

On behalf of: Par Pharmaceutical, Inc. *et al.*

Entered: December 5, 2016

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 IPR2016-00084¹
U.S. Patent No. 5,665,772

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

**SUPPLEMENTAL DECLARATION OF WILLIAM L. JORGENSEN, PH.D.
IN SUPPORT OF PETITIONERS' REPLY IN THE *INTER PARTES*
REVIEW OF U.S. PATENT NO. 5,665,772**

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.

Par Pharm., Inc. Exhibit 1118 Par Pharm., Inc. v. Novartis AG Case IPR2016-00084

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I, William L. Jorgensen, Ph.D. resident of Deep River, Connecticut, hereby declare as follows:

I. INTRODUCTION AND QUALIFICATIONS

1. I am the same William L. Jorgensen, Ph.D. who submitted an opening declaration (Ex. 1003) in support of Par Pharmaceutical, Inc.'s ("Par") petition for the *Inter Partes* Review of U.S. Patent No. 5,665,772 (Ex. 1001, "the '772 Patent"). My qualifications and experience in medicinal and organic chemistry are fully laid out in my opening declaration. (Ex. 1003 ¶¶ 2-9.)

2. I submit this supplemental declaration to respond to certain opinions offered in two declarations submitted by Dr. William Roush (Ex. 2093) and Dr. Alexander Klibanov (Ex. 2092) in support of the Response of Patent Owner Novartis AG ("Novartis") in this proceeding.

3. My work in this matter is being billed at a rate of \$600 per hour, with reimbursement for necessary and reasonable expenses. My compensation is not in any way contingent upon the outcome of any *inter partes* review. I have no financial or personal interest in the outcome of this proceeding or any related litigation.

4. In forming my opinions, I have relied on the '772 Patent's claims, disclosure, and file history, on the materials cited in my opening declaration (Ex. 1003), as well as on materials cited in this supplemental declaration, and my own

experience, expertise, and knowledge of the person of ordinary skill in the art in the relevant timeframe.

II. SUMMARY OF OPINIONS REGARDING THE DECLARATIONS OF DR. ROUSH AND DR. KLIBANOV

5. As I stated in my opening declaration, the prior art taught that rapamycin was a prominent compound that generated intense interest in the medicinal chemistry community and that rapamycin had low water solubility that would have motivated a POSA to make modifications to improve its properties. (Ex. 1003 ¶¶ 132-140.) A POSA would have initially modified rapamycin at its hydroxyl groups, because such groups are the easiest and most straightforward to modify, and in particular would have selected C40 as the primary candidate for modification because the prior art taught that of the three hydroxyl groups it was least involved in binding to FKBP-12 and was not implicated in binding to the then-unknown effector protein. (*Id.* ¶¶ 141-145.) A POSA would have sought to add flexible side chains containing polar groups with known water-solubilizing potential as reflected in the teachings of Yalkowsky and Lemke. (*Id.* ¶¶ 146-156.) A POSA, seeking to maximize the probability of achieving a derivative with immunosuppressant activity and increased water solubility, would have started with the smallest substitutions that included flexible side chains and the most water-solubilizing potential. (*Id.* ¶¶ 150-153.) Among the first modifications that a POSA would have been motivated to use would be the 2-hydroxyethoxy group

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