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Paper: 17
Entered: January 16, 2019

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NOVARTIS PHARMACEUTICALS CORPORATION,
Petitioner,

v.

PLEXXIKON INC.,
Patent Owner.

Case IPR2018-01287
Patent 9,469,640 B2

Before SHERIDAN K. SNEDDEN, JO-ANNE M. KOKOSKI, and KRISTI L. R. SAWERT, *Administrative Patent Judges.*

KOKOSKI, *Administrative Patent Judge.*

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

I. INTRODUCTION

Novartis Pharmaceuticals Corporation ("Petitioner") filed a Petition to institute an *inter partes* review of claims 1, 2, 4–6, 9, 11, and 12 of U.S. Patent No. 9,469,640 B2 ("the '640 patent," Ex. 1001). Paper 2 ("Pet."). Plexxikon Inc. ("Patent Owner") filed a Preliminary Response. Paper 10 ("Prelim. Resp.").

Institution of an *inter partes* review is authorized by statute when "the information presented in the petition . . . and any response . . . shows that 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; *see* 37 C.F.R. § 42.4. Upon consideration of the Petition, the Preliminary Response, and the evidence of record, we determine that the Petition presents substantially the same arguments as those previously presented to the Office, and, thus, exercise our discretion under 35 U.S.C. § 325(d) to deny institution of an *inter partes* review as to claims 1, 2, 4–6, 9, 11, and 12 of the '640 patent.

A. Related Proceedings

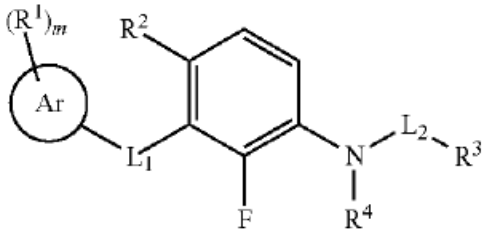
The parties indicate that the '640 patent is being asserted in *Plexxikon Inc. v. Novartis Pharmaceuticals Corp.*, Civil Action No. 4:17-cv-04405 HSG (EDL) (N.D. Cal.). Paper 8, 2; Pet. 4.

B. The '640 Patent

The '640 patent, titled "Compounds and Methods for Kinase Modulation, and Indications Therefor," is directed to compounds "that are active on protein kinases in general," and methods for the use of such compounds "in treating diseases and conditions associated with regulation of the activity" of the protein kinases. Ex. 1001, 1:26–46. The '640 patent

describes a genus of compounds that have the following generic formula ("Formula I"):

Formula I



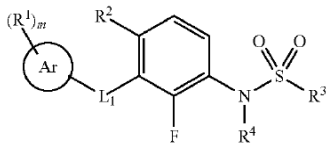
Id. at 1:51–3:64. The '640 patent identifies a number of options for each of Ar, R^1, R^2, R^3, R^4, L_1, L_2, and m. *Id.* For example, the '640 patent states that "Ar is optionally substituted heteroaryl," "R^2 is hydrogen, lower alkyl or halogen," and "R^3 is optionally substituted lower alkyl, optionally substituted $C_{3–6}$ cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl or optionally substituted heteroaryl." *Id.* at 1:65, 2:13, 2:17–20. The '640 patent further discloses a number of sub-genera of Formula I that it identifies as Formulae Ia, Ib, Ic, Id, Ie, If, Ig, Ih, Ii, and Ij. *Id.* at 3:65–13:41.

C. Challenged Claims

Petitioner challenges claims 1, 2, 4–6, 9, 11, and 12 ("the challenged claims") of the '640 patent. Claim 1, the only independent claim, is reproduced below.

1. A compound of formula (Ia):

(Ia)



or a pharmaceutically acceptable salt thereof, wherein:

L_1 is a bond or —N(H)C(O)—;

each R^1 is optionally substituted lower alkyl or optionally substituted heteroaryl;

R^2 is hydrogen or halogen;

R^4 is hydrogen;

R^3 is optionally substituted lower alkyl or optionally substituted aryl;

m is 0, 1, 2, 3, 4, or 5; and

Ar is a monocyclic heteroaryl containing 5 to 6 atoms wherein at least one atom is nitrogen.

