

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

GILEAD SCIENCES, INC.,
Petitioner,

v.

REGENTS OF THE UNIVERSITY OF MINNESOTA,
Patent Owner.

IPR2017-02005
Patent 8,815,830 B2

Before ERICA A. FRANKLIN, ZHENYU YANG, and
CHRISTOPHER G. PAULRAJ, *Administrative Patent Judges*.

YANG, *Administrative Patent Judge*.

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

INTRODUCTION

Gilead Sciences, Inc. (“Petitioner”) filed a Petition (Paper 1 (“Pet.”)), seeking an *inter partes* review of claims 1–9, 11, 12, and 28 of U.S. Patent No. 8,815,830 B2 (Ex. 1301, “the ’830 patent”). Regents of the University of Minnesota (“Patent Owner”) filed a Preliminary Response. Paper 35 (“Prelim. Resp.”).

We have authority under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted “unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a) (2012).

For the reasons provided below, we determine that Petitioner has not demonstrated a reasonable likelihood that it would prevail with respect to at least one of the claims challenged in the Petition. Accordingly, we deny institution of an *inter partes* review.

Related Matters

According to the parties, Patent Owner asserted the ’830 patent against Petitioner in *Regents of the University of Minnesota v. Gilead Sciences, Inc.*, No. 16-cv-02915 (D. Minn.). Pet. viii; Paper 3, 1. The case was later transferred to the U.S. District Court for Northern District of California and was docketed as *Regents of the University of Minnesota v. Gilead Sciences, Inc.*, No. 3:17-cv-06056 (N.D. Ca.). Paper 21, 1.

Petitioner also filed three other petitions (IPR2017-01712, IPR2017-01753, IPR2017-02004), all challenging the claims of the ’830 patent. Pet. viii.

Case History

Petitioner filed the Petition on August 29, 2017. Paper 5. With our authorization, the parties briefed the issue of whether the doctrine of sovereign immunity applies in this proceeding such that we should grant Patent Owner's Motion to Dismiss the Petition. Papers 12, 15, 16.

While the Motion to Dismiss in this case was pending, the Board denied Patent Owner's motions to dismiss based on sovereign immunity in several other *inter partes* review proceedings. *LSI Corp. v. Regents of the Univ. of Minn.*, IPR2017-01068, Paper 19 (PTAB Dec. 19, 2017); *Ericsson Inc. v. Regents of the Univ. of Minn.*, IPR2017-01186, -01197, -01213, -01214, -01200, -01219 (PTAB Dec. 19, 2017). On February 12, 2018, Patent Owner filed a Notice of Appeal, seeking immediate appellate review of those decisions. *See, e.g.*, IPR2017-01186, Paper 22.

Under such circumstances, and at the request of Patent Owner, we suspended this proceeding in view of the appellate adjudication of the state-sovereign-immunity issue. Papers 17, 20, 23. Petitioner then sought, and was granted, leave to intervene in those appeals. Paper 21, 2.

On June 14, 2019, the Federal Circuit affirmed the Board's decision denying Patent Owner's motion to dismiss in those proceedings. *Regents of the Univ. of Minn. v. LSI Corp.*, 926 F.3d 1327, 1330 (Fed. Cir. 2019). On January 13, 2020, the Supreme Court denied Patent Owner's petition for writ of certiorari. *Regents of the Univ. of Minn. v. LSI Corp.*, 140 S. Ct. 908 (Jan. 13, 2020) (No. 19-337). The next day, we denied Patent Owner's Motion to Dismiss and lifted the stay order in this proceeding. Paper 27.

Because Petitioner filed four petitions, challenging largely overlapping claims of the '830 patent, we requested that Petitioner rank them in the order in which it wishes the panel to consider the merits. Paper 32, 2 (citing Office Patent Trial Practice Guide, July 2019 Update,¹ 26). We also invited Patent Owner to respond to Petitioner's notice. *Id.* at 3. The parties have since filed their respective papers. Papers 33, 34.

The '830 Patent

The '830 patent relates to nucleosides with antiviral and anticancer activity. Ex. 1301, 1:1–2.

