

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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SHANGHAI HONGENE BIOTECH CORP.,  
Petitioner,

v.

CHEMGENES CORP.,  
Patent Owner.

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IPR2023-00875  
Patent 8,309,707 B2

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Before JOHN G. NEW, ZHENYU YANG, and CYNTHIA M. HARDMAN,  
*Administrative Patent Judges.*

YANG, *Administrative Patent Judge.*

PRELIMINARY GUIDANCE  
PATENT OWNER'S MOTION TO AMEND

## I. INTRODUCTION

On October 24, 2023, we instituted trial as to claims 1 and 2 of U.S. Patent No. 8,309,707 B2. Paper 6. After institution, Patent Owner filed a Motion to Amend. Paper 11 (“Motion” or “Mot.”). In its Motion, Patent Owner proposes to amend the ’707 patent to replace claims 1 and 2 with substitute claims 4 and 5. Mot. 1–2. Petitioner filed an Opposition to Patent Owner’s Motion. Paper 13 (“Opposition” or “Opp.”).

In the Motion, Patent Owner requested that we provide preliminary guidance concerning the Motion in accordance with the Board’s Pilot Program concerning motion to amend practice and procedures. Mot. 1–2; *see also* Notice Regarding a New Pilot Program Concerning Motion to Amend Practice and Procedures in Trial Proceedings under the America Invents Act before the Patent Trial and Appeal Board, 84 Fed. Reg. 9,497 (Mar. 15, 2019) (providing a patent owner with the option to receive preliminary guidance from the Board on its motion to amend) (“Notice”). We have considered Patent Owner’s Motion and Petitioner’s Opposition.

In this Preliminary Guidance, we provide information indicating our initial, preliminary, and non-binding views on whether Patent Owner has shown a reasonable likelihood that it has satisfied the statutory and regulatory requirements associated with filing a motion to amend in an *inter partes* review and whether Petitioner (or the record) establishes a reasonable likelihood that the substitute claims are unpatentable. *See* Notice, 84 Fed. Reg. at 9,497 (“The preliminary guidance . . . provides preliminary, non-binding guidance from the Board to the parties about the [motion to amend]”); *see also* 35 U.S.C. § 316(d) (statutory requirements for a motion to amend); 37 C.F.R. § 42.121 (regulatory requirements and burdens for a motion to amend); *Lectrosonics, Inc. v Zaxcom, Inc.*,

IPR2018-01129, Paper 15 (PTAB Feb. 25, 2019) (precedential) (providing information and guidance regarding motions to amend).

For purposes of this Preliminary Guidance, we focus on the proposed substitute claims, and specifically on the amendments proposed in the Motion. *See* Notice, 84 Fed. Reg. at 9,497. We do not address the patentability of the originally challenged claims. *Id.* Moreover, in formulating our preliminary views on the Motion and Opposition, we have not considered the parties' other substantive papers on the underlying merits of Petitioner's challenges. We emphasize that the views expressed in this Preliminary Guidance are subject to change upon consideration of the complete record, including any revision to the Motion filed by Patent Owner. Thus, this Preliminary Guidance is not binding on the Board when rendering a final written decision. *See id.* at 9,500.

## II. PRELIMINARY GUIDANCE

As a threshold matter, Patent Owner has not clearly articulated whether the Motion is either: (1) contingent upon a finding in a final written decision that the challenged claims are unpatentable; or (2) non-contingent. "A motion to amend claims may cancel claims and/or propose substitute claims." *Lectrosonics* at 3 (citing 35 U.S.C. § 316(d)(1); 37 C.F.R. § 42.121(a)(3)). A request to substitute claims ordinarily will be treated as contingent. *Id.* "In other words, a proposed substitute claim normally will be considered only if a preponderance of the evidence establishes that the original patent claim that it replaces is unpatentable." *Id.* A patent owner should adopt a claim-by-claim approach to specifying the contingency of substitution, e.g., which claim is to be substituted for which claim, and under what circumstances. *Id.*

For purposes of this Preliminary Guidance, we treat the Motion as contingent upon a finding in a final written decision that the challenged claims are unpatentable. *See Lectrosonics* at 3 (“[A] request to substitute claims ordinarily will be treated as contingent”). However, we advise Patent Owner to expressly state whether the motion is contingent or non-contingent in either a reply in support of the motion to amend or in a revised motion to amend.

#### A. Statutory and Regulatory Requirements

For the reasons discussed below, at this stage of the proceeding, and based on the current record, it appears that Patent Owner has not shown a reasonable likelihood that it has satisfied the statutory and regulatory requirements associated with filing a motion to amend.

##### 1. Reasonable Number of Substitute Claims

Does Patent Owner propose a reasonable number of substitute claims? (35 U.S.C. § 316(d)(1)(B))
Yes. Patent Owner proposes no more than one substitute claim for each challenged claim. Mot. 2, A1–A5 (Appx. A). Petitioner does not argue otherwise.

##### 2. Respond to Ground of Unpatentability

Does the Motion respond to a ground of unpatentability involved in the trial? (37 C.F.R. § 42.121(a)(2)(i))
Yes. It appears that the Motion responds to the grounds of unpatentability. Mot. 10–15. Petitioner does not argue otherwise.

### 3. Scope of Amended Claims

Does the amendment seek to enlarge the scope of the claims? (35 U.S.C. § 316(d)(3); 37 C.F.R. § 42.121(a)(2)(ii))

No. It appears that each proposed substitute claim is narrower in scope than the corresponding original claim. Mot. 3–5, A1–A5 (Appx. A). Petitioner does not argue otherwise.

### 4. New Matter

Does the amendment seek to add new subject matter? (35 U.S.C. § 316(d)(3); 37 C.F.R. § 42.121(a)(2)(ii))

Yes. For the reasons discussed below, on this record, we find that Patent Owner fails to show a reasonable likelihood that the substitute claims introduce no new matter relative to the original disclosure.

Patent Owner asserts that the proposed substitute claims are supported by the specification of the original application, No. 12/584,625 (“the ’625 application”), and U.S. Provisional Application No. 61/191,065 (“the ’065 provisional”). Mot. 5. Patent Owner asserts that proposed substitute claim 4 is supported in claim 1 of the ’707 patent and disclosures in the ’625 application and the ’065 provisional. *Id.* at 6–7. Patent Owner asserts that proposed substitute claim 5 is supported in claim 2 of the ’707 patent and disclosures in the ’625 application and the ’065 provisional. *Id.* at 7–10.

Specifically, Patent Owner asserts that proposed substitute claim 4 is supported by stating that

[e]ach of these elements is recited in original Claim 1 of the ’707 Patent (Ex. 1001, 33:47-35:17), and is supported by, *inter alia*, pages 20:30-23:15, 37:11-38:9, 40:10-43:10, 45:4-23 (Claim 1) of the ’625 Application. Ex. 1002, 23:30-26:15, 39:11-40:9, 42:10-45:10, 47:4-23 (Claim 1); Ex. 2001, ¶77. Each of these elements is also supported by, *inter alia*, pages 14-16, 24, and 26-27 of the ’065 Provisional. Ex. 2002, 21-23, 31, 33-34; Ex. 2001, ¶77.

