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Paper 9
Entered: October 10, 2018

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ALNYLAM PHARMACEUTICALS, INC.,
Petitioner,

v.

SILENCE THERAPEUTICS GMBH,
Patent Owner.

Case PGR2018-00059
Patent 9,695,423

Before JEFFREY B. ROBERTSON, RAMA G. ELLURU, and MONTÉ T. SQUIRE, *Administrative Patent Judges.*

SQUIRE, *Administrative Patent Judge.*

DECISION
Denying Institution of Post-Grant Review
35 U.S.C. § 324

I. INTRODUCTION

A. Background

Alnylam Pharmaceuticals, Inc. ("Petitioner") filed a Petition ("Pet.," Paper 2) requesting post-grant review of claims 1–25 of U.S. Patent No. 9,695,423 ("the '423 patent," Ex. 1001). Silence Therapeutics GMBH ("Patent Owner") filed a Preliminary Response ("Prelim. Resp.," Paper 7). We have authority to determine whether to institute a post-grant review. 35 U.S.C. § 324; 37 C.F.R. § 42.4(a).

The standard for instituting a post-grant review is set forth in 35 U.S.C. § 324(a), which provides that a post-grant review may not be instituted unless "the information presented in the petition filed under section 321, if such information is not rebutted, would demonstrate that it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable." After considering the Petition and Preliminary Response, we determine that Petitioner has not demonstrated that it is more likely than not that at least one of the challenged claims is unpatentable. We, therefore, do not institute post-grant review of any claim of the '423 patent.

B. Related Matters

Petitioner identifies *Alnylam Pharmaceuticals, Inc. v. Silence Therapeutics*, Civil Action No. 1:18-cv-10613-MLW, filed in the United States District Court for the District of Massachusetts, as a pending suit in which Petitioner seeks declaratory judgment of non-infringement of the '423 patent and related patents. Pet. 3; Paper 5. Petitioner also identifies the following applications that claim priority to the '423 patent's filing date: U.S. Patent Application No. 15/589,968, filed on May 8, 2017 (issued as U.S. Patent No. 9,790,501); U.S. Patent Application No. 15/589,971, filed

on May 8, 2017 (issued as U.S. Patent No. 9,758,784); U.S. Patent Application No. 15/594,349, filed on May 12, 2017 (issued as U.S. Patent No. 9,783,802); U.S. Patent Application No. 15/594,438, filed on May 12, 2017 (issued as U.S. Patent No. 9,790,505); and U.S. Patent Application No. 15/678,024, filed on August 15, 2017. Paper 5.

Patent Owner identifies the following post-grant reviews, which involve the same parties and related patents: PGR2018-00067 (filed June 11, 2018); PGR2018-00075 (filed July 9, 2018); PGR2018-00088 (filed July 17, 2018); and PGR2018-00089 (filed July 17, 2018). Paper 8.

C. The '423 Patent

The '423 patent is titled "Interfering RNA Molecules" and issued on July 4, 2017 from U.S. Application No. 14/977,710.[1] Ex. 1001, (21), (22), (54). The '423 patent is directed to interfering ribonucleic acid molecules having a double-stranded structure. *Id.* at 1:28–29. The '423 patent describes small interfering RNA ("siRNA" or "RNAi") molecules and methods for using such molecules, for example, for inhibiting expression of a target gene. *Id.* at 1:34–36, 2:22–24, 6:49–54 (disclosing "a method for inhibiting the expression of a target gene in a cell or derivative thereof comprising introducing a ribonucleic acid according to any of the aspects of

[1] U.S. Application No. 14/977,710 ("'710 application," Ex. 1004), filed December 22, 2015, is a continuation of a series of patent applications and claims priority to European Patent Application No. 02017601, filed August 5, 2002 ("EP1," Ex. 1006); U.S. Provisional Application No. 60/402,541, filed August 12, 2002 ("'541 provisional," Ex. 1007); and European Patent Application No. 03008383, filed April 10, 2003 ("EP2," Ex. 1008). Ex. 1001, (30), (63), 1:6–20. In this Decision, we refer to underlying applications to which the '423 patent claims priority collectively as the "priority applications."

the present invention into a cell in an amount sufficient to inhibit expression of the target gene"), 12:30–32 (disclosing "that all of the ribonucleic acids of the present invention are suitable to cause or being involved in methods of RNA mediated interference"). The target nucleic acid sequence or target nucleic acid is typically "a single stranded RNA" and "more preferably an mRNA" (messenger RNA). *Id.* at 11:61–64.

The '423 patent discloses that the siRNA molecules consist of a ribonucleic acid comprising a double-stranded structure, formed by a first strand and a second strand. *Id.* at 11:25–28. The '423 patent further discloses that the first strand comprises a stretch of contiguous nucleotides that is at least partially complementary to a target nucleic acid, and the second strand comprises a second stretch of contiguous nucleotides that is at least partially identical to a target nucleic acid. *Id.* at 1:30–34, 11:28–31. The '423 patent explains that the "length of the first stretch and second stretch, respectively, is typically about 15 to about 23, preferably 17 to 21, and more preferably 18 or 19 bases." *Id.* at 18:33–35, 3:29–32 ("In an embodiment of the ribonucleic acid according to any aspect of the present invention the double-stranded structure has a length of 17 to 21 nucleotides, preferably 18 to 19 nucleotides.").

The '423 patent discloses that at least one nucleotide of the siRNA molecule has a modification at the 2'-position and the modification is preferably selected from the group comprising amino, fluoro, methoxy, alkoxy and alkyl. *Id.* at 3:50–54, 15:48–51 (disclosing that "modification of the nucleotides may be any form of modification described herein"). The '423 patent describes that a "flanking nucleotide or group of nucleotides is arrayed on both sides of the modified nucleotide or group" and discloses that

"the flanking nucleotide or group either is unmodified or does not have the same modification of the preceding nucleotide or group of nucleotides." *Id.* at 16:30–34.

The '423 patent further discloses that the

> first strand and/or said second strand comprises a plurality of groups of modified nucleotides having a modification at the 2'-position whereby within the strand each group of modified nucleotides is flanked on one or both sides by a flanking group of nucleotides whereby the flanking nucleotides forming the flanking group of nucleotides is either an unmodified nucleotide or a nucleotide having a modification different from the modification of the modified nucleotides.

Id. at 3:54–4:5. *See also id.* at 7:6–12 (stating that the "unmodified nucleotides or unmodified groups of nucleotides referred to as flanking group(s) of nucleotides herein . . . are different from the modification of the nucleotides forming the group(s) of modified nucleotides").

The '423 patent explicitly defines the term "unmodified nucleotide" to mean "either not having any of the aforementioned modifications at the nucleotide forming the respective nucleotide or group of nucleotides, or having a modification which is different from the one of the modified nucleotide and group of nucleotides, respectively." *Id.* at 16:45–50, 16:51–59 (disclosing that modification of the unmodified nucleotide "can be the same or even different for the various nucleotides forming said unmodified nucleotides or for the various flanking groups of nucleotides").

The '423 patent describes several embodiments and examples that illustrate certain advantages and aspects of the claimed invention. *Id.* at 2:25–6:56, 21:52–33:31. In one embodiment, the '423 patent describes a "17 nucleotide long siRNA" molecule, including experimental data suggesting that the molecule showed decreased or reduced activity, as

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