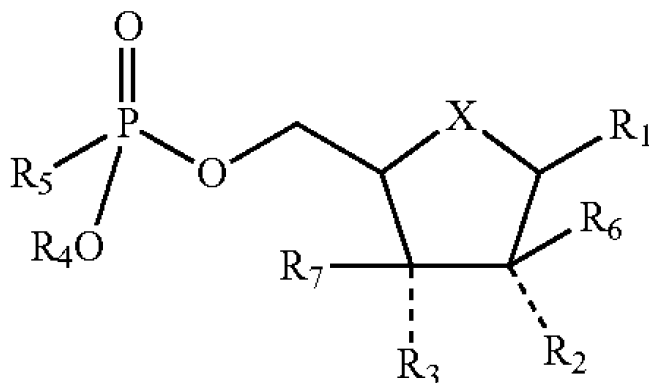
The '830 patent acknowledges that “U.S. Pat. No. 6,475,985 reports certain specific nucleoside phosphoramidate analogs having anticancer and/or antiviral properties.” *Id.* at 1:61–63. It states that there were other, continued interests “in phosphoramidate nucleoside analogs due to their demonstrated utility as prodrugs of antiviral and anticancer nucleoside monophosphates, or pronucleotides.” *Id.* at 1:63–66. But despite the prior-art studies on this topic, there was still “a need for chemotherapeutic agents with antiviral and[/]or anticancer properties.” *Id.* at 2:6–8. According to the '830 patent, its invention provides such “compounds that act as antiviral and[/]or anticancer agents.” *Id.* at 2:48–49.

¹ 84 Fed. Reg. 33,926 (July 16, 2019), available at <https://www.uspto.gov/TrialPracticeGuide3>.

Illustrative Claim

Claim 1 is independent and is reproduced below:

1. A compound of formula I:



wherein:

R₁ is guanine, cytosine, thymine, 3-deazaadenine, or uracil, optionally substituted by 1, 2, or 3 U; wherein each U is independently halo, hydroxy, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkyloxy, (C₁-C₆)alkanoyl, (C₁-C₆)alkanoyloxy, trifluoromethyl, hydroxy(C₁-C₆)alkyl, —(CH₂)₁₋₄P(=O)(OR_w)₂, aryl, aryl(C₁-C₆)alkyl, or NR_xR_y;

R₂ is halo;

R₆ and R₇ are independently H or (C₁-C₆)alkyl;

R₃ is hydroxy;

R₄ is hydrogen, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, aryl(C₁-C₆)alkyl, or 2-cyanoethyl;

R₅ is an amino acid;

X is oxy, thio, or methylene;

each R_w is independently hydrogen or (C₁-C₆)alkyl;

R_x and R_y are each independently hydrogen, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, phenyl, benzyl, phenethyl, or (C₁-C₆)alkanoyl; or R_x and R_y together with the nitrogen to which they are attached are pyrrolidino, piperidino or morpholino;

wherein any (C₁-C₆)alkyl of R₁, R₄-R₇, R_w, R_x, and R_y is optionally substituted with one or more halo, hydroxy, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkyloxy, (C₁-C₆)alkanoyl, (C₁-C₆)alkanoyloxy, trifluoromethyl, azido, cyano, oxo (=O), (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, (C₃-C₆)cycloalkyl(C₁-C₆)alkyl, (C₁-C₆)alkyl-S—(C₁-C₆)alkyl-, aryl, heteroaryl, alkyl(C₁-C₆)alkyl, or heteroaryl(C₁-C₆)alkyl, or NR_{aj}R_{ak}; wherein each R_{aj} and R_{ak} is independently hydrogen, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, phenyl, benzyl, or phenethyl;

and wherein any aryl or heteroaryl may optionally be substituted with one or more substituents selected from the group consisting of halo, hydroxy, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkyloxy, (C₁-C₆)alkanoyl, (C₁-C₆)alkanoyloxy, trifluoromethyl, trifluoromethoxy, nitro, cyano, and amino;

or a pharmaceutically acceptable salt thereof.

Asserted Ground of Unpatentability

Petitioner challenges claims 1–9, 11, 12, and 28 under a single ground, alleging they are unpatentable for obviousness over the combined teachings of the '787 patent² and Brox.³

In support of its patentability challenge, Petitioner relies on the Declaration of David MacMillan, Ph.D. Ex. 1307.

