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Paper No. 7
Entered: July 19, 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 IPR2018-00390
Patent 8,889,159 B2

Before ERICA A. FRANKLIN, GRACE KARAFFA OBERMANN and RICHARD J. SMITH, *Administrative Patent Judges.*

OBERMANN, *Administrative Patent Judge*.

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

I. INTRODUCTION

Petitioner filed a Petition for *inter partes* review of claims 1–37 of U.S. Patent 8,889,159 B2 ("the '159 patent"). Paper 2 ("Pet."). Patent Owner filed a Preliminary Response. Paper 6 ("Prelim. Resp."). We have authority to institute an *inter partes* review only upon a showing that Petitioner is reasonably likely to prevail with respect to at least one challenged patent claim. 35 U.S.C. § 314(a). Applying that standard, we conclude that Petitioner has not established the threshold showing for review and, accordingly, we deny the Petition and do not institute review of any challenged claim.

A. Related Proceedings

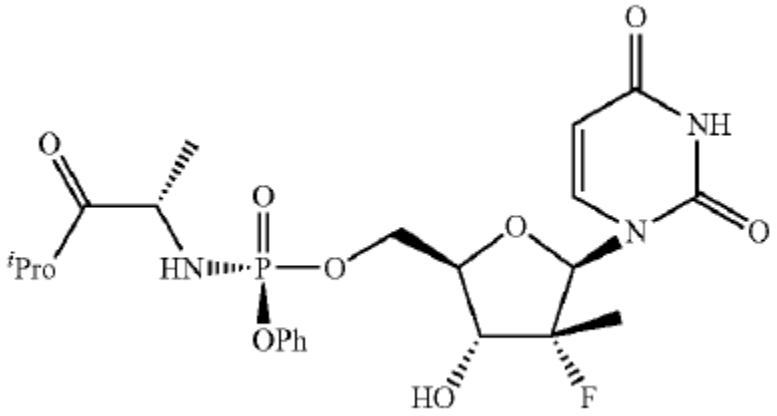
Petitioner identifies as a related matter a pending patent application (U.S. Patent Appl. No. 15/410,438) that claims priority through the '159 patent. Pet. 2. Petitioner avers that it "is not aware of any other matter that would affect, or be affected by, a decision in this proceeding." *Id*.

Patent Owner identifies the same pending application under a heading titled "Related Matters." Paper 3, 2. Patent Owner also identifies a second pending application (U.S. Patent Appl. No. 14/538,736) as a related matter and, further, "notes" that Petitioner filed eight prior petitions for *inter partes* review, none of which was directed to any claims of the '159 patent. *Id*. at 2–3 (citations omitted). "Patent Owner does not concede that any" of those identified matters— "aside from" the '159 patent—"would affect, or be affected by this proceeding." *Id*.

B. The '159 Patent

The '159 patent relates to a pharmaceutical composition and unit dosage form of a specific agent for treating hepatitis C virus ("HCV"). Ex. 1001, Abstract. The specification discloses that (S)-isopropyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3 -hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate is "available from Gilead Sciences, Inc." and, further, is disclosed and claimed in U.S. Pat. No. 7,964,580. Ex. 1001, 7:65–8:2.

The specification states that this HCV agent is, or has been, known variously as "GS-7977," "sofosbuvir," and "PSI-7977." *Id*. at 7:67; 5:20–21. We refer to that agent in this decision as sofosbuvir. According to the '159 patent specification, sofosbuvir has the following general structure:



Id. at 7:65–8:15. Patent Owner directs us to information that sofosbuvir may exist in different crystalline forms known as "polymorphs," which "can, and often do, exhibit different properties." Prelim. Resp. 5–6 (and evidence cited therein).

The '159 patent discloses a polymorphic form of sofosbuvir identified as "Form 6." Ex. 1001, 8:42; 32:24, 31. According to the specification, Form 6 is

characterized by an X-ray powder diffraction ("XRPD") pattern of "2θ-reflections (°) at about: 6.1, 8.2. 10.4, 12.7, 17.2, 17.7, 18.0, 18.8, 19.4, 19.8, 20.1, 20.8, 21.8, and 23.3." *Id*. at 8:18–26, 40–56; *see id*. at 9:51–55 (disclosing "preferred subembodiment" of "crystalline" sofosbuvir having that characteristic XRPD pattern of 2θ-reflections); 11:40–12:55 (disclosing embodiments having that characteristic XRPD pattern of 2θ-reflections).

