Trials@uspto.gov
571.272.7822

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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.

IPR2018-00121
Patent 8,334,270 B2

Before LORA M. GREEN, GRACE KARAFFA OBERMANN, and WESLEY B. DERRICK, *Administrative Patent Judges*.

DERRICK, *Administrative Patent Judge*.

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

I. INTRODUCTION

Initiative for Medicines, Access & Knowledge (I-MAK), Inc. ("Petitioner") requests an *inter partes* review of claims 1, 2, 10–18, and 20–25 of U.S. Patent 8,334,270 B2 (Ex. 1001, "the '270 patent"). Paper 2 ("Pet."). Gilead Pharmasset LLC ("Patent Owner") filed a Preliminary Response. Paper 9 ("Prelim. Resp.").

We have authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314(b); 37 C.F.R. § 42.4(a). We may not institute an *inter partes* review "unless . . . 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(a). Applying that standard, for the reasons set forth below, we decline to institute an *inter partes* review because the Petitioner has not shown a reasonable likelihood that it would prevail in establishing the unpatentability of any challenged claim.

II. BACKGROUND

A. Related Proceedings

The parties identify a concurrently-filed, second petition for *inter partes* review of the '270 patent, IPR2018-00122. Pet., 2; Paper 4, 3. Patent Owner also identifies additional petitions for *inter partes* review of additional patents: IPR2018-00119 and IPR2018-00120 for U.S. Patent No. 7,964,580 B2; IPR2018-00103 for U.S. Patent No. 7,429,572 B2; IPR2018-00125 for review of U.S. Patent No. 8,633,309 B2; and IPR2018-00126 for review of U.S. Patent No. 9,284,342 B2. Paper 4, 3.

B. The ’270 Patent (Ex. 1001)

The ’270 patent is directed to, *inter alia*, phosphoramidate prodrugs of a nucleoside derivative for treatment of viral infections in mammals, its ester, or a stereoisomer thereof. Ex. 1001, Abstract. The ’270 patent also addresses methods of treatment, uses, and processes for preparing such compounds. *Id.* The ’270 patent claims the benefit of priority of two earlier-filed provisional applications, 60/909,315, filed on March 30, 2007 (Ex. 2013), and 60/982,309, filed on October 24, 2007 (Ex. 2014), respectively, “the ’315 application” and “the ’309 application.” Ex. 1001, 1:4–9.

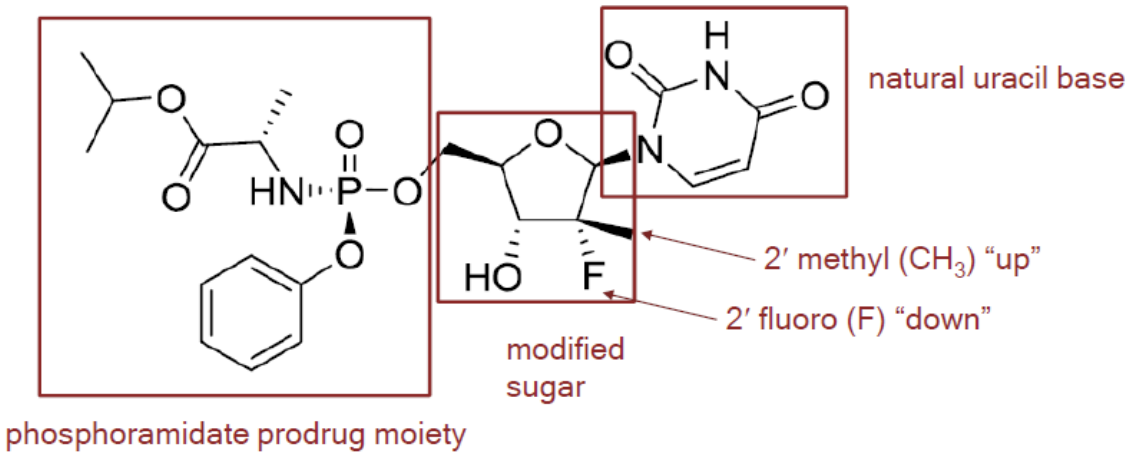
C. Illustrative Claims

Independent claims 1 and 16, each reciting a number of different phosphoramidate nucleoside derivatives, are reproduced below in part:

> 1. A compound selected from among
> . . .
> (S)-isopropyl 2-(((S)-(2R,3R,4R, 5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyl[-]tetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate . . . .
>
> 16. A compound or its stereoisomer thereof selected from among
> . . .
> (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahy-dro-furan-2-ylmethoxy]-phenoxy-phosphorylamino}-propionic acid isopropyl ester . . . .

Ex. 1001, 605:35, 52–55, 607:58–59, 608:58–61.

The compound set forth by name in the reproduced portion of claim 1 above is the Sp stereoisomer of a phosphoramidate nucleoside derivative, known as sofosbuvir, which structure is depicted below:



Prelim. Resp. 3–4. The figure depicts the chemical structure of sofosbuvir with stereochemistry and identifies the compound's phosphoramidate prodrug moiety, modified sugar, and natural uracil base. *Id.* at 4. Claim 16 likewise, in setting forth a compound or stereoisomer of compounds identified by name, including that reproduced above, encompasses the Sp stereoisomer, the Rp stereoisomer, and mixtures of the two. *Id.* at 3–4, 12; *see also* Pet. 28–29.

D. The Asserted Grounds of Unpatentability

Petitioner contends that "[e]ach and every feature of claims 1, 2, 10-18 and 20-25 can be found in the prior art reference[s] identified below."[1]

[1] Although Petitioner contends "[e]ach and every feature . . . can be found" in the cited references (Pet. 27), the analysis that follows of "exemplary disclosure of the cited references" (*id.*) is effectively limited to consideration of a single compound—the 5′-phosphate (phosphoramidate) prodrug of the uridine analog (2′R)-2′-deoxy-2′-fluoro-2′-*C*-methyluridine, wherein the

Pet. 27 (citing Ex. 1002 ¶ 92). More particularly, Petitioner asserts that claims 1, 2, 10–18, and 20–25 are unpatentable based on each of the following grounds. Pet. 3, *see also id.* at 27–55.

References	Statutory Basis
Sofia[2]	§ 102
Sofia and Perrone[3]	§ 103
Ma[4] and Perrone	§ 103

Petitioner supports the Petition with the testimony of Joseph M. Fortunak, Ph.D. (Ex. 1002). Based on Dr. Fortunak's statement of qualifications (*id.* ¶¶ 1–20) and curriculum vitae (Ex. 1003), on this record, we determine that he is qualified to opine from the perspective of a person of ordinary skill in the art.

III. ANALYSIS

A. Level of Skill in the Art

Petitioner contends that a person of ordinary skill in the art would have held either

> (1) a Ph.D. in chemistry or a closely related field with some experience in an academic or industrial laboratory focusing on drug discovery or development, and would also have some

5′-phosphate group is the (phenyl)(isopropyl-L-alaninyl)phosphate group (*id.* at 27–55).

[2] Sofia et al., Poster #P-259, presented at the 14th Int'l Symposium on Hepatitis C Virus and Related Viruses, Glasgow, Scotland, UK, Sept. 9–13, 2007 (Ex. 1004).

[3] Perrone et al., 50 J. MED. CHEM. 1840–1849 (2007) (Ex. 1008).

[4] Ma et al., 282 J. BIOL. CHEM. 29812–29820 (2007) (Ex. 1005).

> familiarity with antiviral drugs and their design and mechanism of action, or
>
> (2) a Bachelor's or Master's degree in chemistry or a closely related field with significant experience in an academic or industrial laboratory focusing on drug discovery and/or development for the treatment of viral diseases.

Pet. 5–6 (citing Ex. 1002 ¶ 35).

Patent Owner does not expressly contest the level of ordinary skill. *See generally* Prelim. Resp.

