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Paper No. 9
Entered: May 24, 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 IPR2018-00125
Patent 8,633,309 B2

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

SMITH, *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") filed a Petition (Paper 2, "Pet.") to institute an *inter partes* review of claims 1–12 of U.S. Patent 8,633,309 B2 (the "'309 patent"). 35 U.S.C. § 311. Gilead Pharmasset LLC ("Patent Owner") filed a Preliminary Response to the Petition (Paper 6), as corrected (Paper 8). ("Prelim. Resp.").

We have authority to determine whether to institute an *inter partes* review under 35 U.S.C. § 314. 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). For the reasons set forth below, we conclude that Petitioner has not established a reasonable likelihood that it would prevail in showing the unpatentability of any challenged claim of the '309 patent. Therefore, we do not institute an *inter partes* review for any challenged claim of the '309 patent.

A. Related Proceedings

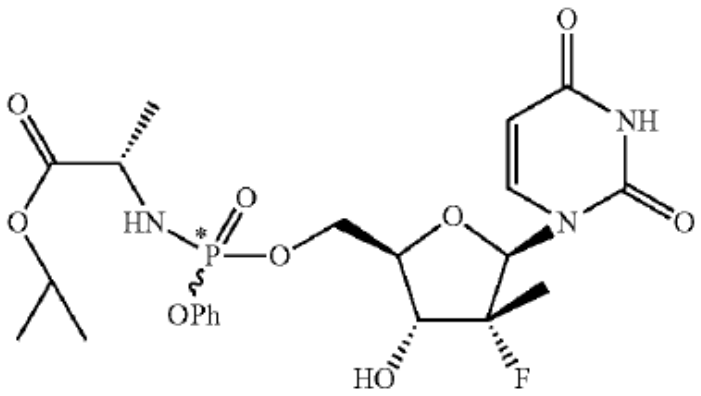
Petitioner also filed two petitions for *inter partes* review of U.S. Patent No. 7,964,580 (Case Nos. IPR2018-00119 and IPR2018-00120); two petitions for *inter partes* review of U.S. Patent No. 8,334,270 (Case Nos. IPR2018-00121 and IPR2018-00122); one petition for *inter partes* review of U.S. Patent No. 7,429,572 (Case No. IPR2018-00103); and one petition for *inter partes* review of U.S. Patent No. 9,284,342 (Case No. IPR2018-00126). Pet. 2; Paper 3, 3.

B. The '309 Patent

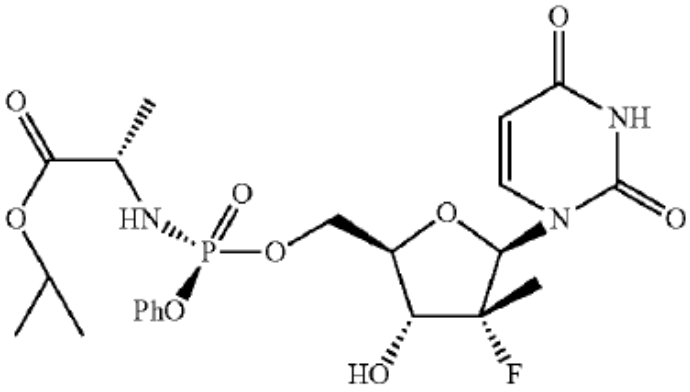
The '309 patent relates to nucleoside phosphoramidates and their use as agents in treating viral diseases, such as hepatitis C. Ex. 1001, 1:12–17. The '309

patent specifically disclose a compound represented by formula 4 and its respective phosphorous-based diastereomers represented by formulas S*p*-4 and R*p*-4, as shown below:

