

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ATEA PHARMACEUTICALS, INC.,
Petitioner,

v.

GILEAD SCIENCES, INC.,
Patent Owner.

PGR2023-00046
Patent 11,642,361 B2

Before SUSAN L. C. MITCHELL, CYNTHIA M. HARDMAN, and
MICHAEL A. VALEK, *Administrative Patent Judges*.

MITCHELL, *Administrative Patent Judge*.

DECISION
Denying Institution of Post-Grant Review
35 U.S.C. § 324(a)

I. INTRODUCTION

On August 7, 2023, Atea Pharmaceuticals, Inc. (“Petitioner”) filed a Petition for Post-Grant Review of claim 1 of U.S. Patent No. 11,642,361 B2 (Ex. 1001, “the ’361 patent”). Paper 2 (“Pet.”). On November 22, 2023, Gilead Sciences, Inc. (“Patent Owner”) filed a Preliminary Response. Paper 6 (“Prelim. Resp.”).

Institution of post-grant review is authorized by statute only when “the information presented in the petition . . . demonstrate[s] that it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable.” 35 U.S.C. § 324; *see* 37 C.F.R. § 42.4. Upon considering the Petition, Preliminary Response, and the cited evidence, we conclude that Petitioner has not satisfied its burden under 35 U.S.C. § 324 to show that it is more likely than not that claim 1 is unpatentable.

A. Real Parties in Interest

Petitioner identifies itself, Atea Pharmaceuticals, Inc., as the real party in interest. Pet. 8. Patent Owner identifies itself, Gilead Sciences, Inc., as the real party in interest. Paper 5, 1.

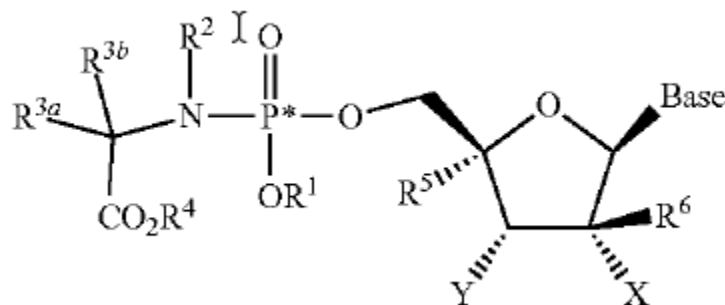
B. Related Matters

Petitioner lists no related matters. *See* Pet. 8. Patent Owner lists the Petition at issue here and the applications in the chain from which the ’361 patent issued as related matters. *See* Paper 5, 1.

C. The ’361 Patent (Ex. 1001)

The ’361 patent, titled “Nucleoside Phosphoramidate Prodrugs,” issued May 9, 2023, identifying Gilead Sciences, Inc. as the applicant and assignee. Ex. 1001, codes (71), (73). The named inventors of the ’361 patent are Jinfa Du, Dhanapalan Nagarathnam, Michael Joseph Sofia, and

Peiyuan Wang. *See id.* at code (72). The '361 patent describes a chemical structure, Formula I, set forth below, for compounds of phosphoramidate prodrugs of nucleoside derivatives (along with their salts, hydrates, solvates, and crystalline forms) for the treatment of viral infections in mammals, and how to prepare such prodrugs. *Id.* at Abst., 5:13–7:59, 12:33–15:3.



Ex. 1001, Abst., 5:20–7:59. The '361 patent provides three columns of possible choices for the substituents of Formula I set forth above, providing myriad possibilities for a particular compound. *Id.* at 5:31–7:59.

The '361 patent concludes that “[a]s can be appreciated from the structure represented by formula I above, there are myriad ways to express the several embodiments and aspects of each embodiment of the present invention.” *Id.* at 15:4–7. The '361 patent describes three embodiments, which in turn are described as “directed to the compound of formula I, each having several aspects, based on the identity of the modified purine or pyrimidine base.” *Id.* at 15:7–10. The '361 patent notes, however, that:

This is not intended to be an explicit or implicit admission that the three embodiments are independent or distinct nor should it be interpreted as such. Rather, it is intended to convey, information so that the full breadth of the present invention can be understood. Furthermore, the following embodiments and aspects thereof, are not meant to be limiting on the full breadth of the invention as recited by the structure of formula I.

Ex. 1001, 15:10–18.

The '361 patent further describes these compounds as “inhibitors of RNA-dependent RNA viral replication and . . . useful as inhibitors of HCV [hepatitis C virus] NS5B polymerase, as inhibitors of HCV replication and for treatment of hepatitis C infection in mammals.” *Id.* at 1:39–44. The '361 patent identifies HCV infection as a serious health risk for those individuals who do not clear the virus. *Id.* at 1:60–64. The '361 patent states:

Once infected, about 20% of people clear the virus, but the rest can harbor HCV the rest of their lives. Ten to twenty percent of chronically infected individuals eventually develop liver-destroying cirrhosis or cancer. The viral disease is transmitted parenterally by contaminated blood and blood products, contaminated needles, or sexually and vertically from infected mothers or carrier mothers to their offspring.

Id. at 1:60–67.

The '361 patent asserts that current immunotherapies are of limited clinical benefit, and with no vaccine for HCV, “there is an urgent need for improved therapeutic agents that effectively combat chronic HCV infection.” Ex. 1001, 1:67–2:6.