On this record, we adopt Petitioner's essentially uncontested definition of the level of ordinary skill. We further note that the prior art itself demonstrates the level of skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that "specific findings on the level of skill in the art . . . [are not required] 'where the prior art itself reflects an appropriate level and a need for testimony is not shown'" (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985))).

B. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to their broadest reasonable construction in light of the specification of the patent in which they occur. 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016) (affirming applicability of broadest reasonable construction standard to *inter partes* review proceedings). Under that standard, we interpret claim terms using "the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant's

specification." *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997). "Under a broadest reasonable interpretation, words of the claim must be given their plain meaning, unless such meaning is inconsistent with the specification and prosecution history." *Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1062 (Fed. Cir. 2016). If an inventor acts as his or her own lexicographer, the definition must be set forth with reasonable clarity, deliberateness, and precision. *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1249 (Fed. Cir. 1998). Only those term which are in controversy need to be construed and only to the extent necessary to resolve the controversy. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017).

Petitioner contends that "there is no reason to give any of the terms of the claims of the '270 [patent] a meaning other than their ordinary and accustomed meaning." Pet. 6.

Patent Owner does not contest that the claim terms should be given their ordinary and accustomed meaning. *See generally* Prelim. Resp. We determine that no claim term requires express construction for the purpose of determining whether to institute review.

C. Prior Art Status

Under 35 U.S.C. § 311(b), in an *inter partes* review, a petitioner may only challenge the claims of a patent based on "prior art consisting of patents or printed publications," and the petitioner has the initial burden of producing evidence to support a conclusion of unpatentability under § 102 or § 103, including that an asserted reference is prior art to the challenged claims under a relevant subsection of § 102. "To satisfy its burden of proving obviousness, a petitioner cannot employ mere conclusory

statements. The petitioner must instead articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness." *In re Magnum Tools Int'l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016).

Petitioner contends that Sofia and Ma are both prior art because the '315 application does not describe the specific compounds claimed by the '270 patent in that "it does not discuss the specific compounds and stereochemistry around the phosphorous atom claimed." Pet. 22; *see also id.* at 24; Ex. 1002 ¶ 72. The relied on declaration evidence, reproduced below in full, states:

> The '315 provisional application does not include a description of the specific compounds claimed by the '270 patent. While the '315 provisional discusses broad genera of compounds, it does not discuss the specific compounds and stereochemistry around the phosphorous atom claimed in the '270 patent.

Ex. 1002 ¶ 72.

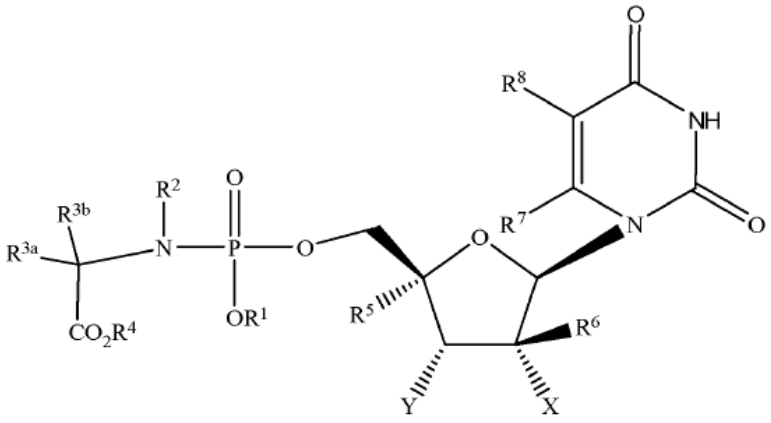
Patent Owner contends the '270 patent is entitled to the benefit of priority of the '315 provisional, and that Petitioner wholly fails to meet its burden of producing evidence that the '270 patent is not entitled to its earliest priority date.[5] Prelim. Resp. 14–15. Patent Owner contends that "neither [Petitioner] nor its expert has presented a legitimate priority analysis." *Id.* at 14.

