Trials@uspto.gov
571-272-7822

Paper 17
Date: August 7, 2023

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SANDOZ INC.,
Petitioner,

v.

ACERTA PHARMA B.V.,
Patent Owner.

IPR2023-00478
Patent 10,272,083 B2

Before ULRIKE W. JENKS, ZHENYU YANG, and RYAN H. FLAX, *Administrative Patent Judges*.

JENKS, *Administrative Patent Judge*.

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

I. INTRODUCTION

Sandoz, Inc. ("Petitioner") filed a petition to institute *inter partes* review of claims 8–12, 19, and 20 of U.S. Patent No. 10,272,083 B2 (Ex. 1001, "the '083 patent"). Paper 1 ("Pet."). Acerta Pharma B.V. ("Patent Owner") filed a Preliminary Response. Paper 10 ("Prelim. Resp."). With our authorization (Ex. 3003) Petitioner filed a Reply to Patent Owner's Preliminary Response (Paper 13 ("Reply")) and Patent Owner filed a Sur-reply (Paper 14 ("Sur-reply")).

The Board has discretion to determine whether to institute *inter partes* review. *See* 35 U.S.C. § 314 (2022); 37 C.F.R. § 42.4(a) (2022). Under 35 U.S.C. § 325(d), "in determining whether to institute [*inter partes* review], 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."

For the reasons stated below, we determine that the same or substantially the same prior art or arguments previously were presented to the Office and Petitioner has failed to show material error in the consideration of that art or argument. *Advanced Bionics, LLC v. Med-El Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8–9 (PTAB Feb. 13, 2020) (precedential)("*Advanced Bionics"*). We, therefore, deny institution of *inter partes* review.

II. BACKGROUND

A. Related Matters

The parties identify the following district-court proceedings as related matters involving the '083 patent: *Acerta Pharma BV v. Cipla Ltd.,* No. 1-22-cv-00162 (D. Del.); *Acerta Pharma BV v. MSN Pharms. Inc.,* No.

1-22-cv-00163 (D. Del.); *Acerta Pharma BV v. Sandoz Inc.*, No. 1-22-cv-00164 (D. Del.); *Acerta Pharma BV v. Alembic Pharms. Ltd.*, No. 1-22-cv-00154 (D. Del.); *Acerta Pharma BV v. Natco Pharma Ltd.*, No. 1-22-cv-00155 (D. Del.). Pet. 3; Paper 4, 2 (Patent Owner's Mandatory Notices).

B. Real Parties in Interest

Petitioner identifies the real party in interest as Sandoz, Inc. Pet. 3. Patent Owner identifies Acerta Pharma B.V., AstraZeneca UK Limited, AstraZeneca Pharmaceuticals LP, and AstraZeneca AB as real parties in interest. Paper 4, 1.

C. Overview of the '083 patent (Ex. 1001)

The '083 patent, titled "Methods of Treating Chronic Lymphocytic Leukemia and Small Lymphocytic Leukemia using a BTK Inhibitor," relates to methods of treating leukemia. Ex. 1001, code (54), (57). "Bruton's Tyrosine Kinase (BTK or Btk) is a TEC[1] family non-receptor protein kinase expressed in B cells and myeloid cells." Ex. 1001, 1:14–16. "The reported role for BTK in the regulation of proliferation and apoptosis of B cells indicates the potential for BTK inhibitors in the treatment of B cell lymphomas. BTK inhibitors have thus been developed as potential therapies." *Id.* at 1:28–32.

Potential therapeutic targets include B cell chronic lymphocytic leukemia (CLL) and the closely related small lymphocytic leukemia (SLL)

[1] The TEC family is a subfamily of non-receptor protein-tyrosine kinases (PTKs) represented by its first member, Tec. Tec kinase is an integral component of T cell signaling and has a distinct role in T cell activation. *See* https://www.ncbi.nlm.nih.gov/gene/7006 (last visited July 24, 2023).

that show rapid cell accumulation and resistance to apoptosis. *See id.* at 1:34–52. The '083 patent also contemplates treating the following hematological malignancies: non-Hodgkin's lymphoma (NHL), diffuse large B cell lymphoma (DLBCL), follicular lymphoma (FL), mantle cell lymphoma (MCL), Hodgkin's lymphoma, B cell acute lymphoblastic leukemia (B-ALL), Burkitt's lymphoma, Waldenstrom's macroglobulinemia (WM), multiple myeloma, or myelofibrosis. *Id.* at 4:25–32.