Ex. 1001, 150:25–47.

D. The Asserted Ground of Unpatentability

Petitioner challenges the patentability of claims 1, 2, 4–6, 9, 11, and 12 of the ’640 patent under 35 U.S.C. § 102(a) as being anticipated by U.S. Patent No. 7,994,185 B2, issued on August 9, 2011 (“the ’185 patent,” Ex. 1006).

II. ANALYSIS

Institution of *inter partes* review is discretionary. *See* 35 U.S.C. § 314(a); 37 C.F.R. § 42.108. Our discretion on whether to institute is guided by 35 U.S.C. § 325(d), which states that “the Director may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office.” Patent Owner contends that Petitioner’s challenge relies on the same or substantially the same arguments that were already considered during the prosecution of the ’640 patent. Prelim. Resp. 9–16.

When evaluating whether the same or substantially the same prior art or arguments previously were presented to the Office under § 325(d), the Board has considered a number of non-exclusive factors, including: (1) the

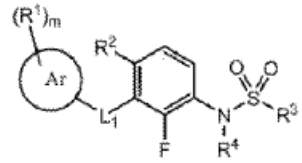
similarity of the asserted art and the prior art involved during the examination; (2) the extent to which the asserted art was considered during examination, including whether the prior art was the basis for rejection; (3) the cumulative nature of the asserted art and the prior art considered during examination; (4) whether Petitioner has pointed out sufficiently how the Examiner erred in its consideration of the asserted prior art; (5) the extent to which the arguments made during examination and the manner in which Petitioner relies on the prior art or the applicant's arguments during examination overlap; and (6) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the asserted prior art. *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, Case IPR2017-01586, slip op. at 17–18 (PTAB Dec. 15, 2017) (Paper 8) (informative). After considering all of the relevant factors and the parties' arguments, we are persuaded, for the reasons set forth below, that the Petition presents substantially the same arguments previously presented to the Office.

A. Relevant Prosecution History of the '640 Patent

The '640 patent issued from U.S. Patent Application Serial No. 15/048,851 ("P5") filed on February 19, 2016 as a continuation of U.S. Patent Application Serial No. 13/926,959 ("P4"), filed on June 25, 2013 as a continuation of U.S. Patent Application Serial No. 13/866,353 ("P3"), filed on April 19, 2013 as a continuation of U.S. Patent Application Serial No. 12/669,450 ("P2"), which is the national phase entry of PCT Application No. PCT/US2008/070124, filed on July 16, 2008. Ex. 1001, (21), (22), (63); *see* Pet. 8–9. P2 claims the benefit of priority to Provisional Application No. 60,959,907 ("P1"), filed on July 17, 2007. Ex. 1001, (60); Pet. 9.

During the prosecution of P4, pending claim 1, and claims 2–8, 10, 16, and 18 that depended, directly or indirectly, therefrom, were rejected for failing to comply with the written description requirement. Ex. 1008, 3.[1] Then-pending claim 1 is reproduced below:

1. (Currently Amended) A compound of formula (Ia)[[(Ic)]]:



(Ia)

or a pharmaceutically acceptable salt thereof,

wherein:

L_1 is a bond, $-N(R^{11})-$, $-N(R^{11})-C(X)-$, $-N(R^{11})-S(O)_2-$, $-N(R^{11})-C(NH)-$, $-N(R^{11})-C(X)-N(R^{11})-$, or $-N(R^{11})-S(O)_2-N(R^{11})-$;

X is O or S;

R^{11} is hydrogen or optionally substituted lower alkyl;

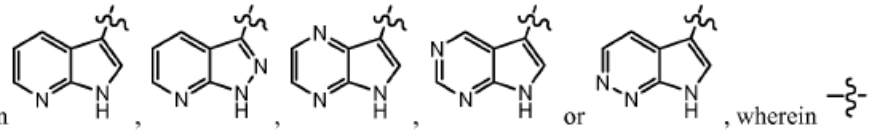
each R^1 is ~~independently selected from~~ optionally substituted lower alkyl or optionally substituted heteroaryl;

R^2 is hydrogen, lower alkyl, or halogen;

R^3 is optionally substituted aryl;

R^4 is hydrogen;

the subscript m is 0, 1, 2, 3, 4, or 5; and

Ar is optionally substituted heteroaryl, with the proviso that Ar is other than  , wherein indicates the point of the attachment to the phenyl moiety in formula (Ia)[[(Ic)]].