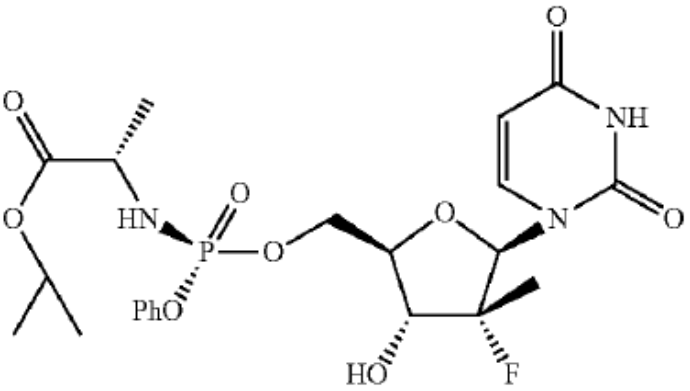
4



S_P-4



R_P-4



Id. at 4:50–5:24. The '309 patent states that "[t]he term 'P*' means that the phosphorus atom is chiral and that it has a corresponding Cahn-Ingold-Prelog designation of 'R' or 'S' which have their accepted meanings." *Id.* at 6:8–10. The compound of formula S*p*-4 is sofosbuvir. Prelim. Resp. 10.

The '309 patent discloses methods of synthesizing the formula 4 compound as a diastereomeric mixture of S_P-4 and R_P-4. Ex. 1001, 31:60–33:56. The '309 patent also discloses methods of obtaining substantially pure S_P-4 from the mixture of diastereomers by chromatography and crystallization of the individual stereoisomers. *Id.* at 36:3–12 (describing crystallization process that resulted in ">99% pure S_P-4"); *id.* at 72:34–61 (describing HPLC purification conditions that resulted in 99.5% pure S_P-4). The '309 patent teaches methods of generating substantially pure isomers by diastereoselective synthesis. *See, e.g.*, *id.* at 49:25–50:7 (describing processes for stereoselective synthesis of the S_P-4 enantiomer, resulting in about 97% chiral purity). The '309 patent also describes biological activity tests in which the potency of each of the compounds of formula 4, R_P-4, and S_P-4 was demonstrated by viral replicon assays. *See id.* at 75:30–56.

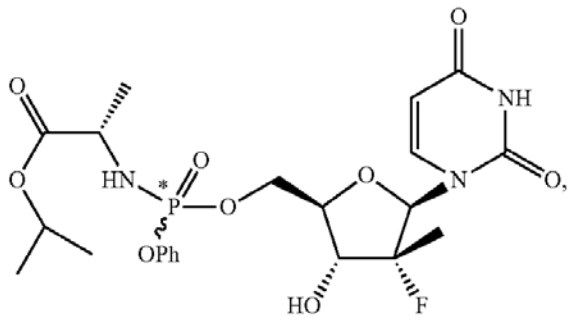
The '309 patent states that "U.S. patent application Ser. No. 12/053,015, which corresponds to WO 2008/121634 [Sofia '634, Ex. 1005] . . . discloses a number of phosphoramidate nucleoside prodrugs, many of which show activity in an HCV assay." *Id.* at 4:42–46.

C. Illustrative Claim

Petitioner challenges claims 1–12 of the '309 patent, of which claim 1 is the only independent claim. Claim 1 is reproduced below:

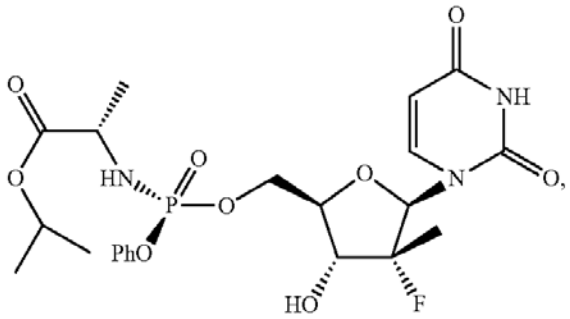
1. A compound represented by the formula (4):

(4)



