UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PAR PHARMACEUTICAL, INC.,

Petitioner,

v.

NOVARTIS AG,

Patent Owner.

Case IPR2016-01479
Patent No. 9,006,224

EXPERT DECLARATION OF DR. MATTHEW H. KULKE

Table Of Contents

I. Introduction....1

II. Qualifications....4

III. Legal Principles....7

IV. Person Of Ordinary Skill In The Art....9

V. State Of The Art....9

VI. Summary Of The '224 Patent....13

VII. No Prior Art In Grounds 3 Or 4 Teaches Or Suggests The Claim Element "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy"....15

A. Boulay 2004 Does Not Teach Or Suggest The Claim Element "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy"....15

B. O'Donnell Does Not Teach Or Suggest The Claim Element "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy"....17

C. Duran Does Not Teach Or Suggest The Claim Element "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy"....18

D. Tabernero Does Not Teach Or Suggest The Claim Element "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy"....22

VIII. A Person Of Ordinary Skill In The Art Would Not Have Had A Reasonable Expectation That Everolimus Would Be Effective In A Method Of Treating "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy" In View Of The Prior Art In Grounds 3 And 4....24

A. Boulay 2004 Does Not Teach Or Suggest That Everolimus Would Be Effective In A Method Of

Treating "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy".....25

B. O'Donnell Does Not Teach Or Suggest That Everolimus Would Be Effective In A Method Of Treating "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy" 26

C. Duran Does Not Teach Or Suggest That Everolimus Would Be Effective In A Method Of Treating "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy" 28

D. Tabernero Does Not Teach Or Suggest That Everolimus Would Be Effective In A Method Of Treating "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy" 29

E. No Other Reference Cited In Connection With Grounds 3 And 4 Teaches Or Suggests That Everolimus Would Be Effective In A Method Of Treating "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy".....31

F. A Person Of Ordinary Skill In The Art Would Not Have Had A Reasonable Expectation That Everolimus Would Be Effective In A Method Of Treating "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy" 33

1. A Person Of Ordinary Skill Would Not Have Extrapolated The Results Reported In O'Donnell Or Tabernero To "Advanced [PNETS] After Failure Of Cytotoxic Chemotherapy".....35

2. A Person Of Ordinary Skill Would Not Have Drawn Conclusions Regarding The Efficacy Of Everolimus From The Preliminary Temsirolimus Data In Duran.....39

3. A Person Of Ordinary Skill Would Have Known That Advanced PNETS After Failure Of Cytotoxic Chemotherapy Would Generally Be More Resistant And Harder To Treat.....41

IX. A Person Of Ordinary Skill In The Art Would Not Have Had A Reasonable Expectation That Everolimus Would Be Effective

In A Method Of Treating "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy" In View Of The Prior Art In Grounds 1 And 2 44

A. Oberg 2004 Does Not Teach Or Suggest That Everolimus Would Be Effective In A Method Of Treating "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy" 45

B. Boulay 2004, O'Donnell And Tabernero Do Not Teach Or Suggest That Everolimus Would Be Effective In A Method Of Treating "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy" 47

C. A Person Of Ordinary Skill In The Art Would Not Have Had A Reasonable Expectation That Everolimus Would Be Effective In A Method Of Treating "Advanced [PNETs] After Failure Of Cytotoxic Chemotherapy" 48

X. The Methods Of Claims 1-3 Of The '224 Patent Have Demonstrated Unexpected Results 50

XI. Conclusion 54

I. Introduction

1. Challenged claims 1-3 of U.S. Patent No. 9,006,224 ("the '224 Patent") recite methods of using everolimus monotherapy for the treatment of patients with pancreatic neuroendocrine tumors (PNETs) "wherein the tumors are advanced tumors after failure of cytotoxic chemotherapy."

2. At this preliminary stage of these proceedings, I have been asked by counsel for Novartis AG ("Novartis") to provide my opinion on three issues: (1) whether any of the prior art relied on by Dr. Mark J. Ratain in Grounds 3 and 4 teaches or suggests the claim element "advanced [PNETs] after failure of cytotoxic chemotherapy"; (2) whether a person of ordinary skill in the art would have had a reasonable expectation that everolimus would be effective in a method of treating "advanced [PNETs] after failure of cytotoxic chemotherapy" in view of the art cited in (a) Grounds 1 and 2 or (b) Grounds 3 and 4; and (3) whether the methods of claims 1-3 of the '224 Patent have demonstrated unexpected results.

3. As to the first issue, in Grounds 3 and 4, Dr. Ratain relies on Boulay 2004, Duran, O'Donnell, and Tabernero. None of those references alone or in combination teaches or suggests the claim element "advanced [PNETs] after failure of cytotoxic chemotherapy." Boulay 2004 reports the results of *in vivo* testing of everolimus against the CA20948 "rat pancreatic tumor model." It does not teach or suggest the use of everolimus for treating "advanced [PNETs] after

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