As to the 5′-phosphate (phosphoramidate) prodrug of the uridine analog (2′R)-2′-deoxy-2′-fluoro-2′-*C*-methyluridine, wherein the 5′-phosphate group is the (phenyl)(isopropyl-L-alaninyl)phosphate group,

[5] Patent Owner "also submits that the Petition should be stayed pending disposition of the *Oil States* appeal" before the Supreme Court relating to the constitutionality of IPR proceedings. Prelim. Resp. 37–38. The request is moot, however, in light of our decision denying institution.

the focus of Petitioner's anticipation and obviousness analysis (Pet. at 27–55), Patent Owner offers a detailed explanation addressing chemical structure, stereochemistry, and synthesis (Prelim. Resp. 15–19).

Patent Owner relies on the '315 provisional's disclosure of IX-25-2 (Ex. 2013, 195), a compound according to Structure IX (*id.* at 187), in which particular constituents in Structure IX, i.e., R^1, R^2, $R3^a$, R^{3b}, R^4, R^5, R^6, X, Y, R^7, and R^8, are specified in Table IX-25 (*id.* at 195). Patent Owner reproduces Structure IX and Table IX-25 (with emphasis), as depicted below:



IX

Table IX-25.

№	R^1	R^2	R^{3a}	R^{3b}	R^4	R^5	R^6	X	Y	R^7	R^8
IX-25-1	Ph	H	H	H	^{i}Pr	H	CH_3	F	OH	H	H
IX-25-2	Ph	H	H	CH_3	^{i}Pr	H	CH_3	F	OH	H	H
IX-25-3	Ph	H	H	$CH(CH_3)_2$	^{i}Pr	H	CH_3	F	OH	H	H
IX-25-4	Ph	H	H	$CH_2CH(CH_3)_2$	^{i}Pr	H	CH_3	F	OH	H	H
IX-25-5	Ph	H	H	CH_2Ph	^{i}Pr	H	CH_3	F	OH	H	H
IX-25-6	Ph	H	H	CH_2-indol-3-yl	^{i}Pr	H	CH_3	F	OH	H	H
IX-25-7	Ph	H	H	$CH_2CH_2SCH_3$	^{i}Pr	H	CH_3	F	OH	H	H
IX-25-8	Ph	*	H	*	^{i}Pr	H	CH_3	F	OH	H	H

*R^2 and R^{3b} joined together by $(CH_2)_3$ to form five-membered ring.

Prelim. Resp. at 16–17; *see also* Ex. 2013, 87 (Structure IX), 195 (Table IX-25). Structure IX itself discloses the stereochemistry for most of the structure, but does not depict the stereochemistry at the potentially chiral centers as the carbon substituted with R^{3a} and R^{3b} and at the phosphorus (P).

Patent Owner directs us to disclosure in the '315 provisional that identifies both chiral configurations at the potentially chiral centers at both the carbon substituted with R^{3a} and R^{3b} and at the phosphorus (P) for each compound, including IX-25-2. Prelim Resp. 17–18 (citing Ex. 2013, 63–64). In particular, as to the carbon center, the compounds disclosed by reference to the depicted structures, including Structure IX, and the tables, including Table IX-25, include those in which "R^{3a} projects towards the viewer while R^{3b} projects away from the viewer" and those in which "R^{3a} projects away from the viewer while R^{3b} projects towards the viewer." *Id.* at 17–18 (emphasis omitted) (citing Ex. 2013, 63). And, as to the phosphorus (P), the compounds disclosed includes those in which "the oxo-substituent projects towards the viewer while the OR^1 substituent projects away from the viewer, and vice versa." *Id.* at 18 (citing Ex. 2013, 63–64).

In sum, the cited disclosure discloses compounds according to IX-25-2 that include both stereochemical orientations at the carbon bearing the specified R^{3a} and R^{3b} constituents, both stereochemical orientations at the phosphorous, and stereochemical orientations elsewhere that are identical to those of sofosbuvir. As such, the cited portions of the '315 provisional constitute disclosure of the Sp stereoisomer (sofosbuvir), as well as the stereoisomers having the opposite stereochemical orientation at either (or both) the carbon bearing R^{3a} and R^{3b} constituents and the phosphorous. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570 (Fed. Cir. 1996) (It is well

settled that "*ipsis verbis* disclosure is not necessary to satisfy the written description requirement of section 112."); *see also In re Ruschig*, 379 F.2d 990, 994–95 (CCPA 1967) (Analogizing the direction sufficient to identify species in a genus as "blaze marks which single out particular trees.").