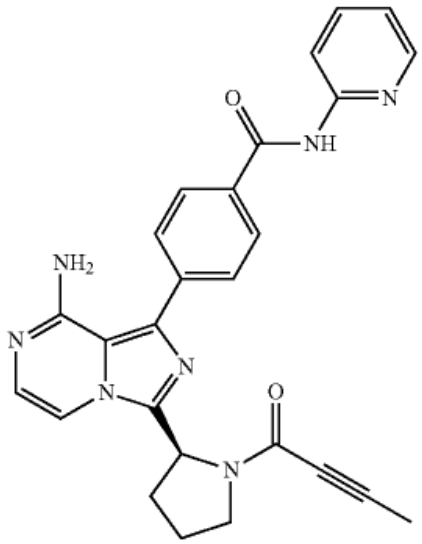
The BTK inhibitor according to the '083 patent is (S)-4-(8-amino-3-(1-(but-2-ynoyl)pyrrolidin-2-yl)imidazo[l ,5-a] pyrazin-1-yl)-N-(pyridin-2-yl)benzamide (Formula II) or a pharmaceutically acceptable salt, solvate, hydrate, cocrystal, or prodrug thereof. *Id.* at 4:21–25. The inhibitor is administered twice daily at a dose of 100 mg. *Id.* at 4: 31–33. Treatment using the Formula II inhibitor may be "continued for >28 days until disease progression or an unacceptable drug-related toxicity occurs." *Id.* at 59:37–39. "The BTK inhibitor of Formula (II) shows much greater selectivity for BTK compared to other kinase[]" inhibitors such as ibrutinib. *Id.* at 57: 22–24. According to the '083 patent "[i]n vitro and in vivo safety pharmacology studies with Formula (II) have demonstrated a favorable nonclinical safety profile." *Id.* at 57:48–50.

D. The Challenged Claims

Petitioner challenges claims 8–12, 19, and 20 of the '083 patent. Pet. 5. Independent claim 8, reproduced below, is illustrative of the subject matter recited in the challenged claims.

> 8. A method of treating a mantle cell lymphoma (MCL) in a human subject suffering therefrom comprising the step of orally administering, to the human subject, a dose of 100 mg twice daily

of a BTK inhibitor, wherein the BTK inhibitor is a compound of Formula (II):[2]



or a pharmaceutically-acceptable salt, hydrate, or solvate thereof.

Ex. 1001, 100:39–65.

[2] The compound of Formula (II) is also known as acalabrutinib. *See* Ex. 1002 ¶¶ 14, 17, 42 ("the '083 patent discloses . . . administering a compound of 'Formula (II),' which is the name that the '083 patent uses for the compound that is known today as acalabrutinib"), ¶ 77 (citing Ex. 1004, 994).

E. Asserted Grounds of Unpatentability

Petitioner asserts the following grounds of unpatentability of claims 8–12, 19, and 20 of the '083 patent:

Claim(s) Challenged	35 U.S.C. §	Reference(s)
8–12, 19, 20	103[3]	Barf,[4] Cheson[5]
8–12, 19, 20	103	Barf-PCT,[6] Cheson

Pet. 5. In support of its patentability challenge, Petitioner relies on, *inter alia*, the Declaration of John P. Fruehauf, M.D. Ph.D. Ex. 1002. Patent Owner disputes Petitioner's asserted grounds of unpatentability. *See generally* Prelim. Resp.

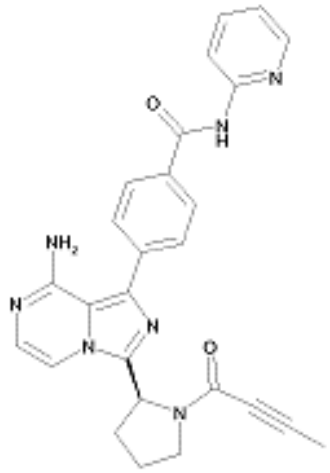
F. The Prior Art

We provide brief summaries of Petitioner's asserted references below.

1. Barf-PCT (Ex. 1006)

Barf-PCT discloses a genus of BTK inhibitor compounds and exemplifies 133 compounds in that genus. *See* Ex. 1006, 77–93. Example 6 discloses the following compound:

[3] The Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) ("AIA"), amended 35 U.S.C. § 103. Petitioner states that "[t]he '083 patent was filed in 2015 and claims priority to provisional applications filed in 2014 (EX1001, 1), after the effective date of March 16, 2013, . . . Thus, this Petition applies the AIA version of Title 35." Pet. 5, fn. 1.
[4] Barf et al., US 9,758,524 B2, issued Sept. 12, 2017 (Ex. 1005).
[5] Cheson (chairman), 11 HEMATOLOGY & ONCOLOGY SUPPLEMENT 12 (International Conference on Malignant Lymphoma: Advancements in the Treatment of B-Cell Malignancies (June 18, 2013)) (Ex. 1008).
[6] Barf et al., WO 2013/010868 A1, published January 24, 2013 (Ex. 1006).



