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Paper No. 7
Filed: June 13, 2018

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INITIATIVE FOR MEDICINES,
ACCESS & KNOWLEDGE (I-MAK), INC.,
Petitioner,

v.

GILEAD PHARMASSET LLC
Patent Owner.

Case IPR2018-00103
Patent 7,429,572 B2

Before LORA M. GREEN, ERICA A. FRANKLIN, and RICHARD J. SMITH, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

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

I. INTRODUCTION

Initiative for Medicines, Access & Knowledge, Inc. ("I-MAK" or "Petitioner") filed a Petition requesting an *inter partes* review of claims 1–19 of U.S. Patent No. 7,429,572 B2 (Ex. 1001, "the '572 patent"). Paper 2 ("Pet."). Gilead Pharmasset LLC ("Patent Owner") filed a Preliminary Response to the Petition. Paper 6 ("Prelim. Resp.").

Institution of an *inter partes* review is authorized by statute when "the information presented in the petition . . . and any response . . . shows that there is 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; *see* 37 C.F.R. §§ 42.4. Upon considering the Petition and the Preliminary Response, we determine that Petitioner has not demonstrated a reasonable likelihood that it would prevail in showing the unpatentability of any of the challenged claims. Accordingly, we decline to institute an *inter partes* review for any challenged claim of the '572 patent.

A. Related Proceedings

Petitioner states that it "is not aware of any other matter that would affect, or be affected by, a decision in this proceeding." Pet. 2. Patent Owner identifies U.S. Patent Application Serial No. 12/878,262, now U.S; Patent No. 8,415,322 B2, as well as U.S. Patent Application Serial No. 11/854,218, which is pending. Paper 3, 2.

Patent Owner also notes

> that Petitioner filed two petitions for Inter Partes Review of U.S. Patent No. 7,964,580 [B2] (Case Nos. IPR2018-00119 and IPR2018-00120); two petitions for Inter Partes Review of U.S. Patent No. 8,334,270 [B2] (Case Nos. IPR2018-00121 and IPR2018-00122), one petition for Inter Partes Review of U.S. Patent No. 8,633,309 [B2] (Case No. IPR2018-00125), and one

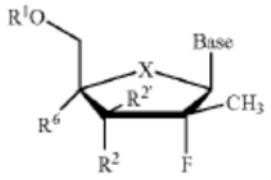
petition for Inter Partes Review of U.S. Patent No. 9,284,342 [B2] (Case No. IPR2018-00126).

Id.

B. The '572 Patent (Ex. 1001)

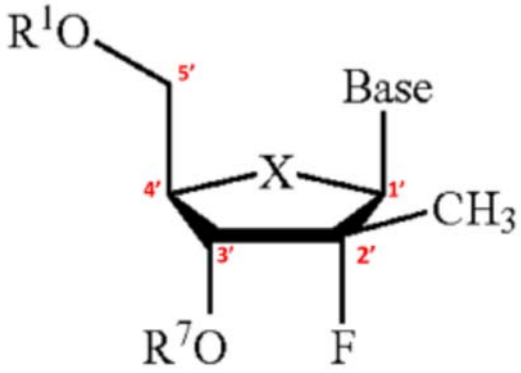
The '572 patent issued September 30, 2008, with Jeremy Clark as the sole listed inventor. Ex. 1001.

According to the '572 patent, "[h]epatitis C virus (HCV) infection is a major health problem that leads to chronic liver disease, such as cirrhosis and hepatocellular carcinoma, in a substantial number of infected individuals, estimated to be 2-15% of the world's population." *Id.* at 1:22–25. The '572 patent "provides a (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β-D or β-L), or its pharmaceutically acceptable salt or prodrug thereof, and the use of such compounds for the treatment of a host infected with a virus belonging to the Flaviviridae family, including hepatitis C, West Nile Virus and yellow fever virus." *Id.* at 10:21–26. In particular, the '572 patent provides compounds of the general formula:



Id. at 11:30–40. As can be seen in the above formula, the fluorine at the 2' position of the sugar ring is below the ring, also referred to as the down position, and the methyl group at the 2' position is above the ring, or the up position. *See* Prelim. Resp. 1 (noting that the "specific 2'-methyl up, 2'-fluoro down ('2'MeF') structure is a central feature of the inventions disclosed and claimed in the '572 patent").