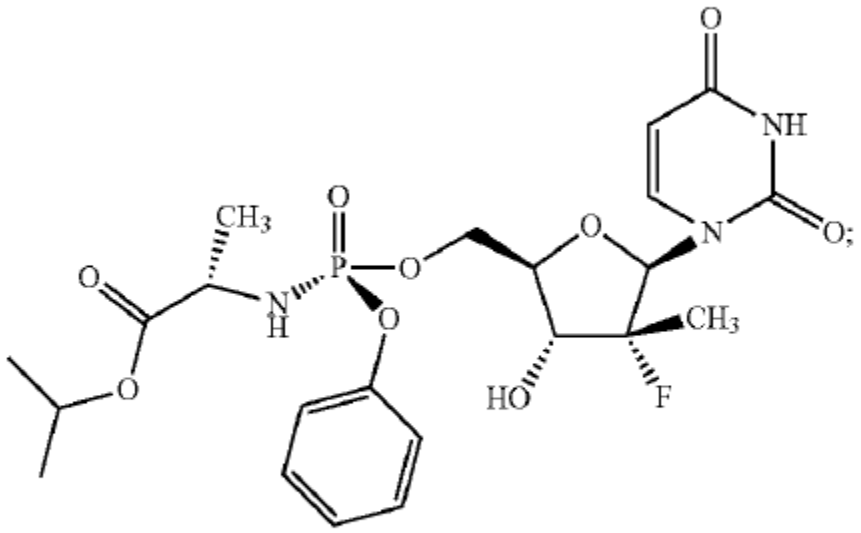
The specification discloses an example that includes instructions for forming "polymorphic Form 6" into a 400 mg tablet dosage form. *Id*. at 32:6–63. Specifically, the '159 patent describes milling Form 6 "with extragranular excipients (microcrystalline cellulose, croscarmellose sodium, colloidal silicon [dioxide], magnesium stearate) to yield a powder blend comprising 33.33% w/w" sofosbuvir, which "was compressed to a target tablet weight of 1200 mg, with each tablet comprising about 400 mg of" sofosbuvir. *Id*. Patent Owner avers that Form 6 is used in its commercial pharmaceutical product known as Sovaldi. Prelim. Resp. 6.

C. Illustrative Claims

Petitioner challenges claims 1–37 of the '159 patent, of which claims 1 and 16 are the only independent claims.

Claim 1 is reproduced below:

1. A pharmaceutical composition comprising:
a) about 25% to about 35% w/w of crystalline GS-7977 having the structure

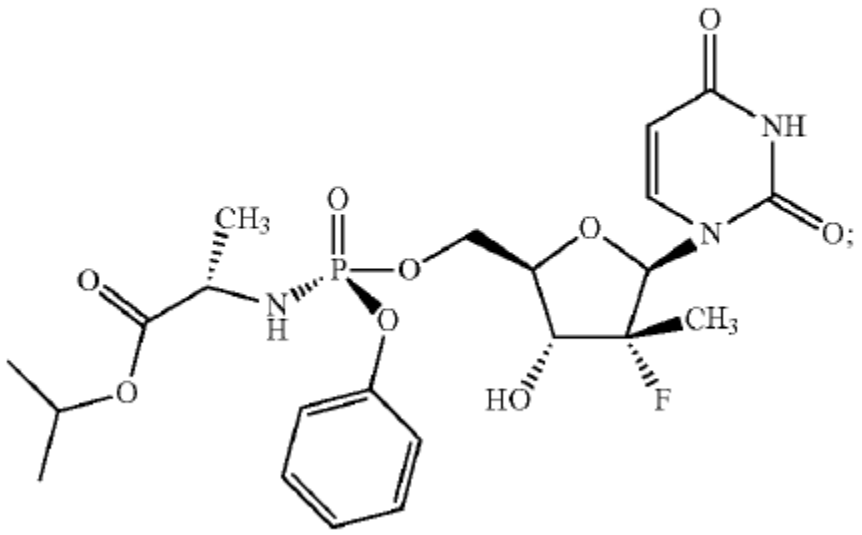


and
b) at least one pharmaceutically acceptable excipient, wherein the crystalline GS-7977 has XRPD 2θ-reflections (°) at about:
6.1 and 12.7.