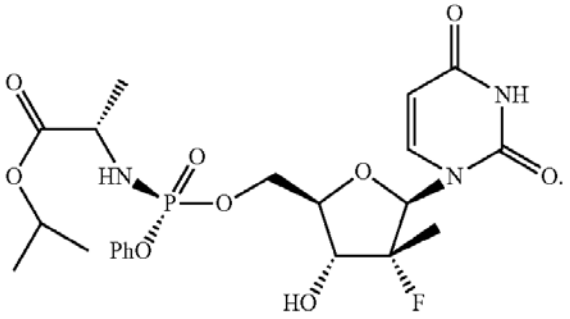
wherein P* represents a chiral phosphorus atom and wherein the compound is at least 97% of the S_P stereoisomer represented by the formula (S_P-4):

(S_P-4)



and not more than 3% of the R_P stereoisomer represented by the formula (R_P-4):

(R_P-4)



Ex. 1001, 76:1–47.

Claims 2–12 depend directly or indirectly on claim 1. *Id.* at 76:48–77:12.

D. The Asserted Grounds of Unpatentability

Petitioner contends that the challenged claims are unpatentable under 35 U.S.C. §§ 102(a) and 103(a) based on the following specific grounds. Pet. 3.

Reference[s]	**Basis**	**Claims challenged**
Sofia '634[1]	§ 102(a)	1–12
Sofia '634 and Congiatu[2]	§ 103(a)	1–12
Clark '147[3] and Congiatu	§103(a)	1–12

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

II. ANALYSIS

A. Person of Ordinary Skill in the Art

Petitioner asserts that a person of ordinary skill in the art would have 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

[1] Sofia et al., WO 2008/121634 A2, published Oct. 9, 2008 ("Sofia '634"). Ex. 1005. Sofia '634 is the PCT publication corresponding to US Application Serial No. 12/053,015, which issued as US Patent No. 7,964,580 B2 on June 21, 2011 ("the '580 patent"). *See* Ex. 1001, col. 4, ll. 42–43.
[2] C. Congiatu et al., *Novel Potential Anticancer Naphthyl Phosphoramidates of BVdU: Separation of Diastereoisomers and Assignment of the Absolute Configuration of the Phosphorus Center*, J. MED. CHEM. 49, 452–55 (2006) ("Congiatu"). Ex. 1006.
[3] Clark, WO 2005/003147 A2, published Jan. 13, 2005 ("Clark '147"). Ex. 1007.

would also have some 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. 9.

Patent Owner's definition of a person of ordinary skill in the art differs from Petitioner's definition. Prelim. Resp. 15. Patent Owner contends that a person of ordinary skill in the art would have either "(1) a Ph.D. in chemistry or a closely related field with some experience in an academic or industry laboratory focusing on drug discovery or development, including compound purification," and "would have some familiarity with the development of antiviral drugs, or work in collaboration with someone who has expertise in the development of antiviral drugs;" 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, including compound purification," and "some familiarity with development of antiviral drugs, or work in collaboration with someone who has expertise in the development of antiviral drugs." *Id.*

On this record and at this stage of the proceeding, we do not discern an appreciable difference in the parties' respective definitions of a person of ordinary skill in the art. Accordingly, we find that a person of ordinary skill in the art would have 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, including (for example) compound purification, and would also have some 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, including (for example) compound purification, for the treatment of viral diseases.

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 regarding ordinary skill level 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 the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 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, and absent any special definitions, we generally give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *See In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *See In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Neither Petitioner nor Patent Owner raise any claim construction issues or proposed constructions, and both acknowledge that the claim terms should be given their ordinary and customary meaning. Pet. 9–10; Prelim. Resp. 15–16. Accordingly, we apply the ordinary and customary meaning to the claims at issue. *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))).

C. Principles of Law

Anticipation requires that "each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (citation omitted). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference.'" *Id.*

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 omitted).

Obviousness also requires "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). A conclusion of obviousness "cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *Id.* (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)).

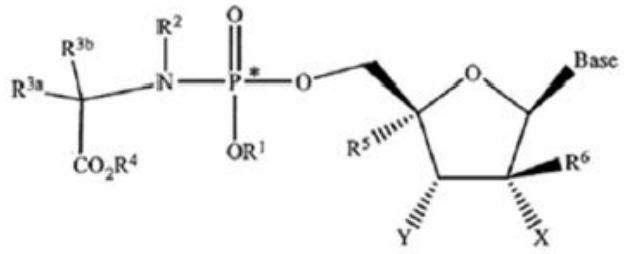
We analyze the asserted grounds of unpatentability in accordance with the above-stated principles.