The following formula also shows the stereochemistry at the 2' position of the sugar ring of the disclosed compounds, and shows the numbering of the carbon atoms on the sugar ring:

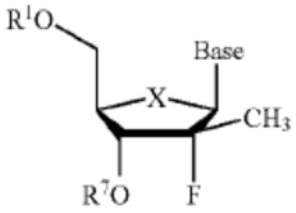


Id. at 5. As noted by Patent Owner, the carbon at the 2' position is a tertiary carbon as it is attached to a methyl group as well as the two adjacent carbon atoms of the sugar ring. *Id.* at 4.

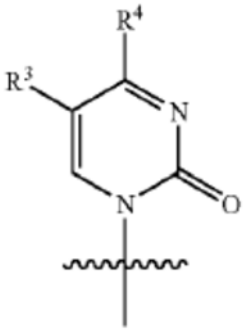
C. Representative Claim

Petitioner challenges claims 1-19 of the '572 patent. Claim 1 is representative, and is reproduced below:

1. A (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside (β-D or β-L) or its pharmaceutically acceptable salt of the structure:



wherein Base is a pyrimidine base represented by the following formula:



X is O; R^1 and R^7 are independently H, a monophosphate, a diphosphate, a triphosphate, a H-phosphonate, alkyl, an alkyl sulfonyl, or an arylalkyl sulfonyl; and

R^3 is H and R^4 is NH_2 or OH.

Ex. 1001, 64:27–57.

Claims 2–5 further limit the genus of claim 1. *Id.* at 64:58–65:3. Claims 6 and 15 are drawn to specific compounds that fall within the genus of claim 1. *Id.* at 65:4–19, 66:24–39. Claims 7–12 and 16 are drawn to pharmaceutical compositions of compounds that fall within the genus of claim 1. *Id.* at 65:20–37, 66:40–42. Claims 13 and 14 are drawn to methods of synthesizing the compounds of claim 1. *Id.* at 65:38–66:4. And finally, claims 17–19 are drawn to liposomal compositions that comprise compounds that fall within the genus of claim 1. *Id.* at 66:43–51.

D. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–19 of the '572 patent on the following grounds (Pet. 3):

References	Basis	Claims Challenged
Klecker[1]	§ 102(b)	1–16

[1] Klecker et al., WO 99/23104 A2, published May 14, 1999 ("Klecker") (Ex. 1005).

References	Basis	Claims Challenged
Sommadossi[2]	§ 102(b)	1–19
Sommadossi and Klecker	§ 103(a)	1–19

Petitioner relies also on the Declaration of Joseph M. Fortunak, Ph.D. Ex. 1002.

II. ANALYSIS

A. Claim Construction

We interpret claims using the "broadest reasonable construction in light of the specification of the patent in which . . . [they] appear[]" 37 C.F.R. § 42.100(b); *see also Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016). Under the broadest reasonable construction standard, claim terms are generally given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc*., 504 F.3d 1249, 1257 (Fed. Cir. 2007). "Absent claim language carrying a narrow meaning, the PTO should only limit the claim based on the specification . . . when [it] expressly disclaim[s] the broader definition." *In re Bigio*, 381 F.3d 1320, 1325 (Fed. Cir. 2004). "Although an inventor is indeed free to define the specific terms used to describe his or her invention, this must be done with reasonable clarity, deliberateness, and precision." *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Petitioner asserts that "there is no reason to give any of the terms of the claims of the [']572 [patent] a meaning other than their ordinary and

[2] Sommadossi et al., WO 01/90121 A2, published November 29, 2001 ("Sommadossi") (Ex. 1006).

accustomed meaning." Pet. 9. Patent Owner does not offer any claim construction. Accordingly, we determine that none of the claim terms require explicit construction in order to determine whether to institute a trial in this case. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Ltd.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) ("[W]e need only construe terms 'that are in controversy, and only to the extent necessary to resolve the controversy'" (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))).

B. Anticipation by Klecker

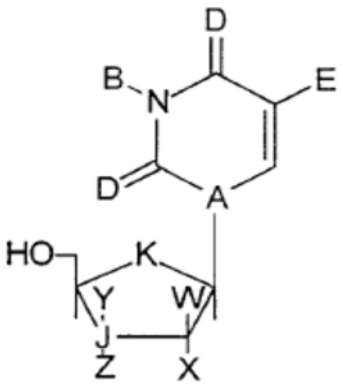
Petitioner asserts that claims 1–16 are anticipated by Klecker. Pet. 32–49. Patent Owner responds that Petitioner has not demonstrated a reasonable likelihood that the claims are anticipated by Klecker. Prelim. Resp. 20–23.

i. Overview of Klecker (Ex. 1005)

Klecker "relates to methods, compounds, and compositions for diagnosing and/or treating tumor cells with anti-tumor agents activated by thymidylate synthase (TS) and/or thymidine kinase (TK)." Ex. 1005,[3] 1:4–

[3] All references to page numbers in a reference are to the original numbering of the reference, and not the page numbers added by a party, unless otherwise indicated.