Mot. 7.

Patent Owner asserts that proposed substitute claim 5 is supported by stating that

[e]ach of these elements is recited in original Claim 2 of the '707 Patent (Ex. 1001, 35:18-36:15), and is supported by, *inter alia*, pages 20:30-23:15, 38:11-26, 40:10-43:10, 45:25-46:15 (Claim 2) of the '625 Application. Ex. 1002, 23:30-26:15, 40:11-26, 42:10-45:10, 47:25-48:15 (Claim 2); Ex. 2001, ¶85. Each of these elements is supported by, *inter alia*, pages 15-16, 24, and 26-27 of the '065 Provisional. Ex. 2002, 22-23, 31, 33-34; Ex. 2001, ¶85. The shading in the depicted chemical formula image in Substitute Claim 5 has been corrected as noted on pages 9-10 of the Institution Decision and is also supported by the cited support in the '625 Application and the '065 Provisional. Ex. 2001, ¶85.

Mot. 9.

Petitioner argues Patent Owner does not properly identify support for proposed substitute claims 4 and 5 because the Motion merely provides string citations. Opp. 1–3. According to Petitioner, “a motion to amend must ‘*describe how* the original disclosure of the patent and any relied upon prior application supports each claim that is added or amended.’ . . . This burden of production is not satisfied by merely string citing parts of the priority document.” *Id.* at 2 (emphasis in original, citations omitted).

Petitioner contends Patent Owner’s identification of support for proposed substitute claims 4 and 5 is insufficient because the Motion does not specify how each limitation is supported, and “merely has a table reciting the claim as a whole, then a single paragraph containing only the conclusory and vague assertion that the claim elements are ‘supported by’ string citations to the '625 Application and the '065 Provisional.” *Id.* at 3.

On this record, we agree with Petitioner that the string cites in Patent Owner’s Motion do not explain how each individual claim limitation is supported. Patent Owner provides only bare citations, leaving it to the Board to discern how and which citation purportedly supports each claim limitation. Thus, it is our preliminary and non-binding view that Patent Owner fails to show a reasonable likelihood that the proposed substitute claims add no new matter.

Petitioner also asserts that proposed substitute claims 4 and 5 lack adequate written description support for the recited 2'-F compounds.

Opp. 4–11. We analyze this issue later in our discussion of written description support under the Patentability section.

## B. Patentability

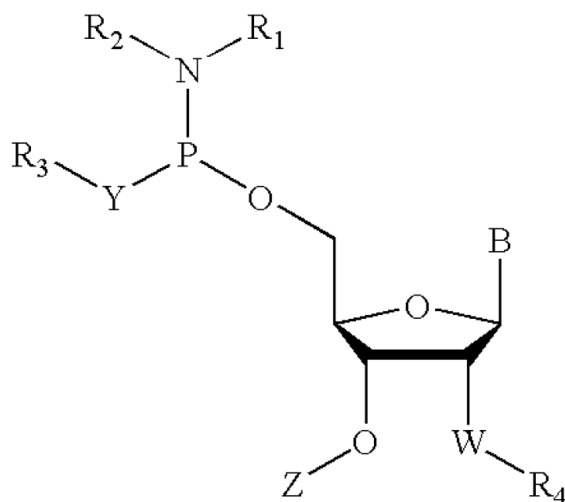
For the reasons discussed below, at this stage of the proceeding, and based upon the current record,<sup>1</sup> it appears that Petitioner has shown a reasonable likelihood that proposed substitute claims 4 and 5 are unpatentable.

Does the record establish a reasonable likelihood that the proposed substitute claims are unpatentable?

### 1. Written Description

Yes. On this record, it appears that Petitioner has shown a reasonable likelihood that proposed substitute claims 4 and 5 are unpatentable as lacking written description support for the 2'-F Limitation.

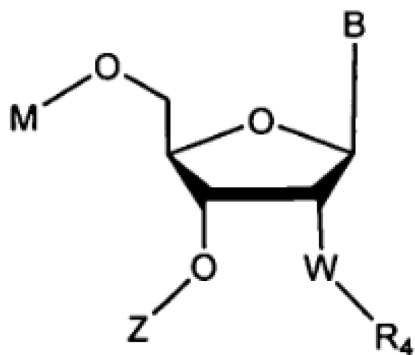
Formula (1) recited in proposed substitute claim 4 is reproduced below.



Mot. A-1.

<sup>1</sup> We express no view on the patentability of original claims 1 and 2 in this Preliminary Guidance. Instead, we focus on the proposed amendments to those claims in the Patent Owner's Motion to Amend.

Formula(2) recited in proposed substitute claim 5 is reproduced below.



Mot. A-3.

According to Petitioner, proposed substitute claims 4 and 5 require “W—R<sub>4</sub>” at the 2′ position and recite “W is selected from the group consisting of an oxygen diradical and a fluorine radical” and “R<sub>4</sub> is selected so that . . . if W is a fluorine radical, then R<sub>4</sub> is not present.” Opp. 4–5 (citing Ex. 1015 ¶¶ 26–27).

Petitioner contends “the specifications<sup>2</sup> lack adequate written description support under 35 U.S.C. § 112 for the many compounds of Substitute Claims 4 and 5 that have a fluorine and nothing else at the 2′-position (collectively referred to herein as the ‘claimed 2′-F compounds’)” because the specifications do not convey to a person of ordinary skill in the art that “the inventors were in possession of any of the claimed 2′-F compounds” and “applicants expressly admitted during prosecution that they did not even begin working on 2′-F compounds until well after the ’707 Patent application was filed.” *Id.* at 4 (footnote added).

We further discuss Petitioner’s arguments below, followed by our analysis.

*A. Summary of Petitioner’s Argument that the Specifications Do Not Reasonably Convey Possession of the Claimed 2′-F Compounds*

Petitioner contends that “[n]o claimed 2′-F compound is disclosed anywhere in the specifications.” Opp. 5 (citing Ex. 1015 ¶ 31). According to Petitioner, instead, “[t]he specifications disclose methods for making compounds having other 2′ substituents, like 2′-O substituents” and “report data on compounds having other 2′ substituents.” *Id.* (citing Ex. 1002, 22, 28–38, Figs. 1–6b; Ex. 2002, 19–20, 24–30, Figs. 1–6; Ex. 1001, 13:65–14:29, 19:1–28:15, Figs. 1–6b; Ex. 1015 ¶ 31) (emphasis omitted). Petitioner points to additional disclosures in the specifications it contends show that “the specifications, read as a whole, individually and collectively, convey that the inventors worked exclusively with compounds that did not have a 2′-F substituent, but instead had a 2′-O-TBDMS or 2′-O-TOM substituent.” *Id.* at 5–6 (citing Ex. 1002, 17–18,



20, 23–25; Ex. 2002, 17, 19, 21–22; Ex. 1001, 11:14–25, 12:64–67, 15:38–16:37; Ex. 1015 ¶ 32) (emphasis omitted).