Ex. 1001, 46:36–56. Claims 2–15 and 33 depend directly or indirectly from claim 1. *Id.* at 46:57–47:50; 49:15–17.

Claim 16, the only other independent claim, is reproduced below:

16. A unit dosage form comprising:
a) about 400 mg of crystalline GS-7977 having the structure



and
b) at least one pharmaceutically acceptable excipient,
wherein the crystalline GS-7977 has XRPD 2θ-reflections (°) at about
6.1 and 12.7.

Ex. 1001, 47:51–48:5. Claims 17–32 and 34–37 depend directly or indirectly from claim 16. *Id*. at 48:6–49:14; 49:18–29.

D. The Asserted Grounds of Unpatentability

The Petition, supported by the declaration of Joseph M. Fortunak, Ph.D. (Ex. 1014), asserts the following grounds of unpatentability against claims 1–37:

Reference	Statutory Basis
Ross '645[1]	§ 102
Ross '645	§ 103
Ross '257[2,3]	§ 102
Ross '257	§103

Pet. 3.

II. ANALYSIS

A. Person of Ordinary Skill in the Art

Petitioner asserts that a person of ordinary skill in the art at the time of the invention would have had 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 and/or development, including formulations, and would also have some familiarity with antiviral drugs and their design and mechanism of action, or"

[1] WO 2011/123645 A2, to Bruce Ross, et al., published Oct. 6, 2011 (Ex. 1008, "Ross '645").

[2] U.S. Pat. Pub. 2010/0298257 A1, to Bruce S. Ross, et al., published Nov. 25, 2010 (Ex. 1005, "Ross '257").

[3] The table of grounds presented in the Petition twice refers to "Ross '237." Pet. 3. We determine that the reference to Ross '237 is a typographical error, given that the arguments and evidence asserted in the analysis sections of the Petition relate to Ross '257. *See, e.g.*, Pet. 23–26, 45–64; Ex. 1005 (asserted prior art reference).

alternatively "(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 formulations, for the treatment of viral diseases." Pet. 8 (citing Ex. 1014 ¶ 39).

Patent Owner, by contrast, contends that a person of ordinary skill in the art would have had either "(1) a Ph.D. in chemistry, pharmacy or a closely related field, with some experience in an academic or industrial laboratory focusing on drug formulation, and would also have some familiarity with the clinical development of antiviral drugs, or work in collaboration with someone who has expertise in the clinical development of antiviral drugs; or" alternatively "(2) a Bachelor's or Master's degree in chemistry, pharmacy, or a closely related field, with significant experience in an academic or industrial laboratory focusing on drug formulation, and some familiarity with clinical development of antiviral drugs, or work in collaboration with someone who has expertise in the clinical development of antiviral drugs." Prelim. Resp. 10.

Based on the information presented, we determine that the prior art asserted in the Petition 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)). To the extent more specific findings are necessary, we adopt Petitioner's proposed definition, which, unlike Patent Owner's counter definition, is supported by declaration testimony. *Compare* Pet. 8 (citing Ex. 1014 ¶ 39), *with* Prelim. Resp. 10 (citing no evidence in support of Patent Owner's proposed definition). However, like Patent Owner, we discern no appreciable difference in the parties'

respective definitions, much less any difference that would alter the outcome of this decision based on our acceptance of one definition over the other. *See* Prelim. Resp. 11 (Patent Owner, arguing that any difference between the parties' proposed definitions "does not affect the arguments" advanced in the Preliminary Response).

B. Claim Construction

In an *inter partes* review, we construe claims an unexpired patent using the "broadest reasonable construction in light of the specification of the patent." 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016) (upholding use of broadest reasonable construction standard in *inter partes* reviews). Under that standard, we apply "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). Neither Petitioner nor Patent Owner raises any disputed claim construction term or proposed construction. On the contrary, both acknowledge that the claim terms should be given their ordinary and customary meaning. Pet. 8; Prelim. Resp. 11.