7. In particular, Klecker teaches the following compounds of the following formula:



wherein: A= N, C;

B = H, hydroxy, halogen, acyl (C_1-C_6), alkyl (C_1-C6,), alkoxy (C_1-C_6);

D = O, S, NH_2;

E = H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkoxy, substituted alkoxy, halogen, or any substituent which is readily cleaved in the body to generate one of the before listed groups;

W, X, Y, Z = H, hydroxy, halogen, alkyl (C_1-C_6), alkoxy (C_1-C_6), a label containing moiety or a label;

J = C, S; and

K = O, C.

Id. at 14:18–15:7.

According to Klecker, in a preferred embodiment, "W is Fluorine and E is H, methyl, iodine[,] or a substituent readily cleaved by the body to generate one of these groups." *Id.* at 15:11–13. Klecker notes further that "F can also be placed below the ring at the 2' - position, X=F." *Id.* at 19:25–26.

ii. Analysis

Claim 1 is drawn to a nucleoside with a methyl group in the 2' up position and a fluorine in the 2' down position. We note further that all of the challenged claims are drawn to compounds, methods of synthesis, pharmaceutical compositions, and liposomal compositions that all require a compound that falls within the genus of claim 1.

Petitioner contends[4] that in the formula provided above, Klecker discloses that the substituents A, B, D, and E "would be selected from typical pyrimidine bases," and that "would then lead one of skill to immediately envisage the generally known cytidine and uridine bases, wherein A would be N, B would be H, D would be O or NH_2 and E would be H." Pet. 34 (citing Ex. 1005, 30:19–22; Ex. 1002 ¶ 91). Petitioner asserts that Klecker teaches that fluorine is a preferred substituent at the X position, and teaches that W can be an alkyl ($C_1 – C_6$). *Id.* (citing Ex. 1005, 19:21–26, 44:11–15). According to Petitioner, the ordinary artisan "would know from general knowledge and common sense that methyl is a preferred lower alkyl in that group." *Id.* (citing Ex. 1002 ¶ 92).

Petitioner asserts further that Klecker teaches that K may be O or C, and the ordinary artisan "would also know from general knowledge and common sense that K being O creates a natural sugar ring commonly found in nucleosides." *Id.* (citing Ex. 1002 ¶ 93; Ex. 1005, 44:16). Acknowledging that Klecker identifies "a number of substituents" at the 3'

[4] We adopt Petitioner's statement (Pet. 8) as to the level of skill of the ordinary artisan for purposes of this Decision. We note that the applied prior art also reflects the appropriate level of skill at the time of the claimed invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).

position of the sugar ring, Petitioner asserts that "C is the first substituent identified for J, and H and OH are the first two substituents identified for Y and Z." *Id.* at 34–35 (citing Ex. 1005, 44:11–15). Petitioner asserts, therefore, that "one of ordinary skill in the art would envisage their implementations, i.e.[,] J as C, Y as H[,] and Z as OH." *Id.* at 35 (citing Ex. 1002 ¶ 94). Petitioner contends, therefore, that "one of ordinary skill in the art reading Klecker would immediately envisage compounds that fall squarely within the compounds of claim 1 of the ['']572 patent." *Id.* (citing Ex. 1002 ¶ 95).

Patent Owner responds that all of the challenged claims "require[ ] a nucleoside with methyl (CH_3) at the 2' up position and a fluorine (F) at the 2' down position." Prelim. Resp. 1. According to Patent Owner, Klecker does not teach a compound with a fluorine in the 2' down position and a methyl group in the 2' up position. *Id.* at 17.

Patent Owner asserts that Petitioner has engaged in improper hindsight, using the "disclosure of the '572 patent as a roadmap to cherry pick substituents and assemble the structure of the claimed invention." Prelim. Resp. 20. Specifically, Patent Owner argues that Klecker discloses a large genus of potentially billions of compounds. *Id.* at 21. Petitioner, Patent Owner asserts, does not point to any example of Klecker that shows a methyl group in the 2' up position, and in fact teaches that fluorine is the preferred substituent in that position. *Id.* at 22 (citing Ex. 1005, 19:21–25). Thus, Patent Owner asserts that "Klecker does not disclose the claimed combination of substituents," and, thus, does not anticipate the challenged claims. *Id.* at 22–23.