In the face of the '315 provisional's disclosure, including even disclosure of the particular compound relied on in Petitioner's contentions of anticipation and obviousness, we agree with Patent Owner that Petitioner fails to sufficiently demonstrate that the '270 patent is not entitled to the priority benefit of the '315 provisional. We accord little weight to Dr. Fortunak's testimony, because Dr. Fortunak does not identify factual support for his opinion and he fails to address portions of the '315 provisional contrary to his position. *See Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 294 (Fed. Cir. 1985) ("Lack of factual support for expert opinion going to factual determinations" is sufficient to "render the testimony of little probative value in a validity determination."). Thus, there is no basis for Petitioner's contentions that Sofia is prior art "because it was published by September 13, 2007" (Pet. 22), and that Ma is prior art "because it was published on October 12, 2007" (*id.* at 24).

D. Alleged Unpatentability of the Challenged Claims

1. Anticipation by Sofia

Petitioner asserts that claims 1, 2, 10–18, and 20–25 are anticipated by Sofia. Pet. 27–32. The unavailability of Sofia as prior art undermines Petitioner's anticipation ground. Accordingly, we are not persuaded the record before us establishes a reasonable likelihood that Petitioner will prevail in showing that the subject matter of claims 1, 2, 10–18, and 20–25 is unpatentable over Sofia.

2. Obviousness over Sofia and Perrone

Petitioner contends that claims 1, 2, 10–18, and 20–25 are unpatentable as obvious over the combination of Sofia and Perrone. *Id.* at 32–44. The unavailability of Sofia undermines Petitioner's obviousness ground, which relies on Sofia as to the nucleoside portion of a prodrug according to the claims, that is, "the uridine analog '(2'R)-2'-deoxy-2'-fluoro-2'-*C*-methyluridine.'" *Id.* at 33. Perrone, relied on as to the phosphoramidate portion of the prodrug (*id.* at 37–42), uses a different uridine analog, 4′-azidourdine (Ex. 1008). Accordingly, we are not persuaded the record before us establishes a reasonable likelihood that Petitioner will prevail in showing that the subject matter of claims 1, 2, 10–18, and 20–25 is unpatentable over Sofia and Perrone.

3. Obviousness over Ma and Perrone

Petitioner contends that claims 1, 2, 10–18, and 20–25 are unpatentable as obvious over the combination of Ma and Perrone. Pet. 44–55. The unavailability of Ma undermines Petitioner's obviousness ground, which relies on Ma as to the nucleoside portion of the claimed pro-drug, and on Perrone as to the phosphoramidate portion of the prodrug. *Id.* Accordingly, we are not persuaded the record before us establishes a reasonable likelihood that Petitioner will prevail in showing that the subject matter of claims 1, 2, 10–18, and 20–25 is unpatentable over Ma and Perrone.

IV. CONCLUSION

Petitioner has not established a reasonable likelihood of prevailing on its assertion that claims 1, 2, 10–18, and 20–25 are unpatentable.

V. ORDER

For the reasons given, it is:

ORDERED that the Petition is *denied* as to all challenged claims of the '270 patent and no trial is instituted.

PETITIONER:

Daniel B Ravicher
RAVICHER LAW FIRM PLLC
dan@ravicher.com

PATENT OWNER:

Dorothy P. Whelan
Michael J. Kane
W. Chad Shear
FISH & RICHARDSON P.C.
whelan@fr.com
kane@fr.com
shear@fr.com

David L. Cavanaugh
Emily R. Whelan
WILMER HALE
david.cavanaugh@wilmerhale.com
emily.whelan@wilmerhale.com