D. Anticipation by Sofia '634

Petitioner asserts that claims 1–12 are anticipated by Sofia '634. Pet. 27–35. On this record, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing that any of claims 1–12 are anticipated by Sofia '634.

1. Sofia '634 (Ex. 1005)

Sofia '634 discloses phosphoramidate prodrugs of nucleoside derivatives represented by formula (I):



I

Ex. 1005, Abstract. Sofia '634 further describes nucleoside phosphoramidates and their use as agents for treating viral diseases, such as hepatitis C virus (HCV) infection. *Id.* at 2:15–21. Example 25 of Sofia '634 is the same as that represented by formula (4) in the '309 patent, except that Example 25 is a mixture of diastereomers at phosphorus. *Id.* at 684. Example 81 of Sofia '634 describes the separation of diastereomeric mixtures of Examples 15, 39, and 49. *Id.* at 693–94. Sofia '634 is referenced in the '309 patent. Ex. 1001, 4:42–46.

2. Analysis

Petitioner argues that "Example 25 in Sofia '634 is the same compound as that represented by formula (4) in claim 1 of the '309 patent," but also acknowledges that "Example 25 is a mixture of diastereomers at phosphorous." Pet. 29–30. Moreover, rather than pointing to any disclosure in Sofia '634 of the

separation of the diastereomers of Example 25, Petitioner argues that "[a] POSA would also expect that the specific disclosures of Examples 15, 39, and 49 would apply to Example 25," because "each of [compounds 15, 39, and 49] is a slightly different phosphoramidate prodrug analog" as compared to "the compound claimed in the '309 patent and each is a close structural analog of Example 25." *Id.* at 30–31. Notably, such argument by Petitioner does not establish that the compound claimed in the '309 patent is disclosed by Sofia '634 as required for a finding of anticipation. *See Robertson*, 169 F.3d at 745.

Regarding the limitations in claim 1 that "the compound is at least 97% of the S*p*stereoisomer represented by the formula (S*p*-4)" and "not more that 3% of the R*p*stereoisomer represented by the formula (R*p*-4)," Petitioner contends that "these arbitrary limits are inherently taught by Sofia '634" and "are not meaningful from a standpoint of antiviral activity." Pet. 33. Petitioner provides no support for those arguments, other than a reference to the Fortunak Declaration that repeats the same words as Petitioner, but without citation to any evidentiary support. Ex. 1002 ¶ 94. In particular, Petitioner makes no showing that any allegedly inherent limitations in claim 1 are "necessarily present" in Sofia '634. *See Robertson*, 169 F.3d at 745; *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981) ("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.") (citation omitted).

Thus, Petitioner fails to persuasively establish that Sofia '634 discloses each and every element of claim 1, either expressly or inherently. *See Robertson*, 169 F.3d at 745. Accordingly, we determine that Petitioner has not shown a reasonable likelihood that it would prevail on its assertion that claim 1 (and dependent claims 2–12, which include the limitations of claim 1) are anticipated by Sofia '634.

E. Obviousness over Sofia '634 and Congiatu

Petitioner contends that claims 1–12 are obvious over Sofia '634 and Congiatu. Pet. 35–45. For the reasons set forth below, we exercise our discretion to decline institution because the same or substantially the same prior art or arguments were previously presented to the Office. *See* 35 U.S.C. § 325(d) ("In determining whether to institute or order a proceeding under this chapter . . . the Director may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office.").[4]

1. Prosecution History

The Examiner rejected issued claims 1–12[5] as obvious over Sofia 2007,[6] finding that Sofia 2007 taught a phosphoramidate prodrug that is a mixture of S*p* and R*p* stereoisomers, and is a potent therapeutic agent for treating HCV infection. Pet. 6; Ex. 1004, 9–13. The Examiner further found that Sofia 2007 does not expressly teach that the Sp stereoisomer is at least 97%, 98%, or 99% and the Rp stereoisomer is not more than 3%, 2%, or 1%. Pet. 6; Ex. 1004, 12. The Examiner concluded that:

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[4] Petitioner does not specifically address Section 325(d). However, Patent Owner argues that institution should be denied based on Sofia '634 and Congiatu pursuant to 35 U.S.C. § 325(d). Prelim. Resp. 48–50.