We agree with Patent Owner that Petitioner has not established a reasonable likelihood that claim 1 is anticipated by Klecker. To anticipate a reference must expressly or inherently disclose "within the four corners of the document not only all of the limitations claimed but also all of the limitations arranged or combined in the same way as recited in the claim." *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1371 (2008). Moreover, "anticipation is not proven by 'multiple, distinct teachings that the artisan might somehow combine to achieve the claimed invention.'" *Microsoft Corp. v. Biscotti, Inc.*, 878 F.3d 1052, 1069 (Fed. Cir. 2017) (internal citation omitted). "[A] disclosed genus may anticipate a claimed species when the genus is so small that one of ordinary skill in the art would 'at once envisage each member of this limited class.'" *Wasica Fin. GmbH v. Continental Auto. Sys., Inc.*, 853 F.3d 1272, 1285 (Fed. Cir. 2017) (quoting *AbbVie Inc. v. Mathilda & Terence Kennedy Inst. of Rheumatology Tr.*, 764 F.3d 1366, 1379 (Fed. Cir. 2014)).

In this case, we agree with Patent Owner that Petitioner is improperly using claim 1 as a roadmap to cherry pick teachings of the Klecker reference to arrive at compounds encompassed by the genus of that claim. For example, we acknowledge that Klecker teaches that a fluorine may be placed below the ring at the 2' position of the sugar ring. Ex. 1005, 19:25–26. Petitioner does not point us to any teaching of Klecker, however, that teaches a compound that has both a methyl group and a fluorine at the 2' position of the sugar ring, regardless of whether the fluorine is in the up position or the down position. That is, although the broad genus of compounds disclosed by Klecker encompasses such compounds, Petitioner does not point us to any teaching, other than the broad disclosure of the

genus, wherein "W, X, Y, [and] Z" may be "H, hydroxy, halogen, alkyl (C_1-C_6), alkoxy (C_1-C_6)a label containing moiety or a label" (Ex. 1005, 15:3–5), that would direct the ordinary artisan to choose X and W such that one of X and W is methyl and the other is fluorine, much less pointing to support of X as fluorine and W as methyl.

Petitioner relies on the Declaration of Dr. Fortunak in asserting that because Klecker teaches the X position may be substituted with fluorine and teaches that W can be an alkyl (C_1 – C_6), the ordinary artisan would understand from "general knowledge and common sense that methyl is a preferred lower alkyl in that group." Pet. 34 (citing Ex. 1002 ¶ 92). Dr. Fortunak, however, merely repeats the statement in the Petition without citing any evidentiary support. *See* Ex. 1002 ¶ 92; *see also id.* ¶¶ 93–95 (discussing choosing other substituents in the structure of Klecker). Conclusory statements by an expert "that does not disclose the underlying facts or data on which the opinion is based is entitled to little or no weight." 37 C.F.R. § 42.65(a). Furthermore, Petitioner's conclusory statements (Pet. 34–35) that because C is the first substituent identified for J, and H and OH are the first two substituents identified for Y and Z and, thus, the ordinary artisan would immediately envisage a compound where J is C, Y is H, and Z is OH, do not sufficiently persuade us that the ordinary artisan would immediately envisage their implementation to arrive at compounds that fall within the genus of claim 1.

Therefore, we determine that, on the record currently before us, Petitioner has not sufficiently shown that the ordinary artisan would immediately envisage a compound that has both a methyl group and a fluorine at the 2' position of the sugar ring, much less a compound in which

the fluorine is in the 2' down position of the sugar ring and methyl in in the 2' up position of the ring. Moreover, Petitioner does not sufficiently demonstrate that the ordinary artisan would also immediately envisage compounds that have the other substituents required by the genus of claim 1.

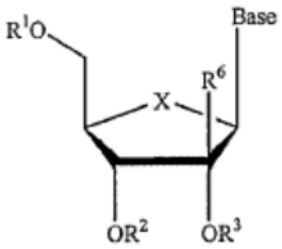
All of the challenged claims require the genus of compounds of claim 1, or a particular compound that falls within that genus. For example, claims 7–12 and 16 are drawn to pharmaceutical compositions of compounds that fall within the genus of claim 1, and claims 13 and 14 are drawn to methods of synthesizing the compounds of claim 1. Ex. 1001, 65:20–37, 66:40–42, 65:38–66:23. As Petitioner does not sufficiently establish that Klecker anticipates the genus of compounds of claim 1, it does not establish that the remaining claims that all require that structure, such as methods of synthesizing the compounds of claim 1, are anticipated by Klecker. Accordingly, we decline to institute trial as to any of the challenged claims as being anticipated by Klecker.

