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**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**

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## **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. 9,561,197<sup>1</sup> (“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

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<sup>1</sup> 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.<sup>2</sup> 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.<sup>3</sup>

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

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<sup>2</sup> 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.

<sup>3</sup> 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.

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