² Christopher McGuigan, U.S. Pat. No. 7,951,787 B2, issued May 31, 2011 (Ex. 1302).

³ L. W. Brox et al., *Studies on the Growth Inhibition and Metabolism of 2'-Deoxy-2'-fluorocytidine in Cultured Human Lymphoblasts*, 34 CANCER RES. 1838 (1974) (Ex. 1306).

ANALYSIS

Discretionary Denial

Patent Owner contends that we should exercise our discretion and deny institution because Petitioner filed four petitions to challenge the claims of the '830 patent. Prelim. Resp. 11–12, 68. According to Patent Owner, “[f]our parallel petitions are inappropriate and have placed a substantial and unnecessary burden on the Board and Patent Owner.” *Id.* at 68.

Petitioner points out that all four petitions were filed in 2017, before the Office started to disfavor multiple petitions against the same patent. Paper 33, 1. According to Petitioner, but for Patent Owner’s “efforts to stop these proceedings before they began” by asserting sovereign immunity, these proceedings would have concluded before the policy shift. *Id.* at 1–2.

Under such circumstances, and because, as explained below, we deny institution based on substantive analysis of the Petition, we decline to consider whether institution should be denied on a discretionary basis.

Claim Construction

In an *inter partes* review based on a petition filed before November 13, 2018, the Board interprets a claim term in an unexpired patent according to its broadest reasonable construction in light of the specification of the patent in which it appears. 37 C.F.R. § 42.100(b) (2017);⁴ *Cuozzo*

⁴ The final rule changing the claim construction standard does not apply here, as the Petition was filed before the effective date of the final rule, November 13, 2018. *See* Changes to the Claim Construction Standard for

Speed Techs., LLC v. Lee, 136 S. Ct. 2131, 2144–46 (2016). Under that standard, and absent any special definitions, we assign claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention, in the context of the entire patent disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Petitioner states that the terms in the '830 patent should be construed under the broadest-reasonable-interpretation standard. Pet. 14. It generally notes that the '830 patent offers some specific definitions. *Id.*

Patent Owner discusses the terms “alkyl” and “aryl.” Prelim. Resp. 37–55. According to Patent Owner, “alkyl” means “a hydrocarbon group containing only single bonds.” *Id.* at 50. It points to McGraw-Hill Dictionary of Scientific and Technical Terms, which defines “alkyl” as “[a]n organic group that results from removal of a hydrogen atom from an acyclic, saturated hydrocarbon;” and “saturated hydrocarbon” as “[a] saturated carbon-hydrogen compound with all carbon bonds filled; that is, there are no double or triple bonds as in olefins and acetylenics.” *Id.* (quoting Ex. 2315, 64. 1754). Patent Owner argues that its construction is consistent with the disclosures of the '830 patent. *Id.* at 50 (noting that in the '830 patent, alkyl denotes “both straight and branched groups”) (quoting Ex. 1301, 5:15–16),

Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board, 83 Fed. Reg. 51,340 (Oct. 11, 2018) (amending 37 C.F.R. § 42.100(b) effective November 13, 2018).

52 (observing that each named group of (C₁-C₆)alkyl in the '830 patent is a hydrocarbon group containing only single bonds) (citing Ex. 1301, 6:37–39). Petitioner, although not offering any construction of the term, acknowledges that “alkyl” is “commonly understood” to include only saturated hydrocarbons. Pet. 21. On this record, we find Patent Owner’s argument persuasive and agree that “alkyl” is “a hydrocarbon group containing only single bonds.”