C. Anticipation by Sommadossi

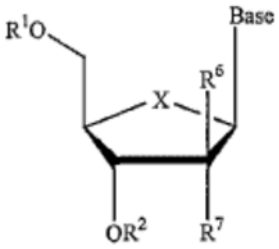
Petitioner asserts that claims 1–19 are anticipated by Sommadossi. Pet. 49–62. Patent Owner responds that Petitioner has not established a reasonable likelihood that the challenged claims are anticipated by Sommadossi. Prelim. Resp. 18–20.

i. Overview of Sommadossi (Ex. 1006)

Sommadossi teaches compounds for the treatment of hepatitis C infections. Ex. 1006, 7:15–17. In particular, Sommadossi teaches compounds of Formulas X and XI, shown below:



(X)



(XI)

wherein:

Base is a purine or pyrimidine base as defined herein;

R^1, R^2[,] and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2[,] or R^3 is independently H or phosphate;

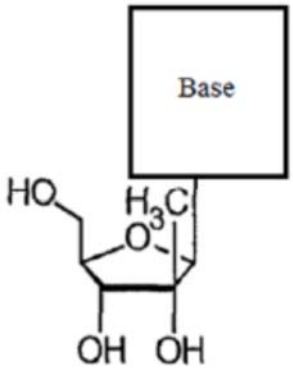
R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^7 is hydrogen, OR^3, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), - O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), - NH(acyl), -N(lower alky)$_2$, -N(acyl)$_2$; and

X is 0, S, SO_2[,] or CH_2.

Id. at 13:6–14:1.

Figure 1 of Sommadossi shows 10 illustrative nucleosides, and Petitioner characterizes some of those illustrated nucleosides as:



(Fig. 1)

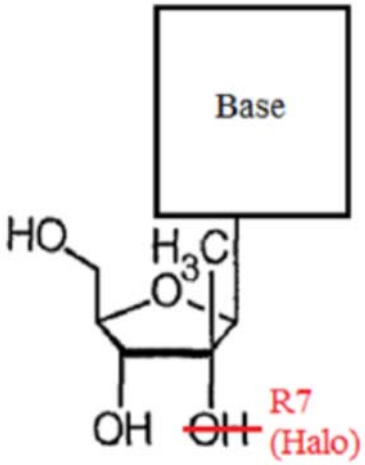
Ex. 1006, Fig. 1; Pet. 51.

Finally, Sommadossi defines the term "halo" as "chloro, bromo, iodo, and fluoro." Ex. 1006, 52:31.

ii. Analysis

Petitioner initially relies on formulas X and XI of Sommadossi, asserting that the formulas are essentially identical to one another, except that X has an "OR^3" group in the 2' down position, and XI has an "R^7" in the 2' down position. Pet. 50–51 (citing Ex. 1006, 13:6–27; Ex. 1002 ¶ 133). Petitioner asserts that Sommadossi, thus, expressly teaches substituting the "R^7" group for the "OR^3" group at the 2' down position. *Id.* at 51.

Next, relying on Figure 1 of Sommadossi, given the above teaching of Sommadossi that the "R^7" group may be substituted for the "OR^3" group at the 2' down position, Petitioner redraws Figure 1 with that substitution. *Id.* (citing Ex. 1006, Fig. 1; Ex. 1002 ¶ 134). That annotated Formula is shown below:



Id. In addition, Petitioner asserts, the annotated figure in which the "R^7" group is substituted for the "OR^3" group at the 2' down position is further annotated to demonstrate that Sommadossi teaches that the "R^7" group may be a halogen. *Id.* (citing Ex. 1002 ¶ 134).

Petitioner notes, however, that Sommadossi teaches in particular that the "R^7" group may be "chlorine, bromine, and iodine," but asserts that the ordinary artisan "would have known that in the field of nucleoside drugs, halogens are substitutable for each other and, thus, Sommadossi's express teaching of 'chloro, bromo[,] and iodo,' also inherently taught fluoro." *Id.* at 51–52 (quoting Ex. 1006, 13:26, citing Ex. 1002 ¶ 135).

