UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Moderna Therapeutics, Inc.

Petitioner

v.

Protiva Biotherapeutics, Inc.

Patent Owner

U.S. Patent No. 9,364,435

Issued: June 14, 2016

Named Inventor: Edward Yaworski, Kieu Lam, Lorne Palmer, Ian MacLachlan

Title: Lipid Formulations for Nucleic Acid Delivery

DECLARATION OF ANDREW S. JANOFF, PH.D. IN SUPPORT OF MODERNA THERAPEUTICS, INC.'S PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 9,364,435

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I, Dr. Andrew S. Janoff, PhD, declare as follows:

I. INTRODUCTION

1. My name is Andrew S. Janoff. I am a consultant in biotechnology and drug delivery, primarily focusing on lipid and liposome technology.

2. I have been engaged by Moderna Therapeutics, Inc. ("Moderna") as an expert in connection with matters raised in the Petition for *Inter Partes* Review ("Petition") of U.S. Patent No. 9,364,435 (the "'435 patent") owned by Protiva Biotherapeutics, Inc. ("Patent Owner").

3. This declaration is based on the information currently available to me. To the extent that additional information becomes available, I reserve the right to continue my investigation and study, which may include a review of documents and information that may be produced, as well as testimony from depositions that have not yet been taken.

II. SUMMARY OF OPINIONS

4. The '435 patent is entitled "Lipid Formulations for Nucleic Acid Delivery." Ex. 1001. The '435 patent is directed to a composition of nucleic acid-lipid particles (*e.g.*, particles that can be used to deliver therapeutic nucleic acid payloads to a patient) comprising three lipid components (*i.e.*, cationic lipid, non-cationic lipid and conjugated lipid), each of which fall within a claimed proportion with regard to the total lipid in the particles. *See, e.g.*, *id.*, cl. 1. The Petition challenges claims 1-20 of the '435 patent.

5. Petitioner's Ground 1 challenges claims 1-20 of the '435 patent as obvious under 35 U.S.C. § 103 in view of Patent Owner's prior disclosures in PCT/CA2004/001051, Publication No. WO2005007196 A2 ("'196 PCT"), Ex. 1002, or U.S. Publication No. US2006/0134189 ("'189 publication"), Ex. 1003. Based on studying the petition and the exhibits cited in the petition as well as other documents, it is my opinion that claims 1-20 of the '435 patent are obvious in view of the '196 PCT or '189 publication.

6. Petitioner's Ground 2 challenges claims 1-20 of the '435 patent as obvious in view of the Patent Owner's prior disclosures in light of Lin (Ex. 1005) and/or Ahmad (Ex. 1006) under 35 U.S.C. § 103. Based on studying the petition and the exhibits cited in the Petition as well as other documents, it is my opinion that claims 1-20 of the '435 patent are obvious in view of the Patent Owner's prior disclosures in light of Lin and/or Ahmad.

7. Petitioner's Ground 3 challenges claims 1-20 of the '435 patent as anticipated by the disclosures in U.S. Publication No. US2006/0240554 ("'554 publication"), Ex. 1004, under pre-AIA 35 U.S.C. § 102(b) or, in the alternative, as obvious under 35 U.S.C. § 103 in view of the '554 publication. Based on studying the petition and the exhibits cited in the petition as well as other documents, it is my opinion that claims 1-20 of the '435 patent are anticipated by the '554 publication. In the alternative, it is my opinion that claims 1-20 of the '435 patent are obvious in view of the '554 publication.

III. QUALIFICATION AND EXPERIENCE

8. I am formally trained as a membrane biophysicist. I obtained my Ph.D. degree in Biophysics from Michigan State University in 1980. Before that, I received my MS in Biophysics from Michigan State University in 1977, and my BS in Biology from The American University in 1971. I received postdoctoral training in Pharmacology at the Harvard Medical School and in Anesthesia at the Massachusetts General Hospital.

9. I have played leadership roles in the discipline of pharmaceutical liposomology from its inception in 1981.

10. After my post-doctoral work, I was recruited from Harvard by the industrialist, Jack Whitehead, and became the first senior founding scientist at the Liposome Company, Inc. I eventually became the Vice President of Research and Development at the Liposome Company. I led the team at the Liposome Company that discovered, formulated, and developed ABELCET, a novel lipid structure that is approved worldwide for systemic fungal infections. I first published the physical chemical characterization of this structure, along with an explanation of why it would yield a less toxic alternative to the traditional micelle formulation in the *Proceedings of the National Academy of Sciences*.

11. I led the team at the Liposome Company that developed Staclot LA, a diagnostic reagent comprised of Hexagonal (II) lipid that is a standard

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