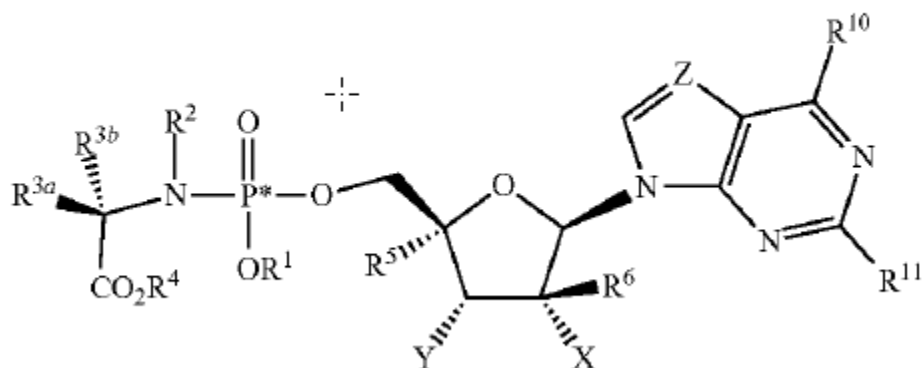
D. Challenged Claim

Petitioner challenges only claim 1 of the three claims of the '361 patent. Pet. 1, 11.

Claim 1 is reproduced below:

1. A compound of formula I-6:

I-6



wherein:

- (a) R¹ is H, -CH₃, phenyl, p-bromo-phenyl, p-chlorophenyl or p-fluoro-phenyl;
- (b) R² is H;
- (c) R^{3a} is H and R^{3b} is H, -CH₃, -CH(CH₃)₂, -CH₂CH(CH₃)₂, -CH(CH₃)CH₂CH₃, -CH₂Ph or lower cycloalkyl;
- (d) R⁴ is CH₃, ethyl, n-propyl, or i-propyl;
- (e) R⁵ is H;
- (f) R⁶ is H, -CH₃, -CH₂F, -CHF₂, -CF₃, or -F;
- (g) X is H, -OH, -OCH₃, -F, -NH₂, or -N₃; with the proviso that X cannot be OH when R⁶ is -CH₃ or -CH₂F;
- (h) Y is -OH, -NH₂, -OCH₃ or -OC(O)CH₃,
- (i) R¹⁰ is -NHR' and R¹¹ is -NH₂;
- (j) Z is N or -CR¹²;
 wherein R¹² is H, halogen, -OR', -NH₂, -NHR', -NR'₂, -NO₂, C₁₋₆ alkyl, -CO₂R', -CONH₂, -CONHR', -CONR'₂, -CH=CHCO₂H or -CH=CHCO₂R';
- (k) R' is C₁₋₆ alkyl; and
- (l) P* is a chiral phosphorus atom;
 or a pharmaceutically acceptable salt thereof.

Ex. 1001, 619:1-37.

E. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claim 1 of the '361 patent on the following grounds, *see* Pet. 11:

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1	§ 112(a)	Lack of Written Description
1	§ 112(a)	Lack of Enablement
1	§ 102(a)(1)	'706 U.S. Publication ¹

Petitioner submits the Declaration of Prof. Alexander M. Klibanov, Ph.D. (Ex. 1015) in support of institution of post-grant review. Pet. 1.

II. ANALYSIS

A. Eligibility for Post-Grant Review

The post-grant review provisions set forth in Section 6(d) of the AIA² apply only to patents subject to the first-inventor-to-file provisions of the AIA. *See* AIA § 6(f)(2)(A) (“The amendments made by subsection (d) . . . shall apply only to patents described in section 3(n)(1).”). Patents subject to the first-inventor-to-file provisions are those that issue from applications “that contain[] or contained at any time . . . a claim to a claimed invention that has an effective filing date as defined in section 100(i) of title 35, United States Code, that is on or after” March 16, 2013. *Id.* § 3(n)(1). Our rules require that each petitioner for post-grant review certify that the challenged patent has an effective filing date that renders the patent available for post-grant review. 37 C.F.R. § 42.204(a) (“The petitioner must certify that the

¹ U.S. Publication 2016/0257706, published Sept. 8, 2016. (Ex. 1020, “’706 U.S. Publication”).

² Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (“AIA”).

patent for which review is sought is available for post-grant review.”). In addition, “[a] petition for a post-grant review may only be filed not later than the date that is 9 months after the date of the grant of the patent or of the issuance of a reissue patent (as the case may be).” 35 U.S.C. § 321(c); *see also* 37 C.F.R. § 42.202(a) (accord).

Petitioner asserts that this Petition was timely filed because the ’361 patent issued May 9, 2023, and the Petition was filed on or before the date that is nine months after this date. Pet. 9. This Petition was filed on August 7, 2023, which is within nine months after the May 9, 2023, issue date of the ’361 patent. *Id.* at code (45). Therefore, we determine that the Petition was timely filed.

On this record, however, we determine that the ’361 patent is ineligible for post-grant review based on our analysis on the merits that is set forth below.

Petitioner contends:

The ’361 patent is available for PGR [post-grant review], because claim 1 has an effective filing date on or after March 16, 2013, as it is not entitled to any priority date earlier than November 15, 2022, the date PO [Patent Owner] amended its March 19, 2021 claim amendment to facilitate allowance (and not that date either), as discussed further below. Claim 1 as issued lacks written description support and is not enabled by the specification as required by § 112(a).

Pet. 10 (citing *Eli Lilly & Co. v. Genentech, Inc.*, PGR2019-00043, Paper 11, 11–12 (Oct. 7, 2019); *Daiichi Sankyo, Inc. v. Seagen, Inc.*, PGR2021-00030, Paper 17, 8–10 (Apr. 7, 2022)).

