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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MODERNA THERAPEUTICS, INC.,
Petitioner,

v.

PROTIVA BIOTHERAPEUTICS, INC.,
Patent Owner.

Case IPR2018-00739
Patent 9,364,435 B2

Before SHERIDAN K. SNEDDEN, SUSAN L.C. MITCHELL, and RICHARD J. SMITH, *Administrative Patent Judges*.

MITCHELL, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
35 U.S.C. § 314(a)

I. INTRODUCTION

Moderna Therapeutics, Inc. ("Petitioner") filed a Petition to institute an *inter partes* review of claims 1–20 of U.S. Patent 9,364,435 B2 (the "'435 patent"). Paper 2 ("Pet."). Protiva Biotherapeutics, Inc. ("Patent Owner")[1] filed a Preliminary Response to the Petition. Paper 12 ("Prelim. Resp.").

We have authority under 35 U.S.C. § 314(a) to determine whether to institute an *inter partes* review. To institute an *inter partes* review, we must determine that the information presented in the Petition shows "a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). On April 24, 2018, the Supreme Court held that a decision to institute under 35 U.S.C. § 314(b) may not institute review on less than all claims challenged in the petition. *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1355–56 (2018). Also, in accordance with USPTO Guidance, "if the PTAB institutes a trial, the PTAB will institute on all challenges raised in the petition." *See Guidance on the Impact of SAS on AIA Trial Proceedings* (April 26, 2018) (available at https://www.uspto.gov/patents-application-process/patent-trial-and-appeal-board/trials/guidance-impact-sas-aia-trial).

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[1] According to Patent Owner, Protiva Biotherapeutics, Inc. ("Protiva") existed as a wholly-owned subsidiary of Arbutus Biopharma Corporation and was amalgamated into Arbutus Biopharma Corporation in January 2018. Paper 14, 2. Patent Owner identifies Arbutus Biopharma Corporation (fka "Tekmira"), Genevant Sciences, Ltd., and its fully owned subsidiaries: Genevant Sciences Holding, Ltd., Genevant Sciences Corporation, Genevant Sciences, Inc., and Genevant Sciences, GmbH, as the real parties in interest. *Id*.

Applying those standards, and upon consideration of the information presented in the Petition and the Preliminary Response, we conclude that Petitioner has established a reasonable likelihood that it would prevail in showing the unpatentability of at least one challenged claim of the '435 patent. Therefore, we institute an *inter partes* review for claims 1–20 of the '435 patent.

A. Related Proceedings

Patent Owner identifies the following related matters:

Moderna Therapeutics, Inc. v. Protiva Biotherapeutics, Inc., IPR2018-00680 regarding U.S. Patent No. 9,404,127 B2; and European Patent Office Opposition proceedings regarding EP 2 279 254. Paper 14, 2.

B. The '435 Patent (Ex. 1001)

The '435 patent relates to "stable nucleic acid-lipid particles (SNALP) comprising a nucleic acid (such as one or more interfering RNA), methods of making the SNALP, and methods of delivering and/or administering the SNALP." Ex. 1001, Abstract. The '435 patent states that "[t]he present invention is based, in part, upon the surprising discovery that lipid particles comprising from about 50 mol % to about 85 mol % of a cationic lipid, from about 13 mol% to about 49.5 mol % of a non-cationic lipid, and from about 0.5 mol % to about 2 mol % of a lipid conjugate provide advantages when used for the in vitro or in vivo delivery of an active agent, such as a therapeutic nucleic acid (e.g., an interfering RNA)." *Id.* at 5:55-62. The '435 patent further states that

> the present invention provides stable nucleic acid-lipid particles (SNALP) that advantageously impart increased activity of the encapsulated nucleic acid (e.g., an interfering RNA such as siRNA) and improved tolerability of the formulations in vivo, resulting in a significant increase in the therapeutic index as

> compared to nucleic acid-lipid particle compositions previously described. Additionally, the SNALP of the invention are stable in circulation, e.g., resistant to degradation by nucleases in serum and are substantially non-toxic to mammals such as humans.

Id. at 5:62–6:5.

The '435 patent identifies specific SNALP formulations that encapsulate siRNA as the nucleic acid, such as the 1:57 SNALP and the 1:62 SNALP, and states that "the Examples herein illustrate that the improved lipid particle formulations of the invention are highly effective in downregulating the mRNA and/or protein levels of target genes." *Id*. at 6:5–30.

C. Illustrative Claim

Petitioner challenges claims 1–20 of the '435 patent. Claim 1 is illustrative and reproduced below:

> 1. A nucleic acid-lipid particle comprising:
> (a) a nucleic acid;
> (b) a cationic lipid comprising from 50 mol % to 85 mol % of the total lipid present in the particle;
> (c) a non-cationic lipid comprising from 13 mol % to 49.5 mol % of the total lipid present in the particle; and
> (d) a conjugated lipid that inhibits aggregation of particles comprising from 0.5 mol % to 2 mol % of the total lipid present in the particle.

Ex. 1001, 89:55–63.

Claim 1 is the only independent claim, and claims 2–20 are directly or indirectly dependent on claim 1. *Id*. at 89:55–92:22.

D. The Asserted Grounds of Unpatentability

Petitioner contends that the challenged claims are unpatentable under 35 U.S.C. §§ 102 and 103 based on the following grounds. Pet. 5.

Reference[s]	Basis	Claims challenged
WO 2005/007196 A2[2] and US 2006/0134189 A1[3]	§ 103	1–20
'196 PCT, '189 Publication, Lin,[4] and Ahmad[5]	§ 103	1–20
US 2006/0240554 A1[6]	§§ 102 and 103	1–20

Petitioner also relies on the Declaration of Dr. Andrew S. Janoff, Ph.D. ("Janoff Declaration" or "Decl."). Ex. 1007; *see generally* Pet.

II. ANALYSIS

A. Person of Ordinary Skill in the Art

Petitioner asserts that a person having ordinary skill in the art ("POSITA") "would have specific experience with lipid particle formation and use in the context of delivering therapeutic payloads, and would have a Ph.D., an M.D., or a similar advanced degree in an allied field (*e.g.*, biophysics, microbiology, biochemistry) or an equivalent combination of education and experience." Pet. 5 (citing Ex. 1007 ¶¶ 31–32). Petitioner

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[2] Ian MacLachlan et al., WO 2005/007196 A2, published Jan. 27, 2005 ("'196 PCT"). Ex. 1002.
[3] Ian MacLachlan et al., US 2006/0134189 A1, published Jun. 22, 2006 ("'189 Publication"). Ex. 1003.
[4] Alison J. Lin et al., *Three-Dimensional Imaging of Lipid Gene-Carriers: Membrane Charge Density Controls Universal Transfection Behavior in Lamellar Cationic Liposome-DNA Complexes*, 84 BIOPHYSICAL J. 3307–16 (2003) ("Lin"). Ex. 1005.
[5] Ayesha Ahmad et al., *New Multivalent Cationic Lipids Reveal Bell Curve for Transfection Efficiency Versus Membrane Charge Density: Lipid-DNA Compleses for Gene Delivery*, 7 J. GENE MED. 739–48 (2005) ("Ahmad"). Ex. 1006.
[6] Tongqian Chen et al., US 2006/0240554 A1, published Oct. 26, 2006 ("'554 Publication"). Ex. 1004.

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