Reproduced above is the structure of the compound that is now known as acalabrutinib[7] having the following chemical name: (S)-4-(8-amino-3-n-but-2-vnoylpyrrolidin-2-vnimidazo[1,5-alpyrazin-1-yl)-N-(pyridin-2-yl)benzamide. *Id.* at 1 (code (54)), 10:19–16:27, 35:16–36:2 (Example 6). Barf-PCT discloses that its compounds "can be used in therapies to treat or prevent [ ] Bruton's Tyrosine Kinase (Btk) mediated disorders." *Id.* at 21:19–20. "Proliferative diseases that can be treated or prevented include, among others, non-Hodgkin lymphoma (in particular the subtypes diffuse large B-cell lymphoma (DLBCL) and mantle cell lymphoma (MCL)), B cell chronic lymphocytic leukemia and acute lymphoblastic leukemia (ALL) with mature B cell, ALL in particular." *Id.* at 22:15–18.

Barf-PCT provides tables containing data related to the exemplified compounds' potency against several enzymes, including BTK. Barf-PCT discloses that "[a]ll compounds of the invention have an EC50[8] of 10 mM or lower" for inhibiting Btk kinase activity. *Id.* at 16:35–36.

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[7] *See above* note 1.

[8] "The term EC50 means the concentration of the test compound that is required for 50% inhibition of its maximum effect in vitro." Ex. 1006, 17:4–5.

Dosing information in Barf-PCT is general to all the compounds in the specification, and broadly discloses "a dosage for humans preferably contains 0.0001-25 mg per kg body weight." *Id.* at 20:16, 20:24–25. Barf-PCT discloses that administration may be as a single daily dose "or as multiple subdoses administered at appropriate intervals throughout the day, or, in case of female recipients, as doses to be administered at appropriate daily intervals throughout the menstrual cycle." *Id.* at 20:25–27.

2. Barf (Ex. 1005)

Barf has the same specification as Barf-PCT, including the same disclosed genus of compounds, the same broad and general dosing information related to that genus, the same disclosure that compounds in the genus are useful in treating BTK-mediated disorders including MCL, the same example compounds, and the same tables containing EC50 potency data. *See e.g.* Ex. 1005, 9:9–14:26, 17:62-18:1, 19:39–41, 27:36–74:49, 145:1–24 (Table 1).

3. Cheson (Ex. 1008)

Cheson[9] is a compilation article from the International Conference on Malignant Lymphoma held on June 18, 2013. Cheson teaches that the Btk inhibitor "[i]brutinib has demonstrated activity in a variety of B-cell malignancies, including indolent non-Hodgkin lymphoma (NHL), [chronic

[9] The compilation article contains chapters from various authors including John G. Gribben, MD, DSc, FMedSci ("B-Cell Receptor Pathway Inhibitors – Rationale and Potential"); Bruce D. Cheson, MD ("The Potential for Eliminating Chemotherapy in Indolent Non-Hodgkin Lymphoma"); Susan O'Brien, MD ("The Changing Landscape in CLL"); and Andre Coy, MD ("Mantle Cell Lymphoma: The Changing Landscape"). The article is collectively referred to as "Cheson."

lymphocytic leukemia] CLL, and mantle cell lymphoma (MCL)." Ex. 1008, 4. Cheson teaches that ibrutinib is a small-molecule inhibitor of key B-cell receptor signaling pathways. Figure 4 in Cheson is reproduced below:

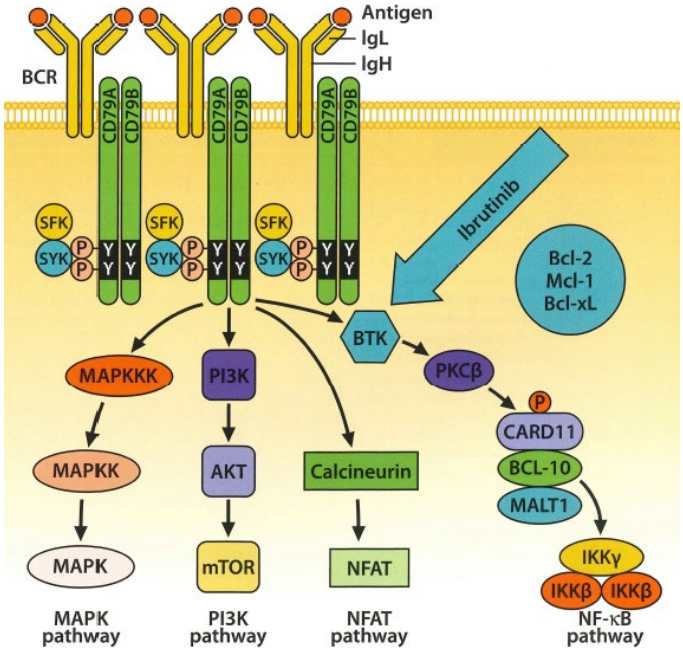

Figure 4 shows the location of the target for the small-molecule inhibitor ibrutinib in the B-cell receptor signaling pathway. *Id.* at 6. "[T]he BTK inhibitor ibrutinib (Figure 4) demonstrated antitumor activity in patients with various relapsed/ refractory B-cell malignancies." *Id.* at 7.

Cheson teaches that "[m]antle cell lymphoma [(MCL)] is an aggressive, biologically heterogeneous lymphoma subtype that is typically associated with a poor prognosis." *Id. at* 11. "The BTK inhibitor ibrutinib has also been evaluated in MCL[, a]fter a phase 1 study suggested antitumor activity of ibrutinib in MCL." *Id.* at 14.

III. DISCRETIONARY DENIAL UNDER 35 U.S.C. § 325(d)

Patent Owner argues that we should exercise our discretion under § 325(d) and deny institution. Prelim. Resp. 19–45. Specifically, Patent

Owner argues that the same or substantially the same prior art and arguments that Petitioner relies on for its grounds of unpatentability—namely, Barf, Barf-PCT, and Cheson—were presented previously to the Office. *Id.* at 19. Patent Owner argues that Barf-PCT is the international application counterpart of Barf, containing the same disclosures as Barf, including acalabrutinib, treating MCL, and the overlapping dosing range. *Id.* at 20.

Petitioner argues that "Barf (EX1005), was not before the Examiner" and specifically that the claims in Barf are not part of Barf-PCT and therefore not before the Examiner. Reply 1; Pet. 26 ("Barf and Barf-PCT share the same material disclosure; only their claims are different."). Petitioner further contends that Examiner cited Barf-PCT "only as a secondary reference in combination with two other references—Smyth and Evarts—that Petitioner does not rely on." Reply 2; Pet. 68. Petitioner argues that, "[e]ven where a petition relies on the same prior art cited during prosecution, panels have repeatedly instituted review where, as here, the petition addresses alleged unexpected results that were the basis for allowance." Reply 4; *see* Pet. 54–66.

A. Legal Standard

Section 325(d) provides that the Director[10] may "reject the petition" if "the same or substantially the same prior art or arguments previously were presented to the Office." The Board analyzes this issue under a two-part framework:

> (1) [determining] whether the same or substantially the same art previously was presented to the Office or whether the same or

[10] The Board institutes trial on behalf of the Director. 37 C.F.R. § 42.4(a).

> substantially the same arguments previously were presented to the Office; and (2) if either condition of [the] first part of the framework is satisfied, [determining] whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims.

Advanced Bionics, Paper 6 at 8.

In analyzing whether the same or substantially the same art or arguments were previously presented to the Office, we consider factors including: (i) the similarities and material differences between the asserted art and the prior art previously presented to the Office; (ii) the cumulative nature of the asserted art and the prior art previously evaluated by the Office; and (iii) the extent of the overlap between the arguments made before the Office and the manner in which the petitioner relies on the prior art or the patent owner distinguishes the prior art. *Id.* at 8–10; *see also Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8, 17–18 (Dec. 15, 2017) (precedential as to § III.C.5, first paragraph) ("*Becton, Dickinson*").

In analyzing whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims, we consider factors including: (iv) the extent to which the asserted art was evaluated by the Office, including whether the prior art was the basis for rejection during examination; (v) whether the petitioner has pointed out sufficiently how the Office erred in its evaluation of the asserted prior art; and (vi) the extent to which additional evidence and facts presented in the petition warrant reconsideration of prior art or arguments. *Advanced Bionics*, 8–10; *Becton, Dickinson*, 17–18.

B. Analysis

1. Part 1: Whether the same or substantially the same art or arguments were presented previously to the Office

The first part of the *Advanced Bionics* framework requires us to determine whether the Petition advances the same or substantially the same art or arguments that were previously presented to the Office. *Advanced Bionics*, 8. For the reasons explained below, we determine that the same or substantially the same art was previously presented, and thus, the first part of the framework is satisfied.