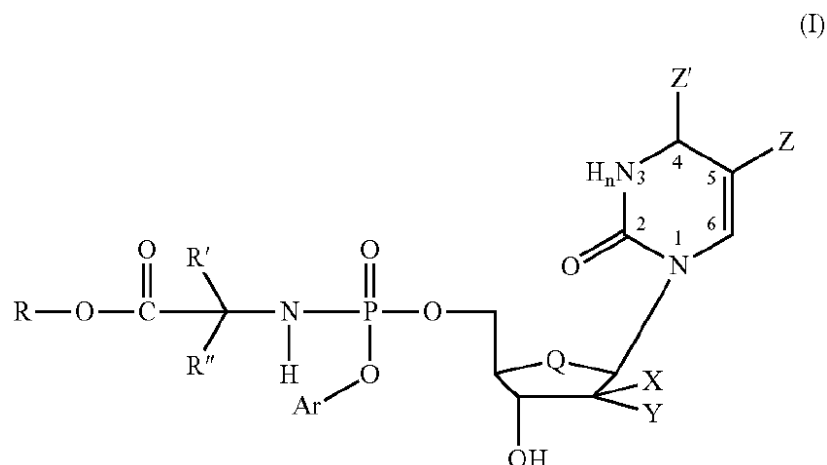
Patent Owner points to the '830 patent for defining “aryl” as “a phenyl radical or an ortho-fused bicyclic carbocyclic radical having about nine to ten ring atoms in which at least one ring is aromatic.” Prelim. Resp. 41 (quoting Ex. 1301, 5:14–22). The parties agree that this definition excludes heteroaryl groups, that is, “ring systems with heteroatoms (i.e., atoms that are not carbon or hydrogen) incorporated into the ring(s).” *Id.* at 42; Pet. 21.

Claim terms need only be construed to the extent necessary to resolve the controversy. *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011). On this record and for purposes of this Decision, we see no need to construe any other term expressly.

Prior-Art Disclosures

The '787 Patent

The '787 patent describes phosphoramidate derivatives of nucleotides and their use in the treatment of cancer. Ex. 1302, Abstract. It teaches a compound of formula I:



wherein

R is selected from the group comprising alkyl, aryl and alkylaryl;

R' and R'' are, independently, selected from the group comprising H, alkyl and alkylaryl, or R' and R'' together form an alkylene chain so as to provide, together with the C atom to which they are attached, a cyclic system;

Q is selected from the group comprising $-O-$ and $-CH_2-$;

X and Y are independently selected from the group comprising H, F, Cl, Br, I, OH and methyl ($-CH_3$);

Ar is a monocyclic aromatic ring moiety or a fused bicyclic aromatic ring moiety, either of which ring moieties is carbocyclic or heterocyclic and is optionally substituted;

Z is selected from the group comprising H, alkyl and halogen;
 and

n is 0 or 1,

wherein

when n is 0, Z' is $-NH_2$ and a double bond exists between position 3 and position 4, and

when n is 1, Z' is $=O$;

or a pharmaceutically acceptable derivative or metabolite of a compound of formula I;

with the proviso that when n is 1, X and Y are both H, R is methyl

(–CH₃), one of R' and R'' is H and one of R' and R'' is methyl (–CH₃), then Ar is not phenyl (–C₆H₅).

Id. at 3:30–4:3.

Brox

Brox teaches that nucleoside 2'-deoxy-2'-fluorocytidine (FCdR) inhibits the growth of various human lymphoblastic cell lines in culture. Ex. 1306, Abstract, 1839.

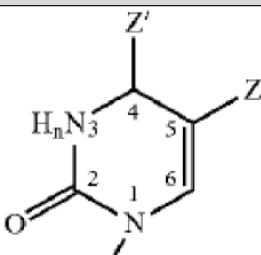
Analysis

Petitioner asserts that claims 1–9, 11, 12, and 28 would have been obvious over the combination of the '787 patent and Brox. Pet. 33–59. Based on this record, we determine Petitioner has not established a reasonable likelihood that it would prevail in this assertion.

Petitioner argues that the '787 patent “discloses a genus of nucleoside phosphoramidate compounds that are an obvious subgenus that is almost entirely within the scope of the genera claimed in the '830 patent, and/or substantially overlaps those genera.” *Id.* at 33 (citing Ex. 1307 ¶ 24, 75), *see also id.* at 38 (“The Markush group selections in the '787 patent fall largely within the Markush group selections of the claims of the '830 patent.”). Petitioner states that “[t]he '787 patent subgenus is slightly broader in its available substituent choices at the 2'-position than the claims of the '830 patent.” *Id.* at 44. Petitioner relies on Brox for the “narrowing selections” at this position. *Id.* at 46–49. Petitioner argues that an ordinarily skilled artisan would have been motivated to combine the teachings of the '787 patent and Brox. *Id.* at 48–49. Thus, Petitioner concludes that the challenged claims would have been obvious over the '787 patent and Brox. *Id.* at 52–59.

