Paper No. ___
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

APOTEX INC., APOTEX CORP., ARGENTUM PHARMACEUTICALS LLC, ACTAVIS ELIZABETH LLC, TEVA PHARMACEUTICALS USA, INC., SUN PHARMACEUTICAL INDUSTIRES, LTD., SUN PHARMACEUTICAL INDUSTRIES, INC., AND SUN PHARMA GLOBAL FZE,
Petitioners,

v.

NOVARTIS A.G.,
Patent Owner.

IPR2017-00854[1]
Patent No. 9,187,405

PETITIONERS' MOTION FOR OBSERVATIONS REGARDING THE CROSS-EXAMINATION OF DR. LAWRENCE STEINMAN

[1] Cases IPR2017-01550, IPR2017-01946, and IPR2017-01929 have been joined with this proceeding.

Petitioners hereby submit observations on the deposition testimony of Novartis's declarant Dr. Lawrence Steinman given on April 5, 2018 (EX1061).

1. In EX1061 at 37:2-39:7, Dr. Steinman testified that the "standard of care" "often" used for treating relapses in RRMS patients is using corticosteroids to blunt the relapse and "alleviate the variety of different manifestations of a relapse." He also testified that "if they did have a relapse, I would be giving steroid as well" as fingolimod. This is relevant to Dr. Jusko's assertion that MS patients treated with corticosteroids provided a skewed weight average. EX1064 (04/10/2017 Jusko Depo), 139:12-141:22; *see also* EX2022 (1st Steinman Decl), ¶¶33-34, 38.

2. In EX1061 at 39:24-41:20, 44:18-48:4 Dr. Steinman testified that one cannot know when administering fingolimod whether it will be effective in a particular patient, that he "can't provide any guarantees," that "it would be hard" to talk in a scientific manner about slowing progression of RRMS in an individual patient. This is relevant to Novartis's proposed construction that the original and proposed amended claims require actual efficacy as a claim element because it demonstrates that their proposed construction is unreasonable, indefinite, and lacks support and enablement in the '405 patent. EX2096, ¶¶5, 7, 9-17; Paper 63, 2-5.

3. In EX1061 at 48:5-23, 52:4-56:16, 57:20-58:14, Dr. Steinman testified that treating RRMS is broad enough to include each of slowing progression and preventing relapses but broader than just those two and described a Venn diagram

illustrating how different categories can have overlapping subject matter without being co-extensive. He disagreed that "all patients whose relapses are under control are no longer in need of slowing progression of RRMS," and agreed that "an RRMS patient whose relapses are controlled may still be in need of slowing progression of RRMS." *Id.*, 57:20-58:14. This is relevant to Novartis's argument that the claims require an intention of efficacy because the independent claims otherwise would allegedly be rendered duplicative. Dr. Steinman's testimony establishes that each independent claim has a different scope. EX2096, ¶¶11-17; Paper 63, 2-5; Paper 61, 8; Paper 64, 2-3, 7-8; Paper 2, 24-25; EX1002, ¶¶43-47.

4. In EX1061 at 112:5-113:18, 114:15-117:22, Dr. Steinman agreed it was known fingolimod was being developed as a DMT, that DMTs had only been approved to treat RRMS, not PPMS, that the default understanding of a POSA was that a DMT for treating MS referred to RRMS, and that he "would probably think yes, it was about RRMS" prior to June 2006 if discussing treatment of MS using fingolimod. This is relevant to Dr. Steinman's assertion that a POSA would not understand Kovarik's 0.5 mg daily maintenance dose for treating an autoimmune disease (*e.g.*, MS) as relevant to RRMS. EX2096, ¶¶57-66; Paper 63, 13-14.

5. In EX1061 at 118:7-23, Dr. Steinman agreed that a POSA would have been more skeptical of a fingolimod clinical trial for PPMS than RRMS. This is relevant to Novartis's assertion that the failure to include a 0.5 mg dose of fingolimod in the

INFORMS trial for PPMS indicates skepticism that the 0.5 mg dose of fingolimod would be effective against RRMS. Paper 63, 9-12; EX2097, ¶¶14-17.

6. In EX1061 at 121:19-122:16, Dr. Steinman agreed that the '405 patent discloses a 200-fold dose range for fingolimod (0.1-20 mg/kg) in rats for significant inhibitory activity and 0.3 mg/kg to fully inhibit activity. This is relevant to Novartis's assertion that the animal data in the specification supports efficacy against RRMS of the 0.5 mg dose in humans. EX2096, ¶¶53-54, 65; Paper 63, 2-5, 7-8. It is relevant because Dr. Jusko converts 0.1 mg/kg in rats to 1.43 mg in humans, not 0.5 mg. EX2095, ¶¶22-26, 31, 39-41. This is also relevant to Dr. Steinman's assertion that a POSA should ignore the Chiba reference's disclosure of a range of effective doses encompassing 0.5 mg because it is in a "thousand-fold range" of 0.01 mg to 10 mg. EX2022, ¶179.

7. In EX1061 at 122:17-128:17, Dr. Steinman testified that the '405 patent's only discussion of lymphopenia addresses 50% lymphopenia and that "I don't think it addresses the Webb threshold at all." This is relevant to Novartis's argument that "at least" 70% lymphopenia was required to see any efficacy. *See, e.g.*, EX2096, ¶¶25-40, 72-73; Paper 63, 5-6, 9-12. It is relevant because the patent reflects the same understanding as the prior art (*e.g.*, Kovarik (EX1004), 2) that lymphopenia of at least 70% was not a threshold for any efficacy. EX2096, ¶¶3, 62, 65; Paper 63, 5-6, 9; *see also*, *e.g.*, Paper 56, 11-12; EX1047, ¶¶38-48, 99.

8. In EX1061 at 128:18-132:7, 203:5-13, Dr. Steinman argued that the claims of the '405 patent are where it allegedly teaches that the 0.5 mg dose is effective and agreed that the specification only describes administering that dose in the prophetic clinical trial for investigating clinical benefit in an experimental setting. This is relevant to Novartis's argument that the claims require at least intended efficacy as a claim element. It is relevant because the pre-2011 patent specification does contain the claim language Dr. Steinman relies upon. EX1009, 0188-89.

9. In EX1061 at 157:11-158:20, 264:18-268:13, Dr. Steinman agreed that scientists in June 2006 believed that fingolimod did not work exclusively by sequestering lymphocytes and that Webb teaches that its non-lymphopenia mechanism of action may produce the therapeutic benefit. This is relevant to Novartis's argument that "at least" 70% lymphopenia was required to see any efficacy. *See, e.g.*, EX2096, ¶¶3-5, 25-40, 50, 52, 72-73; Paper 63, 5-7.

10. In EX1061 at 190:17-191:25, Dr. Steinman testified that the claims of the '405 patent are complete once the steps are performed regardless of whether the steps results in an effect on the subject. This is relevant to Novartis's arguments that the claims require efficacy because it demonstrates there is no efficacy element. *See, e.g.*, EX2096, ¶¶5, 7, 9-17; Paper 63, 2-5.

11. In EX1061 at 209:24-210:17, 213:6-215:222, Dr. Steinman testified that the '405 patent claims provide no limitation for the number of days of administration

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