UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Moderna Therapeutics, Inc.

Petitioner

v.

Protiva Biotherapeutics, Inc.

Patent Owner

Case No. IPR2019-00554
U.S. Patent No. 8,058,069

PETITIONER'S REPLY TO PROTIVA'S RESPONSE

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TABLE OF AUTHORITIES

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Cases

LIST OF EXHIBITS RELIED UPON IN THE REPLY

Exhibit No.	References
1020	Declaration of Thomas J. Anchordoquy, Ph.D. iso Petitioner's Reply to Protiva's Response ("Anchodoquy")
1021	Curriculum Vitae of Thomas J. Anchordoquy
1022	Final Written Decision in IPR2018-00739, Paper 51, Entered September 11, 2019
1023	Onpattro Labeling, Application No. 210922Orig1s000
1024	Ian MacLachlin, Liposomal Formulations for Nucleic Acid Delivery (2007)
1025	Deposition of David H. Thompson, Ph.D. taken January 15, 2020
1026	Akinc *et. al.*, Onpattro story and clinical translation of nanomedicines containing nucleic acid-based drugs, Nature Nanotechnology, Vol. 14, Dec. 2019, pp. 1084-1087
1027	Zimmerman *et. al.*, RNAi-mediated gene silencing in non-human primates, 2006 Nature Publishing Group
1028	U.S. Patent No. 7,799,565 issued to MacLachlan, Sept. 21, 2010

I. INTRODUCTION

The Board ordered an IPR over the'069 patent with respect to grounds 1-3 for claims 1-22. In response, Patent Owner Protiva relies upon the mistaken premises that (1) the prior art references do not teach overlapping ranges for the phospholipid component (Response, 12-18) and (2) the disclosed ranges are too broad to support routine optimization (*id.*, 19-30). Both are demonstrably false. First, Protiva's expert admits that the cited references disclose an overlapping phospholipid range and actual prior art testing demonstrating phospholipid concentrations overlapping with the claimed range. Second, Protiva's own prior test data confirms the regular practice in the field of optimizing lipid concentrations and provides a starting point for such routine optimization.

Protiva relies heavily on its expert's belief that all the "cationic lipids should be minimized" because of toxicity concerns. Response, 29. This oversimplification evinces Protiva's expert's inexperience with lipid carrier particles. It was well known years before the '069 patent that ionizable cationic lipids can be used in high amounts to create particles that are substantially non-toxic. *See, e.g.*, EX1004, [0151].

Faced with prior disclosures of particle formulations with overlapping ranges for all claimed lipid components rendering the claims *prima facie* obvious, Protiva seeks to cloud the matter as much as possible. For example, Protiva points to the

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