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 No. IPR2018-01423
Patent No. 9,266,951

PETITIONER'S OPPOSITION TO PATENT OWNER'S MOTION TO STRIKE

I. Introduction

Lilly's Reply, accompanying exhibits, and supporting declarations respond to new issues raised in Teva's POR and by Teva's experts and therefore are within the proper scope of a reply. Teva claims that Lilly's Reply and exhibits "present new evidence and theories of invalidity," but there is nothing to support those conclusory statements. Instead, Teva uses its Motion to argue its substantive validity positions and level unsupported attacks on Lilly's experts. Teva's Motion should be denied.

II. Argument

A petitioner in an IPR proceeding may introduce arguments at the reply stage in response to arguments raised in a POR. *Anacor Pharm., Inc. v. Iancu*, 889 F.3d 1372, 1380-81 (Fed. Cir. 2018); 37 C.F.R. § 42.23(b). The Board routinely allows new evidence, including declarations from new experts, in reply. *See e.g.*, *Belden Inc. v. Berk–Tek LLC*, 805 F.3d 1064, 1078 (Fed. Cir. 2015). New reply evidence is also appropriate if it is used "to document the knowledge that skilled artisans would bring to bear in reading the prior art identified as producing obviousness." *Anacor,* 889 F.3d at 1380-81.

Striking portions of a party's brief is "an exceptional remedy" not warranted here. A reply or reply evidence may be excluded if it introduces an entirely new theory of obviousness or new evidence that is necessary to make out a *prima facie* case of patentability. *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d

1359, 1369-70 (Fed. Cir. 2016). By contrast, exclusion is inappropriate where, as here, a reply "expands the same argument made in its Petition." *Ericsson Inc. v. Intellectual Ventures I LLC*, 901 F.3d 1374, 1381 (Fed. Cir. 2018).

A. Exhibit 1287 and Related Sections of Lilly's Reply

Exhibit 1287 and Lilly's related argument (Reply, 3, 11-12) are directly responsive to assertions newly made in Teva's POR. Teva and its experts incorrectly argued that Tan 1995, an asserted reference, was a "basic research paper" that would not have motivated a POSA to make humanized antibodies. POR, 2, 4, 14, 42, 45; Ex. 2211, ¶¶ 61, 63-64; Ex. 2229, ¶¶ 50, 77. Teva further alleged to have personal knowledge of co-authors of the Tan references, implying they never considered antibody humanization. POR, 45; Ex. 2211, ¶¶ 70, 76. Teva also argued that certain blood pressure data presented in Tan 1995 would have discouraged further research. POR, 22-25, 41-42.

Exhibit 1287, which was written by Dr. Tan in 1994 and describes his and his co-authors' work in Tan 1995, directly contradicts Teva's arguments. With first-hand knowledge of the blood pressure results in Tan 1995, Dr. Tan wrote there was "no reason" why humanized anti-CGRP monoclonal antibodies should not be investigated and used as "therapeutic agents" for migraine and other diseases. Ex. 1287, 247; Reply, 11-12. Exhibit 1287 is therefore proper reply evidence.

Teva's Motion mischaracterizes Lilly's Reply as using Ex. 1287 as "an alleged

'contemporaneous' teaching of motivation." The *actual text* of Lilly's Reply is clear: for "further motivation," it cites only the Petition, Tan 1994 (Ex. 2021), Tan 1995 (Ex. 2022), and Ex. 1303. Reply, 3. Exhibit 1287 is included to provide contextual information, made necessary by Teva's allegations that blood pressure readouts reported in Tan 1995 would have raised safety concerns. *See, e.g.*, Ex. 2229, ¶¶ 77-82. This is explained at pages 11-12 of Lilly's Reply, which Teva fails to address.

Thus, Ex. 1287 and its use in Lilly's Reply are plainly proper rebuttal. *Belden*, 805 F.3d at 1082 ("the function of rebuttal [is] to explain, repel, counteract, or disprove the evidence of the adverse party").

B. Lilly's Evidence and Discussion of Aptamers Is Properly Responsive to Teva's POR

Teva incorrectly seeks to strike evidence and reply briefing concerning CGRP-binding aptamers (Reply, 9; Ex. 1240; Ex. 1309; Ex. 1321, ¶¶ 38, 51, 52, 54, 60, 69; Ex. 1322, ¶¶ 17, 31, 74, 77). But anti-CGRP aptamer evidence was originally presented with the Petition. Pet., 39, 58. Lilly also properly used that evidence to directly respond to multiple Teva arguments.

Teva argued that a POSA would have had safety concerns associated with directly antagonizing CGRP, particularly for compounds with a long half-life. POR, 19-29; Ex. 2229, ¶ 73-82; Ex. 2211, ¶¶ 12, 27-70. Teva further argued a POSA would not have targeted CGRP, as opposed to its receptor, because of (1) hypothetical safety concerns about preventing CGRP from binding to receptors other than the CGRP-

receptor (cross-binding) and (2) hypothetical efficacy concerns based on the "spare receptor theory." POR, 29-31; Ex. 2229, ¶¶ 23-42, 88-95.

Lilly rebuts those positions in part with evidence that CGRP-binding aptamers—recognized in the prior art as "analogs to antibodies"—were being developed to treat migraine. These aptamers had long half-lives yet displayed no safety risks. Reply, 9; Ex. 1240; Ex. 1309; Ex. 1321, ¶¶ 48-70; Ex. 1322, ¶¶ 17, 31, 74, 77. Lilly's Reply further cites this aptamer evidence to illustrate the unsupported and hypothetical nature of Teva's "spare receptor" and cross-binding arguments, as notwithstanding Teva's purported concerns researchers were actually developing anti-migraine agents targeting CGRP directly. Reply, 16-19; Ex. 1321, ¶¶ 40-47; Ex. 1322, ¶¶ 17, 65-75.

Teva misleadingly refers to Lilly's rebuttal evidence related to aptamers as "an entirely new aptamer-based theory." Teva is incorrect. The fact that evidence related to aptamers contradicts more than one of Teva's new arguments does not make it a "new theory." Moreover, Teva ignores Dr. Charles's (and Tan's) position that targeting the CGRP ligand or its receptor were "alternative, complementary strategies." Ex. 1004, ¶ 124; Ex. 1022, 566, 571. Researchers' pursuit of CGRP-binding aptamers provides further objective evidence that CGRP antagonism and CGRP-receptor antagonism were in fact considered alternatives.

Thus, Lilly's Reply arguments and evidence relating to aptamers are wholly

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