Petitioner relies on three references in its asserted grounds of unpatentability: Barf, Barf-PCT, and Cheson. Pet. 5. Petitioner argues that "[t]he Examiner did not consider Barf's claims" and that the Barf-PCT was only considered "as a secondary reference in combination with Smyth '172 and Evarts, which Petitioner does not rely on." *Id.* at 68. Petitioner cites Barf (and Barf-PCT) as teaching that "doses within its range 'may be presented as one dose or multiple subdoses administered at appropriate intervals throughout the day.'" *Id.* at 40 (citing Ex. 1005, 17:63–66), *see id.* at 52 ("Barf-PCT's teaching of 'multiple subdoses administered at appropriate intervals throughout the day'"). Petitioner additionally cites "Cheson[, which] teaches that 'BTK inhibitors are being evaluated in a twice-daily schedule in an attempt to overcome the synthesis of new BTK molecules within those cells.'" *Id.* at 40 (citing Ex. 1008, 4; Ex. 1002 ¶ 144), *id.* at 52 (citing Ex. 108, 4, 10; Ex. 1002 ¶ 196).

Patent Owner argues that Barf, Barf-PCT, and Cheson "are identical to or substantially the same as the prior art references presented to the Office during the prosecution of the '083 patent." Prelim. Resp. 19–20. We agree, as explained below.

There can be no dispute that Barf-PCT was before the Office. Barf-PCT was listed on a form PTO-892 by the Examiner and is listed on the face of the '083 patent as a considered-reference. Ex. 1004, 911 (entry N); Ex. 1001, code (56). Moreover, the Examiner was aware of the international search report and written opinion for PCT/IB2015/000645 which is the national stage benefit application of the '083 patent from which the '083 patent claims priority benefit. *Id.* at 1052 (entry 32, 33). The search report and written opinion listed the Barf-PCT as relevant to the claimed subject matter. *Id.* at 967, *see also id.* at 955 ("D1 [WO 2013/010868 (which is Ex. 1006)] discloses the use of Btk inhibitors in the treatment of Btk-mediated disorders (abstract)"). The Examiner certified that all references listed in the IDS "except where lined through" were considered, and PCT/IB2015/000645 search report and written opinion are not lined through. *Id*. Additionally, the Examiner cited Barf-PCT in an office action indicating that the disclosed BTK inhibitor compounds are useful in treating various inflammatory conditions including cancers including such as lymphomas. *Id.* at 909, 1035. Accordingly, Barf-PCT is "[p]reviously presented art." *See Advanced Bionics*, 7–8 (indicating that "previously presented art" includes "art made of record by the Examiner").

On the other hand, Barf and Cheson were not, themselves, before the Office during examination of the application that issued as the '083 patent and therefore are not the "same art" previously presented to the Office. *Advanced Bionics*, 13–14. But, Patent Owner argues, art substantially similar to these references was before the Office during examination. *See* Prelim. Resp. 11–22. Patent Owner argues that "Barf has the same specification as Barf-PCT, . . . [t]he only difference between Barf and

Barf-PCT are their claims," and that "Barf-PCT is the international[11] application counterpart to Barf," and "provides the same disclosures as Barf, including acalabrutinib, treating MCL, and the overlapping dosing range."; *Id.* at 11, 20. Patent Owner also argues that "Cheson is substantially the same as, and cumulative of, other references the Examiner cited during prosecution as teaching twice-daily administration." *Id.* at 22.

As to Barf,[12] Patent Owner argues that "Barf and Barf-PCT have identical specifications, including the same dosing language of '0.0001-25 mg per kg body weight' which Sandoz cites from Barf's specification and claim 12." *Id.* at 21, *see also id.* at 26 ("Barf and Barf-PCT share the same material disclosure; only their claims are different"). Patent Owner contends that the Board has found references to be substantially similar when their specifications are the same, but their claims are different. Prelim Resp. 21 (citing "*Alarm.com, Inc., v. Vivint, Inc.*, IPR2022-00728, Paper 6 at 19-20 (P.T.A.B. Nov. 1, 2022); *Ivantis, Inc. et al v. Sight Sciences, Inc.* IPR2022-01530, Paper 14 at 13-14 (P.T.A.B. Mar. 27, 2023)). Patent Owner asserts that "Examiner's rejections reflect that he understood and found that Barf-PCT itself disclosed acalabrutinib in an example, and disclosed its use in treating 'cancers including lymphomas,' even if it did not include a specific claim to that subject matter." Prelim Resp. 21 (citing Ex. 1004, 909, 1034–35; Ex. 1006, 22:15–16, 35:15–36:2). Having considered the record,