The earliest application in the line of continuation applications leading to the ’361 patent, which Petitioner agrees contains the same specification as the ’361 patent, was filed on March 21, 2008. Ex. 1001, code (60); Pet. 25

(stating Petitioner accepts U.S. Application No. 12/053,015 (filed March, 21, 2008) contains the same specification as the '361 patent). Patent Owner asserts that the priority date for the '361 patent is in 2007, relying on the provisional applications to which the '361 patent claims priority, the earliest of which was filed March 30, 2007. Prelim. Resp. 15. These dates fall before March 16, 2013.

We understand Petitioner's argument, however, to assert that the Specification of the '361 patent does not contain sufficient written description for claim 1. *See* Pet. 26–116. Therefore, according to Petitioner's argument, claim 1 of the '361 patent would not be entitled to an effective filing date based on any application in the chain of continuations from which the '361 patent issued, or even the filing date of the '361 patent itself. *See* Pet. 10; 35 U.S.C. § 100(i)(1)(A). At this stage of the proceeding, Patent Owner has not directly challenged the eligibility of the '361 patent for post-grant review.

Because we determine as set forth below that Petitioner has not provided sufficient evidence at the institution stage to support its assertions that claim 1 of the '361 patent lacks written description in the Specification and because Petitioner agrees that the written description in the Specification is the same for the chain of continuation applications that date back to the March 21, 2008 application, we find that it has not been shown that the '361 patent is ineligible for post-grant review. We address the merits of Petitioner's written description ground, as well as Petitioner's related enablement challenge, as support for our bases for this determination.

B. Person of Ordinary Skill in the Art

Factual indicators of the level of ordinary skill in the art include “the various prior art approaches employed, the types of problems encountered in the art, the rapidity with which innovations are made, the sophistication of the technology involved, and the educational background of those actively working in the field.” *Jacobson Bros., Inc. v. U.S.*, 512 F.2d 1065, 1071 (Ct. Cl. 1975); *see also Orthopedic Equip. Co. v. U.S.*, 702 F.2d 1005, 1011 (Fed. Cir. 1983) (quoting with approval *Jacobson Bros.*).

According to Petitioner, a person of ordinary skill in the relevant art (“POSA”) would have been a person with:

- (a) a Ph.D. in organic chemistry, medicinal chemistry, or a closely related discipline in the pharmaceutical area that includes drug discovery experience, or
- (b) an M.S. degree in organic chemistry, medicinal chemistry, or a closely related discipline in the pharmaceutical area with three or more years of drug discovery experience (some of which could be during his/her postgraduate work) (Ex. 1015 ¶ 22). Because the subject matter of the ’361 patent is directed to compounds for the treatment of viral diseases, a POSA would normally be able to interpret relevant biological testing and its results (*id.*).

Pet. 15.

Patent Owner responds that a POSA would consist “of a team of scientists with experience in various aspects of drug development.” Prelim. Resp. 21. Patent Owner provides its own definition of such a team that closely resembles Petitioner’s definition of a POSA, but adds 2 years of post-doctoral experience in drug discovery for a Ph.D., and four versus three years of experience in drug discovery for a POSA with a bachelor’s or a master’s degree in organic, synthetic, or medicinal chemistry. *Id.* at 20.

Patent Owner also expands the relevant fields for the skilled artisan to include virology, microbiology, or molecular biology. *Id.*

Patent Owner also asserts that Petitioner's definition of a skilled artisan with a Ph.D. does not include any relevant experience in drug discovery. Prelim. Resp. 22. Petitioner's definition set forth above, however, does include experience in drug discovery, albeit within the confines of achieving a Ph.D. *See* Pet. 15 ("a Ph.D. in organic chemistry, medicinal chemistry, or a closely related discipline in the pharmaceutical area that ***includes drug discovery experience***") (emphasis added). Patent Owner concludes that "the Board should deny the Petition under either party's proposed definition of a skilled artisan because the Petitioner has failed to meet its burden" Prelim. Resp. 22–22; *see also* Pet. 15 n.1 (stating Petitioner's declarant, Dr. Klivanov, considered Patent Owner's definition of a POSA from IPR2017-01712 and "determined that none of his conclusions contained in his Declaration would change when using it instead of his proposed POSA").

The major differences between Petitioner's and Patent Owner's definitions of a skilled artisan include the number of years of drug discovery experience that is necessary and the breadth of the fields of endeavor with which a POSA should be familiar. We agree with Patent Owner that a POSA includes a team of skilled artisans with skill sets in the various aspects of drug development, but determine that Petitioner has addressed those necessary skill sets in its definition. We also determine on this record that Petitioner has assessed adequately the level of experience needed, and do not agree with Patent Owner that greater years of experience are necessary for a POSA in this instance. *See KSR Int'l Co. v. Teleflex Inc.*,

550 U.S. 398, 421 (2007) (“A person of ordinary skill in the art is also a person of ordinary creativity, not an automaton.”).

Because Petitioner’s definition of a person of skill in the art appears commensurate with the level of skill reflected in the asserted art in this case as well as the ’361 patent itself, we apply Petitioner’s proposed level of ordinary skill in the art to determine whether it is more likely than not that Petitioner would prevail on its challenges to claim 1. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (stating prior art itself can reflect the appropriate level of ordinary skill in the art).