Patent Owner contends that we should deny the Petition because, among other reasons, the premise of the obviousness challenge, that is, the genus of the '787 patent "substantially overlaps" with that of the challenged claims, is flawed. Prelim. Resp. 6–9, 37–58. Patent Owner argues that "[t]he '787 Patent defines 'alkyl' and 'aryl' far more broadly than the meaning of those terms in the '830 Patent." *Id.* at 38. As a result, Patent Owner concludes that "the claimed '830 Patent genus neither substantially overlaps nor virtually encompasses the '787 genus (even if modified according to Brox)." *Id.* at 40. We find Patent Owner's argument more persuasive.

The Petition includes a chart comparing the Markush group selections in the '787 patent with those of challenged claim 1:

Prior Art '787 Patent	The '830 Patent
 N is 0 or 1 Wherein When n is 0, Z' is—NH₂ and a double bond exists between position 3 and position 4 (cytosine), and When n is 1, Z' is =O (thymine or uracil); Z is selected from the group comprising H, alkyl and halogen.	R₁ is guanine, cytosine, thymine, 3-deazaadenine, or uracil, optionally substituted by 1, 2, or 3 U; wherein each U is independently halo, hydroxy, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, (C₁-C₆)alkoxy, (C₃-C₆)cycloalkyloxy, (C₁-C₆)alkanoyl, (C₁-C₆)alkanoyloxy, trifluoromethyl, hydroxy(C₁-C₆)alkyl, —(CH₂)₁₋₄P(=O)(OR_w)₂, aryl, aryl(C₁-C₆)alkyl, or NR_xR_y.

Oxygen protecting group is Ar wherein Ar is aryl	R ₄ is hydrogen, (C ₁ -C ₆)alkyl, (C ₃ -C ₆)cycloalkyl, aryl, aryl(C ₁ -C ₆)alkyl, or 2-cyanoethyl
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Pet. 43 (highlighting in original).

For the R₄ position, Petitioner argues that “aryl, aryl(C₁-C₆)alkyl” of the ’830 patent encompasses the “Ar” of the ’787 patent. *Id.*, *see also id.* at 40 (“[B]oth the ’787 patent and the ’830 patent include an aryl substituent.”). We find that for the following two reasons, despite using the same term “aryl,” the R₄ substituent options claimed in the ’830 patent does not encompass the “Ar” substituent selections of the ’787 patent.

First, as discussed in the claim-construction section, the parties agree that “aryl,” as defined in the ’830 patent, excludes heteroaryl groups. *Supra* at 9; Pet. 21; Prelim. Resp. 42. “Aryl” in the ’787 patent, in contrast, “may be a heteroaromatic group containing one, two, three or four” heteroatoms. Ex. 1302, 4:65–5:3, *see also id.* at 3:56–58 (“Ar is a monocyclic aromatic ring moiety or a fused bicyclic aromatic ring moiety, either of which ring moieties is carbocyclic or heterocyclic and is optionally substituted.”).

Second, when “aryl” is an ortho-fused bicyclic carbocyclic radical, the ’830 patent limits the system to “about nine to ten ring atoms.” Ex. 1301, 5:14–22. In contrast, in the ’787 patent, “an aryl group means an aromatic group containing 5 to 14 ring atoms.” Ex. 1302, 4:65–66. Because of at least these two differences, the “Ar” substituent selections of the ’787 patent are broader than the “aryl” substituent selections of the claims of the ’830 patent.

Similarly, we find that the '787 patent discloses broader selections corresponding to the R₁ position of the '830 patent. At R₁, Petitioner argues that the U substituents of “halo” and “(C₁-C₆)alkyl” of the '830 patent encompass the “H, alkyl and halogen” Z substituents of the '787 patent. Pet. 43, *see also id.* at 38–39 (arguing that the '787 patent discloses “an alkyl or halogen substituted derivative thereof as options at R₁ . . . all of which are contained within the '830 patent claims”). Pet. 38–39. For the following two reasons, we disagree.

