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. IPR2018-01710
Patent No. 8,586,045

PETITIONER'S RESPONSE TO TEVA'S SUPPLEMENTAL BRIEF REGARDING *FOX FACTORY, INC. v. SRAM, LLC*

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GLOSSARY

FDA	U.S. Food and Drug Administration
IPR	*Inter partes* review
Italicized text	Emphasis added unless otherwise indicated
Lilly or Petitioner	Eli Lilly and Company
pM	picomolar
Teva or Patent Owner	Teva Pharmaceuticals International GmbH
'045 patent	U.S. Patent No. 8,586,045 (Ex. 1001)
'614 patent	U.S. Patent No. 9,340,614 (Ex. 1001 in IPR2018-01422)
'614 Hearing Tr.	Record of Oral Hearing (Paper 71 in IPR2018-01422)
'951 patent	U.S. Patent No. 9,266,951 (Ex. 1001 in IPR2018-01423)
'881 patent	U.S. Patent No. 9,346,881 (Ex. 1001 in IPR2018-01424)
'794 patent	U.S. Patent No. 8,007,794 (Ex. 2024)

I. Teva Failed to Establish that Amino Acid Sequence Is Insignificant

Having represented to the FDA that it engineered Ajovy®'s amino acid sequence to achieve its therapeutic profile, Teva's repeated failure to address the criticality of sequence confirms that no presumption applies. Ex. 2217, 8-9; Reply, 21-22; *Fox Factory, Inc. v. SRAM, LLC*, 944 F.3d 1373, 1375-76 (Fed. Cir. 2019). Teva's mere attorney argument that sequence is insignificant is baseless. Br., 5.

Depending on their specific sequence, anti-CGRP antibodies within the broad scope of the 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*, (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, 101:15-104:19; Ex. 1014, ¶175. These unclaimed features would lead to materially different properties (*e.g.*, no efficacy or significant adverse events) compared to Emgality® and Ajovy® and were identified by FDA as directly bearing on "*critical quality attributes*" (CQAs). Ex. 2216, 17; Ex. 2217, 6-9.

Teva's unsupported argument that "sequences are not driving the praise" (because Emgality® and Ajovy® have different sequences) is therefore inconsistent with the admissions of its expert, contrary to its representations to FDA, and contrary

to the fundamental principle of antibody biology that sequence determines function. Br., 5; Ex. 1063, 59, 63; Ex. 1062, 41; Ex. 1301, 93:14-20; Reply, 21-22.

II. Teva Failed to Meet Its Burden of Establishing Coextensiveness

In an effort to argue away its admission that Ajovy® and Emgality® are *not* "coextensive" with its overbroad claims, Teva contends they form a representative number of species within the claimed genus. '614 Hearing Tr., 63; Br. 2, n.1, 5-7. But this is mere attorney argument, unsupported by any evidence.[1]

Teva's argument also lacks merit. Two sequence-engineered, FDA-approved antibody drugs are *not* representative of broad genus claims seeking to cover using *all* human or humanized anti-CGRP antibodies, *regardless of sequence*, for treating migraine (among at least 250 other forms of headache). Ex. 1304, 74:17-75:12. Indeed, as held in *Celltrion, Inc. v. Genentech, Inc.*, a sequence-engineered, FDA-approved antibody drug lacks nexus to even sub-genus claims reciting specific mutations. IPR2017-01374, Paper 85 at 45, 48 (PTAB Nov. 29, 2018) (relying on

[1] Teva's representative species argument is waived, as Teva failed to raise it before the oral argument. *See* POR, 55-56; Sur-reply, 27; *Cablz, Inc. v. Chums, Inc.*, 708 F. App'x 1006, 1011-12 (Fed. Cir. 2017). Moreover, Teva's new arguments alleging praise and success for Alder's antibody are also waived, as Teva argued Alder *only* in the context of a license agreement. POR, 63-64.

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