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Paper No. 51
Entered: September 11, 2019

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*.

FINAL WRITTEN DECISION

Determining Claims 1–6, 9, 12, 14, and 15
Unpatentable in *Inter Partes* Review
35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

Determining Claims 7, 8, 10, 11, 13, and 16–20
Not Unpatentable in *Inter Partes Review*
35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

Denying Patent Owner's Motion to Amend
35 U.S.C. § 316(d) and 37 C.F.R. § 42.121

I. INTRODUCTION

This is a final written decision in *inter partes* review of claims 1–20 of U.S. Patent No. 9,364,435 B2 (Ex. 1001, "the '435 patent") entered pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons set forth below, we determine that Petitioner has shown by a preponderance of the evidence that claims 1–6, 9, 12, 14, and 15 of the '435 patent are unpatentable under 35 U.S.C. § 102. *See* 35 U.S.C. § 316(e). We also determine that Petitioner has not shown by a preponderance of the evidence that claims 7, 8, 10, 11, 13, or 16–20 are unpatentable.

Because we have found only some of the challenged claims unpatentable, we address Patent Owner's contingent Motion to Amend concerning proposed substitute claims for those unpatentable claims, which are proposed substitute claims 21–26, 29, 32, 34, and 35. We also find that Patent Owner's proposed substitute claims 21–26, 29, 32, 34, and 35 are unpatentable. Therefore, we deny Patent Owner's Motion to Amend.

A. Procedural History

Moderna Therapeutics, Inc. ("Petitioner")[1] filed a Petition to institute an *inter partes* review of claims 1–20 (the "challenged claims") of the '435 patent. Paper 2 ("Pet."); *see* 35 U.S.C. §§ 311–319. Petitioner relied upon the Declaration of Andrew S. Janoff, Ph.D. to support its challenge.

[1] Petitioner states that the name of its parent has been changed to Moderna, Inc., and that Moderna, Inc.'s intellectual property matters are now conducted under the name of ModernaTX, Inc., which is a fully-owned subsidiary of Moderna, Inc. Paper 46, 2.

See generally Pet. Protiva Biotherapeutics, Inc. ("Patent Owner")[2] filed a Preliminary Response to the Petition. Paper 12 ("Prelim. Resp.").

Pursuant to 35 U.S.C. § 314(a), on September 12, 2018, we instituted an *inter partes* review of challenged claims 1–20 (Paper 15, "Inst. Dec." or "Institution Decision") instituting *inter partes* review of all challenged claims under all asserted grounds. Inst. Dec. 33. Patent Owner filed a Response (Paper 24, "PO Resp.") supported by the Declaration of David H. Thompson, Ph.D (Ex. 2009). Petitioner filed a Reply (Paper 28, "Reply") supported by a second Declaration of Dr. Janoff (Ex. 1021), and Patent Owner filed an authorized Sur-reply (Paper 34, "Sur-reply"). *See* Papers 16, 19 (authorizing Patent Owner's Sur-Reply).

Patent Owner filed a contingent motion to amend (Paper 26 (corrected), "Mot.") supported by a Declaration of Dr. Thompson (Ex. 2040), which Petitioner opposed (Paper 29, "Opposition to Motion to Amend") with a supporting Declaration of Dr. Janoff (Ex. 1020). Patent Owner filed a Reply to Petitioner's opposition. Paper 33, "Reply Opp."

At the request of both parties, we held an oral hearing on June 6, 2019, and the transcript of that hearing has been entered into the record. Paper 49 ("Tr.").

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[2] 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*.

B. 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.

C. 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.

D. 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.

E. The Instituted Grounds of Unpatentability

We instituted the instant trial based on the following grounds of unpatentability. Inst. Dec. 5, 33.

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