According to Petitioner, "there is no discussion in Sommadossi of why R^7 could not be fluoro to contradict this common knowledge, and Sommadossi taught that R^6 could be 'chloro, bromo, fluoro, iodo.'" *Id.* at 52 (citing Ex. 1002 ¶ 135; Ex. 1006, 13:23). Petitioner further cites McAtee[5] as

[5] J. JeffreyMcAtee et al., *A Completely Diastereoselective Electrohilic Fluorination of a Chiral, Noncarbohydrate Sugar Ring Precursor: Application to the Synthesis of Several Novel 2'-Fluoronucleotides*, 63 J. ORG. CHEM. 2161–2167 (1998) ("McAtee") (Ex. 1009).

evidence that it was "common knowledge . . . that fluorine was not only a possible substitute for hydroxy at the 2' position, but a preferred one." *Id.* (citing Ex. 1002 ¶ 136; Ex. 1009). Petitioner asserts further, citing Briton,[6] that it was common knowledge "that fluorine was successful in the 2' down position when methyl was in the 2' up position." *Id.* (citing Ex. 1002 ¶ 136; Ex. 1011). Petitioner asserts, therefore, that when the disclosure of Sommadossi is viewed in light of that common knowledge, the ordinary artisan "would at once envisage F in the 2' down position because CH^3 was in the 2' up position." *Id.* (citing Ex. 1002 ¶ 136).

Patent Owner, in reply, argues that Sommadossi does not teach a compound with a fluorine in the 2' down position and a methyl group in the up position. Prelim. Resp. 17–18. In response to Petitioner's argument that the ordinary artisan would view Sommadossi's failure to disclose using a fluorine at the 2' down position of the sugar ring as a typographical error, Patent Owner contends that "argument is nonsense," as "Sommadossi . . . simply does not teach 2'-fluorine down." *Id.* at 18–19.

We agree with Patent Owner. In particular, Petitioner's arguments that the ordinary artisan in this field would have understood that halogens are substitutable for each other, and that as there is no discussion in Sommadossi of why R^7 could not be fluoro to contradict this common knowledge (Pet. 51–52), are an obviousness argument and not an anticipation argument.

To the extent that Petitioner (Pet. 51–52) is invoking inherency in arguing that the express teaching of Sommadossi that R^7 may be chloro,

[6] Britton et al., U.S. Patent 5,420,266, issued May 30, 1995 (Ex. 1011).

bromo and iodo, is also an express teaching that R^7 may be fluoro, we disagree that the use of fluoro as the R^7 group is inherent in the teachings of Sommadossi. "Inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999), *quoting In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981). Even though the ordinary artisan may have understood that fluoro is also a halogen and may be substituted for chloro, bromo, or iodo, the fact remains that Sommadossi taught the use of, *inter alia*, chloro, bromo, or iodo at the R^7 position, specifically, rather than a halogen element, generally. Ex. 1006, 13:24–27.

Petitioner's argument (Pet. 52) that "Sommadossi taught that R^6 could be 'chloro, bromo, fluoro, [or] iodo,'" is actually counter to Petitioner's assertions. That is, that statement demonstrates that Sommadossi knew that "fluoro" could be included in the list of halogens. Moreover, Sommadossi defined the term "halo" as "chloro, bromo, iodo, and fluoro." Ex. 1006, 52:31. Thus, to avoid inadvertently excluding a halogen, Sommadossi could have used the term "halo" in listing the possible substituents for the R^7 group, but chose not to do so.

Accordingly, we determine that Petitioner has not sufficiently established that Sommadossi anticipates the compounds of claim 1. Because, as discussed above in our analysis of the anticipation ground over Klecker, all of the claims require the compound of that claim, or a particular compound that falls within the genus of claim 1, Petitioner has also not sufficiently demonstrated that any of the challenged claims are anticipated

by Sommadossi. Accordingly, we decline to institute trial as to any of the challenged claims on the basis that the claim is anticipated by Sommadossi.