Based on the information presented, including the disclosures of the '159 patent specification and the asserted prior art references, we agree with the parties that no claim term requires express construction for purposes of this decision. *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. Anticipation by Ross '645

Petitioner asserts that claims 1–37 are anticipated by Ross '645. Pet. 26. We agree with Petitioner that Ross '645 discloses Form 6 of sofosbuvir. *Id*. at 29 (citing Ex. 1008, 20:16–18; 116:17–18). We further agree that Ross '645 discloses that "[a] typical preparation will contain from about 5% to about 95% active compound or compounds (w/w)." *Id*. at 30 (citing Ex. 1008, 21:22–23). We disagree, however, that the mere fact that the range specified in independent claim 1 ("about 25% to about 35% w/w") falls within the range disclosed in Ross '645 ("about 5% to about 95%") shows sufficiently that the reference anticipates the narrower claimed range. *Id*. at 30–31 (Petitioner's conclusory argument that the encompassing prior art range disclosed in Ross '645 necessarily anticipates the narrower range specified in claim 1, and citing, by way of support, only bare opinion testimony that repeats the conclusory argument verbatim without any analysis (Ex. 1014 ¶ 98)).

A reference that discloses a broad range encompassing a narrower claimed range anticipates the narrower claimed range only if the reference describes the narrower claimed range "with sufficient specificity." Prelim. Resp. 15 (quoting *Atofina v. Great Lakes Chem. Corp*., 441 F.3d 991, 999 (Fed. Cir. 2006)). Patent Owner persuasively argues that the "sufficient specificity" requirement demands a showing (which is entirely absent in the Petition) that an ordinarily skilled artisan "would 'at once envisage' the claimed arrangement or combination," which, in this

case, requires a composition of Form 6 of sofosbuvir in a percentage range of about 25% to about 35% (w/w). Prelim. Resp. 15 (quoting *Kennametal, Inc. v. Ingersoll Cutting Tool Co.*, 780 F.3d 1376, 1381 (Fed. Cir. 2015)). The Petition does not address, much less show sufficiently, how or why a person of ordinary skill in the art "would 'at once envisage'" a formulation of about 25% to about 35% (w/w) of Form 6, as required by claim 1, from the much broader range of "about 5% to about 95%" (w/w) that is disclosed in Ross '645 in the general context of any "active compound or compounds." Ex. 1008, 21:22–23; *see* Pet. 30–31 (citing Ex. 1014 ¶ 98) (Petitioner and Dr. Fortunak, failing to address that key point).

Patent Owner, for its part, directs us to persuasive information that the broad range disclosed in Ross '645 for any "active compound" does not suggest the narrower range required by claim 1 for Form 6. Prelim. Resp. 12–16. On that point, we agree with Patent Owner that the range disclosed in Ross '645 is so broad that it suggests "almost all percentages of active ingredient(s)" and reveals a "lack of any direction about a sub-range." *Id*. at 16; *see* Ex. 1008, 21:22–23 (Ross '645, disclosing a range of "about 5% to about 95%" without any suggestion of a preferred sub-range of percentages for Form 6 or any other particular polymorph of sofosbuvir).

Patent Owner identifies compelling authority that a broad range must be shown to describe a narrower claimed range "with sufficient specificity" to represent an anticipatory disclosure. Prelim. Resp. 15. For example, in *Atofina*, our reviewing court held that a prior art disclosure of a temperature range of 100 to 500° C did not anticipate a claimed range of 330 to 450° C "with sufficient specificity." *Atofina*, 441 F.3d at 999. Similarly, the Petition contains no analysis tending to show that the broad percentage range disclosed in Ross '645 teaches,

"with sufficient specificity" (*id.*), the narrower range required by claim 1. Instead, the Petition rests on a faulty assumption that a broad encompassing range disclosed in the prior art necessarily anticipates a narrower claimed range. Pet. 30–31.

The Federal Circuit's opinion in *OSRAM Sylvania, Inc. v. Am. Induction Techs., Inc.*, 701 F.3d 698 (Fed. Cir. 2012) also is instructive. There the dispute centered on whether a prior art disclosure of "approximately 1 torr or less" anticipated a claim limitation that required "less than 0.5 torr." *Id.* at 706. Our reviewing court there reversed a district court's grant of summary judgment of anticipation on those facts. *Id.* Similar to Petitioner in this case, the patent challenger in *OSRAM Sylvania* relied on "the conclusory claim that less than 0.5 torr necessarily falls within 'approximately 1 torr or less' as a matter of fact." *Id.* The Federal Circuit explained that "the inquiry does not end there." *Id.* "[H]ow one of ordinary skill in the art would understand the relative size of a genus or species in [the] particular technology is of critical importance." *Id.*

The Petition nowhere addresses that critical inquiry. Accordingly, we find that Petitioner fails to show sufficiently that the broad range disclosed in Ross '645 anticipates the narrower range required by claim 1. Pet. 30–31 (bridging paragraph, for totality of Petitioner's argument on that point).