[5] Issued claims 1–12 were numbered claims 82–93 during prosecution. Ex. 1004, 4–5.

[6] Sofia, M.J., *beta-D-2'-Deoxy-2'-fluoro-2'-C-methyluridine Phosphoramidates: Potent and Selective Inhibitors of HCV RNA Replication*, 2nd International Workshop on HCV—Resistance and New Compounds, Oct. 31, 2007 ("Sofia 2007"). Petitioner did not submit a copy of Sofia 2007, but Sofia 2007 appears from the record to include this paper and/or a corresponding poster (#7) exhibited at the referenced workshop.

> It would have been obvious to one of ordinary skill in the art at the time the invention was made to separate the mixture of Sp and Rp stereoisomers and formulate it into a pharmaceutical composition for treating HCV infection.
>
> One having ordinary skill in the art at the time the invention was made would have been motivated to separate the mixture of Sp and Rp stereoisomers and formulate it into a pharmaceutical composition for treating HCV infection because the disclosed phosphoramidate prodrug containing a mixture of Sp and Rp isomers is known to have potential therapeutic effect and usefulness in treating HCV infection, and separation [of] the two isomers of a known therapeutic drug and identifying the therapeutic potency of each isomer are well known in the art. One of ordinary skill in the art would have reasonably expected [] success because separating the isomers of the known therapeutic agents and identifying the potency of each isomer and formulat[ing] into a pharmaceutical composition is well within the ordinary and routine level of one skilled in the art.

Pet. 6–7; Ex. 1004, 12–13.

Patent Owner contested the rejection and, according to Petitioner, argued (in part) that "neither [Sofia 2007] nor any other cited reference supported the assertion that one skilled in the art would have been motivated to separate the Rp and Sp stereoisomers and obtain compounds of at least 97%, 98% and 99% of the Sp stereoisomer." Pet. 7. Patent Owner also argued "unexpected results," particularly that "the Sp stereoisomer (*S*p-**4**) is more potent [than] the mixture of the two phosphorous-based stereoisomers (**4**) and > 20-fold more potent than the corresponding Rp stereoisomer (*R*p-**4**)." Ex. 1004, 24; Pet. 7–8. The Examiner replied:

> Applicant's arguments, submitted May 21, 2013, with respect to the rejection of instant claims 82-93 under 35 USC 103(a) for being obvious over [Sofia 2007], have been fully considered and found to be persuasive to remove the rejection as Applicant has demonstrated that

> the enantiomer Sp-4 is unexpectedly more potent in inhibiting HCV replication than the Rp-4 enantiomer, thereby overcoming the *prima facie* case of obviousness.

Pet. 8; Ex. 1004, 39.

In the Reasons for Allowance, the Examiner said:

> The claimed invention is novel and non-obvious over the prior art. While it is known in the art to make phosphoramidate compounds such as the instantly claimed ones, for example as described in [the '580 patent] and furthermore to resolve chiral compounds into individual enantiomers, Applicant has discovered that the Sp enantiomer of the claimed compound is unexpectedly more potent in inhibiting HCV replication as disclosed on p. 97 of the specification as originally filed. Therefore any *prima facie* case of obviousness is overcome by this finding of unexpected results. For these reasons the claims meet the requirements of 35 USC 102 and 103.

Pet. 8; Ex. 1004, 56.