D. Obviousness over the Combination of Sommadossi and Klecker

Petitioner asserts that claims 1–19 are rendered obvious by the combination of Sommadossi and Klecker. Pet. 62–90. Patent Owner responds that Petitioner has not established a reasonable likelihood that any of the challenged claims are rendered obvious by the combination of Sommadossi and Klecker. Prelim. Resp. 23–30.

i. Analysis

Petitioner asserts that "[t]he only possible difference between Sommadossi and claim 1 of the ['']572 patent is the presence of fluorine at the 2' down position instead of hydroxyl." Pet. 63 (citing Ex. 1002 ¶ 159). Petitioner contends that it would have been obvious to place fluorine at the 2' down position given the teachings of Klecker and the general knowledge in the art. *Id.* That is, Petitioner asserts, McAtee and Britton both demonstrate that "F was not only substitutable for OH at the 2' down position in anti-viral nucleosides, it was actually preferred, especially when methyl is in the 2' up position." *Id.* at 64 (citing Ex. 1002 ¶ 161; Ex. 1009; Ex. 1011). According to Petitioner, the ordinary artisan "would have also had a reasonable expectation of success in being able to make this substitution because, as discussed above, many methods were known to successfully fluorinate nucleosides, as shown by[ ] Codington,[7]

[7] John F. Codington et al., *Nucleosides XIV. Synthesis of 2'-Deoxy-2'Fluorouridine*, 83 J. AM. CHEM. SOC. 5030-5031 (1961) ("Codington") (Ex. 1012).

Pankiewicz,[8] McAtee and Watanabe.[9]" *Id.* at 64 (footnotes added, citations omitted).

Patent Owner argues that the Board has determined "in interference proceedings involving the '572 patent that because of the 'highly unpredictable' nature of nucleoside chemistry and the lack of teaching in the prior art in 2003, it would have required undue experimentation to synthesize a 2'MeF nucleoside." Prelim. Resp. 1 (citing Ex. 2002, 21 (Interference 105,871); Ex. 2006, 35 (Interference 105,981)), *see also id.* at 24 (same). Among other things, Patent Owner asserts that the Board found during the interference proceedings that "although organic fluoridation techniques were well-known in the art, fluoridation of ***tertiary*** alcohols to produce the claimed 2'MeF nucleoside was neither taught nor suggested." *Id.* at 2, *see also id.* at 29–30 (same). That conclusion, Patent Owner asserts, was affirmed by the Federal Circuit. *Id.* at 2–3 (citing *Storer v. Clark,*[10] 860 F.3d 1340, 1352 (Fed. Cir. 2017) (relating to Interference number 105,981) (hereinafter, "*Storer*")). According to Patent Owner, Petitioner "completely ignores the Board's previous decisions and the Federal Circuit's opinion." Prelim. Resp. 3.

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[8] Krysztof W. Pankiewicz, *Review: Fluorinated Nucleosides*, 327 CARBOHYDRATE RES. 87–105 (2000) (Ex. 1010).

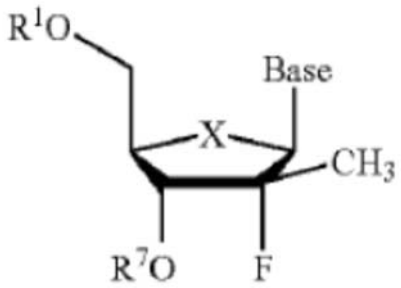
[9] Kyoichi A. Watanabe et al., *Nucleosides. 129. Synthesis of Antiviral Nucleosides: 5-Alkenyl-1-(2-Deoxy-2-Fluoro-β-D-Arabinofuranosyl)Uracils*, 27 J. MED. CHEM. 91–94 (1984) ("Watanabe") (Ex. 1013).

[10] This decision of the Court of Appeals for the Federal Circuit was entered into the record of this proceeding by Patent Owner as Exhibit 2010.

As to Petitioner's reliance on Britton, Patent Owner argues that "Britton does not disclose the 2'MeF structure," but, rather, lists provides identical lists of substituents for the 2' down and 2' up positions, in which both "fluoro" and "alkyl" are mentioned. *Id.* at 27–28 (citing Ex. 1011, 2:48–52). Otherwise, according to Patent Owner, "there is no suggestion or teaching disclosed in Britton that would lead a person of ordinary skill to combine a 2' up methyl with a 2' down fluorine, or indicate that such a combination could be readily synthesized by a person of ordinary skill at that time." *Id.* Similarly, Patent Owner asserts, McAtee does not provide any examples in which the substituent at the 2' up position is anything other than hydrogen. *Id.*

We agree with Patent Owner that Petitioner has not sufficiently established that the combination of Klecker and Sommadossi renders the compounds of claim 1 obvious. Obviousness "requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Int'l Corp*., 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)). "In determining whether obviousness is established by combining the teachings of the prior art, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art." *In re GPAC Inc.*, 57 F.3d 1573, 1581 (Fed. Cir. 1995) (internal quotations and citations omitted). In addition, "[a]n obviousness determination requires finding both 'that a skilled artisan would have been motivated to combine the teachings of the prior art . . . and that the skilled artisan would have had a reasonable expectation of success in doing so.'" *In re Stepan Co.*, 868 F.3d 1342, 1345–46 (Fed. Cir. 2017) (quoting *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.,* 821 F.3d 1359, 1367–68 (Fed. Cir. 2016)).

