Paper No. ___
Filed: February 16, 2018

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

PETITIONER'S REPLY
37 C.F.R. §42.24(c)

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

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I. INTRODUCTION

Novartis Response (Paper 27, "POR") continues to misconstrue or ignore prior art while tacitly conceding efficacy does not depend on loading doses. Failing that, Novartis asks the Board to import result limitations into the claims that are simply not there. Novartis also relies heavily on an alleged teaching away based on animal studies, but these studies instead confirm that the 0.5 mg dose was expected to work. Moreover, anticipatory prior art Novartis disclosed with its POR decimate its erroneous teaching away and objective evidence arguments. Finally, Novartis fails to identify Section 112 support in the priority documents for the no-loading-dose element of the claims. Petitioners have established by a preponderance of the evidence that claims 1-6 are unpatentable under each of Grounds 1-3.

II. POR FAILS TO UNDERMINE *PRIMA FACIE* OBVIOUSNESS.

A. Novartis Misreads and Ignores Prior Art.

The Petition established that a loading dose regimen increases the speed of efficacy but is not required to make a maintenance dose effective for MS treatment. Pet. 4-8, 30-31, 34-39, 41-43; Paper 11 at 18; EX1002, ¶¶67, 70-72, 108-09, 112-13, 117-22, 126. Petitioner thereby demonstrated the error in Novartis's prosecution argument that the 0.5 mg maintenance therapy disclosed in Kovarik should be disregarded because it was allegedly dependent on the loading dose regimen. Novartis and its experts have now conceded this point, as they must.

EX2024, ¶131 ("achieve the effect of the drug faster"); EX2022, ¶¶157-58 (used to avoid delay); POR 48 (Kappos showed no loading dose needed); *see also* EX1047, ¶¶31-37.

Novartis's continued effort to ignore Kovarik because it used a loading dose is particularly disingenuous because Novartis's "teaching away" and "unexpected results" arguments repeatedly rely on references describing transplant studies, in which context loading doses were used. POR 9-14, 34-35, 37 (transplant studies provide "insight" for "patients with multiple sclerosis"); EX1019 at 685 (loading dose); EX1031 at 1084 (when rapid effect is "critical"). Novartis's argument that the Board should ignore Kovarik because it discloses "loading dose methods" should be rejected.

Novartis wrongly contends Kovarik's 0.5 mg maintenance therapy was merely a hypothetical "input" for illustrating loading dose regimens for an unspecified autoimmune disease. POR 4, 36. But the 0.5 mg maintenance therapy was not a hypothetical input, it was "part of a preferred embodiment." Pet. 7-11; EX1004 at 13, 15, 17; EX1047, ¶¶25-30. Kovarik placed MS at the head of a small list of preferred autoimmune disease targets of the medication. Pet. 10; EX1004 at 14, 17. Novartis's argument is contrary to the express teachings of the reference and should be rejected.

Novartis's identification of RR-MS as the point of novelty also fails. Novartis does not contest that RR-MS patients constituted the vast majority of MS patients, that RR-MS was the target of prior disease-modifying therapies (DMTs), and that reducing relapses and slowing progression in RR-MS patients were the known targets and results of fingolimod treatment. POR 49 (agreeing "Kovarik identifies multiple sclerosis as an autoimmune disease," and "RRMS is the most common form"), 5 (Thomson reviewed fingolimod's application to RRMS); EX1042 at 16:6-23:11, 25:8-29:2 (known DMTs reduced relapses and slowed progression in RR-MS patients; progression slowed by reducing relapses). Novartis's latest attempt to misread Kovarik should be rejected.

Unable to rewrite Kovarik, Novartis asks the Board to err by pretending Kovarik does not exist. *Randall Mfg. v. Rea*, 733 F.3d 1355, 1362-63 (Fed. Cir. 2013) (reversing Board for ignoring prior art references); *Coal. for Affordable Drugs V LLC v. Biogen MA, Inc.*, IPR2015-01993, Paper 63 at 6 (POSA "presumed to be aware of" all art "from the same or analogous fields"). Novartis argues that only hindsight identifies Kovarik and Thomson as prior art and that Kovarik was "seized…from the file history." POR 46-49. But Dr. Giesser explained that she analyzed Kovarik and Thomson because they were published before June 2006 and describe "properties of fingolimod" and its "treatment for MS." EX2039 at 89:3-21. In other words, like the patent, each reference describes

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