C. Claim Construction

We construe claims “using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. [§] 282(b).” 37 C.F.R. § 42.200. Therefore, we construe the challenged claims under the framework set forth in *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–19 (Fed. Cir. 2005) (en banc). Under this framework, claim terms are given their ordinary and customary meaning, as would be understood by a person of ordinary skill in the art, at the time of the invention, in light of the language of the claims, the specification, and the prosecution history of record. *Id.* Only those terms that are in controversy need be construed, and only to the extent necessary to resolve the controversy. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, *Matal*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (citing *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

Both parties agree that we need not construe any claim terms here to resolve the issues in this proceeding. *See* Pet. 16; Prelim. Resp. 18–19. We

agree with the parties that we need not construe any claim terms in this proceeding to resolve whether to institute a post-grant review.

D. Lack of Written Description

Petitioner asserts that the compound set forth in claim 1 of the '361 patent is a claimed subgenus of a broader genus described in the Specification of the '361 patent. Specifically, Petitioner states:

The Summary of the Invention presents an enormously broad chemical formula that seeks to cover an almost incalculable number of nucleotide phosphoramidates with variables at every possible position, and wherein each of the variables covers a huge scope of layered substituent possibilities [referred to by Petitioner as the '361 Supergen]. To place in context, the number of compounds in subgenus claim 1 reaches the billions.

Pet. 27–28 (citing Ex. 1001, 5:25–38; Ex. 1015 ¶¶ 19, 93). Petitioner further asserts that there are no “blaze marks that single out particular trees in a forest” to “reasonably lead” a POSA to the claimed subgenus. *Id.* at 26–27. Petitioner concludes that the '361 Supergen described in 524 columns of tables of compounds in the Specification does not teach a single species that falls within claim 1 and actually points away from the claim 1 subgenus. Pet. 78–85.

For instance, Petitioner points to the negative proviso in claim 1 “that X cannot be OH when R⁶ is –CH₃ or –CH₂F,” which it asserts does not have written description support from any blaze mark. Pet. 34–39. The support for claim 1 and this proviso is asserted in the prosecution history of the '361 patent to include “pages 19, 51, 61, and 67–68 and Examples 67–80.” Ex. 1002, 91. Petitioner asserts that pages 67–68 correspond to the

fourteenth aspect of the third embodiment in the Specification of the '361 patent. Pet. 35 (citing Ex. 1001, 37:46–38:10).

Petitioner argues that “[t]he actual proviso in the fourteenth aspect of the third embodiment as set out in the specification and which focuses on R⁵ is indefinite, not to mention vague, because it is amenable to at least three distinct interpretations.” Pet. 36. Petitioner asserts that the proviso provided in the fourteenth aspect of the third embodiment defines R⁵, whereas the proviso of claim 1 eliminates reference to R⁵ and instead defines X. *Id.* at 38. Petitioner posits that during prosecution, Patent Owner “converted an R⁵ proviso to become an X proviso” to remove the alleged ambiguity with respect to the R⁵ proviso set forth in the Specification. *Id.* Petitioner further asserts that the R⁵ proviso in the Specification does not provide sufficient support for the proviso in claim 1 because it is “indefinite” in that it is subject to at least three interpretations. Pet. 36–39. Petitioner concludes:

In the case of the '361 patent claim 1, a reasonable POSA could interpret the negative limitation in the definition of R⁵ of the fourteenth aspect of the third embodiment in at least . . . three distinct ways . . . thus making the proviso indefinite. And PO’s attempt to circumvent this indefiniteness by rewriting the proviso into an “X” proviso from an “R⁵” proviso leads to a written description problem by using language in claim 1 that is not unambiguously provided in the patent specification.

Pet. 39 (citing Ex. 1015 ¶ 62).

Petitioner also asserts that “there is no written description support for the breadth of the claim.” Pet. 59 (citing Ex. 1015 ¶¶ 64–96). Prof. Klibanov testifies that he finds “no indication that the fourteenth aspect of the third embodiment would be a more likely starting point for a POSA than any other embodiment of the patent application other than through use of

impermissible hindsight (i.e., looking at the claim first and then finding the ‘closest’ embodiment).” Ex. 1015 ¶ 68, *cited in* Pet. 61.

Even starting with the fourteenth aspect of the third embodiment, Prof. Klibanov testifies that “claim 1 is still very different from the subgenus disclosed in the patent specification,” and lists these differences in Table 2 of the Petition. Ex. 1015 ¶ 68, *cited in* Pet. 61–63. Petitioner applied the following “combinatorial analysis” to arrive at the alleged number of different possible “combinations of variables of Formula I-6 set forth in the fourteenth aspect of the third embodiment”:

$$\text{number of possible combinations} = n! / [(n-m)! \times m!]$$

Pet. 65. Based on this analysis, Petitioner asserts that “[t]he fourteenth aspect of the third embodiment includes over 10^{27} different possible combinations of variables from which PO [Patent Owner] selected just a single specific combination.” Pet. 59–60 (citing Ex. 1005 ¶¶ 64–96).

Petitioner points to the differences between Formula I-6 described in the fourteenth aspect of the third embodiment and the compound of claim 1, namely, specific variables that have been chosen for narrowed R groups R^4 , R^{10} , R^{11} , and R' , and the differing proviso. Pet. 62–64. Petitioner concludes:

Prof. Klibanov found no “blaze marks” for the specific combination of Markush Elements which PO selected from narrowed substituents R^4 , R^{10} , R^{11} , and R' . Additionally, PO chose to modify only variables R^4 , R^{10} , R^{11} , and R' but did not modify variables R^1 , R^2 , R^{3a} , R^{3b} , R^5 , R^6 , X, Y, Z, or R^{12} . This represents just one combination of selections out of over 10^{27} possible combinations.