One of the previous interference proceedings, Patent Interference 105,871 (the '871 Interference"), was between Jean-Pierre Sommadossi, Paolo LaColla, Richard Storer, and Giles Gosselin as the junior party, Application 12/131,868 and Jeremy Clark, the '572 patent, as the senior party. Ex. 2002. The count in that interference was drawn to a compound of the formula:



Id. at 2. In that proceeding, Clark argued that at the time of Sommadossi's invention, there was a "lack of knowledge about how make a compound within the scope of Count 1 at the time of Sommadossi's asserted conception." *Id.* at 19. The Board determined that the evidence of record supported that the skilled artisan would not have the necessary skill to synthesize the compounds of the count, and, thus, it was not merely a matter of routine experimentation to synthesize such compounds. *Id.* at 20–21. Therefore, the Board entered judgment in favor of Clark. Ex. 2003, 2.

Similarly, at issue in Interference 105,981 (the '981 Interference) was whether the ordinary artisan would be able to synthesize a nucleoside in which a fluoro is in the 2' down position without undue experimentation. Ex. 2006, 8. The Board found that a "high amount of experimentation is necessary to synthesize a 2'-fluoro-2'-methyl nucleoside with the fluoro moiety in the 'down' position requiring at least two years of a high priority experimentation by persons skilled in the art, including multiple

consultations with experts at the top of their fields and additional formal training." *Id.* at 19. That finding was affirmed by the Court of Appeals for the Federal Circuit in *Storer*, which concluded that substantial evidence supported that finding. *Storer*, 860 F.3d at 1352.

Petitioner (Pet. 64) cites Britton, Codington, Pankiewicz, McAtee, and Watanabe as evidence that it would have been obvious to place fluorine at the 2' down position given the teachings of Klecker and the general knowledge in the art, with those references providing a reasonable expectation of success of achieving the claimed compounds. Importantly, however, Petitioner does not explain how the teachings of the above cited references remedy the finding of the Board in the '871 interference, as well as the '981 interference, and affirmed by the Federal Circuit in *Storer*, that the skilled artisan would not have the necessary skill to synthesize the claimed nucleosides in which a fluorine is in the 2' down position and a methyl group is in the 2' up position. That is, as argued by Patent Owner (Prelim. Resp. 2), Petitioner does not point us to any evidence of record that teaches or suggests fluoridation of tertiary alcohols to produce the claimed nucleoside wherein the fluorine is in the down position and the methyl group is in the up position at the 2' position of the methyl ring, as required by the nucleosides of the formula of claim 1.

We determine, therefore, that the evidence currently of record does not sufficiently support Petitioner's argument that the ordinary artisan would have had a reasonable expectation of success of synthesizing the compounds of the formula of claim 1, wherein a fluorine is in the down position and a methyl group is in the up position at the 2' position of the sugar ring. Consequently, Petitioner has not sufficiently established that the

combination of Sommadossi and Klecker renders obvious the compounds of claim 1. In addition, as all of the challenged claims requires a compound of that claim, or a particular compound that falls within the genus of that claim, Petitioner has not sufficiently demonstrated that claims are rendered obvious by the combination of Sommadossi and Klecker.

Accordingly, because Petitioner has not demonstrated a reasonable likelihood that any of the challenged claims are rendered obvious by the combination of Sommadossi and Klecker, we decline to institute *inter partes* review on that basis.[11]

III. CONCLUSION

For the foregoing reasons, we are persuaded that the Petition fails to establish a reasonable likelihood that Petitioner would prevail in showing that any of the challenged claims of the '572 patent are unpatentable.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is *denied* as to all challenged claims of the '572 patent and no trial is instituted.

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[11] Patent Owner argues also that we should deny the Petition under 35 U.S.C. § 325(d), as Petitioner's challenges are based on arguments that have already been presented to the Board. Prelim. Resp. 30. That is, Patent Owner asserts, Petitioner does not acknowledge the previous interference proceedings, and does not address the previous findings of the Board. *Id.* at 30–31. Patent Owner's arguments in this regard may have merit. However, as we deny institution based upon Petitioner's failure to demonstrate a reasonable likelihood that the challenged claims are rendered obvious by the combination of Sommadossi and Klecker, we need not reach this issue.

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