UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SAMSUNG BIOEPIS CO., LTD.,
Petitioner

v.

ALEXION PHARMACEUTICALS, INC.,
Patent Owner

Case IPR2023-00999
U.S. Patent No. 9,725,504 B2

PETITIONER'S REPLY TO
PATENT OWNER'S PRELIMINARY RESPONSE

Samsung respectfully submits the following preliminary reply to address Alexion's discretionary denial arguments under §§ 314(a) and 325(d). (Paper 6 ("POPR"), 17-32; EX3001.) Under *Advanced Bionics*, the Board considers (1) whether the same or substantially the same art or arguments were presented during the original prosecution, and if so, (2) whether the Examiner materially erred as to patentability. (*See* Paper 2 ("Pet."), 66.)

I. Samsung's Petition Presents New Prior Art and Arguments

As detailed below, the first element of *Advanced Bionics* is not satisfied.

A. Bowdish, Mueller PCT, and Tacken Were Never Considered during Prosecution of the '504 Patent

Alexion concedes that Bowdish and Mueller PCT never appeared on an IDS and were never cited, discussed, or relied on as the basis for any rejection. (POPR, 18.) Nevertheless, Alexion argues that citation of related references, US7,482,435 (parent of Bowdish) and Mueller 1997, is sufficient to satisfy the first element of *Advanced Bionics*. (POPR, 21-22.) It is not. Neither reference was cited, discussed, or relied on as the basis for any rejection. As the mere citation of the reference itself on an IDS is often insufficient to satisfy the first element of *Advanced Bionics*, the mere citation of a *counterpart* to the reference in an IDS is even more insufficient. *See, e.g.*, *CODE200, UAB v. Bright Data Ltd.*, IPR2022-00353, Paper 8, 10 (PTAB July 1, 2022) (Finding that when a reference is not the basis of rejection, and merely

cited in an IDS, it weighs "strongly against" exercising discretionary denial.). Alexion's contention that Mueller PCT is cumulative to Mueller 1997 is also wrong. (*Id.*, 18, 20 n.9.) Mueller PCT discloses the complete IgG2/G4 constant domain used in eculizumab, Mueller 1997 does not. (Pet., 67-68, 68 n.6.)

Similarly, despite conceding that Tacken and the Mueller PCT never appeared on an IDS, or were cited or relied on as the basis for any rejection by the Examiner during '504 prosecution, (POPR, 18), Alexion asserts that submission of Amgen's IPRs during prosecution of the '189 and '809 related patents is sufficient to satisfy the first element of *Advanced Bionics*. (POPR, 22-23.) This argument fails too, because the Examiner did not address either reference in the Office Action or Reasons for Allowance, despite Tacken's express teaching that eculizumab contains the IgG2/G4 constant region, and Mueller PCT's disclosure of that sequence. (Pet., 71-73; EX1003, ¶¶180-181.) *See, e.g., Cisco Sys., Inc. v. Netsocket, Inc.*, IPR2023-00607, Paper 11, 22 (PTAB Sept. 26, 2023) ("[E]ven if there is substantial overlap, a reference that was neither applied against the claims nor discussed by the Examiner does not weigh in favor of exercising discretion under § 325(d).")

B. The Petition Presents New Arguments

Alexion mischaracterizes Samsung's newly-presented obviousness Grounds, arguing that Samsung's "basic combinations" are the same as in the Amgen IPR.

(POPR, 25-26.) Setting aside the vagueness of what the term "basic combination" means, the undeniable fact is that none of the Samsung's obviousness combinations including Tacken (Grounds 1-4) were considered during prosecution of the '504 patent or later child patents. Nor could they have been, since none of the grounds presented in the Amgen IPRs included Tacken. (*Compare* Pet., 4 *with* EX1024, 10.) The Petition is also based on new arguments supporting obviousness rationales and expert testimony that was not of record during original examination. (*See, e.g.*, Pet., 70 n.7; EX1003, ¶¶111-168); *see Boehringer Ingelheim Int'l GMBH v. Abbvie Biotech. Ltd*., IPR2016-00409, Paper 9, 8 (PTAB July 7, 2016); *Fellowes, Inc. v. Treefrog Devs., Inc*., IPR2020-01435, Paper 12, 19-20 (PTAB Feb. 22, 2021). The Petition thus does not present "the same or substantially the same" arguments under 35 U.S.C. §325(d) and *Advanced Bionics*.

II. The Examiners Erred Materially During Prosecution of the '504 Patent and its Related Patents

Even if the first element of *Advanced Bionics* was satisfied (it is not), the second element is also not satisfied because the Petition identifies multiple material errors by the Examiners during prosecution of the '504 patent and its related patents.