Pet. 64 (citing Ex. 1015 ¶ 71).

Prof. Klibanov also testifies that even if we focus only on the particular selections made to arrive at claim 1 from Formula I-6, i.e., 4 elements of 20 for R^4 , 1 element of 15 for R^{10} , 1 element of 15 for R^{11} , and 1 element of 4 for R' , “the number of possible combinations of R group substituents is still overwhelming This results in well over four million possible combinations of R group substituents for R^4 , R^{10} , R^{11} , and R' even when all other numbers of selections and other variables are ignored ($4,845 \times 15 \times 15 \times 4 = 4,360,500$).” Ex. 1015 ¶ 85, *cited in* Pet. 70–71.

Also, Petitioner asserts, the Specification of the '361 patent describes only a single synthesized compound covered by claim 1, Compound 72. Pet. 72 (citing Ex. 1001, 607). Petitioner concludes: “In Prof. Klibanov’s opinion the synthesis of a single compound cannot create sufficient ‘blaze marks’ for a POSA to visualize the entire huge subgenus of claim 1,” which Petitioner asserts covers over 15 billion compounds. *Id.* (citing Ex. 1015 ¶¶ 88, 93). Petitioner concludes that “the over 12,000 recited examples which are not covered by the claims teach away from claim 1 of the '361 patent and show PO lacked possession of the claimed invention.” *Id.* at 77; *see also id.* at 78–85 (discussing Tables II-1 through XXXII-50 that describe no compounds within claim 1 and provide “multiple flashing red signs . . . that would convincingly point a POSA away from the claim 1 subgenus”) (citing Ex. 1015 ¶ 99).³

³ Although Patent Owner addresses the remaining arguments of Petitioner under the written description ground as in the Petition, we address these arguments, e.g., the '361 patent alleged failure “to disclose how to make the full scope of breadth of nucleotides within the claim 1 phosphoramidates,” and Patent Owner’s alleged inconsistent statements in other fora (*see* Pet. 85–116), in our analysis of the enablement ground. We find the enablement

Patent Owner asserts the Petition is meritless because it makes no attempt to apply the law or relevant legal tests in *Ariad Pharma., Inc. v. Eli Lilly and Co.*, 598 F.3d 1336 (Fed. Cir. 2010) (en banc) or *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), for lack of written description or lack of enablement, respectively, to the facts. Prelim. Resp. 3–4, 25. Specifically, Patent Owner asserts, Petitioner does not apply the law set forth in *Ariad* setting forth the test that written description support “requires the disclosure of either (1) a representative number of species falling within the scope of the genus or (2) structural features common to the members of the genus so that one of skill in the art can visualize or recognize the members of the genus.” 598 F.3d at 1350, *cited in* Prelim. Resp. 26.

Patent Owner describes the facts as follows. Patent Owner asserts that the ’361 patent results from work that led to sofosbuvir, an oral nucleotide analogue for the treatment of chronic HCV infection approved by the FDA as Patent Owner’s Sovaldi product. Prelim. Resp. 1, 6. Patent Owner describes the breadth of the disclosure in the ’361 patent as follows.

The disclosure spans 320 pages and 618 columns. The inventors first lay out ten generic structural formulas for their nucleotide prodrugs, each with various “aspects” that refine the substituents in their inventive compounds. The inventors proceed to provide 31 groups of tables with 12,400 “contemplated species of the various aspects of the disclosed embodiments.” The patent then teaches how to make the disclosed nucleotide prodrugs, including references to earlier applications that teach how to make the “nucleoside analog” portion of the compounds, including the previously difficult to synthesize 2’methyl-up, 2’fluoro-down nucleotide analogs . . . and 12 synthetic examples teaching how to synthesize the full

ground to provide the more appropriate rubric for addressing these arguments.

prodrug compounds. In total, the inventors included 75 examples of nucleotide prodrugs that they had synthesized, NMR data for all but six of those examples, and anti-HCV activity data for 19 of them. Example 25 is sofosbuvir.

Prelim. Resp. 6–7 (citing Ex. 1001, 1:41–44, 12:33–54:16, 54:17–579:39, 584:51–596:50, 590:9–617:20, 597–598).

Patent Owner asserts that claim 1 starts with Formula I-6 as set forth in the fourteenth aspect of the third embodiment described in the Specification of the '361 patent, but with narrower group of preferred substituents for R⁴, R¹⁰ (including R') and R¹¹ and slightly different, but consistent, proviso language. Prelim. Resp. 23. Patent Owner explains that the slightly different proviso in claim 1 has appropriate written description support in the fourteenth aspect of the third embodiment set forth in the Specification of the '361 patent because a POSA would have understood that the proviso in the fourteenth aspect should be read as “when X is OH, [and] R⁶ is CH₃ or CH₂F, R⁵ cannot be H.” Prelim. Resp. 29–30. Patent Owner concludes:

With that typo addressed, the meaning of the proviso in the fourteenth aspect is clear: if X is OH and R⁶ is CH₃ or CH₂F, the R⁵ cannot be H. Conversely, if R⁵ is H, as is claimed [in claim 1], then it cannot be true that both X is OH and R⁶ is CH₃ or CH₂F. That is precisely what the challenged claims dictate: the applicants decided to define R⁵ as H and, as a result, required that X could not be OH if R⁶ is CH₃ or CH₂F, consistent with the proviso in the fourteenth aspect.

Prelim. Resp. 30.

Patent Owner provides the following reasons why Petitioner's lack of written description challenge fails when the appropriate law is applied to the

facts of this proceeding. *See* Prelim. Resp. 33–42. We will address each of these reasons in our analysis.