Petitioner further argues that “[a]lthough the specifications allude to 2′-F substituents elsewhere, such references would not have conveyed to a POSA that the inventors were in possession of the claimed 2′-F compounds.” *Id.* at 6 (citing Ex. 1015 ¶ 33). According to Petitioner:

- “[T]he specifications describe the use of conventional 2′-F phosphoramidites in the prior art (*i.e.* where the phosphoramidite group is at the 3′ position). . . . But none of those compounds has the phosphoramidite, hydroxyl, or linker group at the 5′ position, as required by Substitute Claims 4 and 5.” *Id.* at 6–7 (citing Ex. 1002, 8:1–5; Ex. 2002, 10; Ex. 1001, 2:41–3:27, 4:58–62; Ex. 1015 ¶ 33).
- “[T]he specifications describe and depict 2′-F phosphoramidites in the ‘arabino’ (*i.e.*, ‘ara’) stereochemical configuration, in which the 2′-F substituent projects above the plane and the 3′ substituent projects below the plane” such that a person of ordinary skill in the art “would have understood that such compounds are directed to ‘ANAs’ (arabino nucleic acids), not ‘RNAs’ (ribo nucleic acids)” as recited in proposed substitute claims 4 and 5. *Id.* at 7 (emphasis omitted, citing Ex. 1002, 7:15–8:5, 10:16–20, 43:14–17, 44:16–19, 45:13–18; Ex. 2002, 9–10, 12, 33–34; Ex. 1001, 3:1–15, 31:6–11, 31:42–52, 32:16–21; Ex. 1015 ¶ 34).
- “[A]lthough the specifications depict the same two formulae (1) and (2) in Substitute Claims 4 and 5 and state that ‘W’ can be fluorine, the formulae in the specifications do not allow R<sub>4</sub> in formula (1) or R in formula (2) to be absent” and “require that, when ‘W’ is fluorine, R<sub>4</sub> and R are present as one of a specified group, such as ‘silyl ether such as TBDMS, triisopropylsilyl oxymethylene, Fmoc, alkyl, aryl, or acetyl.” *Id.* at 7–8 (citing Ex. 1002, 39–40, 47–48 (claims 1, 2); Ex. 2002, 31, claims 1, 2; Ex. 1001, 28:41–29:29; Ex. 1015 ¶ 35). Petitioner contends a person of ordinary skill in the art would have known that “fluorine cannot form two covalent bonds at the same time as required in formulae (1) and (2) in the specifications” and “if the inventors were in possession of such compounds, they would have realized that no R<sub>4</sub>

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<sup>2</sup> According to Petitioner, “[t]he salient disclosures (and lack thereof) are essentially the same in the ’707 Patent specification, the ’625 Application, and the ’065 Provisional. Accordingly, for brevity, Petitioner refers to these disclosures collectively as the ‘specifications.’” Opp. 4 n.2.

or R group could be present when ‘W’ is fluorine.” *Id.* at 8 (citing Ex. 1015 ¶ 36).

Petitioner concludes that “[b]y failing to describe the absence of R<sub>4</sub> or R when ‘W’ is fluorine, and in light of the specifications’ emphasis on 2’-O substituents, the specifications would not have reasonably conveyed to a POSA that the inventors were in possession of the claimed 2’-F compounds where R<sub>4</sub> is absent.” *Id.* at 8–9 (citing Ex. 1015 ¶ 37).

*B. Summary of Petitioner’s Argument that the File History Confirms the Failure to Describe the Claimed 2’-F Compounds*

Petitioner contends the file history for the ’707 patent shows that the ’625 application does not provide written description support for the 2’-F compounds because the applicants expressly admitted that they did not begin working on a 2’-F compound “until well after filing the ’625 Application.” Opp. 9.

According to Petitioner, “[t]he Examiner rejected the original claims with respect to 2’-F compounds, noting that they were ‘directed in part to subject matter not adequately described in the instant disclosure[.]’” and noting that “the specification indicated that ‘additional synthetic work directed to . . . 2’-fluoro analogues had not yet been started as of the date of filing, and that the synthetic details have not been either disclosed in detail or claimed in detail.’” *Id.* at 9–10 (citing Ex. 1002, 166–67; Ex. 1015 ¶ 39).

Petitioner also argues that “the Examiner faulted the original claims for encompassing the situation where W was fluorine and R<sub>4</sub> is present,” to which the applicants responded by amending the claims to add the claim limitation reciting that if W is fluorine, R<sub>4</sub> is absent. *Id.* at 10 (citing Ex. 1002, 168, 192, 194; Ex. 1015 ¶¶ 39–40). Petitioner contends the applicants explained that “[t]hey found that when W=fluoro radical, R<sub>4</sub> is absent’ and that the ‘inventors have developed synthesis of 2’-fluoro-n-protected-ribonucleosides-5’-phosphoramidites [*sic*], and the records will be provided by way of supplemental declaration(s).” *Id.* (citing Ex. 1002, 201; Ex. 1015 ¶ 40).

Petitioner explains that the applicants filed a declaration for support from Suresh C. Srivastava, one of the inventors named on the ’707 patent, which “detailed the synthesis and characterization of the 2’-F ‘compound 9[.]’” and “admitted that ChemGenes did not even begin working on that 2’-F analogue until June 23, 2010—more than nine months after the ’625 Application was filed on September 8, 2009.” *Id.* (citing Ex. 1002, 254–64; Ex. 1015 ¶¶ 41–42) (emphasis omitted).

*C. Analysis*

On this record, we agree with Petitioner that proposed substitute claims 4 and 5 likely lack adequate written description support for the recited 2'-F compounds.

The test for sufficiency of the written description support is “whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date sought.” *Ariad Pharm., Inc. v. Eli Lilly and Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). This “possession” test “requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art.” *Id.* Possession shown by evidence “outside of the specification is not enough,” and “a description that merely renders the invention obvious does not satisfy the requirement.” *Id.* at 1352. Instead, it is the specification itself that must demonstrate possession. *Id.*

On the current record, we find Petitioner’s argument persuasive that the specifications likely do not disclose the claimed 2'-F compounds, which require R<sub>4</sub> in formulae (1) and (2) to be “not present.” Opp. 5–8. This is especially so in view of the prosecution history showing that the applicants apparently did not gain possession of the claimed 2'-F compounds until after the filing date of the '625 application. *See* Ex. 1002, 201, 254.