A. Errors During Prosecution of the '504 Patent

Alexion's arguments rely on two findings by the Examiner during prosecution of the '504 patent (POPR, 14); both were erroneous. First, the findings that "none

of the art recited an antibody with a heavy chain consisting of SEQ ID NO: 2 and a light chain consisting of SEQ ID NO: 4" and that "SOLIRIS® and its unique sequence was not 'accessible to the public' as of March 15, 2007" are clearly in error given: (1) Tacken's disclosure that eculizumab contains an IgG2/G4 constant domain, (2) Mueller PCT's disclosure of the sequences for the constant regions of SEQ ID NOS:2 and 4, and (3) Bowdish's disclosure of the sequence for antibody 5G1.1, including the complete sequence for IgG2/G4 constant domain claimed in SEQ ID NO: 2. (Pet., 69-70; EX1003, ¶178.)

Second, the Examiner's finding that a POSA "would not have been easily guided to mak[e] antibodies with these recited sequences" fails to account for the multiple enabling routes in the prior art to make the exact eculizumab antibody that is recited in claim 1 as SEQ ID NOS:2 and 4; similarly, the Examiner also clearly overlooked the teachings of Wang regarding doses and formulations. (Pet., 69-70; EX1003, ¶¶176-179.) The Examiner thus failed to appreciate both: (1) Mueller PCT's disclosure of eculizumab's hybrid IgG2/IgG4 heavy chain constant region sequence, and methods of how to make and use an antibody with this hybrid constant region, and (2) the integrated disclosures of Bowdish and Evans which teach the same. (*Id.*)

B. Errors During Prosecution of the '189 and '809 Related Patents

As for the related patents, Alexion argues that the Petition "presents no evidence that the Examiners did not 'appreciate Tacken's and Mueller PCT's disclosure' other than an observation that those references were not cited in an Office Action or Notice of Allowance." (POPR, 30-31.) But, as Dr. Ravetch explains, Tacken and Mueller PCT teach the very thing that the Examiner mistakenly concluded was missing from the prior art—that eculizumab contains the IgG2/G4 constant domain. (Pet., 71-73; EX1003, ¶¶181-182.) Had the Examiner appreciated Tacken's and Mueller PCT's disclosure he could not have reasonably concluded such information was missing from the prior art. The absence of any discussion of these references from the Office Actions and Notice of Allowance is evidence that the Examiner must have misapprehended the significance of those references.

The Examiner error can be traced back to Alexion's repeated misrepresentation of the art. For example, Alexion represented that "the literature as of March 15, 2007 … consistently identified 'eculizumab' as the antibody described in the 'Thomas' publication,' … which has a naturally-occurring 'IgG4' heavy chain constant region," ignoring that the Tacken article, published in 2005 by its own employees, expressly discloses that eculizumab contains an IgG2/G4 isotype. (EX1003, ¶182.) Alexion's Response repeats this misrepresentation and

ignores the extensive explanation by the Petition and Dr. Ravetch of why a POSA, by 2007, would not have been misled by citations to Thomas, because of Tacken. (Pet., 11-14, 29-30, 40-41, 60-61; *see also* EX1003, ¶¶112, 130, 165.)

The Examiner erred in a second way by relying on Alexion's misleading alignment of Evans' 5G1.1 *mouse* antibody variable regions with Bowdish's sequence rather than using Evans' 5G1.1 *humanized* variable region in his reasons for allowance. (Pet., 73-75; EX1035, 006-07; EX1003, ¶¶183-184.) The Examiner also mistakenly relied on Alexion's mischaracterization that Evans discloses "multiple options" for heavy chain CDR3 sequence, when in fact Evans discloses a single unique HCDR3 sequence. (Pet., 75-76; EX1003, ¶¶185-186.) The Examiner erred a third time by misapprehending the many reasons why Alexion's secondary considerations evidence failed, and a fourth time in misevaluating Wang. (Pet., 76-78; EX1003, ¶¶187-189.) Alexion's arguments relating to these errors stand unrebutted, as Alexion provided no substantive response at all in its POPR as to Samsung's Errors 2, 3, and 4 (POPR, 32), and should be precluded from doing so in any surreply.

III. Conclusion

The Board should exercise its discretion under §§ 314(a) and 325(d) and institute a trial based on the Grounds in Samsung's Petition.

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Respectfully submitted,

COOLEY LLP
ATTN: Patent Group
1299 Pennsylvania Avenue NW
Suite 700
Washington, DC 20004
Tel: (650) 843-5505
Fax: (650) 849-7400

By: / Michelle S. Rhyu /
Michelle S. Rhyu
Reg. No. 41,268
Counsel for Petitioner

CERTIFICATE OF SERVICE

I hereby certify, pursuant to 37 C.F.R. Section 42.6, that a complete copy of the attached **PETITIONER'S REPLY TO PATENT OWNER'S PRELIMINARY RESPONSE** and related documents, are being served via electronic mail on October 5, 2023, upon Patent Owner by serving Patent Owner's counsel of record in this proceeding as follows:

Gerald J. Flattmann, Jr.
gflattmann@cahill.com
Andrew Cochran
acochran@cahill.com
CAHILL GORDON & REINDEL LLP

DATED: October 5, 2023

/ Michelle S. Rhyu /
Michelle S. Rhyu
Reg. No. 41,268