Paper No. __
Filed: November 24, 2015

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NEPTUNE GENERICS, LLC

PETITIONER

V.

ELI LILLY & COMPANY

PATENT OWNER

CASE NO.: UNASSIGNED
PATENT NO. 7,772,209
FILED: JULY 11, 2007
ISSUED: AUGUST 10, 2010
INVENTOR: CLET NIYIKIZA

TITLE: ANTIFOLATE COMBINATION THERAPIES

DECLARATION OF W. ARCHIE BLEYER, MD, FRCP[GLASG]

Teva – Fresenius

I, W. Archie Bleyer, MD, FRCP hereby declare as follows:

I. INTRODUCTION

1. I am over the age of eighteen (18) and otherwise competent to make this declaration.

2. I have been retained as an expert witness on behalf of NEPTUNE GENERICS, LLC for the above-captioned *inter partes* review ("IPR"). I understand that the petition for *inter partes* review involves U.S. Patent No. 7,772,209 ("the '209 patent"), Exhibit 1001, which issued from U.S. Patent Application No. 11/776,329 (the "'329 Application"), filed July 11, 2007. (Ex. 1001 at Front Cover.) The '209 Patent claims priority to U.S. Patent App. No. 60/215,310 (filed June 30, 2000). The '209 Patent names Clet Niyikiza as an inventor. The '209 Patent issued on August 10, 2010. (*Id*.)

3. In preparing this Declaration, I have reviewed the '209 Patent and considered each of the documents cited herein, in light of general knowledge in the art as of June 30, 1999. In formulating my opinions, I have relied upon my experience, education and knowledge in the relevant art. In formulating my opinions, I have considered the viewpoint of a person of ordinary skill in the art prior to June 30, 1999.

II. BACKGROUND AND QUALIFICATIONS

4. I am a Clinical Research Professor in the Department of Radiation

Medicine at The Knight Cancer Institute at the Oregon Health and Sciences University, Portland; a Professor of Pediatrics at The University of Texas Medical School at Houston; and a Senior Advisor for the Children's Oncology Group Adolescent and Young Adult Committee.

5. My teaching responsibilities are primarily based in adolescent and young adult oncology.

6. I received an undergraduate degree (B.S.) (1965) in Life Sciences from the Massachusetts Institute of Technology, Cambridge, Massachusetts, and a medical degree (M.D.) (1969) from the University of Rochester School of Medicine and Dentistry, Rochester, New York.

7. After medical school, I completed my internship (1970) and residency (1971) in medicine/pediatrics and pediatrics at the University of Washington and Children's Hospital and Medical Center, Seattle, Washington.

8. Following residency, I completed fellowships in pediatric oncology at the National Cancer Institute, Bethesda, Maryland (1974), Seattle Children's Hospital and the University of Washington, Seattle, Washington (1975).

9. I received Board Certification in Pediatrics and Pediatric Hematology/Oncology from the National Board of Medical Examiners (1970), American Board of Pediatrics (1975), and the American Board of Pediatrics (1976).

10. I served as a Lieutenant Commander in the United States Public Health Services, and as a Clinical Associate at the National Cancer Institute, NIH, Bethesda, Maryland (1971-1974).

11. I am a Fellow of the American Board of Pediatrics and the Royal College of Physicians (Glasgow).

12. I am a member of multiple regional, national, and international organizations relating to pediatric, medical, and adolescent/young adult oncology.

13. I have authored more than 250 peer-reviewed articles and over 60 book chapters on pediatric oncology, medical oncology, adolescent/young adult oncology, and neuro-oncology, including articles and book chapters on the same topics.

14. I am an Editor of the 8 books, monographs and special issues of oncology journals. The most important book is *Cancer in Adolescents and Young Adults* (Springer Verlag Publishers, 2007) that has 73 authors from 9 countries on 4 continents, 534 pages, 199 figures, and 90 tables. A 2nd edition that will nearly double the contents is in preparation.

15. I have prescribed and administered a wide variety of intravenous, intramuscular, subcutaneous and intrathecal medications, including antifolates.

16. I consider myself to be an expert in the fields of pediatric oncology, adolescent/young adult oncology, neuro-oncology and cancer screening.

17. I am being compensated at a rate of $300/hour.

18. Additional details of my education and experience are listed in my *curriculum vitae*, a copy of which is attached as Attachment 1 (Ex. 1024).

III. LIST OF DOCUMENTS CONSIDERED IN FORMULATING OPINION

19. In formulating my opinion, I have considered the following documents: (a) the '209 Patent (Ex. 1001), (b) portions of the '209 Patent prosecution file history (Ex. 1002), and (c) the prior art relevant to the Petition – (1) Allen et al., "Diagnosis of Cobalamin Deficiency I: Usefulness of Serum Methylmalonic Acid and Total Homocysteine Concentrations." American Journal of Hematology, 34, 1990, 90-98 ("*Allen*") (Ex. 1017); (2) Refsum H & Ueland PM, "Clinical significance of pharmacological modulation of homocysteine metabolism." Trends in Pharmacol. Sci., Vol. 11, No. 10, 1990, pp. 411-416 ("*Refsum*") (Ex. 1012); (3) Morgan et al., "The Effect of Folic Acid Supplementation on the Toxicity of Low-Dose Methotrexate in Patients with Rheumatoid Arthritis." Arthritis and Rheumatism, Vol. 33, No. 1, January 1990, pp. 9-18 ("*Morgan*") (Ex. 1023); (4) U.S. Patent No. 5,217,974 ("the *'974 Patent*") (Ex. 1009); (5) European Patent Application No. 0,595,005 A1 ("*EP 005*") (Ex. 1010); (6) Zervos et al., "Functional folate status as a prognostic indicator of toxicity in clinical trials of the multitargeted antifolate LY231514." Proceedings of ASCO, Vol. 16, 1997, pg. 256a ("*Zervos*") (Ex. 1016); (7) Brönstrup et al.,

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