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Paper 8
Entered: February 15, 2017

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 9,006,224 B2

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

CRUMBLEY, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
35 U.S.C. § 314(a) and 37 C.F.R. § 42.108

I. INTRODUCTION

Par Pharmaceutical, Inc. filed a Petition requesting an *inter partes* review of claims 1–3 of U.S. Patent No. 9,006,224 B2 (Ex. 1001, "the '224 patent"). Paper 1 ("Pet."). Novartis AG, the owner of the '224 patent, filed a Preliminary Response to the Petition. Paper 7 ("Prelim. Resp.").

Pursuant to 35 U.S.C. § 314(a), an *inter partes* review may not be instituted unless the information presented in the Petition and any Preliminary Response shows "there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." Taking into account the information presented, we conclude that the record establishes a reasonable likelihood that Par will prevail in proving that claims 1–3 of the '224 patent are unpatentable. Accordingly, we institute an *inter partes* review of these claims.

A. Related Matters

We are informed that the '224 patent has been asserted in two patent infringement actions in the United States District Court for the District of Delaware: *Novartis Pharm. Corp. et al. v. Roxane Labs., Inc.*, No. 15-474-RGA, and *Novartis Pharm. Corp. et al. v. Par Pharm., Inc.*, No. 15-475-RGA. Pet. 3; Paper 4, 2–3. Claims 1 and 2 of the '224 patent were challenged by a different petitioner in IPR2016-01461; the Board denied institution of trial in that proceeding.

B. The '224 Patent

The '224 patent, titled "Neuroendocrine Tumor Treatment," issued April 14, 2015, from U.S. Patent Application No. 12/094,173. Ex. 1001,

(54), (45), (21). The patent describes treating neuroendocrine tumors using mTOR (mammalian target of rapamycin) inhibitors, including rapamycin and its derivatives. *Id*. at 1:2–5, 1:17–43. One specifically listed rapamycin derivative is 40-O-(2-hydroxyethyl)-rapamycin, also known as everolimus. *Id*. at 1:46–47; 11:50.

The '224 patent discloses that mTOR inhibitors have activity as immunosuppressants, and have also been found useful for the treatment of solid tumors, particularly advanced solid tumors, including pancreatic neuroendocrine tumors (PNETs). *Id*. at 2:35–67. PNETs are particularly lethal, having a 5-year patient survival rate of 55.3%; the '224 patent states that most are malignant at the time of diagnosis, and 60% or more present with liver metastases. *Id*. at 3:1–10. The '224 patent concludes that there is an unmet need for treatment of PNETs in patients whose disease has progressed following one or more courses of chemotherapy. *Id*. at 3:10–12.

The '224 patent describes a method of treatment using mTOR inhibitors, specifically with everolimus ("compound A"). *Id*. at 11:66–67. The patent proposes a clinical study in which patients with advanced PNETs are treated with 10 mg/day of everolimus after failure of cytotoxic chemotherapy. *Id*. at 26:56–60.

C. Illustrative Claim

Of the challenged claims, claims 1 is independent and illustrative of the challenged claims:

> 1. A method for treating pancreatic neuroendocrine tumors, comprising administering to a human subject in need thereof a therapeutically effective amount of 40-0-(2-hydroxyethyl)-

> rapamycin as a monotherapy and wherein the tumors are advanced tumors after failure of cytotoxic chemotherapy.

Ex. 1001, 26:66–27:4. Claim 2 specifies a unit dose of 10 mg/day, and claim 3 requires that the tumor be an islet cell tumor. *Id*. at 27:5–8.

D. Asserted Grounds of Unpatentability

Par challenges claims 1–3 of the '224 patent on the following grounds of unpatentability:

References	**Basis**[1]	**Challenged Claims**
Öberg 2004,[2] Boulay 2004,[3] and O'Donnell[4]	§ 103(a)	1–3
Öberg 2004, Boulay 2004, O'Donnell, and Tabernero[5]	§ 103(a)	2

[1] The relevant sections of the Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112–29, took effect on March 16, 2013. Because the application from which the '224 patent issued was filed before that date, our citations to Title 35 are to its pre-AIA version.

[2] K. Öberg, *Treatment of neuroendocrine tumors of the gastrointestinal tract*, 27 ONCOLOGIA 57 (2004) (Ex. 1027).

[3] A. Boulay et al., *Antitumor efficacy of intermittent treatment schedules with the rapamycin derivative RAD001 correlates with Prolonged Inactivation of Ribosomal Protein S6 Kinase 1 in Peripheral Blood Mononuclear Cells*, 64 CANCER RES. 252 (2004) (Ex. 1005).

[4] A. O'Donnell et al., *A phase I study of the oral mTOR inhibitor RAD001 as a monotherapy to identify the optimal biologically effective dose using toxicity, pharmacokinetic (PK) and pharmacodynamics (PD) endpoints in patients with solid tumors*, 22 PROC. AM. SOC'Y OF CLINICAL ONCOLOGY 200(803ab) (2003) (Ex. 1029).

[5] J. Tabernero et al., *A phase I study with tumor molecular pharmacodynamics (MPD) evaluation of dose and schedule of the oral mTOR-inhibitor Everolimus (RAD001) in patients (pts) with advanced solid*

References	Basis[1]	Challenged Claims
Boulay 2004, O'Donnell, and Duran[6]	§ 103(a)	1–3
Boulay 2004, O'Donnell, Duran, and Tabernero	§ 103(a)	2

Par contends that Öberg 2004, Boulay 2004, and O'Donnell are prior art to the '224 patent under 35 U.S.C. § 102(b), whereas Duran and Tabernero are prior art under 35 U.S.C. § 102(a). Pet. 29–36. Novartis does not, at this stage of the proceeding, challenge the prior art status of any reference.

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, we construe claims by applying the broadest reasonable interpretation in light of the specification. 37 C.F.R. § 42.100(b); *see also In re Cuozzo Speed Techs., LLC*, 136 S. Ct. 2131, 2144–46 (2016). Under the broadest reasonable interpretation standard, and absent any special definitions, claim terms are given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art in the context of the entire disclosure. *In re Translogic Tech. Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms or phrases

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tumors, 23 J. CLINICAL ONCOLOGY 3007 (2005) (Ex. 1038).

[6] I. Duran et al., *A Phase II Trial of Temsirolimus in Metastatic Neuroendocrine Carcinomas (NECs)*, 23 SUPPLEMENT TO J. CLINICAL ONCOLOGY 3096 (2005) (Ex. 1011).

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