1. Petitioner is incorrect in asserting that there must be some indication or “blaze mark” that points to the fourteenth aspect of the third embodiment as “a more likely starting point” for a skilled artisan;
2. Petitioner’s argument that the fourteenth aspect of the third embodiment includes over 10^{27} different possible combinations of variables is a fallacy relying on an inappropriate “combinatorial” approach;
3. Petitioner inappropriately “writes off” large portions of the Specification of the ’361 patent as irrelevant; and
4. Petitioner has failed to provide sufficient analysis to establish that the claimed subgenus is too broad.

Prelim. Resp. 33–42.

I. Analysis

In defining the written description requirement of 35 U.S.C. § 112, the Federal Circuit has stated this requirement

Implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves both to satisfy the inventor’s obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed. The written description requirement thus satisfies the policy premises of the law, whereby the inventor’s technical/scientific advance is added to the body of knowledge, as consideration for the grant of patent exclusivity.

The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence.

Capon v. Eshhar, 418 F.3d 1349, 1357 (Fed. Cir. 2005) (citations omitted); *see Ariad*, 598 F.3d at 1345 (stating written description describes “the

invention sufficiently to convey to a person of skill in the art that the patentee had possession of the claimed invention at the time of the application, i.e., that the patentee invented what is claimed”).

In reviewing genus claims in particular, the Federal Circuit in *Ariad* confirmed that the following test applies.

[A] sufficient description of a genus . . . requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can “visualize or recognize” the members of the genus. . . . [A]n adequate written description requires a precise definition, such as by structure, formula, chemical name, physical properties, or other properties, of species falling within the genus sufficient to distinguish the genus from other materials.

Ariad, 598 F.3d at 1350.

In applying this test, the Federal Circuit has explained that for genus claims, a POSA must look “for blaze marks within the disclosure that guide attention to the claimed species or subgenus.” *Regents of the Univ. of Minn. v. Gilead Sciences, Inc.*, 61 F.4th 1350, 1356 (Fed. Cir. 2023) (citing *e.g.*, *In re Ruschig*, 379 F.2d 990, 994–95 (CCPA 1967)). In evaluating whether such blaze marks exist, merely disclosing some structural features common to the members of a genus does not demonstrate possession of the claimed genus—such structural features must enable a POSA to “visualize or recognize” the members of the genus. *Id.* at 1359. In making such a determination, the Federal Circuit stated “[r]egarding whether common structural features must exist between a claim and a putative disclosure, those features must constitute the near-entirety of the structures being compared.” *Id.*; see also *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119

F.3d 1559, 1568 (Fed. Cir. 1997) (“Every species in a genus need not be described in order that a genus meet the written description requirement.”).

In applying this rubric to the challenged claims here, we determine that Petitioner has not shown on the record before us that it is more likely than not that it will prevail in establishing challenged claim 1 lacks written description.

Petitioner insists that we look for blaze marks to get us to the fourteenth aspect of the third embodiment that Patent Owner asserted in the prosecution history of the ’361 patent is part of what provides written description disclosure for claim 1. *See* Pet. 61; Ex. 1002, 91. Petitioner also asserts that the extensive disclosure in the Specification of the ’361 patent that does not describe compounds within claim 1 actually “teach[es] away” and shows lack of possession of the compounds of claim 1. Pet. 26–27, 78–85. As Patent Owner notes, this is simply not the test for determining whether a claim has sufficient written description support.

In applying the rubric set forth in *Ariad* to determine whether claim 1 has appropriate written description support, we can look for structural features common to the members of the subgenus of claim 1 so that one of skill in the art can “visualize or recognize” the members of the subgenus. *See Ariad*, 598 F.3d at 1350. To do this, we look “for blaze marks within the disclosure that guide attention to the claimed species or subgenus.” *See Regents of the Univ. of Minn.*, 61 F.4th at 1356. In this regard, the fourteenth aspect of the third embodiment *is* the blaze mark that points to the subgenus of claim 1. We do not need to find blaze marks that identify the fourteenth aspect of the third embodiment as the only formula of merit or the only one that should be claimed. Rather, we look to the written description

to see if it describes sufficient structural features common to the members of the subgenus of claim 1 such that a POSA can visualize or recognize the members of that subgenus, thereby demonstrating that the inventors possessed the subject matter of the claim at the time they filed their application.

As Patent Owner points out, of the five generic embodiments, i.e., two pyrimidine and three purine base embodiments, “the third purine embodiment is further refined in a series of nineteen ‘aspects’ that limit the options at one or more variable groups.” Prelim. Resp. 32–33 (citing Ex. 1001, 28:34–41:39). We do not need to determine whether a POSA would have selected the fourteenth aspect to arrive at claim 1; we need only determine that the written description describes that aspect and from that description a POSA “would necessarily recognize that the compounds [of claim 1] were disclosed as a combination that might be selected if desired” *Nelson v. Bowler*, Interference No. 101,217, 1986 WL 83353, at *4 (BPAI 1986).

Petitioner first asserts that the proviso in the fourteenth aspect of the third embodiment is indefinite and cannot provide written description support for the proviso of claim 1. Pet. 34–59. We disagree.

As Patent Owner points out, it is *claims* we examine to determine indefiniteness, not embodiments in a specification. Prelim. Resp. 31 (citing 35 U.S.C. § 112(b)). We do not need to determine every permutation defined by the proviso in the Specification, only whether such proviso provides appropriate support for the proviso in claim 1.