See id. at 5–6. The Examiner stated that "[t]he only disclosure, is in the form of general formula with lists of possible groups," and "[t]his kind of disclosure is not representati[ve] of any species." *Id.* at 6. The Examiner also stated that "[a]ll disclosed compounds have a linker moiety between the

[1] Citations to Exhibits 1004, 1005, and 1007–1017 are to the page numbers added by Petitioner to the bottom right-hand corner of the page.

phenyl and the Ar[,] i.e., L1 in formula I is not a bond," and P4 does not provide any "convincing evidence, or rationale that the biological activity of disclosed compounds would have been retained if the L1 in formula I is a bond instead of those linking moieties." *Id.* at 7. Therefore, according to the Examiner, "it is not understood what specific structures for the claimed variables will lead to compounds that have the instantly claimed activity." *Id.* at 7. Finally, the Examiner stated that

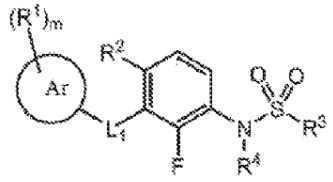
> [t]he structure/activity relationship (SAR) for binding and activity is elucidated upon analysis of IC_{50} data of multiple compounds with various types of structural modifications. These types of studies provide insight into the structural limitations that are required for activity, i.e.[,] specific structural elements tolerated for the claimed activity. In the absence of such correlation, it is not possible to determine what structural modifications will allow for the preservation of the desired activity.

Id.

In response, Applicant amended the claims "to be directed to a more focused genus of compounds." Ex. 1009, 6. The amended claims were also rejected for failure to comply with the written description requirement, for the same reasons set forth above. Ex. 1010, 3–8. In a subsequent Examiner Interview, the Examiner "agreed that the application has support for L1 as amide or a bond, and Ar as bicyclic nitrogen-containing heteroaryl with the proviso in the claims." Ex. 1011, 1 (emphasis omitted).

P5 was then filed as a continuation of P4, wherein claims 1–20 were cancelled and new claims 21–33 were added. Ex. 1014, 3–4. Claim 21 was the only independent claim, and is reproduced below:

21. (New) A compound of formula (Ia):



(Ia)

or a pharmaceutically acceptable salt thereof,

wherein:

L_1 is a bond, -N(H)C(O)-, -N(H)-, -N(H)-$S(O)_2$-, or -N(H)-C(NH)-;

each R^1 is optionally substituted lower alkyl or optionally substituted heteroaryl;

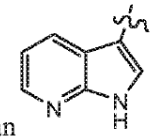
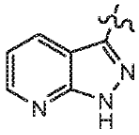
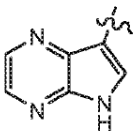
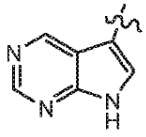
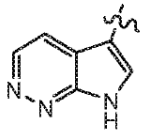
R^2 is hydrogen or halogen;

R^4 is hydrogen;

R^3 is optionally substituted lower alkyl or optionally substituted aryl;

m is 0, 1, 2, 3, 4, or 5; and

Ar is a monocyclic heteroaryl containing 5 to 6 atoms or a bicyclic heteroaryl containing 8 to 10 atoms wherein at least one atom is nitrogen,

with the proviso that Ar is other than  ,  ,  ,  or  , wherein indicates the point of the attachment to L_1.