Therefore, as indicated in the prosecution history, the Examiner found that it was known in the art to make phosphoramidate compounds (for example as described in the '580 patent, the US counterpart to Sofia '634), and to resolve chiral compounds into individual enantiomers. *Id.*

2. Analysis

When evaluating whether the same or substantially the same prior art or arguments were previously presented to the Office under § 325(d), the Board has considered a number of non-exclusive factors, including, for example: (1) the similarity of the asserted art and the prior art involved during the examination; (2) the extent to which the asserted art was considered during examination, including whether the prior art was the basis for rejection; (3) the cumulative nature of the asserted art and the prior art considered during examination; (4) whether Petitioner has pointed out sufficiently how the Examiner erred in its consideration of the

asserted prior art; (5) the extent of the overlap between the arguments made during examination, and the manner in which Petitioner relies on the prior art or the applicant's arguments during examination; and (6) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the asserted prior art. *Juniper Networks, Inc. v. Mobile Telecomm'ns Techs., LLC*, Case IPR2017-00642, slip op. at 8–9 (PTAB July 27, 2017) (Paper 24); *see also Becton, Dickinson & Co. v. B. Braun Melsungen AG*, Case IPR2017-01586, slip op. at 17–28 (PTAB Dec. 15, 2017) (Paper 8) (informative). After considering these factors, we are persuaded that the Petition presents substantially the same prior art or arguments previously presented to the Office with respect to the asserted grounds of obviousness based on Sofia '634 and Congiatu. *See* 35 U.S.C. § 325(d).

Petitioner's Arguments

Petitioner states that "[d]uring prosecution, the Examiner made a similar obviousness rejection of the '309 patent's claims. EX1004 at 12-13. Patent Owner was only able to overcome the obviousness rejection by arguing the claimed invention had purported unexpected results. EX1004 at 24." Pet. 44.

Notwithstanding the "similar obviousness rejection" during prosecution and the Examiner's express consideration of the US counterpart to Sofia '634, Petitioner advances arguments that "Sofia '634 taught that the different diastereomers of its compounds, including compound 25, could be separated, and that these diastereomers would be expected to have substantially different antiviral activity." Pet. 23. Petitioner further contends that "a POSA would know [from Sofia '634] that the phosphorous diastereomers of any phosphoramidate nucleoside drug candidate must be separated and tested individually to determine which diastereomer provide[s] the predominant antiviral activity." *Id.* at 39. According to Petitioner, Sofia '634 also taught "separation of diastereomers by

chromatography" (*id.* at 41), that "[t]he compounds of Sofia '634 were also known to exist as different diastereomers at phosphorous" (*id.* at 19), and that Example 81 of Sofia '634 teaches that, although "[t]he absolute stereochemistry of the P-chiral center of the diastereomers were not determined. . . . chromatographic resolution of these two diastereomers provides for isomers that are characterized as fast eluting and slow eluting isomers." *Id.*, quoting Ex. 1005, 693–694.

Similar to its arguments regarding Sofia '634, Petitioner contends that Congiatu taught separation of phosphorous diastereomers, that it would not be unexpected that the diastereomers would have different biological activity (approximately 15-fold), that the diastereomers would need to be tested to determine which is preferred, that mixtures of diastereomers at phosphorus are readily obtained and the R*p* and S*p* diastereomers may be separated by chromatography and their stereochemistry assigned. Pet. 43.

Recognizing that Patent Owner argued unexpected results during prosecution, Petitioner contends that

> the claimed invention did not have unexpected results, as it would have been entirely expected that one of the two diastereomers would be highly more potent than the other. EX1002 at ¶124. As discussed above, a POSA would have been motivated to separate a compound into its diastereomers and test their separate potencies. *Id*. A POSA would also expect that one diastereomer might be much more potent than the other since many such examples existed, and would be highly motivated to perform this test. *Id*. Thus, Patent Owner did not show during prosecution of the '309 patent that its claims had unexpected results. *Id*.

Pet. 44.

We address the above factors under Section 325(d) in view of the prosecution history and Petitioner's arguments.