We agree with Patent Owner that because R⁵ is defined as H in claim 1, the proviso defines what X cannot be (OH) if R⁶ is CH₃ or CH₂F,

which is consistent with and supported by the proviso in the fourteenth aspect of the third embodiment that explains the reverse: What R^5 cannot be (H) when X is OH and R^6 is CH_3 or CH_2F . *See* Ex. 1001, 37:61–62.

Turning again to the fourteenth aspect of the third embodiment, we also agree with Patent Owner that Petitioner inappropriately inflates the number of possible combinations of the different variables to arrive at 10^{27} combinations using a “combinatorial” approach. Patent Owner explains:

For example, the fourteenth aspect of the third embodiment lists twenty potential options at R^4 . In calculating the number of possible subgenera, Petitioner does not start with those twenty possible options, but instead first morphs the twenty options number into **1,048,575** possible *combinations* of those options at R^4 alone. Similarly, Petitioner asserts that the fifteen possible options at each of R^{10} and R^{11} results in 32,767 possible combinations at each of those variables, and the 4 possible options at R' result in fifteen possible combinations at that variable. Petitioner then multiplies those already exaggerated numbers together to arrive at its number of possible subgenera.

Prelim. Resp. 35–36.

Petitioner applies this approach ostensibly premised on a similar approach that Patent Owner took in another case. *See* Pet. 65 (citing 1015 ¶ 72); *see* Ex. 1015 ¶ 73 n.7 (noting Patent Owner used the same combinatorial approach in its petition challenging U.S. Patent No. 8,815,830). Petitioner asserts that because “there is no teaching in the specification that discusses a preference for only choosing four specific elements [for R^4] out of a list of twenty, as compared to instead choosing one, two, three, five, six, etc. elements,” Petitioner applied a combinatorial analysis. Pet. 65.

As Patent Owner points out, other Board panels have previously rejected such an approach when Petitioner has not provided sufficient evidence or argument to show that the Specification teaches more than one class of substituent at each position. *See* Prelim. Resp. 36; *Gilead Sciences, Inc. v. Regents of the Univ. of Minn.*, IPR2017-01712, Paper 67, 36 (PTAB may 21, 2021) (Ex. 1024) (Board expressing concerns regarding “combinatorial” approach applied in Patent Owner’s petition challenging U.S. Patent No. 8,815,830). Similar concerns arise here, which Petitioner has not sufficiently reconciled.

For instance, Prof. Klibanov states that he applies Petitioner’s proffered combinatorial analysis as “a standard mathematical method for determining the number of possible combinations of selections that can be made from a set that has distinct members” using a colored marble analogy, without assessing whether a POSA would have viewed all of these combinations as appropriate in light of the teachings of the Specification of the ’361 patent. *See* Ex. 1015 ¶¶ 73–87. Thus, on the facts of this case, Petitioner has not sufficiently demonstrated that the combinatorial analysis it applies represents what a POSA would have understood from reading the ’361 patent’s written description as a whole.

In addition, Petitioner provides Table 1 in the Petition setting forth the embodiments and aspects described in the Specification of the ’361 patent that do not cover the subgenus of claim 1 and which Petitioner labels as irrelevant. *See* Pet. 39–59. Patent Owner takes issue with Petitioner’s lack of analysis of the *entirety* of the teachings of the Specification to determine whether there is written description support for claim 1.

For example, Patent Owner asserts that Petitioner dismisses many of the embodiments/aspects listed in Table 1 because they have a pyrimidine base versus a purine base as in claim 1 (citing Pet. 39–59), or do not include the exact proviso language as in claim 1 (citing Pet. 40, 48, 51). Prelim. Resp. 37–38. Patent Owner also takes issue with Petitioner’s dismissal of the 12,400 species disclosed in the Specification of the ’361 patent that have a purine base, but not the exact same substituents on the base as recited in claim 1. *Id.* at 38 (citing Pet. 78–83). Patent Owner points out that Petitioner does not acknowledge the statement in the Specification that any one of the exemplified nucleoside bases can be used in combination with any one of contemplated species with particular combinations of substituents. *Id.* (citing Ex. 1001, 54:23–27).

Patent Owner concludes:

Given that it incorrectly ignored large parts of the disclosure, Petitioner’s conclusion that the specification does not provide “any guidance” for the “individual selections” at R⁴, R¹⁰ and R¹¹ should not be given any weight. As just one example, Petitioner and its expert fail to even acknowledge that at least 7,440 of the embodiments disclosed in Tables II-1 to XXXII-50 include the claimed methyl, ethyl, or propyl substituents at R⁴. Petitioner’s (and its expert’s) approach of simply ignoring large portions of the disclosure is legally wrong, and their conclusions are based on an incomplete and deficient analysis.

Prelim. Resp. 39 (citing Ex. 1001, 55:1–579:39).

We agree with Patent Owner that Petitioner has not provided sufficient analysis of the disclosure in the Specification of the ’361 patent to determine whether claim 1 lacks sufficient written description support. Petitioner appears to apply an *ipsis verbis* test for a majority of the disclosure and fails to look for blaze marks within that disclosure to

determine whether adequate written description support is provided in the Specification of the '361 patent. *See* Pet. 40–59 (stating embodiment irrelevant if not an exact match with the compound of claim 1). We determine that on this record, Petitioner has not provided sufficient evidence and explanation as to why claim 1 lacks sufficient written description support.

2. Conclusion

Petitioner has failed to show that it is more likely than not that it would prevail in showing that claim 1 lacks written description support.