Thus, it is our preliminary and non-binding view that Petitioner has shown a reasonable likelihood that the specifications do not provide adequate written description support for the 2'-F compounds in proposed substitute claims 4 and 5.

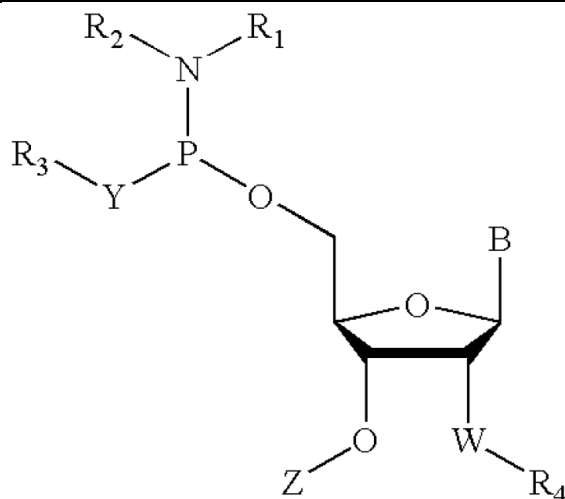
We emphasize that our position on written description is preliminary, and invite the parties to address this issue in further briefing and/or in a revised motion to amend.

2. Prior Art (Anticipation and Obviousness)

Yes. On this record, it appears that Petitioner has shown a reasonable likelihood that proposed substitute claim 4 is unpatentable as anticipated, and proposed substitute claims 4 and 5 are unpatentable as obvious, as discussed below.

*Proposed Substitute Claim 4*

In proposed substitute claim 4, Patent Owner proposes “delet[ing] the species in Claim 1 that Petitioner alleged [were] anticipated in Ground I.” Mot. 10. Formula (1) recited in proposed substitute claim 4 is reproduced below.



Mot. A-1.

We discuss below our preliminary views regarding proposed substitute claim 4 in the context of the prior art Petitioner raises in its Opposition.

## I. Anticipation

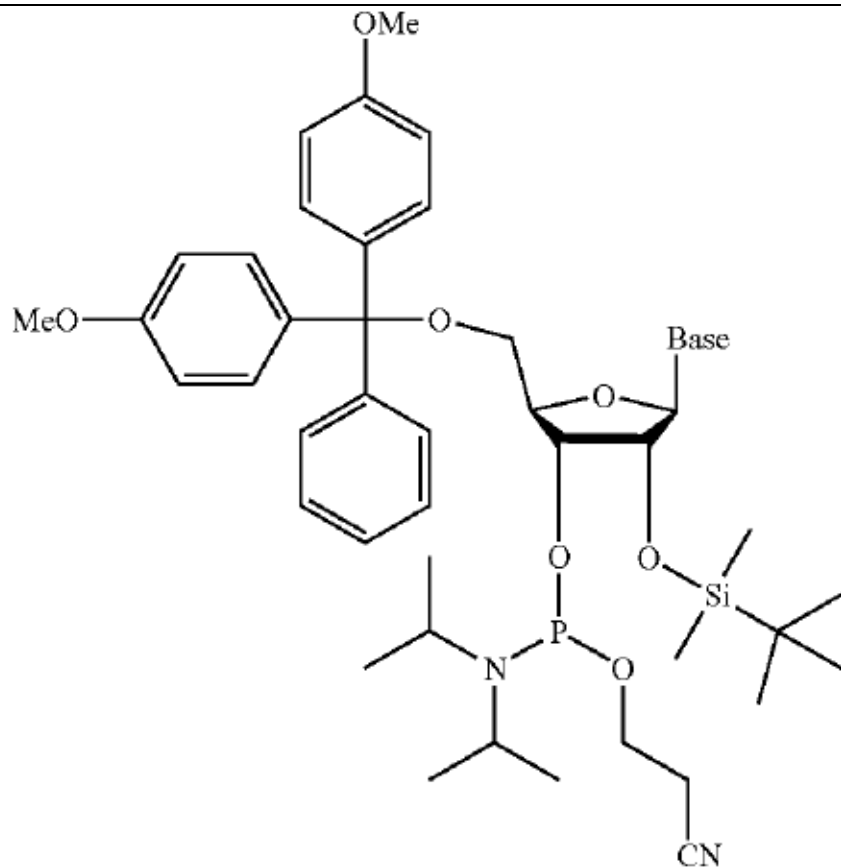
### A. U.S. Patent No. 7,897,758 (“the ’758 patent”)<sup>3</sup>

At this stage in the proceeding, and based on the current record, it appears that Petitioner has shown a reasonable likelihood of establishing that proposed substitute claim 4 is unpatentable under 35 U.S.C. § 102 as anticipated by the ’758 patent.

Petitioner relies on structures (11), (23), and (26) from the ’758 patent for support. Structure (11) from the ’758 patent is reproduced below.

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<sup>3</sup> U.S. Patent 7,897,758 B2, issued March 1, 2011 (Ex. 1019).



(11)

Ex. 1019, 9:1–22.

Petitioner asserts that “structure (23) is an example of the general structure (11) where the ‘Base’ is adenine protected at the N<sup>6</sup> position with a tertbutylphenoxyacetyl group (i.e., 9-(N<sup>6</sup>-tert butyl phenoxyacetyladeninyl)-.” Opp. 15 (citing Ex. 1015 ¶ 61).

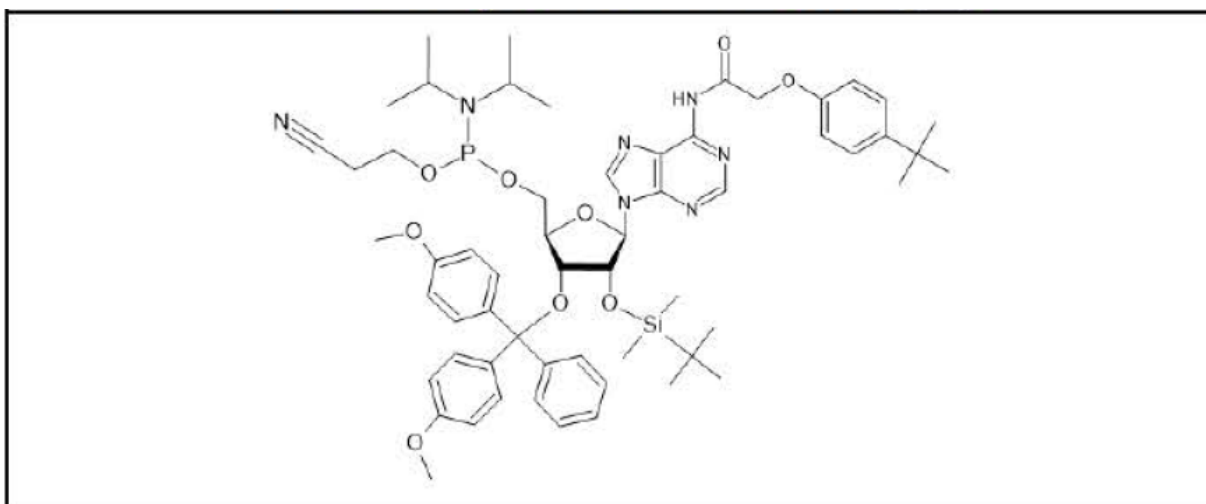
Petitioner also contends that “structure (26) is an example of the general structure (11) where the ‘Base’ is cytosine protected at the N<sup>4</sup> position with a tertbutylphenoxyacetyl group (i.e., 1-(N<sup>4</sup>-tertbutylphenoxyacetylcytosinyl)).” *Id.* at 16 (citing Ex. 1019, 21:1–22; Ex. 1015 ¶¶ 65–66).

