Filed on behalf of: Par Pharmaceutical, Inc. et al.

Entered: January 19, 2017

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PAR PHARMACEUTICAL, INC., BRECKENRIDGE PHARMACEUTICAL, INC., AND ROXANE LABORATORIES, INC.
Petitioners

v.

NOVARTIS AG
Patent Owner

Case IPR2016-00084[1]
U.S. Patent No. 5,665,772

Before LORA M. GREEN, CHRISTOPHER L. CRUMBLEY, and ROBERT A. POLLOCK, *Administrative Patent Judges*.

PETITIONERS' RESPONSE TO PATENT OWNER'S IDENTIFICATION OF PORTIONS OF PETITIONERS' REPLY

[1] Breckenridge Pharmaceutical, Inc. was joined as a party to this proceeding via a Motion for Joinder in IPR2016-01023; Roxane Laboratories, Inc. was joined as a party via a Motion for Joinder in IPR2016-01102.

Pursuant to the Board's email of January 6, 2017, Petitioners submits a responsive numbered list of citations to the record that provide support for where the arguments objected to by Patent Owner were previously raised by Petitioner, or citations to arguments by Patent Owner to which the objected-to portions are responsive with a one-sentence description of the relevance.

1. **Patent Owner:** Page 3, line 20 – page 4, line 3, and page 4, lines 13-15. Petitioners assert a new basis for selecting rapamycin as a lead compound ("potency") that could and should have been raised as part of their prima facie case, but was not included in the Petition.

Petitioners' response: Petitioners asserted in the petition that rapamycin's immunosuppressant potency is a basis for selecting it as a lead compound (Pet. 16-17, 26-27, 41-42 (citing, *e.g.*, Ex. 1003 ¶ 133)), and the reply responded to arguments to the contrary in the patent owner response (POR 48-49).

2. **Patent Owner:** Page 4, lines 10-12 and 17-20 (see also page 1, lines 17-20). Petitioners assert a new basis for selecting rapamycin as a lead compound ("researchers regularly selected rapamycin") that relies on evidence (exhibits cited in Ex. 2093 ¶¶ 63-83) that could and should have been raised as part of their prima facie case, but were not included in the Petition.

Petitioners' response: The petition asserted that researchers were regularly selecting rapamycin as evidence that a POSA would have selected it as a lead compound (Pet. 18, 26, 41 (citing, *e.g.*, Ex. 1003 ¶¶ 89-100, 136)), and the reply responded to arguments to the contrary in Patent Owner's Response (POR 47-50) by, *e.g.*, pointing to additional examples provided by Novartis in its Ex. 2093 ¶¶ 63-83.

3. **Patent Owner:** Page 6, lines 3-16. Petitioners rely on new evidence (Ex. 1034 at 116; Ex. 1118 ¶¶ 25-26) to assert that it was known in the art that rapamycin's solubility led to formulation problems, when this argument and evidence could and should have been raised as part of their prima facie case, but were not included in the Petition.

Petitioners' response: The petition established that rapamycin's poor solubility led to formulation problems (Pet. 4, 17, 26-27, 41-42, citing, *e.g.*, Ex. 1003 ¶¶ 75-76, 138-140 and Ex. 1005 (Morris)), and the reply and Ex. 1118 ¶¶ 25-26 responded to arguments in POR 51-55 and Ex. 2092 ¶¶ 150-160; *see also* POR 29 ("Par's case is premised on its assertion that rapamycin's water solubility was sufficiently problematic to limit pharmaceutical utility"); Ex. 1118 ¶¶ 25-26 (expressly responding to Ex. 2092); Novartis's Motion to Exclude ("Mot. Excl.")

5-7 (Ex. 1034), 8-10 (Ex. 1118 ¶¶ 25-26) (Paper 54); Petitioners' Opposition ("Opp. Mot. Excl.") 5-7 (Ex. 1034), 7-9 (Ex. 1118 ¶¶ 25-26) (Paper 59).

4. **Patent Owner:** Page 6, lines 5-16. Petitioners rely on new evidence (Ex. 1034; Ex. 1118 ¶¶ 26, 32-35) to assert a motivation to chemically modify rapamycin, when this evidence could and should have been raised as part of their prima facie case, but was not included in the Petition.

Petitioners' response: The petition established that rapamycin's poor solubility limited its use in drug formulations (Pet. 4, 17, 23-24, 26-27, 32-34 41-42, citing, *e.g.*, Ex. 1003 ¶¶ 75-76, 138-140 and Ex. 1005 (Morris)), and the reply and Ex. 1118 ¶¶ 26, 32-35 responded to arguments at POR 51-55 and Ex. 2092 ¶¶ 150-160; *see also* Item 3 (above); POR 29; Mot. Excl. 8-10; Opp. Mot. Excl. 5-7, 7-9.

5. **Patent Owner:** Page 10, lines 10-12 and 14-17. To the extent Petitioners are arguing that (i) Lemke (Ex. 1008) discusses internal entropy and/or (ii) Yalkowsky (Ex. 1007) discusses polar groups and hydrophilicity, these arguments could and should have been raised as part of their prima facie case, but were not included in the Petition.

Petitioners' response: Petitioners are not alleging that Lemke discusses internal entropy or that Yalkowsky discusses polar groups and hydrophilicity; rather, Petitioners are alleging that "Lemke and Yalkowsky together taught that adding flexible side chains (to increase internal entropy) containing polar groups (to increase hydrophilicity) is likely to improve solubility" as stated at Reply 10 (citing Pet. 44-48 where this issue was raised); *see also* Reply 11 n.2 (including citations); Mot. Excl. 9 (re: the cites to Ex. 1118 in this portion of Reply); Opp. Mot. Excl. 8-9 (same).

6. **Patent Owner:** Page 12, line 1 – page 14, line 9, and page 15, line 13 – page 16, line 1. Petitioners attempt to explain how Yalkowsky is relevant to the instant case, including why everolimus qualifies as a long-chain derivative of rapamycin with more than 6 atoms in the chain, when such arguments and evidence could and should have been raised as part of their prima facie case, but were not included in the Petition, and when Petitioners' declarant, Dr. Jorgensen, refused to answer questions at his August 9, 2016 deposition about the length of everolimus's side chain (see Novartis's Patent Owner Response, Paper 27 at 22 and 22 n.4).

Petitioners' response: The petition established why Yalkowsky is relevant (Pet. 7, 23, 32-33, 44-48), the reply at 12-14 expressly responded to Novartis's

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