Filed: December 24, 2018

Filed on behalf of: Eli Lilly and Company

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ELI LILLY AND COMPANY
Petitioner

v.

TEVA PHARMACEUTICALS INTERNATIONAL GMBH
Patent Owner

Case IPR2018-01422 (Patent No. 9,340,614)
Case IPR2018-01423 (Patent No. 9,266,951)
Case IPR2018-01424 (Patent No. 9,346,881)
Case IPR2018-01425 (Patent No. 9,890,210)
Case IPR2018-01426 (Patent No. 9,890,211)
Case IPR2018-01427 (Patent No. 8,597,649)[1]

PETITIONER'S REPLY TO PATENT OWNER'S POPR

[1] The word-for-word identical paper is filed in each proceeding identified in the caption, pursuant to the Board's order. For the Board's convenience, citations refer to papers filed in IPR2018-01422 involving Teva's Patent No. 9,340,614. Emphases are added unless otherwise noted.

I. Introduction[2]

Teva's § 325(d) arguments are unavailing. First, none of Lilly's asserted references was used to reject *any* of the claims of the Teva patents during prosecution. Second, the asserted references are not cumulative of those used to reject the claims. Indeed, Lilly's asserted references and expert testimony establish an explicit motivation to humanize anti-CGRP antagonist antibodies, which Teva argued was missing during prosecution. Third, Lilly also specifically addressed, *inter alia*, how Teva's one-sided arguments during prosecution regarding Tan 1995 were incorrect. Thus, the *Becton* factors strongly favor institution.

II. Lilly's Asserted References Were Not Used to Reject Any Claims

During prosecution of the six challenged patents, the Examiner did not reject any claims over—or even mention—any of the asserted references: Tan 1995, Queen, Wimalawansa, and Doods. Ex. 2005, 159-66. In fact, as Lilly's cited evidence demonstrates, Wimalawansa was *not even of record* until the last-to-issue '210 and '211 patents. Pet., 58 (citing Exs. 1176-1181); Ex. 2043, 255; Ex. 2042, 260. Thus, the Examiner did not consider Wimalawansa during examination of the '649, '614, '881, and '951 patents, much less in combination with Tan 1995, Queen, and/or Doods. These facts weigh heavily against a § 325(d) denial. *Navistar, Inc. v. Fatigue Fracture Tech., LLC*, IPR2018-00853, Paper 13 at 16-17

[2] Lilly does not acquiesce to any of Teva's arguments not addressed herein.

(PTAB Sept. 12, 2018) ("[T]he fact that [references] were of record, but not applied in any rejection by the Examiner . . . provides little impetus for us to exercise our discretion" under §325(d)).[3]

III. Lilly's Asserted References Are Not Cumulative of Pisegna and Frobert

Wimalawansa is also not cumulative of the Pisegna and Frobert references used to reject certain claims during prosecution of the '649 patent. Teva asserts that a "critical issue regarding patentability of the [challenged] patent[s] is whether a POSA would have had a *reason to humanize* an anti-CGRP antibody." POPR, 22-23 (emphasis in original). Wimalawansa provides that purportedly "critical" disclosure, expressly describing *humanized* anti-CGRP antibodies (Ex. 1096, 567) and stating that they "*should be explored*" for a variety of therapeutic applications (*id.*, 570). As explained by Dr. Charles in unrebutted expert testimony, Wimalawansa "advocated for making and using *humanized* anti-CGRP antagonist antibodies for therapeutic purposes." Ex. 1008, ¶ 106 (emphasis in original). That is precisely what Teva argued was missing from Pisegna and Frobert during prosecution, contradicting Teva's argument that Wimalawansa is cumulative. Ex. 1136, 3-4 ("Pisegna also does not cure the failure of Frobert to teach or suggest a

[3] Teva's reliance on *Omega* and *Microsoft v. Multi-Tech Sys., Inc.* (POPR, 14-15) is misplaced. Those cases concern claim construction and prosecution history estoppel, not § 325(d).

human or *humanized anti-CGRP antagonist antibody*"). Teva's reversal of its position about the teachings of the prior art, unsupported by expert testimony, compels a trial on the merits. *Coherus Biosci. Inc. v. AbbVie Biotech. Ltd.*, IPR2016-00172, Paper 9 at 19 (PTAB May 17, 2016) ("factual disputes [are] best resolved during trial").[4]

Tan 1995 is also not cumulative of Frobert and Pisegna. Teva incorrectly attempts to cabin Lilly's reliance on Tan 1995 to its disclosure of murine anti-CGRP antibodies. POPR, 23. But, as Lilly and its experts have established, Tan 1995 is not so limited. Indeed, Tan 1995 establishes that anti-CGRP antibodies (1) may selectively bind human α-CGRP (and not amylin) (Pet., 17, 23); (2) effectively block the CGRP pathway *in vivo*; (3) "clearly diffuse[] into the synaptic cleft," i.e., the site of action that Teva alleges is necessary for *in vivo* effectiveness (Pet. 38-43; Ex. 1022, 571); and (4) were known alternatives to using receptor

[4] Sveinsson, Salmon, and the '438 patent, like Wimalawansa, further demonstrate the motivation in the art to humanize anti-CGRP antibodies. Pet., 24-27, 43. Teva did not respond to these references under § 325(d) and instead incorrectly argued that the Board should ignore them. POPR, 29-30; *Genzyme Therapeutic Prods. Ltd. P'ship v. Biomarin Pharm. Inc.*, 825 F.3d 1360, 1369 (Fed. Cir. 2016) (the Board should consider references illustrating the state of the art under § 103).

antagonists—a class of compounds Teva discusses at length (POPR, 4-10)—for blocking the CGRP pathway. Pet., 17-18, 23, 27-29, 38-43; Ex. 1008, ¶ 114 (citing Ex. 1022, 571).

Neither Frobert nor Pisegna contains any of these disclosures. Nor do they describe Tan 1995's *in vivo* testing or its guidance to use higher doses and longer distribution times, which Teva followed in its specification's examples. Pet., 38-43; Ex. 1008, ¶¶ 91-103. Rather, Frobert relates to an immunoassay for measuring CGRP, while Pisegna describes antibodies targeting the CGRP *receptor* as Teva argued during prosecution (rather than anti-CGRP antibodies like Tan 1995 and Wimalawansa). Ex. 1032, 275; Ex. 2005, 181-82; *e.g.*, Ex. 2049, ¶¶ [0002], [0009].

Teva's argument about Queen's humanization processes is also irrelevant because Teva itself concedes that preparing humanized antibodies was "known" and "conventional." POPR, 19; Pet., 7 (citing Ex. 1001, 27:61-67, 29:8-31).

Teva also fails to explain how the one art-based rejection made in the earliest application is applicable to all the claims (no matter the limitations) that issued from the same family. *Vizio, Inc. v. Nichia Corp*., IPR2017-00551, Paper 9 at 8 (PTAB July 7, 2017) (rejecting § 325(d) argument where there was "no evidence that the Examiner considered[] [the prior art] *in the context of the claims of the [challenged] patent*"). In contrast, Lilly addresses each claim limitation and how the prior art renders obvious the claims as a whole. Pet., §§ VII-VIII.

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