First, as discussed in the claim-construction section, the parties agree that “alkyl” as defined in the '830 patent, includes only saturated hydrocarbons. *Supra* 8; Pet. 21; Prelim. Resp. 50. In contrast, in the '787 patent, an “alkyl” group includes either “saturated or unsaturated (e.g. alkenyl or alkynyl) hydrocarbonyl radical.” Ex. 1302, 4:58–60.

Second, as, the '830 patent limits the claimed U substituents to “(C₁-C₆)alkyl.” Ex. 1301, 19:13. In contrast, the '787 patent does not limit the number of carbon atoms. Because of at least these two differences, the “alkyl” substituent selections of the '787 patent are broader than the “(C₁-C₆)aryl” substituent selections of the claims of the '830 patent.

Petitioner acknowledges that “the '787 patent expressly broadens the commonly understood definitions of ‘alkyl’ (to include unsaturated hydrocarbons) and ‘aryl’ (to include heteroaryls), but the corresponding definitions in the '830 patent do not contain those broadened definitions.” *Id.* at 21; *see also id.* at 39 n.3 (“[T]he '787 patent’s specific definition [of “alkyl”] somewhat broadens this shared substituent terminology by allowing ‘alkyl’ to encompass unsaturated hydrocarbons more commonly known as

‘alkenyl’ or ‘alkynyl.’”); *id.* at 40 n.5 (“The ’787 patent has specifically broadened the term ‘aryl’ beyond its commonly understood definition to include heteroatoms.”).

Despite these admissions, Petitioner contends that an ordinarily skilled artisan “would regardless understand” “alkyl” and “aryl” as they are “commonly understood.” *Id.* at 39 n.3, *id.* at 40 n.5. As support, Petitioner relies on the testimony of Dr. MacMillan, who chalks up the broadened definitions of “alkyl” and “aryl” in the ’787 patent as a “minor difference” from the challenged patent. Ex. 1307 ¶ 99 n.3. According to Dr. MacMillan, an ordinarily skilled artisan would be “naturally directed towards the common and shared definition of both of those terms in each of the ’787 patent and the ’830 patent, meaning that the resulting genus of compounds disclosed in the ’787 patent will be entirely within those claimed in the ’830 with respect to those choices.” *Id.* We are not persuaded.

Dr. MacMillan relies on the challenged patent itself to support his opinion. *See, e.g., id.* ¶ 88 n.1 (“[A]s between the definitions of alkyl in the ’787 patent and the ’830 patent, a person of skill would understand the term ‘alkyl’ to be focused on the commonly understood definition of alkyl, namely saturated hydrocarbon chains, as defined in the ’830 patent.”) (citing Ex. 1301, 5:15–19). “The inventor’s own path itself,” however, “never leads to a conclusion of obviousness; that is hindsight.” *Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1296 (Fed. Cir. 2012). Instead, “[w]hat matters is the path that the person of ordinary skill in the art would have followed, as evidenced by the pertinent prior art.” *Id.* Here, that prior-art evidence is missing. Because Dr. MacMillan’s opinion on this issue is not properly

supported, we accord it little weight. *See* 37 C.F.R. § 42.65(a) (“Expert testimony that does not disclose the underlying facts or data on which the opinion is based is entitled to little or no weight.”).

In sum, both “aryl” and “alkyl” are broader in the ’787 patent than in the ’830 patent. Thus, even if an ordinarily skilled artisan, based on the teachings of Brox, would have modified the formula I genus of the ’787 patent, such modified genus would not be “almost entirely within the scope of” the genus of the challenged claims. As a result, Petitioner has not sufficiently demonstrated the obviousness of the challenged claims over the ’787 patent and Brox.

CONCLUSION

For the reasons explained above, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing that at least one of the challenged claims is unpatentable as obvious over the combination of the ’787 patent and Brox.

ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is denied, and we do not institute *inter partes* review of any claim of the ’830 patent based on the ground asserted in the Petition.

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