. I remained at SmithKline Beckman Pharmaceuticals (and its subsequent corporate identities) for approximately 17 years, over which time I rose to the position of Senior Vice President and Director of Biological Sciences Worldwide, where I was responsible for a staff of approximately 500 scientists. During my last year at the company, I became the Senior Vice President and Director of all Discovery Research for the Corporation Worldwide, which included all of the areas of Biological Sciences, Chemical Sciences, Medicinal Chemistry, Physical Chemistry, Process Chemistry, Molecular and Cellular Biology, and Genetics, with responsibility for a staff of approximately 1,700 scientists and an annual budget of approximately $1.2 billion.

7. It was during my tenure at SmithKline Beckman Pharmaceuticals (and its subsequent corporate identities) that I was personally responsible for the discovery and subsequent development of Coreg® (carvedilol) for the treatment of chronic congestive heart failure, for which I was awarded the *Discoverers Award* in 2008 by the Pharmaceutical Research and Manufacturers Association (PhRMA), which is the major trade association for the

DOCKET ALARM

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

**LAW FIRMS**
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

**FINANCIAL INSTITUTIONS**
Litigation and bankruptcy checks for companies and debtors.

**E-DISCOVERY AND LEGAL VENDORS**
Sync your system to PACER to automate legal marketing.