That finding is consistent with prior Board decisions identified by Patent Owner. Prelim. Resp. 15–16. Specifically, the Board previously held that a disclosure of a dosage range of 1–1000 mg, with a preferred dosage range of 1–100 mg, did not anticipate a claimed amount of 2.5 mg or 5 mg. *Mylan Pharm. Inc. v. Boehringer Ingelheim Int'l GmbH*, Case IPR2016-01566, Paper 15, 6–7 (P.T.A.B. Feb. 3, 2017). Applying the same principles, the Board also previously held that a concentration range of 0.01% to 4% w/w, with a preferred range of 0.1–0.2% w/w,

did not anticipate a claimed concentration of 0.3% w/w. *Complex Innovations, LLC v. Astrazeneca AB*, Case IPR2017-00631, Paper 13, (P.T.A.B. July 24, 2017).

Given that the Petition is devoid of analysis tending to establish that the broad range of about 5% to about 95% (w/w) disclosed in Ross '645 anticipates with sufficient specificity the narrower range of about 25% to about 35% (w/w) specified in claim 1, we conclude that Petitioner fails to show a reasonable likelihood of prevailing as to claim 1 (and claims 2–15 and 33, which depend directly or indirectly therefrom).

Our reasoning applies with equal force to independent claim 16 (and claims 17–32 and 34–37, which depend directly or indirectly therefrom). Claim 16 requires a unit dosage of 400 mg. Patent Owner persuasively points out that the Petition does not show sufficiently "that Ross '645's broad generic disclosure of a dosage range" of "10 to 10,000 mg" anticipates the narrower range of "400 mg" required by claim 16. Prelim. Resp. 19. The decisions in *Atofina*, *Mylan*, and *Complex Innovations*, discussed above in connection with claim 1, apply with equal force to claim 16, and refute Petitioner's contention that the broad dosage range disclosed in Ross '645 anticipates "all incremental values" falling between the endpoints of the prior art range. Pet. 38. The Petition lacks information or analysis from which we reasonably can conclude that the 400 mg unit dosage required by claim 16 (and all claims that depend directly or indirectly therefrom) is disclosed "with sufficient specificity" in Ross '645. *Atofina*, 441 F.3d at 999.

Accordingly, on this record, we find that Petitioner does not demonstrate a reasonable likelihood of prevailing at trial in showing that any challenged claim of the '159 patent is anticipated by Ross '645.

D. Obviousness over Ross '645

Petitioner also asserts that the subject matter of claims 1–37 would have been obvious from the disclosure of Ross '645. Pet. 26. The Petition does not provide a separate analysis of the obviousness challenge, but rather, asserts obviousness in a conclusory fashion as part of the anticipation challenge. Pet. 26–31. The information presented in the Petition does not include reasoning with a rational underpinning sufficient to show how or why a person of ordinary skill in the art would have been led to modify the disclosure of Ross '645 to arrive at the claimed invention. *Id*.

Specifically, when discussing independent claim 1, the Petition states only that Ross '645 renders the invention obvious because a person of ordinary skill in the art "would have been motivated to prepare a suitable pharmaceutical composition with the known HCV agent," namely, Form 6 of sofosbuvir. Pet. 31 (citing Ex. 1014 ¶ 98). When discussing independent claim 16, the Petition states only that a person of ordinary skill in the art would have understood from Ross '645 and "common knowledge" that the prior art would "at least" have "rendered" claim 16 "obvious." Pet. 38 (citing Ex. 1014 ¶ 129). Those conclusory statements are insufficient to support trial institution. A petitioner in our forum cannot satisfy its burden of proving obviousness by employing "mere conclusory statements" regarding the motivations of an ordinarily skilled artisan. *In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016).

Notably, by way of evidentiary support, the Petition directs us only to opinion testimony of Dr. Fortunak, which merely repeats verbatim the conclusory statements set forth in the Petition, without providing any factual analysis or citing any supporting objective proof. *See* Ex. 1014 ¶¶ 98, 129 (the portions of Dr. Fortunak's declaration testimony relied upon to establish the ground based on

obviousness). Even if we accept that Dr. Fortunak is qualified to testify from the perspective of a person of ordinary skill in the art, his inadequately supported opinion on the question of obviousness "is entitled to little or no weight." 37 C.F.R. § 42.65(a); *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" that underpin an obviousness determination "may render the testimony of little probative value in a validity determination.").