[11] Petitioner acknowledges that Barf-PCT is the international application counterpart to Barf, published in 2013. Pet. 2.
[12] Patent Owner additionally asserts that "Barf is not prior art because it is exempt as joint research subject matter under 35 U.S.C. § 102(b)(2)(C) and § 102(c)." Prelim. Resp. 20. Because the petition is denied we do not need to resolve this issue.

we agree with Patent Owner that, because Barf is nearly identical to Barf-PCT in its disclosure – Barf is "substantially the same art" as Barf-PCT, which was previously presented to the Office. *Advanced Bionics*, 8.

As to Cheson, Patent Owner argues that this reference is "used solely to argue that the 'twice-daily' limitation is obvious." Prelim Resp. 22. Patent Owner contends that, during the prosecution of the '083 patent, "in both office actions, the Examiner relied on Smyth which he noted taught 'BTK inhibitors similar to those recited in the instant claims' administered orally 'as much as 2 to 4 times a day.'" Prelim Resp. 23 (citing Ex. 1004, 908–909, 1034). Patent Owner explains that the Examiner additionally "relied on Evarts as teaching 'specific dosage amounts' to treat MCL, including an express teaching that '[t]he dosage form can be administered twice daily,' to 'provide an optimal treatment regimen.'" *Id.*

Having considered the record, acknowledging Petitioner's point that Cheson was not actually of record during prosecution, we agree with Patent Owner that Cheson is cumulative to the teaching in Smyth and Evarts relied on by the Examiner for multiple daily dosing of a BTK inhibitor and, therefore, is "substantially the same art" as that previously presented to the Office. *Advanced Bionics*, 8.

We are not persuaded by Petitioner's contention that the teachings in Barf-PCT, Smyth, and Evarts directed to administering a BTK inhibitor over multiple doses throughout the day are not cumulative to the teaching in Cheson. *See* Reply 2 ("'BTK inhibitors are being evaluated in a twice daily schedule in an attempt *to overcome the synthesis of new BTK molecules*,' which 'appeared to be *more effective*, perhaps with *more rapid responses*,'

than once-daily dosing"). Cheson may have provided additional explanation on why multiple dosing may be preferred. Ex. 1008, 4 (use of a twice daily administration schedule to overcome new BTK molecule synthesis), 10; Pet. 40–41. However, scientific explanation for the cellular response to a multiple dosing regimen of a BTK inhibitor that was already suggested in the art does not detract from that teaching already of record in Barf-PCT, Smyth, and Evarts.

For these reasons, we determine that all the references that Petitioner asserts in the Petition (i.e., Barf, Barf-PCT, and Cheson) are the same or substantially the same art that were previously presented to the Office. Accordingly, we determine that the first part of the *Advanced Bionics* framework is satisfied.

2. Part 2: Whether the Petitioner Demonstrates Material Error

Next, we consider "whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims." *Advanced Bionics*, 8. Patent Owner argues that "Petitioner has not demonstrated that the Office erred." Prelim. Resp. 28 (citing *Advanced Bionics*, 8–9). Patent Owner also argues that Petitioner "has not come close to demonstrating that the Examiner's treatment of the art or arguments was unreasonable, much less incorrect." *Id.*

Petitioner argues that "the Examiner erred in considering Barf-PCT. The Examiner repeatedly found acalabrutinib disclosed in Example 1, which is incorrect, and did not consider Example 6 that actually discloses it." Pet. 68. Petitioner argues that Examiner materially erred in allowing the claims. Reply 3. Specifically, Petitioner contends that the alleged unexpected results with twice daily dosing of 100 mg as asserted during

prosecution led to error because that result is expected. *See id.* at 3–4 (citing Pet. 55–63; Ex. 1002 ¶¶ 227–244; Ex. 1017, 5, 20; Ex. 1009, 12).

Patent Owner acknowledges that the Examiner misidentified acalabrutinib as appearing in Example 1, rather than Example 6, of Barf-PCT. Prelim. Resp. 14, fn 3 (citing Ex. 1004, 909). During prosecution, however, Patent Owner alerted the Examiner to the fact that the compound of "Formula (II) specified in the pending claims is not identical to the compound of Example 1 of the '868 application [Ex. 1006]. Applicant note[d] for the record, however, that the compound of Formula (II) is disclosed as Example 6 on page 30 of the '868 application [Ex. 1006]." Ex. 1004, 997. Thus, the Examiner's initial misidentification during prosecution, when considered in light of Patent Owner's rectifying that misidentification is not ultimately a mistake, as alleged by Petitioner, giving rise to error material to patentability. Accordingly, we agree with Patent Owner that "[t]he Examiner's rejections reflect that he understood and found that Barf-PCT itself disclosed acalabrutinib in an example, and disclosed its use in treating 'cancers including lymphomas.'" Prelim. Resp. 21.

