UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SANDOZ INC.,
Petitioner,

v.

ACERTA PHARMA B.V.,
Patent Owner.

Case IPR2023-00478
Patent 10,272,083 B2

PETITIONER'S AUTHORIZED REPLY TO PATENT OWNER'S PRELIMINARY RESPONSE

I. Patent Owner's request to deny review under § 325(d) is unwarranted.

Under both parts of the *Advanced Bionics* test (Pet. 67–68; Prelim. Resp. 19), there is no basis to deny institution of the Petition under 35 U.S.C. § 325(d).

A. The same prior art and arguments were not previously presented.

Patent Owner's assertion that the same or substantially the same art and arguments were presented under *Advanced Bionics* Part 1 is incorrect. Prelim. Resp. 19–28. Two out of three references were not before the Examiner, and the arguments the Examiner considered are materially different than Petitioner's.

First, it is undisputed that Petitioner's primary reference, Barf (EX1005), was not before the Examiner. Patent Owner argues only that Barf is "substantially" the same as Barf-PCT (EX1006) (Prelim. Resp. 20), yet it admits that only Barf specifically claims "a method of treating MCL with the compound now known as acalabrutinib" using a dosing range that overlaps with the '083 patent's claimed regimen (Prelim. Resp. 11; EX1005, cls. 1, 12). These claims, which are presumed enabled (Pet. 31), are not in Barf-PCT and thus were not before the Examiner.[1]

[1] Patent Owner also argues that "Barf is not prior art" (Prelim. Resp. 20) but later clarifies that Barf merely "*would* not qualify as prior art" if the '083 patent were "correct[ed]" to identify parties to an alleged joint research agreement (*id*. at 45 (emphasis added)). No such certificate of correction has been issued or even

Second, it is undisputed that Petitioner's combination reference, Cheson (EX1008), also was not before the Examiner. Patent Owner argues only that Cheson is "cumulative" of references cited by the Examiner as teaching dosage forms that potentially "*can* be administered twice daily" or "as much as 2 *to 4 times* a day." Prelim. Resp. 23 (emphasis added). These generic statements that dosage forms "can" be administered multiple times a day are not cumulative of Cheson's specific motivations that "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. EX1008, 4, 10 (emphasis added); Pet. 40–41.

Third, while Barf-PCT in Ground 2 was disclosed, the Examiner cited it only as a secondary reference in combination with two other references—Smyth and Evarts—that Petitioner does not rely on. As Patent Owner admits, the Examiner applied Smyth as a primary reference teaching a different dosing regimen for ibrutinib and only cited Barf-PCT to substitute acalabrutinib's structure. Prelim. Resp. 13–14; EX1004, 908–09. The Examiner later added

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requested. Regardless, any hypothetical correction after the Petition was filed would not apply retroactively to this proceeding. *See, e.g.*, *Emerson Elec. Co. v. SIPCO, LLC*, IPR2016-00984, Paper 52 at 17–25 (PTAB Jan. 24, 2020).

Evarts as teaching yet another dosing regimen. Prelim. Resp. 16; EX1004, 1034–35. While *Patent Owner* included Barf-PCT's dosing range in a block quote (Prelim. Resp. 15; EX1004, 1000), *the Examiner* never cited or relied on it. Moreover, while the Examiner generically found a skilled artisan could "optimize the treatment of leukemia" (Prelim. Resp. 26; EX1004, 1035), the Examiner did not consider the Petition's arguments that a skilled artisan would have arrived at the claimed dosing regimen using clinical data, FDA guidance, and routine animal studies (Pet. 29–44). Thus, substantially the same arguments were not presented.

B. The Examiner materially erred in allowing the claims.

Even if the same art and arguments were considered, discretionary denial would still be unwarranted under *Advanced Bionics* Part 2 because the Examiner materially erred in allowing the claims. As Patent Owner admits, the claims were allowed based on alleged unexpected results. Prelim. Resp. 32–33; EX1004, 1382. The Petition and Petitioner's declarant, Dr. Fruehauf, show extensively how these results were neither probative nor unexpected. Pet. 55–63; EX1002 ¶¶ 227–44.

In defending the notice of allowance, Patent Owner merely rehashes its argument from prosecution that it was unexpected the claimed 100 mg twice-daily dose of acalabrutinib (totaling 200 mg per day) would achieve maximal BTK occupancy because ibrutinib was approved at a higher once-daily dose of 560 mg. Prelim. Resp. 40. Patent Owner ignores the Petition's detailed showing that this

result was expected because both the Advani study and FDA's own clinical pharmacology reviews showed that a far lower dose of ibrutinib—2.5 mg/kg, equivalent to 175 mg for an average weight of 70 kg—"resulted in maximum BTK occupancy and maximum clinical response," suggesting that "doses lower than the [FDA-approved] doses are expected to have sustained occupancy of the BTK active site in vivo." EX1017, 5, 20; Pet. 57–59; *see also* EX1009, 12.

Neither FDA's pharmacology reviews nor Advani were considered by the Examiner, who also lacked the benefit of Dr. Fruehauf's declaration applying these references to show that the alleged results were expected. EX1002 ¶¶ 232–35. Even 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. *See Red Diamond, Inc. v. Southern Visions, LLP*, PGR2019-00045, Paper 9 at 20 (PTAB Oct. 15, 2019) ("Petitioner's arguments that the Examiner erred in allowing the claims based on alleged unexpected results persuade us that we should not exercise our discretion to deny the Petition under § 325(d)."); *Prollenium US Inc. v. Allergan Industrie, SAS*, IPR2020-00084, Paper 12 at 45 (PTAB April 10, 2020) ("[H]ad [Petitioner's] evidence been before the Examiner, there is a reasonable likelihood that the Examiner would have sustained the *prima facie* conclusion of obviousness under Section 103, discounting what was then interpreted as evidence of unexpected

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