Accordingly, on this record, we find that Petitioner is not reasonably likely to prevail at trial in showing that the subject matter of independent claim 1 or 16 would have been obvious to an ordinarily skilled artisan from the disclosure of Ross '645. Given that Petitioner's arguments pertaining to the dependent claims rest on the same insufficient showing made in connection with independent claims 1 and 16, we find also that Petitioner fails to meet the threshold showing required to support institution of trial with respect to any challenged claim on the ground based on obviousness over Ross '645. *See* Pet. 31–45 (for analysis of the challenges directed to dependent claims 2–16 and 17–37).

E. Grounds Based on Ross '257

The Petition asserts that claims 1–37 are anticipated by, or obviousness over, the disclosure of Ross '257. Pet. 23–26, 45–64. Petitioner acknowledges, however, that during patent prosecution, "the Examiner made only one prior art rejection of the pending claims"—a rejection based on obviousness over Ross '257 in view of two other references. *Id*. at 6–7. Petitioner also acknowledges that, in response to that "obviousness rejection, Patent Owner amended the claims to recite polymorphic Form 6" of sofosbuvir; an amendment that resulted in withdrawal of the rejection and allowance of the claims to issue in their present form. *Id*. The

Examiner fully considered Ross '257 but, nonetheless, determined that "the claimed polymorph appears to be free of art." *Id*. at 7 (quoting prosecution history (Ex. 1002, 114)). Under these circumstances, we agree with Patent Owner that a question arises whether it is "unnecessary and wasteful to re-adjudicate" those issues previously considered and decided by the Office. Prelim. Resp. 62.

Patent Owner invites us to exercise our discretion to deny the grounds that assert Ross '257 because those grounds present "the same or substantially the same prior art or arguments previously" "presented to the Office." *Id*. at 60 (quoting 35 U.S.C. § 325(d)). We agree with Patent Owner that the Examiner fully considered, and expressly rejected, the argument that Ross '257 discloses or suggests Form 6 of sofosbuvir. *See id*. at 61–62 (directing us to the relevant portions of the prosecution history (Ex. 1002, 85, 88–89, 114, 141–142)). Patent Owner's argument in support of an application of our discretion under Section 325(d), therefore, is not without merit. *Id*. at 60–62. However, we determine on the merits, based on our own analysis, that Petitioner has not met the threshold showing necessary to support trial institution on the grounds based on Ross '257. *See* Pet. 23–26, 45–64 (argument pertaining to Ross '257).

Based on the information presented in the Petition and Preliminary Response, we agree with the Examiner that Ross '257 "does not disclose or suggest the claimed polymorph" required by each challenged claim; namely, Form 6 of sofosbuvir, which is characterized by "XRPD 2θ-reflections (°) at about: 6.1 and 12.7." Ex. 1002, 141. The Examiner found, and we agree, that the reference on its face teaches crystalline sofosbuvir having "XRPD 2θ-reflections (°) at about: 5.0, 7.3, 9.4 and 18:1." *Id*.; Ex. 1005 ¶ 99. Petitioner's argument that the further disclosure of a "substantially pure crystalline" form of sofosbuvir represents a teaching of "a genus" that would have included "any additional

crystalline forms" is not persuasive. Pet. 47. Petitioner directs us to information insufficient to show that the specific polymorph required by each challenged claim (that is, Form 6, having characteristic XRPD 2θ-reflections (°) at about: 6.1 and 12.7) is anticipated by, or would have been obvious from, any of the "six crystalline forms" disclosed in Ross '257. Pet. 47 (citing Ex. 1005 ¶¶ 98–106).

Accordingly, on this record, we determine that Petitioner is not reasonably likely to prevail at trial in showing that any challenged claim of the '159 patent is unpatentable under either ground that asserts Ross '257.

III. CONCLUSION

Based on the information presented in the Petition and Preliminary Response, we conclude that Petitioner has not established a reasonable likelihood of prevailing at trial in showing that any of claims 1–37 of the '159 patent are unpatentable.

IV. ORDER

It is

ORDERED that the Petition is *denied* and an *inter partes* review is not instituted.

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