According to Petitioner, a person of ordinary skill in the art “would have understood that structure (11) above has a 3′-phosphoramidite group and a 5′-DMT group for synthesis in the 3′→5′ direction (i.e., a 3′-phosphoramidite).” *Id.* at 13 (citing Ex. 1015 ¶ 57). Petitioner contends the ’758 patent discloses that the 3′-phosphoramidite group and the 5′-DMT group can be reversed, for example, to form a 5′-phosphoramidite-3′-DMT compound (i.e., a 5′-phosphoramidite) for reverse synthesis. *Id.* (citing

Ex. 1019, 11:21–38; Ex. 1015 ¶¶ 58–59) (emphasis omitted); *see also id.* at 13–14 (citing Ex. 1019, 11:21–38, 11:64–12:7; Ex. 1015 ¶¶ 58–59).

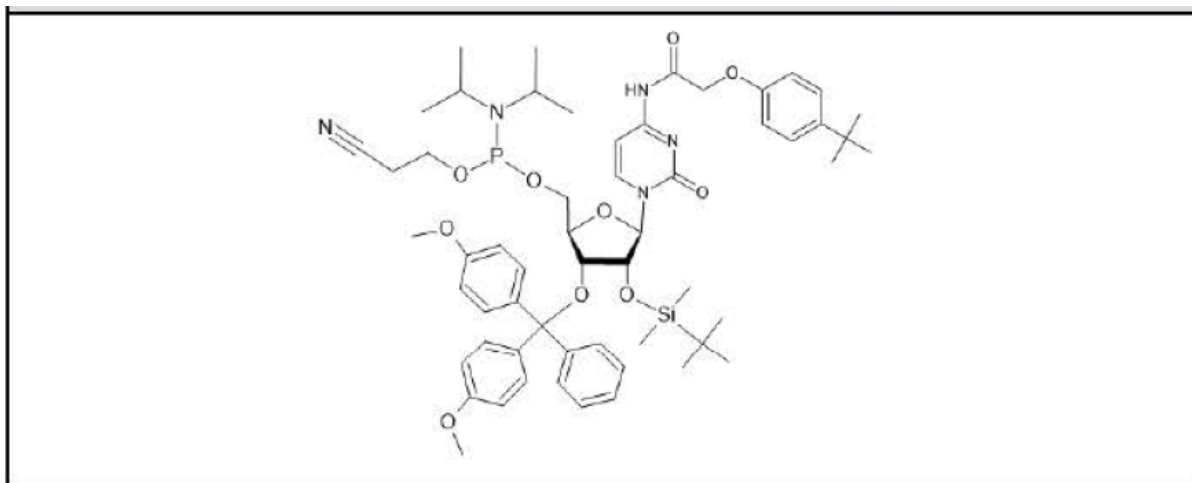
Petitioner argues that “[g]iven the emphasis on reverse synthesis in the ’758 Patent itself, a POSA would have immediately envisaged that structure (11) included not only the 5’-DMT-3’-phosphoramidite configuration (depicted above), but also the reverse 5’-phosphoramidite-3’-DMT configuration.” *Id.* at 14 (citing Ex. 1015 ¶ 60). Thus, Petitioner continues, “a POSA would have immediately envisaged the 5’-phosphoramidite” of structures (23) and (26). *Id.* at 15–17 (citing Ex. 1015 ¶¶ 61–62, 67).

Petitioner contends that reverse structure (23) has the following structure:



*Id.* at 15 (citing Ex. 1015 ¶¶ 61–62). According to Petitioner, reverse structure (23) has “the same structure of Substitute Claim 4 where Y is an oxygen atom, R<sub>1</sub> and R<sub>2</sub> are each an alkyl radical (specifically, isopropyl), R<sub>3</sub> is a cyanoethyl radical, Z is dimethoxytriphenylmethyl (DMT), W is an oxygen diradical, R<sub>4</sub> is tert butyl dimethyl silyl (TBDMS), and B is 9-(N<sup>6</sup>-tert butyl phenoxyacetyl)adeninyl-.” *Id.* (citing Ex. 1015 ¶¶ 63–64).

Petitioner also asserts that reverse structure (26) has the following structure:



*Id.* at 17 (citing Ex. 1015 ¶¶ 67). Petitioner argues that reverse structure (26) has “the same structure of Substitute Claim 4 where Y is an oxygen atom, R<sub>1</sub> and R<sub>2</sub> are each an alkyl radical (specifically, isopropyl), R<sub>3</sub> is a cyanoethyl radical, Z is dimethoxytriphenylmethyl (DMT), W is an oxygen diradical, R<sub>4</sub> is tert butyl dimethyl silyl (TBDMS), and B is 1-(N<sup>4</sup>-tertbutylphenoxyacetylcytosinyl)-.” *Id.* (citing Ex. 1015 ¶¶ 68–69).

Petitioner contends the ’758 patent would have enabled a person of ordinary skill in the art to make the 5’-phosphoramidites of structures (23) and (26) without undue experimentation because “[t]he ’758 Patent discloses a general scheme for making its phosphoramidites” and incorporates Robles<sup>4</sup> by reference, which “discloses the preparation of 5’-phosphoramidites 12(a,b,c).” Opp. 18–19 (citing Ex. 1015 ¶¶ 70–76, 119; Ex. 1019, 11:34–38, 23:21–25; Ex. 1021, 41:55 (Fig. 3), 41:59–60). According to Petitioner, “[a]lthough the 5’-phosphoramidites 12(a,b,c) of Robles are DNA phosphoramidites, a POSA would have understood that the process could be applied to the RNA 5’-phosphoramidites depicted in the ’758 Patent with routine adjustments, if needed.” *Id.* (citing Ex. 1015 ¶¶ 73–74).