Id. at 3. In the accompanying remarks, Applicant requested that "the Office review the Interview Summary of parent application [P4], filed on even date herewith," and noted that "the Office agreed that the application has support for L1 as amide or a bond, and Ar as nitrogen-containing bicyclic heteroaryl and monocyclic heteroaryl." *Id.* at 7. In the P4 Interview Summary, Applicant stated that

> numerous embodiments of the claimed compounds wherein L1 is a bond can be found throughout the specification, including but not limited to paragraphs [0007], [0009], and [0021]. Further, Scheme 2 provides exemplary methods of making compounds where L1 is a bond. The Office agreed that "the

> application has support for L1 as amide or a bond . . . [.]" Applicant-Initiated Interview Summary dated January 22, 2016.

Ex. 1012, 2. Thereafter, P4 went abandoned. Ex. 1013.

The Examiner rejected pending claims 21–33 in P5 as "failing to comply with the written description requirement," repeating the rationale from rejections of similar claims during the prosecution of P4. Ex. 1015, 3–7. In particular, the Examiner concluded that

> (i) substantial structural variation exists in the genus/subgenus embraced by claims 21-33; (ii) No disclosure of species supporting the genus; (iii) common structural attributes of the claimed genus/subgenus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art. Thus, the specification fails to provide adequate written description for the genus of compounds claimed and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, has possession of the entire scope of the claimed invention.

Id. at 7.

In response, Applicant amended claim 21 to recite that "L_1 is a bond or –N(H)C(O)–" and "Ar is a monocyclic heteroaryl containing 5 to 6 atoms wherein at least one atom is nitrogen," and cancelled claim 29. Ex. 1016, 2–3. In the accompanying remarks, Applicant stated that during an interview with the Examiner "the Office agreed that the application provides support for L_1 as amide or a bond and support for Ar as a monocyclic or bicyclic nitrogen-containing heteroaryl as discussed below and during the prosecution of the parent application" P4. *Id.* at 5. Applicant pointed to paragraphs [0007], [0009], [0011], and [0021] of the specification as providing "embodiments for claimed L_1, including L_1 is a bond," and further

pointed to Scheme 2 as providing "exemplary methods [for] making compounds where L_1 is a bond." *Id.* at 6.

In response to Applicant's amendment, a Notice of Allowability of pending claims 21–28 and 30–33 was issued. Ex. 1017. In the Reasons for Allowance, the Examiner stated that "[t]he amendments of the claims, limiting the Ar in general formula (Ia) to monocyclic heteroaryl, and the L1 is limited to a bond or –N(H)C(O)– is sufficient to overcome the rejections under 35 U.S.C. [§] 112, first paragraph as set forth in prior office action." *Id.* at 6.

B. Same or Substantially the Same Arguments

Petitioner contends that the challenged claims "are not entitled to the benefit of the July 16, 2008 filing date of P2 or the earlier provisional application because P2 does not satisfy the written description and enablement requirements of 35 U.S.C. § 112 (pre-AIA) as required for benefit under 35 U.S.C. § 120." Pet. 1. Petitioner contends that "P2 discloses enormous genera of chemical compounds which cover an effectively incalculable number of compounds, but provides no 'blaze marks' to direct a person of ordinary skill to the subgenera of the Challenged Claims." *Id.* at 1–2. Petitioner contends that "while the subgenera of the Challenged Claims cover trillions of compounds, there are only three examples in P2 that fall within the scope of the claims, and none where L_1 is a bond." *Id.* at 2. Petitioner further contends that "P2 does not enable a person of ordinary skill to *make* the full scope of compounds in these claims where L_1 is a bond, which constitute approximately half of the compounds covered by the claims." *Id.* at 41. According to Petitioner, P2 also "fails to disclose how to *use* such compounds where L_1 is a bond" because "P2

provides no data showing that any of the claimed compounds where L_1 is a bond has activity on kinase proteins and a person of ordinary skill would not have believed such compounds where L_1 is a bond would have such activity." *Id.* (citing Ex. 1002 ¶ 106).

