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. IPR2018-01427
Patent No. 8,597,649 B2

PETITIONER'S RESPONSE TO TEVA'S SUPPLEMENTAL BRIEF

REGARDING *FOX FACTORY, INC. v. SRAM, LLC*

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I. Teva Failed to Meet Its Burden of Establishing Coextensiveness

Fox Factory rejected changing the coextensiveness requirement to an analysis of whether a claim "cover[s]" products cited for secondary considerations. *Fox Factory v. SRAM, LLC*, 744 F.3d 1373, 1377 (Fed. Cir. 2019). Yet in its substantive briefing, Teva merely alleged that the claims "*cover* one or both of Ajovy® and Emgality®" without addressing coextensiveness, the broad scope of the claims, or the materiality of unclaimed features. POR, 55; Sur-reply, 25-26; Ex. 2137, ¶118.

Although Teva reaffirmed at the oral hearing that its position was that the claims "cover" the products and that the claims are *not coextensive*, Teva now contends that coextensiveness exists because Ajovy® and Emgality® "*are* humanized anti-CGRP antagonist antibodies" within the broad scope of the claims. Br., 1-2, 5; Paper 69, 63 ("Your Honor, I'm not saying they're co-extensive"). This is a distinction without a difference, as Teva fails to address the incredible breadth of the claims or its many admissions that unclaimed features materially impact function.

II. Teva Failed to Meet Its Burden of Showing Insignificance of Unclaimed Features and Other Patents

Lilly identified multiple features encompassed by the claims but not recited as limitations that materially affect function—such as amino acid sequence, pM-level binding affinity, antibody format, and antibody class. Reply, 21-24. Despite bearing the burden of establishing that unclaimed features are "insignificant," *Fox Factory*, 944 F.3d at 1374-75, Teva offered *no response*. Sur-reply, 25-26.

Indeed, Teva fails to offer *any* evidence contradicting the universally understood principle that sequence is critical and dictates antibody function. Teva represented to the FDA that it introduced multiple specific mutations into Ajovy®—out of more than 20^{220} possible mutations—to achieve pM-level binding affinity and eliminate ADCC and CDC. Ex. 2217, 8-9; Ex. 1142, 392 (mutating sequence to achieve "picomolar range" affinity can have "*profound effects* on the utility of antibodies as therapeutic and prophylactic agents"); Ex. 1301, 91:25-92:22. This is highly analogous to *Fox Factory*, where a patentee's representations in its marketing materials confirmed lack of nexus due to unclaimed features. 944 F.3d at 1375-76. Emgality®'s specific sequence and resulting properties, with mutations to eliminate ADCC and CDC, were likewise highlighted to the FDA. Ex. 2216, 17, 21-22, 41.

Teva concedes that Ajovy® and Emgality® have different sequences, but fails to support its baseless (and belated) assertion that sequence is insignificant to its secondary considerations evidence. Br., 4-5. Sequence matters: depending on their specific sequence, anti-CGRP antibodies within the broad scope of all challenged claims would have (1) binding affinity *orders of magnitude worse* than Ajovy® and Emgality®, (2) strong effector functions having the *undesired side effect of killing cells* (cytotoxicity), (3) an antibody fragment format that Dr. Tomlinson testified would be *useless as a therapeutic*, and/or (4) an antibody class *never successfully used before* in any FDA-approved antibody. Reply, 21-24; Ex. 1301, 27:25-28:6,

134:14-25, 34:9-35:1, 36:16-39:11, 102:1-104:19; Ex. 1002, ¶162. These unclaimed features would lead to materially different properties (e.g., no efficacy or significant adverse events) as compared to Ajovy® and Emgality®. Reply, 21-24. Notably, even these antibodies have fundamentally different properties: Lilly's Emgality® is FDA-approved to treat cluster headache while Teva's Ajovy® failed clinically. Ex. 2153, 1.

Teva newly argues that antibodies with different sequences are "associated with the same praise." Br., 4. But this alleged praise is directed to *only two* high-affinity, sequence-optimized antibodies (Ajovy® and Emgality®) and is not representative of the broad challenged claims.[1] *See AbbVie Deutchsland GmbH v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1291-92, 1301 (Fed. Cir. 2014) (even *300 antibodies* do not represent a functionally defined genus). Moreover, the alleged praise extends to compounds *outside* the scope of the claims such as anti-CGRP *receptor* antibodies and small molecule inhibitors. Reply, 24-25. As Dr. Rapoport admitted, the *only* property he considered for nexus is the ability of antibodies to "block the CGRP pathway," which is legally insufficient because this mechanism of action was already disclosed to treat migraine. Reply, 24; Ex. 1304, 142:1-8.

[1] Teva argued Alder only in the context of a license agreement. POR, 63-64. Teva's new arguments alleging praise and success for Alder's antibody should be rejected. *Cablz, Inc. v. Chums, Inc.*, 708 F. App'x 1006, 1011-12 (Fed. Cir. 2017).

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