Factors 1–3

Sofia ’634 is the same as, or substantially similar to, the ’580 patent that the Examiner expressly addressed in the Notice of Allowance. Ex. 1004, 56; n.1, *supra*. Moreover, based on the Examiner’s position regarding Sofia 2007 during prosecution, Sofia 2007 appears to be substantially similar to Sofia ’634. *See* Ex. 1004, 12–13. Petitioner also relies on Congiatu for teachings that are substantially the same as Sofia ’634, such that the alleged teachings of Congiatu are cumulative to the alleged teachings of Sofia ’634. We thus find that the asserted art (Sofia ’634 and Congiatu) and the prior art involved in, and considered during, the examination of the ’309 patent, are the same or substantially the same. *See* Section 325(d) factors 1–3 above.

Factor 5

As set forth above, Petitioner’s arguments regarding separation of diastereomers overlap those made by Patent Owner, and addressed by the Examiner, during prosecution. *See* Section 325(d) factor 5 above.

Factors 4 and 6

Petitioner contends that the Examiner erred in determining that Patent Owner established unexpected results. Pet. 44. However, the citation to Exhibit 1002, paragraph 124, in the above quoted argument regarding unexpected results is to a statement in the Fortunak Declaration that repeats verbatim the statements asserted by Petitioner, without citing evidentiary support. *See* Ex. 1002 ¶ 124. Moreover, Congiatu adds nothing to Petitioner’s argument regarding unexpected results as it is merely cumulative to Sofia ’634. (*Compare* Pet. 23: “Sofia ’634 taught . . . that these [phosphorous] diastereomers would be expected to have substantially different antiviral activity” *with* Pet. 43: “Congiatu taught that . . . it would not be unexpected for there to be a very substantial . . . difference in

biological activity of phosphorous diastereomers.”). Therefore, Petitioner has neither sufficiently pointed out how the Examiner erred nor provided additional evidence or facts that warrant reconsideration of the Examiner’s decision. *See* Section 325(d) factors 4 and 6 above.

Accordingly, pursuant to 35 U.S.C. § 325(d), we exercise our discretion and decline to institute on the ground of obviousness over Sofia ’634 and Congiatu.

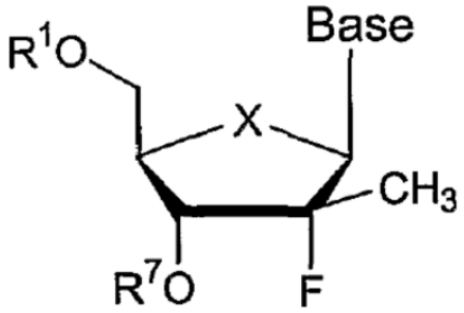
F. Obviousness over Clark ’147 and Congiatu

Petitioner contends that claims 1–12 are obvious over Clark ’147 and Congiatu. Pet. 46–52. On this record, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing that any of claims 1–12 are obvious over Clark ’147 and Congiatu.

1. Clark ’147 (Ex. 1007)

Clark ’147 is directed to compositions and methods for treating a *Flaviviridae* infection, such as hepatitis C virus, using (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleosides. Ex. 1007, Abstract. Clark ’147 claims:

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



wherein Base is a purine or pyrimidine base; and substituents X, R^1, and R^7 are respectively one of a group of elements or compounds. *Id.* at 101. Clark ’147 was cited during the prosecution of the ’309 patent. Ex. 1001, 3.

2. Analysis

Petitioner argues that "[a] POSA would have been motivated to combine the teachings of Clark '147 and Congiatu because they both related to nucleoside phosphoramidate prodrugs." Pet. 46. Petitioner argues that Clark '147's "teaching of diastereomers inherently taught compounds of 97–99% of the preferred diastereomer," and that the recited diastereomeric purities of 97%, 98%, and 99% are "arbitrary limits" and "not meaningful from a standpoint of antiviral activity." *Id.* at 49.