Patent Owner responds that, during the prosecution of the '640 patent, "the Examiner explicitly consider[ed] the § 112 support for the challenged claims" and "addressed head-on the specific arguments about the L_1 substituent, which are now at the heart of Petitioner's case." Prelim. Resp. 9. In that regard, Patent Owner argues that the Examiner "rejected the claims several times because they 'read on numerous possible distinct species [and] there is no substantial feature shared by all species.'" *Id.* at 10 (quoting Ex. 2001, 4). Patent Owner argues that "the Examiner, like the Petitioner here, focused on the L_1 substituent," namely, when the L_1 substituent is a bond, and that "Applicant amended the claims to be directed to a more focused genus of compounds claiming L_1 as, *inter alia*, a bond, and identified where its amendments found support in the specification under § 112." *Id.* at 10–11 (citing Ex. 1008, 6–7; Ex. 1009, 2–5).

Patent Owner further argues that, in allowing the claims, the Examiner explicitly stated that "[t]he amendments of the claims, limiting the Ar in general formula (Ia) to monocyclic heteroaryl, ***and the L_1 is limited to a bond of –N(H)C(O)– is sufficient to overcome the rejections under 35 U.S.C. § 112, first paragraph***, as set forth in the prior office action." *Id.* at 12 (quoting Ex. 1017, 6). According to Patent Owner, because "the Office has already decided the dispositive § 112 issue and Petitioner has not presented any new argument or evidence to justify reaching a different

conclusion," the Board should "deny institution pursuant to § 325(d)." *Id.* at 15–16.

We agree with Patent Owner that Petitioner's arguments regarding whether P2 provides § 112 support for the challenged claims are substantially the same as those considered by the Examiner during the prosecution of the '640 patent.

As set forth above, the Examiner repeatedly rejected the pending claims because: (1) "[t]he only disclosure, is in the form of general formula with lists of possible groups," and "[t]his kind of disclosure is not representati[ve] of any species" (Ex. 1005, 9; Ex. 1008, 6; Ex. 1010, 6; Ex. 1015, 6); (2) "[a]ll disclosed compounds have a linker moiety between the phenyl and the Ar," but the application does not provide any "convincing evidence, or rationale that the biological activity of [the] disclosed compounds would have been retained if the L1 in formula I" vary with the scope defined in the pending claims (Ex. 1005, 9; Ex. 1008, 7; Ex. 1010, 6; Ex. 1015, 7); and (3) in the absence of information regarding "the structural limitations that are required for activity, i.e. specific structural elements tolerated for the claimed activity," "it is not possible to determine what structural modifications will allow for the preservation of the desired activity" (Ex. 1005, 9–10; Ex. 1008, 7; Ex. 1010, 7; Ex. 1015, 7). Here, Petitioner argues that: (1) P2 does not provide sufficient disclosure of the subgenera (i.e., species) (Pet. 1–2, 14–40); (2) "P2 does not guide one of ordinary skill to focus on" the bond or –N(H)C(O)– options for L_1, "particularly in combination with each of the other specific substituents in the Challenged Claims" (*id.* at 27–35); and (3) P2 does not provide information regarding activity data or other guidance to establish "that

compounds in which L_1 is a bond might work as kinase inhibitors, or for any other pharmacological purpose" (*id.* at 57; *see generally id.* at 56–61). We conclude that Petitioner's arguments are substantially the same as those considered by the Examiner during the prosecution of the '640 patent.

C. Discretion to Deny Institution of Trial

Petitioner contends that claims 1, 2, 4–6, 9, 11, and 12 of the '640 patent are unpatentable under 35 U.S.C. § 102(b) as anticipated by the '185 patent, which issued on August 9, 2011. Pet. 61–64. Petitioner's contentions are premised on its argument that the challenged claims are not entitled to the benefit of the July 16, 2008 filing date of P2 for failure to satisfy the requirements of § 112. *Id.* at 62 ("Because the Challenged Claims are not entitled to the benefit of the July 16, 2008 filing date of P2, their earliest possible priority date is April 19, 2013. As such, the Challenged Claims are anticipated under § 102(b) by the '185 patent, which issued on August 9, 2011, more than one year prior to the earliest possible priority date of the Challenged Claims."). Having found that the Petition raises the same arguments regarding § 112 as those previously considered by the Office, we now decide whether to exercise our discretion to deny institution under § 325(d).