E. Lack of Enablement

Petitioner does not provide a separate analysis for its argument that claim 1 is not enabled. *See generally* Pet. Petitioner, however, does discuss how the '361 patent disclosure allegedly “fails to disclose how to make the full scope of breadth of nucleotides within the claim 1 phosphoramidates.” Pet. 85 (citing Ex. 1015 ¶ 102). For instance, Petitioner asserts that none of the four references provided in the Specification of the '361 patent “teach[] how to make compounds within the full scope of claim 1 of the '361 patent; in fact, all of these references are limited to the same 2'-alkyl-up-2'-F-down structural motif.” Pet. 87 (citing Ex. 1015 ¶ 105). Petitioner concludes:

Thus, the entire scope of synthetic examples in the '361 patent is drawn to merely one embodiment—nucleotides with 2'-methyl (or alkyl)-up and 2'-fluoro-down. This is not sufficient to teach a POSA how to make compounds across the full claimed scope of compounds with varied 2'-substituents, or even to point them in that direction.

Pet. 89 (citing Ex. 1015 ¶¶ 106–107 (specifically Table 9)).

Petitioner also addresses alleged inconsistent statements made by Patent Owner in other proceedings concerning how difficult or impossible it would be to make compounds similar to the subgenus of claim 1. *See* Pet. 89–116.

Patent Owner responds that Petitioner “fails to at all address the amount of experimentation needed to practice the claimed inventions, much less explain why any such experimentation is undue or unreasonable.” Prelim. Resp. 44. For instance, the fact that some experimentation may be necessary to synthesize compounds with other substituents at the 2’ position does not establish that such experimentation is undue. Prelim. Resp. 45 (citing *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1576, 1576–77 (Fed. Cir. 1984)). Patent Owner also asserts that Petitioner’s arguments are based on statements made in different proceedings, about different claims, with a different priority date. *Id.* (citing Pet. 92–96).

Patent Owner concludes:

Petitioner does not even attempt to demonstrate the amount of experimentation needed to practice the claimed invention, much less that it is “undue,” particularly in light of the nature of the invention, the state of the art, and the level of ordinary skill in the art.

Prelim. Resp. 45 (citing *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988)).

I. Analysis

The specification must enable a person of ordinary skill in the art to make and use the claimed invention. *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997). The disclosure of the specification also must be commensurate in scope with the claim under consideration. *See In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991).

Furthermore, Section 112(a) requires that the patent specification enable “those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.” *Koito Mfg. Co., Ltd. v. Turn-Key-Tech, LLC*, 381 F.3d 1142, 1155 (Fed. Cir. 2004). The factors set forth by our reviewing court in *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), may be considered when determining whether a disclosure calls for undue experimentation. These factors are: “(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.” *Wands*, 858 F.2d at 737.

We determine that on the record before us Petitioner has failed to establish that it is more likely than not that it would prevail in showing claim 1 lacks enablement. First, we note that Petitioner has not made clear in the Petition which arguments relate to its lack of enablement challenge. *See* Prelim. Resp. 43 (stating the Petition only uses the words “enable” or “enablement” twice in discussing the support for the grounds). Further, as Patent Owner points out, Petitioner describes how the Specification of the ’361 patent sets forth how to make a compound within claim 1 that has the same 2’-alkyl-up-2’-F-down structural motif, but does not assess what further experimentation is necessary, if any, to make compounds within claim 1 using different substituents for the 2’ position. *Id.* at 45.

Petitioner attempts to use allegedly inconsistent statements from the Patent Owner to establish lack of enablement, but these statements were made concerning an earlier time period, 2003, compared to the 2007 priority

date that Patent Owner asserts applies to claim 1, and is certainly before the 2021 priority date that Petitioner seeks to assign to claim 1. Petitioner does not address whether these statements concerning the difficulties in making certain compounds allegedly within the scope of claim 1 would remain true in 2007 or 2021. Thus, without this further explanation, we cannot determine if the allegedly inconsistent statements Petitioner relies upon are relevant to show that claim 1 was not enabled as of the priority date of the '351 patent. Again, it is the petitioner's burden to make such connections sufficiently for institution, but Petitioner here has not done so.

2. Conclusion

Petitioner has failed to show on this record that it is more likely than not that it would prevail in showing that claim 1 is not enabled.

F. Prior Art Challenge

Petitioner asserts that claim 1 is anticipated by the '706 U.S. Publication published on September 8, 2016. Pet. 11, 116–112. We determine on the record before us that Petitioner has not demonstrated that the '706 U.S. Publication qualifies as prior art.

We have determined that Petitioner has not established that it is more likely than not claim 1 lacks written description support, and Petitioner agrees that the same specification is provided in the chain of continuations that resulted in the '361 patent, the first of which was filed on March 21, 2008. *See* Pet. 25; Prelim. Resp. 47. Therefore, on this record, the '706 U.S. Publication, which was published after March 21, 2008, does not qualify as prior art, and we determine that Petitioner has not shown that it is

more likely than not that it would prevail in its prior art challenge as to claim 1 of the '361 patent.

III. CONCLUSION

For the foregoing reasons, we conclude that the information presented in the Petition does not establish that it is more likely than not that Petitioner will prevail in showing that challenged claim 1 of the '361 patent is unpatentable based on any ground presented in the Petition. Accordingly, we do not institute a post-grant review of claim 1 of the '361 patent.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is denied; and

FURTHER ORDERED that the requested post-grant review is not instituted with respect to claim 1 of the '361 patent.

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Patent 11,642,361 B2

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