Petitioner argues that Congiatu taught separation of phosphorous diastereomers, that it would not be unexpected that the phosphorous diastereomers would have different biological activity (approximately 15-fold), that the diastereomers must be tested to determine which is preferred as a drug candidate, that mixtures of diastereomers at phosphorus are readily obtained, and that the R*p* and S*p* diastereomers may be separated by chromatography and their stereochemistry at phosphorous assigned. Pet. 50.

Petitioner also repeats the same argument regarding a lack of unexpected results that Petitioner advanced in connection with the asserted ground of obviousness based on Sofia '634 and Congiatu above. *Id.* at 51. However, Petitioner cites to paragraph 142 of the Fortunak Declaration which, like the citation to paragraph 124 of the Fortunak Declaration in the above quote, is also to a statement that repeats verbatim the statements asserted by Petitioner, but without citation to evidentiary support. *See* Ex. 1002 ¶ 142.

On this record, we are not persuaded that Petitioner has established a reasonable likelihood that it would prevail in showing that claim 1 would have been obvious over Clark '147 and Congiatu. As an initial matter, Petitioner does not explain how or whether Clark '147 discloses or even suggests the compound of

formula 4 (claim 1). Furthermore, Petitioner fails to establish any teaching or suggestion of the compound of formula 4 by Clark '147 or Congiatu, alone or in combination. *See CFMT*, 349 F.3d at 1342; *GPAC Inc.*, 57 F.3d at 1581. Moreover, other than citations to unsupported paragraphs of the Fortunak Declaration, Petitioner provides no persuasive explanation of how Clark '147 inherently teaches diastereomeric purities of 97%, 98%, and 99%. In particular, Petitioner fails to persuasively explain how such purities "necessarily must be present" in Clark '147. *See Par Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1194–96 (Fed. Cir. 2014) (discussing inherency in the obviousness context).

Petitioner's argument that Congiatu taught "that it would not be unexpected for there to be a very substantial (in this case approximately 15-fold) difference in biological activity of phosphorous diastereomers," as well as its argument that "the claimed invention did not have unexpected results," do not sufficiently address the finding of unexpected results that, according to Petitioner, was the "only" reason the Examiner allowed the claims of the '309 patent. Pet. 44. Objective indicia of unexpected results must be considered before any conclusion regarding obviousness is reached, and may be the most probative evidence of nonobviousness. *Millennium Pharms., Inc. v. Sandoz Inc.*, 863 F.3d 1356, 1367–68 (Fed. Cir. 2017) (citing cases). However, Petitioner's arguments regarding a lack of unexpected results amount to little more than conclusory statements that are insufficient to support a conclusion of obviousness. *See KSR*, 550 U.S. at 418.

Petitioner also fails to set forth any persuasive reason to combine the teachings of Clark '147 and Congiatu. Instead, Petitioner supports the combination with a conclusory statement that relies on the same statement in the Fortunak Declaration that lacks citation to evidentiary support. *See* Pet. 46; Ex. 1002 ¶ 129. Again, such conclusory statements are insufficient to establish obviousness. *See*

KSR, 550 U.S. at 418.

On this record, we find that Petitioner has failed to persuasively show that the cited references alone or in combination taught or suggested the limitations in claim 1. Further, Petitioner has not persuasively demonstrated that the cited references or the skill in the art would have provided a reason that would have prompted a POSA to combine the teachings of Clark '147 and Congiatu. Accordingly, we determine that Petitioner has not shown a reasonable likelihood that it would prevail on its assertion that claim 1, and thus, dependent claims 2–12, which include the limitations of claim 1, are unpatentable as obvious over Clark '147 and Congiatu. *See In re Fine*, 837 F.2d 1071, 1076 (Fed. Cir. 1988) ("Dependent claims are nonobvious under section 103 if the independent claims from which they depend are nonobvious.").

III. CONCLUSION

For the foregoing reasons, we conclude that Petitioner has not established a reasonable likelihood of prevailing on its assertion that any of claims 1–12 of the '309 patent are unpatentable.

IV. ORDER

In consideration of the foregoing, it is hereby ORDERED that the Petition is *denied*.

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