Our discretion under § 325(d) involves a balance between several competing interests. *See Neil Ziegman, N.P.Z., Inc. v. Stephens*, Case IPR2015-01860, slip op. at 12–13 (PTAB Feb. 24, 2016) (Paper 11). "On the one hand, there are the interests in conserving the resources of the Office and granting patent owners repose on issues and prior art that have been considered previously." *Fox Factory, Inc. v. SRAM, LLC*, Case IPR2016-01876, slip op. at 7 (PTAB Apr. 3, 2017) (Paper 8). "On the other hand,

there are the interests of giving petitioners the opportunity to be heard and correcting any errors by the Office in allowing a patent—in the case of an *inter partes* review—over prior art patents and printed publications." *Id.*

As discussed in Section II(B) above, Petitioner relies on substantially the same arguments with respect to whether P2 provides § 112 support for the challenged claims as those considered by the Examiner during the prosecution of the '640 patent. Petitioner does not present any argument distinguishing the Office's previous decisions on substantially the same issues or to provide a compelling reason why we should readjudicate substantially the same arguments considered by the Examiner during prosecution. Petitioner argues that the Examiner failed to provide an explanation as to why he agreed that there was adequate support in the application for L_1 as a bond or amide, but does not point us to additional facts or evidence that would warrant our reconsideration of the arguments on the basis of Examiner error.[2] Pet. 33–35 ("[W]hile the Examiner ultimately did allow claims where L_1 is a bond, no meaningful reasons were provided to explain the change in position or basis for this allowance."). The Declaration of Phil S. Baran, Ph.D. (Ex. 1002), which Petitioner submitted to support the challenges presented in the Petition, does not provide additional evidence or facts that warrant reconsideration of the disclosures in

[2] We note that Petitioner also argues that "[t]he proper question is whether the entire claimed subject matter, including each specific selection of each of the variable (L_1, R^1, R^2, R^3, R^4, *m*, and Ar) in combination as they appear in the Challenged Claims, was disclosed in P2." Pet. 35. Given the Examiner's thorough consideration of the § 112 support for L_1 and Ar, we infer the Examiner did not consider such support to be lacking for the other listed variables.

P2 that are substantially the same as the disclosures already considered by the Office.

We recognize that Petitioner has a direct interest in pursuing the instant Petition, but we also recognize the burden and expense to Patent Owner in having to defend the '640 patent based on substantially the same arguments already considered by the Office. We find that the disclosures in P2 were substantively considered by the Examiner with respect to whether the challenged claims met the requirements of § 112, and that we have been shown no reason sufficient to reevaluate those disclosures with respect to any of the challenged claims. *See Unified Patents Inc. v. John L. Berman*, Case IPR2016-01571, slip. op. at 12 (PTAB Dec. 14, 2016) (Paper 10) (informative); *see also Cultec, Inc. v. StormTech LLC*, Case IPR2017-00777 (PTAB Aug. 22, 2017) (Paper 7) (informative) (denying institution of *inter partes* review under § 325(d) because the same or substantially the same prior art or arguments previously were presented to the Office during prosecution); *Hospira, Inc. v. Genentech, Inc.*, Case IPR2017-00739 (PTAB July 27, 2017) (Paper 16) (informative) (denying institution of *inter partes* review under § 325(d) because the Office already decided the dispositive issue of whether the asserted references qualified as prior art with respect to the challenged patent). Consequently, we exercise our discretion and decline to institute review of claims 1, 2, 4–6, 9, 11, and 12 under 35 U.S.C. § 102 as anticipated by the '185 patent.

III. CONCLUSION

Based on the arguments in the Petition and the Preliminary Response, and the evidence of record, we conclude that the instant Petition raises the

same or substantially the same arguments as those previously presented to and considered by the Office. In light of the circumstances of the present case, we exercise our discretion under 35 U.S.C. § 325(d) and decline to institute *inter partes* review of the '640 patent.

IV. ORDER

In consideration of the foregoing, it is hereby

ORDERED that the Petition is *denied*.

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