Patent Owner (then applicant) submitted evidence of unexpected results during prosecution in order to overcome the Examiner's finding of obviousness. Specifically, Patent Owner submitted Byrd (Ex. 1010) to support the position that providing continuous BTK target occupancy of greater than 95% over a 24-hour period can be achieved with twice daily dosing of acalabrutinib using a significantly lower dose as compared to ibrutinib. *See* Ex. 1004, 1000–1002, 1004; Sur-reply 2–3 (citing Byrd (Ex. 1010)).

According to Byrd,

> [t]he short half-life and selective properties of acalabrutinib allow twice-daily dosing with virtually complete and continuous BTK inhibition without increased toxic effects. Thus far, twice-daily dosing of ibrutinib has not been pursued and may not be possible owing to the potential for drug accumulation given the ibrutinib half-life of 4 to 13 hours.

Ex. 1004, 1001; Ex. 1010, 9. Byrd additionally teaches that "the safety profile of acalabrutinib was also favorable, despite prolonged, continuous administration. Adverse events were mostly grade 1 or 2 and selflimiting, and most resolved over time." Ex. 1010, 9. Acalabrutinib also does not inhibit EGFR, ITK, and TEC kinase, and no cases of atrial fibrillation have been associated with the drug. *Id.*

Because the Examiner allowed the claims it is reasonable to conclude that Examiner found this evidence sufficiently persuasive to overcome the rejection over Barf-PCT. Ex. 1004, 1382; Sur-reply 3. Specifically, the Examiner, in the notice of allowance, found that

> other BTK inhibitor compounds, are known in the prior art, they differ[] chemically from the instant invention. Further the 100 mg, twice daily oral dosage i[s] unexpectadtly superior for BTK inhibition without increase[d] toxicity. The close[s]t[] chemical compound in the prior art is ibrutinib, but the half[]life is such that a twice daily dosage would not be effective.

Ex. 1004, 1382. In other words, the Examiner relied on the superior safety profile of acalabrutinib as the reason for allowing the claims over the prior art (noted above as the same or substantially the same art as that asserted now).

Finally, we are also not persuaded by Petitioner's contention that the Examiner failed to consider Advani (Ex. 1009) or FDA's pharmacology

reviews (Ex. 1017), which Petitioner alleges has a bearing on the argued unexpected results during prosecution. Reply 4. Petitioner cites Advani or FDA's pharmacology reviews in conjunction with their expert declaration to support that the claimed dosing regime is obvious. *See* Pet. 32 (citing Ex. 1002 ¶ 122; Ex. 1009, 9–12). However, neither ground of unpatentability asserted by Petitioner relies on Advani or FDA's pharmacology reviews.

As Patent Owner points out, Advani was cited "in the provisional application to which the '083 patent claims priority," as well as in the Specification of the '083 patent. Sur-Reply 3 (citing Ex. 1004, 527, 573; Ex. 1001, 56:19–26, 72:3–12). Patent Owner further asserts that "[t]he data in the FDA review that Sandoz and its expert cite is the same Advani data." *Id.* at 4 (citing Pet. 19–20, Reply 4). That Petitioner, and Petitioner's expert, cite different references to teach twice daily dosing scheme does not convince us that the Examiner materially erred. Here, the Examiner cited Evarts (Ex. 1034 (U.S. Patent Application Publication No. 2014/0179673) for treating mantle cell leukemia with a BTK inhibitor by orally administering 100–150 mg of an active agent twice daily. Ex. 1004, 1035. We find that Petitioner's reliance in the Petition on references that are not part of the prosecution record considered by the Examiner, and are not even asserted against the claims in Petitioner's asserted grounds for unpatentability as set out in the Petition, fails to demonstrate "that the Office erred in a manner material to the patentability of challenged claims." *Advanced Bionics*, 8–9.