Based on the current record, we find Petitioner’s arguments persuasive. Petitioner does not argue that the ’758 patent discloses 5’-phosphoramidite compounds with all the substituents arranged or combined in the same way as recited in proposed substitute claim 4. A reference, however, can anticipate a claim “even if it does not expressly spell out all the limitations arranged or combined as in the claim, if a person of skill in the art, reading the reference, would at once envisage the claimed arrangement or combination.” *Microsoft*

*Corp. v. Biscotti, Inc.*, 878 F.3d 1052, 1068 (Fed. Cir. 2017) (quotation marks and brackets omitted).

As Petitioner correctly points out, the '758 patent expressly discloses that the 3'-phosphoramidite group and the 5'-DMT group can be reversed to form a 5'-phosphoramidite. Opp. 13–14 (citing Ex. 1019, 11:21–38, 11:64–12:7). Thus, Petitioner has argued persuasively that “a POSA would have immediately envisaged the 5'-phosphoramidite” of structures (23) and (26). *Id.* at 15–17. Petitioner also has shown sufficiently that reverse structures (23) and (26) are two species within the scope of the genus of proposed substitute claim 4. *Id.* Thus, it is our preliminary, non-binding opinion that Petitioner has established a reasonable likelihood that the '758 patent anticipates proposed substitute claim 4.

*B. U.S. Patent App. Pub. No. 2006/0247431 A1 (“the '431 publication”)*<sup>5</sup>

According to Petitioner, “[t]he '431 Publication is the publication of U.S. Patent App. No. 11,380,227, which issued as the '758 Patent described above.” Opp. 19 (citing Ex. 1019, cover; Ex. 1020, cover). Petitioner contends the '431 publication anticipates proposed substitute claim 4 for the same reasons discussed above for the '758 patent because “[t]he '431 Publication contains the same disclosures as the '758 Patent.” *Id.* at 19–20 (citing Ex. 1015 ¶¶ 81–82, 121).

Based on the current record, Petitioner’s arguments are persuasive for the same reasons discussed above for the '758 patent. Thus, it is our preliminary, non-binding opinion that Petitioner has established a reasonable likelihood that the '431 publication discloses the limitations of proposed substitute claim 4.

## **II. Obviousness**

*A. The '758 Patent or the '431 Publication Alone*

At this stage in the proceeding, and based on the current record, it appears that Petitioner has shown a reasonable likelihood of establishing that proposed

<sup>4</sup> Robles et al., *Solid-phase synthesis of a nucleopeptide from the linking site of adenovirus-2 nucleoprotein, -Ser(p<sup>5'</sup> CATCAT)-Gly-Asp-. Convergent versus stepwise strategy*, 23(20) NUCLEIC ACIDS RES. 4151–61 (1995) (Ex. 1021).

<sup>5</sup> U.S. Patent App. Pub. 2006/0247431 A1, published November 2, 2006 (Ex. 1020).



substitute claim 4 is unpatentable under 35 U.S.C. § 103 as obvious over the '758 patent (or the '431 publication, which has the same disclosures as the '758 patent) alone.

Petitioner contends that the '758 patent discloses the 3'-phosphoramidite structures (23) and (26), and based on the teachings in the '758 patent, an ordinarily skilled artisan would have been motivated to make the corresponding 5'-phosphoramidite-3'-DMT compounds of structures (23) and (26).

Opp. 20–21 (citing Ex. 1019, 11:21–38, 11:64–12:7; Ex. 1015 ¶ 87). According to Petitioner, “the '758 Patent explicitly includes 5'-phosphoramidites in its description of the nucleoside phosphoramidites ‘as used herein’ the '758 patent” and “recognizes that such 5'-phosphoramidites can be used in the synthesis of oligonucleotides in the 5' to 3' direction.” *Id.*

Petitioner further contends a person of ordinary skill in the art “would have been motivated to make such compounds for 5' to 3' oligonucleotide synthesis because reverse synthesis and its advantages were known” and a person of ordinary skill in the art “would have understood that 5'-phosphoramidites had various potential uses, including in RNA research such as branched oligonucleotide synthesis.” *Id.* at 21 (citing Ex. 1011, 2027; Ex. 1022, 11319; Ex. 1023, 856–57; Ex. 1024, 5688; Ex. 1025, 421; Ex. 1015 ¶¶ 19–21, 88–89).

Petitioner argues a person of ordinary skill in the art would have had a reasonable expectation of success for the same reasons that the '758 patent is enabling, as discussed in the anticipation ground. *Id.*

Based on the current record, we find Petitioner's contentions persuasive. Petitioner sufficiently describes the scope and content of the '758 patent and the '431 publication, and points out the differences between the proposed substitute claims and the prior art. *See* Opp. 13–17, 19–20. Petitioner also persuasively argues that an ordinarily skilled artisan would have had a reason to make the 5'-phosphoramidite compounds of structures (23) and (26), arriving at the subject matter of proposed substitute claim 4, and would have had a reasonable expectation of success in doing so. *Id.* at 18–19.

Thus, it is our preliminary, non-binding opinion that Petitioner has established a reasonable likelihood that the '758 patent or the '431 publication alone would have rendered proposed substitute claim 4 obvious.

*B. The '758 Patent or the '431 Publication in View of  
the 1999 ChemGenes Catalog,<sup>6</sup> the '719 Patent,<sup>7</sup> and Sinha<sup>8</sup>*

Petitioner argues that “[i]n addition to the reverse structures (23) and (26) of the '758 Patent described above, the remaining 1' base groups and 2' substituents” of proposed substitute claim 4 would have been obvious over either the '758 patent or the '431 publication in view of the knowledge of a person of ordinary skill in the art, as illustrated by the '758 patent, the 1999 ChemGenes Catalog, the '719 patent, and Sinha. Opp. 22. At this stage in the proceeding, and based on the current record, it appears that Petitioner has shown a reasonable likelihood of prevailing in this assertion.

Petitioner contends that the remaining eleven options for “B” represent “conventional, known bases and protecting groups.” *Id.* (citing Ex. 1015 ¶¶ 91, 128). Petitioner contends a person of ordinary skill in the art would have been motivated to use any of the additional options for “B” with a reasonable expectation of success based on the '758 patent, and “to have a complementary library of phosphoramidite reagents for 5' → 3' synthesis.” *Id.* at 22–23 (citing Ex. 1015 ¶¶ 92–93). Specifically, Petitioner contends a person of ordinary skill in the art would have been motivated to include the following bases:

- 1-uracilyl- and 1-(5-methyl-uracilyl)- based on the '758 patent because “[u]racil and thymine (5-methyl uracil) were well-known nucleobases” and the '758 patent “discloses that its nucleobases may be ‘the pyrimidine bases thymine, cytosine and uracil’” (*id.* at 23 (citing Ex. 1015 ¶¶ 94, 128; Ex. 1019, 9:65–10:14));
- -9-(N<sup>6</sup>-benzoyladeniny)-, 1-(N<sup>4</sup>-benzoylcytosiny)-, and 9-(N<sup>2</sup>-isobutyrylguaniny)- based on the '758 patent and the '719 patent because “N-benzoyl protection of adenine and cytosine, and N-isobutyryl protection of guanine, were well-known” and the '758 patent “discloses that its nucleobases may be ‘N6-benzoyladenine, N4-benzoylcytidine, [and] N2-isobutyrylguanine[.]’” (*id.* (citing Ex. 1015 ¶¶ 95, 128; Ex. 1019, 10:10–12; Ex. 1027, 4:29–37));
- 9-(N<sup>6</sup>-phenoxyacetyladeniny)- and 1-(N<sup>4</sup>-phenoxyacetylcytosiny)- based on the 1999 ChemGenes Catalog and the '719 patent because “N-phenoxyacetyl (N-PAC) protection of adenine and cytosine was well-known” and “[t]he 1999 ChemGenes Catalog discloses N-PAC protection of adenine and cytosine” (*id.* (citing Ex. 1015 ¶¶ 96, 128; Ex. 2005, 53; Ex. 1027, 4:29–37));
- 9-(N<sup>2</sup>-tertbutylphenoxyacetylguaniny)- based on Sinha because “[t]ertbutylphenoxyacetyl (t-BPA) protection of guanine was well-known”

and “Sinha discloses t-BPA protection of guanine” (*id.* at 24 (citing Ex. 1015 ¶¶ 97, 128; Ex. 1028, 3120));

- 9-(N<sup>6</sup>-acetyladeninyl)- and 1-(N<sup>4</sup>-acetylcytosinyl)- based on the 1999 ChemGenes Catalog and the ’719 patent because “[a]cetyl protection of adenine and cytosine was well-known”, “[t]he 1999 ChemGenes Catalog discloses acetyl protection of cytosine”, and “the ’719 Patent discloses acetyl protection of adenine” (*id.* (citing Ex. 1015 ¶¶ 98, 128; Ex. 2005, 52; Ex. 1027, 4:29–37)); and
- -(5-fluoro-uracilyl)- based on the 1999 ChemGenes Catalog because “5-fluoro uracil was a well-known modified nucleobase” and “[t]he 1999 ChemGenes Catalog discloses 5-fluoro uridine” (*id.* (citing Ex. 1015 ¶¶ 99, 128; Ex. 2005, 60)).

Regarding the additional options for W and R<sub>4</sub> recited in proposed substitute claim 4, which recite that W is fluorine and R<sub>4</sub> is absent, and W is oxygen and R<sub>4</sub> is TOM, Petitioner contends a person of ordinary skill in the art “would have been motivated to make each of these options with a reasonable expectation of success based on the ’758 Patent” because the ’758 patent discloses that “its oligonucleotides consist ‘either entirely or to a large part . . . of ribonucleotides or 2’-modified ribonucleotides like . . . 2’-fluororibonucleotides””; “its phosphoramidites include ‘2’-fluoronucleosides””; and “its 2’-O-protective groups include the ‘(triisopropylsilyl)oxymethyl (“TOM”) group””. Opp. 24–25 (citing Ex. 1015 ¶ 100; Ex. 1019, 7:56–61, 9:52–65, 10:49–56).

Based on the current record, we find Petitioner’s contentions persuasive. Petitioner sufficiently shows that an ordinarily skilled artisan would have known the remaining 1’ base groups and 2’ substituents of proposed substitute claim 4 are conventional. *See* Opp. 22–25. Petitioner also persuasively argues that an ordinarily skilled artisan would have had a reason to use any of these known options, arriving at the subject matter of proposed substitute claim 4, and would have had a reasonable expectation of success in doing so. *Id.* at 22–23.

Thus, it is our preliminary, non-binding opinion that Petitioner has established a reasonable likelihood that the ’758 patent or the ’431 publication in view of

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<sup>6</sup> ChemGenes Corporation, *Bio technology products & manufacturer of DNA-RNA intermediates* (1999) (Ex. 2005).

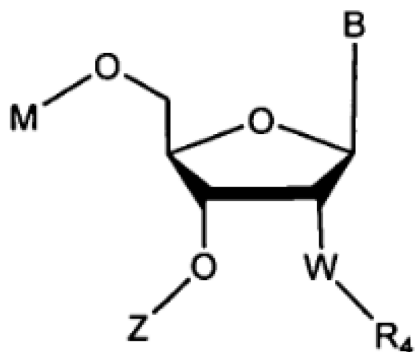
<sup>7</sup> U.S. Patent 5,525,719, issued June 11, 1996 (Ex. 1027).

<sup>8</sup> Sinha et al., *Synthesis of oligodeoxynucleoside methylphosphonates utilizing the tert-butylphenoxyacetyl group for exocyclic amine protection*, 22(15) NUCLEIC ACIDS RES. 3119–23 (Ex. 1028).

the 1999 ChemGenes Catalog, the '719 Patent, and Sinha would have rendered proposed substitute claim 4 obvious.

*Proposed Substitute Claim 5*

In proposed substitute claim 5, Patent Owner proposes “delet[ing] the species in Claim 2 that Petitioner alleged [were] anticipated in Ground II.” Mot. 10. Formula (2) recited in proposed substitute claim 5 is reproduced below.



Mot. A-3. Petitioner argues that formula (2) of proposed substitute claim 5 is directed to the same compounds as formula (1) of proposed substitute claim 4, “except that M is a hydrogen or a linker at the 5’-position instead of a 5’-phosphoramidite.” Opp. 12 (citing Ex. 1015 ¶¶ 13, 16); *see also* Mot. A-3 (“M is a hydrogen radical or a linker.”).

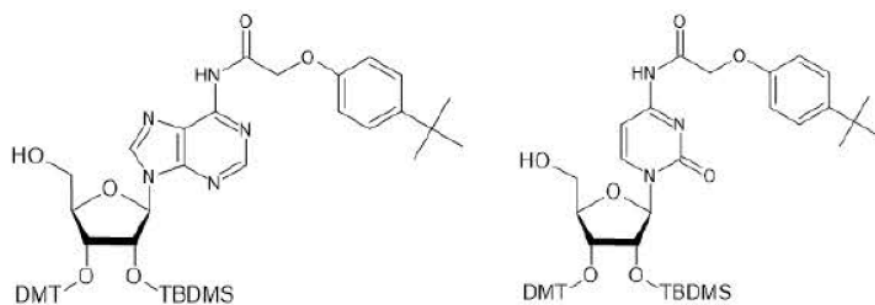
We discuss below our preliminary views regarding the proposed amendments in the context of the prior art Petitioner raises in its Opposition.

**I. Anticipation**

*A. The '758 patent*

At this stage in the proceeding, and based on the current record, it appears that Petitioner has not shown a reasonable likelihood of establishing that proposed substitute claim 5 is unpatentable under 35 U.S.C. § 102 as anticipated by the '758 patent.

