

John E. Flaherty
Ravin R. Patel
McCARTER & ENGLISH LLP
Four Gateway Center
100 Mulberry St.
Newark, NJ 07102
Telephone: (973) 622-4444

*Attorneys for Plaintiff Horizon
Therapeutics LLC*

Robert F. Green
Caryn C. Borg-Breen
Ann K. Kotze
Rachel C. Bell
GREEN, GRIFFITH & BORG-BREEN LLP
City Place
676 N. Michigan Avenue, Suite 3900
Chicago, Illinois 60611
Telephone: (312) 883-8000

*Of Counsel for Plaintiff Horizon Therapeutics
LLC*

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY**

HORIZON THERAPEUTICS LLC,

Plaintiff,

v.

PAR PHARMACEUTICAL, INC.,

Defendant.

Case No. 2:17-cv-5901-KM-MAH

Motion Date: See Dkt. No. 57

**DECLARATION OF INVENTOR BRUCE F. SCHARSCHMIDT, M.D., IN SUPPORT
OF PLAINTIFF HORIZON'S OPPOSITION TO PAR'S MOTION FOR SUMMARY
JUDGMENT OF INVALIDITY UNDER 35 U.S.C. § 101**

TABLE OF CONTENTS

I. INTRODUCTION 1

II. EDUCATION AND CAREER..... 1

III. UREA CYCLE DISORDERS 2

IV. DEVELOPMENT OF RAVICTI®..... 6

V. URINARY PAGN OUTPUT..... 8

VI. BLOOD AMMONIA LEVELS 9

VII. THE PAA:PAGN RATIO..... 11

I. INTRODUCTION

1. I, Bruce F. Scharschmidt, M.D., submit this declaration on behalf of Horizon Therapeutics, LLC (“Horizon Therapeutics”) in support of its Opposition to Par’s Motion for Summary Judgment of Invalidity Under 35 U.S.C. § 101.

2. I currently serve as a consultant to Horizon Pharma, Inc. (“Horizon Pharma”). Horizon Therapeutics, the plaintiff in this case, is a subsidiary of Horizon Pharma.

3. I am one of the named inventors of U.S. Patent No. 9,561,197¹ (“the ’197 Patent”), entitled “Methods of Therapeutic Monitoring of Phenylacetic Acid Prodrugs” and issued on February 7, 2017.

II. EDUCATION AND CAREER

4. I completed my undergraduate and medical studies as part of Northwestern University’s Honors Program in Medical Education, an accelerated program that combined the traditional four years of undergraduate education and four years of medical education into a six-year degree. I graduated with my M.D. in 1970.

5. I am Board Certified in Internal Medicine and Gastroenterology.

6. After completing my residency and fellowship at the University of California, San Francisco, I continued my career there for the next 19 years, eventually serving as the Chief of Gastroenterology and a Professor of Medicine. During this time I also served as Editor-in-Chief of the Journal of Clinical Investigation and was elected President of the American Society for Clinical Investigation.

7. I spent the next ten years at Chiron Corporation, where, as Vice President of Clinical Development, I headed the clinical development, clinical operations and biostatistics

¹ Attached to the Declaration of Rachel C. Bell, Esq. (“Bell Declaration” or “Bell Decl.”), submitted contemporaneously, as Ex. A.

and clinical data management groups before being elevated to the corporate group as VP of Scientific Affairs. Chiron was acquired by Novartis International AG in April 2006. I continued working at Novartis as a Vice President until April 2008.

8. I served as the Chief Medical Officer and subsequently Chief Medical & Development Officer of Hyperion Therapeutics, Inc. (“Hyperion”) from April 2008 to May 2015, at which time it was acquired by Horizon Pharma. I also served as a Senior Vice President at Hyperion.

9. I was listed as an inventor on every patent application filed by Hyperion during my tenure there.

10. I have authored over 200 scientific articles over the course of my career.

III. UREA CYCLE DISORDERS

11. The '197 Patent generally is directed to an improved method of treating a patient with a urea cycle disorder (“UCD”). The method involves measuring the ratio of plasma phenylacetate (“PAA”) to plasma phenylacetylglutamine (“PAGN”) in the same blood sample of a UCD patient who has previously taken glycerol phenylbutyrate or another PAA prodrug, and, if the ratio is *outside* of the range from 1:1 to 2:1 (or, alternatively, outside of the range from 1:1 to 2.5:1) and, in particular, if the PAA to PAGN ratio is above 2:1 or 2.5:1, administering to the UCD patient glycerol phenylbutyrate in an amount that is effective to cause the UCD patient to achieve a PAA to PAGN ratio that is within the target range.

12. UCDs are a class of inherited metabolic diseases characterized by a partial or complete absence of one or more enzymes or transporters involved in the metabolic pathway for disposing of waste nitrogen from the human body in the form of urea, which is excreted in urine. Disruption of the urea cycle leads to an accumulation of waste nitrogen and a corresponding increase in ammonia in a patient’s bloodstream. Ammonia is a potent neurotoxin which, when

present in sufficiently high concentrations in the bloodstream, results in a clinical condition referred to as hyperammonemia. Hyperammonemia manifests as central nervous system dysfunction of varying severity up to and including irreversible neurological damage and death if left untreated. Symptoms of neurotoxicity associated with UCDs include the following: somnolence (sleepiness), fatigue, lightheadedness, headache, irritability, poor feeding, hyperventilation, vomiting, disorientation, impaired memory, coma, irreversible neurological injury and death.

13. Prior to the advent of drug therapy, patients severely affected by UCDs typically died. In one longitudinal study, two-thirds of the severely affected babies diagnosed with a UCD during the first month of life died by the age of 6, even with the administration of sodium phenylacetate/sodium benzoate 10%/10% rescue treatment (AMMONUL®) during hyperammonemic crises.² With the development of newer chronic treatments, survival rates increased, but one out of five of severely affected newborns diagnosed with a urea cycle disorder within the first month of life still died from the condition within the first year of life.³

14. Dietary restriction is a key component of managing treatment of a UCD patient. Physicians decrease a patient's protein intake, thereby reducing the amount of waste nitrogen which must be cleared from the body through a genetically impaired urea cycle. With less waste nitrogen, patients are less prone to develop elevated blood ammonia levels. However, severe dietary protein restriction may also decrease the intake of essential amino acids below the levels

² Marshall Summar et al., *Diagnosis, symptoms, frequency and mortality of 260 patients with urea cycle disorders from a 21-year, multicenter study of acute hyperammonemic episodes*, 97 ACTA PAEDIATRICA 1420, 1423 & Fig. 3 (2008), attached as Exhibit B to the Bell Declaration.

³ See Food & Drug Administration Division Director's Summary Review of New Drug Application No. 203284 (the RAVICTI® (glycerol phenylbutyrate) NDA) at p. 3 of 33, attached as Exhibit C to the Bell Declaration.

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.