Having considered the record, we agree with Patent Owner that Petitioner has failed to demonstrate that the Office erred in its evaluation of

the cited art (now asserted) as required by *Advanced Bionics*. *Advanced Bionics* cautions that "[i]f reasonable minds can disagree regarding the purported treatment of the art or arguments, it cannot be said that the Office erred in a manner material to patentability." Paper 6, 9. *Advanced Bionics* also explains the rationale for this rule: "At bottom, this framework reflects a commitment to defer to previous Office evaluations of the evidence of record unless material error is shown." *Id.* Here, we discern no error in the Office's previous consideration of the prior art of record during prosecution, which is the same and/or substantially the same as that asserted here. We find that Petitioner's reliance on the Examiner's citation to a reference's Example 1 instead of its Example 6, and then being expressly corrected on the mistake on the record, followed by an allowance of the claims, does not demonstrate "that the Office erred in a manner material to the patentability of challenged claims." *Advanced Bionics*, 8–9 ("If a condition in the first part of the framework is satisfied and the petitioner fails to make a showing of material error, the Director generally will exercise discretion not to institute inter partes review.").

C. Summary

For the reasons discussed above, we determine that both parts of the two-part framework of *Advanced Bionics* are satisfied. Thus, we exercise our discretion pursuant to 35 U.S.C. § 325(d) to deny institution of trial.

IV. MOTION FOR LEAVE TO FILE CERTIFICATE OF CORRECTION

On May 23, 2023, we granted Patent Owner authorization to file a motion for leave to file a Certificate of Correction. Ex. 3002. Patent Owner seeks correction for the '083 patent to reference a written joint research

agreement ("JRA") between Acerta's predecessor-in-interest and a third party, MSD Oss BV ("Merck"). Mot. 1 (citing *Honeywell Int'l Inc. v. Arkema Inc.*, 939 F.3d 1345, 1349 (Fed. Cir. 2019)).

The '083 patent claims priority to several provisional applications. Provisional application No. 62/035,777, filed on August 11, 2014, provisional application No. 61/974,665, filed on April 3, 2014, and provisional application No. 61/929,742, filed on January 21, 2014. Ex. 1001, code (60). Patent Owner asserts that the "invention disclosed in the '083 patent is the subject of a timely, written joint research agreement, EX2004, but the patent mistakenly does not reference it." *Id.* Patent Owner asserts that the JRA was effective by January 21, 2014, which is the '083 patent's earliest effective filing date. Patent Owner submits a copy of its JRA with MSD Oss BV (a predecessor-in-interest to Merck Sharp & Dohme B.V.) (Ex. 2004), and identifies the text it proposes to insert at the beginning of the '083 patent specification (Mot. 4). The correction sought could bear on whether art cited in the Petition (Ex. 1005) is prior art to the '083 patent. Pet. 5; Prelim. Resp. 18; Mot. 3–4; Opp. 1.

Petitioner opposes Patent Owner's Motion. Specifically, Petitioner argues that Patent Owner's failure to disclose Merck on the face of the '083 patent was not a mistake made in good faith. Opp. 2. According to Petitioner, Patent Owner does not provide any evidence in support of the assertion that the mistaken omission was inadvertent. *Id.* Additionally, "Patent Owner has not identified when it allegedly discovered its 'mistake,' so there is no basis (let alone a sufficient basis) to evaluate Patent Owner's 'good faith' in seeking correction." *Id.* at 3.

Our role, however, is not to decide whether Patent Owner's request for a certificate of correction is meritorious; instead, we are tasked with simply assessing whether there is a sufficient basis to support Patent Owner's position. If so, it is up to the Director to decide whether to exercise the authority under § 255 and issue a certificate of correction. We have reviewed the arguments in the Motion and conclude that "there is a sufficient basis supporting Patent Owner's position that the mistake may be correctable." *Honeywell*, 939 F.3d at 1349.

However, because as discussed above (*see supra* Section III), we deny institution here pursuant to our discretion under Section 325(d), we find that whether Barf is or is not prior art is immaterial to this proceeding and Patent Owner's request and any certificate of correction here is moot. Therefore, we *deny* as moot the Motion for leave to file a Certificate of Correction.

V. CONCLUSION

Having considered the Petition, the Preliminary Response, and the evidence of record, we exercise our discretion under 35 U.S.C. § 325(d) and deny institution. Accordingly, the Petition is *denied*, and no trial is instituted.

VI. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is *denied*, and no trial is instituted;

FURTHER ORDERED that Patent Owner's Motion for leave to file Certificate of Correction is *denied*.

For PETITIONER:

Jovial Wong
WINSTON & STRAWN LLP
jwong@winston.com

For PATENT OWNER:

Stanley Fisher
David Berl
WILLIAMS & CONNOLLY LLP
sfisher@wc.com
dberl@wc.com