Petitioner argues that when the 5’-position M is hydrogen, the 3’-position is DMT, the 2’-position is O-TBDMS, and “B” is 9-(N6-tert butyl phenoxyacetyladeninyl)- or 1-(N4-tertbutylphenoxyacetylcytosinyl)-, the two species of proposed substitute claim 5 are:



Opp. 17 (citing Ex. 1015 ¶ 113).

Petitioner again relies on the reverse structures (23) and (26). Opp. 18.

Petitioner acknowledges that in those structures, “the 5′-position is a phosphoramidite instead of hydrogen.” *Id.* (citing Ex. 1015 ¶ 114). According to Petitioner, however, an ordinarily skilled artisan would have understood that “the last step of forming a phosphoramidite is converting the 5′-hydroxyl (OH) group of a nucleoside to a phosphoramidite, as reflected in Scheme 2 in the ’758 Patent,” and thus, “would have immediately envisaged the two compounds of Substitute Claim 5 above where M is hydrogen as an intermediate to obtaining the phosphoramidites of Substitute Claim 4 described above.” *Id.* (citing Ex. 1019, 2:50–3:13; Ex. 1015 ¶ 114).

Petitioner further contends that in the reverse structures (23) and (26), “the 5′-phosphoramidite could, instead, be a 5′-linker group such as a succinate for attaching the first nucleotide to the solid support.” *Id.* (citing Ex. 1015 ¶¶ 116–18). Thus, Petitioner concludes that an ordinarily skilled artisan “would have immediately envisaged the two compounds of Substitute Claim 5 above where M is a conventional succinate linker.” *Id.* (citing Ex. 1015 ¶ 118).

Based on the current record, Petitioner’s arguments are not persuasive.

“[U]nless a prior art reference discloses 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, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate under 35 U.S.C. § 102.” *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1371 (Fed. Cir. 2008). Petitioner does not argue that the ’758 patent discloses 5′-hydrogen or 5′-linker compounds with all the substituents arranged or combined in the same way as recited in proposed substitute claim 5.

In addition, the allegedly anticipated species deviate from the structures (23) and (26) of the ’758 patent by several steps: first, reverse the 3′-phosphoramidite group and the 5′-DMT group to form a 5′-phosphoramidite; then, seek the

intermediate or swap a linker group for the phosphoramidite. Thus, on the current record, we are not persuaded by Petitioner's assertions that an ordinarily skilled artisan would have immediately envisaged the 5'-hydrogen or 5'-linker compounds of proposed substitute claim 5.

Thus, it is our preliminary, non-binding opinion that Petitioner has not established a reasonable likelihood that the '758 patent discloses the limitations of proposed substitute claim 5.

### *B. The '431 publication*

Because the '431 Publication contains the same disclosures as the '758 Patent, Petitioner contends the '431 publication anticipates proposed substitute claim 5 for the same reasons discussed above for the '758 patent. Opp. 19–20 (citing Ex. 1015 ¶¶ 81–82, 121).

For the same reasons discussed above for the '758 patent, it is our preliminary, non-binding opinion that Petitioner has not established a reasonable likelihood that the '431 publication discloses the limitations of proposed substitute claim 5.

## **II. Obviousness**

### *A. The '758 Patent or the '431 Publication Alone*

At this stage in the proceeding, and based on the current record, it appears that Petitioner has shown a reasonable likelihood of establishing that proposed substitute claim 5 is unpatentable under 35 U.S.C. § 103 as obvious over the '758 patent or the '431 publication alone.

In addition to the same arguments advanced in challenging proposed substitute claim 4, Petitioner further contends that an ordinarily skilled artisan would have been motivated to make the corresponding 5'-H-3'-DMT compounds and 5'-linker-3'-DMT compounds of structures (23) and (26) based on the teachings in the '758 patent. Opp. 20–21 (citing Ex. 1019, 2:50–3:13, 11:21–38, 11:64–12:7, 19:7–23, 20:1–23; Ex. 1015 ¶¶ 85, 87, 125–26).

According to Petitioner, an ordinarily skilled artisan “would have understood that the last step of forming a phosphoramidite is converting the hydroxyl (OH) group of a nucleoside to a phosphoramidite”; and “would have understood that a succinate group is commonly used to attach the first nucleotide to the solid support.” *Id.* (citing Ex. 1019, 2:50–3:13, 11:21–38, 11:64–12:7; Ex. 1015 ¶¶ 87, 125–26).

Based on the current record, we find Petitioner's contentions persuasive. Petitioner sufficiently describes the scope and content of the '758 patent and the '431 publication, and points out the differences between the proposed substitute claims and the prior art. *See* Opp. 17–18. Petitioner also persuasively argues that an ordinarily skilled artisan would have had a reason to make the 5'-hydrogen and 5'-linker compounds of reverse structures (23) and (26), arriving at the subject matter of proposed substitute claim 5, and would have had a reasonable expectation of success in doing so. *Id.* at 20–21.

Thus, it is our preliminary, non-binding opinion that Petitioner has established a reasonable likelihood that the '758 patent or the '431 publication alone would have rendered proposed substitute claim 5 obvious.

*B. The '758 Patent or the '431 Publication in View of  
the 1999 ChemGenes Catalog, the '719 Patent, and Sinha*

Petitioner advances the same arguments here as those in challenging proposed substitute claim 4 on the same ground. For the same reasons explained above, it is our preliminary, non-binding opinion that Petitioner has established a reasonable likelihood that the '758 patent or the '431 publication in view of the 1999 ChemGenes Catalog, the '719 Patent, and Sinha would have rendered proposed substitute claim 5 obvious.

### III. CONCLUSION

This concludes the Preliminary Guidance, which is Patent Owner's first option under the Board's Pilot Program. Notice, 84 Fed. Reg. at 9,497. Patent Owner has the additional option under the Board's Pilot Program to file a revised motion to amend by June 3, 2024 (Due Date 3). Paper 8, 2. These two options are in addition to Patent Owner's original option to file a reply brief in response to Petitioner's opposition to the motion to amend.

In addition to those two options under the Board's Pilot Program and the option to file a reply brief, Patent Owner is reminded that amendments of the challenged claims may also be pursued in a separate reissue or reexamination

proceeding before, during, or after an AIA trial proceeding, including subsequent to the issuance of the Final Written Decision. We draw Patent Owner's attention to the April 2019 *Notice Regarding Options for Amendments by Patent Owner Through Reissue or Reexamination During a Pending AIA Trial Proceeding*. See 84 Fed. Reg. 16,654 (Apr. 22, 2019). If Patent Owner chooses to file a reissue application or a request for reexamination of the challenged patent, we remind Patent Owner of its continuing obligation to notify the Board of any such related matters in updated mandatory notices. See 37 C.F.R. § 42.8(a)(3), (b)(2).



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